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Egyptian Journal of Psychiatry

Aims and Scope

EJP focuses primarily on psychological medicine, integrating it with various allied disciplines as psychology, social, basic and clinical medical sciences.

Editorial Policy

Today, the amount of new research knowledge doubles every six years the vast number of psychiatric and medical journals available clearly indicates the proliferation of present research activity. However, the practicing psychiatrist and others hardly find the time to read all relevant literature, even when they have access to it.

The Egyptian Journal of psychiatry (EJP) in its new form publishes editorials, original research articles, reviews and mini-reviews intended as a way To bridge the gap between basic psychiatric research and clinical relevance, clinical messages including ask the expert, case reports, commentaries, and drug focus, invited symposia and conference reports cowering topical subjects, book reviews and journal search in which the editors have tried to make a representative selection of books and journal summaries grouped in the order they arrive at our office, and every summary is preceded by the title. the names and initials of up to three authors, the abbreviated journal title, year, volume, issue, and page numbers Letters to the editors accepted fix publication comprise comments, view points and preliminary communications, discussion reports and students studies.

Material submitted in the EJP also address historical articles on mental hospitals in Egypt as well as tributes to dedicate the contribution of the Egyptian pioneers in the field. Our Mission is to provide the reader with an issue that will enhance and increase their understanding of the Egyptian psychiatric practice. In this respect, pearls from Arabic language were also quoted.

The spectrum of EJP extends to cite news, announcements, and scientific highlights on meeting invitations, national and international congress directory, listing of websites and an access to relevant organizations and journals. Material selected for publication includes those papers of merit, not already published or accepted for publication elsewhere, that have been subjected to independent peer review. All subscriptions will be available for electronic access starting from this issue. Noteworthy, EJP is a peer-reviewed journal that will publish two issues in 2003 and it is intended as a free service to you. Your suggestions will be greatly appreciated.

Editor in chief

Anyone reading the EJP in its new form would Not Report the issue with a feeling of déjà vu!!! and is kindly requested to ask: What Changes (if any) it has made in her/his practice?

Revolution and mental health

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Introduction

Volumes have been written on revolutionary human behaviour, and both historians and other scholars have addressed the subject in great detail. It has been considered not only from a socioeconomic stand point but also from a political perspective. An infinite variety of reasons have been explored, presenting both justification for revolution and purely emotional and even irrational reasons for man's behaviour in this regard. Has a 'gold thread' appeared in history that can shed some light on the causes of revolts? The Latin word *revolutio* means to turn around, take an opposite direction, or make often drastic changes (Jones, 2011).

The Egyptians seemed to find an acceptable social structure and were able to live without revolt, except for the Amarna experience, which was short lived. The Romans and the Greeks had a social contract, but there was one revolt after another. The concept of addressing issues by force of arms was well established and continues into the 21st century. Fear of punishment or the hope of reward were the two motivating factors (Jones, 2011).

The Middle Ages taught man how to accept his anger and control it. The 19th century taught man to consider his collective power to make vital changes to circumstances. The slave revolts in ancient Rome were minor when compared with the revolt as seen today (Jones, 2011).

Revolution, regardless of how it is called, acts of rage and acts of violence are all manifestations of individuals seeking to acquire what to them is absent in their lives.

Types of revolutions

Scientific revolutions, Le Bon claims, are the most important but the least attentive of revolutions. It is as if these scientific wonders can be absorbed without consequences when they change the structure of society radically in a 'cut and control' phenomenon.

Beneath scientific revolutions are religious and political revolutions. 'While scientific revolutions derive solely from rational elements, political and religious beliefs are sustained almost exclusively by affective and mystic factors'.

By the insistence of absolute truth a belief necessarily becomes intolerant. This explains the violence, hatred and persecution that are habitually associated with the Protestant Reformation and the French Revolution.

> In religious revolutions no experience can reveal to the faithful that they are deceived, since they would have to go to heaven to make the discovery. In political revolutions experience quickly demonstrates the error of a false doctrine and forces men to abandon it (Le Bon, 1913).

The revolutionary mentality

Revolutionists are characterized by a restless spirit, instability and discontent and are ready to rebel against any established order of affairs. They are spurred by the mere love of revolt, and if some magic power could realize all their desires they would simply revolt again. This special mentality often results from a pecuiliar adaptation of the individual to his surroundings, or from an excess of mysticism, or adoption of certain ideals and principles; it may also be merely a question of temperament or, in some cases, may arise from pathological disturbances. Perpetual rebels are generally highly impressionable beings, whose mind is obsessed with fixed ideas. Despite the apparent energy indicated by their actions they are really weak characters and are incapable of mastering control over themselves sufficiently to resist the impulses that rule them. The mystic spirit that drives them furnishes pretexts for their violence and enables them to regard themselves as great reformers (Le Bon, 1913).

There are certain affective elements whose development during revolution contributes to modify individual or collective personalities. In particular, we can mention: hatred, fear, ambition, jealousy or envy, vanity and enthusiasm (Le Bon, 1913). Keeping aside the influence of affective, rational and collective logic, we will occupy ourselves solely with the considerable part played by the

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mystic elements that have prevailed in so many revolutions. The chief characteristic of the mystic temperament consists of the attribution of a mysterious power to superior beings or forces, which are incarnated in the form of idols, fetishes, words or formulae. Mystic logic constitutes the might of the great popular movements. Men who would be by no means ready to allow themselves to be killed for the best of reasons will readily sacrifice their lives to a mystic ideal that has become an object of adoration. The principles of the revolution speedily inspire a wave of mystic enthusiasm analogous to those provoked by the various religious beliefs that had preceded it.

Even in the case of science, revolutions fail to produce their full effect until they penetrate the soul of the multitude. The crowd is a manifestation of the mystic personality where the conscious individuality of man vanishes in the unconscious personality of the crowd.

Here, the collective mind dominates the unconscious in what Le Bon calls 'collective logic', which is marked by infinite credulity, exaggerated sensibility, shortsightedness and a capacity to slavishly respond to affirmation, contagion, repetition and prestige. The revolutionary becomes a veritable nonperson, as personal characteristics vanish in the crowd. 'The miser becomes generous, the skeptic a believer, the honest man a criminal, the coward a hero'.

The crowd is on automatic pilot with unconscious forces dominating their collective soul, doing and saying what they would not do or say under other circumstances. 'A crowd is in reality inaccessible to reason; the only ideas capable of influencing it will always be sentiments evoked in the form of images'. This is true in any mass movement.

The unpredictability and uncertainty of revolution

The depressed fruit seller in Tunisia who set himself on fire and touched off protests that toppled former President Zine el Abidine ben Ali has inspired copycats in recent days in Egypt, Algeria and Mauritania (Hassan, 2011).

The protesters were as astonished as they were angry. Not long before, no one had imagined that the regime was vulnerable. Now the streets were filled with millions of people marching and shouting 'Mubarak has to go'.

For those struggling to understand what is happening in Egypt, and what will happen, the Iranian revolution of 1978–1979 is an obvious reference point. It is also handy for lazy pundits. The Shah used violent repression? Then violent repression will fail in Egypt. The Iranian revolution ultimately produced an Islamist government? Then Egypt is going Islamist.

The 25 January 2011 white revolution triumphed against tyranny in Egypt by a combination of the youth's vision and their technological expertise, good fortune and the armed forces' tacit endorsement of their fundamental legitimate demands for democracy, a respect for human rights and social justice.

The majority of young people congregate at websites like Twitter and Facebook; hence, when the Egyptian Revolution took to the social networks, today's youth were given a front row seat and watched it all unfold. That reason alone makes the Egyptian Revolution particularly special and meaningful and will certainly leave a much more indelible impression on the next generation of world citizens and leaders (Kelly, 2011).

Their good fortune lay primarily in the government's slow response to a few of their demands, coupled with Hosni Mubarak's much delayed arrogant speeches. This led to their realization that the whole regime had to be abolished (El-Shazly, 2011).

When all of us worried that the demonstrators would suffer from exhaustion, or that the protests could fizzle out, a number of tragic events outraged public opinion greatly, namely, what we now call the 'battle of the camels', which left many young bright promising protesters dead and the public breakdown in tears on a TV channel of Wael Ghoneim, a Google manager in Dubai and online activist. He had just been released after being arrested and kept blindfolded for 12 days shortly after the protests began. Hence, the crowds kept streaming to Tahrir Square over the following days, but they never lost their courtesy, grace and humour (El-Shazly, 2011).

For ordinary people, the moment of crisis was both thrilling and terrifying. Being in a revolution is such a confusing time. It is a time when you do not know, literally, what tomorrow will bring. If you plan to go to a demonstration, you do not know if you are going to be the only one out there, or one in a sea of millions. Whether the police will shoot you, or join you in the streets protesting against the regime.

There was overwhelming uncertainty. Coping with it was a constant struggle. To deal with this uncertainty, people were obsessive about talking politics; they talked politics with everybody.

Protests are a game of numbers. If huge crowds turn out, there is relative safety and a greater chance of success. If not, those present are more likely to fail and die. Predicting what other people will do is a matter of life and death. People are trying to sample outside their family and friend network to find out what everyone else is going to do.

Should I go to the protest? Should I join the strike? Millions of people asked these questions every day. Their decisions depended on what they thought everyone else would do, and their decision was liable to change right up until the very moment of acting upon it. In this tense atmosphere, rumours and emotions surged through the population like electric charges. Excitement could give way to terror in an instant. Despair to hope. And back again. You cannot read off people's attitudes from a year before, a month before, even a day before, and predict what they are going to do on any given day under these circumstances.

Even what people wanted was liable to sudden, startling change. 'What your end goal is depends on what you think is possible. If the fall of a dictatorial government suddenly seems achievable, then that may be the most important thing in your life today. Whereas yesterday it may have seemed pie-in-the-sky and you would go about your business and not even form an opinion about the topic because it seems so unviable'.

This is precisely what is happening in Egypt now. There are many possible outcomes and no way of predicting what will actually happen. People are constantly asking where the country is going to, and no one knows correctly.

Collective mind

The stability and malleability of the national psyche is as much in question as that of the individual. Le Bon sees revolutions occurring when there is a collective sickness of the collective mind. Because of internal stress and accelerating and unanticipated demands made on it by change, it is unable to cope successfully. Sentiments, traditions and prejudices constitute this national mind, always ripe to project its missteps to others (Fisher, 2012).

When elements within society not only clash but also take on the character of half-castes, Le Bon sees the situation ungovernable and vulnerable to open rebellion.

> From the moment when the Revolution descended from the middle to the lower classes of society, it ceased to be a domination of the instinctive by the rational and became the effort of the instinctive to overpower the rational (Le Bon, 1913).

The social climate festers and boils and then become increasingly chaotic and phlegmatic but will go nowhere until it finds a leader.

Ideas, leaders, armies and crowds constitute the essential elements of a revolution. Rarely does the crowd understand the revolution. The crowd is unhinged from meaning. It shouts because others are shouting, it revolts because others are revolting, it crashes into police barriers because others are, having no idea why or what caused it to be unhinged (Fisher, 2012).

Once the crowd has prevailed, the governmental ideal 'is always the very simple, something very like dictatorship. This is why, from the times of the Greeks to our own, dictatorships has always followed anarchy' (Le Bon, 1913).

The predominant characteristics of the revolutionary spirit reflected in the collective personality are race, religion, traditional hatred, customary fears, vanity, ambitions and envy. Out of this grows the temperament of the mystic mentality that is moved by idols, fetishes, words and formulae. It flatters itself that it alone is in possession of the absolute truth and meaning (Fisher, 2012).

Revolution and violence

Some revolutions were violent, others were not. A nonviolent revolution is a revolution using mostly campaigns of civil resistance, including various forms of nonviolent protest, to bring about the departure of governments seen as entrenched and authoritarian. In some cases a campaign of civil resistance with a revolutionary purpose may be able to bring about the defeat of a dictatorial regime only if it obtains a degree of support from the armed forces, or at least their benevolent neutrality (Wikipedia, March 2011).

An effective campaign of civil resistance, and even the achievement of a nonviolent revolution, may be possible in a particular case despite the controlling government taking brutal measures against protesters; the commonly held belief that most revolutions that have happened in dictatorial regimes were bloody or violent uprisings is not borne out by historical analysis. Nonviolent revolutions in the 20th century became more successful and more common, especially in the 1980s as Cold War political alliances that supported status quo governance waned (Wikipedia, March 2011).

The beginnings of the nonviolence movement lie in the satyagraha philosophy of Mahatma Gandhi, who guided the people of India to independence from Britain. According to the socialist Fourth International, Karl Marx acknowledged a theoretical possibility of 'peaceful' revolutions, but the Fourth International articles also say 'The development and preservation of good relations with the military forces is one of the absolute priorities of preparatory revolutionary work' (Dan Jakopovich, 2008).

Violent revolutions are those started and continued forcibly and in which was used a lot of violence to extinguish the old resisting regime – for example French, Russian, Romanian, Libian and Syrian revolutions.

Mental health at times of revolution

The WHO defines mental health as 'a state of well being in which an individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community'.

The WPA Regional Meeting was held in Cairo, 26–28 January 2011. This scientific meeting coincided with the Egyptian Revolution for change. The guests were able to view the Tahrir Square from their Hotel in the Center of Cairo (WPA, 2011).

A psychiatrist is not a politician; however, he/she should be aware of the political system of the country. This political system can change many issues in the norms of the people and in the healthcare system used by them. An environment that protects and respects basic human, political, socioeconomic and cultural rights is also fundamental to mental health promotion. It is usually easier to say that dictators are crazy but it is more difficult to know the truth about their health (Elsayed, 2011).

Countries torn by dictatorship face higher levels of distress, and yet they are the most in need of productive, healthy citizens. Treating or reducing the psychological impacts of dictatorship and promoting resilience in otherwise physically healthy individuals are critical to helping rebuild these countries (Elsayed, 2011).

Across Egypt, when the police forces vanished, the youngsters were stationed at street intersections. Never was traffic as regulated as when they were in charge, and drivers cooperated beautifully. No driver tried to 'burn' a red traffic light, something unheard of for many years.

At the same time, when garbage collectors also disappeared, housewives, youngsters in their 20s and teenagers swept the streets, gathered the garbage in sacks and stacked them at street corners and also painted tramway stations and walls that had been damaged by anti-Mubarak graffiti (El-Shazly, 2011).

It seems like every individual has a story to tell – some faced death, others saw loved ones die, whereas others have been greatly affected by the violence that followed the end of the revolution. Although every individual deals with this emotional impact in their own way, experts say that there is little doubt that people will continue to deal with these traumatic events for some time.

'I have been dealing with a lot of patients who are dealing with postrevolutionary stress', says Anne Justus, a clinical psychologist and an assistant professor at the American University in Cairo. She notes that, even if a person watched the event only on TV, there is always a chance he or she could be traumatized or experience psychological repercussions.

Psychologist and neuroscientist Dalia Danish explains that there are three criteria that classify an event as traumatic for an individual. The first is the person's proximity to the event. The second is assessing how severe it is. Severe events usually involve violence, shootings, wars or life-threatening disasters.

The final determinant depends on whether or not there is a social network of support to help people process these violent events and put them in context. This social support network usually consists of family, friends and even the media, although in terms of the revolution Danish believes the media has not been helpful. 'Obviously that is non-existent because if you look at the media, they are scaring everyone and are heating up the issue instead of calming people down' (El Tahawy, 2011).

Has the father–children relationship come to an end?

In some countries including Egypt people used to considering the leader as the father of the nation (family). However, what kinds of fathers are these leaders of their countries? Sometimes, of course, they are benign, beloved, or both. At other times they are tough and exacting, but fair. Some are tyrannical, iron-fisted. Then there are the cruel and even murderous.

It is clear that Hosni Mubarak was leaning towards the extreme end of the dictator/thug end of the spectrum. We have watched his henchmen mow down innocent protestors in the streets. We have seen his inability to give up his position at the helm of his nation, even when the nation was screaming for his removal and young people were willing to die to make him go (Fein, 2011).

In short, Hosni Mubarak was an abuser. And perhaps it is no accident that the 'children' of the abuser fought back, were willing to die to get him out of their lives. It is the father's role to protect the family, care for its well-being, keep it safe. When the supposedly protective father is abusive, the children endure, often suffer in silence, may be inwardly filled with rage, or may give up.

We have seen in Egypt, and in Tunisia, that when young children dare to band together, they can fight back. They have their own 'secret' language on Facebook and Twitter. It does not matter if the older children do not understand them or their means of communication. It does not matter if the older children are afraid; the younger ones are not. They have each other. No longer isolated or alone, helping each other, caring for each other like siblings, they can 'out' the abusive father and, once emboldened, will stop at nothing to put an end to the abuse and remove the abuser (Fein, 2011).

The abuser refused to be humiliated, to give up his power, to yield to the young children of Egypt. He used threats, force and violence. He manipulated some of the older children (the police) to carry out his will. He was willing to inflict death on the young rather than cede his position at the head of the national family. He insisted he keep Egypt from chaos, that he maintain order. He hung on beyond the point when everyone thought he would go. For a moment there, near the end, it looked horrible – as though the abusive father would stop at nothing to retain control. And then, in a moment no one will ever forget, an announcement was made: the tyrant was stepping down, leaving the palace, handing over power. The abused children had won!

When Mubarak surrendered, the young people of Egypt thought that the abuser had gone and that the abuse had come to an end and that there would be no dictator after him in Egypt. Is it true, or is it just a dream?.

Psychological challenges in the transitional period

Uncertainity

Danish says one of the most important factors affecting nearly everyone right now is uncertainty – they are living in an uncertain future that requires them to make important political decisions.

'Not only can't you predict [the outcome], you're close to the events. The events are severe, but you also need to make decisions that will put your country in a different position', she says. 'Are we going to be […] an Islamic state or a secular state? Everyone is confused' (El Tahawy, 2011).

Feeling insecure

Any sense of security was shattered during the first few days of the revolution. On the night of 28 January, the police withdrew from the country, leaving the streets unprotected while allegedly opening prison doors to allow some of the country's most dangerous criminals to escape. Gunshots rang out through almost every neighbourhood of every city in the country. In some areas, looting and burning of shops became an almost daily occurrence.

'When the police withdrew and the thugs were roaming [the streets] of Egypt, we were all at least in a war-like situation and your life was totally jeopardized', says Danish. 'People were defenceless, and it was bound to affect everyone'.

With rumours of murders and thefts spreading throughout the country, many people were paralysed with fear. Justus explains that the very fact that no one was actually sure of what was true and what was a lie was even more frightening. 'It's very stressful when things are not transparent, when you have difficulty finding out if things are true or not', Justus says. 'Fear gives more strength to the rumour' (El Tahawy, 2011).

Coping with loss

Many protestors were killed or lost, and their families are suffering considerably and asking for revenge. Families are focussing on investigating their children's murders, and they want to know more about the people who directly killed them and how they were released from prison.

People lost confidence in authorities as they saw officers and soldiers who were accused of killing their relatives released from prison as no proof could be collected to justify their trial, which could open the door for personal revenge.

When people are grieving for someone, there are stages that they go through. One of the stages is anger, the second is denial and the last is sadness. After the stage of sadness, they are supposed to enter a stage of either recovery or depression according to their surrounding environment.

Lasting effects

It is normal to experience stress, anxiety and other emotional reactions to the traumatic events of the revolution. According to specialists, being directly involved in the violence is a much more intense experience. Justus says that people who were in or close to Tahrir Square have significantly higher chances of developing full-fledged post-traumatic stress disorder (PTSD).

Danish explains that, in simple terms, PTSD is characterized by recurring thoughts or flashbacks related to a traumatic event. Typically, people with PTSD have nightmares related to the events. Many experience terror attacks, whereas others will typically try to avoid anything related to the event. Other symptoms include an increase in aggressive behaviour; the person might also withdraw from daily life (El Tahawy, 2011).

'You are most likely to get post-traumatic stress if your life is jeopardized, whether you participated in it [the event] or witnessed it, or heard about it, it doesn't matter. You don't have to be actually there', says Danish.

The impact of trauma can be far reaching. Danish is concerned that beyond simply living in fear many people are so caught up with what is happening in the country that they are ignoring their mental health. 'I feel most people are taking decisions based on fear rather than based on thought', she says. 'Obviously you cannot have political awareness or rebuild Egypt if [you are] mentally not capable of making rational decisions'.

Given the violent and stressful events of the revolution and the ongoing uncertainty of the future, Danish feels that it is normal for people to experience mental health problems right now, noting, 'I think psychological help is very important'.

People have to be aware of the problems and acknowledge their fears in order to help themselves. In terms of coping with daily stress, it is recommended to practise relaxation techniques such as breathing exercises. Other advices are: 'Don't risk your life, make sure you are in secure places, try to think rationally'. 'If you set yourself goals for the day, you feel that you have some sense of control over your life. At that moment we don't feel that' (El Tahawy, 2011).

Changes in the Egyptian mental condition

For many decades Egyptians had a negative self-image: helplessness, hopelessness, loss of control on the future, inability to change governmental attitudes towards people, sense of rejection, poverty, persecution, etc.

This negative self-image underwent a change early with the 25th January Revolution, when Egyptians believed that they would be able to change the dictatorial regime within 18 days, pushing Mubarak out and putting him in jail, exerting pressure on the new authorities to perform how the people wanted them to, giving up the chronic fear they had, demanding loudly for their rights, being ready to go to Tahrir and other squares all over the country to confirm their freedom, fighting against anyone who was trying to bring them back to a dictatorial system, feeling proud about being an Egyptian patriot and so on (Elmahdy, 2011).

It is only natural that a sense of national euphoria should follow a popular uprising that has toppled a tyrant who had been in power for 30 years. However, what happens next to the country's collective psyche is less clear.

The potential for great change exists. Many Egyptians suggest that there still exists tremendous pride and optimism, even if it is tempered with caution (Afify, 2012).

Shawky al-Akabawy, a prominent Egyptian psychiatrist, says that it would take years and a lot of work to turn the new-found positivity and national pride among Egyptians from a temporary high into a sustainable change.

'Sudden wars don't allow people to take their time to change. Principles will cause change, not slogans', said al-Akabawy, urging Egyptians to stick to the principles of the revolution to dispel the negativities that decades of oppression have instilled in the Egyptian character.

Basma Abdel Aziz, a psychologist at the Egyptian Mental Health Secretariat and El Nadeem Center for Rehabilitation of Victims of Violence, describes the Egyptian personality before the revolution as passive aggressive and defeatist. Egyptians used to channel the anger resulting from their oppression in various wrong directions, she says, such as slacking at work or destroying public property, while simultaneously accepting the status quo.

Saneya Abdel Atty, a teacher, exemplifies that change. She says that she used to isolate herself in her house when she faced a problem. Now, whenever she has something to say, she heads to Tahrir Square.

Like many Egyptians, Abdel Atty's relief is mixed with apprehension. 'I am now living in a state of imbalance. I'm wondering whether the blood of the martyrs will pay off or go to waste?'

The triumph of the people's will, which was crowned by Mubarak's resignation in response to their demands, gave the Egyptian people a feeling of dignity and empowerment that many say has changed them drastically.

Al-Akabawy says that the revolution filled the people with pride, dignity and confidence after they succeeded in changing what they thought was unchangeable.

Many Egyptians had a gloomy outlook on the future before the revolution, but now a sense of hope has been ignited that Egypt and its people are headed for a better future.

'After we were sure that there was no hope, the youth who started the revolution opened the door, and the whole population who had been suffering from corruption followed', says Akabawy.

The removal of the fear barrier took a huge burden off the shoulders of Egyptians. Abdel Aziz says that Egyptians were finally able to speak out against their rulers, who they regarded as father figures before, making them off limits for criticism. The unrealistic expectation that some Egyptians had regarding the results of the revolution might lead to disappointment, which would halt the change in their personalities.

'For the first time in 30 years, Egyptians are feeling that the world is looking at them with admiration and respect, which has restored the sense of national dignity that had been lost', explains al-Akabawy.

Amira Khallaf, an English teacher, says that she is motivated by the feeling that Egypt is her country and that it is her responsibility to develop it.

Many who were depressed by the thought that Egyptians are negative and unwilling to fight for change got a huge boost when they saw millions of people participating in the demonstrations that led to Mubarak's fall (Afify, 2012).

Akabawy says that the extent to which the people's hopes will be materialized during the next phase will determine whether this shift in Egyptian morale will last or fade away, leaving them in a state of despair similar to that which was common before the revolution.

Abdel Aziz believes that a radical transformation in the educational system, from teaching memorization and passivity to encouraging creative thinking and initiative, is crucial to sustaining a long-lasting change in the Egyptian personality (Afify, 2012).

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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Impairment in working memory in multiple sclerosis

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Aim

The aim of the current study was to assess the relation between working memory dysfunction and clinical and MRI findings in relapsing remitting multiple sclerosis.

Participants and methods

This study was conducted on 50 patients with clinically definite relapsing remitting multiple sclerosis, they were recruited from the Outpatient Clinic of Alexandria University Hospitals; and 25 healthy controls matched for age, sex, and educational level. All participants were subjected to neuropsychological assessment that included: digit span, visual span, *N*-nack task, and Wisconsin card sorting test. The patient group was further subjected to: Expanded disability status scale (EDSS) and brain MRI.

Results

Clinically, the present study found no statistically significant correlations between working memory dysfunction and age, age at onset, sex, number of relapses, affected functional system, or EDSS status. Alternatively, there were statistically significant positive correlations between working memory dysfunction and the duration of illness.

Conclusion

This study suggests that according to the resources utilized by cognitive tasks, working memory tasks may be classified into high-demanding working memory tasks (2-back task and WCST) and low-demanding working memory tasks (1-back task and digit and visual span), and in relapsing remitting multiple sclerosis working memory dysfunction includes mainly high-demanding working memory tasks.

Keywords:

MRI, multiple sclerosis, working memory

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Introduction

Cognitive impairment is a common clinical feature of multiple sclerosis (MS), occurring in up to 65% of patients with this disorder (Foong *et al.*, 1998). Repeatedly, it has been suggested that the cognitive impairment in MS patients is strongly associated with limitations in work and social activities (DeSousa *et al.*, 2002).

Neuropsychological studies have provided evidence indicating that deficits in working memory (WM) may be involved in MS (Amato *et al.*, 2001). However, the brain mechanisms underlying these deficits continue to be a subject of ongoing investigations, as their patterning and specificity still remain unclear. This is particularly evident in psychophysiological research. The existing evidence indicates that the multifocal demyelination of MS leads to a disruption of the multiple interconnected brain areas, which form the substrate of the WM (Amato *et al.*, 2001).

The term 'working memory' was introduced into the literature of cognitive psychology by Miller *et al.* (1960). Their definition is surprisingly modern; they did foresee the goal-directed and executive components of WM:

> When we have decided to execute some particular plan, it is probably put in some special state or place where it can be remembered while it is being executed. Particularly if it is a transient, temporary kind of plan that will be used today and never again, we need some special place to store it. …we should like to speak of the memory we use for the execution of our plans as a kind of quick access, working memory.

They did not stop with a cognitive definition of WM, but went on and proposed an anatomical localization of these functions in the brain:

> This most forward position of the primate frontal lobe appears to us to serve as 'working memory' where plans can be retained temporarily when they are being formed, or transformed, or executed.

WM has a content and capacity. WM content is the task-relevant representations (representations are symbolic codes for information) temporarily held on-line during the delay of WM tasks. The content in WM is not only maintained (which is more in line with the definition of short-term memory), but can be manipulated by different operations, with the prospective aim of facilitating goal-directed behavior (external as motor execution or internal such as decision making). The content in WM is retained transiently (for seconds) and is not stored in long-term memory. If not actively maintained,

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the content disappears. One way to actively maintain the information in WM is to rehearse it (repetitively direct attention to it). Rehearsal supports WM, and protects the information from fading and possibly also from interference from competing stimuli (Raye *et al.*, 2002; Cowan, 2005).

WM capacity is the number of items of information that can be held active in parallel in WM. The capacity of WM is limited and a popular view is that seven (± 2) items of information can be processed simultaneously in WM, although one item can constitute a chunk of information (a chunk is a cluster of logically connected items, maintained as one), and thus extending the perimeter of seven. WM load quantifies the relative processing resources required to perform a WM task (Cowan, 2005; Klingberg, 2008).

A complex cognitive process such as WM is likely to be mediated by a distributed network of distinct brain regions (Mesulam, 1990). However, evidence from neuropsychological, electrophysiological, and functional neuroimaging studies in both animals and humans supports a role of the frontal lobes as a critical node in the network supporting WM (Groenewegen *et al.*, 1990). The frontal lobes make up over one-third of the human cerebral cortex and can be divided into three major subdivisions: the prefrontal cortex, the premotor/motor cortex, and the paralimbic cortex (which includes the anterior cingulated gyrus) (Uylings and Van Eden, 1990; Goldman-Rakic and Friedman, 1991). The prefrontal cortex is therefore situated to receive inputs from regions involved in the encoding and storage of information (i.e. parietal and temporal cortices), while projecting to regions involved in response initiation (i.e. basal ganglia). Such an anatomical profile is required for a structure involved in using internal representations to guide action (Selemon and Goldman-Rakic, 1988).

WM uses a network of cortical and subcortical areas. As it is dependent on this network, it may be disrupted by many neuropsychiatric disorders, including Alzheimer's disease, frontotemporal dementia, vascular dementia, Parkinson's disease, MS, head injuries, tumors, strokes, attention deficit hyperactivity disorder, schizophrenia, and reading disorder. The mechanisms by which these disorders cause deficits in WM are variable, complex, and, in most instances, poorly understood. The following mechanisms have been suggested: structural damage to the cortical or the subcortical network, demyelination and disconnection (MS), reduced prefrontal size, and disregulated prefrontal activity as a result of a reduction in subcortical input into the frontal cortex (reduced prefrontal catecholamine input) (Grace, 1991; Braver and Cohen, 1999; Friedman *et al.*, 1999; Durstewitz *et al.*, 2000; Russell *et al.*, 2000).

Aim of the work

The aim of the present work is to determine the relation between WM dysfunction and clinical and MRI findings in relapsing remitting MS.

Materials

This study was carried out on (a) 50 patients with clinically definite MS (according to Posers criteria) (Poser *et al.*, 1983) and a relapsing remitting course (according to the definition of Lublins and Reingolds) (Lublin and Reingold, 1996). They were recruited from the Outpatient Clinic of Alexandria University Hospitals in the period from October 2008 to August 2009. And (b) 25 healthy controls matched for age, sex, and educational level.

All participants were either included or excluded according to their fulfillment of the criteria below:

Inclusion criteria

(1) Age between 20 and 40 years.
(2) Sex; both men and women were included in the study.
(3) Written consent from each participant after explaining the nature, steps, and aim of the study.
(4) The study was approved by the Ethical Committee of the Alexandria Faculty of Medicine.

Exclusion criteria

(1) A current or a past medical or psychiatric disorder other than MS that could affect cognitive domains.
(2) Neurological impairment that might interfere with evaluation.
(3) MS relapse or corticosteroid use within the past 6 weeks.

Subjects and methods

All participants (patients and healthy controls) were subjected to the following:

(1) Complete history taking.
(2) A clinical assessment was carried out including the following:
    (a) Thorough physical, neurological, and psychiatric examination.
(3) A neuropsychological assessment was carried out including the following:
    (a) *Digit span subtest from the Wechsler adult intelligence scale-revised (Wechsler, 1981)*: This test requires the examiner to verbally present digits at a rate of one per second. The forward test requires the participant to repeat the digits verbatim. The backward test requires the participant to repeat the digits in the reverse order. The number of digits increases by one until the participant consecutively fails two trials of the same digit span length. The score for each participant was the maximum number of digits repeated correctly.
    (b) *Visual span subtest from the Wechsler memory scale-revised (Wechsler, 1987)*: This assessed participants' ability to remember a sequence of boxes lighting up on a computer screen. The visual span was calculated as the longest sequence that the participant could recall accurately on at least one of the two trials. For each trial, eight randomly

arranged white squares were shown on the screen. Some of the squares lit up in color, one by one, in a variable sequence and participants were instructed to remember the sequence. At the end of the presentation, the participant was required to touch each of the boxes that had lit up in the same order as they were originally presented. The task began with the simplest level of a two-box sequence. After each successful trial, the number of boxes in the sequence was increased by one to a maximum of nine. If the participant's response was incorrect at any particular level, an alternate sequence of the same length was presented. This continued until the participant failed two consecutive trials at any one level, whereupon the test was terminated. The visual span was calculated as the longest sequence that the participant could recall accurately on at least one trial.

(c) *N-back task (Parmenter et al., 2006)*: In this, the participant had to indicate whether a visual stimulus presented on the screen (the 'target' stimulus) was similar to or different from a previously presented stimulus (the 'cue' stimulus). This procedure required the relevant information to be maintained and updated in WM. The task was computerized. Participants were seated in front of a personal computer screen. Each *N*-back task consisted of three blocks of 15 responses to cue/target stimuli (16 stimuli presented to examine N-1 back task and 17 stimuli presented to examine N-2 back task). The maximal score for each task was 45 (15 trials × 3 blocks). Each stimulus was presented on the screen for 3000 ms. The participant had 3 s in which to answer 'same' or 'different'. After a 1000 ms interstimulus interval, a new stimulus appeared on the screen. All patients were given a training block of trials for the two levels of *N*-back task.

(d) *Wisconsin card sorting test (WCST) (64 card version) (Heaton, 1981*; *Gold et al., 1997)*: The participant was given one deck of 64 cards. The cards are printed with one to four different symbols (triangle, star, cross, and circle) and in one of four different colors (red, green, yellow, blue). The participant's task was to place the cards, one by one, under one of four different stimulus cards according to an undisclosed principle. The stimulus cards also contain symbols that differ according to number, shape, and color. The examiner informed the participant after each sort whether his or her placement was 'right' or 'wrong'. The participant had to deduce the principle on the basis of the feedback provided by the examiner. After a run of 10 consecutive correct placements, the underlying principle changed without this being disclosed to the participant. The test was concluded once a participant completed three correct runs of 10 correct placements or had exhausted all of the cards. Gold *et al.* (1997) have stated that 'successful WCST performance requires the subject to remember his or her prior response and associated feedback and to use this information to select a new response, a form of working memory'. A number of different scores can be derived, including the number of perseverative errors (the number of errors where the participant has used the same rule for their choice as the previous choice) and categories achieved (the number of run of 10 correct responses).

The patient group was further subjected to the following:

(1) *Expanded disability status scale (EDSS) (Kutzke, 1983)*: A patient was evaluated on the EDSS according to the signs and symptoms observed during a standard neurological examination. These clinical observations were classified into functional systems. There are eight functional systems, each grading the signs and symptoms for different neurological functions. The eight functional systems are pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral, and other.

(2) Brain MRI including a T_1 pulse sequence, a T_2 pulse sequence, and a FLAIR pulse sequence. The site and number of MS plaques were determined in different regions of the brain.

Results

Demographic characteristics of the patients and the control groups

The age of the participants ranged between 21–39 and 21–37 years, with a mean of 29.32 ± 5.60 and 28.38 ± 5.32 for the patient and the control groups, respectively. There was no statistically significant difference between the patient and the control groups in terms of age ($P = 0.49$).

The patient group included 13 men (26.0%) and 37 women (74.0%), whereas the control group included 10 men (40.0%) and 15 women (60.0%). There was no statistically significant difference between the patient and the control groups in terms of sex ($P = 0.21$).

In terms of the educational level, 21 patients (42.0%) had primary or preparatory education, 18 (36.0%) had secondary education, 10 had higher education (20.0%), and one (2.0%) had postgraduate education, whereas among the control participants, 11 individuals (44.0%) had primary or preparatory education, seven (28.0%) had secondary education, six (24.0%) had higher education, and one (4.0%) had postgraduate education. There was no statistically significant difference between the patient and the control group in terms of education ($P = 0.87$) (Table 1).

Clinical findings

Table 2 shows that age at onset of the disease ranged from a minimum of 16 years to a maximum of 35 years, with a mean of 25.4 and a SD of 5. The duration of illness ranged between 1.00 and 11.00 years, with a mean of 4.18 ± 2.57. The number of relapses ranged between 2.0 and 11.0,

Table 1 Characteristics of the patients and the control groups in terms of age, sex, and education

Demographic variables	Patients	Controls	*t*	*P*
Age				
Range	21–39	21–37	0.697	0.49
Mean	29.32	28.38		
SD	5.596	5.327		
Sex				
Male	13 (26.0%)	10 (40.0%)	1.54	0.21
Female	37 (74.0%)	15 (60.0%)		
Education				
Primary or preparatory	21 (42.0%)	11 (44.0%)	0.71	0.87
Secondary	18 (36.0%)	7 (28.0%)		
Higher education	10 (20.0%)	6 (24.0%)		
postgraduate	1 (2.0%)	1 (4.0%)		

P is significant if <0.05.

Table 2 Clinical findings

Clinical variables	Minimum	Maximum	Mean	SD
Age at onset (years)	16.00	35.00	25.42	4.97
Duration of illness (years)	1.00	11.00	4.18	2.58
Number of relapses	2.00	11.00	4.36	1.98
Expanded disability status scale	0.00	3.50	2.29	0.99

with a mean of 4.36 ± 1.97. The EDSS ranged between 0.0 and 3.50, with a mean of 2.29 ± 0.99.

Magnetic resonance image findings

Table 3 shows the number of the lesions among the patient group. Five patients (10.0%) had a normal-appearing brain, 13 patients (26.0%) had less than five lesions, 16 patients (32.0%) had 5–10 lesions, nine patients (18.0%) had more than 10 lesions, and seven patients (14.0%) had dirty-appearing white matter.

Table 4 shows the level of lesions in the patient group. It shows that five patients (10%) had a normal-appearing brain, 26 patients had supratentorial lesions (52%), seven patients (14%) had infratentorial lesions, and 12 patients (24%) had lesions at both levels.

Table 3 Number of lesions

Number of lesions	Number of patients (%)
Normal-appearing brain	5 (10.0%)
<5	13 (26.0%)
5–10	16 (32.0%)
>10	9 (18.0%)
Dirty-appearing white matter	7 (14.0%)

Table 4 Level of lesions

Level of lesions	Number of patients (%)
Normal-appearing brain	5 (10%)
Supratentorial	26 (52%)
Infratentorial	7 (14%)
Both	12 (24%)

Table 5 Digit span: comparison of the results of the patients and the control participants

Digit span	Patients	Controls	*t*	*P*
Forward digit span				
Range	4–8	4–8	1.08	0.28
Mean	5.90	6.24		
SD	1.29	1.26		
Backward digit span				
Range	3–6	3–6	0.81	0.42
Mean	4.38	4.56		
SD	0.901	0.917		

P is significant if <0.05.

Results of neuropsychological assessments

Digit span

Table 5 shows the digit span – comparison of the results of the patients and the control participants. Forward digit span ranged between 4 and 8, with a mean of 5.90 ± 1.29 for the patient group, whereas for the control participants, it ranged between 4 and 8, with a mean of 6.24 ± 1.26. Backward digit span ranged between 3 and 6, with a mean of 4.38 ± 0.90 and 4.56 ± 0.91, for the patient and the control group, respectively. There were no statistically significant differences between the two groups studied in terms of forward digit span and backward digit span ($P = 0.28$ and 0.42, respectively).

Visual span

Table 6 shows the visual span – comparison of the results of the patient and the control group. Forward visual span ranged between 4 and 8, with a mean of 5.52 ± 1.35 and 6.12 ± 1.33 for the patient and the control group, respectively. Backward visual span ranged between 3 and 7, with a mean of 4.44 ± 1.12 and 4.92 ± 1.11 for the patient and the control group, respectively. There were no statistically significant differences between the patient and the control group in terms of visual span ($P = 0.072$ and 0.083, respectively).

N-back task

Table 7 shows the *N*-back task – comparison of the results of the patient and the control group. Performance of the studied groups in the 1-back task ranged between 35 and 45, with a mean of 40.20 ± 3.14 for the patient group, whereas for the control participants, it ranged between 37 and 45, with a mean of 41.60 ± 2.27; there was no statistically significant difference between them in the 1-back task ($P = 0.052$). Performance of the studied groups in the 2-back task ranged between 29 and 44, with a mean of 35.60 ± 4.10 for the patient group, whereas for the control participants, it ranged between 33 and 44, with a mean of 37.88 ± 4.02; there was a statistically significant difference between them in the 2-backtask ($P = 0.025$).

Wisconsin card sorting test

The results of the studied groups in the WCST are presented in Table 8. Categories achieved ranged between 0 and 3, with a mean of 1.84 ± 0.86 and 2.36 ± 0.90 for the patient and the control group, respectively. Perseverative errors ranged between 5 and 18, with a mean of 9.98 ± 2.535 for the patient group, and 6–16, with a mean of 8.36 ± 2.325 for the control participants. There were statistically significant differences

Table 6 Visual span: comparison of the results of the patients and the control participants

Visual span	Patients	Controls	*t*	*P*
Forward visual span				
Range	4–8	4–8	1.82	0.072
Mean	5.52	6.12		
SD	1.35	1.33		
Backward visual span				
Range	3–7	3–7	1.75	0.083
Mean	4.44	4.92		
SD	1.12	1.11		

P is significant if <0.05.

Table 7 *N*-back task: comparison of the results of the patient and the control group

N-back task	Patients	Controls	*t*	*P*
1-back task				
Range	35–45	37–45	1.98	0.052
Mean	40.20	41.60		
SD	3.14	2.27		
2-back task				
Range	29–44	33–44	2.03	0.025*
Mean	35.60	37.88		
SD	4.10	4.02		

*Significant difference between patients and control.
P is significant if <0.05.

Table 8 Wisconsin card sorting test (categories achieved and perseverative errors): comparison of the results of the patient and the control group

Wisconsin card sorting test	Patients	Controls	*t*	*P*
Categories achieved				
Range	0–3	0–3	2.4	0.018*
Mean	1.84	2.36		
SD	0.866	0.907		
Perseverative errors				
Range	5–18	6–16	2.67	0.009*
Mean	9.98	8.36		
SD	2.535	2.325		

*Significant difference between patients and control.
P is significant if <0.05.

between the patient and the control group in the categories achieved and perseverative errors ($P = 0.018$ and 0.009, respectively).

Correlations between working memory dysfunction and clinical findings

Table 9 and Figs 1–3 show statistically significant positive correlations between the duration of illness and the patients' performance on the WCST (perseverative errors and categories achieved) and the 2-back task, respectively ($P = 0.041$, 0.012, and 0.036).

Correlations between working memory dysfunction and radiological findings

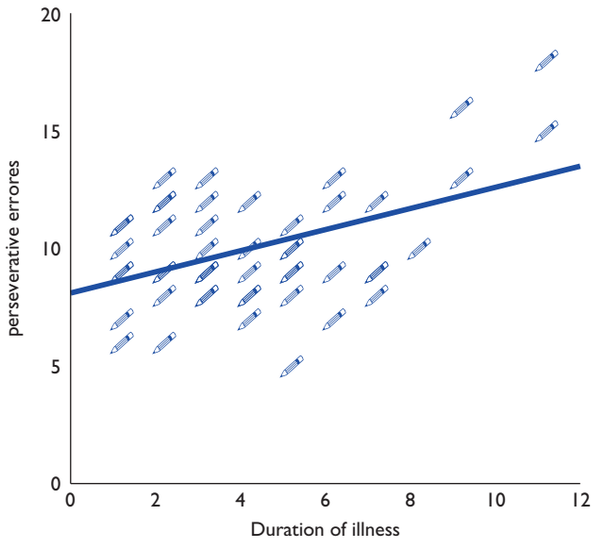
Table 10 and Figs 4–6 show that there were statistically significant positive correlations between the number of lesions and the patients' performance on the WCST (perseverative errors and categories achieved) and the 2-back task, respectively ($P = 0.041$, 0.004, and 0.048, respectively).

Table 9 Correlations between the duration of illness and the patients' performance on the 2-back task and the Wisconsin card sorting test (categories achieved and perseverative errors)

Duration of illness	*r*	*P*
WCST (perseverative errors)	0.457	0.041
WCST (categories achieved)	−0.453	0.012
2-Back task	−0.352	0.036

P is significant if <0.05.
WCST, Wisconsin card sorting test.

Figure 1



Correlation between the duration of illness and patients' performance on the Wisconsin card sorting test (perseverative errors).

Discussion

The current study proposed different psychometric tools to examine the different subcomponents of WM:

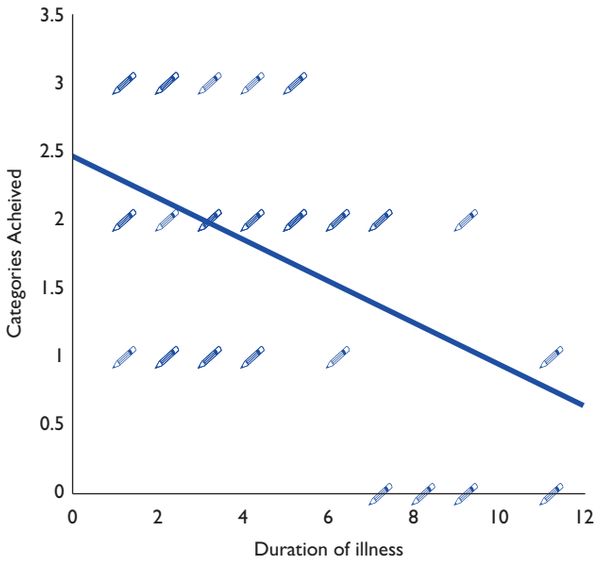
(1) Forward digit and visual span to evaluate controlling attention.
(2) Backward digit and visual span to measure controlling attention and the retentive subcomponent.
(3) *N*-back task to assess controlling attention, retentive, and updating subcomponents.
(4) WCST for task of controlling attention, retentive, updating and executive subcomponents.

There is no general agreement in the definition of reliable cut-off points for impairments in WM; thus, the present study defines dysfunction in WM as statistically significant differences between the patient and the control participants.

We found no statistically significant differences between the patients and the control participants in the performance on both the forward and the backward digit span test, in agreement with other authors (Rao *et al.*, 1991; Andrade *et al.*, 1999; Balsimelli *et al.*, 2007).

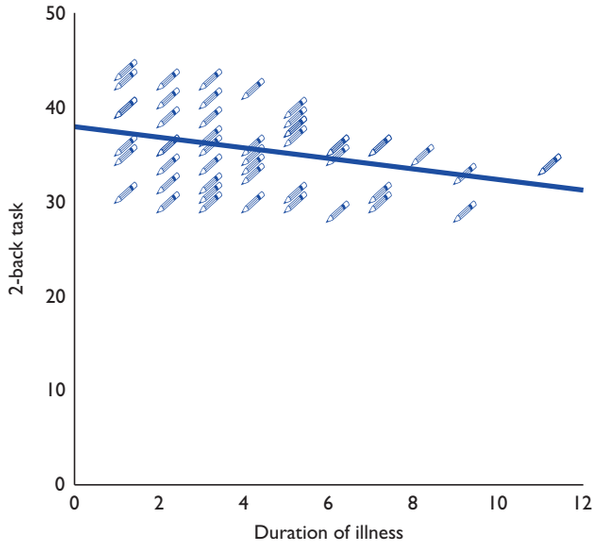
This results are not in agreement with those reported by Grigsby *et al.* (1994) and Sfagos *et al.* (2003), who found

Figure 2



Correlation between the duration of illness and the patients' performance on the Wisconsin card sorting test (categories achieved).

Figure 3



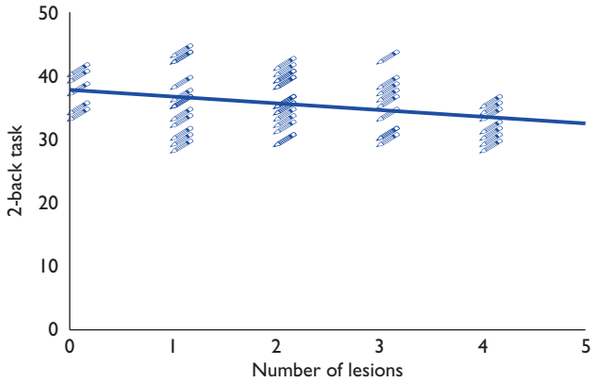
Correlation between the duration of illness and the patients' performance on the 2-back task.

Table 10 Correlations between the number of lesions and the patients' performance on the 2-back task and the Wisconsin card sorting test (categories achieved and perseverative errors)

Number of lesions	*r*	*P*
WCST (perseverative errors)	0.290	0.041
WCST (categories achieved)	−0.396	0.004
2-Back task	−0.281	0.048

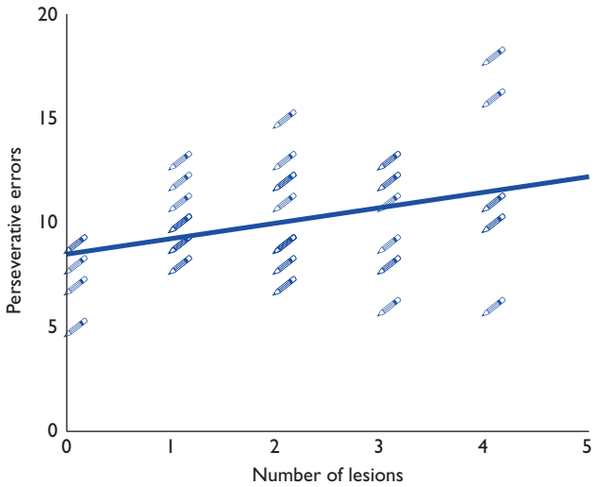
P is significant if <0.05.
WCST, Wisconsin card sorting test.

Figure 4



Correlation between the number of lesions and the patients' performance on the 2-back task.

Figure 5

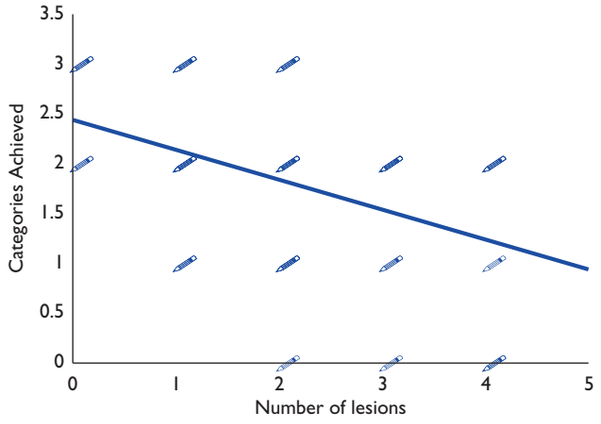


Correlation between the number of lesions and the patients' performance on the Wisconsin card sorting test (WCST) (perseverative errors).

statistically significant differences between the patients and the control participants in the performance on both the forward and the backward digit span test. The differences in these studies may be attributed to the fact that Grigsby and Sfagos carried out their studies on patients with a progressive course and recent relapse.

The current study showed no statistically significant differences between the patients and the control participants on visual span (forward and backward). This in agreement with Foong *et al.* (1998), who found statistically significant differences between the patients and the control participants in the performance on the visual span during relapse, but these differences did not exist during remission. However, in disagreement with our study, Foong *et al.* (1999) found statistically significant differences between the patients and the control participants in performance on the visual span. This

Figure 6



Correlation between the number of lesions and the patients' performance on the Wisconsin card sorting test (WCST) (categories achieved).

contradiction may be attributed to the differences in the selection criteria of the patients. In the current study, the maximum age of the patients was less than 40 years, patients on corticosteroid were excluded, the minimum time from the last relapse was 45 days, and the study was restricted to patients with a relapsing remitting course. Although in Foongs' study the maximum age of the patients was less than 50 years, other courses were involved and the minimum time from the last relapse was 30 days.

In the present study, there was no statistically significant difference between the patients and the control participants in performance on the 1-back task, but there was a statistically significant difference between the patient and the control group in performance on the 2-back task.

In the current study, there were statistically significant differences between the patient group and the control participants in performance on the WCST; the MS patients achieved fewer categories and made more perseverative errors than the control participants, confirming the results of several previous studies (Heaton *et al.*, 1985; Beatty *et al.*, 1990a; Mendozzi *et al.*, 1993; Beatty and Monson, 1996).

These results suggest that according to the resources utilized by cognitive tasks, WM tasks may be classified into high-demanding WM tasks (2-back task and WCST) and low-demanding WM tasks (1-back task and digit and visual span), and in relapsing remitting MS, dysfunction in WM includes mainly high-demanding WM tasks. That nature of dysfunction in WM in MS, which includes high-demanding working tasks, is different from the nature of dysfunction in WM in mania and schizophrenia, which includes low-demanding and high-demanding WM tasks (Conklin *et al.*, 2000; Perry *et al.*, 2001; Glahn *et al.*, 2006).

Clinically, this study found no significant correlations between dysfunction in WM and age, age at onset, sex, number of relapses, the functional system affected, or EDSS status. Alternatively, we found statistically significant positive correlations between dysfunction in WM and the duration of illness, which can be attributed to the degenerative nature of the illness (Frischer *et al.*, 2009).

The influence of disease characteristics on the cognitive processes in MS is a subject of controversy. Studies have shown an ambiguous relationship between duration of disease and cognition. Graf *et al.* (1984), McIntosh-Michaelis *et al.* (1991). Rao *et al.* (1987) reported no correlation between duration of disease and cognition. In contrast, a trend toward a higher frequency of poor scores in a memory test in patients with a longer disease duration was reported by Maurelli *et al.* (1992). Conflicting results have also been reported on the role of physical disability (measured using the Extended Disability Status Scale in most cases). Maurelli *et al.* (1992), Rao *et al.* (1987), and Stenager *et al.* (1989) reported significant correlations between physical disability and cognitive functioning. However, Beatty *et al.* (1990b) found that there were no significant correlations between physical disability and cognitive functioning.

Maurelli *et al.* (1992) and Rao *et al.* (1987) reported that the degree of cognitive impairment evident in individuals with MS seems to be unrelated to their neurological disability status or duration of disease. This is considered to be because of the variability in lesion sites. A patient with a predominantly spinal cord or optic nerve involvement may be severely physically disabled, but may have little or no cerebral demyelination and may therefore show little cognitive change. Feinstein *et al.* (1992) found that although duration of disease and disability were unrelated to cognitive impairment in their sample, the disease course seemed to be a sensitive marker of cognitive decline. They reported that a chronic-progressive disease course was associated with greater impairment in cognitive as well as sensory and motor domains.

However, the more commonly reported finding of an absence of any correlation between physical and cognitive functioning in patients with MS indicates that the latter cannot be ascertained from a neurological examination. Hence, a neuropsychological assessment may be valuable.

Radiologically, the present study found statistically positive correlations between the number of lesions and dysfunction in WM. An increase in the number of lesions led to more injury to intracortical and/or intercortical fibers. Injuries to this interconnecting white matter cause disconnection in WM and important processing regions. This study suggests disconnection as a potential mechanism for dysfunction in WM in MS. This is in agreement with Dineen *et al.* (2009), who suggested disconnection as a mechanism for cognitive dysfunction in MS.

Franklin *et al.* (1988) and Fulton *et al.* (1999) found that lesion volume was correlated with cognitive dysfunction in MS. They reported that the degree and pattern of cognitive dysfunction were correlated significantly with the amount of white-matter disease in the cerebral

hemispheres, as evidenced by MRI. This suggests that cerebral lesions result in cognitive dysfunction.

The present study found no correlation between dysfunction in WM and specific sites of lesions, and this may be attributed to the following: dependence of WM on diffuse, extensive neuronal circuits that include cortical and subcortical structures and the inability of conventional MRI to detect lesions in normal-appearing white matter. Therefore, the lesions are more diffuse and involve more sites than those that appear as MRI hyperintensities.

To enhance specificity, a considerable number of studies have focused on identifying the relationship between the location of MS lesions and cognitive dysfunction. These studies fall into two general classes of examination: effects of 'disconnection' and effects of regionally circumscribed lesion load. As focal lesions are quite common and often extensive in the cerebral white matter, disconnection syndromes would be expected to be common. However, numerous correlations have been reported between the location of MS lesions and cognitive impairment (Sperling *et al.*, 2001; Rovaris *et al.*, 2006). Many of these studies have yielded conflicting results, which can partially be attributed to the heterogeneous pathological substrate of multiples sclerosis lesions. Beyond methodological concerns, particularly for MS, the significance of the results is limited because of the lack of the pathological specificity of contrast-enhanced MRI, the heterogeneous pathological substrate, and its inability to detect magnetic resonance-related diffuse changes in normal-appearing brain tissue. The application of quantitative magnetic resonance techniques, such as magnetization transfer imaging, diffusion tensor imaging, and magnetic resonance spectroscopy, has been shown to at least partially overcome the lack of pathological specificity of conventional MRI. The evidence that normal-appearing white matter is not normal remains central for understanding the mechanisms of dysfunction in WM in MS.

Conclusion and recommendation

(1) According to the resources utilized by cognitive tasks, WM tasks may be classified into high-demanding WM tasks and low-demanding WM tasks.
(2) WM dysfunction in relapsing remitting MS includes high-demanding working tasks.
(3) There were no statistically significant correlations between dysfunction in WM and age, sex, age at onset, number of the relapses, intensity of clinical disability, or the functional system affected.
(4) There were statistically significant positive correlations between dysfunction in WM and the duration of illness.
(5) There were no statistically significant correlations between dysfunction in WM and site of the lesions.
(6) There were statistically significant positive correlations between dysfunction in WM and the number of lesions.

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Conflicts of interest

There are no conflicts of interest.

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Correlates of antenatal bonding: an Egyptian Study

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Background
The relationship between mother and child develops and progresses throughout the pregnancy period. In recent times there has been increasing interest in antenatal maternal–foetal bonding and its relationship with different variables, as well as the impact of this bonding on the child's mental health.

Objectives
To investigate the pattern of maternal–foetal relationship during pregnancy, and its relationship to maternal depression and to different sociodemographic and pregnancy-related factors, as well as to the perception of intimate relation with spouse.

Methods
One hundred expectant Egyptian mothers attending obstetric outpatient clinics for regular follow-up of their pregnancy were recruited into the study. They were asked to fill the Maternal–Fetal Attachment Scale (MFAS), the Intimate Bond Measure and the Edinburgh Postnatal Depression Scale.

Results
Maternal antenatal bonding was significantly higher on the MFAS in expectant mothers with longer gestational age. Women with assisted pregnancy had significantly higher scores on the MFAS total score and Role Taking and Attribution subscales. However, if the cause of infertility was unexplained or related to female-oriented factors, the aforementioned MFAS scores tended to be significantly lower than when infertility was related to male-oriented or both factors. Primiparous women had significantly higher scores on the MFAS total score and Role Taking and Differentiation subscales compared with multiparous women. Women who perceived themselves as being healthy had significantly higher scores on the Interaction subscale of MFAS. In this study the intimate relationship with the spouse, and not the marriage duration, showed significant differences in relation to maternal bonding. Expectant mothers who reported a positive attitude towards their marital relationship (Optimal Intimacy and Affectionate Constraint) had significant higher means on the total score of the MFAS and on the Interaction, Giving of Self and Role Taking subscales. The study showed that expectant women with previous loss of foetus and those with no depressive symptoms had better bonding despite the lack of significance.

Conclusion
Maternal antenatal bonding is associated with multiple factors including longer gestational age, parity, previous loss of foetus, assisted pregnancy, perceived good maternal health and intimacy with partner.

Keywords:
antenatal bonding, Edinburgh Postnatal Depression Scale, Intimate Bond Measure, Maternal–Fetal Attachment Scale, maternal–foetal relation

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Introduction

It was believed for many years that attachment between the mother and her child starts in the few hours following delivery (Honjo *et al.*, 2003). As early as 1967 Rubin stated that the immediate bond between a mother and her neonate existed as a result of prenatal processes (Rubin, 1967). However, it was not until the 1980s that research reflected the increasing recognition that the relationship between a mother and her child starts to develop while the child is a foetus. To date, the significance of antenatal bonding is not as well studied as maternal–infant postpartum bonding (Alhusen, 2008). According to Brockington (1996) this prenatal affiliation develops in a way similar to the mother–infant relationship after birth. Cranley (1981) was the first to create a theoretical construct and an antenatal attachment scale called the Maternal–Fetal Attachment Scale (MFAS), an instrument that continues to be the most frequently used in studies on the antenatal period (Beck, 1999). Although it was developed originally in the USA, the MFAS was used later in different western cultures (Müller and Ferketich,

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1992; Seimyr *et al.*, 2009) and in nonwestern countries like Korea (Chang *et al.*, 2004) and Japan (Narita and Maehara, 1993). There is a dearth of research on the maternal–foetal bonding in Egypt and Arab countries. To the best of our knowledge this issue has not been investigated in our culture.

Maternal–foetal bonding has been defined by many researchers as the extent to which women engage in behaviours that represent affiliation and interaction with their unborn child (Cranley, 1981). During pregnancy the expectant mother goes through multiple dynamic psychological and physiological changes that affect her relationship with her unborn child. The maternal–foetal bonding is suggested to be related to three main aspects: cognitive, affective and altruistic. The cognitive component of attachment is related to the desire to know about the infant. The affective component represents the pleasure accompanying thoughts of or interaction with the foetus. The altruistic component is the desire for providing protection to the coming child (Shieh *et al.*, 2001).

With the increasing recognition that maternal–foetal attachment (MFA) is an important requirement for optimal maternal–infant adaptation (Fuller, 1990; Müller, 1996; Bryan, 2000), it is essential for mental health professionals to monitor it as it has important implications for the mental health of both the mother and the person to be (the child). Research has demonstrated a correlation between prenatal and postnatal attachment (Fleming *et al.*, 1988; Müller, 1996). As such, early intervention starts in the antenatal period, particularly as it is well documented that optimal attachment in early infancy is an integral component in the future development of the child (Oppenheim *et al.*, 2007). In addition, there is emerging research suggesting that low levels of prenatal attachment may be related to forms of foetal abuse (Pollock and Percy, 1999; Laxton-Kane and Slade, 2002). In contrast, there is growing evidence that the prevalence of depression during pregnancy is comparable to postpartum rates (Green, 1998; Evans *et al.*, 2001; Austin, 2003, 2004). Hart and McMahon (2006) found that women having low quality of foetal attachment reported significantly higher levels of depression and anxiety (state and trait). Lindgren (2001, 2003) reported that women with lower depression scores had higher levels of MFA and that MFA had significant direct effects on the health practices of mothers.

Aim of the study

To investigate the pattern of maternal–foetal relationship during pregnancy and factors positively and negatively associated with it.

Hypothesis

Maternal antenatal bonding is positively associated with longer gestational period, method of conception and previous loss of foetus or a newly born child and negatively associated with depression and poor marital relationship.

Participants and methods

Study type

This is a cross-sectional descriptive study conducted on a convenient sample.

Site of study

Participants were recruited from six prenatal clinics located in two governorates: Giza and Cairo.

Participants

One hundred expectant Egyptian mothers attending gynaecology and obstetric outpatient clinics for follow-up of their pregnancy between October 2010 and June 2011 were selected for the study. Exclusion criteria were participants suffering from life-threatening conditions or threatened abortion. A verbal explanation of the purpose of the study and of the questionnaires and forms entailed in the study was given. Those who agreed to participate were given the questionnaires to be filled in without assistance from the prenatal clinic team.

Tools

A structured information sheet covering the following:

(1) *Sociodemographic*: data about both parents, pertaining to age, education, occupation and duration of marriage.
(2) *Pregnancy*: duration of pregnancy; if current pregnancy is wanted, planned; mode of conception; mother's health during pregnancy; desired sex; expected sex if known; number of foetuses; previous pregnancies; previous miscarriages or loss of baby.

The Maternal–Fetal Attachment Scale (Cranley, 1981)

The MFAS version used is a 22-item scale (Brockington, 1996) scored on a five-point scale from 1 (definitely not) to 5 (definitely yes), with 5 being the most positive statement. It consists of five subscales:

(1) Role Taking: three items.
(2) Differentiation of Self from Fetus: three items.
(3) Interaction with Fetus: six items.
(4) Attributing Characteristics to Fetus: five items.
(5) Giving of Self: five items.

The Edinburgh Postnatal Depression Scale (Cox et al., 1987)

This is a self-reporting 10-item questionnaire scored on a four-point scale from zero to three specifically designed to screen for postnatal depression in community samples. Five of the items concern dysphoric mood, two concern anxiety and the remaining items deal with guilt, suicidal ideation and an inability to cope.

The authors recommend a cut-off score of 9/10 for screening purposes for women in the postpartum period (Cox *et al.*, 1987). Although the Edinburgh Postnatal Depression Scale (EPDS) was developed specifically for the screening and assessment of postpartum depression, it is now widely used during the entire perinatal period (Brandon *et al.*, 2008).

Both the MFAS and EPDS were translated into Arabic and back translated by the authors and revised with Prof. Ian Brockington, and the Arabic versions were used.

Intimate Bond Measure (Wilhelm and Parker, 1988)
It is a 24-item self-report scale assessing the nature of partner relationship. It comprises two subscales: care and control. The care subscale covers aspects such as affection, consideration and understanding, whereas control assesses the extent to which the participant feels dominated, intruded upon, criticized and controlled by the partner.

Wilhelm and Parker (1988) defined four broad styles of intimate relationships that they label as:

(1) Optimal Intimacy: high care, low control.
(2) Affectionate Constraint: high care, high control.
(3) Affectionless Control: low care, high control.
(4) Absence of Intimacy: low care, low control.

The scale was translated into Arabic and back translated. Permission to use the scale was obtained by the first author from Kay Wilhelm, after she approved the translation and back translation.

Statistical analysis
Data were statistically analysed using Statistical Package for Social Sciences, version 16 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics for numerical data were means and SD, whereas those for categorical data were number and percentage. Inferential analyses used for quantitative variables were the Student *t*-test and the χ^2-test for qualitative data. Level of significance was taken at *P* values less than 0.05.

Ethical issues
Study approval was received from the research and ethics committees of the Department of Psychiatry, Cairo University. A verbal consent was obtained from all the participants, describing the objectives of the study and the questionnaires required to be filled. It was clearly stated to all expectant mothers that participation in the study was voluntary and that they had the right to withdraw from the study without affecting their regular care at the obstetric clinics.

Description of participants
Sociodemographic characteristics
Age
The age of the participants ranged from 22 to 43 (mean: 28.86 ± 4.72). Of them, 70.1% ($n = 68$) were in the 21–30 age group and 24.7% ($n = 24$) were in the 31–40 age group. Only 5.2% ($n = 5$) were older than 40 years (Table 1).

Marriage duration
The majority of the participants (50%) had been married for 1–5 years. Of the married participants 22 and 23% had been married for periods less than a year and more than 5 years, respectively.

Table 1 Sociodemographic characteristics

	N (%)
Age ($n=100$)	
Range: 22–43	
Mean ± SD: 28.86 ± 4.72	
21–30	68 (68)
31–40	24 (24)
>40	5 (5)
Unstated	3 (3)
Marriage duration (years) ($n=100$)	
≤1	22 (22)
>1–5	50 (50)
6–10	17 (17)
>10	6 (6)
Unstated	5 (5)
Education ($n=100$)	
Preparatory	1 (1)
Secondary	7 (7)
University	47 (47)
Postgraduate studies	4 (4)
Unstated	41 (41)
Occupation ($n=100$)	
Housewife	22 (22)
Professional	19 (19)
Managerial and semiprofessional	16 (16)
Skilled	2 (2)
Unstated	41 (41)

Education
Out of the 59 participants who stated their educational level, 86.4% ($n = 51$) were university graduates.

Occupation
In all, 37.2% ($n = 22$) of the participants stated their occupation as housewives, whereas the remaining 62.8% ($n = 37$) were professionals, for example, physicians, pharmacists and engineers; 27.1% ($n = 16$) were in managerial and semiprofessional jobs (e.g. accountants, human resources and public relation employees), and only 3.3% ($n = 2$) were in a skilled job.

Pregnancy-related data
Pregnancy duration
As shown in Table 2, the majority of the participants were in the third (46) or second trimesters (43%). Only 8% were in the first trimester.

Health-related problems
An overall 23% ($n = 23$) reported variable health-related problems (diabetes mellitus, removal of an ovary, hypotension, hyperemesis and perceived poor health). In contrast, 74% ($n = 74$) negated the presence of any health problem and considered themselves healthy.

Parity
In all, 60.9% ($n = 56$) were primiparous, whereas 39.1% ($n = 36$) were multiparous.

Previous foetal or neonatal loss
Of those who answered, 7.5% ($n = 6$) reported previous foetal loss.

Mode of conception
Of those who answered, 45.4% ($n = 44$) had an assisted pregnancy, whereas 54.6% ($n = 53$) reported natural pregnancy.

Table 2 Pregnancy related data

	N (%)
Pregnancy duration	
First trimester	8 (8)
Second trimester	43 (43)
Third Trimester	46 (46)
Health-related problems	
None	74 (74)
Yes[a]	23 (23)
Unstated	3 (3)
Planned pregnancy	
Yes	79 (79)
No	18 (18)
Unstated	3 (3)
Desired pregnancy	
Yes	94 (94)
No	3 (3)
Unstated	3 (3)
First pregnancy	
Yes	56 (56)
No	36 (36)
Unstated	8 (8)
Previous foetal or neonatal loss	
Yes	6 (6)
No	74 (74)
Unstated	20 (20)
Desired sex for mother	
Boy	19 (19)
Girl	27 (27)
Both	5 (5)
No preference	20 (20)
Unstated	29 (29)
Foetus sex	
Boy	26 (26)
Girl	26 (26)
Both	8 (8)
Unstated	40 (40)
Number of foetuses	
1	79 (79)
2	15 (15)
Unstated	6 (6)
Mode of conception	
Natural	53 (53)
Assisted	44 (44)
Unstated	3 (3)
Cause of infertility in assisted pregnancy ($n=44$)	
Male	21 (47.7)
Female	14 (31.8)
Both	4 (9)
Unexplained	5 (11.4)
Psychiatric history	
Negative	88 (88)
Positive[b]	6 (6)
Unstated	6 (6)

[a]Diabetes mellitus, removal of an ovary, hypotension, hyperemesis, poor health.
[b]Three reported depression, one anxiety and two nonspecified.

Cause of infertility in assisted pregnancy

Among the 44 participants who had assisted pregnancy, the cause of infertility was due to a male factor in 47.7% ($n = 21$), due to a female factor in 31.8% ($n = 14$) and due to both male and female factors in 9% ($n = 4$). 11.4% ($n = 5$) had infertility due to unexplained factors.

Results

Antenatal bonding as measured by Maternal–Fetal Attachment Scale

As shown in Table 3, the MFAS total scale ranged from 50 to 105, with a mean score of 84.53 ± 11.29. Table 4 shows the responses of expectant mothers on the MFAS subscales. On the Role Taking subscale, 93% of expectant mothers were eagerly looking forward to holding their babies and 90% were imagining themselves taking care of the baby; however, only 75% were able to picture themselves feeding the baby. On the Differentiation of Self from Fetus subscale 98% of expectant mothers were looking forward to seeing how their baby looks like and about 90% enjoyed watching their tummy jiggle. A higher percentage of expectant mothers had decided on a girl's name (55%) than a boy's (40.8%). On the Interaction with Fetus subscale grasping the foot of the baby through the tummy to move it received the highest percentage of negative answers (76.3%) and was also the question not answered the most number of times (20%). On the Attributing Characteristics to the Fetus subscale, the item that received the highest number of positive answers was wondering whether the baby could hear while inside the mother's womb (92%), followed by whether the child could feel and think (89%). The highest percentage of uncertainty was regarding the implication behind the foetus kicking (33%) and ability to guess the baby's personality from the way he/she moved around (24%). The highest percentage of negative answers concerned the baby getting hiccoughs (56%). On the Giving of Self subscale, 91% of expectant mothers stated that they were engaging in activities to try to stay healthy, which they would not otherwise do had they not been pregnant, with 82% eating meat and vegetables to ensure that the baby gets a good diet and 84% giving up certain habits to help their baby grow healthy; 88% of the participants felt that all the trouble of being pregnant was worth it, whereas 52% felt that their body was ugly.

Table 3 Maternal–Fetal Attachment Scale total scale and subscale mean scores ($n=100$)

	Mean	SD	Range
Total	84.53	11.29	50–105
Role Taking	12.87	2.2	6–15
Differentiation of Self from Fetus	12.49	1.79	8–15
Interaction with Fetus	17.44	3.8	8–25
Attributing Characteristics to Fetus	21.84	4.16	9–29
Giving of Self	20.05	3.2	6–25

Sociodemographic correlates of antenatal bonding

Maternal bonding across age

The mean values obtained by the different age groups did not differ significantly. However, the older group tended to obtain higher mean scores on the total scale as well as on the Role Taking and Attribution subscales (Table 5).

Maternal bonding according to marriage duration

Bonding did not differ significantly with the duration of marriage of expectant mothers. However, as shown in Table 6, there was a tendency for those married for more than 10 years to obtain higher mean scores on the total scale and all subscales except the Differentiation subscale.

Pregnancy-related correlates of antenatal bonding

Maternal bonding across pregnancy

Expectant mothers with longer gestational periods (in the third trimester) obtained significantly higher mean scores

Table 4 Distribution of answers to the items of Maternal–Fetal Attachment Scale according to subscales

		N (%)				
		Definitely yes	Yes	Uncertain	No	Definitely no
Role Taking						
4	Picture myself feeding baby ($n=98$)	43 (42.2)	32 (31.4)	8 (7.8)	14 (13.7)	1 (1)
8	Imagine myself taking care of baby ($n=98$)	48 (49)	39 (39.8)	6 (6.1)	5 (5.1)	0 (0)
17	Can hardly wait to hold baby ($n=100$)	59 (59)	34 (34)	5 (5)	1 (1)	1 (1)
Differentiation of Self from Fetus						
3	Enjoy watch tummy jiggle as baby kicks ($n=97$)	61 (61.9)	27 (27.8)	6 (5.9)	4 (4.4)	0 (0)
5	Looking forward to see how the baby look ($n=100$)	75 (75)	23 (23)	1 (1)	1 (1)	0 (0)
10	Decided on a name for a girl ($n=98$)	19 (19.7)	35 (35.7)	7 (7.1)	3 (33.7)	4 (4.1)
3	Enjoy watch tummy jiggle as baby kicks ($n=97$)	61 (61.9)	27 (27.8)	6 (5.9)	4 (4.4)	0 (0)
Interaction with Fetus						
1	Talk to my unborn baby ($n=100$)	41 (41)	45 (45)	2 (2)	1 (1)	1 (1)
7	Refer to baby by nickname ($n=98$)	33 (33.7)	35 (35.7)	7 (7.1)	23 (23.5)	0 (0)
16	I poke to get him/her to poke back ($n=96$)	17 (17.7)	38 (39.6)	4 (4.2)	36 (37.5)	1 (1)
18	I stroke my tummy to quite baby ($n=97$)	34 (35.1)	37 (38.1)	9 (9.3)	16 (16.5)	1 (1)
22	I grasp baby foot to move it around ($n=80$)	3 (3.8)	6 (7.8)	10 (12.5)	50 (62.5)	11 (13.8)
Attributing Characteristics to Fetus						
6	Wonder if baby feels cramped in there ($n=100$)	28 (28)	42 (42)	9 (9)	19 (19)	2 (2)
9	Can guess what my baby's personality will be ($n=99$)	25 (25.3)	27 (27.3)	24 (24.2)	17 (17.2)	6 (6.1)
12	Wonder if baby can hear inside ($n=100$)	36 (36)	56 (56)	2 (2)	6 (6)	0 (0)
13	Wonder if baby thinks and feels inside ($n=98$)	34 (34.7)	53 (54.1)	5 (5.1)	6 (6.1)	0 (0)
15	Baby kicks to tell me it is eating time ($n=97$)	18 (18.6)	32 (33)	32 (33)	12 (12.4)	3 (3.1)
19	Can tell baby has hiccoughs ($n=98$)	7 (7.1)	20 (20.4)	16 (16.3)	41 (41.8)	14 (14.3)
Giving of Self						
2	Feel the trouble of being pregnant is worth it ($n=98$)	54 (55.1)	32 (32.7)	8 (8.2)	3 (3.1)	1 (1)
11	Do things to stay healthy ($n=100$)	42 (42)	49 (49)	4 (4)	4 (4)	1 (1)
14	I eat meat and vegetable to be sure my baby gets good diet ($n=100$)	41 (41)	41 (41)	9 (9)	9 (9)	0 (0)
20	Feel my body is ugly ($n=99$)	21 (21.2)	31 (31.3)	16 (16.2)	28 (28.3)	3 (3)
21	Give up doing things to help my baby ($n=99$)	33 (33.3)	50 (50.5)	6 (6.1)	9 (9.1)	1 (1)

Table 5 Maternal bonding across age

	21–30 years	31–40 years	>41 years	*F*	*P*
Total	85.43 ± 11.95	82.52 ± 9.34	85.6 ± 13.63	0.589	0.557
Role Taking	13.01 ± 2.21	12.25 ± 2.33	14.6 ± 1.67	2.627	0.078
Differentiation	12.57 ± 1.89	12.25 ± 1.59	12.4 ± 1.52	0.291	0.748
Interaction	17.97 ± 3.83	15.81 ± 3.35	17.4 ± 4.56	2.931	0.058
Attribution	21.98 ± 4.43	21.71 ± 2.99	23.4 ± 3.71	0.354	0.703
Giving of Self	19.95 ± 3.38	20.5 ± 2.67	20.2 ± 2.17	0.265	0.768

on the whole scale as well as on all the different subscales (Table 7).

Maternal bonding according to mode of conception

Expectant mothers with assisted conception obtained significantly higher means on the total scale and the subscales of Role Taking, Interaction with Fetus and Attributing Characteristics to Fetus. Those who conceived normally did not differ from those with assisted conception on Differentiation and Giving of Self subscales (Table 8).

Maternal bonding according to cause of infertility

The mean scores differed significantly according to the cause of infertility on the scale as a whole and on two subscales, namely, the Role Taking and the Attribution subscales. Higher means were obtained in case of male-oriented factors or if both spouses had a problem than if the reason for infertility had been a female-oriented factor or was unexplained (Table 9).

Maternal bonding according to previous loss of foetus or neonate

Those who reported previous loss of a foetus or a neonate obtained lower means on all subscales except the Interaction subscale, in which they scored higher; however, all differences were statistically insignificant (Table 10).

Maternal bonding according to parity

Expectant mothers who were pregnant for the first time obtained a significantly higher mean score compared with multiparous mothers on the scale as a whole, as well as on the subscales of Role Taking and Differentiation (Table 11).

Maternal bonding according to mothers' health during pregnancy

Expectant mothers reporting poor health or health-related problems during their pregnancy obtained lower means except on the Differentiation subscale; however, the difference was statistically significant only on the Interaction subscale (Table 12).

Perception of expectant mothers of their marital relation on Intimate Bond Measure

The most frequent style of marital relationship as perceived by the expectant mothers was Affectionate Constraint (36.6%, $n=23$), followed by Absent Intimacy (25.4%). Optimal Intimacy and Affectionless Control were represented equally (19%).

Bonding according to style of intimate relation as perceived by expectant mothers

Comparing the four styles of intimate relation, the Affectionate Constraint group (high care, high control) showed significantly higher total MFAS mean scores as well as higher scores on Interaction and Giving of Self. As shown in Table 13 the optimal style group showed significantly higher Role Taking mean scores.

Table 6 Maternal bonding according to marriage duration

	<1 year	1–5 years	>5–10	>10 years	*F*	*P*
Total	83.63 ± 11.68	84.96 ± 11.84	84 ± 11.7	89 ± 8.49	0.364	0.779
Role Taking	13.11 ± 2.02	12.94 ± 2.09	12.82 ± 3.26	13 ± 1.55	0.057	0.982
Differentiation	12.64 ± 1.68	12.48 ± 1.76	12.52 ± 1.97	11.5 ± 2.07	0.649	0.586
Interaction	17.3 ± 4.93	17.94 ± 3.43	15.47 ± 3.52	19.17 ± 2.2	2.243	0.089
Attribution	20.63 ± 3.89	22.1 ± 4.38	22.47 ± 3.6	25 ± 1.9	2.035	0.115
Giving of Self	20 ± 2.94	19.76 ± 3.42	20.82 ± 2.94	20.3 ± 2.25	0.493	0.688

Table 7 Maternal bonding across pregnancy ($n = 97$)

	First trimester	Second trimester	Third trimester	*F*	*P*
Total	72.24 ± 12.81	83.76 ± 9.6	87.6 ± 11.22	6.817	0.002
Role Taking	11 ± 2.62	13.13 ± 1.92	13.13 ± 1.67	3.78	0.026
Differentiation	10.25 ± 1.49	12.53 ± 1.74	12.87 ± 1.56	8.755	0.000
Interaction	15.88 ± 4.11	16.6 ± 3.71	18.47 ± 3.72	3.495	0.034
Attribution	18.19 ± 4.37	21.88 ± 3.58	22.48 ± 4.37	3.865	0.024
Giving of Self	17.53 ± 4.81	19.84 ± 3.04	20.87 ± 2.72	4.084	0.020

Table 8 Bonding according to the way of conception ($n = 97$)

	Assisted	Normal	*t*	*P*
Total	86.62 ± 11.87	81.48 ± 9.99	3.22	0.002
Role Taking	13.79 ± 1.49	12.16 ± 2.48	3.836	0.000
Differentiation	12.41 ± 1.91	12.55 ± 1.7	−0.376	0.708
Interaction	18.33 ± 3.5	16.64 ± 3.94	2.205	0.03
Attribution	23.73 ± 4.13	20.55 ± 3.42	4.151	0.000
Giving of Self	20.72 ± 3.39	19.58 ± 2.87	1.79	0.076

Maternal bonding in relation to depression

Out of the 100 participants 96 answered the EPDS. Applying the cut-off score of above nine points, 59.4% ($n = 57$) of participants were scored as depressed. There were no significant differences between those who were scored as depressed on the EPDS and those who did not on the MFAS scale as a whole or on any of its subscales. However, the nondepressed group tended to score higher mean values than the depressed group except on Differentiation and Giving of Self subscales (Table 14).

Discussion

This study showed that the antenatal bonding was significantly higher on the MFAS total score and on all subscales in expectant mothers with longer gestational periods. This is in line with the works of Grace (1989), Heidrich and Cranley (1989), Lerum and LoBiondo-Wood (1989), Righetti *et al.* (2005), Tsartsara and Johnson (2006) and Hjelmstedt *et al.* (2006), in which gestational age was consistently demonstrated to have significant correlation with maternal development of antenatal bonding. A plausible explanation is that the longer the gestational age, the more likely the mother will adapt to the new role transition and progress in the attachment process with her unborn child.

This study showed that the mode of conception has an impact on antenatal bonding. Gravidas with assisted conception (44% of the sample) had significantly higher scores on the MFAS total score as well as on the Role Taking and Attribution subscales. As suggested by Alhusen (2008) these women with long-awaited pregnancies usually suffer from lengthy periods of infertility, thereby raising their investment in the pregnancy and their perception of the foetus as being precious. This finding is consistent with the studies by Eugster and Vingerhoets (1999) and McMahon *et al.* (2011) who reported the presence of significant association between assisted conception and more intense foetal attachment. In contrast, Hjelmstedt *et al.* (2006) found no significant differences in maternal bonding between women who conceived by means of in-vitro fertilization versus those who conceived naturally.

It is noteworthy that the cause of infertility in women with assisted pregnancy had a significant impact on maternal bonding. In this study, statistically significant lower mean scores on the total MFAS and on the Role Taking and Attribution subscales were observed if the cause of infertility was unexplained or was due to factors related to the female partner. This could be attributed to the fact that stress levels may be higher in gravidas when they are the cause of infertility. When the reason for infertility is unknown, women tend to be blamed in our culture, adding to their stress and possibly affecting the ability to bond with the unborn child. The different dynamics underlying each cause of infertility seem an interesting area that needs in-depth study.

In the current study, primiparous women had significantly higher scores on the MFAS total score and on the Role Taking and Differentiation subscales than did multiparous women. The higher bonding in mothers who were pregnant for the first time may indicate their eagerness to assume a new role that had never been experienced before. This is consistent with the study by Grace (1989) and the meta-analytic study by Yarcheski *et al.* (2009) that reported that parity correlated negatively with antenatal bonding and is considered one of the predictors of MFA.

Although a significant difference was not found in the total scores on MFAS among the mothers based on the presence or absence of a previous loss of a foetus, the mothers with previous loss had lower bonding. This may reflect the mothers' worries that affected MFA. This is in line with the study by Armstrong and Hutti (1998) who reported that expectant mothers with previous loss of a foetus had significantly greater levels of anxiety and significantly lower

Table 9 Maternal bonding according to the cause of infertility

	Male factor	Female factor	Both	Unexplained	*F*	*P*
Total	91.55 ± 9.03	85.77 ± 16.4	89.76 ± 5.6	83.6 ± 9.94	3.8	0.007
Role Taking	14.14 ± 1.11	13.21 ± 1.76	14.25 ± 1.5	13.6 ± 1.95	4.348	0.003
Differentiation	12.9 ± 2.05	12.5 ± 1.83	11.0 ± 1.41	11.2 ± 0.85	1.689	0.159
Interaction	18.67 ± 3.41	18.46 ± 4.03	18.75 ± 1.5	16.2 ± 3.77	1.578	0.186
Attribution	24.48 ± 3.06	22.57 ± 5.75	25.78 ± 2.1	22.2 ± 3.42	5.847	0.000
Giving of Self	21.42 ± 2.61	19.81 ± 2.61	20.75 ± 1.5	20.4 ± 3.44	1.447	0.225

Table 10 Maternal bonding according to previous loss of foetus or neonate

	No loss	Loss	*t*	*P*
Total	85.54 ± 11.1	80.54 ± 16.74	1.018	0.312
Role Taking	13.1 ± 2.15	12.17 ± 3.37	0.981	0.330
Differentiation	12.62 ± 1.8	11.67 ± 1.75	1.250	0.215
Interaction	17.44 ± 3.85	19 ± 3.36	− 0.960	0.340
Attribution	22.35 ± 3.95	20 ± 6.07	1.343	0.183
Giving of Self	20.24 ± 2.95	17.71 ± 5.68	1.866	0.066

Table 11 Maternal bonding according to parity

	Primiparous	Multiparous	*t*	*P*
Total	87.24 ± 10.77	81.73 ± 11.25	2.235	0.021
Role Taking	13.44 ± 1.91	12.14 ± 2.45	2.722	0.008
Differentiation	12.88 ± 1.74	12.03 ± 1.75	2.121	0.037
Interaction	17.9 ± 3.79	16.91 ± 3.71	1.221	0.225
Attribution	22.62 ± 4.23	21.19 ± 3.78	1.646	0.103
Giving of Self	20.65 ± 2.85	19.39 ± 3.46	1.898	0.061

Table 12 Maternal bonding according to mothers' health during pregnancy

	Good	Poor	*t*	*P*
Total	85.44 ± 11.39	82.41 ± 11.37	1.113	0.269
Role Taking	12.98 ± 2.05	12.65 ± 2.77	0.615	0.542
Differentiation	12.39 ± 1.78	12.78 ± 1.83	0.113	0.364
Interaction	17.84 ± 3.9	16 ± 3	2.051	0.043
Attribution	22.1 ± 4.01	21.54 ± 4.29	0.599	0.55
Giving of Self	20.15 ± 3.36	19.96 ± 2.4	0.252	0.801

levels of prenatal attachment. The review by Alhusen (2008) showed that several studies have reported that MFA is lower in women with previous loss. The explanation given is that when a mother experiences such a loss she may grieve for a long time, and a subsequent pregnancy may evoke a degree of apprehension, thereby disrupting attachment. This is also in line with the study by Tsartsara and Johnson (2006) who stated that women with a history of miscarriage reported significantly higher pregnancy-specific anxiety at the first trimester. It is worthy to investigate the impact of worries and anxieties on maternal bonding in future studies.

This study showed that maternal bonding tended to be associated with older age of mothers, despite the lack of significance. This finding is consistent with the work of McMahon *et al.* (2011) who reported that older mothers appeared to have some psychological advantages over their younger counterparts. They tended to be more resilient and reported lower symptoms of depression and anxiety during pregnancy. This may give them an advantage in bonding with their infants.

Although participants with life-threatening conditions were excluded from the sample, other participants with general medical conditions ($n = 23$) were included, unlike most other research work that studied bonding only among healthy mothers (Brandon *et al.*, 2008). This enabled the study to examine the effect of poor general health of mothers on bonding with their unborn children. In the current study, expectant mothers with poor general health obtained statistically significant lower mean scores on the Interaction subscale of MFAS. This finding suggests that healthcare providers for pregnant women may have to assess antenatal attachment especially when the mother does not perceive herself as healthy. It might be recommended that these women be educated about the importance of interaction by talking and playing with their foetuses, which may reflect in better attachment and healthy relation with the infants in the future (Ahern and Ruland, 2003). In Alhusen's (2008) critical review of literature, it was found that MFA predicts engagement in health practices such as attending prenatal care, maintaining a nutritionally sound diet, and getting regular exercise that reflected positively on the mothers' health and in greater MFA.

In this study, intimate relations with the spouse, and not marriage duration, showed significant differences in maternal bonding. This may point to the importance of marriage perception as a quality, not just its duration. This is in line with the work of Cranley (1981) and Wilson *et al.* (2000) who concluded that social support, not necessarily marriage duration, may influence attachment.

In this study expectant mothers who reported a positive attitude towards their marital relation (Optimal Intimacy and Affectionate Constraint) had significantly higher mean scores on the total score of the MFAS as well as on the Interaction, Giving of self and Role Taking subscales. This finding is in line with most of the literature that reported good marital relation and social support as important predictors of antenatal bonding (Yarcheski *et al.*, 2009).

Although a significant difference was not found between the depressed and nondepressed groups of expectant mothers on the MFAS total score or on any of its subscales, it is noteworthy that the depressed group tended to have lower mean scores than the nondepressed group. A consistently reported finding of studies by Robertson *et al.* (2004), Seimyr *et al.* (2009) and McFarland *et al.* (2011) is that mothers with depressive symptoms are less positive about their pregnancy and show lower scores on MFAS. Further, Brandon *et al.* (2008) stated that mothers showing strong MFA reported less depressive symptoms.

Table 13 Bonding according to style of intimate relation as perceived by expecting mothers

	Absent	Affectionless	Affectionate	Optimal	*F*	*P*
Total	84.4 ± 10.25	78.7 ± 12.15	90.9 ± 10.47	85.8 ± 7.5	4.335	0.007
Role Taking	12.59 ± 2.57	12 ± 2.85	13.58 ± 1.72	14.07 ± 0.96	3.058	0.034
Differentiation	12.47 ± 1.42	11.77 ± 1.83	12.69 ± 1.87	12.8 ± 1.93	0.974	0.410
Interaction	16.8 ± 3.04	16.08 ± 3.57	19.38 ± 3.32	16.6 ± 3.36	4.211	0.009
Attribution	22.94 ± 3.51	20.62 ± 3.93	23.85 ± 3.6	22.97 ± 3.2	2.268	0.089
Giving of Self	19.76 ± 2.59	19.15 ± 2.94	21.41 ± 2.56	19.4 ± 2.5	3.146	0.031

Table 14 Maternal bonding in relation to depression ($n = 96$)

	Nondepressed	Depressed	*t*	*P*
Total	85.38 ± 11.69	84.07 ± 11.28	0.550	0.584
Role Taking	13.26 ± 1.85	12.78 ± 2.25	1.091	0.278
Differentiation	12.46 ± 1.76	12.51 ± 1.82	−0.126	0.90
Interaction	17.56 ± 3.84	17.25 ± 3.88	0.378	0.706
Attribution	22.33 ± 4.53	21.58 ± 3.95	0.868	0.388
Giving of Self	19.84 ± 3.71	20.18 ± 2.91	−0.490	0.625

Clinical implications

When poor levels of MFA are identified during the course of pregnancy, appropriate interventions should be implemented to assist the expectant mother to achieve a physically and psychologically sound pregnancy in an effort to best optimize maternal and foetal health.

When factors known to threaten MFA, such as depression, anxiety, substance abuse and lack of social support, are present or suspected, both mental and maternity healthcare communication is highly advised. Together, an early and effective intervention can be implemented.

Research implications

Future studies should include longitudinal designs to enhance our understanding of the maternal–foetal relationship over time. A prospective study using a larger, randomly selected sample to examine the development of maternal bonding across the gestational period and postnatal period would aid in studying the relationship between antenatal attachment and postnatal bonding with the infant and allow generalization.

It is recommended to perform further studies to investigate the presence of anxiety and depressive subthreshold symptoms and clinical diagnoses among expectant women and their impact on the process of maternal–foetal bonding.

It is worth studying the bonding before and after performing an ultrasound. The option and ability to view the foetus as an independent being at an earlier point in pregnancy is likely to contribute to the development of maternal–foetal relationship at a much earlier point in foetal development.

Further research on high-risk pregnancy mothers is needed for adding knowledge to the interplay between obstetric complications and development of antenatal bonding.

Study limitations

The cross-sectional design of the study prevented causal inferences. In addition, this study recruited a convenient sample with a relatively high level of education. The participants in this study were well educated. Of the women in this study 51% reported a university degree or above. This does not represent the level of education in the Egyptian population. The last census in 2006 reported that only 8% of Egyptian women had a university degree or above (Central Agency for Public Mobilization and Statistics (CAPMAS, 2006). This discrepancy may limit the generalizability of the study results.

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Conflicts of interest

There are no conflicts of interest.

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Sexual risk among substance users and its relation to personality profile

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Objectives
To study sexual behavior among substance users, to find an association between substance use and risky sexual behaviors, and to determine whether there is an association between personality traits and risky sexual behaviors among substance users.

Participants and methods
Our participants (100) were divided into two groups: group 1 (cases) included 50 individuals (diagnosed with substance abuse according to the DSM-VI criteria) recruited from the Kasr El Aini psychiatric inpatient ward and group 2 (controls) included 50 normal control individuals, matched for age, sex, and socioeconomic status. All patients were men, ranging age from 18 to 40 years, were taking substances for at least 6 months, and all of them could read and write. Those with a comorbid axis I diagnosis were excluded from the study. Both groups were subjected to a full psychiatric sheet, risk assessment battery (RAB), and the Eysenck personality questionnaire. The Addiction Severity Index was determined for cases, urine sampling was carried out using drug screening strips, and a laboratory test was performed for HIV and hepatitis C virus detection.

Results
Both groups showed nonsignificant differences in terms of age, education, employment, education, and social status. The most prevalent substance used was tramadol (96%), followed by cannabis (72%) and heroin (58%). Hepatitis C virus infection was detected in (16%); none of the patients had HIV (AIDS). There were statistically significant differences in extroversion and neuroticism between the cases and the controls. There was a statistically significant difference between the cases and the controls in terms of the sexual subscale of RAB. There was a significant correlation between psychoticism and criminality subscales in Eysenck Personality Questionnaire and the RAB in the case group.

Conclusion
Patients with substance abuse have more sexual risk than normal controls. Sexual risk is not related to the severity of addiction, but to psychoticism and criminal behavior of personality.

Keywords:
personality, sexual risk, substance abuse

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Introduction

Substance users are at a risk of sexual transmission of HIV through high-risk sexual behavior such as engaging in unprotected intercourse, having multiple sexual partners, exchanging sex for money and/or drugs, and combining sex and substance use (Booth *et al.*, 2000; UNAIDS/WHO/UNICEF, 2008).

Certain patterns of substance use have been shown to be associated with an increased risk for sexual transmission of HIV. Both injection and noninjection heroin use have been associated with high-risk sexual activity (Chitwood *et al.*, 1995; Sánchez *et al.*, 2002).

Several studies of men who have sex with men have found an association between sexual risk behavior and alcohol and recreational drug use (Dolezal *et al.*, 2000; Chaudhury *et al.*, 2010).

The relationship between alcohol and sexual risk taking is complex, and may be explained in a number of ways. Alcohol use may influence high-risk behaviors by affecting judgment and increasing disinhibition. Alcohol use may be a marker of a risk-taking personality; individuals who consume alcohol in huge amounts may also be more likely to engage in high-risk sexual behaviors (Leigh *et al.*, 1994; Haynes *et al.*, 2008).

The use of alcohol or other drugs has been proposed to be a contributing factor to sexual risk-taking. Because alcohol and drugs are believed to interfere with judgment and decision making, it has been suggested that their use

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in conjunction with sexual activity might increase the probability that risky behavior will occur (Graves and Leigh, 1995; Marshall *et al.*, 2010).

Several hypotheses have been offered to explain the association between substance use and sexual risk behavior, including pharmacological effects, social context, situation specific rituals, and personality traits. Yet, few studies have sought to verify these explanatory hypotheses (Dolezal *et al.*, 2000).

Preliminary evidence has indicated that impulsivity and related traits such as novelty, sensation, and risk seeking appear to account for some unique variance in sexual risk behavior, at least in some populations (Stein *et al.*, 2006).

It has been well established that substance use disorders and personality disorders frequently co-occur. (James and Taylor, 2007; Fridberg *et al.*, 2011).

Aim of the work

(a) To study sexual behavior among substance users. (b) To find an association between substance use and risky sexual behavior. (c) To find an association between personality traits and risky sexual behavior among substance users.

Participants and methods

Our participants (100) were divided into two groups: group 1 included 50 individuals [diagnosed with substance abuse according to the DSM-VI criteria (American Psychiatric Association, 2000)] recruited from the Kasr El Aini psychiatric inpatient ward. Group 2 included 50 (selected on consultation with a statistical consultant) normal control individuals, matched for age, sex, and socioeconomic status. Individuals ranging in age between 18 and 40 years, men, with substance abuse during the last 6 months, those who could read and write, and those who provided informed consent were included in the study.

Exclusion criteria

Patients with a comorbid psychiatric condition on Axis I were excluded.

Methods

A cross-sectional study was carried out using the following tools: (a) a full psychiatric examination (semistructured interview): based on a Kasr Al Ainy psychiatric interview, with a special focus on substance use. (b) The risk assessment battery (RAB, Navaline *et al.*, 1994): the RAB is a self-administered questionnaire designed for use with substance-using populations. It was developed to provide a rapid (<15 min) and confidential, noninterview method of assessing both needle use practices and sexual activity associated with HIV transmission. There are two global sections in the RAB: (a) drug and alcohol use during the past 30 days and (b) needle use and sexual behavior during the past 6 months. Sexual risk behavior was assessed using the sex risk subscale of the RAB. This questionnaire was translated into Arabic and back translated by a staff member of the psychiatric department of Cairo University Faculty of Medicine. This questionnaire was administered to both the patient and the control group. (c) Eysenck's Personality Questionnaire (EPQ; Eysenck and Eysenck, 1975) was used to assess neuroticism, psychoticism, introversion/extroversion, criminality, and Lie scale.

The questionnaire has 90 questions to be answered by a yes or a no response. Each one of the five dimensions has certain questions and each question has a score; then, the total score for each dimension is calculated. For patients in group 1, (d) the Addiction Severity Index (ASI) was used (McLellan *et al.*, 1992). The ASI is a widely used structured clinical interview that assesses substance use/abuse and psychosocial functioning in a variety of domains including medical, employment, legal, family/social, and psychiatric. (e) Urine sampling was performed using drug screening strips. (f) A laboratory test was performed for HIV and hepatitis C virus (HCV) detection.

Ethical issues

Participation of the patients was voluntary. Patients received an explanation of the aim of the research as well as instructions for filling in the questionnaires. This research was funded by the researcher without any outside financial support.

Data management and analysis

All the questionnaires collected were checked for completeness and logical consistency. Precoded data were entered into a computer using a database developed for data entry on Microsoft Office Excel program for Windows, 2003. Data were then transferred to the statistical package of social science, version 16 (SPSS, IBM, Chicago, Illinois, USA), for data analysis.

Results

Both the groups showed nonsignificant differences in terms of age, education, employment, education, and social status. The most commonly used substance was tramadol (96%), followed by cannabis (72%), heroin (58%), benzodazepines (40%), and alcohol (16%). Among these substance abusers, 90% were using more than one substance, that is they were polysubstance dependent. In addition, 58% were substance drug injectors (SDI), injecting themselves with heroin. HCV infection was detected in 16%; none of the patients had HIV (AIDS) Table 1.

Table 2 shows that there were statistically significant differences in extroversion and neuroticism between the cases and the controls.

Table 3 shows that there was a significant difference between the cases and the controls on the sexual subscale of RAB.

Our patients had medical problems because of drug dependence ranging from mild (18%) to moderate (10%), to severe (20%), and 52% did not have any medical problems.

For the employment subscale, 4% did not have any problem, 14% had mild problems, 32% had moderate problems, and 50% had severe problems.

On the drug abuse scale, 34% had moderate problems and 66% had severe problems.

No abnormality was found on the legal problem scale (18%), followed by 24% with mild problems, 22% with moderate problems, and 36% with severe problems.

The family history scale was normal in 20% of the patients, followed by 36% with a mild degree, 14% with a moderate degree, and 30% with a severe degree of problems.

Table 4 shows a nonsignificant correlation between the RAB and the ASI.

Table 5 shows a significant correlation between psychoticism and criminality subscales in EPQ and the RAB in the case group.

Table 1 Demographic data of the cases and the controls

		N (%)		
	Factor	Cases (*N*=50)	Control (*N*=50)	*P* value
Age	Mean	25.88	27.64	0.158
	SD	5.68	6.09	
Education	Primary	8 (16)	4 (8)	0.367
	Preparatory	9 (18)	6 (12)	
	Secondary	6 (12)	12 (24)	
	Diploma	13 (16)	11 (22)	
	University	14 (28)	17 (34)	
Employment	Professional	12 (24)	15 (30)	0.582
	Skilled laborers	30 (60)	23 (46)	
	Nonskilled laborers	5 (10)	9 (18)	
	Not working	3 (6)	3 (6)	
Social status	Married	15 (30)	14 (28)	0.378
	Single	30 (64)	31 (62)	
	Divorced	3 (6)	5 (10)	
Substance abuse	Alcohol	8 (16)		
	Tramadol	48 (96)		
	Heroin	21 (58)		
	Cannabis	36 (72)		
	Benzodiazepines	20 (40)		
	>1 substance at a time	45 (90)		
	Injecting substance	21 (58)		
Laboratory investigation	HIV	0 (0)		
	HCV	8 (16)		

HCV, hepatitis C virus.

Table 6 shows a nonsignificant correlation between any subscale in EPQ and RAB in the controls.

Table 7 shows a significant correlation between psychoticism, family history, and social relation status. Also, there was a significant correlation between extroversion and legal state, criminality, and family history.

Discussion

In terms of the demographic data of the sample, there were no statistically significant differences between the case group and the control group including age, marital status, education, and occupation. This indicated that the samples were well matched and eligible for the study and comparison. The mean age of the patients was 25.88 years, whereas that of the controls was 27.64 years; although the mean age in the controls was slightly higher, there was no statistically significant difference between the two groups. This is in agreement with many researchers such as Hafeiz (1995), who found, in a study of 116 patients admitted to the Al-Amal Hospital in Dammam, that 83% of the patients ranged in age from 21 to 32 years, which also indicates that most substance users fall within this age range; this is also in agreement with another Egyptian research carried out on 52 psychoactive substance users by Mubasher *et al.* (2008) on disinhibited risky behaviours and plasma serotonin among drug addicts, where the mean age of the cases was 26.9 years. In terms of education, among the cases, 16% had completed primary education, 18% had completed preparatory education, 12% had completed secondary education, 26% had a diploma (technical education), and 28% had university education.

However, in the control group, 8% had completed primary education, 12% had completed preparatory education, 24% had completed secondary education, 22% had a diploma, and 34% had university education. This shows that controls had higher levels of education compared with cases, but there was no statistically significant difference between the two groups. This may reflect the adverse effects of substance abuse on education. In terms

Table 3 Sexual subscale of the risk assessment battery

	Minimum	Maximum	Mean	SD	*P* value
Cases	0	1	0.1822	0.387358	0.05
Control	00	0.050	0.001	0.007	

Table 2 Eysenck Personality Questionnaire in cases and controls

	Cases				Controls				
	Minimum	Maximum	Mean	SD	Minimum	Maximum	Mean	SD	*P* value
Psychoticism (p)	1	18	6.9	3.48	1	15	6.46	3.35	0.464
Extroversion (E)	3	18	11.96	3.09	9	18	13.48	2.41	0.023
Neuroticism (N)	3	23	15.04	4.69	5	22	13.14	4.00	0.032
Lie Scale (L)	3	19	10.04	3.83	2	19	9.48	3.39	0.441
Criminality (C)	5	27	15.66	4.90	4	23	14.44	4.41	0.194

Table 4 Correlation between the risk assessment battery and the Addiction Severity Index in the case group

	ASI social relation status category	ASI legal status category	ASI family history category	ASI drug and alcohol abuse status category	ASI occupation category	ASI medical status category
Sexual risk subscale of the risk assessment battery						
r factor	0.254	0.015	0.234	0.251	0.249	0.051
P value	0.075	0.920	0.102	0.079	0.081	0.724

ASI, Addiction Severity Index.

Table 5 Correlation between risk assessment battery and Eysenck Personality Questionnaire in the cases

RAB	Psychoticism	Neuroticism	Extroversion	Lie	Criminality
r factor	0.374*	0.264	0.218	−0.147	0.390*
P value	**0.007**	0.063	0.128	0.309	**0.005**

RAB, risk assessment battery.
*Highly significant correlation.

Table 6 Correlation between risk assessment battery versus Eysenck Personality Questionnaire in the controls

RAB	Psychoticism	Neuroticism	Extroversion	Lie	Criminality
r factor	0.154	0.099	−0.085	−0.105	0.139
P value	0.285	0.492	0.558	0.468	0.336

RAB, risk assessment battery.

of occupation, among the cases, 24% were professional workers, 60% were skilled workers, 10% were nonskilled workers, and 6% were not working and were unemployed.

This is in agreement with Kleyn and Lake (1990), who found that injection drug users who were working were significantly less willing to enter treatment because, among other difficulties, treatment is time consuming and can limit job-related travel. Also, there is a risk of employment termination if employers learn of treatment entry and, thereby, of drug use, although earlier studies have not only failed to find adverse effects, but often found positive impacts of illicit drug use on labor market success (Kaestner 1991, 1994; Andrew and Michaels, 1992; Charles and Williams, 1992). Thomas and Zuvekas (1998) suggest that these studies failed to adequately discriminate between moderate drug consumption and heavy drug consumption or abuse/addiction. When differentiating moderate drug users from more problematic users, expected negative labor market effects of drug problems were found, and more recent studies have found that chronic use or substance abuse substantially reduces the probability of employment (Pieere and French, 2004).

In our study, although only 6% were unemployed, the other patients had current employment problems, and this may be explained by the small sample of our study (i.e. 50 patients). In terms of marital status, the majority of the cases were single (64%), 30% were married, and 6% are divorced, in agreement with other results as in a Survey on Hard Drug Users in Nepal: Practice for Policy Analysis and Advocacy (2010), in which similar results were found, that is, 65.4% of patients were single, 29.7% were married, and 4.1% were divorced.

Also, Abdel Mohsen *et al.* (2009) found that 21.1% of the patients were married, 64.2% were single, and 14 (14.7%) were separated. This trend may be attributed to several social problems, including marital, associated with substance abuse and also the lack of responsibility among substance abusers. In terms of the type of substance used in our study, the most commonly used substance was tramadol (96%), followed by cannabis (72%), heroin (58%), benzodiazepines (40%), and then alcohol (16%); (90%) of the patients were using more than one substance, that is polysubstance dependent, also (58%) where SDI for heroin injection and that's why they have same percentage.

Our results are in agreement with the results of the study of Hatata (2004), who found that opiates were used by 61.9% of the patients, cannabis by 18.5%, followed by sedatives (15.8%) and alcohol (3.9%). Our results were not in agreement with those of Abdel-Wahhab *et al.* (2006), who carried out a study on a sample of Egyptian adolescents, and found that among 40 patients, the most common substance used was cannabis (70%), followed by alcohol (65%), bango (62.5%), sedative hypnotics (57.5%), heroin (25%), codeine (10%), and tramadol (2.5%). This inconsistency can be attributed to the nature of the sample used in both studies; in the former study, the patients were adolescents, and the use of cannabinioids at this age is experimental and believed to be a proof of maturity.

In the study by Fawzi (2011), of 640 patients, 67.9% were taking tramadol in prescribed or nonprescribed form. Tramadol is the most commonly used drug because of its wider availability and cheaper price compared with other types of drugs. The unplanned indirect media advertising for tramadol abuse movies and TV also played a remarkable role in promoting tramadol abuse. Out of 50 patients, 16% had HCV infection; none of the patients had HIV (AIDS). Although Egypt is one of the countries with a low prevalence of HIV and AIDS, evidence shows that unless concerted efforts are made, this might not remain true for long (NSP, 2007). Egypt has a low prevalence of HIV among the general population (below 0.1%). Until the end of 2009, 3919 HIV cases were detected in Egypt, of which 2920 were Egyptians. Among these, 1078 (27.5%) developed AIDS. However, Egyptians have the highest prevalence of HCV in the world. The recently released Egyptian Demographic Health Survey tested a representative sample of the entire country for the HCV antibody. The sample included both urban and rural populations and included all 27 governorates of Egypt. Over 11 000 individuals were tested. The

Table 7 Correlation of Eysenck Personality Questionnaire and Addiction Severity Index

	ASI social relation status category	ASI legal status category	ASI family history category	ASI drug and alcohol abuse status category	ASI occupation category	ASI medical status category	ASI psychoticism problem
EPQ psychoticism							
r factor	0.432**	0.237	0.320*	0.140	0.118	0.041	0.097
P value	0.002	0.097	0.023	0.332	0.414	0.778	0.504
EPQ neuroticism							
r factor	0.057	0.063	0.218	0.078	0.032	0.107	0.140
P value	0.696	0.666	0.128	0.591	0.827	0.460	0.333
EPQ extroversion							
r factor	0.141	0.287*	0.192	0.207	0.208	0.195	0.087
P value	0.329	0.043	0.181	0.150	0.147	0.176	0.548
EPQ lie							
r factor	−0.221	−0.137	−0.117	−0.260	−0.186	0.022	−0.138
P value	0.123	0.344	0.419	0.068	0.197	0.880	0.341
EPQ criminality							
r factor	0.220	0.194	0.303*	0.125	0.113	0.105	0.255
P value	0.125	0.177	0.033	0.388	0.433	0.466	0.074

ASI, Addiction Severity Index; EPQ, Eysenck Personality Questionnaire.
*Significant correlation.
**Highly significant correlation.

overall prevalence (percentage of people) positive for the antibody to HCV was 14.7% (Ungass Country Progress Report, 2009).

Our results were in agreement with a Chinese study carried out by Garten *et al*. (2005), which reported that HCV was present in 95.1% of HIV-positive heroin users. HCV is highly prevalent in SDI throughout southern China as a result of parenteral and sexual transmission. Our patients had medical problems because of drug dependence ranging from mild (18%), to moderate (10%), to severe (20%), and 52% did not have any medical problems; our results were in agreement with those of Mohsen *et al.* (2001), who found that 66% of patients did not have any medical problems, and 15% had mild, 6% had moderate, and 13% had severe medical problems.

In terms of the employment subscale, 4% did not have any problem, 14% had mild problems, 32% had moderate problems, and 50% had severe problems. This was in agreement with Mohsen *et al.* (2001), who found that 5% of his patients had mild, 18% had moderate, 28% had severe, and 48% had extreme problems, and this indicates the negative effects of substance abuse on work performance. In the drug abuse scale, 34% had moderate problems and 66% had severe problems. Our results were in agreement with those of Abdel-Wahhab *et al.* (2006), who found that 70% of the patients had severe problems, followed by 10% with moderate problems; this can be attributed to the nature of the sample. Both samples were selected from the Kasr Elini Hospital clinic. In the legal problem scale, ~18% of the patients showed no abnormality, followed by 24% with mild problems, and 22% with moderate problems, and 36% with severe problems. This could be explained by Easton *et al.* (2000) who found that crimes of violence and against property are associated with reduction of adherence to treatment and readiness to change substance use. The family history scale was normal in 20% of the patients, followed by 36% with mild problems, 14% with moderate problems, and 30% with severe problems. This is in agreement with Mohsen *et al.* (2001), who found that 1% of the patients had mild problems, 38% had moderate problems, 23% had severe problems, and 36% had very severe problems on the family history scale. Our study showed that there were statistically significant differences between the case group and the normal control group on the extraversion scale, with a mean of (11.96 ± 3.09) for the case group compared with (13.48 ± 2.41) for the control group, and this is not in agreement with other studies that have reported higher extraversion scores among substance users (Walton and Roberts, 2004). However, some researchers such as Rankin *et al.* (1982) observed low extraversion in heavy users and, similarly, in terms of the five-factor model of personality, individuals who use intoxicating substances have been characterized by low extraversion. Also, Homayouni (2011) found that addicted individuals scored higher on neuroticism, openness to experience, and external religious orientation, and lower on extroversion, agreeableness, and conscientiousness than normal individuals.

However, Fridberg *et al*. (2011) found the same extraversion among controls and cases; this study was carried out on 62 current cannabis users and 45 healthy drug-naïve controls. This may be attributed to the self-medication theory of addiction, as individuals with a high E-score are sociable and substance users may use substance intake as a kind of self-medication to help them overcome anxiety and to become more extroverted and interactive, enhance relaxation, relieve stress and anxiety, increase alertness, help them cope with daily life, aid mood alteration, seek pleasure, to improve performance, or enhance creativity, and also for social facilitation. Also, our study showed statistically significant differences between the case group and the normal group in terms of the neuroticism scale, with a mean of (15.04 ± 4.69) for the case group compared with (13.14 ± 4.00) for the control group, and this was in agreement with Sher *et al.* (2000), who reported that heavy users appear to score high on measures of neuroticism, and this may indicate the inner hidden anxiety associated with substance drug use. Our study showed that there were statistically significant

differences between the two groups in the sexual subscale RAB; the case group had a mean value of (0.1822 ± 0.387) and the controls had a mean value of (0.001 ± 0.007), with a P value of 0.05. This result was in agreement with the (alcohol/drug model); in this model, the definition was expanded to include individuals who used both alcohol and drugs. An individual under the influence of drugs may have casual sex with unknown partners and may not use a condom, and potentially engage in other risky sexual behaviors (Dew *et al.*, 2007; Marshall *et al.*, 2010). Schafer *et al.* (1994) hypothesized that those under the influence of a substance may have impaired judgment, lower inhibitions, and decreasing sensitivity toward pain during intercourse, which may lead to an infection and sexually transmitted diseases. Our study showed that there was a significant positive correlation between the sexual subscale of RAB and the criminality scale of EPQ, and this is in agreement with Margolis *et al.* (2006), who found that out of 550 participants, men aged 18–29 years, in state prisons in California, Mississippi, Rhode Island, and Wisconsin, 71% had multiple sex partners, 65.1% had sex with a partner they perceived as risky, and 45.3% had engaged in unprotected sex with multiple partners. Our study showed that there was a positive significant correlation between the legal status scale of ASI and the extraversion scale of EPQ, as extraverts are 'sensation seeking' as reported by Zuckerman (1979), who defined the sensation seeking personality trait as follows: 'the need for varied, novel, and complex sensations and experiences and the willingness to take physical and social risks for the sake of such experience'. This trait has been related to the proneness to high stimulating activities such as adventure sports, exotic meals, intake of drugs, sex, and illegal activities. There was a significant positive correlation between the severity of a family history of substance intake and the psychoticism scale of EPQ, as individuals who score a high score on psychoticism may be aggressive and antisocial.

This result was in agreement with a study that reported that patients with a family history of substance abuse showed higher antisocial behaviors (Giancola, 2003), and the children of parents with alcohol and other drug use disorders (i.e. high-risk children) have increased rates of antisocial behaviors. Also, drug addiction is strongly linked to a family history of drug abuse, and relatives of drug-dependent individuals have an eight-fold increased risk of developing substance abuse disorders compared with the general population (Merikangas *et al.*, 1998).

Limitations

The results of the present study should be interpreted in light of the following limitations:

First, our sample size was small.

Second, we restricted our sample to a hospital that serves patients belonging to a lower social class, which might not be representative of hospitals serving patients of higher social classes, who might have different profiles.

Third, female patients and those with a comorbid psychiatric diagnosis were not included, who might have a different profile of substance abuse and risky sexual behaviors.

Conclusion

Patients with substance abuse show more risky sexual behaviors than normal controls, which might be because of impaired judgment.

This high risk is not related to the severity of addiction, but to psychoticism and criminal behavior of personality.

Psychoticism and criminal behavior in our patients were related to a family history of substance abuse.

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Conflicts of interest

There are no conflicts of interest.

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Assessment of controlled substances, dependence on them, and their management by pharmacists

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Introduction
Substance abuse is more than just a health problem; it is a formidable moral, social, and economic challenge of pandemic proportions. Palestine is not an exception to this problem, and the trend of use is increasing. Healthcare providers, primary care physicians, pharmacists, patients themselves, and their families, can all play a role in identifying and preventing prescription drug abuse.

Methodology
The study population included 205 public pharmacies distributed across the Gaza Strip governorates. Data was collected by means of an interview questionnaire administered to pharmacists working in the pharmacies.

Study objectives
The aim of the study was to identify and verify several variables and attributes affecting drug abuse, including the knowledge, attitudes, and practices of pharmacists, and to study and analyze the drug abuse situation in the Gaza Strip.

Results
The majority of pharmacists (90.2%) acknowledged drug addiction as an existing phenomenon in the Gaza Strip society, and 32.2% of pharmacists believed that the physician, the pharmacist, and the inspection department all shared the responsibility for its existence. Most pharmacists believed that the increased anxiety and tension in the community was the most common reason for this increase in demand for drugs. Approximately 50.2% of pharmacists did not believe that their colleagues dispensed any of the controlled drugs without a doctor's prescription. Approximately 89.8% of pharmacists were convinced of the need for a medical prescription to dispense any of the drugs listed, and of these 89.8%, 84.8% did not dispense any of the controlled drugs to a person they suspected of being dependent on drugs, even if that person had a medical prescription. Hence, the study showed no significant relationship.

Conclusion
The study showed that drug abuse is an existing phenomenon in the Gaza Strip and there is a lack of attention to reduce its spread and impact on society. There are similarities between female and male pharmacists in the Gaza Strip with regard to knowledge about drug abuse; however, there are differences in practice and attitude among them.

Recommendation
Physicians, pharmacists, and the inspection department should assume their respective responsibilities toward prevention of drug abuse as a shared responsibility in order to ensure a safe future for the entire community.

Keywords:
addiction, controlled substance, pharmacist, tramadol

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Introduction

Substance abuse is more than just a health problem; it is a formidable moral, social, and economic challenge of pandemic proportions. Not a single country in the world can be called 'drug free'. The question we need to face and find an answer to is the following: Why, despite all efforts, do the issues related to substance abuse continue to increase in seriousness? (WHO report, 2004).

The risks for addiction to prescribed drugs increase when the drugs are used for reasons other than for those prescribed. Healthcare providers, primary care physicians, pharmacists, and patients themselves, can all play roles in the identification and prevention of prescription drug abuse. The pharmacist, physician, and patient each has a role in the drug abuse problem.

Preventing or stopping prescription drug abuse is an important part of patient care. However, healthcare

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providers should not avoid prescribing or administering stimulants, central nervous system depressants, or opioid pain relievers if needed.

Physicians should be aware of prescription drug abuse and the fact that the supply of these drugs comes initially from family and friends. Clinicians need skills to tailor addiction treatment according to the treatment group, including women, different sociocultural groups, age-specific groups, the medically ill, and people with legal problems. Addiction treatment, especially psychotherapy and psychopharmacology, is still an art (Tommasello, 2004).

The American Society of Health-System Pharmacists believes that pharmacists possess the unique knowledge, skills, and responsibilities required for assuming an important role in substance abuse prevention, education, and assistance. Pharmacists, similar to healthcare providers, should be actively involved in reducing the negative effects that substance abuse has on society, healthcare systems, and the profession of pharmacy (ASHP, 2003).

The role of a pharmacist in supervising and educating the public on prescription drug misuse has been steadily increasing over the past several decades. However, there continues to be confusion regarding the roles and responsibilities of pharmacists in recognizing prescription drug abuse and suitably intervening to prevent it (Cohen and McCormick, 2008).

Greater attention has been given to integrating treatment for co-occurring psychiatric disorders; medical conditions such as HIV/AIDS, hepatitis, and tuberculosis; and the psychosocial problems that complicate addictive illness.

According to the data from United Nations Office on Drugs and Crime, globally, there are an estimated 200 million people who make use of one or another type of illicit substance. The most common is cannabis, followed by amphetamines, cocaine, and opioids. Illicit substance use is more prevalent in the male population compared with the female population, much more so than cigarette smoking and alcohol consumption. Substance use is also more prevalent among young people than among those belonging to an older age group. An estimated 205 million people around the world use illicit drugs, including 25 million who suffer from illicit drug dependence. This constitutes a public health, socioeconomic, developmental, and security problem for both industrialized and developing countries alike (UNODC and WHO, 2008).

Drug use in Egypt remains a problem. The number of drug users in Egypt ranges from 1 million to 6 million, with most drug users being in the 15–25 years age group. Accurate statistics are difficult to obtain, given the taboo nature of drug abuse and the stigma associated with being an addict (WHO, 2010).

Treatment facilities are not evenly distributed throughout Egypt, and the most widespread drug used at present is 'Bango' (cannabis derivative) (Abdel-Gawad, 2002).

Thousands of young men in Gaza are becoming addicted to a prescription painkiller used to alleviate the stress of living in the besieged Palestinian territory. Students, laborers, and even professionals are buying large quantities of tramadol, a synthetic opioid painkiller similar to morphine, although milder, on the black market. It is estimated that the number of drug abusers in the Gaza Strip and the West Bank and East Jerusalem is 32 000–45 000, of whom 20% are addicts. It is estimated that up to 30% of men in Gaza between the ages of 14 and 30 years take tramadol regularly, with around 15 000 showing signs of addiction (ANGA, 2005).

Subjects and methods

A cross-sectional study was conducted on the pharmacies in the Gaza Strip governorates.

They were selected by means of a stratified random sampling method. The study was conducted from April to July 2009 in five governorates in the Gaza Strip. The number of pharmacies in the Gaza strip is 411, distributed in each governorate as follows: (Palestinian Enterprise Development PED project, medicine consumption and supply study November 2007).

The sample of 205 pharmacies in the present study represented 49.87% of all pharmacies distributed across all regions of the Gaza Strip based on the proportion of pharmacies in each region [North Gaza (37), Gaza city (90), Middle governorate (26), Khanyounis (36), and Rafah (16)]. Data were collected by means of an interview questionnaire administered to the pharmacists working in the pharmacies. Interviews were conducted using the questionnaire and information pertaining to the pharmacist with regard to knowledge, attitudes, practices, sociodemographic factors, sex, age, number of years of experience, year of graduation, the University and state from which he/she graduated, and the way he/she dealt with narcotic drugs and hazardous materials was collected in the following manner: 12 medicines were selected and questions were asked on whether these drugs were available without prescription, whether the holder of this prescription was an addict, and whether the pharmacists were convinced of the need for a prescription for dispensing these drugs in all cases, and, if not, the reasons for nonpersuasion. The questionnaire inquired about concern for the phenomenon of addiction to narcotic drugs and hazardous materials in terms of the following: the belief that the phenomenon of addiction exists, who bears responsibility and knowledge of pharmacopoeia and of legislation relating to medicines, awareness of knowledge centers caring for addicts, whether there was an increase in the demand for these drugs and, if so, the reasons for such an increase. Finally, comments or suggestions from the pharmacist were also taken.

Statistical analyses were performed with SPSS for windows (version 18; SPSS Inc., Chicago, Illinois, USA). It included frequency distributions of the events of interest. Pearson's χ^2-test was used for comparing categorized variables, and P-value less than 0.05 was considered statistically significant.

Results

This study included 205 pharmacies distributed across the Gaza Strip governorates, which were selected randomly according to a stratified sampling procedure. The age range of the pharmacists was 25–30 years (44.9%), and most of them were men (59.5%) with 1–3 years of experience (35.6%). The sociodemographic characteristics of the pharmacists are presented in Table 1.

About 86.8% of pharmacies relied on books and journals as sources of information, whereas 17.6% relied on websites (Table 2).

The majority of drug users were over the age of 24 years (74.1%), and most of them were employed (Table 3).

The study showed that the demand for drugs was mostly in the evening and night (39.02%; Table 4).

The number of inspections carried out by the Department of Drug Control in terms of the number of visits made to pharmacies in the Gaza Strip according to the pharmacists is shown in Table 5.

The study demonstrates the fallbacks of the system involved in the inspection and control of the illegal dispensing and use of these controlled drugs (Table 6).

Table 7 shows that about 50.2% of pharmacists do not believe that their colleagues dispense the items listed without a doctor's prescription, although 45.4% believe they do.

When asked whether the pharmacist dispensed medication to a person suspected of being an addict although he or she possessed a doctor's prescription, only 14.1% of the pharmacists admitted to doing so (Table 8).

This study shows that the three most commonly demanded drugs in the pharmacy were Tramal (Germany), pulmadrin compound, and xanagis (Table 9).

More than 90% agreed that there existed a phenomenon of addiction to narcotic drugs and that more than one person or institution is responsible for it (Table 10).

Most pharmacists (66.3%) did not attend any courses or seminars on drug addiction, and 89.3% of the pharmacists felt the need for such courses and seminars. Despite a lack of these courses, the study shows that 51.7% of pharmacists contributed to or tried to find a solution to this phenomenon of addiction.

With regard to the knowledge on the existence of centers providing medical care to addicts, the study showed that 30.2% were aware of the existence of such centers, whereas 69.8% were not. The study also showed a strong lack of knowledge on the existence of centers providing education to addicts (92.2%).

More than 70% (70.7%) of pharmacists noted an increase in the demand for narcotic drugs in their pharmacies (Table 11).

With regard to the causes of drug addiction, pharmacists believed that increased anxiety and tension in the com-

Table 1 Distribution of pharmacists by socio-demographic factors

Characteristics	*N* (%)
Sex	
Male	122 (59.5%)
Female	83 (40.5%)
Age	
Less than 25	52 (25.4%)
25–30	92 (44.9%)
More than 30	61 (29.7%)
Years of experience	
1–3	73 (35.6%)
4–6	55 (26.8%)
7–10	36 (17.6%)
11 or more	41 (20.0%)
The country of graduation	
Palestine	160 (78.0%)
Arabic countries	21 (10.2%)
Others	24 (11.8%)

Table 2 The availability of information resources in Gaza strip pharmacies included in the study

Availability of information resources	
Availability of books, journals	178 (86.8%)
Availability of computer	69 (33.7%)
Availability of websites	36 (17.6%)

Table 3 The classes of majority of whom demand these drugs according to the outer appearance of them

Characteristics	*N* (%)
Rich and affluent people	8 (3.9%)
Staff and middle-class income	36 (17.56%)
Workers and artisans class	108 (52.68%)
The poor class	19 (9.27%)
Nonspecified	34 (16.59%)

Table 4 The most times of demand of these drugs

Characteristics	*N* (%)
Morning	6 (2.93%)
Afternoon until evening	24 (11.71%)
Evening and night	80 (39.02%)
Unspecified	95 (46.34%)

Table 5 The number of inspection department (department of drug control) visits to the pharmacy each year

Characteristics (number of visit)	*N* (%)
None	40 (19.5%)
Once a year	53 (25.9%)
Twice a year	62 (30.2%)
More than twice a year	50 (24.4%)

Table 6 The effectiveness of the system used in the inspection and control

Characteristics (effectiveness)	*N* (%)
Effective	43 (20.98%)
Not effective	140 (68.29%)
Do not know	22 (10.73%)
Total	205 (100%)

Table 7 The dealing with narcotic drugs and hazardous materials from pharmacist point of view

General trend	Repetition (%)
No	103 (50.2%)
Yes	93 (45.4%)
Neutral	9 (4.4%)
Total	205 (100%)

Table 8 The pharmacists dispense the medication to a person whom they doubt even though he had a doctor's prescription

General trend	Repetition (%)
No	158 (77.1%)
Yes	29 (14.1%)
Neutral	18 (8.8%)
Total	205 (100%)

Table 9 The most three types of medicines in demand in your pharmacy

Drug	Order	*N* (%)
Tramal	1	201 (32.8%)
Pulmadrin compound	2	116 (18.9)
Xanagis	3	69 (11.3)

Table 10 Who bears the responsibility of this phenomenon

Who bears the responsibility for this phenomenon?	
Physician	3 (1.5%)
Pharmacist	34 (16.6%)
Inspection Service and the General administration of Pharmacy	46 (22.4%)
Physician and pharmacist	56 (27.3%)
Others: more than one	66 (32.2%)

Table 11 The demand for narcotic drugs in their pharmacies

Is there a marked increase in the demand for narcotic drugs in your pharmacy	
Yes	145 (70.7%)
No	48 (23.4%)
Do not know	12 (5.9%)
Total	205 (100%)

Table 12 Causes of drug addiction phenomena

Decline in the prices of these drugs	11 (7.6%)
Increased anxiety and tension in the community	98 (67.6%)
Both reasons	25 (17.2%)
Other reasons	11 (7.6%)

munity was the most common reason (67.6%) for the increase in demand for narcotic drugs in the Gaza Strip pharmacies (Table 12).

Inferential analysis

The relationship between the dispensing any of these controlled drugs by a pharmacist only on submission of a prescription in all cases and the possibility of dispensing one of these drugs to a person suspected of being addicted to drugs but who has a prescription is presented in Table 13.

Data in Table 13 show that 89.8% of pharmacists are convinced of the need for a medical prescription to dispense any of the drugs listed in all cases and that, of these 89.8%, 84.8% do not dispense any of these drugs to a person they suspect of being an addict even if that person has a medical prescription.

With regard to the relationship between the inspection system and pharmacies in terms of the number of annual visits made to the pharmacies by the Department of Inspection, data showed that 18.7% of the pharmacies had not been subjected to any inspection during the year; 26.1% of the pharmacies covered by the study had been inspected only once; and 24.6% of the pharmacies had been inspected more than twice. With respect to differences between governorates in terms of the number of annual inspections, the test statistics revealed that differences between governorates were real (moral) and that Rafah was the governorate that received the most number of inspection visits, twice annually (75%) (Table 14).

With regard to the relationship between the increase in demand for narcotic drugs and years of experience of pharmacists, Table 15 shows that 81.4% of pharmacists who noted a marked increase in the demand for narcotic drugs had experience of 3 years or less, whereas 83.0% had 4–6 years of experience.

Discussion

The present study was conducted to investigate the sociodemographic characteristics, knowledge, attitude, and practices of pharmacists. In addition, the sociodemographic characteristics of drug abusers from the pharmacists' point of view in the Gaza Strip were studied as being important indicators for the pharmacists' practice.

Distribution of pharmacists according to sex and age group showed a male predominance of 59.5%, as against 40.5% of women. It is known that after marriage women do not agree to work in pharmacies because of the long hours of work, which does not fit in with their married life, and because of the low salary paid for this work; hence, they prefer staying at home, unlike men, who have no choice but to work because of the responsibility of providing for their family.

The study showed that the majority of pharmacists (44.4%) were of an average age of 25–30 years and 24.9% were of an average age of less than 25 years. This is logical because a pharmacist graduates at an average age of 23–25 years and those who are unable to work immediately after graduation need further training to obtain work. Pharmacists aged more than 30 years are those who would have obtained jobs other than in public pharmacies. Hence, most pharmacists are of an average age of 25–30 years.

The major sources of scientific information available to pharmacies were books and journals. However, the researchers noticed that the pharmacists considered the medic book as an information resource, although the medic is, in fact, an alphabetical and pharmacological index and not a source of scientific information.

Table 13 The relationship between the conviction of pharmacists about dispensing

	Conviction of the need to dispense any of the medications listed under a medical prescription in all cases		
	No	Yes	Total
Dispensing medication to a person requesting one of these drugs but you suspect that he is an addict and is in possession of a doctor's prescription			
No	88.9%	84.8%	85.2%
Yes	11.1%	15.2%	14.8%
Total	10.2%	89.8%	100.0%

χ^2-square value=0.214; n=176; P=0.264, not significant.

Table 14 The relationship between the inspection system to pharmacies and the governorates

	Number of annual inspection visits (%)				
Governorate	None	Once	Twice	More than twice	Total
Gaza	31.0	26.4	25.3	17.2	100.0%
North	17.9	28.2	30.8	23.1	100.0%
Middle	0	19.2	42.3	38.5	100.0%
Khan yunis	8.6	34.3	45.7	11.4	100.0%
Rafah	6.3	12.5	6.3	75.0	100.0%
Total	18.7	26.1	30.5	24.6	100.0%

Cramer's value=0.282; n=203; P=0.0001, significant.

The study showed that most drug abusers were of an average age of 24 years or more. However, the pharmacist noted an increase in the number of drug users who were of an average age of less than 24 years, which is indicative of a dangerous situation in Gaza schools and universities. It is known from many published studies that most drug users are of this average age (Yusef, 2010).

The majority of drug abusers were workers and artisans (52.7%), which could be because of two main reasons:

(1) The years spent working and living in Israel among Israeli people, leading to adoption of a particular lifestyle;
(2) The difficult economic conditions and unemployment that these people suffer from following the closure of the borders, making life difficult and leading to a state of despair and frustration.

Political, economic, and social conditions have changed in recent years. Rapid changes have adversely affected the country's stability, and citizens face a lot of problems in adapting to the changes. Adaptation problems lead to others, which affect the members belonging to the weakest section of society. Such unstable conditions are conducive to the spread of drugs in society (Stonkutė and Magnus, 2000). However, an increasing number of pharmacists (16.6%) believe that drug users belong to all strata of the society (Research and Social Survey Unit of Democracy Watch, 2001). Socioeconomic factors related to drug use include low educational levels and dropping out of school at an early age; unemployment, low salaries, and difficult jobs; low income and debt; insecurity of accommodation and homelessness; mortality and drug-related diseases; poor access to care; and social stigma (European monitoring center for drugs and drug addiction, 2003).

Demand for drugs is more frequent during the evening and night because of three main reasons:

(1) The pharmacist knows that inspection mainly takes place in the morning and afternoon; hence, he will be more flexible in dispensing these controlled drugs without a prescription in the evening and at night, reflecting a trend created by the pharmacist himself.
(2) Drug users may note that the pharmacist is more flexible in dispensing drugs at this time; further, the pharmacist himself may inform drug users about the time of inspection, as a result of which drug addicts avoid these times for demanding drugs.
(3) In Gaza, pharmacists working in the morning and afternoon are usually women, who usually do not agree to dispense these drugs without a prescription. The drug users can note this easily.

Most pharmacists (30.2%) reported that the inspection department visited the pharmacies twice a year; however, 68.3% of pharmacists believed that the inspection was not effective. From the pharmacists' point of view, inspection was routine, nonserious, and usually on non-registered Egyptian medications and tramadol. They also recommended that inspection be carried out on stores and pharmaceutical companies and at doctor's clinics by reviewing prescriptions. The researcher noticed an increase in drug abuse, indicating that the inspection was not effective.

The study showed that most pharmacists (83.9%) were convinced that dispensing any medication in the list needed a medical prescription, and 77.1% of the pharmacists did not dispense medication to a person whom they suspected of being an addict even though he/she had a doctor's prescription. In practice, this implied that there was a gap between pharmacists and doctors in terms of confidence and collaboration because of the absence of regulation in prescription, which makes it easy to obtain one.

Pharmacists noticed that tramadol tablets or capsules were the most commonly demanded drugs, followed by pulmadrin compound syrup and xanagis tablets. Gazans cannot travel outside the Strip; they have very few places to go to for fun and are faced with a failing economy. These factors could be the reason for the boom in the popularity of tramadol, a painkiller known here by the common brand name 'Tramal'. The drug's popularity has been propelled by its availability, as large quantities have been smuggled through tunnels under the Gaza–Egypt

Table 15 The relationship between the increase in the demand for narcotic drugs and the years of experience

	There is a marked increase in the demand for narcotic drugs in your pharmacy		
Years of experience	Yes	No	Total
3 years or less	57 (81.4%)	13 (18.6%)	73 (100.0%)
4–6 years	44 (83.0%)	9 (17.0%)	53 (100.0%)
7–10 years	24 (70.6%)	10 (29.4%)	34 (100.0%)
11 or more	20 (55.6%)	16 (44.4%)	36 (100.0%)
Total	145 (75.1%)	48 (24.9%)	193 (100.0%)

Cramer's value = 0.239; $n = 193$; $P = 0.012$, significant.

border. Tramadol has spread widely and very fast because, until 2009, it was available over the counter in pharmacies and is now available in the illegal market.

The majority of drug users are between 24 and 34 years of age. There are 8000 cases of drug use in courts and 3000 cases of trafficking and distribution. Most drug crimes are committed by men. There are about 40 000 drug users in Gaza. There are usually more drug users in places where there is an absence of police force (UNODC, 2008).

Most pharmacists believed that more than one person or institution is responsible for this phenomenon (32.2%). This means that physicians, pharmacists, and the inspection department all share the burden of this responsibility, which is very logical because all of them have an active role in spreading this phenomenon and we cannot exclude any of them.

Pharmacists and physicians need more efficient methods to communicate with each other so as to more effectively share information about specific clients/patients and to access more general community-wide and province-wide trends in fraudulent prescriptions and prescription drug abuse and misuse.

Furthermore, although some health professionals may contribute to the misuse and abuse of prescription drugs because of inappropriate prescribing behavior, others may provide inadequate pharmacotherapy for pain and other conditions because of the fear that their patients will become addicted or that they will incur regulatory scrutiny (NIDA, 2008).

The study showed that 51.7% of pharmacists contributed to or tried to find a solution to this problem; however, the researcher noticed that the solution used was mostly refusal to dispense the drugs and nothing else.

Inferential analysis

Data showed that 85% of pharmacists said that they were convinced of the need for a medical prescription in all cases. They claimed that they did not dispense medication to a person they suspected was an addict. Hence, apart from a medical prescription, pharmacists also considered the external appearance of the patient before dispensing drugs.

Several studies have associated quality of dispensing with factors such as pharmacist's age, educational background, and social and demographic factors. The pharmacists' opinions about their practice have been proposed as potential determinants of the quality of dispensing. However, these factors have been analyzed individually, and so far no comprehensive theoretical model has been proposed to explain their effect (Field, 2008).

The study showed that the pharmacists who have fewer years of experience (3 years or less) are those who notice an increase in the demand for narcotic drugs in their pharmacies (81.4%). This is because the pharmacist with more number of years of experience would be familiar with the identity of the drug user and will refuse his or her request. At the same time, the drug user, realizing this fact, would avoid going to that particular pharmacist and try to find a newly graduated pharmacist, exploiting the new pharmacist's lack of experience in this field, to ask for one of these drugs.

The study showed that Rafah is the governorate that was subjected to the most number of inspections (75% twice annually). Because of its proximity to the border with Egypt, and therefore being considered a center for smuggling of narcotic drugs through the tunnels, inspectors are keen to search Rafah pharmacies more than they are others.

The tunnels have been used to smuggle foreign currency, weapons, cigarettes, narcotics, alcohol, electronic items, and prostitutes from Egyptian Rafah to the Palestinian areas of the Gaza Strip. At the same time it is noticeable that weapon smuggling is more concerning from the perspective of world governments in comparison with smuggling of narcotics because of the relation of weapon smuggling with Israeli security (Sharp, 2008).

Conclusion

This cross-sectional analytic study was conducted in Gaza Strip pharmacies from April 2009 to July 2009. An overall conclusion can be summarized as follows:

(1) Drug abuse is an existing phenomenon in the Gaza Strip but sufficient attention has not been paid to curb its spread and reduce its impact on society, particularly among young people. It is considered a public health issue in the region, but it is not declared as such by the government.
(2) Drug abuse is predominant among men of an average age of 24 years or more, although there is a growing increase in the number of drug users among school and university students.

(3) Tramadol is the most commonly demanded drug in the Gaza Strip pharmacies and is the most important medication in terms of being subjected to strict inspection and control measures compared with other drugs, which do not receive the same attention.
(4) Most pharmacists lack knowledge about recent regulations and rules.
(5) The majority of pharmacists have never attended lectures or seminars on drug abuse even though they are convinced about the importance of such lectures or seminars.
(6) No adequate treatment for drug abusers exists in the Gaza Strip.
(7) Socioeconomic factors related to drug use include low educational levels, early school leaving; unemployment, low salaries, and difficult jobs; low income and debt; insecurity of accommodation and homelessness; and bad political situation, all of which contribute to the increase in drug abuse in the Gaza society.
(8) Although the inspection visits to pharmacies are conducted mostly twice a year, the inspection is still ineffective against drug abuse increase from the pharmacist's point of view.
(9) More than one person or institution should bear the responsibility of the phenomenon of drug abuse. Hence, physicians, pharmacists, and the inspection department all of them share the burden of this responsibility; no one is excluded.
(10) The majority of pharmacists do not advise all individuals who request these controlled substances all the time; they advice individuals based on the extent of their belief in a patient's response to their advice about the danger of addiction.

Recommendations

(1) More attention should be focused on the increase in the number of drug abusers among school and university students and among workers in order to find a logical and practical solution to reduce them.
(2) More workshops, courses, and specialized seminars should be held for pharmacists to provide adequate information regarding this subject in terms of laws of exchange and the classification schedules.
(3) Pharmacy colleges must have resources to prepare students to care for addicts. In addition to strengthening the undergraduate experience, pharmacy colleges must develop residency programs that produce experts in the field.
(4) Conducting sessions to educate new graduates and students of the Faculty of Pharmacy and Medicine to sensitize them to the dangers of this phenomenon and inform them about what they could be subjected to by means of practical training in pharmacies and clinics.
(5) Full awareness programs should be held by syndicates and universities to sensitize various sections of society toward addiction risks and symptoms and ways to overcome them.
(6) All parties, such as physicians, pharmacists, and the inspection department, should assume responsibility for this phenomenon and not burden the other parties because ensuring a safe future for the entire community should be a shared responsibility.
(7) There must be restriction on who can write the prescription containing any of these controlled substances through Ministry of Health new laws.

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Conflicts of interest

There are no conflicts of interest.

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Emotional involvement and burden in caregivers of patients with Alzheimer's disease

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Background
There has been relatively little research on caregivers of patients with Alzheimer's disease and those with cognitive disorders for long durations.
Aim
To examine the psychological dimensions, defensive styles strategies, and distress in caregivers of Alzheimer's patients.
Methods
Caregivers of 40 patients with Alzheimer's disease were interviewed and compared with a group of caregivers of diabetic patients on the experience of caregiving, emotional stress, and burden. Caregivers of patients with Alzheimer's disease were assessed using the Defense-Style Questionnaire and the Involvement Evaluation Questionnaire.
Results
Caregivers of patients with Alzheimer's disease used mature, neurotic, and immature defensive strategies to cope with the patient's symptoms and difficult behavior, and experienced more worry about these problems and led to increased supervision. There were sex differences among caregivers; female caregivers were more prone to worry and overinvolvement than male caregivers.
Conclusion
Caregivers of patients with Alzheimer's disease have to cope with a wide range of problems and develop coping defensive strategies. Caregivers worried most about the difficult behavior and symptoms of patients with Alzheimer's disease. The increased levels of worry, tension, negative feelings, and overuse of mature defenses in caregivers are associated with personal and sociodemographic variables, rather than variables related to the illness itself.

Keywords:
Alzheimer's disease, behavioral and psychological symptoms, caregivers, psychological burden

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Introduction

It has been found that a patient's illness may have an impact on several aspects of family life (Georges *et al.*, 2008), but it is unclear why some family members are more adversely affected than others. Caring for a family member with Alzheimer's disease is extremely stressful and contributes toward the development of psychiatric and physical illnesses among caregivers (Belle *et al.*, 2006). Numerous potential factors have been examined, including sociodemographic characteristics of the patients and the caregivers, patients' clinical characteristics, and family setting and members. However, generally, the findings have been inconsistent, possibly reflecting differences in the conceptualization and measurement of caregivers' experiences (Thompson and Spilsbury, 2007). Provision of better ways to support family caregivers is a major public and psychiatric health challenge.

Most studies have found that the severity of symptoms of patients with Alzheimer's disease is strongly related to their caregivers' burden (Conde-Sala *et al.*, 2009), although a few have found no association; for example, Wilson *et al.* (2007).

Coresident caregivers, especially spouses, are of primary importance in situations in which patients with Alzheimer's disease are cared for in their own homes in their community rather than in institutional settings, which may be costly and may result in social stigma (Schneider *et al.*, 1999).

Negative attitudes are prevalent in the society toward individuals with any mental illness. Discrimination occurs across every aspect of social and economic existence. Research has documented stigma, with its negative impacts on individuals with mental, cognitive, or psychiatric illness (Boucharlat *et al.*, 2006).

Stigma not only affects individuals with psychiatric illness but also their families, a process by which an individual is stigmatized by virtue of association with another

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stigmatized individual (Gormley, 2000), that is, 'associative stigma'.

Families are more actively involved in the long-term care of their relatives who have severe cognitive and behavioral impairments. Caregivers' experiences encompass distress, stigma, worry, shame, and guilt, and positive emotions such as Care giver satisfaction to that effort (Huang *et al.*, 2009). Studies have consistently shown that approximately one-third of caring relatives have elevated levels of anxiety or depression linked to their role as caregivers (Yeung *et al.*, 2007), especially caregivers of patients with Alzheimer's disease, who are mainly elderly spouses (Aguglia *et al.*, 2004).

Methods

A consecutive sample of forty previously diagnosed patients with Alzheimer's disease and their caregivers attending Kasr El-Aini psychiatric outpatient clinics were included in the study. A group of 40 caregivers of diabetic patients were used as controls. Patients were recruited over a period of 6 months (September 2010–March 2011). Caregivers younger than 21 years of were excluded.

A psychiatrist assessed the patients using a semistructured interview and confirmed a previously assigned diagnosis according to the (DSM IV) criterion for Alzheimer's disease of a history of at least 2 years of illness. The psychiatrist interviewed the patient and sought consent to interview the caregiver. This study was designed as an outpatient cross-sectional study after receiving the approval of the ethical research committee, and conformed to the provisions of the World Medical Association's Declaration of Helsinki.

Caregivers were sons, spouses, siblings, and others (distant relatives). For each participant recruited in the study, a main caregiver was identified as the individual who was most available (contact) and most supportive either emotionally or financially. To be eligible, caregivers were required to be 'responsible'; that is, older than 21 years of age and with reasonable contact with the patient face to face at least twice weekly. An informed consent was obtained for participation in the study.

Psychological and psychiatric assessment of the caregivers was performed and the following tools were used:

(1) Psychiatric sheet for the caregiver.
(2) Involvement Evaluation Questionnaire (IEQ) (Schene and Wijngaatchen, 1992): This questionnaire assesses the main aspects of burden such as worry, tension, and supervision, and assesses the negative and positive emotions associated with caregiving. The IEQ is one of the most valid and simple instruments used for the evaluation of caregivers (Reine *et al.*, 2003). The worrying part covers the painful interpersonal factors as concern about the patient safety, general health, and the help they receive. Tension involves a strained interpersonal atmosphere between the caregivers and the patient: quarrels, annoyance, and occasional threats. Supervision involves caring about the medications, sleep, and dangerous behavior. The questionnaire also measures the negative and positive aspects of caregiving. Negative aspects (caregiver distress) include negative symptoms, stigma, effect on the family, and the need to provide backup and dependency.
(3) Defensive Style Questionnaire (DSQ40) (Soliman, 1996, 1997): The Arabic version of the DSQ40 was applied for an assessment of ego defenses of the caregivers. Defenses include anticipation, suppression, humor, sublimation, pseudoaltruism, idealization, reaction formation, undoing, acting out, denial, devaluation, displacement, dissociation, autistic fantasy, isolation, passive aggression, projection, rationalization, somatization, and splitting. The DSQ40 can yield 20 individual scores and three higher order factor scores, namely, mature, immature, and neurotic.
(4) Clinical dementia rating scale (CDR) (Washington University, 1998): The CDR is a five-point scale used to characterize six domains of cognitive and functional performance applicable to Alzheimer's disease and related dementias. It assesses memory, orientation, judgment, problem solving, home and hobbies, and personal care, with scores of 0 = normal, 0.5 = very mild, 1 = mild, 2 = moderate, and 3 = severe. The research methodology was approved by the ethical committee of the psychiatric department of Cairo University (Kasr El-Aini).

Statistical analysis

Descriptive statistics were presented including frequency tables, means, SD, and range whenever appropriate.

The analytic tests used included an unpaired Student's *t*-test for comparing the means of the two groups, a paired *t*-test for comparing the values before and after analysis of variance (i.e. *t*-test) for comparison of the means of more than one group.

The χ^2-test was used for contingency table analysis correlation, and regression analysis was also carried out.

The threshold of significance was fixed at a 5% level (*P* value). A *P* value more than 0.05 was considered not significant. A *P* value less than 0.05 was considered significant.

Results

No statistically significant difference was found in terms of the sex of the caregivers of patients with Alzheimer's disease and diabetes. The relationship of the caregivers with the patients showed a statistically significant difference (spouses were the caregivers for 40% of the patients with Alzheimer's disease) (sons were the caregivers in 45% of the control group) ($P = 0.019$). Marital status of the caregivers showed a statistically

Table 1 Comparative data of caregivers of patients with Alzheimer's disease and control caregivers

	N (%)		
	Case	Control	*P*
Caregiver sex			0.6
Male	12 (30%)	15 (37.5%)	
Female	28 (70%)	25 (62.5%)	
	40 (100%)	40 (100%)	
Caregiver relation			0.019
Spouse	16 (40%)	4 (10%)	
Sibling	10 (25%)	13 (32.5%)	
Son	10 (25%)	18 (45%)	
Distant relative	4 (10%)	5 (12.5%)	
	40 (100%)	40 (100%)	
Marital status			0.000
Married	28 (70%)	14 (35%)	
Single	5 (12.5%)	18 (45%)	
Widow	3 (7.5%)	8 (20%)	
Divorced	4 (10%)	0 (0%)	
	40 (100%)	40 (100%)	

significant difference between the two groups (70% of the caregivers in the Alzheimer group were married and 35% of the controls were married) ($P = 0.000$) (Table 1).

Alzheimer caregivers' perceived stigma to the illness was statistically significant than the diabetic caregivers (52.5% while it was only 5% in the diabetic caregivers; $P = 0.000$). Caregivers of patients with Alzheimer's disease expressed significantly more worry than diabetic caregivers (77.5 vs. 45%; $P = 0.005$). Fears were expressed significantly more by the caregivers of patients with Alzheimer's disease than diabetic caregivers (67.5 vs. 12.5%; $P = 0.000$). Loss and grief were expressed significantly more by the caregivers of patients with Alzheimer's disease than diabetic caregivers (82.5 vs. 0%; $P = 0.000$). Negative feelings were expressed significantly more by the caregivers of patients with Alzheimer's disease than diabetic caregivers (55 vs. 20%; $P = 0.002$) (Table 2).

Baseline data showed that patients with Alzheimer's disease were predominantly men (62.5%); only 52.5% were married. In terms of area of residence, 60% mainly lived in urban areas and 40% lived in rural areas. For most patients, the duration of illness was long. The mean duration of illness was 3 years (Table 3).

A total of 70% of the caregivers were women and 30% were men. The mean age of the caregivers was 49 years. A total of 40% were partners (spouse), 25% were sons, 25% were siblings, and 10% had another relationship (relative, neighbor) with the patient. Of the caregivers 37.5% were working, of whom 20% were skilled manual workers, 12% were semiskilled manual workers, and 38% were unskilled manual workers. 62.5% were not working. 70% of the caregivers were living with the patient in the same household. Of the caregivers of patients with Alzheimer's disease, 70% were married, 12.5% were single, 10% were divorced, and 7.5% were widowed (Table 4).

There was no statistically significant difference ($P = 0.1$) in terms of sex in the types of defenses used by caregivers. Psychological defenses for coping used by the caregivers were mainly mature (67.5%), neurotic (17.5%), and immature (15%). Female caregivers showed defenses that were mature (45%), neurotic (15%), and immature (10%), with no significant difference compared with male caregivers ($P = 0.1$) (Table 5).

Table 2 Involvement Evaluation Questionnaire for the case and the control group

	N (%)		
Involvement Evaluation Questionnaire	Case	Control	*P*
Perceived stigma			0.000
Absent	19 (47.5%)	38 (95%)	
Present	21 (52.5%)	2 (5%)	
	40 (100%)	40 (100%)	
Worries			0.005
Absent	9 (22.5%)	22 (55%)	
Present	31 (77.5%)	18 (45%)	
	40 (100%)	40 (100%)	
Fears			0.000
Absent	13 (32.5%)	35 (87.5%)	
Present	27 (67.5%)	5 (12.5%)	
	40 (100%)	40 (100%)	
Loss and grief			0.000
Absent	7 (17.5%)	40 (100%)	
Present	33 (82.5%)	0 (0%)	
	40 (100%)	40 (100%)	
Negative feelings			0.002
Absent	18 (45%)	32 (80%)	
Present	22 (55%)	8 (20%)	
	40 (100%)	40 (100%)	

Table 3 Characteristics of the patients with Alzheimer's disease

Patients' characteristics	*N* (%)
Sex	
Male	25 (62.5%)
Female	15 (37.5%)
Marital status	
Married	21 (52.5%)
Unmarried	19 (47.5%)
Residence	
Urban	24 (60%)
Rural	16 (40%)

Table 4 Characteristics of caregivers of patients with Alzheimer's disease

Caregivers' data	*N* (%)
Sex	
Males	12 (30%)
Females	28 (70%)
Relation to the patient	
Son	10 (25%)
Spouse	16 (40%)
Sibling	10 (25%)
Others	4 (10%)
Marital status	
Single	5 (12.5%)
Married	28 (70%)
Divorced	4 (10%)
Widowed	3 (7.5%)
Employment	
Working	15 (37.5%)
Unemployed	25 (62.5%)
Residence with patient	
Living with patient	28 (70%)
Not living with patient	12 (30%)

Statistically significant differences were found in the defensive styles of caregivers according to their employment ($P = 0.001$).

Nonworking caregivers showed a higher frequency of mature defenses than those who were working (50%). The difference was statistically significant ($P = 0.001$) (Table 6).

There were statistically significant differences in caregiver defenses according to their relationship with the patient ($P = 0.001$). Spouses showed significantly higher mature defenses (40%), followed by sons (15%) (Table 7).

Table 5 Sex and defenses

	N (%)		
Types of defenses	Males	Females	Total
Neurotic	1 (2.5%)	6 (15%)	7 (17.5%)
Mature	9 (22.5%)	18 (45%)	27 (67.5%)
Immature	2 (5%)	4 (10%)	6 (15%)

Table 6 Work and defenses

	N (%)		
Types of defenses	Working	Not working	Total
Mature	7 (17.5%)	20 (50%)	27 (67.5%)
Neurotic	3 (7.5%)	4 (10%)	7 (17.5%)
Immature	5 (12.5%)	1 (2.5%)	6 (15%)
Total	21 (100%)	9 (100%)	40 (100%)

Table 7 Relationship and defenses

	N (%)				
Types of defenses	Sons	Spouses	Siblings	Others	Total
Mature	6 (15%)	16 (40%)	5 (12.5%)	0 (0%)	27 (67.5%)
Neurotic	1 (2.5%)	0 (0%)	4 (10%)	2 (5%)	7 (17.5%)
Immature	3 (7.5%)	0 (0%)	1 (2.5%)	2 (5%)	6 (15%)

Table 8 Defensive styles in relation to the marital status of caregivers

	N (%)			
Defenses styles	Widowed	Married	Single	Divorced
Immature	0 (0%)	3 (50%)	1 (16.6%)	2 (33.3%)
Mature	3 (11.1%)	22 (81.5%)	0 (0%)	2 (7.4%)
Neurotic	0 (0%)	3 (42.8%)	4 (57.2%)	0 (0%)

Married caregivers showed significantly more mature defenses ($P = 0.008$) (Table 8).

Fears were expressed significantly more by married caregivers ($P = 0.000$). Loss and grief was expressed significantly more by married caregivers ($P = 0.000$). Negative feelings were expressed significantly more by married caregivers (86.4%), followed by divorced caregivers (13.6%) ($P = 0.006$). The perception of stigma was significantly higher among widowed caregivers (42.9%), followed by married caregivers (33.3%), and to a lesser extent by single caregivers (23.8%) ($P = 0.014$) (Table 9).

Caregivers of patients with Alzheimer's disease of a severe degree on CDR expressed significantly greater perception of stigma (85.7%; $P = 0.003$), fears (81.5%; $P = 0.001$), and negative feelings and depression (100%), compared with caregivers of patients with Alzheimer's disease of a moderate degree ($P = 0.000$) (Table 10).

Trapped feelings were expressed significantly more by employed caregivers compared with those who were not working (68.2 and 31.8%; $P = 0.000$). Worries were expressed significantly more by nonworking than by working caregivers (51.6%; $P = 0.008$) (Table 11). Females expressed significantly higher trapped emotion ($P = 0.09$) (Table 12).

Worries were expressed the most by caregivers who were spouses (45.2%), followed by sons (32.3%), and finally siblings (9.7%). The difference was statistically significant ($P = 0.000$). Perception of stigma was reported by the most by caregivers who were sons (42.9%), followed by spouses (33.3%), and siblings (23.8%); the difference was statistically significant ($P = 0.014$) (Table 13).

Loss and grief were expressed the most by caregivers who were spouses, followed by sons, and siblings ($P = 0.000$). Trapped emotions were highest among the sons followed by siblings followed by others ($P = 0.000$). Depression

Table 9 Results of the Involvement Evaluation Questionnaire according to marital status

	N (%)					
	Married	Single	Widow	Divorced	Total	*P*
Fears						0.000
Absent	3 (23.1%)	5 (38.5%)	3 (23.1%)	2 (15.4%)	13 (100%)	
Present	25 (92.6%)	0 (0%)	0 (0%)	2 (7.4%)	27 (100%)	
Loss and grief						0.000
Absent	1 (14.3%)	4 (57.1%)	0 (0%)	2 (28.6%)	7 (100%)	
Present	27 (81.8%)	1 (3%)	3 (9.1%)	2 (6.1%)	33 (100%)	
Negative feelings						0.006
Absent	9 (50%)	5 (27.8%)	3 (16.7%)	1 (5.6%)	18 (100%)	
Present	19 (86.4%)	0 (0%)	0 (0%)	3 (13.6%)	22 (100%)	
Stigma						0.014
Absent	9 (47.4%)	5 (26.3%)	1 (5.3%)	4 (21.1%)	19 (100%)	
Present	7 (33.3%)	5 (23.8%)	9 (42.9%)	0 (0%)	21 (100%)	

was highest among caregivers who were spouses, followed by sons ($P = 0.000$) (Table 14).

Discussion

Strong evidence from previous research indicates that the caregiving role is very demanding, frequently distressing, and may adversely affect the health and quality of life of the caregivers (Schulz *et al.*, 2004). This study aimed to assess the distress levels, defensive styles, and variables of involvement among caregivers of patients with Alzheimer's disease, in relation to certain disease parameters such as the degree of severity of illness and caregivers' personal factors.

Unsurprisingly, the severity of Alzheimer's disease was correlated with the multiple effects suffered by the caregivers, especially when the mean duration of the illness was long (>2 years).

Earlier research has reported on the factors affecting caregivers' burden, including the severity of symptoms and duration of illness (Donaldson *et al.*, 1997). However, more recent research found these factors to be less effective. Elliottt *et al.* (2010) suggested that caregivers' burden is not directly linked to the severity of psychopathological symptoms, but rather a deficit in a patient's sphere of functioning (Burns, 1993). This might not only be linked to problems related to the illness but also a number of nonspecific factors related to the family such as poor living conditions, difficulties at work, the responsibility of physical caring, and financial responsibility (Benbow, 2001).

In order to investigate the effect of Alzheimer's disease on caregivers, it was necessary to compare caregivers of Alzheimer's disease with a control group. Caregivers of patients with diabetes mellitus were chosen, as it is a lifelong illness and in the long term, requires a degree of continuous supervision by the caregiver to prevent life-threatening complications such as hypoglycemic or hyperglycemic coma. On comparing caregivers of patients with Alzheimer's with the caregivers of patients with diabetes mellitus, it was found that the caregivers of patients with Alzheimer's disease showed higher levels of burden, especially caregivers of patients with more severe behavioral and cognitive impairments. This is in agreement with the results of Donaldson *et al.* (1998), who compared caregivers of patients with Alzheimer's disease and those with chronic medical conditions.

In this study, most caregivers perceived their patient's illness to be severe in the preceding two years. This provides an explanation for the relationship of severity of illness to caregivers' burden. Conde-Sala *et al.* (2009), studying spouses of patients with Alzheimer's disease, found that stable partnerships seem to be achievable when the partner's impairment is perceived as moderate

Table 10 Results of the Involvement Evaluation Questionnaire in relation to the severity of clinical dementia rating scale

	N (%)			
	Moderate CDR	Severe CDR	Total	*P*
Stigma				0.003
Absent	12 (63.2%)	7 (36.8%)	19 (100%)	
Present	3 (14.3%)	18 (85.7%)	21 (100%)	
Fears				0.001
Absent	10 (76.9%)	3 (23.1%)	13 (100%)	
Present	5 (18.5%)	22 (81.5%)	27 (100%)	
Negative feelings				0.000
Absent	15 (83.3%)	3 (16.7%)	18 (100%)	
Present	0 (0%)	22 (100%)	22 (100%)	
Depression				0.000
Absent	15 (88.2%)	2 (11.8%)	17 (100%)	
Present	0 (0%)	23 (100%)	23 (100%)	

CDR, clinical dementia rating scale.

Table 11 Trapping and worries in relation to caregivers' work

	N (%)			
	Working	Nonworking	Total	*P*
Feeling trapped				0.000
Absent	0 (0%)	18 (100%)	18 (100%)	
Present	15 (68.2%)	7 (31.8%)	22 (100%)	
Worries				0.008
Absent	0 (0%)	9 (100%)	9 (100%)	
Present	15 (48.4%)	16 (51.6%)	31 (100%)	

Table 12 Caregivers' fears, worries, and feelings of being trapped in relation to sex

	N (%)			
	Male	Female	Total	*P*
Trapped				0.09
Present	9 (40.9%)	13 (59.1%)	22 (100%)	
Absent	3 (16.7%)	15 (83.3%)	18 (100%)	
Worries				0.8
Present	9 (29%)	22 (71%)	31 (100%)	
Absent	3 (33.3%)	6 (66.7%)	9 (100%)	
Fears				0.9
Present	8 (29.6%)	19 (70.4%)	27 (100%)	
Absent	4 (30.8%)	9 (69.2%)	13 (100%)	

Table 13 Caregivers' relation to the patient and perception of stigma and worries

	N (%)					
	Spouse	Son	Sibling	Other	Total	*P*
Stigma						0.014
Negative	9 (47.4%)	1 (5.3%)	5 (26.3%)	4 (21.1%)	19 (100%)	
Present	7 (33.3%)	9 (42.9%)	5 (23.8%)	0 (0%)	21 (100%)	
Worries						0.000
Negative	2 (22.2%)	0 (0%)	7 (77.8%)	0 (0%)	9 (100%)	
Present	14 (45.2%)	10 (32.3%)	3 (9.7%)	4 (12.9%)	31 (100%)	

Table 14 Caregivers' relationship with the patient and feelings of loss, grief, trapping and depression

	N (%)					
	Spouse	Sibling	Son	Others	Total	*P*
Loss and grief						0.000
Absent	0 (0%)	3 (42.9%)	0 (0%)	4 (57.1%)	7 (100%)	
Present	16 (48.5%)	7 (21.2%)	10 (30.3%)	0 (0%)	33 (100%)	
Trapped						0.000
Absent	15 (83.3%)	3 (16.7%)	0 (0%)	0 (0%)	10 (100%)	
Present	1 (4.5%)	7 (31.8%)	10 (45.5%)	4 (18.2%)	22 (100%)	
Depression						0.000
Absent	5 (29.4%)	9 (52.9%)	0 (0%)	3 (17.6%)	17 (100%)	
Present	11 (47.8%)	1 (4.3%)	10 (43.5%)	1 (4.3%)	23 (100%)	

or moderately severe. Moraes and Silva (2009) reported that the most important factor affecting caregivers' burden was the change in the relationship occurring in 'severe' illness that could be accompanied with persecution or infidelity delusions and behavioral changes are the most important factors that affect negatively the care giver relationship with the patient. Especially when there are delusions of persecution and infidelity related to the care giver.

The high rate of unemployment among the caregivers of patients with Alzheimer's disease in this study, with its impact on the financial situation of the family, correlated with both the use of more mature defenses and more worry and stress among the caregivers. Different findings have been obtained in other studies. Coen *et al.* (1997) reported that most of the spouses and children of the patients experience the disadvantages of caring even if it did not cause them serious problems in their lives. Alison *et al.* (2000) found that financial burdens are usually compounded by other problems, such as dealing with aggressive episodes and worry about the future. This difference could be attributed to differences in the community support system and medical insurance of these patients, which covered the expenses of medications and did not place additional financial constraints on the caregivers; in contrast, in this study, the family covered all the medical expenses of the patient, which imposed additional burden financially and emotionally.

The caregivers interviewed in this study faced emotional and practical challenges as a result of caring for a patient with Alzheimer's disease. In terms of the demographic characteristics, the findings of this study showed that the majority of caregivers (72%) lived in the same house with the patient. Among them, unemployed (62.5%), there were more female caregivers; thus, they had closer and more frequent contact with the patient, which resulted in more direct exposure to day to day caring issues.

It can be argued that this finding may simply reflect the living circumstances of the general population (Office for National Statistics, 1998), and thus may be representative of the socioeconomic and cultural context. This contrasts with some western studies; for example, Coen *et al*. (1999), who found that less than half of the patients (40%) lived with their families.

In this study, with the use of the IEQ, female caregivers were found to experience nonsignificantly higher levels of distress than their male counterparts. Women expressed more worry (71%), especially among those who were unemployed; this was not significant. They also expressed more fears (70.4%), feelings of being trapped (59.1%), and significantly more loss and feelings of grief than male caregivers. Female caregivers were also more involved in the supervision of the patient, and thus felt trapped. This can be attributed to cultural factors. In Egypt, daughters and wives are more involved than husbands and sons in the care of chronically ill patients.

Whether the degree of exposure and involvement with the patient can explain this sex difference is difficult to assess. Some studies have emphasized the role of continuous involvement in increasing the caregivers' burden (Mittelman *et al.*, 2004). By being exposed to their relative's illness on a daily basis, they are exposed to many burdens, which has a negative impact on their own well-being (Burns *et al.*, 2005). In contrast, Alison *et al.* (2000) found that the stress levels and burden of caregivers living apart were similar to those who were living with the patients.

The sex differences in worries, fears, loss, and grief may be related to sex-specific factors. Moraes and Silva (2009) suggested that male caregivers avoid contact because they find the situation distressing; Aguglia *et al.* (2004), however, reported that female caregivers experience greater strain than male caregivers and have more behavioral and emotional problems, whereas Tarrier *et al.* (2002) found that male caregivers of psychiatric patients experienced more anxiety than female caregivers. Belle *et al.* (2006) have reported that men may respond to the challenges of providing care in a more task-oriented manner and with less emotional involvement.

Actually, all the previously mentioned factors are believed to play a role in the sex differences observed in this study, and cannot be considered without an understanding of cultural influences specific to our society. The role of a woman as the main domestic caregiver, with men playing a greater role outside the home, may be attributed to the higher degree of involvement and thus stress. It should also be kept in mind that men in our society tend to underplay the strain they are under and may be less expressive in terms of their feelings of distress.

The defensive styles reported in this study represent a cross-section of the caregivers' coping styles. Most caregivers used mature defenses (67.5%), mainly sup-

pression, followed by neurotic defenses (17.5%), mainly pseudoaltruism and reaction formation, and immature defenses (15%). This is in agreement with the findings of the use of mature practical coping mechanisms as the main strategy among caregivers in a European study carried out by Aguglia *et al.* (2004). It is hard to relate our results to other studies results. There are cultural and community services in the European societies that help the care givers to cope better.

Again, sex differences were found, which were nonsignificant, with 45% of female caregivers using mature defenses and only 22% of male caregivers using mature defenses, followed by neurotic defenses, which can be considered as an attempt by the male caregivers to develop 'mastery' over the situation, a finding also reported by Moraes and Silva (2009).

Several studies have suggested that factors related to illness and the personal characteristics of caregivers have a significant influence on how they cope with caring for patients with Alzheimer's disease (Belle *et al.*, 2006). It seems, however, that sociodemographic factors may play a minor role, whereas the coping methods used to deal with problems may play the most significant role (Jönsson *et al.*, 2006). Most of the studies available have reported results that are in agreement with the findings of this study on the use of mature defenses and coping mechanisms by caregivers of patients with Alzheimer's disease; Scneider *et al.* (1999) have reported that caregivers of patients with chronic psychiatric illnesses frequently use nonpassive methods of coping.

The somatization defense, which was high in this study (17%), was also found by Connell *et al.* (2001) who found that those who were living with chronic psychiatric patients had more frequent general practioners visits. Campbell (2009) suggested that the severity of the patient's disease is a significant predictor of psychosomatic symptoms. In our culture the somatization defense is known to be high, particularly among females.

A reason given by Tarrier *et al.* (2002), might apply to the results of this study of increased mature defenses. They suggested that the family caregivers' knowledge had an indirect impact on the burden through active coping, and adapting, indicating that the less caregivers' knowledge, the more caregivers use of negative coping strategies.

Mature defenses were found to be used significantly more by caregivers who were unemployed, and stress and worry were also expressed significantly more by this group. However, trapped emotions were significantly higher among the employed group. Although employment can play a role as a buffer for feelings of helplessness and help care giver in distracting his negative feelings. Yet it also acts as extra efforts that make the care giver feel trapped all the time. Other mature defensive styles and coping strategies that were not explored in this study might have also been used by working caregivers. Schneider *et al.* (1999) suggested that denial, problem solving, and religious beliefs play an important role in helping to cope with the stress of caring for mentally ill patients.

Caregivers' distress

Seventeen percent of the caregivers in this study had psychiatric morbidity. The results showed that a relatively higher proportion of caregivers considered that the patients' illness had affected their relationship with others and had also led to mental health problems in them.

Previous research seems to support this finding. Aguglia *et al.* (2004) found, in a study carried out in Italy, that despite the advancements in hospital and community services, there are still many caregivers who are not only under stress but also have psychiatric and physical illnesses that go unnoticed. Caregivers of patients with Alzheimer's disease had a considerably higher prevalence of depressive disorders compared with that in the general population (Tarrier *et al.*, 2002). The figures for psychiatric morbidity range from 25% (Belle *et al.*, 2006), one-third (Alison *et al.*, 2000), up to 41% (Schneider, 1999). The relatively lower level of psychiatric morbidity in this study can be attributed to the methodology: the use of a semistructured interview rather than a diagnostic instrument.

Married caregivers had significantly greater negative feelings toward the patient than divorced and single caregivers, especially when the patients had a severe degree of impairment. Married caregivers not only face illness-specific burdens but also burdens resulting from their partnership and family roles. The burdens of everyday living can markedly affect the quality of life, and satisfaction with the relationship with the patient (Aguglia *et al.*, 2004).

In everyday life with the patient, spouses and sons experience a major burden that can affect their living situation and well-being (Burns *et al.*, 2005).

Spouses expressed significantly greater worries and feelings of loss and grief in relation to the patient. They also used mature defenses more often. These findings are understandable because spouses have a longer binding relation and more exposure to the patient than sons, and are more directly responsible than siblings who have other aspects of their lives to worry about. Moraes and Silva (2009) reported that Alzheimer's spouses are overburdened because of their long-term caring role. The long duration of exposure to the patient could also explain their greater feelings of loss and grief. Coen *et al.* (1999) suggested that levels of grief increased over time, especially when there is infidelity or persecutory delusions.

Spouses of Alzheimer's patients in this study expressed significantly greater worry and used mature defenses significantly more. This could be attributed to the spouse effort to deal with behavioral and cognitive changes due to the illness (Moraes and Silva, 2009). Difference in caregivers' responses in this study are related to sex and personal differences in the coping mechanisms used, which is in accordance with Alison (2000).

Stigma

The literature suggests that burden could arise because of the stigma associated with individuals with mental or behavioral illness (Georges *et al.*, 2008). Alzheimer's disease, because of its distinctive symptoms of cognitive impairment, disruptive or disinhibited behavioral symptoms, emotional instability, and perceived dangerousness, that could result out of delusions of persecution or infidelity (Donaldson *et al.*, 1997), is particularly a target for stigma and discrimination.

Cognitive dysfunction worsens progressively over time in patients with Alzheimer's disease and could be followed by many behavioral changes. As a consequence, the family may prefer social isolation, and may develop feelings of frustration, anxiety, low self-esteem, and helplessness (Etters *et al.*, 2008). Evidence exists indicating that stigma and worry may be associated with lower levels of self-reported physical well-being among caregivers of patients with Alzheimer's disease (Burns *et al.*, 2005).

The present study found that several factors were independently related to the perceived magnitude of the effect of stigma on both the patient and the family. The perceived effect of stigma was greater if the patient had more severe behavioral symptoms, if the caregiver had a relatively low education level, and if the family lived in an urban area.

Stigma is more observed in urban areas where the patients' behavior is more supervised by people around (Kaufer *et al.*, 2005).

Daughters and wives were more vulnerable to the negative effects of stigma emotionally and socially than sons and husbands. Georges *et al.* (2008) noted that stigma as a negative societal attitude acts as a stress and augments negative emotions, worries, tension, loss and grief, and negative feelings of the caregiver toward the patient. Campbell (2009) found that family members who are not over anxious in response to the patients' illness perceive stigma in less threatening way.

Limitation

This study has some limitations.

- The sample of the present study may not be representative of the larger population of caregivers of patients with dementia, as they were recruited from a single center and included those from a certain socioeconomic class and with certain educational levels.
- The sample size of 40 patients is relatively modest and if solely used on cross-sectional basis limited the power of the study.
- The study did not include a comparison group who were cared for in care homes and assess the burden and the direct involvement of their relatives.
- There were great problem to assess the financial costs of therapy of the patient that could have an impact in the caring style of the patient.
- This study was cross sectional and focused only on the primary caregiver; therefore, the results cannot be generalized to the family of Alzheimer's patients as a whole.
- Not all the disease-related factors were correlated in depth with the stress and defenses of the caregivers.

Implications

Interventions might be planned on the basis of existing defensive coping strategies among caregivers as well as focusing on improving patients' cognitive symptoms and associated behavioral problems, which might help to reduce caregivers' burden.

Empowering the role of old age psychiatry services in hospitals that could be reached in all areas for better quality of life of the patient and the care giver.

Family education and mutual support groups for caregivers may be a useful approach as it was found that many caregivers believed that the negative symptoms are under the patient's control.

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Conflicts of interest

There are no conflicts of interest.

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Psychiatric morbidity of chronic institutionalized patients with schizophrenia: implications for future community care

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Background

In many western countries, deinstitutionalization of chronically mentally ill patients was established after the mass introduction of neuroleptics in the late 1960s and the early 1970s. Deinstitutionalization was proven to be successful when there were strong ideological or humanitarian motives and when psychiatric reform was a priority and was completed with a comprehensive system of community. However, its long-term effects should be examined and questioned in terms of improving quality of life and functional abilities.

Aim and objectives

The research aimed at studying the morbidity profile and impact of schizophrenia on chronic institutionalized mentally ill patients as baseline data for planning of deinstitutionalization and a Community care program.

Methods

Data on sociodemographics, course of illness, treatment history, rate of admission, duration of hospital stay, and medical condition were collected retrospectively, followed by a cross-sectional study of a total of 95 patients with a schizophrenia spectrum using psychopathological rating scales such as PANSS, MMSE, CGI-S. Diagnosis according to DSM-IV and an interview using SCID were carried out by two different psychiatrists for high inter-rater reliability. The sample was recruited from among long-stay hospital patients.

Results

The mean age of onset of schizophrenia among the patients was 48.9 ± 10.3 and 21.2 ± 5.7 years. The mean duration of illness was 27.5 ± 9.3 years, whereas the mean duration of repeated admission was 19.07 ± 12.5 years. With respect to the median percentage of total hospital stay, 30% could be attributed to the patients' median age and 55% to illness duration, whereas with respect to chronic hospitalization 20% could be attributed to the patients' median age and 35% to illness duration. Of the patients, 85% were men; 70% were single and unemployed with a low socioeconomic status; 25% lacked private housing; 30% had diabetes mellitus and/or hypertension; 80% were obese and overweight; and 50% were on antilipid drugs. Delusion, hallucination, and conceptual disorganization were the highest-scoring positive symptoms in 50% of cases. Negative symptoms also scored higher (7.4) on all items in 60% of cases. Eighty percent had compromised cognitive deficits. Early age of onset of schizophrenia and being older were powerful predictors for repeated admission, a long duration of illness, and chronic hospitalizations. Severity of illness is also a powerful predictor for long hospital stay.

Conclusion

Schizophrenia is a chronic devastating illness that impacts function and cognitive abilities, and is characterized by a high rate of admission, chronic course of illness as well as chronic institutionalization. For continuity of care and a favorable prognosis, early comprehensive, multidisciplinary, and multimodel programs are required for patients with mental illness from the date of first hospital contact.

Keywords:
community care, deinstitutionalization, schizophrenia, social welfare

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Introduction

Schizophrenia is a heterogeneous disorder with variations in the severity of symptoms and in course and presentation (Davidson and McGlashan, 1997), of which cognitive and functional impairments are core features (Mohamed *et al.*, 1999). Such functional disability results in low employment rates and is a hallmark of many patients with schizophrenia (Lehman *et al.*, 2002). Accordingly, psychiatric rehabilitation may improve social inclusion and

functioning in patients with severe mental illness (Wilcock, 2005).

Comprehensive treatment of patients with schizophrenia focuses on alleviating psychotic symptoms, improving psychosocial function, and decreasing the rate of rehospitalization. Many studies have shown that readmission in schizophrenia is a multifactorial phenomenon whose probability is increased by early onset of the disorder (Vyas *et al.*, 2007), male sex (Lin *et al.*, 2006), substance abuse (Linszen *et al.*, 1994), marital status (i.e. being unmarried) (Lacro *et al.*, 2002), higher number of previous hospitalizations (Roick *et al.*, 2004), and short length of previous hospital stay. Nonadherence to medication and a low-quality support system (Olesen and Mortensen, 2002) are additional risk factors for rehospitalization.

Length of stay depends on not only the number of beds available in the area but also the possibility to refer the patients discharged from the hospital to community services for further care. This follow-up is particularly important for patients with schizophrenia and related disorders, who require continuity of care over prolonged periods of time (Moreno Küstner *et al.*, 2001). In Canada, as in other countries, the rates of rehospitalization or readmission for mental illness are very high relative to those for most other diseases. Among mental illnesses, readmission rates for schizophrenia and psychotic disorders are among the highest. The chronic, highly debilitating, and refractory nature of these disorders means that stabilization of an individual's condition regularly requires long stays in hospital (Canadian Institute for Health Information, 2006, 2007; Madi *et al.*, 2007).

The course and outcome of schizophrenia have received considerable attention since the condition was first described as dementia praecox by Kraepelin in 1896. Although a century's research has given rise to an extensive literature regarding its natural history, some of the original questions on the prognosis and outcome of schizophrenia are just as pertinent today. Kraepelin originally considered dementia praecox to have a deteriorating course, altering this view when he found that some of his severe hospital-based patients showed spontaneous remission (Rosen and Garety, 2005).

Although there has been a tendency to dichotomize outcome into either a chronic, deteriorating course or a full remission one, research has increasingly viewed the outcome of schizophrenia spectrum psychosis (hereafter, 'psychosis') as being on a continuum (Vaillant, 1963, 1964, 1978; Strauss and Carpenter, 1972), and has emphasized both its heterogeneity and complexity (Strauss, 1969; Strauss and Carpenter, 1977; Carpenter and Strauss, 1991; Harding *et al.*, 1992). Although it is now generally accepted that the course of illness is heterogeneous, there is little consensus on the complexity of this heterogeneity, where Ciompi (1980a, 1980b) have described eight main patterns of illness outcome, Huber *et al.* (1980) have described 12 possible courses, whereas Shepherd *et al.* (1989) have described only four.

It appears that the lack of economic resources of families and the related support system and the existing unemployment influence the course of illness, preventing recovery and causing relapses and readmissions; in the 1930s, Faris and Dunham (1939) had reported in their ecologic study in Chicago that the highest treated rates for 'dementia praecox' were concentrated in the slum areas of the greater Chicago area (seven cases per 1000 adults in the slum areas in contrast to two to five per 1000 in the upper class areas); this study was replicated in several other cities of the USA, yielding the same findings.

In Europe and North America, discharges of patients with chronic schizophrenia from mental hospitals began in the 1950s, before the widespread use of antipsychotic drug treatment. Avoiding admission, or early discharge, combined with domestic and industrial rehabilitation in open hospitals, may prevent the accumulation of long-stay 'institutionalized' patients and allow a proportion of them to return to full participation in community life (Wing and Brown, 1970). The therapeutic community movement (Jones, 1952), seen as an ideology rather than a therapeutic theory, did not originate in mental hospitals but spread to them later and, along with concern about institutional neurosis (Barton, 1959), the social breakdown syndrome, (Gruenberg, 1966), and asylum, had a considerable impact socially and politically (Goffman, 1961). Thus, the community care movement was born. In patients with chronic schizophrenia, the success of such care depends on the validity of sociological theories about the causes of defect states; the effectiveness of new drug treatments in alleviating the acute and often bizarre symptoms of mental illness; the patients' compliance with both drug and social treatments; and the provision of suitably staffed amenities such as day hospitals, day centers, industrial units, and local hostels (Goffman, 1961).

In the new millennium, the majority of the world's countries belong to the category of lower-middle level of economic development, which is reflected on the existing mental healthcare and psychosocial rehabilitation services, with an increasing incidence of mental disorders imposing a huge global burden (Murray and Lopez, 1996).

The WHO Mental Health Atlas reflects several observable marked discrepancies in the existence of community-based mental health services and the specialized services for chronically mentally ill patients (rehabilitation services); only half of the lower economically developed countries provide community-based psychiatric services, disability benefits, and rehabilitation services in contrast to 97.4–100% of the higher economically developed countries (WHO, 2000, 2001a, 2001b, 2005).

Aim and objectives

The aim of the current research was to study the morbidity profile and the impact of schizophrenia on chronic institutionalized mentally ill patients as baseline

data for planning deinstitutionalization and a Community care program.

Patients and methods

Place of the study

The current study was carried out at the state psychological medicine hospital of Kuwait, which is the only governmental psychiatric hospital in Kuwait, where the services are limited only to the hospital resources, lacking comprehensive, multidisciplinary, and community care. It is considered the third hospital in Kuwait in terms of patients' capacity, with 764 beds (575 beds for the general psychiatric service and 189 for addiction). The bed occupation rate is 69.2%, with an average length of stay of 52.9 days. It has 97 psychiatrists, 656 nurses, and 361 other staff members (psychologists, pharmacists, and medical paramedical coworkers). It has 130 beds for long-stay hospital patients, with 22.6% of beds for the general psychiatric service. In 2010, the Ministry of Heath in Kuwait reported a total of 56 209 visits for outpatient department and 5654 for psychiatric emergencies (Ministry of Health Kuwait 2010 year report.)

Duration of the study and participants

The study was carried out in the period between 1 January up to the end of June 2009, wherein all patients of long-stay wards (other than those in the Geriatric wards) were recruited.

Tools

All cases were subjected to the following:

(1) *Structured Clinical Interview for DSM-IV Axis I diagnosis Clinical Version* (*DSM-IV SCID-I*) (First *et al.*, 1995): It is a semistructured diagnostic interview based on an efficient but thorough clinical evaluation administered by an experienced trained bilingual researcher for Arabic-speaking patients.
(2) *Positive and Negative Syndrome scale* (*PANSS*) (Kay *et al.*, 1987): It includes 30 items on three subscales, with seven items covering positive symptoms, seven items covering negative symptoms, and 16 covering general psychopathology. Each item is scored on a seven-point item-specific scale ranging from 1 to 7; thus, the positive and negative subscales each range from 7 to 49, and the general psychopathology scale ranges from 16 to 112. It is a standard tool for assessing clinical outcome in treatment studies of psychotic disorders and useful for tracking severity in clinical practice.
(3) *Mini-Mental State Examination* (*MMSE*) (Folstein *et al.*, 1975): It is a 30-point cognitive test developed for the bedside assessment of cognitive functions including orientation, memory, attention, construction, and language.
(4) *Clinical Global Impression scale-Severity Index* (*CGI-S*) (Guy, 1976): It is a seven-point scale that requires the clinician to rate the severity of the patient's illness at the time of assessment, relative to the clinician's past experience with patients who have the same diagnosis. Considering the total clinical experience, a patient is assessed on the severity of mental illness at the time of rating.
(5) *Fahmy and El-Sherbini Social Classification scale* (Fahmy and El-Sherbini, 1983): Personal and socioeconomic data include age, sex, level of education and occupation of the parents, family size, estimated economic level, and sanitation in the house. All data were scored; the total socioeconomic score is 30. A score of 25 or higher indicates a high socioeconomic class, 20–24 middle class, 16–20 low social class, and 15 or less very low socioeconomic class.

Procedure

The study included two phases.

(1) *Phase 1*: This was a retrospective part, in which all the files of the patient were received from the file department and reviewed meticulously to collect data related to sociodemographics, as well as clinical and treatment data.
(2) *Phase 2*: This was a cross-sectional study in which patients with the diagnosis of schizophrenia and schizoaffective disorder were enrolled and assessed as follows:
    (a) Diagnosis confirmed by the DSM-IV (SCID-I), and accordingly, 95 cases were included in our study, except the following:
        (i) 8 cases of nonschizophrenia psychosis,
        (ii) 23 cases of mental subnormality,
        (iii) 1 case of personality disorder.
    (a) Clinical picture and psychopathology were assessed by the PANSS.
    (b) Cognitive functions were assessed by the MMSE.
    (c) Severity of illness was assessed by the CGI-S.
    (d) Social class of the patients was determined using the Fahmy and El-Sherbibi Social Classification scale.
    (e) Anthropometric measures such as BMI and waist circumference were obtained.

Interview and rating scales were processed by two different psychiatrists for higher reliability.

Ethical issues

Approval from the local research ethical committee of the hospital was obtained, besides oral and/or written informed consent from patients and/or their families after an explanation of the study procedures and aims was provided; the patient were free to withdraw from the study at any time if they wished.

Statistical analysis

Data were collected and reviewed by analysis using SPSS version 17 (IBM, New York, USA); the following tests were used: Independent-samples *t*-test as a parametric test of significance for comparison between two sample means after performing Levene's test for equality of

variances, the χ^2-test (or likelihood ratio) as a nonparametric test of significance for comparison between the distribution of two qualitative variables, Fisher's exact test as a nonparametric test of significance for comparison between the distribution of two qualitative variables whenever the χ^2-test was not appropriate; it yields the *P*-value directly. A paired-sample *t*-test was used as a parametric test of significance for comparison between before and after values of quantitative variables, one-way analysis of variance (*f*-test) was used as a parametric test of significance for comparison between more than two sample means using either Scheffe's or Tauham's post-hoc tests for the results of homogeneity testing, and the Pearson correlation coefficient (χ^2) was used as a parametric measure of mutual relationship between two normally distributed quantitative variables.

Results

Sociodemographic data

Study of the demographic data of 95 cases of chronic schizophrenia with a long hospital stay showed that 84.2% patients (80) were men, 71.6% were single, and 72.6% did not have a job; 27.4 and 63.4% were from a very low and a low social class, respectively; 27.4% lacked private housing; 50.5% of cases had a positive family history of psychiatric illnesses; and 31.6% had a family history of medical illness (diabetes mellitus, hypertension, and dyslipidemia), as shown in Table 1.

Table 1 Distribution of sociodemographics of patients with chronic schizophrenia (*N*=95)

	N (%)
Sex	
Female	15 (15.8)
Male	80 (84.2)
Marital status	
Single	68 (71.6)
Married	12 (12.6)
Divorced	13 (13.7)
Widow	2 (2.1)
Nationality	
Non-Kuwaiti	23 (24.2)
Kuwaiti	72 (75.8)
Job history	
Jobless	69 (72.6)
Professional	1 (1.1)
Retired	25 (26.3)
Education	
Illiterate	22 (23.2)
Low grade	53 (55.8)
High school	17 (17.9)
University	3 (3.2)
Social standard	
Very low	26 (27.4)
Low	60 (63.2)
Moderate	8 (8.4)
High	1 (1.1)
Housing	
No private	26 (27.4)
Private	69 (72.6)
Family history of psychiatric illnesses	
Positive	47 (49.5)
Negative	48 (50.5)
Medical family history (DM, HTN, dyslipidemia)	
Positive	65 (68.4)
Negative	30 (31.6)

DM, diabetes mellitus; HTN, hypertension.

Clinical and medical characteristics

As can be seen in Table 2, 72 patients (75.8%) experienced the onset of schizophrenia with positive psychotic symptoms. Undifferentiated and paranoid schizophrenia were the most common subtypes (43.2 and 23.2%, respectively). It was also found that the incidences of diabetes mellitus, hypertension, and dyslipidemia were 29.5, 30.5, and 48.4%, respectively.

However, 51.6% patients (49) were obese, with BMI of at least 30, and 30.5% were overweight (BMI 25–29.9). Pathological waist circumference of at least 102 was found in 43.3% of men, whereas all women had a pathological waist circumference, with cut-off point of at least 88, as shown in Table 3.

The mean age at onset of schizophrenia was 48.9 ± 10.3 years, the mean duration of illness was 21.2 ± 5.7 years, the mean age of illness chronicity was 27.5 ± 9.3 years, and the mean frequency of repeated hospital admissions was 19.07 ± 12.5, with a duration of stay of 3.3 ± 3.9 months. The mean duration of last hospital admission was 9.8 ± 6.2 years and the total hospital stay was 14.6 ± 7.4 years.

As shown in Fig. 1, the mean total positive PANSS subscore was 17.8 ± 7.08 with 46.3, 50.5 and 47.3% of cases scoring at least 4 on delusions, conceptual disorganization, and hallucinatory behavior, respectively. Figure 2 shows that the mean total negative score mean was 28.4 ± 10.9, with (69.4%) of cases scoring of at least 4 in stereotyped thinking and blunted affect, 64.2% in poor rapport, 60.5% in emotional withdrawal, and 56.8% in passive social withdrawal. In contrast, the mean score of general psychopathology was 38.5 ± 9.4, with 44.2% scoring at least 4 in preoccupation, 43.1% in unusual thoughts and active social

Table 2 Distribution of medical state and clinical presentation for chronic patients with schizophrenia (*N*=95)

	Frequency (%)
Symptom onset	
Negative symptoms	3 (3.2)
Positive symptoms	72 (75.8)
Mixed	20 (21.1)
DM	
Negative	67 (70.5)
Positive	28 (29.5)
DM/drug used (at onset)	
Conventional	16 (57.1)
Atypical	12 (42.9)
DM/illness course	
Before illness	1 (3.5)
After illness	10 (35.8)
During test stay	17 (60.7)
HTN	
Negative	66 (69.5)
Positive	29 (30.5)
HTN/drug used (at onset)	
Conventional	18 (62.06)
Atypical	11 (37.94)
HIN/illness course	
Before illness	0
After illness	8 (27.6)
During test stay	21 (72.4)
Dyslipidemia	
Negative	49 (51.6)
Positive	46 (48.4)

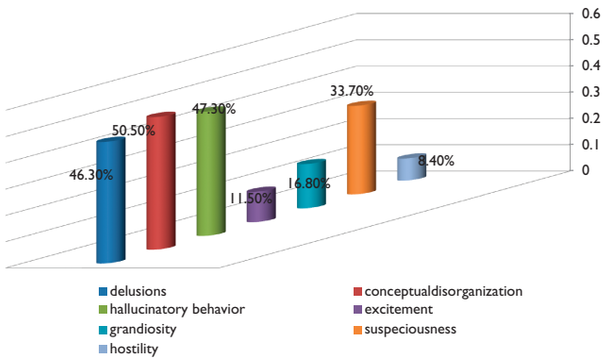
DM, diabetes mellitus; HTN, hypertension.

Table 3 Distribution of medical and anthrapometric characteristics of patients with chronic schizophrenia (*N*=95)

	Frequency (%)
Dyslipidemia drug at onset	
Conventional	14 (30.4)
Atypical	32 (69.6)
Dyslipidemia illness course	
Before illness	2 (4.3)
After illness	4 (8.6)
During test stay	40 (86.9)
Other medical illness	
CVS	7 (7.4)
Hepatitis	4 (4.2)
Renal	1 (1.1)
COPD	5 (5.5)
CNS	1 (1.1)
Hypothyroid	7 (7.4)
Blood disease (ITP)	3 (3.2)
Psoriasis	2 (2.2)
Cancer	1 (1.1)
BMI	
≥30	49 (51.6)
25–29.9	29 (30.5)
<25	17 (17.9)
Waist circumference (male)	
>102	35 (43.2)
94–101.9	19 (20)
<94	41 (36.8)
Waist circumference (female)	
≥88	15 (15.6)

CNS, central nervous system; COPD, chronic obstructive pulmonary disease; CVS, cerebrovascular stroke; ITP, idiopathic thrombocytopenia.

Figure 1



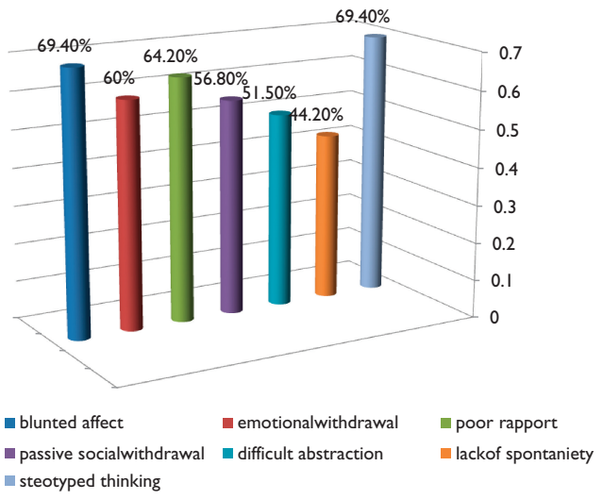
PANSS-positive subscores. PANSS, Positive and Negative Syndrome scale.

withdrawal, 9.5% in both somatic concern and mannerisms, and only 1% in motor retardation, as shown in Figs 3 and 4.

In terms of the severity of illness and assessment of cognitive functions, Table 4 shows that 86.3% of cases scored at least 4, indicating moderate to extremely ill. Moreover, the MMSE showed that 43.1% of cases had a definite cognitive deficit, scoring less than 20 on MMSE, 20% had a suspected cognitive deficit, and 36.8% had a normal range.

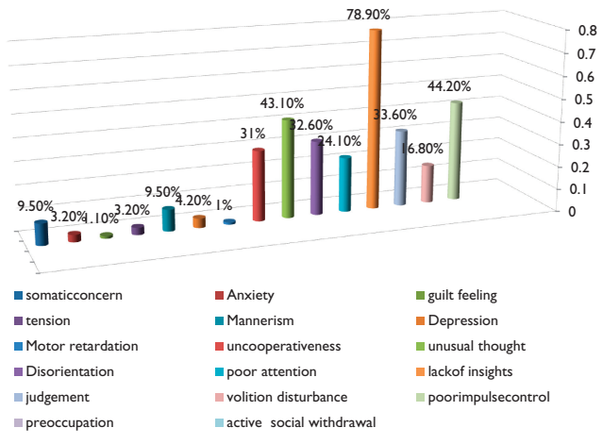
There were two previous failed treatment trails with a full therapeutic dose (400–1000 mg chlorpromazine equivalent) for at least 3–6 months, but with nonresponsiveness. Conventional antipsychotic prescriptions were highly significantly ($P = 0.000$) decreased across the three stages of treatments (85, 37, and 24.2%), whereas atypical groups showed a reversed increase (14, 51, and 75.8%).

Figure 2



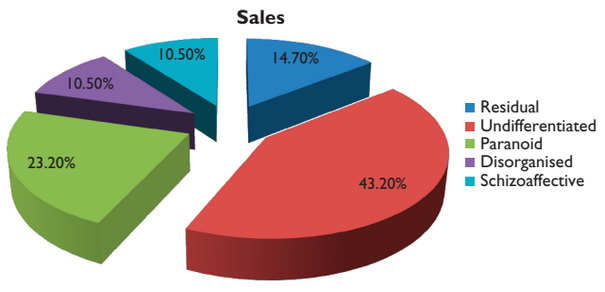
PANSS-negative subscore. PANSS, Positive and Negative Syndrome scale.

Figure 3



General psychopathology subscores.

Figure 4



Distribution of schizophrenia subtypes.

Review of their medical treatment data showed that 49.5% of them had received antihyperlipidemic agents, 31.6% had received antihypertensives, and 28.5, 20, and

Table 4 Clinical Global Impression scale-Severity Index and Mini-Mental State Examination

	N (%)
CGI-S	
Moderate to extremely ill	82 (86.3)
MMSE	
<20: definite cognitive deficient	41 (43.1)
20–40: suspected cognitive deficient	19 (20)
25–30: normal cognitive function	35 (36.8)

CGI-S, Clinical Global Impression scale-Severity Index; MMSE, Mini-Mental State Examination.

9.5% had received oral hypoglycemics, cardiac medications, and insulin, respectively. However, drugs for nonmetabolic disturbances, such as antacids, vitamins, and minerals, and for other specific treatments such as thyroxin, cardiac, bronchodilators, and topical ointments had been used by less than 20%, as shown in Figs 5–7.

Illness chronicity

The chronicity of illness was indicated by a long duration of illness (27.5 ± 9.3 years). Table 5 shows a statistically highly significant correlation with age, repeated admissions, long hospital stay, and total years of hospitalization ($P = 0.000$) each.

Patients with a chronic course of illness showed more severe cognitive dysfunction indicated by a highly significant statistical correlation with a lower MMSE score and higher scores on the disorientation item ($P = 0.000$), as shown in Table 5.

In terms of psychopathology, chronic patients with schizophrenia were significantly less delusional ($P = 0.05$) and suspicious ($P = 0.003$), with significantly less somatic concern ($P = 0.008$ and 0.003). In contrast, conceptual disorganization and difficult abstraction were more statistically significant in chronic patients enrolled in the study ($P = 0.005$ and 0.02, respectively; Table 6).

As can be seen in Table 7, the correlation between the duration of illness in our schizophrenia cases and their medical profile showed that those with a longer duration of illness were significantly more prone to hypertension versus those with a lower duration of illness (32.03 ± 7.8 vs. 25.5 ± 9.3, $P = 0.002$) and more significantly prone to metabolic syndrome versus those with a lower duration of illness (29.63 ± 9.3 vs. 21.6 ± 8.3, $P = 0.04$).

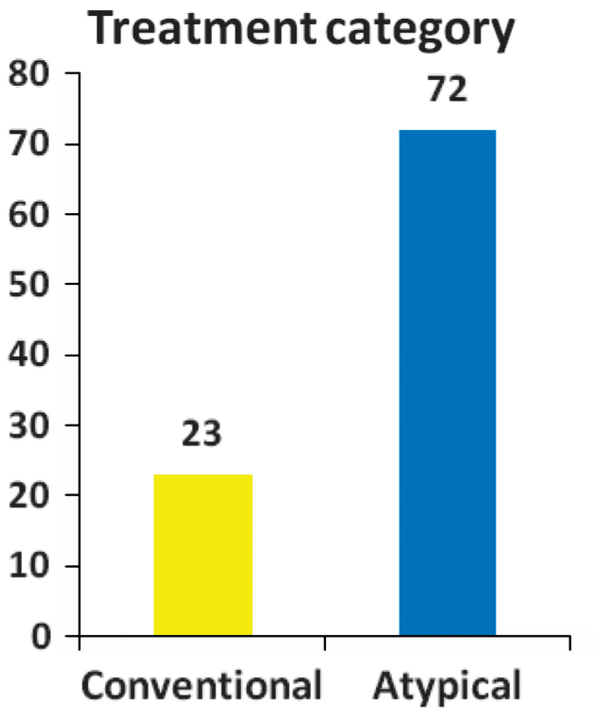
At the same time, there was a significant difference between patients with a longer duration of illness (34.0 ± 9.1 years), and those with a shorter duration of illness (25.5 ± 8 years, $P = 0.04$), in the severity of the illness using the GCI-S; those with a longer duration of illness were found to be borderline mentally ill versus those with a shorter duration, who were found to be extremely ill, as shown in Table 7.

Illness chronicity and medications

Table 8 shows that conventional antipsychotics were prescribed more for those with a longer duration of illness (30.4 ± 9.7) than the atypical group with a less duration of illness (26.5 ± 9.1), but was statistically insignificant ($P = 0.08$). Meanwhile, it was found that both clozapine and olanzapine were significantly more prescribed for those with a shorter duration of illness (25.3 ± 8.4 and 24.1 ± 8.7, respectively).

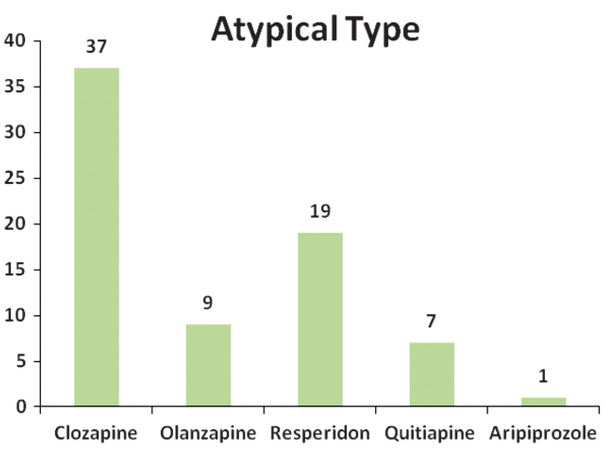
Using the multiple logistic regression model ($f = 2.704$, $P < 0.000$ and $R^2 = 0.991$), the most powerful significant predictors for illness chronicity were being older (0.987) and an early age of onset of schizophrenia (1.008); other

Figure 5



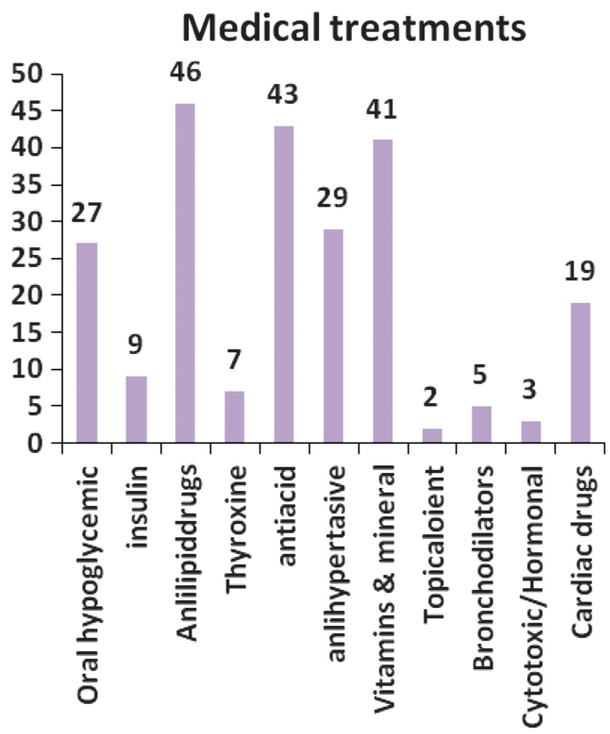
Distribution of treatment among cases.

Figure 6



Distribution of atypical antipsychotics used.

Figure 7



Treatment of medical conditions.

variables such as sex, social standard, family psychiatric history, scores of MMSE, PANSS, and CGI-s had no predictive value, as shown in Table 9.

Repeated hospital admission

There was a highly significant direct correlation between the mean number of repeated hospital admissions and each of age ($P = 0.001$), and duration of illness ($P = 0.000$), total period of hospitalization ($P = 0.01$), as well as being retired ($P = 0.03$), as shown in Table 6.

Table 10 shows that there was also a highly statistically significant difference between our chronic schizophrenia cases with respect to housing in relation to repeated relapses and hospital admission, wherein those with no private housing were more prone to repeated admissions ($P = 0.007$). In contrast, higher rates of repeated relapses and hospital admission were significantly highly associated with a moderate to high socioeconomic standard ($P = 0.002$).

Also, patients who have been currently diagnosed with residual schizophrenia or schizoaffective disorder had a history of significantly higher rates of repeated admission ($P = 0.04$), as shown in Table 7. At the same time, volition disturbance was significantly higher ($P = 0.03$) with repeated hospitalization, as shown in Table 6.

The multiple logistic regression model ($f = 2.907$, $P < 0.004$, $R^2 = 0.268$) showed that the most powerful predictors for repeated relapses and a high rate of hospitalization were being older (+ 0.706) and having an early age of onset of schizophrenia (1.035 years). Other variables lacked the power of prediction such as sex social standard, family history , and PANSS, MMSE, and CGI-S scores, as shown in Table 9.

Longer hospitalization and chronic institutionalization

The mean total hospitalization stay per year was 14.6 ± 7.4 and 9.8 ± 6.2 for chronic institutionalization. The longer hospitalization is indicated by the sum of duration of repeated admissions and the last continuous hospital stay period.

Patients with schizophrenia with longer durations of hospitalization are those with a longer course of illness ($P = 0.000$), older patients ($P = 0.000$), and of course those with a high rate of admission ($P = 0.001$) and chronic institutionalization ($P = 0.000$). They had higher scores on disorientation ($P = 0.03$) and volition disturbance ($P = 0.04$), as well as conceptual disorganization ($P = 0.02$). This means that these symptoms may have a role in their long hospitalization, as shown in Table 5. Also, these patients were more significantly likely to have dyslipidemia ($P = 0.03$), as shown in Table 7, and conventional antipsychotics were more significantly prescribed for these patients ($P = 0.04$).

With respect to the median percentage of total hospital stay, 30% could be attributed to the patients' median age and 55% to illness duration, whereas in the case of chronic hospitalization, 20% could be attributed to patients' median age and 35% to illness duration, as shown in Table 11.

As shown in Table 9, the multiple logistic regression model for total hospital stay ($f = 6.979$, $P < 0.001$, $R^2 = 0.492$) showed that the most powerful predictors were being older (10.519), early onset age of schizophrenia (0.0723), higher scores on the positive PANSS scale (0.233), and high psychopathological severity, as evidenced by CGI-S (1.732).

The most powerful predictors for chronic continuous institutionalization (significant model; $f = 2.70$, $P < 0.07$, $R^2 = 0.273$) were older age (0.328) and early age onset of schizophrenia (0.043), as shown in Table 9.

Discussion

Need for community care services

Long-stay patients with chronic schizophrenia represent a small proportion of all patients with such an illness, but in many cases, these patients account for a majority of the cases associated with the treatment of the illness (Harvey *et al.*, 2000). Meanwhile, deinstitutionalization is a multifunctional process to be viewed in a parallel with the existing unmet socioeconomical needs of the person to be discharged in the community and the development of care alternatives (Mechanic and Rochefort, 1990; Madianos, 2002).

The Psychological Medicine Hospital of Kuwait is the only and official state hospital that still depends on a hospital-based service. It has 764 beds for psychiatric and addiction services (575 for psychiatric general services

Table 5 Correlation of duration of illness, relapse number, duration, and total and last stay with age, onset age, cognitive parameters, and Positive and Negative Syndrome scale scores in 95 cases of schizophrenia

	Duration of illness	Relapse number	Relapse duration	Total hospital stay	Last stay duration
Duration of illness					
R		0.449	0.083	0.440	0.608
P		0.000	0.424	0.000	0.000
Relapse number					
R	0.449	1	−0.166	0.002	0.259
P	**0.000**		0.108	0.986	0.011
Relapse duration					
R	0.083	−0.166	1	−0.077	0.196
P	0.424	0.108		0.456	0.058
Last stay duration (years)					
R	0.440	0.002	−0.077	1	0.807
P	**0.000**	0.986	0.456		**0.000**
Total stay					
R	0.608	0.259	0.196	0.807	1
P	0.000	0.011	0.058	0.000	
Mini-Mental State Examination					
R	−0.378	−0.014	0.007	−0.172	−0.146
P	**0.000**	0.894	0.949	0.096	0.158
Total positive PANSS					
R	−0.136	−0.002	−0.084	0.045	0.057
P	0.188	0.982	0.421	0.665	0.585
Total negative PANSS					
R	0.040	−0.079	0.101	−0.105	−0.068
P	0.701	0.446	0.329	0.313	0.510
Disorientation score					
R	0.382	0.174	0.168	0.125	0.223
P	**0.000**	0.092	0.103	0.229	**0.030**
Lack of attention score					
R	0.193	0.070	0.144	0.116	0.156
P	0.061	0.497	0.162	0.262	0.132
Age					
R	0.816	0.322	0.158	0.335	0.458
P	**0.000**	**0.001**	0.127	**0.001**	**0.000**
Age at onset					
R	−0.151	−0.141	0.056	−0.136	−0.206
P	0.145	0.174	0.586	0.19	**0.045**

Bold indicates *P*-value was significant or highly significant.
PANSS, Positive and Negative Syndrome scale.

and 189 for addiction). The percentage of bed occupancy is 68.2 and 72.3%, respectively; the duration of admissions is 52.4 days for both, with a turnover rate of 25.4 and 28.5 (Ministry of Health report, 2009). The total population of the country is 3 566 737; there is one bed for 4668.1 and one psychiatrist for 37 150 patient population (Kuwait census, 2009).

The total number of beds for long hospital stays is 130, representing 22.6% of the total psychiatric hospital beds (575), which includes nongeriatric patients with different diagnoses with a 96.9% occupancy rate. Patients with disorders in the schizophrenia spectrum represent 79.3% of patients with chronic institutionalization (mean 9.8 ± 6.2 years). Patients with mental illness suffer from inadequate availability of community-based psychiatric services, specialized services for chronic mental illness, and specialized mental health programs for children and adolescents. However, a specific program for elderly patients has been developed recently focusing on their mental and physical problems; a disability benefit policy has also been formulated recently. These findings are not consistent with higher socioeconomic status and social welfare in the Kuwait community.

The substantial cost because of unmet needs for patients with chronic schizophrenia with a long hospital stay highlights the importance of the current study, which points out the nature of this group of mentally ill patients.

Outcome of participants

Our sample of patients with chronic schizophrenia with a long hospital stay has shown some indicators for poor outcomes, wherein 50% of them have a moderate to severe degree of positive and negative symptoms with a positive family history. At the same time, more than 70% were men, never married, unemployed, or retired, with a low educational level and a low socioeconomic standard, besides a high rate of admission and long stay in the hospital. Moreover, 50% were obese, 90% had a risk of metabolic syndrome, and only 20% had intact cognitive functions. These findings of sample characteristics are in agreement with those of other studies (Curson *et al.*, 1988), and in agreement with the study by Harvey *et al.* (2000), who concluded that hospital patients had severe negative and cognitive symptoms as well as functional defects.

Our patient characteristics lack the known good prognostic factors such as being married (Shepherd *et al.*, 1989; Wiersma *et al.*, 1998), having a higher level of education (Geddes *et al.*, 1994), and being female (only 15% of our sample are female patients) (Watt *et al.*, 1983; Jablensky *et al.*, 1992; Leff *et al.*, 1992; Harrison *et al.*, 1996; Murray and Van Os, 1998; Moriarty *et al.*,

Table 6 Correlation of duration of illness, relapse number, duration and total hospital stay, and last hospital stay with Positive and Negative Syndrome scale subscores

	Duration of illness		Relapse number		Relapse duration		Last stay duration		Total stay duration	
	Pearson's correlation	Significance (two tailed)	Pearson's correlation	Significance (two tailed)	Pearson's correlation	Significance (two tailed)	Pearson's correlation	Significance (two tailed)	Pearson's correlation	Significance (two tailed)
Positive PANSS subscores										
Delusion	−0.199	**0.050**	−0.109	0.295	−0.071	0.492	0.039	0.706	0.059	0.572
Conceptual disorganization	0.283	**0.005**	0.048	0.644	0.128	0.216	0.172	0.096	0.233	**0.023**
Hallucinating behavior	−0.142	0.171	−0.022	0.832	0.059	0.568	−0.009	0.929	−0.009	0.933
Excitement	−0.091	0.382	0.071	0.494	−0.094	0.364	0.046	0.657	0.034	0.746
Grandiosity	−0.007	0.949	0.000	0.996	−0.114	0.272	−0.015	0.883	0.018	0.861
Suspiciousness	−0.297	**0.003**	−0.015	0.886	−0.222	**0.031**	−0.015	0.883	−0.069	0.509
Hostility	−0.170	0.100	0.066	0.528	−0.121	0.244	−0.033	0.752	−0.045	0.665
Negative PANSS subscores										
Blunted effect	0.056	0.590	−0.070	0.500	0.089	0.392	0.037	0.721	0.035	0.740
Emotional withdrawal	−0.042	0.686	−0.084	0.417	0.000	0.997	−0.093	0.368	−0.105	0.311
Poor rapport	−0.018	0.859	−0.070	0.498	0.082	0.429	−0.148	0.153	−0.110	0.287
Passive social withdrawal	−0.053	0.611	−0.075	0.473	0.053	0.608	−0.210	**0.041**	−0.180	0.082
Difficult abstraction	0.225	0.028	0.033	0.748	0.188	0.068	0.020	0.845	0.123	0.235
Lack of spontaneity in conversation	−0.016	0.880	−0.100	0.333	0.087	0.400	−0.120	0.249	−0.081	0.436
Stereotyped thinking	0.132	0.204	−0.081	0.434	0.103	0.320	−0.027	0.795	−0.022	0.835
General psychopathology subscores										
Somatic concern	−0.270	**0.008**	−0.090	0.385	−0.001	0.991	−0.004	0.973	−0.076	0.461
Anxiety	−0.062	0.548	−0.008	0.937	−0.101	0.332	−0.051	0.622	−0.076	0.466
Guilt feeling	−0.083	0.425	0.060	0.565	−0.085	0.413	−0.162	0.117	−0.176	0.087
Tension	−0.071	0.494	0.048	0.645	−0.086	0.406	0.027	0.796	−0.008	0.938
Mannerism	0.071	0.494	−0.060	0.566	0.188	0.068	−0.029	0.778	−0.028	0.787
Depression	−0.186	0.071	0.114	0.273	−0.163	0.115	−0.189	0.066	−0.154	0.136
Motor retardation	−0.110	0.287	−0.045	0.664	0.004	0.966	−0.156	0.132	−0.159	0.124
Uncooperativeness	−0.094	0.364	0.060	0.560	−0.107	0.303	−0.128	0.216	−0.098	0.346
Unusual thought	−0.185	0.072	−0.099	0.340	−0.166	0.108	−0.065	0.530	−0.132	0.201
Disorientation	0.382	**0.000**	0.174	0.092	0.168	0.103	0.125	0.229	0.223	0.030
Poor attention	0.193	0.061	0.070	0.497	0.144	0.162	0.116	0.262	0.156	0.132
Lack of insights/ judgment	0.062	0.548	−0.074	0.474	−0.014	0.896	−0.027	0.795	−0.011	0.916
Violent disturb	−0.173	0.094	−0.221	**0.031**	0.028	0.790	−0.126	0.223	−0.211	**0.041**
Poor impulse control	−0.047	0.654	−0.008	0.938	−0.113	0.277	0.100	0.335	0.048	0.645
Preoccupation	−0.060	0.563	0.154	0.137	−0.196	0.057	−0.080	0.441	−0.054	0.606
Active social avoidance	−0.009	0.928	−0.052	0.615	0.005	0.960	−0.152	0.140	−0.130	0.209

Highly significant if $P<0.001$.
Significant if $P<0.05$. Bold indicates P-value was significant or highly significant.
PANSS, Positive and Negative Syndrome scale.

2001). Other good prognostic factors include no family history of psychiatric illness (Vaillant, 1964; Murray and Van Os, 1998) as well as an older age at onset (Shepherd *et al.*, 1989; Jablensky *et al.*, 1992; Loebel *et al.*, 1992). However, our sample of patients lacked all these predictors of a good prognosis, especially the latter factor; in contrast, younger age of onset of illness (<20 years) was a powerful predictor for repeated admission, longer hospital stay, and chronicity of illness in our study, which are all considered as indices for poor outcomes.

The negative effect of schizophrenia was evident in our sample of patients: they have spent 50% of their lives suffering from the illness and have lived around 30% of their lives in hospitals, with 20% of their lives having been lost in chronic institutionalization.

In a study comparing between different groups of patients with schizophrenia who had experienced deinstitutionalization across different periods, Honkonen *et al.* (1992) found that patients had shown more satisfaction with their current situation, without an increased rate of mortality, and a low rate of homelessness. Also, Sytema *et al.* (2002) reported extra benefits for deinstitutionalization with an available community-based program that shortens the length of stay and provides a potentially low rate of rehospitalization, rather than hospital-based ones.

In our sample, the prevalence of acute psychotic illness as well as the negative symptoms that affect the patients' social skills and coping abilities forewarn of the problems that may develop if community services are insufficiently comprehensive and insufficiently organized and funded. Thus, a careful assessment of patients in a deinstitutionalization program should be based on functional scores (Odes *et al.*, 2011) and life skill profiles for assessment of disability profiles (Eu *et al.*, 2001). Moreover, we should

Table 7 Comparison of duration of illness, relapse number, duration of last stay, and total stay duration (h) according to medical, anthropometric, and clinical characteristics

		Duration of illness		Relapse number		Relapse duration		Last stay duration		Total stay duration	
	N	*M*±SD	*P*	*M*±SD	*P*	*M*±SD	*P*	*M*±SD	*P*	*M*±SD	*P*
Diabetes mellitus											
Negative	67	27.6±9.5	0.89	19.0±12.5	0.93	3.05±1.8	0.26	9.5±6.1	0.47	14.6±7.7	0.88
Positive	28	27.3±9.2		19.2±12.7		4.1±6.7		10.5±6.6		14.8±6.8	
Hypertension											
Negative	66	25.5±9.3	**0.002**	17.8±11.1	0.15	3.06±1.8	0.21	9.2±5.9	0.21	13.8±7.6	0.11
Positive	29	32.03±7.8		21.8±14.9		4.1±6.6		11.03±6.8		16.5±6.7	
Dyslipidemia											
Negative	49	26.4±9.0	0.27	16.9±11.8	0.08	2.9±1.6	0.30	8.7±6.6	0.07	13.1±7.3	**0.03**
Positive	46	28.6±9.7		21.3±12.9		3.8±5.9		11.0±5.6		16.3±7.2	
Metabolic syndrome											
Normal	9	21.6±8.3	**0.04**	15.8±8.2		2.6±1.4		7.9±7.1	0.77	11.0±8.1	0.16
Risky	17	31.8±9.5		20.5±13.1	0.34	3.2±2.4	0.31	10.5±6.9		17.6±9.6	
High risky	47	28.5±8.9		17.4±12.4		2.9±1.6		10.05±6.4		14.2±6.9	
Definite cases	22	28.6±9.5		22.6±13.8		4.7±7.5		9.5±4.9		14.8±5.8	
BMI											
≥30	49	26.4±9.3	0.50	19.1±12.2	0.87	3.8±5.1		9.0±5.3	0.44	13.6±5.8	0.38
25–29.9	29	28.4±8.8		18.2±13.2		2.7±1.9	0.45	10.8±7.5		15.8±8.4	
<25	17	29.0±10.3		20.2±12.2		3.0±1.6		10.3±6.3		15.5±9.6	
Schizophrenia subtypes											
Residual	14	34.1±8.6	**0.005**	28.1±14.8	**0.04**	2.9±1.6	0.79	12.9±5.5	0.32	19.4±8.4	0.19
Undifferentiated	41	25.5±8.3		17.5±12.9		4.05±5.7		8.9±5.7		13.3±6.7	
Paranoid	22	24.1±8.7		15.5±9.5		2.7±1.6		9.4±6.9		13.4±7.4	
Disorganized	10	32.0±7.07		17.5±8.4		3.4±1.7		8.0±5.3		15.5±8.6	
Schizoaffective	8	30.4±11.1		25.0±11.6		2.0±0.64		10.2±8.2		14.4±7.3	
Clinical Global Impression scale-Severity Index											
Borderline ill	13	34.0±9.1	**0.04**	20.0±13.7	0.08	6.0±8.1	0.33	13.0±7.2	0.34	23.0±7.9	0.43
Moderate ill	18	23.0±7.6		16.9±12.1		3.3±1.8		10.08±7.1		4.0±7.1	
Marked ill	27	27.0±9.5		23.4±13.1		2.9±1.4		9.5±6.3		15.03±7.02	
Severity ill	21	31.6±9.1		20.2±13.7		2.6±2.2		11.3±6.6		15.7±8.9	
Extremely	16	25.5±8.4		12.4±9.9		±0.7		±		±	

Highly significant if $P<0.001$.
Significant if $P<0.05$. Bold indicates *P*-value was significant or highly significant.

Table 8 Comparison of duration of illness, relapse number, duration of last stay, and total stay duration (h) according to the treatment characteristics of 95 patients with schizophrenia

		Duration of illness		Relapse number		Relapse duration		Last stay duration		Total stay duration	
	N	*M*±SD	*P*	*M*±SD	*P*	*M*±SD	*P*	*M*±SD	*P*	*M*±SD	*P*
Treatment category											
Conventional	23	30.4±9.7	0.08	23.0±14.2	0.08	3.04±1.5	0.62	11.2±6.2	0.2	17.3±8.4	**0.04**
Atypical	72	26.5±9.1		17.8±11.7		3.5±4.4		9.3±6.2		13.8±6.9	
Current treatment type											
Clozapine	37	25.3±8.4	**0.02**	19.1±12.0	0.36	2.7±1.6	0.5	9.1±6.7	0.45	13.1±7.2	0.16
Olanzapine	9	24.3±8.9		18.6±11.1		2.6±1.7		10.6±6.8		14.2±6.4	
Risperidone	19	27.4±10.4		15.1±3.6		4.5±7.8		9.5±5.4		14.2±6.8	
Quitiapine	7	31.1±11.1		15.8±4.2		5.5±2.7		7.8±6.1		14.9±8.2	
Aripiprazole	1	27.0±0.00		30.0±0.00		1.2±0.00		11.0±0.00		14.0±0.0	
Haldol	23	33.3±7.2		24.2±14.3		3.5±1.5		12.2±5.7		18.9±8.07	
Treatment history											
Trial I											
Conventional	81	27.7±10.09	0.74	19.07±12.5	0.15	8.1±1.7	**0.002**	8.6±4.04	0.55	12.9±5.4	0.81
Atypical	14	28.2±8.4		23.0±21.2		4.0±2.6		7.8±3.8		14.6±7.4	
Trial II											
Conventional	36	28.4±9.5	0.69	19.0±8.9	0.09	3.3±3.9	0.41	9.8±6.2	0.12	15.6±8.1	0.21
Atypical	59	28.7±10.1		18.1±10.1		3.4±1.9		7.1±5.6		14.5±7.7	

Bold indicates *P*-value was significant or highly significant.

not rely heavily on the efficiency of new drug treatment nor on the ability and willingness of the family to tolerate deviant social behavior in one of its members and his poor compliance even on long-acting injection (Curson *et al.*, 1988).

Claims of underfunding as the main obstacle to adequate community services should be tempered by criticisms of the high cost of repeated admissions, long hospital stay as well as poor coordination of health services. The community psychiatric services should not only be well organized but should also provide inpatient services. Facilities, albeit at a local level, will be required to offer genuine asylum for the patients who are most severely ill, with the needs of the patient being based on their social

Table 9 Multiple logistic regression model for significant predictors of chronicity, repeated admissions, total institutionalization period, chronic institutionalization

Multiple logistic regression model for significant predictors of chronicity for 95 patients with schizophrenia	
Duration of illness (years)	= 2.817 (constant) + 0.987 × current age (years) − 1.008 × age at onset of schizophrenia (years)
$F = 795.76$, $P < 0.000$, $R^2 = 0.991$	
Logistic regression model for significant predictors for repeated number of hospitalizations for 95 patients with schizophrenia	
Repeated hospitalization number	= 4.548 (constant) + 0.706 × age (years) − 1.035 × onset age of schizophrenia
$F = 2.907$, $P < 0.004$, $R^2 = 0.268$	
Multiple logistic regression model for significant predictors of the total institutionalization period for patients with chronic schizophrenia	
Total institutionalization period	= 4.541 (constant) + 0.579 × age (years) − 0.723 × onset age of schizophrenia + 0.233 total positive score of the PANSS scale + 1.732 × CGI-S score
$F = 6.979$, $P < 0.001$, $R^2 = 0.492$	
Multiple logistic regression model for significant predictors of chronic institutionalization (years) for 95 patients with schizophrenia	
Long continuous hospital stay	= 6.145 (constant) + 0.328 × current age (years) − 0.403 × age at onset of schizophrenia
$F = 2.704$, $P < 0.007$, $R^2 = 0.273$	

CGI-S, Clinical Global Impression scale-Severity Index; PANSS, Positive and Negative Syndrome scale.

disablement (Wing and Furlong, 1986; Crumpton, 1988; Griffiths, 1988).

Finally, the results highlight a problem that is still imperfectly understood by policy makers and administrators in health authorities who are responsible for planning and implementing services for integrative, comprehensive, and continuous psychiatric care with cost benefit and humanitarian motives in a community characterized by a high socioeconomic standard and social welfare for mentally ill patients since their first contact with psychiatric services.

Conclusion and recommendation

Schizophrenic patients with long hospital stays and chronic illness have poor prognostic factors, functional deficits, and weak coping skills that require multimodel comprehensive deinstitutionalization and rehabilitation programs depending on careful assessment, care continuity with cost effectiveness, and humanitarian motivation and social welfare support.

Deinstitutionalization is effective in reducing the quality of life for the chronically ill, whereas community programs are useful for psychiatric patients who are highly motivated. An effective institution with well-trained, flexible staff may be more able to meet the needs of those who are chronically ill.

Table 10 Comparison of duration of illness, relapse number, duration (per month), total stay duration (per year), and last stay duration (years) according to sociodemographics

		Duration of illness/year		Relapse number		Relapse duration/month		Last stay duration/year		Total stay duration/year	
	N	*M* ± SD	*P*	*M* ± SD	*P*	*M* ± SD	*P*	*M* ± SD	*P*	*M* ± SD	*P*
Sex											
Female	15	27.2 ± 9.6	0.88	18.7 ± 11.7	0.900	4.5 ± 1.7	0.23	10.06 ± 6.0	0.87	16.5 ± 6.5	0.29
Male	80	27.5 ± 9.3		19.1 ± 12.7		3.1 ± 4.2		9.7 ± 6.3		14.3 ± 7.6	
Marital status											
Single	68	26.2 ± 8.3	0.13	17.7 ± 11.3	0.060	3.6 ± 4.5	0.71	10.02 ± 6.3	0.55	14.7 ± 7.0	0.64
Married	12	32.1 ± 12.05		20.6 ± 10.1		2.3 ± 1.7		11.1 ± 5.3		15.3 ± 6.4	
Divorced	13	30.35 ± 10.6		26.2 ± 17.7		3.3 ± 1.9		8.0 ± 6.3		14.8 ± 10.3	
Widow	2	25.5 ± 13.4		6.5 ± 4.9		1.7 ± 0.35		7.0 ± 8.4		8.0 ± 7.7	
Job											
Jobless	60	26.7 ± 9.1	0.46	17.06 ± 11.3	**0.030**	3.6 ± 4.4	0.62	10.07 ± 6.5	0.37	14.9 ± 7.7	0.42
Professional	1	30.0 ± 0.0		20.0 ± 0.0		2.4 ± 0.0		1.5 ± 0.0		5.5 ± 0.0	
Retired	25	29.4 ± 10.0		24.6 ± 14.4		2.7 ± 2.1		9.4 ± 5.4		14.2 ± 6.5	
Education											
Illiterate	22	30.7 ± 9.3		18.6 ± 17.7		5.1 ± 7.9		10.6 ± 6.6		16.2 ± 9.2	
Low grade	53	27.3 ± 9.5	0.42	20.4 ± 13.09	0.820	2.8 ± 1.5	0.24	9.7 ± 6.4	0.90	14.7 ± 7.09	0.72
High school	17	25.7 ± 8.5		16.7 ± 8.9		3.0 ± 2.1		9.7 ± 5.7		13.4 ± 6.3	
University	3	24.0 ± 9.8		17.3 ± 20.03		3.3 ± 1.3		7.0 ± 6.0		10.8 ± 9.2	
Social standard											
Very low	26	30.2 ± 8.7		21.5 ± 12.4		2.7 ± 1.5		12.1 ± 6.7		16.8 ± 8.4	
Low	60	25.7 ± 9.4	0.09	16.1 ± 11.3	**0.002**	3.8 ± 4.8	0.45	8.9 ± 6.2	0.15	13.7 ± 7.2	0.30
Moderate	8	31.1 ± 9.1		30.7 ± 12.09		2.1 ± 0.76		8.7 ± 2.9		14.08 ± 4.1	
High moderate	1	35.0 ± 0.0		40 ± 0.00		2.1 ± 0.00		13.0 ± 0.00		20.0 ± 0.0	
Housing											
No private	26	29.08 ± 7.4	0.32	24.6 ± 14.7	**0.007**	2.8 ± 1.6	0.41	8.3 ± 5.6	0.16	13.3 ± 6.4	0.27
Private	69	26.9 ± 10.0		16.9 ± 10.9		3.5 ± 4.2		10.3 ± 6.4		15.1 ± 7.7	
Family history of psychiatric illness											
Negative	47	28.1 ± 9.9	0.51	18.3 ± 13.2	0.570	3.8 ± 5.2	0.22	9.6 ± 6.1	0.74	14.5 ± 7.6	0.89
Positive	48	26.9 ± 8.8		19.7 ± 11.8		2.9 ± 1.8		10.03 ± 6.4		14.7 ± 7.3	
Family history of DM, HTN, dyslipidemia											
Negative	65	27.9 ± 9.4	0.47	19.2 ± 12.8	0.850	3.5 ± 4.6	0.46	9.8 ± 6.2	0.99	14.7 ± 7.6	0.97
Positive	30	26.56 ± 9.2		18.7 ± 11.8		2.9 ± 1.8		9.8 ± 6.2		14.6 ± 7.1	

Bold indicates *P*-value was significant or highly significant. DM, diabetes mellitus; HTN, hypertension.

Table 11 Median of percent of total hospitalization and period of chronic institutionalization in relation to age and illness course duration of the studied cases (*N* = 95)

	Total hospital stay duration		Chronic hospital stay	
Variables	Age	Duration	Age	Duration
Min–maximum	2.1–61.29	7.14–98.28	1.09–55.59	1.67–83.33
*Q*1	21.82	38.71	10.64	18.75
Median	**30.16**	**55.0**	**20.0**	**34.78**
*Q*3	38.28	68.75	27.27	52.00

Bold indicates *P*-value was significant or highly significant.

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Conflicts of interest

There are no conflicts of interest.

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Metabolic syndrome and type 2 diabetes in chronic institutionalized patients with schizophrenia

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Introduction

Schizophrenia is a life-threatening illness with a mortality rate that is twice as high as that of the general population. Over 60% of deaths in schizophrenic patients are due to natural causes such as cardiovascular illness. Patients with schizophrenia and schizoaffective or bipolar disorder may have a predisposition to metabolic syndrome that is exacerbated by a sedentary life, poor dietary habits, possible limited access to care, and antipsychotic drug-induced adverse effects. It has been found that the prevalence rate of metabolic syndrome among schizophrenic patients ranges from 32 to 51%, with a two- to three-fold higher mortality rate due to heart attack compared with those without metabolic syndrome.

Aim and objectives

The current study aimed at detecting the prevalence and patterns of metabolic syndrome in chronic institutionalized patients with schizophrenia, comparing patients with metabolic syndrome - defined by different criteria- and lastly trying to find the predictor factors for metabolic syndrome and for diabetes mellitus.

Methods

Ninety-five patients with schizophrenia and schizoaffective disorder were recruited from long-stay hospital wards, were interviewed using structured clinical interview, and were diagnosed according to *Diagnostic and Statistical Manual of Mental Disorders, 4th ed*. They were subjected to a cross-sectional assessment by psychopathological rating scales including positive and negative syndrome scale, mini mental state examination, and clinical global impression – severity index scale and also to anthropometric measurement taking (BMI and waist circumference). Sociodemographic and clinical characteristics as well as treatment history were collected from data files. Cases were classified into four groups according to the International Diabetes Federation criteria: definite cases with metabolic syndrome (IDF criteria); the high-risk group (lacking one criterion); risky cases with risk for central obesity; and patients with no apparent risk. Data were collected and statistically analyzed.

Results

Twenty-two patients (23.15%) had definite metabolic syndrome according to IDF criteria, 47 patients (49.4%) had high risk, 17 patients (17.8%) had risk factors of metabolic syndrome, and only nine cases (9.4%) had no apparent risk for metabolic syndrome. Sociodemographic and clinical characteristics and psychopathological rating scores were not predictors for metabolic syndrome, nor for diabetes mellitus. BMI and waist circumference had the highest sensitivity, predictive value, and diagnostic accuracy for metabolic syndrome compared with the presence of diabetes, hypertension, or dyslipidemia. Diabetes mellitus occurred earlier and was of longer duration compared with other metabolic disturbances.

Conclusion

(1) The high risk of MS among patients with chronic schizophrenia mandates careful monitoring and elimination of risk factors.
(2) BMI and WC as well as blood sugar and lipid profile are considered simple measures for detecting risk factors.
(3) Attempts towards toward eliminating risk factors such as poor lifestyle, obesity, and metabolic disturbances is vital for long stay hospitalised patients.

Keywords:

cardiovascular disease, diabetes mellitus, metabolic syndrome, schizophrenia

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Introduction

The metabolic syndrome (MS) encompasses a cluster of metabolic risk factors associated with increased risk for type 2 diabetes mellitus and cardiovascular diseases (Black and Fisher, 1992; Sattar *et al*., 2003). It has been defined as the presence of three of five quantitatively defined markers: abdominal obesity, high triglyceride levels, low level of HDL cholesterol, high blood pressure, and elevated fasting glucose levels (Adult Treatment Panel III, 2001).

The prevalence of MS has varied from 10 to 22% (Ford *et al*., 2002). Vanhala *et al*. (1997) reported that the prevalence of MS was 8% in women and 17% in men. It is estimated that around a quarter of the world's adult population suffer from this syndrome (Dunstan *et al*., 2002) and they are twice as likely to die from it and three times as likely to have a heart attack (Isomaa *et al*., 2001). In addition, patients suffering from this syndrome have a five-fold higher risk of developing type 2 diabetes (Stern *et al*., 2004). The clustering of cardiovascular disease (CVD) risk factors that typify the MS is now considered to be the driving force behind the CVD epidemic.

Schizophrenia has a mortality rate that is twice as high as that of the general population (Brown, 1997). It was found that life expectancy among schizophrenic patients is 20% shorter than that of the general population (Newman and Bland, 1991) and those who are in their 40s have a life expectancy that is 6–7 years lower than that of the general population (Hannerz *et al*., 2001). Over 60% of the deaths in schizophrenic patients are due to natural causes such as cardiovascular illness (Brown *et al*., 2000).

Prevalence of type 2 diabetes varied between 6 and 21%, being two- to three-fold higher among patients with schizophrenia than in the general population (American Diabetic Association, 2004; Cohen *et al*., 2006).

Impaired fasting glucose tolerance was found in first-episode drug-naive patients with schizophrenia, suggesting that defective regulation of glucose may be partially associated with the disease process (Ryan *et al*., 2003). Many factors may contribute to increased risk for MS, diabetes mellitus, and CVD in this population – for example, their eating behaviors, exercise habits, lifestyle, history of glucose dysregulation, pre-existing hypertension, and drug use (Brown *et al*., 1999; Kane *et al*., 2004).

Antipsychotics are an important component in the medical management of many psychotic conditions. With the introduction of second-generation antipsychotics in the last decade the use of these medications has soared. Although they have many benefits compared with their early counterparts, their use has been associated with reports of marked weight gain, diabetes, and an atherogenic lipid profile; however, the relative contribution of second-generation antipsychotics to MS in patients with schizophrenia is unclear (Henderson, 2002).

The current study aimed at detecting the prevalence and patterns of metabolic syndrome in chronic institutionalized patients with schizophrenia, comparing patients with metabolic syndrome - defined by different criteria- and lastly trying to find the predictor factors for metabolic syndrome and for diabetes mellitus.

Methods

The study was conducted during the first 6 months of 2010 at the Psychological Medicine Hospital, Kuwait. This is the only psychiatric hospital in the State of Kuwait. It has five general units, in addition to one rehabilitation, one forensic, one geriatric, casualty, and child psychiatry unit, and an addiction center.

There are six long-stay hospital wards (five wards for male and one ward for female patients) with a total capacity of 132 beds.

Approval by the local hospital ethical committee was a prerequisite.

Sampling and participants

All patients in the long-stay hospital wards, with at least 6 months of hospital stay at their last admission, were screened.

Inclusion criteria: Patients suffering from schizophrenia or schizoaffective disorder, of both sexes, who were over 18 years of age and who had provided an informed consent, either by themselves or through a relative, were eligible for being inclusion in the study.

Exclusion criteria: patients with mental subnormality, organic brain syndrome, patients receiving diabetogenic drugs such as corticosteroids, and those with long periods of absence from the hospital (> 3 months) during the last year were excluded.

A total number of 126 patients were examined; 31 patients were excluded (23 had mental retardation, two women suffered from psychosis due to epilepsy, one had bipolar disorder, one woman had mixed personality disorder, two men were absent from the hospital for more than 3 consecutive months, and two men refused to give consent). The resultant 95 patients had been institutionalized for a considerable period of time under the same living conditions and lifestyle, including balanced diets, restricted smoking, and sport activity.

Procedure

The design of the current study consisted of two parts: first, all files of the selected cases were retrospectively reviewed and data pertaining to their sociodemographics, clinical examination, treatment history, mental state with review of their medications, medical history, current investigations, and a cross-sectional study in which patients had to be interviewed using a structured clinical interview in order to be diagnosed according to the *Diagnostic and Statistical Manual of Mental illness 4th ed*. were collected. All recruited patients had to have measurements taken of their vital signs, BMI, and waist circumference (WC). They were then subjected to the following psychometric assessments: positive and negative syndrome scale (PANSS; Kay *et al*., 1986), mini mental state examination

(MMSE; Folstein *et al.*, 1975), and clinical global impression – severity index scale (CGIS; Guy and Bonato, 1970).

Defining metabolic syndrome

There are different criteria for defining MS such as those stated in the International Diabetes Federation IDF (2006), the WHO 1999, the American Medical Association (2001), and the updated NCEP (2001).

As there is lack of epidemiological data for defining central obesity with specific cutoff points for eastern Mediterranean and Middle East (Arab) and Gulf populations, modified criteria for definitions of MS were used by the researchers, dividing patients into four groups according to their pragmatic BMI and WC cutoff points.

Patients with definite metabolic syndrome

Patients were diagnosed with MS if their central obesity was indicated by WC greater than or equal to 102 cm (40 inches) in the case of men or greater than or equal to 88 cm (35 inches) in the case of women and/or BMI was greater than or equal to 30; and when they fulfilled two of the following four conditions: blood sugar level greater than or equal to 5.6 mmol/l, blood pressure level greater than or equal to 130/85, elevated triglyceride levels greater than or equal to 1.7 mmol/l, reduced HDL levels of less than 1.03 mmol/l for men and less than 1.29 mmol/l for women, or if they were under treatment for any of the above-mentioned conditions (IDF criteria).

Patients with high-risk metabolic syndrome

Patients were diagnosed with high-risk MS when their WC and/or BMI cutoff points were as mentioned before and they fulfilled only one criterion from those of blood sugar, blood pressure, or lipid disturbances or being on treatment for it.

Patients at risk for metabolic syndrome

Patients were diagnosed as being at risk for MS when their WC cutoff points were greater than the range of 94–101.9 for men or greater than the range of 84–87.9 for female patients and/or their BMI was between 25 and 29.9 with or without disturbances in blood sugar, blood pressure, or lipid profile.

Patients with a normal metabolic state

Patients with a WC of less than 94 cm for men or less than 84 cm for women, BMI less than 25, and with no disturbances in blood pressure, blood sugar level, or lipid profile, nor undergoing treatment for the same, were reported as having a normal metabolic state.

Statistical analysis

Data were collected and coded. They were then entered into an IBM compatible computer, using SPSS version 17 (IBM; Illinois, Chicago, USA). The entered data were checked for accuracy and normality using the Kolmogorov–Smirnov test. Qualitative variables were expressed as number and percentage and quantitative variables as mean ($\bar{x}$) and SD. The arithmetic mean ($\bar{x}$) was used as a measure of central tendency and SD as a measure of dispersion.

The following statistical tests were used:

The independent sample *t*-test was used as a parametric test of significance for comparison between two sample means after conducting Levene's test for determining equality of variances.

The χ^2 test (or the likelihood ratio) was used as a nonparametric test of significance for comparison between the distribution of two qualitative variables.

Fisher's exact test, which yields a *P* value directly, was used as a nonparametric test of significance for comparison between the distributions of two qualitative variables whenever the χ^2 test was not appropriate.

A paired sample *t*-test was used as a parametric test of significance for comparison between the before and after values of quantitative variables.

The one-way analysis of variance (*F*-test) was used as a parametric test of significance for comparison between more than two sample means using either Scheffe's or Tauhane's post-hoc tests for homogeneity testing.

The Pearson correlation coefficient (*r*) was used as a parametric measure of the mutual relationship between two normally distributed quantitative variables.

Validating parameters – sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy (DA) – were calculated for the individual criteria of MS in patients with chronic schizophrenia:

sensitivity = the ability of the test to detect those with the condition;
specificity = the ability of the test to exclude those without the condition;
PPV = the ability of the test to detect those with the condition among those positively screened;
NPV = the ability of the test to exclude those without the condition among those negatively screened;
DA = the percentage of total agreement of both methods with respect to true positives and true negatives.

Multivariable logistic regression analysis for prediction of MS and diabetes mellitus.

A 5% level was chosen as the level of significance in all statistical significance tests.

Results

Comparison between patients with metabolic syndrome defined by different criteria and those with a normal metabolic profile

On applying the IDF criteria on the 95 patients included in the study, 22 patients (23.15%) were found to have definite MS, 47 (49.4%) were identified as high-risk

Table 1 Sociodemographics of patients with different criteria defining metabolic syndrome and patients with a normal metabolic profile

		Metabolic syndrome				
	Normal metabolic profile ($n=9$)	Risky ($n=17$)	High risky ($n=47$)	Definite ($n=22$)	Total ($n=95$)	Person $\chi^2(3)$ LLR $\chi^2(3)$
Sex						
Female	0	0	11	4	15	
Male	9	17	36	18	80	0.01*
Marital status						
Single	9	11	36	12	68	
Married	0	2	3	7	12	
Divorced	0	3	7	3	13	0.07
Widow	0	1	1	0	2	
Job						
Jobless	7	12	36	14	69	
Professional	0	0	1	0	1	0.78
Retired	2	5	10	8	25	
Education						
Illiterate	3	5	9	5	22	
Low grade	5	9	27	12	53	
High grade	1	3	9	4	17	0.97
University	0	0	2	1	3	
Socioeconomic status						
Very low	1	4	14	7	26	
Low standard	8	10	31	11	60	0.30
Moderate	0	3	2	3	8	
Highly moderate	0	0	0	1	1	

LLR, likelihood ratio.
*Significant if $P<0.05$.

cases, 17 (17.8%) were identified as risky patients, and only nine patients (9.4%) were identified as having a normal metabolic profile. Definite and high-risk cases for MS were significantly more among men and found only in exclusive cases among women ($P=0.01$). No other significant difference was observed between the studied groups with respect to their sociodemographic status (Table 1).

Definite cases for MS and high-risk cases were significantly older than those with a normal metabolic profile (51.4 ± 9.8, 51.9 ± 9.3, and 47.9 ± 10.1 years, respectively; $P=0.01$) (Table 2). Moreover, MS was found to be directly correlated with the duration of illness, representing a significant difference between patients with MS and those with a normal metabolic profile ($P=0.04$; Table 2).

Positive symptoms were significantly predominant at the time of onset of schizophrenia, especially in patients with definite MS and/or in patients at high risk compared with other groups ($P=0.05$; Table 3).

As regards the PANSS score, patients with a normal metabolic profile and those who are less prone to MS obtained significantly higher scores on the negative subscale (34.6 ± 9.1 and 33.5 ± 10.5, respectively) compared with patients with definite MS and at high risk ($P=0.007$; Table 2).

No other significant differences were found between patients with MS defined by different criteria and those with a normal metabolic profile as regards CGIS scores ($P=0.42$; Fig. 1), MMSE scores ($P=0.19$; Table 2), or treatment history [type of medication used, either monotherapy or polytherapy ($P=0.62$), conventional antipsychotics or atypical antipsychotics ($P=0.26$)].

Diabetes mellitus and pattern of metabolic disturbances

Among the 95 studied patients, 28 (29.47%) suffered from diabetes, 29 (30.52%) were hypertensive, and 49 (51.57%) had dyslipidemia. The mean duration of diabetes (10.43 ± 7.3 years) was longer than that for hypertension (7.3 ± 5.05 years) or dyslipidemia (4.6 ± 3.4 years).

At onset of medical illness, conventional antipsychotics were used more frequently by patients suffering from diabetes mellitus ($n=16$, 57.14%) or hypertension ($n=18$, 62.07%), whereas atypical antipsychotics were more frequently used by patients who developed dyslipidemia ($n=32$, 56.31%).

Interestingly, the onset of diabetes mellitus, hypertension, and dyslipidemia for most of the cases was during the period of chronic institutionalization, especially at the time of last admission ($n=17$, 60.71%; $n=21$, 72.41%; and $n=40$, 81.63%, respectively). Only one patient with diabetes mellitus and two patients with dyslipidemia were reported before the onset of schizophrenia.

There were no significant differences between diabetic and nondiabetic patients with respect to their sociodemographic features (Table 4), clinical characteristics, MMSE scores (Tables 4–6), CGIS scores (Fig. 2), history of previous use of conventional or atypical antipsychotics ($P=0.38$), or even current treatment type and dose of medications used (Table 7).

As shown in Table 8, most diabetic patients have coincident hypertension ($n=18$, 54.28%; $P=0.000$) or dyslipidemia ($n=22$, 78.57%; $P=0.000$). Moreover, a high percentage of diabetic patients were significantly more obese ($n=20$, 71.42%; $P=0.04$) and had a larger but nonsignificant WC ($n=19$, 67.85%; $P=0.13$).

Table 2 Correlation between patients with metabolic syndrome defined by different criteria and patients with normal metabolic profile according to age, clinical data, and clinical scale scores

		Metabolic syndrome				
	Normal metabolic profile ($n=9$)	Risky ($n=17$)	High risky ($n=47$)	Definite ($n=22$)	Total ($n=95$)	*P* value
Age (years)	40 ± 10.3	51.9 ± 9.3	47.9 ± 10.1	51.4 ± 9.8	48.9 ± 10.3	0.01*
Age at onset (years)	19 ± 3.9	20.4 ± 4.06	21.2 ± 6.4	22.7 ± 5.4	21.2 ± 5.7	0.34
Duration of illness (years)	19.6 ± 8.3	31.8 ± 9.5	26.5 ± 8.9	28.6 ± 9.5	27.5 ± 9.3	0.04*
Number of relapses	15.8 ± 8.2	20.5 ± 13.1	17.4 ± 12.4	22.6 ± 13.4	19.07 ± 12.5	0.34
Relapse duration (months)	2.6 ± 1.4	3.2 ± 2.4	2.9 ± 1.6	4.7 ± 7.5	3.3 ± 3.9	0.31
Last stay duration (years)	7.9 ± 7.1	10.5 ± 6.9	10.06 ± 6.4	9.5 ± 4.9	9.8 ± 6.2	0.77
Total stay duration (years)	11.0 ± 8.1	17.6 ± 9.6	14.2 ± 6.9	14.8 ± 5.8	14.6 ± 7.4	0.16
MMSE scores	18.8 ± 5.2	16.2 ± 5.5	19.6 ± 7.8	21.0 ± 7.05	19.4 ± 7.1	0.19
PANSS positive subscale score	18.6 ± 7.9	18.6 ± 7.4	17.1 ± 6.9	18.4 ± 6.7	17.8 ± 7.0	0.83
PANSS negative subscale score	34.6 ± 9.1	33.5 ± 10.5	27.9 ± 10.01	23.1 ± 11.4	28.4 ± 10.9	0.007**
BMI	20.7 ± 1.8	26.7 ± 2.03	32.89 ± 6.8	36.9 ± 8.2	31.58 ± 7.8	0.000**
Waist circumference	85.1 ± 4.5	93.50 ± 6.9	103.4 ± 18.2	108.57 ± 26.2	101.1 ± 19.4	0.004**

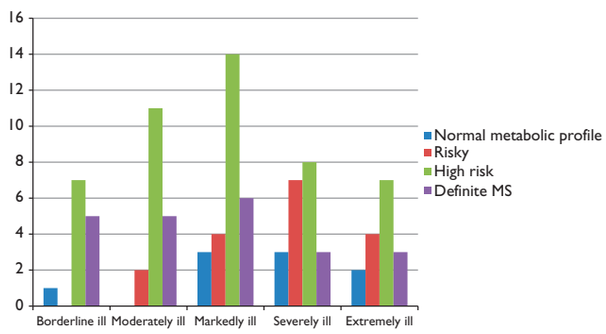
MMSE, mini mental state examination; PANSS, positive and negative syndrome scale.
*Significant if $P<0.05$.
**Highly significant if $P<0.001$

Table 3 Clinical characteristics of patients with metabolic syndrome defined by different criteria and patients with a normal metabolic profile

		Metabolic syndrome				
	Normal metabolic profile	Risky	High	Risky definite	Total ($n=95$)	Person $\chi^2(3)$ LLR $\chi^2(3)$
Symptoms at onset						
Negative	2	0	0	1	3	
Positive	5	14	34	19	72	
Mixed	2	3	13	2	20	0.05*
Total	9	17	47	22	95	
Schizophrenia subtypes						
Residual	1	3	7	3	14	
Undifferentiated	4	9	18	10	41	
Paranoid	2	3	13	4	22	0.92
Disorganized	1	1	7	1	10	
Schizoaffective	1	1	2	4	8	
Family psychiatric history						
Negative	4	9	25	9	47	
Positive	5	8	22	13	48	0.78
Family medical history						
Negative	7	12	33	13	65	
Positive	2	5	14	9	30	0.71

LLR, likelihood ratio.
*Significant if $P<0.05$.

Figure 1



Illness severity among the four studied groups using the clinical global impression severity index (CGIS). Note: the higher the CGIS score, the more severe the illness ($P=0.42$). MS, metabolic syndrome.

The pattern of medical illness (metabolic disturbances)

Figure 3 shows that the median time of onset of diabetes was 20 years after the onset of schizophrenia, but hypertension and dyslipidemia occurred 24 years after the onset of schizophrenia. The mean duration of the schizophrenic course was 27.5 years, and a median duration of 9.8 years of those metabolic disturbances occurred during chronic hospitalization.

Predictive value and diagnostic accuracy for metabolic syndrome criteria

Among all the criteria for MS, BMI (≥25) was the most specific criterion correctly identifying the presence of MS (DA = 78.95). The DA and PPV were higher for MS with BMI of at least 25, followed by male WC or greater than or less than 101 (DA = 73.75). Diabetes mellitus and hypertension were the least reliable criteria for DA or PPV (Table 9).

When each of the following factors, age, sex, socioeconomic standard, family history of diabetes mellitus, hypertension, and dyslipidemia, chronic schizophrenia course, chronic hospitalization, PANSS, MMSE and CGIS scores, were entered in a logistic regression model, none of them were of significant predictive value for the presence of MS or diabetes mellitus (χ^2 model = 21.096, significant $P = 0.02$, $R^2 = 0.318$).

Table 4 Sociodemographics of diabetic (*n*=28) and nondiabetic (*n*=67) patients

	Nondiabetic	Diabetic	Total	Person $\chi^2(3)$ LLR $\chi^2(3)$
Sex				
Female	11	4	15	–
Male	56	24	80	0.79
Marital status				
Single	51	17	68	–
Married	6	6	12	–
Divorced	8	5	13	0.19
Widow	2	0	2	–
Job				
Jobless	51	18	69	–
Professional	1	0	1	0.30
Retired	15	10	25	–
Education				
Illiterate	15	7	22	–
Low grade	38	15	53	0.99
High grade	12	5	17	–
University	2	1	3	–
Socioeconomic status				
Very low	18	8	26	0.40
Low	44	16	60	–
Moderate	5	3	8	–
Highly moderate	0	1	1	–

LLR, likelihood ratio.

Table 5 Clinical characters of diabetic (*n*=28) and nondiabetic (*n*=67) patients

	Nondiabetic	Diabetic	Total	Person $\chi^2(3)$ LLR $\chi^2(3)$
Symptom at onset				
Negative	2	1	3	–
Positive	49	23	72	–
Mixed	16	4	20	0.56
Schizophrenia subtypes				
Residual	10	4	14	–
Undifferentiated	28	13	41	–
Paranoid	16	6	22	–
Disorganized	8	2	10	0.64
Schizoaffective	5	3	8	–
Family psychiatric history				
Negative	37	10	47	–
Positive	30	18	48	0.83
Family medical history				
Negative	46	19	65	–
Positive	21	9	30	0.93

LLR, likelihood ratio.

Discussion

Patients with schizophrenia are at high risk for physical comorbidities such as metabolic dysregulation and CVD, leading to increased mortality (Phelan *et al.*, 2001; Lawrence *et al.*, 2003; Thakore, 2005).

In the current study the prevalence of definite cases of MS according to the International Diabetes Federation criteria 2004 was 23.15% and that for high risk was 49.4%. Those at risk represented 17.8% of cases.

The prevalence rate observed in this study is commensurate with the general prevalence of 10–22% found in the study by Ford *et al.* (2002) and almost similar to the prevalence found in the study by Straker *et al.* (2005) (29.2%) but lower than that in the studies by Correll *et al.* (2007) (47%) and Heiskanen *et al.* (2003) (37%) and significantly different from the 52.5% found in a similar study conducted on chronic, long-stay hospital patients with schizophrenia (El-Tayebani, 2007).

The wide variation between the current and other studies could mainly be because of different methodological diagnostic criteria defining MS, such as in the study by El-Tayebani (2007), who studied a similar sample depending mainly on American Medical Association (2001) and WHO 1999 in which lipid, sugar, and blood pressure levels are cardinal. Hence, cases that did not undergo treatment for metabolic dysregulations based on control of diet and lifestyle measures were included, besides excluding patients at risk who fulfilled only one or two criteria. This was not the case in the current study, in which only cases undergoing treatment for diabetes mellitus, hypertension, and dyslipidemia were included. Variability could also be explained by cultural differences and genetic predispositions; for example, USA has a higher prevalence of obesity and MS than does the UK (Ford *et al.*, 2002).

However, the overall risk for MS in the current study was very high; 90.6% of patients had either a degree of variable risk or actual MS.

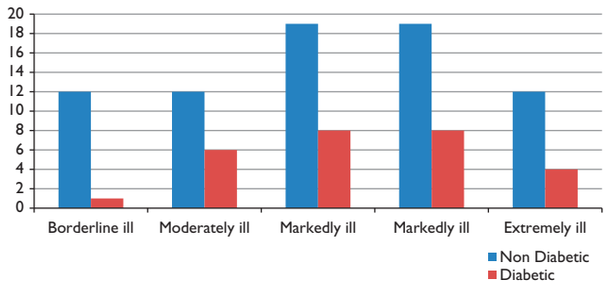
The higher risk of MS in this study may have been because of one or more risk factors, such as schizophrenia itself,

Table 6 Age, clinical data, and mini mental state examination scores of diabetic (*n*=28) and nondiabetic (*n*=67) patients

	Nondiabetic	Diabetic	Total	Person $\chi^2(3)$ LLR $\chi^2(3)$
Age (years)	48.07 ± 10.5	50.2 ± 9.8	48.9 ± 10.3	0.35
Age at onset (years)	22.8 ± 4.9	20.5 ± 5.8	21.2 ± 5.7	0.06
Duration of illness (years)	27.3 ± 9.2	27.6 ± 9.5	27.5 ± 9.3	0.89
Number of relapses	19.2 ± 12.7	19.0 ± 12.5	19.07 ± 12.5	0.93
Relapse duration (months)	4.1 ± 6.7	3.09 ± 1.8	3.3 ± 3.9	0.44
Last stay duration (years)	10.5 ± 6.6	9.5 ± 6.1	9.8 ± 6.2	0.47
Total stay duration (years)	14.8 ± 6.8	14.6 ± 7.7	14.6 ± 7.4	0.88
MMSE score	20.8 ± 6.8	18.9 ± 7.2	19.4 ± 7.1	0.24

LLR, likelihood ratio; MMSE, mini mental state examination.

Figure 2



Illness severity CGI scores among diabetic ($n=28$) and nondiabetic ($n=67$) patients with chronic schizophrenia ($P=0.43$). Note: the higher the CGIS score, the more severe the illness ($P=0.43$).

Table 7 Current treatment characteristics of diabetic ($n=28$) and nondiabetic ($n=67$) patients

	Nondiabetic	Diabetic	Total	Person $\chi^2(3)$ LLR $\chi^2(3)$
Current treatment category				
Conventional	18	5	23	–
Atypical	49	23	72	0.35
Treatment number				
Monotherapy	56	24	80	–
Polytherapy	11	4	15	0.79
Treatment dosage				
≥1000 mg cpz equivalent	62	25	87	–
<1000 mg cpz equivalent	5	3	8	0.86
Current differential drug types				
Clozapine	26	11	37	–
Resperidone	13	7	20	–
Olanzapine	5	4	9	–
Quitiapine	6	0	6	–
Aripiprazole	1	0	1	0.30
Haldol	14	4	18	–
Sulpride	2	1	3	–
Pimozide	1	1	2	–

Cpz, chlorpromazine; LLR, likelihood ratio.

chronicity, long duration of hospital stay, antipsychotic treatments, anthropometric characteristics, medical state (obesity and metabolic dysregulations), sociodemographics, clinical characteristics, and finally lifestyle or complex interactions for all of the above-mentioned risks.

Schizophrenia as a risk factor

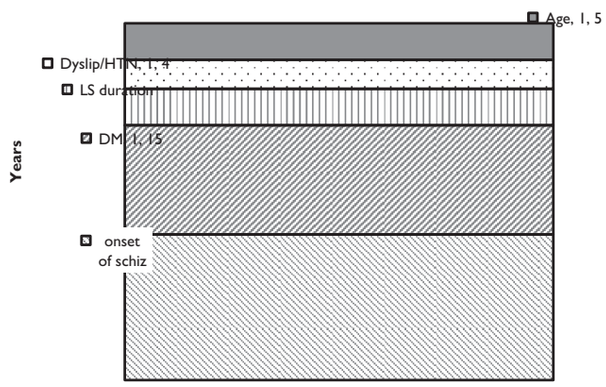
Heiskanen *et al.* (2003) found that the frequency of MS was two to four times higher in a group of people with schizophrenia, treated with typical and atypical neuroleptics, than in an appropriate reference population. This could be explained by the disease itself, wherein unaffected first-degree relatives of people with schizophrenia have high rates of type 2 diabetes mellitus (19–30%), pointing toward a genetic predisposition toward both illnesses (Mukherjee *et al.*, 1989). Further, over 15% of drug-naive individuals with first-episode schizophrenia have impaired fasting glucose levels, hyperinsulinemia, and high levels of the stress hormone cortisol (Ryan *et al.*, 2003).

Table 8 Medical illness and physical state among diabetic ($n=28$) and nondiabetic ($n=67$) patients

	Nondiabetic	Diabetic	Total	Person $\chi^2(3)$ LLR $\chi^2(3)$
Hypertension				
Negative	56	10	66	–
Positive	11	18	29	0.000**
Dyslipidemia				
Negative	43	6	49	0.000**
Positive	24	22	46	–
BMI				
≥30	29	20	49	–
25–29.9	24	5	29	0.04*
<25	14	3	17	–
Waist circumference (cm)				
≥102 male ≥88 female	31	19	50	–
94–101.9 male 84–87.9 female	16	3	19	0.13
<94 male <84 female	20	6	26	–

LLR, likelihood ratio.
*Significant if $P<0.05$.
**Highly significant if $P<0.001$.

Figure 3



Median values of age, onset of schizophrenia, last stay duration (LS), onset of diabetes mellitus, hypertension and dyslipidemia in years.

Schizophrenia is a long-standing stress factor with hypercortisolemia due to hypothalamic pituitary adrenal axis overactivity or defective feedback leading to obesity and metabolic changes. Hence, high risk of MS such as in melancholic depression and Cushing syndrome is associated with physical illness related to hypercortisolemia (Thakore, 2001; Ryan *et al.*, 2004). In addition, schizophrenia may increase the predisposition to MS by exacerbating and potentiating other risk factors such as sedentary life, poor dietary habits, limited access to care, and antipsychotic drug-induced adverse effects (Narasimhan and Raynor, 2010).

In our study the role of schizophrenia itself is unclear because unfortunately there is no control group having other similar psychiatric disorders to be compared against and prove the illness itself as risk. Also, the median time to onset of diabetes, hypertension, and dyslipidemia in our case is far from the age at onset of schizophrenia

Table 9 Predictive value and diagnostic accuracy for individual criteria of metabolic syndrome in chronic patients with schizophrenia

Criterion	Sensitivity	Specificity	PPV	NPV	DA
BMI ≥ 25	77.53	100	100	23.08	78.95
Male waist circumference (cutoff point ≥ 101 cm)	68.52	84.62	90.24	56.41	73.75
Diabetes mellitus	100.00	38.81	40.58	100.00	56.84
Hypertension	93.1	36.36	39.13	92.31	53.68
Dyslipidemia	86.96	40.82	57.97	76.92	63.16

DA, diagnostic accuracy; NPV, negative predictive value; PPV, positive predictive value.

(15, 24, and 24 years, respectively) and thus lack the temporary relation to the major constituents of MS.

Chronicity

The current results indicate that aging, longer duration of illness, and chronic course are significantly associated with both risky cases and definite cases for MS.

This may be understandable in the context of the suggestive finding of one or more risk factors for chronic MS, such as diabetes mellitus, hypertension, and dyslipidemia. This is also supported by results indicating a higher incidence of diabetes mellitus with age; Wild *et al.* (2004) concluded that the most important demographic change across the world in relation to diabetes prevalence appears to be an increase in the proportion of people aged 65 years and above. Further Al Kalaf *et al.* (2010) reported that age was the first significant independent predictor for the incidence of diabetes mellitus in a sample of Kuwaiti people. The dependency of the prevalence of MS on age is seen in most populations around the world (Anthony, 2008).

Chronic institutionalization

In our sample there was no significant association between risk of MS and long hospital stay or total stay period ($P = 0.77$ and 0.16) despite the fact that risky and definite cases for MS were distributed among patients with long duration of hospital stay. The lack of significance may indicate that chronic institutionalization may not be a powerful risk factor in our study in which controlled diet, smoking restriction, and sport activity helped to eliminate risk. This is supported by the results of Sugawara *et al.* (2011), in which higher prevalence of MS was seen in outpatients (48.1%) than in inpatients (15.8%) pointing to the importance of monitoring and minimizing the risk associated with changing lifestyles.

Antipsychotic medications

The relation of antipsychotic medication to type 2 diabetes and MS is unclear. In the present study we cannot ignore the effect of antipsychotic drugs on metabolic dysregulations and high prevalence of risks for MS despite a lack of significant association with either current medications or drugs at onset, as well as with various previous drug trails to treat MS and diabetes mellitus. Similar results were observed in Heiskanen *et al.* (2003), Cohn *et al.* (2004), and Straker *et al.* (2005).

This could be explained by the fact that most of our patients had repeated admissions, which was mainly because of noncompliance to treatment. The only period when compliance was obtained was during the last long hospital stay, in which adjusted environments may have decreased the risk of antipsychotic medication. Furthermore, with chronicity, the environmental factors can overcome the effect of drugs on weight gain, which predisposes diabetes mellitus and MS (Zipursky *et al.*, 2005).

Reports on the incidence of diabetes mellitus and metabolic dysregulation on drug-naive and first-episode schizophrenia have been documented in Ryan *et al.* (2003).

Obesity

Central obesity is a key feature of MS, reflecting the fact that its prevalence is driven by a strong relationship between WC and increased adiposity (BMI). However, despite the importance of obesity, patients of normal weight may also be insulin resistant and may suffer from MS (Anthony, 2008). Ryan and Thakore (2002) highlighted the potential role of visceral fat in cancer, cardiovascular illness, type 2 diabetes, and dyslipidemia. This was related to antipsychotic drugs (American Diabetic Association 2004) or may be independent of drugs and possibly due to HPA axis dysfunction (Rosmond and Björntorp, 2000). It was also reported to be present in drug-naive patients three times more than in the matched group (Thakore *et al.*, 2002).

In the current study there was a highly significant relationship between BMI and WC, indicating an association of general adiposity and visceral obesity with increased risk and definite cases of MS. Presence of type 2 diabetes was also significantly associated with BMI ($P = 0.04$) but not with WC ($P = 0.13$).

The value of BMI compared with WC in detecting the relative risk for diabetes mellitus and MS is under debate. Vazquez *et al.* (2007) demonstrated that BMI, WC, and waist/hip ratio have a similar association with incident diabetes. This was replicated by Ho *et al.* 2001, but Wang *et al.* (2007) reported that BMI was as reliable as or better than WC in predicting lipid risk and cardiometabolic factor. In contrast, Denke *et al.* (1994) indicated the importance of WC for detecting risk of cardiometabolic illness independent of BMI.

Our results indicate that BMI (cutoff point ≥25) has the highest sensitivity and predictive value as well as DA in detecting risk for MS, which may show the importance of this simple measure for detecting risk. However, WC of greater than or equal to 84 was powerful for detecting MS in women, as all studied women ($n = 15$) with schizophrenia lay in the high-risk ($n = 11$) and definite MS group ($n = 4$).

The lack of data about cutoff points for WC in the Mediterranean and Middle East (Arab) region, where the study was conducted, led to confusion in determining male and female scores. IDF 2004 recommends at least 94 cm for men and at least 80 cm for women, whereas El-Tayebani, (2007) used the cutoff point of at least 102 cm for men and at least 89 cm for women. Al Khalaf *et al.* (2010) used the same criteria, with both studies utilizing the NCEP and American Heart Association/updated NCEP guidelines (Grundy *et al.*, 2004). Using different cutoff points led to different results.

The current results concluded that BMI of at least 25 and WC of at least 94 for men and of at least 84 for women can detect the substantial risk of MS in the Arab culture, whereas cutoff points for BMI of at least 30 and for WC of at least 102 for men and of at least 88 for women can detect actual cases with definite MS.

Metabolic dysregulation

Diabetes, hypertension, and dyslipidemia were highly associated with MS ($P = 0.000$). Diabetes mellitus was also highly associated with hypertension and dyslipidemia ($P = 0.000$). Moreover, the sensitivity and NPV of these factors in relation to MS were high, but with modest specificity and DA. These results are commensurate with those of El-Tayebani (2007).

From the above data we can conclude that regularly monitoring simple measures such as BMI, WC, blood sugar, lipid profile, and blood pressure in patients with chronic schizophrenia is highly helpful for avoiding cardiometabolic risk.

Sociodemographics and clinical characters

There was no significant association between sociodemographics and schizophrenia characteristics in patients with diabetes mellitus in this study, nor for MS. Regarding gender, women were found to have high risk and actual MS (P=0.01), however, men were highly represented in both groups. This is consistent with the results of Sugawara *et al.* (2011).

Interestingly, patients with high negative scores on PANSS had lower risk for MS. This is consistent with a significant inverse association of total negative score with BMI ($P = 0.002$, $r = -0.319$) and higher negative PANSS scores in nondiabetic cases (30.3 ± 10.6 for negative cases versus 24.8 ± 10.9 for positive cases with diabetes mellitus, $P = 0.03$).

The weak predictive value of clinical and sociodemographics for MS in our findings was also documented by Heiskanen *et al.*, 2003. This may indicate that the risk for metabolic dysregulation is complex and is an outcome of the interaction between multiple factors such as centeral obesity and insulin resistance (Nakamura *et al.*, 1994; Bonora *et al.*, 1998; Anderson *et al.*, 2001; Nesto, 2003; Carr *et al.*, 2004).

Lifestyle predisposition

According to the WHO, Ministry of Health in Kuwait (2007) and 2005, which studied the Kuwaiti general population, Kuwaiti men within the age group of 40–60 years (matched with our patient age group) had the following risk factors: 23.2% were smokers (10–20 cigarettes/day); 42.1% had significantly reduced physical activity; 41.1% had hypertension; 19.7% were diabetic; 78.8% had WC of at least 93 cm; 50.5% had total cholesterol level of at least 5.2 mmol/l; 9.8% had a high cholesterol level of at least 6.5 mmol/l; and finally 50.5% of them had three or more of the above risk factors.

This means that Kuwaiti men are highly vulnerable to cardiometabolic risks, which may have a role in the ethnic predisposition toward such a problem (WHO, Ministry of Health in Kuwait, 2007 and 2005). The study on ethnic and cultural predisposition for cardiometabolic risk is quite important and needed in future research.

Conclusion and recommendation

(1) The risk of MS is high among patients with chronic schizophrenia, which mandates careful monitoring and elimination of risk factors.
(2) BMI and WC as well as blood sugar and lipid profile are considered simple measures for detecting risk factors.
(3) Studying cardiovascular risk, which is very important for patients with chronic schizophrenia with high mortality due to natural causes, is mandatory for highly vulnerable patients.

Limitations

(1) For the diagnosis of MS, the current study depended on actually treated cases of metabolic dysregulation, which may have disregarded cases with disturbed biochemistry dependent on diet and lifestyle management.
(2) Absence of a control group comprising the general population or other matched groups may limit the generalization of data.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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Dehydroepiandrosterone sulfate and testosterone levels correlate with negative symptoms in male patients with schizophrenia

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Background
Clinical studies have shown greater sex differences in symptoms of schizophrenia, with men having more negative symptoms than women, which may be related to the action of the reproductive hormones.

Objective
The aim of this study was to determine the relationship between negative symptoms and the plasma levels of testosterone and dehydroepiandrosterone sulfate (DHEAS) in male patients with schizophrenia.

Participants and methods
The participants were 50 male patients with chronic schizophrenia. The psychopathology of the patients was assessed using the Positive and Negative Syndrome Scale (PANSS). The Calgary Depression Scale for Schizophrenia (CDSS) and the Drug-induced Extrapyramidal Symptoms Scale (DIEPSS) were also used to exclude the effects of depression or drug-induced extrapyramidal symptoms.

Results
The PANSS negative scores showed a significant inverse correlation with the serum testosterone levels without a correlation with serum DHEAS.

Conclusion
This study indicates that testosterone but not DHEAS may play an important role in the severity of negative symptoms in male patients with schizophrenia.

Keywords:
dehydroepiandrosterone sulfate, negative symptoms, schizophrenia, testosterone

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Introduction

The diagnosis of schizophrenia is currently made using criterion-based systems, including positive (e.g. hallucinations and delusions) and negative (e.g. a volition and alogia) symptoms (Shirayama *et al.*, 2002).

The correlation between negative symptoms and loss of social function among schizophrenics has been increasingly recognized. The diagnosis of schizophrenia has therefore shifted toward the presence of negative symptoms (Akhondzadeh *et al.*, 2006).

Sex differences have been reported in schizophrenia and involve various aspects of the disease. The existence of sex differences in these areas strongly suggests a vital role played by gonadal hormones; the observations of an association between age of onset and reproductive age led some researchers to suggest an important pathogenic role of both estrogen and testosterone, and their interactions with neurotransmitters' system in specific brain regions (Goldstein, 1988; Goldstein and Tsuang, 1990).

Dehydroepiandrosterone (DHEA) and its sulfate conjugate (DHEAS) are neurosteroids that mediate several neurotransmitter systems coupled to ion channels, such as γ-aminobutyric acid (GABAA), *N*-methyl-D-aspartate (NMDA), and sigma receptors (Wen *et al.*, 2001).

DHEA metabolism has been reviewed recently; briefly, DHEA sulfotransferase catalyzes the transformation of DHEA into DHEAS (Falany *et al.*, 1995). Androstenedione is synthesized from DHEA by 3h-hydroxysteroid dehydrogenase/D5–D4 isomerase and from progesterone through 17-OH-progesterone by 17a-hydroxylase and 17,20-lyase (Rupprecht, 2003). The conversion of androstenedione into testosterone is catalyzed by 17h-hydroxysteroid dehydrogenase (King *et al.*, 1999). Previous studies investigating DHEA blood levels in concentrations in psychosis or schizophrenia have reported either low (Harris *et al.*, 2001), elevated (Di Michele *et al.*, 2005), or no differences in DHEA levels (Ritsner *et al.*, 2004) compared with matched healthy controls. In addition, they have unaltered (Mason *et al.*, 1988; Markianos *et al.*, 1999) or significantly lower serum testosterone levels, especially among patients treated with high-dose first-generation antipsychotic agents (Rinieris *et al.*, 1989; Kaneda and Fujii, 2000; Kaneda, 2003), and in male schizophrenia patients before and during treatment, but not after recovery (Taherianfard and Shariaty, 2004). The inconsistencies in the findings published may be because

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of the wide clinical variability, small sample sizes, or differences in the age and duration of illness of patients (Cleare *et al*., 2004). The majority of studies do not report repeat data on serum DHEA and their key metabolites in patients compared with healthy controls over time controlling for confounding factors.

Although there exist a few studies on the relationship between the plasma levels of testosterone and negative symptoms in patients with schizophrenia, the exact role of reproductive hormones in the pathophysiology of the schizophrenia is still emerging (Seeman, 1996; Shirayama *et al*., 2002; Akhondzadeh *et al*., 2003; Goyal *et al*., 2004).

The goals of this study were to determine whether alterations in serum DHEAS and testosterone occur in treated chronic schizophrenia patients compared with healthy controls and to evaluate the relationship between the plasma level of testosterone and DHEAS and the severity of negative symptoms in patients with chronic schizophrenia.

Participants and methods

Participants

Two groups of patients were invited to participate in the study.

Patients

A total of 50 patients were recruited from among consecutive attenders of the psychiatric inpatient department and outpatient clinics of Zagazig University Hospitals from April 2010 to March 2011, with a diagnosis of schizophrenia according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV).

All patients had chronic schizophrenia, defined as having symptoms of schizophrenia for at least 2 years before recruitment.

Their psychiatric symptoms were stable before the examination, and their doses of antipsychotic medications and other concomitant psychotropic medications such as benzodiazepines, antiparkinsonian agents, mood stabilizers, and/or hypnotics were fixed for at least 2 weeks before participation in this study.

The patients were considered symptomatically stable if there had been no appreciable change in their psychotic symptoms during the 4 weeks before participation in this study, irrespective of the severity of their symptoms.

They had no abnormal medical findings as evidenced by assessment of medical histories and physical examinations and no other chronic medical illness, substance abuse (including anabolic steroids), or substance dependence in the past year.

Patients with a BMI less than 20 kg/m^2 or more than 30 kg/m^2, those with drug-induced extrapyramidal symptoms, and depressed patients were excluded.

Controls

An equal number of apparently healthy men, matching the recruited patients as much as possible in terms of age, and with no history of treatment for any neuropsychiatric disorder were recruited.

An informed consent was obtained from all the participants after the procedures had been fully explained. The study was approved by the ethical committee of the institution.

Methods

Assessments

Clinical assessment: semistructured interview

Participants were subjected to a semistructured psychiatric interview, using a specially designed interview derived from the Psychiatric Department sheet of Zagazig University.

The semistructured interview included a full psychiatric sheet, which allowed each patient to receive a psychiatric diagnosis at the end of the interview, during which the DSM-IV-TR (American Psychiatric Association, 2000) diagnosis of a schizophrenia disorder was confirmed.

Psychometric procedures

The following scales were administered:

Positive and Negative Syndrome Scales (*PANSS*) (Kay *et al*., 1987): This is a 30-item, psychopathology rating scale, based on a semistructured clinical interview. The scale was designed to measure positive and negative schizophrenic symptoms, and related variables such as cognitive, affective, and social functioning. It has been evaluated rigorously from a psychometric perspective and has been used widely in several clinical studies. The scale yields five scores: a positive symptom score, a negative symptom score, a general psychopathology score, a total score, and a composite score.

The Calgary Depression scale for Schizophrenia (Addington *et al*., 1990): The Calgary Depression scale for Schizophrenia (CALG) is used to assess the mood state of schizophrenic patients. The patients were asked about (a) depression (his mood over the last 2 weeks), (b) hopelessness (how do you see the future), (c) self-depreciation, (d) guilty ideas of reference, (e) pathological guilt, (f) morning depression, (g) early awakening, (h) suicide, and (i) observed depression (on the basis of interviewers' observations). These items were described according to the severity (absent, mild, moderate, and severe).

The Drug-induced Extrapyramidal Symptoms Scale (*DIEPSS*) (Inada, 1996): The DIEPSS, which consists of eight individual items and one global item, was used to assess treatment-emergent extrapyramidal symptoms.

The eight individual items include (1) gait, (2) bradykinesia, (3) sialorrhea (increased salivation), (4) muscle rigidity, (5) tremor, (6) akathisia, (7) dystonia, and (8) dyskinesia. The global item is overall severity. Extrapyramidal syndromes, as measured by the DIEPSS,

were grouped into four categories: (a) parkinsonism, (b) akathisia, (c) dystonia, and (d) dyskinesia.

The parkinsonism syndrome consisted of DIEPSS items 1–5. The akathisia, dystonia, and dyskinesia syndromes consisted of DIEPSS items 6, 7, and 8, respectively. The severity of each item was rated from 0 (normal) to 4 (severe).

The patients filled in a questionnaire consisting of nine comprehensive questions aimed to detect typical symptoms of parkinsonism including akathisia, dystonia, and dyskinesia.

Body mass index

BMI a statistical measure of the weight of an individual scaled according to height, sometimes referred to as body weight index. It is defined as the individual's body weight divided by the square of their height.

Patients with a BMI below 18.5 kg/m^2 were categorized as underweight, 18.5–24.9 kg/m^2 were categorized as normal, 25.0–29.9 kg/m^2 were categorized as overweight, and at least 30 kg/m^2 were categorized as obese according to the WHO classification.

Laboratory Investigations

Ten milliliters of blood sample was collected in a tube to determine the levels of total testosterone and DHEAS. Blood samples for the hormone estimation were collected from 8:00 to 9:00 a.m. The sera were prepared and stored at $-20^{\circ}C$ until the time of analysis. Testosterone and DHEAS were assayed by a radioimmunoassay.

Statistical analysis

Data were statistically described in terms of mean ± SD, frequencies (number of cases), and percentages when appropriate. A comparison of the quantitative variables between the study groups was performed using the Student *t*-test for independent samples. For comparison of categorical data, the χ^2-test was carried out. The exact test was used when the expected frequency was less than 5. The correlation between various variables was determined using the Pearson moment correlation equation for a linear relation in normally distributed variables and the Spearman rank correlation equation for non-normal variables. *P* values less than 0.05 were considered statistically significant. All statistical calculations were carried out using computer programs Microsoft Excel 2007 (Microsoft Corporation, New York, USA) and statistical package for the social science (SPSS Inc., Chicago, Illinois, USA) version 15 for Microsoft Windows.

Results

The sociodemographic and clinical characteristics of the patients and the control group are presented in Table 1. Because of the selection procedures, the patients and the controls were comparable in terms of age, BMI, and education. Table 1 also shows that there was a statistically significant difference between the group of patients and the control individuals in the level of serum testosterone hormone, but there were no statistically significant differences in the DHEAS level. Table 1 indicates that the mean age at onset of the disease was 19.4 ± 3.4 years (range between 15 and 28 years) and the duration of illness was 9.3 ± 61 years (range between 2 and 23 years); the mean values of the PANSS score were as follows: total 84.8 ± 12.6, positive 20.6 ± 4.7, negative 22.1 ± 4.5, and psychopathology 41.8 ± 7.3.

Table 1 Sociodemographic and clinical characteristics of the patients and the control group

	$\bar{X}$ ± SD		
Sociodemographic data	Patients (*N*=50)	Controls (*N*=50)	Significance
Age (years)			
X±SD	28.7±6.6	29.7±3.6	*t*=0.94
Range	20–40	21–37	*P*=0.34
BMI			
X±SD	25.6±2.97	26.2±203	*t*=1.13
Range	20–30	21–29	*P*=0.26
Education level			
0	2±4.0	4±8.0	*t*=5.22
1	12±24.0	4±8.0	*P*=0.26
2	12±24.0	14±28.0	
3	18±36.0	22±44.0	
4	6±12.0	6±12.0	
Serum testosterone level			
X±SD	3.88±1.6	5.8±1.5	*t*=5.98
Range	1.4–7.8	2.9–7.9	*P*<0.001
DHEAS level			
X±SD	223.6±100.7	229.96±26.6	*t*=0.43
Range	50–501	180–273	*P*=0.66
Age at onset			
X±SD	19.4±3.4		
Range	15–28		
Duration of illness			
X±SD	9.3±61		
Range	2–23		
PANSS			
Total	84.8±12.6 (65–122)		
Positive	20.6±4.7 (14–31)		
Negative	22.1±4.5 (15–32)		
General	41.8±7.3 (30–59)		

DHEAS, dehydroepiandrosterone sulfate; PANSS, Positive and Negative Syndrome Scale.
Statistically significant difference ($P \leq 0.05$).

Table 2 shows that there was no statistically significant difference between the serum testosterone level and the age of the patients, age at onset, BMI, and duration of illness, but there was a statistically significant difference in the PANSS score. The PANSS negative scores showed a significant inverse correlation with the serum testosterone level ($r = -0.481$, $P < 0.001$) and there was no significance difference between the DHEAS level and the age of the patients, age at onset, BMI, duration of illness, and the PANSS negative score.

Table 3 shows the correlation between serum testosterone and the DHEAS level and the severity of negative symptoms, and indicates that there was a highly significant negative correlation between the severity of different negative symptoms and serum testosterone level as, when testosterone decreases, the severity of negative symptoms increases, but there was no correlation between negative symptoms and the serum level of DHEAS.

Table 2 Correlation between serum testosterone, dehydroepiandrosterone sulfate, and other parameters

	Serum testosterone		DHEAS	
Patients parameters	*r*	*P*	*r*	*P*
Age of patients	−0.17	>0.05	−0.13	>0.05
Age at onset	−0.12	>0.05	−0.14	>0.05
Duration of illness	−0.11	>0.05	−0.1	>0.05
BMI	−0.19	>0.05	−0.22	>0.05
PANSS				
Total	−0.56	<0.001	0.31	<0.05
Positive	−0.40	<0.05	0.33	<0.05
Negative	−0.481	<0.001	0.19	>0.05
General	−0.48	<0.001	0.47	<0.001

DHEAS, dehydroepiandrosterone sulfate; PANSS, Positive and Negative Syndrome Scale.
Statistically significant difference ($P \leq 0.05$).

Table 3 Correlation between serum testosterone and dehydroepiandrosterone sulfate level and the severity of negative symptoms

	Serum testosterone		DHEAS	
Negative scale of PANSS	*r*	*P*	*r*	*P*
Blunted affect	−0.65	<0.001	−0.19	>0.05
Emotional withdrawal	−0.41	<0.001	−0.22	>0.05
Poor rapport	−0.42	<0.001	−0.13	>0.05
Passive social withdrawal	−0.59	<0.001	−0.12	>0.05
Difficulty in abstract thinking	−0.38	<0.001	−0.18	>0.05
Lack of spontaneity and flow of conversation	−0.02	>0.05	−0.19	>0.05
Stereotyped thinking	−0.43	<0.001	−0.11	>0.05

DHEAS, dehydroepiandrosterone sulfate; PANSS, Positive and Negative Syndrome Scale.
Statistically significant difference ($P \leq 0.05$).

Discussion

The results of this study indicate that in medicated male patients with chronic schizophrenia, compared with healthy controls, the serum concentration of testosterone was found to be increased, but the DHEAS level was normal, and that the serum total testosterone level is inversely correlated with negative symptoms. Moreover, there was no any correlation between testosterone and DHEAS or between DHEAS and the clinical characteristics of the patients. Decreased serum testosterone levels among our patients have also been reported by Ko *et al*., 2007, who found strongly decreased serum testosterone levels in a group of 35 male inpatients with schizophrenia, and the serum testosterone level was inversely correlated with negative symptoms in male patients with chronic schizophrenia. These findings suggest that lower total and free testosterone levels may reflect more severe negative symptoms in male patients with schizophrenia.

Our results are also supported by the finding reported by Akhondzadeh *et al.* (2006). The results of this study are in agreement with previous studies reporting the relationship between gonadal hormones and negative symptoms in male patients with chronic schizophrenia (Shirayama *et al.*, 2002; Goyal *et al.*, 2004).

With respect to DHEAS (sulfate conjugate of DHEA), some studies have reported low DHEA levels in schizophrenic patients compared with healthy controls (Harris *et al.*, 2001); however, other studies have not reported any differences between patients with schizophrenia and normal controls (Brophy *et al.*, 1983; Ritsner *et al.*, 2004, 2006). Another study reported higher DHEAS levels in young male patients with schizophrenia (Oades and Schepker, 1994) and higher DHEAS levels in first-episode schizophrenia patients (Strous *et al.*, 2004). Plasma levels of DHEA were found to be strongly elevated in a group of schizophrenic patients compared with that of control individuals as reported by Di Michele *et al*. (2005).

However, Goyal *et al.* (2004) reported that both serum testosterone and DHEAS levels were lower in a patient group with predominantly negative symptoms than in a patient group with predominantly positive symptoms.

Previous studies investigating DHEA and testosterone blood levels in psychosis or schizophrenia have reported either low DHEA (Harris *et al.*, 2001), elevated DHEA (Di Michele *et al*., 2005), or no differences in DHEA levels (Ritsner *et al.*, 2004) compared with matched healthy controls. DHEAS levels have been reported to be elevated (Strous *et al.*, 2004) or in the control range (Ritsner *et al.*, 2004).

In addition, unaltered (Markianos *et al.*, 1999) or significantly lower serum testosterone levels have been reported (Kaneda, 2003). The inconsistencies in published findings may be because of the wide clinical variability, small sample sizes, or differences in the age and duration of illness of patients (Cleare *et al*., 2004). The majority of studies have not reported repeat data on serum DHEA and their key metabolites in patients compared with healthy controls.

Many factors affect serum androgen levels as serum testosterone levels decrease with age, starting from the fifth decade of life (Gray *et al.*, 1991). Maximal values of circulating DHEAS are attained between the ages of 20 and 30 years (Orentreich *et al.*, 1984); the serum testosterone level has a diurnal variation, with the highest values at 8:00 a.m. and the lowest values in the late afternoon (Bremner *et al.*, 1983); adiposity, as assessed by the BMI, is a negative determinant of serum testosterone levels (Zumoff *et al.*, 1990).

Therefore, to reduce the effects of these factors on androgen levels, we recruited young male schizophrenic patients aged between 20 and 39 years, taking blood samples between 8:00 and 9:00 a.m., and excluded patients who were obese, that is, those with a BMI of over 30 kg/m^2 in this study.

Previous studies have reported controversial results on the relationship between serum testosterone level and negative symptoms in male schizophrenia patients.

However, these previous studies provide possible explanations for the role of testosterone in the negative symptoms of schizophrenia through its effects on

receptors of gonadal hormones that are concentrated in hypothalamic and limbic systems involved in perception, cognition, and behavior (Stevens, 2002).

Testosterone modulates the action of various neurotransmitters and neuropeptides (Białek *et al*., 2004) and through the neuroprotective or neurotrophic actions of testosterone on motor and autonomic neurons (Białek *et al*., 2004).

This study had some limitations. First, we did not measure other related hormone levels, including the gonadotropin-releasing hormone, luteinizing hormone, adrenocorticotropic hormone, prolactin, cortisol, and estradiol, and thus we did not identify their associations with testosterone and DHEAS levels. Second, the number of participants in this study was small; therefore, a larger sample size is recommended for further studies.

Finally, all patients included in our study received antipsychotic drugs; therefore, it is recommended that in further studies, patients who are not under any treatment be studied in order to exclude the effect of those drugs on the level of serum hormones.

However, this study indicates that testosterone but not DHEAS may play an important role in the severity of negative symptoms in male patients with schizophrenia.

Conclusion

There is a need to determine the serum total testosterone hormone level in male schizophrenia patients with predominantly negative symptoms as it may reflect an associative relationship of testosterone with the severity of negative symptoms in male schizophrenic patients.

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Conflicts of interest

There are no conflicts of interest.

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