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MIDDLE EAST CURRENT PSYCHIATRY

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Aims and Scope

MECPsych is one of the Middle East's leading psychiatric journals. It covers all branches of the subject, with particular emphasis on the clinical aspects of each topic. *MECPsych* is committed to keeping the field of psychiatry in the Middle East updated and relevant by publishing the latest advances in the diagnosis and treatment of mental illness. *MECPsych* publishes high-quality, scientific articles in English, representing clinical and experimental work in psychiatry. The journal acts as an international forum for the dissemination of information advancing the science and practice of psychiatry *MECPsych* encourages articles in compliance with the Madrid and Helsinki Declarations.

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The effect of commonly used antidepressant drug groups on sleep profile with major depression: a case–control study

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Objectives

One of the adjuvant of an ideal antidepressant is its desirable effect on sleep. Nevertheless, head-to-head comparisons between different antidepressants, designed specifically to test their sleep effects in a clinical setting are still scarce. This study aimed at comparing the effect of commonly used antidepressant groups on sleep profile as measured by Polysomnogram of depressed patients in a clinical setting.

Materials and methods

Thirty newly diagnosed nonmedicated depressed patients were recruited from the outpatient and inpatient departments of the Institute of Psychiatry, Ain Shams University Hospitals, in the period May to November 2008. All patients were diagnosed according to International Classification of Diseases-10 research diagnostic criteria of major depression with a score of greater than 14 on the Hamilton Depression Rating Scale, and screened for eligibility in the study using full physical examination, routine laboratory tests, electroencephalogram, and the psychiatric history and mental state examination sheet of the Institute of Psychiatry, Ain Shams University. They were classified according to the prescribed antidepressants according to their treating doctor into tricyclics antidepressants (TCAs) group (15 patients) and selective serotonin reuptake inhibitors (SSRIs) group (15 patients). The control group consisted of 10 healthy individuals matched with patients for age and sex. Recruited depressed patients as well as controls were subjected to (i) structured sheet for sleep disorders, (ii) Hamilton Depression Rating Scale-17 for measuring the efficacy of antidepressants, and (iii) Polysomnographic study. Patients were subjected to these assessments two times, before antidepressant start and 1 month after antidepressant start. Controls were subjected to these assessments once immediately after recruitment.

Results

TCAs improved all sleep parameters, except for sleep stage I and III and slow-wave sleep percentage (SWS %). SSRIs improved all sleep parameters, except for sleep stages I, II, III, and IV and SWS%. TCAs led to a more significant decrease in sleep latency, arousal index, sleep stage I as well as a more significant increase in sleep efficiency, sleep stages III and IV, and SWS% than with SSRIs. SSRIs led to a more significant decrease in rapid eye movement percentage (REM%) and to a more statistically significant increase in sleep stage II than with TCAs. There was no statistically significant difference between the two drug groups regarding their effect on REM density, REM latency, and periodic limb movement index.

Conclusion

Commonly used antidepressants in clinical practice have a positive effect on objective sleep parameters, except for sleep microstructure. TCAs significantly improved objective sleep quality away from its antidepressant therapeutic effect compared with SSRI. Selecting the proper antidepressant for depression with profound sleep problems is an art, which needs future research.

Keywords:
antidepressants, depression, sleep

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Introduction

Sleep disturbance is a prevalent key feature of depression that affects the course of illness, treatment compliance, and treatment response [1]. More than 80% of people with depression experience sleep disturbances, such as early morning waking or frequent awakenings throughout the whole night [2,3]. Even in chronic low-grade depression, which affects roughly 3% of people, insomnia and/or sleepiness may be the most prominent symptom [4].

Disturbed sleep in depression is either objective as shortened rapid eye movement (REM) latency, disruption of sleep continuity, early morning waking, and reduction of slow-wave sleep (SWS) [5] or subjective as total sleep time (TST), difficulty in initiating sleep, and interrupted sleep. This subjective sleep disturbance affects the patient satisfaction by the antidepressant [6,7], that is, does my antidepressant improve my sleep?

One of the adjuvants of an ideal antidepressant is its desirable effect on sleep. Antidepressants that reduce restless sleep and awakening with no REM suppression and that improve alertness are considered ideal [8]. The efficacy of antidepressants generally appears to be equal [9]. However, some compounds claim advantages over others related to specific side effects such as sexual dysfunction and/or sleep disturbance. Nevertheless, head-to-head comparisons between the commonly used antidepressant designed specifically to test these claims in a clinical setting are still scarce [10].

Polysomnogram (PSG) translates subjective sleep complaints to objective findings that help us to quantify the effect of different antidepressants on sleep, which will help in predicting the patient's satisfaction and in enhancing his/her compliance [7,11].

This study aimed at comparing the effect of commonly used antidepressant groups on sleep profile as measured by PSG of depressed patients in a clinical setting.

Patients and methods

Consecutive newly diagnosed nonmedicated depressed patients attending both the outpatient and inpatient departments of the Institute of Psychiatry, Ain Shams University Hospitals, in the period May to November 2008 were invited to participate in the study. Depression was diagnosed according to International Classification of Diseases-10 research diagnostic criteria of major depression with a score of greater than 14 on the Hamilton Depression Rating Scale (HAMD).

The depressed patients who agreed to participate in this study were asked for written consent and were screened for eligibility in the study using full physical examination, routine laboratory tests including blood chemistry, thyroid functions, liver functions, urine analysis, electroencephalogram (EEG), and the psychiatric history and mental state examination sheet of the Institute of Psychiatry, Ain Shams University.

Depressed patients were excluded if they were younger than 20 years and older than 40 years, had comorbid psychiatric disorder other than depression (including bipolar depression), were already maintained on antidepressant(s), had a history of use of antidepressants within the last 6 months, had a history of treatment-resistant depression (nonresponsive to a single antidepressant at therapeutic doses for at least 6 weeks), had a past/current history of epilepsy as confirmed by EEG, had a past/current history of head trauma, had comorbid physical condition and/or drugs that could affect the sleep EEG, had a medical contraindication to antidepressant drugs (including pregnancy, lactation, or not using contraception while of childbearing potential in women), had serious suicide risk, were unable to maintain a consistent sleep pattern (such as shift workers), had current sleep/wake disorder, and/or were on psychoactive substances (including benzodiazepines) in the last 6 weeks before the study as a washout period.

Patients were classified according to the prescribed antidepressant according to their treating doctor into two groups: group 1 had been receiving tricyclics antidepressants (TCAs) and group 2 had been receiving selective serotonin reuptake inhibitors (SSRIs). We had 15 patients in each group after dropouts, which were five in each group mainly because of intolerable side effects of drugs and/or severe sleep complaint that needed rapid intervention.

Control group consisted of 10 healthy individuals who were selected from among the hospital employees after being screened for eligibility of the study in the same way similar to patients. They were matched with patients for age and sex.

Recruited depressed patients as well controls were subjected to (i) structured sheet for sleep disorders, derived from the sleep disorder questionnaire of Douglass *et al.* [12] that contained 72 questions regarding past or current history of sleep disturbance, sleep disorder, psychiatric disorder, and drug history; (ii) HAMD-17 for measuring the efficacy of antidepressants; and (iii) PSG study conducted for three successive nights; we considered the values of the last night in order to take the most valid reading after the patient felt comfortable with the study place.

Patients were subjected to these assessments two times: before antidepressant start and 1 month after antidepressant start. Controls were subjected to these assessments once immediately after recruitment.

Tools

HAMD [13] is a valid reliable multidimensional measure covering wide dimensions of depressive symptomatology, including depressed mood, vegetative symptoms, anxiety, agitation, and insight [14] and being sensitive to treatment change [15]. Reduction of 50% of pretreatment depressive symptoms assessment considered response to treatment and score less than or equal to 7 considered clinical remissions [16]. In antidepressant clinical trials, HAMD-17 has been the gold standard instrument for establishing and comparing the efficacy of new treatments [17,18]. Cutoff point and scoring of depression severity as determined by HAMD-17 are as follows: no depression (≤ 7), mild (8–13), moderate (14–18), severe (19–22), and very severe (> 23).

Overnight polygraph sleep recording (PSG) was carried out by a remote cable that used a 16-channel polygraph including EEG, submental chin electromyelogram, and electro-occulogrpahy. Sleep was recorded automatically with visual correction by an experienced sleep scorer according to standard Rechtschaffen and Kales [19]

criteria. Many parameters were derived from the PSG study including sleep staging time, TST, number of awaking, sleep latency, wakefulness after sleep onset, sleep efficiency, REM latency, REM density, periodic limb movement index (PLMI), and arousal index.

Statistical analysis

Data coded and revised were introduced to an EXCEL database to be manipulated and analyzed later using the 16th version of SPSS (SPSS, Inc., Chicago, IL, USA). For the sake of description, categorical data were presented as number and percentage; means, standard deviation, and 95% confidence limit were used to describe continuous variables. One-way analysis of variance was used to test any significant differences between more than two groups. Kruskall–Wallis test was used to analyze differences of continuous variables between more than two groups. The paired *t*-test was used to analyze the difference within individual group before and after treatment of normally distributed variables. Statistically significance level was set at a value of less than or equal to 0.05; highly significant level was at a value less than 0.01; and very highly significant level was at a value less than 0.001.

Results

Two groups of depressed patients were identified in our study. Each group included 15 patients. The first group (1) received TCAs (11 received amitriptyline and four received imipramine) within the therapeutic dose (75–100 mg/day); their mean age was 34.73 ± 4.89 years with eight of them being women (53.3%) and seven of them being men (46.6%). The second group (2) received SSRIs (12 received paroxetine and three received citalopram) within the therapeutic dose (20 mg/day); their mean age was 34.60 ± 5.36 years with nine of them being women (60%) and six of them being men (40%).

The third group in our study was of healthy controls (3) matched with patients for sex and age. Their mean age was 33 ± 4.42 years with five of them being women (50%) and five of them being men (50%). There was no statistically significant difference between patients and controls regarding age and sex ($P > 0.05$).

In comparing sleep parameters of both TCAs group (1) and SSRIs group (2) versus controls (3) at the baseline (pretreatment), there was statistically significant longer sleep latency, poorer sleep efficiency, higher arousal index, longer stage one, shorter stage three and four and SWS, higher REM percentage and density, and shorter REM latency in patients than in controls. With regard to PLMI, it was higher only in group 1 than in controls with no statistically significant difference ($P = 0.357$) found between group 2 and controls (Table 1).

In comparing sleep parameters of TCAs group 1 versus SSRIs group 2 at the baseline (pretreatment), there was no statistically significant difference in all parameters between the two groups, except for significantly longer stage four and higher SWS percentage (SWS%) and PLMI in group 1 than in group 2 (Table 2).

In assessing the response to treatment in the two groups by comparing the scores on HAMD before and after treatment, there was statistically significant lowering of the HAMD score in both groups; however, it reached the response level (lower than 50% from the initial score) only in group 1. There was no statistically significant difference between the two groups after treatment as regards the HAMD score (Table 3).

With regard to the effect of TCAs on sleep parameters, all parameters were improved after receiving TCAs, except for sleep microstructure where stage one showed no statistically significant shortening after treatment and stage 3 and SWS% showed significant prolongation but still below the normal values (Table 4).

With regard to the effect of SSRIs on sleep parameters, all parameters were improved after receiving SSRIs, except for sleep microstructure, where stage one showed no statistically significant shortening after treatment, stages 2, 3, and 4 showed significant prolongation, and SWS% showed a significant increase, but all were still below the normal values (Table 5).

Table 1 Comparing sleep parameters of depressed patients maintained on TCAs (group 1) versus controls and depressed patients maintained on SSRIs (group 2) versus controls at the baseline pretreatment level

Sleep parameter	TCAs group (mean ± SD)	SSRIs group (mean ± SD)	Controls (mean ± SD)	*P* value
Sleep latency	42.53 ± 7.74	41.6 ± 10.7	19 ± 2.4	0.000
Sleep efficiency	37.35 ± 5.08	40.58 ± 7.3	91.18 ± 2.47	0.000
Arousal index	17.93 ± 1.31	17.4 ± 1.79	5.78 ± 1.83	0.000
Sleep stage 1	8.19 ± 1.2	10.18 ± 3.49	7.78 ± 12.04	0.00
Sleep stage 2	51.41 ± 0.92	52.55 ± 3.17	19.43 ± 2.6	0.00
Sleep stage 3	6.67 ± 10.07	3.87 ± 0.96	9.99 ± 0.71	0.00
Sleep stage 4	3.77 ± 0.71	2.76 ± 1.03	10.12 ± 0.52	0.000
SWS%	7.87 ± 0.87	6.63 ± 1.41	20.17 ± 0.61	0.000
PLMI	2.73 ± 0.65	2.29 ± 0.47	2.08 ± 0.46	0.006 0.357
REM%	31.87 ± 3.25	30.65 ± 5.25	25.21 ± 1.20	0.001
REM density	26.75 ± 0.74	26.03 ± 1.63	20.74 ± 0.83	0.000
REM latency	44.40 ± 12.40	46.24 ± 13.03	68.4 ± 5.93	0.00

Statistical significance level was set at a value ≤ 0.05, highly significant level at a value < 0.01, and very highly significant level at a value < 0.001.
PLMI, periodic limb movement index; REM, rapid eye movement; SSRIs, selective serotonin reuptake inhibitors; SWS, slow-wave sleep; TCAs, tricyclic antidepressants.

Table 2 Comparing sleep parameters of depressed patients maintained on TCAs (group 1) versus depressed patients maintained on SSRIs (group 2) at the baseline pretreatment level

Sleep parameter	TCA group (mean ± SD)	SSRI group (mean ± SD)	*P* value
Sleep latency	42.53 ± 7.74	41.67 ± 10.71	0.774
Sleep efficiency	37.35 ± 5.08	40.58 ± 7.31	0.124
Arousal index	17.93 ± 1.31	17.47 ± 1.79	0.452
Stage 1	8.19 ± 1.2	10.18 ± 3.49	0.12
Stage 2	51.41 ± 0.92	19 ± 2.4	0.61
Stage 3	6.67 ± 10.07	3.87 ± 0.96	0.14
Stage 4	3.77 ± 0.71	2.76 ± 1.03	0.002
SWS%	7.87 ± 0.87	6.63 ± 1.41	0.003
PLMI	2.73 ± 0.65	2.29 ± 0.47	0.030
REM%	31.87 ± 3.25	30.65 ± 5.25	0.388
REM density	26.75 ± 0.74	26.03 ± 1.63	0.102
REM latency	44.40 ± 12.40	46.24 ± 13.03	0.57

Statistical significance level was set at a value ≤ 0.05, highly significant level at a value <0.01, and very highly significant at a value <0.001.
PLMI, periodic limb movement index; REM, rapid eye movement; SSRIs, selective serotonin reuptake inhibitors; SWS, slow-wave sleep; TCAs, tricyclic antidepressants.

On comparing the effect of TCAs and SSRIs on sleep parameters, TCAs led to a more statistically significant decrease in sleep latency, arousal index, sleep stage 1 as well as a more statistically significant increase in sleep efficiency, sleep stages 3 and 4, and SWS% than with SSRIs. In contrast, SSRIs led to a more significant decrease in REM% and a more statistically significant increase in sleep stage 2 than with TCAs. There was no statistically significant difference between the two drug groups regarding their effect on REM density, REM latency, and PLMI (Table 6).

Discussion

At pretreatment baseline, our depressed patients in the two treatment groups had sleep disturbance in the form of longer sleep latency, poorer sleep efficiency, higher arousal index, longer stage one, shorter stages three and four (SWS), higher REM percentage and density, and shorter REM latency than in controls. These findings are in accordance with most of the scientific studies regarding sleep disturbance in depression as those of Thase *et al.* [20], Rush *et al.* [21], Rechtschaffen *et al.* [22], and Doghramji [6] who found the same findings.

There were no statistically significant pretreatment differences between the two groups on nearly all the sleep measures, except for TCAs group that had significantly longer stage four and higher SWS%, which reflects better sleep and higher PLMI, which further reflects poorer sleep than the SSRIs group. These differences entirely occurred by chance as we selected patients already after prescription of the drug for the two groups randomly. Moreover, it may reflect the prescription habits in our practice, which differentiate between TCAs and SSRIs according to drug cost and/or severity of depression, with more TCAs being prescribed for severe depression [23,24]. To our knowledge, no research reflecting actual prescription habits of antidepressants in our culture is available.

Home sleep recording performed by Hicks *et al.* [25] could be comparable with our study, which provided valid data for sleep assessment on three successive nights as a period of adjustment to the unfamiliar surroundings reflecting the most comfort for the patient. They found higher SWS compared with most sleep laboratory studies in depression. This supports the use of home sleep than sleep center recordings as it reflects better sleep quality.

Table 3 Comparing HAMD score of depressed patients maintained on TCAs (group 1) versus depressed patients aintained on SSRIs (group 2) before and after treatment

Group 1 (before treatment)	Group 1 (after treatment)	*P* value
34.53 ± 3.72	15.93 ± 3.83	0.00
Group 2 (before treatment)	Group 2 (after treatment)	*P* value
32 ± 4.49	19.67 ± 6.16	0.00
Group 1 (after treatment)	Group 2 (after treatment)	*P* value
15.93 ± 3.83	19.67 ± 6.16	0.056

Statistical significance level was set at a value ≤ 0.05, highly significant level at a value <0.01, and very highly significant at a value <0.001.
HAMD, Hamilton Depression Rating Scale; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants.

Table 4 Comparing sleep parameters in depressed patients maintained on TCAs (group 1) before and after receiving TCAs

Sleep parameter	Before (mean ± SD)	After (mean ± SD)	*P* value
Sleep latency	42.53 ± 7.74	20.27 ± 4.40	0.00
Sleep efficiency	37.35 ± 5.08	69.20 ± 7.43	0.00
Arousal index	17.93 ± 1.31	9.92 ± 1.50	0.00
Stage 1	8.19 ± 1.2	7.53 ± 1.21	0.07
Stage 2	51.41 ± 0.92	52.93 ± 1.03	0.00
Stage 3	6.67 ± 10.07	7.09 ± 0.97	0.01
Stage 4	3.77 ± 0.71	7.43 ± 1.40	0.00
SWS%	7.87 ± 0.87	14.51 ± 2.07	0.00
PLMI	2.73 ± 0.65	2.79 ± 0.64	0.52
REM%	31.87 ± 3.25	25.00 ± 2.78	0.00
REM density	26.75 ± 0.74	22.39 ± 1.49	0.00
REM latency	44.40 ± 12.40	62.80 ± 5.39	0.00

Statistical significance level was set at a value ≤ 0.05, highly significant level at a value <0.01, and very highly significant at a value <0.001.
PLMI, periodic limb movement index; REM, rapid eye movement; SWS, slow-wave sleep; TCAs, tricyclic antidepressants.

Table 5 Comparing sleep parameters in depressed patients maintained on SSRIs (group 2) before and after receiving SSRIs

Sleep parameter	Before (mean ± SD)	After (mean ± SD)	*P* value
Sleep latency	41.67 ± 10.71	27.80 ± 7.38	0.00
Sleep efficiency	40.58 ± 7.31	58.49 ± 8.59	0.00
Arousal index	17.47 ± 1.79	13.07 ± 2.18	0.00
Stage 1	10.18 ± 3.49	8.87 ± 1.94	0.08
Stage 2	52.55 ± 3.17	54.11 ± 13.32	0.01
Stage 3	3.87 ± 0.96	5.89 ± 1.05	0.00
Stage 4	2.76 ± 1.03	5.89 ± 1.05	0.00
SWS%	6.63 ± 1.41	11.76 ± 1.26	0.00
PLMI	2.29 ± 0.47	2.52 ± 0.50	0.03
REM%	30.65 ± 5.25	21.57 ± 2.77	0.00
REM density	26.03 ± 1.63	22.11 ± 1.63	0.00
REM latency	46.24 ± 13.03	62.40 ± 6.46	0.00

Statistical significance level was set at a value ≤ 0.05, highly significant level at a value <0.01, and very highly significant at a value <0.001.
PLMI, periodic limb movement index; REM, rapid eye movement; SSRIs, selective serotonin reuptake inhibitors; SWS, slow-wave sleep.

Table 6 Comparing sleep parameters of depressed patients maintained on TCAs (group 1) versus depressed patients maintained on SSRIs (group 2) at the post-treatment level

Sleep parameter	After TCAs (mean ± SD)	After SSRIs (mean ± SD)	*P* value
Sleep latency	20.27 ± 4.40	27.80 ± 7.38	0.00
Sleep efficiency	69.20 ± 7.43	58.49 ± 8.59	0.00
Arousal index	9.92 ± 1.50	13.07 ± 2.18	0.00
Stage 1	7.53 ± 1.21	8.87 ± 1.94	0.02
Stage 2	52.93 ± 1.03	54.11 ± 13.32	0.00
Stage 3	7.09 ± 0.97	5.89 ± 1.05	0.00
Stage 4	7.43 ± 1.40	5.89 ± 1.05	0.00
SWS%	14.51 ± 2.07	11.76 ± 1.26	0.00
PLMI	2.79 ± 0.64	2.52 ± 0.50	0.21
REM%	25.00 ± 2.78	21.57 ± 2.77	0.00
REM density	22.39 ± 1.49	22.11 ± 1.63	0.62
REM latency	62.80 ± 5.39	62.40 ± 6.46	0.86

Statistical significance level was set at a value ≤ 0.05, highly significant level at a value < 0.01, and very highly significant at a value < 0.001.
PLMI, periodic limb movement index; REM, rapid eye movement; SSRIs, selective serotonin reuptake inhibitors; SWS, slow-wave sleep; TCAs, tricyclic antidepressants.

The linkage between sleep disturbance and depression in a clinical setting has long been recognized; however, many points are not much discussed. One of these points is compliance and its relation to sleep improvement by antidepressant. In our study, 25% of patients (five out of 20) in each group stopped their antidepressant secondary to intolerable side effects of drugs and/or severe sleep complaint that needs rapid intervention. This confirmed the unmet need of considering sleep effect and/or side effect as a key factor in tailoring antidepressant treatment in order to decrease the ratio of noncompliance on antidepressant with a high rate of early dropout in the course of treatment.

No difference in the dropout ratio in both TCAs and SSRIs groups was found in this study, which supports the findings of the meta-analyses carried out on SSRIs versus TCAs antidepressants that there were no significant differences in crude indices of compliance between fluoxetine and dothiepin, despite marked differences in side effect profile and dose regimen. This could be explained by the fact that studies that have examined compliance with antidepressants as a primary objective have usually been carried out in hospital outpatients, whereas the majority of prescriptions for antidepressants are made in primary care. However, most studies conducted in this setting have been small and almost all have relied on self-reports of tablet consumption by patients or on tablet counts by doctors. TCAs prescriptions in primary care are often at subtherapeutic doses, which will favor their compliance [7,26].

Assessment in this study was conducted 1 month after antidepressant start, which represented the midpoint in the duration needed (2–6 weeks) for antidepressant therapeutic action and was considered as a suitable time for assessing the drug effects on sleep, apart from either the effect of pretreatment depressive disorder or post-treatment recovery. If it was less than 4 weeks, it might have reflected the sleep disturbance of depression itself as the antidepressant did not yet exert its effect, and the symptoms are at their peak. If it was more than 4 weeks, it may have reflected the sleep improvement as a part of depression' remission [24].

SSRIs and TCAs are the antidepressants widely used in clinical practice [9,27] including ours. SSRIs have become a first-line treatment of depression over the past decade [28]. They offer significant advantages compared with the old compounds including TCAs and monoamine oxidase inhibitors (MAOI), such as fewer side effects and nonlethality in overdose [29]. However, some useful properties of the TCA, such as the promotion of sleep, do not apply to SSRIs. Indeed, the SSRIs can increase wakefulness, reduce TST, and sleep efficiency, having an alerting effect in acute treatment, although sleep disruption can ease with long-term treatment [30]. Further sleep disruption by antidepressant can lead either to disaffection with the treatment and early dropout or poor compliance, negatively affecting the overall outcome, or it could require additional treatment with a hypnotic [24].

The main TCA in our sample was amitriptyline (11 out of 15 patients) and the main SSRI was paroxetine (12 out of 15 patients). This practice appears similar to that of Netherlands where paroxetine is the most prescribed antidepressant, followed by amitriptyline, citalopram, and venlafaxine [24].

In our study, both TCAs and SSRIs were well tolerated and equally effective in treating depression. Both were effective in lowering the HAMD score; however, there was a statistically insignificant bias toward TCAs over SSRIs, which reached the sufficient response level defined as at least a 50% reduction in self-reported or observed symptoms. This difference in potential therapeutic effects of both groups could be explained by the severity of depression in our patients (all were moderate or severe scored > 14 on HAMD), and pretreatment difference between both groups on sleep parameters, which reflect to some extent better sleep quality in the TCA group.

All sleep parameters in our study were improved by both TCAs and SSRIs, except for sleep microstructure, which was not affected by both, where shortening of light sleep (stages 1 and 2) and prolongation of deep sleep (stages 2 and 4 and SWS%) showed either nonsignificant difference or significant difference but were still below the normal values. This highlighted an observation that sleep staging restoration may be a part of the remission or the recovery of the depression itself and not merely the sleep effects of antidepressant. This goes with Hicks *et al.* [25] who stated that significant drug effects on sleep, such as TST, sleep efficiency, and wakefulness after sleep onset, occurred early in treatment but stage 1 sleep and number of awakenings showed significant treatment effects more obviously at 8 weeks when the difference between different antidepressants on sleep quality disappeared. In addition, sleep microstructure may need the neuroadaptive changes that occur in the brain with prolonged administration and depression improves [31].

This observation confirmed the explanation postulated by Wilson *et al.* [30] who stated a postantidepressant treatment discrepancy between subjective and objective sleep findings, where subjective complaints about poor sleep were decreased when patients improved, in spite of lack of significant changes in objective measures of sleep as measured by PSG.

In contrast, nonimprovement of sleep microstructure found in this study could be considered as residual symptoms as reported by Nierenberg *et al.* [32] and Menza *et al.* [33], who found 44% of individuals who had achieved remission of depression, and yet had persistent sleep abnormalities.

In this study, TCAs were accompanied by more desirable sleep effects in comparison with SSRIs. All desirable sleep effects as represented in good sleep efficiency (decrease sleep latency and arousal index), shortening of light sleep (decrease in sleep stages 1 and 2), prolongation of deep sleep (increase in sleep stages 3 and 4, and SWS%) were more statistically significant in TCAs than in SSRIs group. This was not expected as our SSRIs group mainly used paroxetine, which is known as the most common SSRIs having sedative properties [34].

This weak sedative property of SSRIs in comparison with TCAs could be explained by the consequence of increased serotonin function, which leads to sleep disturbance early in treatment [35] as well as by the weak anticholinergic effects as reported by Rush *et al.* [21]. Furthermore, this finding accords Wilson and Nutt [36] findings of increased sleep disturbance after paroxetine, and Wilson *et al.* [30] who stated that TCAs tend to improve sleep fragmentation acutely, whereas SSRIs decrease sleep continuity, until there is resolution because of improvement of the depressive illness.

However, REM suppression as evident only in a decrease in REM% was more statistically significantly increased in SSRIs than in TCAs group. This finding egress the findings of Sharpley *et al.* [37] who found that REM sleep suppression remained marked throughout treatment with paroxetine in comparison with nefazodone, which had a small nonsignificant promoting effect on REM. There was no statistically significant difference between the two drug groups regarding their effect on both REM density and latency, a finding that contradicts other studies, which showed early changes of REM sleep latency and percentage and considered it as predictors of treatment outcome [38]. This contradiction may be related to the difference in time of assessment found in-between studies.

Antidepressants that increase serotonin function by blocking reuptake or by inhibiting metabolism have the greatest effect on REM sleep. The decrease in the amount of REM sleep appears to be greatest early in treatment, and gradually diminishes during long-term treatment, except after MAOIs when REM sleep is often absent for many months [39].

REM suppression occurred with all major antidepressant drugs, except trimipramine, mirtazapine, and nefazodone [40]. The MAOIs almost completely suppress REM sleep, whereas the TCAs and SSRIs have been shown to produce immediate (40–85%) and sustained (30–50%) reductions in REM sleep [41]. The clinical efficacy of antidepressant largely derives from their suppressant effects on REM sleep [42], Even though REM sleep time may be decreased, the density of REM periods may increase during antidepressant therapy [43].

However, REM suppression makes a conflict for the concept of ideal antidepressant [44] as, despite being responsible for the clinical efficacy of antidepressant, it often causes increased fatigue in patients who take large doses of antidepressants for extended periods of time. Such fatigue can occasionally interfere with a patient's everyday activities [38].

In conclusion, commonly used antidepressants in clinical practice have a positive effect on objective sleep parameters, except for sleep microstructure. TCAs significantly improved objective sleep quality away from its antidepressant therapeutic effect compared with SSRIs.

We hoped this study to be a cornerstone in future serials concerned with the effect of the new antidepressants on sleep quality early in the treatment, in order to enhance compliance with antidepressant, and to provide descriptive guidelines for effective treatment for sleep problems in depression. Selecting proper antidepressant for depression with profound sleep problems is an art that needs future research considering properties of an ideal antidepressant regarding its effect on sleep disturbances, including improving both subjective and objective sleep complaints, not causing either further sleep disruption or marked REM suppression, and rapidly improving the distribution of sleep symptoms of depression.

Limitations of this study include the small number of our sample, no comparison between subjective and objective sleep complaints for both groups, the absence of placebo group (used for comparison), and the nonseparation of the pretreatment baseline difference from the sleep effects.

There is no conflict of interest to declare.

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الملخص العربي

تأثير عقاقير الاكتئاب الأكثر استخداما علي صورة النوم فى مرضى الاكتئاب: دراسة مع عينة ضابطة

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هدف البحث: من متطلبات علاج الاكتئاب الأمثل أن يكون له تأ ثير مرغوب فيه علي النوم, لكن الدراسات التى تقارن تأثير المجموعات الدوائية بعضها ببعض مازالت قليلة في هذا المجال. و تهدف هذه الدراسة إلي مقارنة تأثير مجموعات أدوية الاكتئاب الأكثر استعمالا علي شكل النوم باستخدام معمل النوم في نسق إكلينيكي. **طريقة البحث:** و قد شملت عينة البحث 30 حالة اكتئاب جسيم جديدة مشخصة تبعا للتقسيم العالمى العاشر, لم يتعاط أفرادها أدوية كما سجل جميعهم أكثر من 14 على مقياس هاملتون. وقد خضع جميع أفراد العينة لعمل: فحص جسمانى شامل, الاختبارات المعملية الروتينية, رسم مخ, بالإضافة إلي فحص الحالة العقلية باستخدام نموذج مستشفى جامعة عين شمس. و قد تم تقسيم العينة الي مجموعتين: 1) مجموعة تعالج بمضادات الاكتئاب ثلاثية الحلقات (15 مريضا), 2) مجموعة تعالج بأدوية السيروتونين (15 مريضا). و تم اختيار 10 من الأصحاء متلائمين فى الجنس والعمر مع عينة البحث يمثلون العينة الضابطة. و خضع أفراد العينتين إلى: -استبيان مقنن لاضطرابات النوم, - مقياس هاملتون للاكتئاب, - معمل قياسات النوم. و تم تطبيق هذه الفحوص علي العينتين قبل استعمال الدواء ثم أعيد تطبيقها مرة ثانية علي أفراد عينة البحث فقط بعد شهر من العلاج. **نتائج البحث:** و قد أظهرت النتائج تحسنا عاما في صورة النوم باستعمال كلا المجموعتين- فيما عدا بعض التراكيب الدقيقة للنوم- مع بعض الفروق الطفيفة لصالح الأدوية ثلاثية الحلقات و خاصة في احساس المريض بالتحسن في النوم. **الاستنتاج:** و قد أكد البحث علي أهمية اختيار العقار المناسب في وجود مشاكل شديدة في النوم مما يجعلها نوعا من الفن (الحرفية) التي تحتاج إلى دراسات أكثر في المستقبل.

Burden of care on female caregivers and its relation to psychiatric morbidity

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Background
Recently, there have been increasing numbers of caregivers who provide care to their chronically ill family members. Care can represent a heavy burden and may put caregivers, who are mostly women (mother or wife), under a high level of stress. Culturally, such caregivers are expected to cope and not to complain.

Aim
To evaluate and compare the burden (objective and subjective) on female caregivers (mother or wife) who provide full-time care to family members who are suffering from either psychiatric or physical disorder.

Materials and methods
This study included 300 female caregivers (wife or mother) with 150 caring for patients suffering from a psychiatric illness and 150 looking after individuals suffering from a chronic physical illness. No male caregivers were included as culturally men are expected to be the breadwinners and if they have to provide care, this is likely to be as part time as most of their time would be dedicated for working outside home. This could provide men with an alternative time for ventilation or an outlet, which may bias the study results. Samples for the study were taken from the attendees of the outpatient clinics, University Hospital, Al-Azhar Faculty of Medicine, New Damietta, in the period 1 June 2007 to 31 May 2008. An approval was obtained from the ethics and scientific committee and informed consent was obtained from the individuals. All caregivers were assessed as follows: the Semistructured Clinical Interview using the diagnostic criteria of the Diagnostic and Statistical manual IV Text Revised (American Psychiatric Association), the Caregiver Strain Index, and Zarit Burden Interview (all these were translated, validated, culturally compatible, and doctor rated).

Results
The total sample included 300 female caregivers divided into two groups: the first group included 150 care providers of patients with psychiatric disorders, including 121 (80.7%) mothers and 29 (19.3%) wives, whereas the second group consisted of 150 female caregivers of individuals with chronic physical illness individuals, including 19 (12.7%) mothers and 131 (87.3%) wives. There was a significant difference between both groups with regard to distribution of nature of the relationship of female caregivers with the care recipients (mother or wife), their age, residence, and educational level. No significant difference regarding their job (the majority in both groups were unemployed) was observed. The objective burden was the highest in cases of poststroke disabilities, schizophrenia, chronic renal failure, chronic liver cell failure, and in those with bipolar disorder (<0.001). Similar distribution was observed in the subjective burden (<0.001). Caregivers suffered major depression in 102 cases (34.0%) and generalized anxiety disorders in 67 cases (22.3%). There was a statistically significant difference between mothers and wives regarding subjective burden and distribution of psychiatric disorders.

Conclusion
The study results may indicate that the burden (objective and subjective) of caregivers and the prevalence of psychiatric disorders in caregivers depend on the impact of the disease on the functional level of the patient. The level of subjective burden and prevalence of psychiatric disorders are higher in wives compared with mothers, which may be attributed to the difference in their appreciation of the caregiving situation and in their appreciation of their responsibility toward the individual needing care.

Keywords:
burden, caregivers, psychiatric morbidity

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Introduction

Providing care for a family member with mental illness is an overwhelming experience for the caregiver. On average, 250 000 patients with chronic mental illness discharge to the care of their families annually in USA [1].

Providing care for a patient with mental illness can be debilitating, stressful, and burdensome for the caregiver. In contrast, providing care to chronically ill or incapacitated family members may have an impact on family caregivers, such as increased self-respect or self-satisfaction from fulfilling a responsibility [2].

Previous studies have showed that caregivers have poor physical health and frequently experience social, emotional, and financial losses [3,4]. Interestingly, caregivers' stress and support are an integral element of an individual patient's assessment in most of the developed countries, for example, the UK [5].

Caregiver burden is defined as persistent hardship, stress, or negative experiences resulting from the provision of care by caregivers [6]. Caregiver burden is strongly related to sleep disturbances [7] and depressive symptoms [8]. It was reported that caregiver burden is negatively related to health-related quality of life, particularly mental health [9].

Researchers advanced the definition of burden when they distinguished between objective and subjective factors. Objective burden consisted of the concrete factors seen to disrupt family life and is subdivided according to specific effects on the family household, the health of other family members, family routine, and in particular, abnormal behavior likely to cause distress. Subjective burden refers to the subjective experience or psychological or emotional impact (i.e. feeling worried or strained) of caring for someone with a mental illness [10].

Living with the patient, patient behavior, demographic characteristics, and socioeconomic status have all been associated with different levels of burden [11]. One study found that caregivers of patients with dementia appeared more vulnerable to depression as a consequence of their experience [12]. White *et al.* [13] found that caregivers of people who had suffered a stroke had lower mental health-related quality of life compared with their counterparts who were not caregivers. Another study used the same questionnaire (SF-36) to measure caregivers' health-related quality of life and found that caregivers of people with cerebrovascular disease or diabetes had significantly negative mental health-related quality of life [14].

The physical consequences of caregiving have received less attention than psychiatric outcomes. One study indicated that caregivers often experience several physical problems, including back injuries, arthritis, high blood pressure, gastric ulcers, and headaches [15].

The aim of this study was to evaluate and compare the burden (objective and subjective) on female caregivers (mother or wife) who provide full-time care to family members who are suffering from either psychiatric or physical disorders.

Patients and methods

This descriptive study included 300 women (either wife or mother, caring for patients with psychiatric disorders or patients with chronic physical illness), selected from the outpatient clinics of psychiatry and other specialties (University Hospital, Al-Azhar Faculty of Medicine; New Damietta) in the period 1 June 2007 to the end of March 2008.

Patients were classified into two groups. The first group included 150 women who are caring for patients with psychiatric disorders of at least 2 years or more and not suffering a chronic mental illness. Psychiatric disorders included schizophrenia, substance dependence, bipolar disorder, and attention-deficit hyperactivity disorder (ADHD). Patients with comorbid chronic physical disorders were excluded. The second group included 150 women who are caring for patients with chronic physical disorders of at least 2 years duration or more. Physical disorders included hepatic failure, renal failure, disabilities because of cerebrovascular strokes, and other neurological disorders. Any physically ill patient who has comorbid chronic psychiatric disorder was excluded.

The duration of illness for selected patients was two years or more for both groups depends on the results of Pim and Heleen [16] study, which indicated that the burden is more manifest after 2 years duration of illness.

In this study, psychiatric disorders include schizophrenia, bipolar disorder, substance dependence, and ADHD. In contrast, the chronic physical diseases include renal or hepatic failure and cerebrovascular stroke. Each subgroup of disorder was composed of at least 30 patients.

All included women were subjected to the following: Semistructured Clinical Interview using the diagnostic criteria of the DSM IV TR, Caregiver Strain Index [17], and Zarit Burden Interview [18]. These instruments were translated into Arabic language by translators who are not psychologists or psychiatrists and then retranslated into English. Face validity was judged by two Professors of Psychiatry (Al-Azhar University) who corrected some words and phrases. Reliability of the translated instruments was tested through application on 30 cases and then reapplication 2 weeks later and was found to be 0.97 for the Zarit Burden Interview and 0.87 for the Caregiver Strain Index. The scores of Zarit Burden Interview vary from 0 to 88, and the higher scores indicate higher burden. The Caregiver Strain Index is composed of 13 questions and positive responses for seven questions or more indicate a high level of burden.

Statistical analysis of data

The collected data were organized, tabulated, and statistically analyzed using the statistical package for social science (SPSS), version 13 (SPSS Inc., Chicago, Illinois, USA). For qualitative data, the number and

percentage distribution were calculated, and χ^2 was used for comparison between groups; and for quantitative data, the mean and standard deviation were calculated and for comparison between two means the Student's *t*-test was used. Tests were considered statistically significant when *P* value was less than or equal to 0.05.

Results

In this study, the caregivers of patients with psychiatric disorders were 150 women, 121 of them (80.7%) were mothers and 29 (19.3%) were wives. In contrast, the caregivers of nonpsychiatric patients were 150 women, 19 of them (12.7%) were mothers and 131 (87.3%) were wives. The mean age of women in group 1 (psychiatric) was 37.20 ± 10.17 years, whereas the mean age in group 2 was 47.36 ± 6.91 years. Fifty-two percent of women in group 1 lived in rural area compared with 65.3% who lived in rural area in group 2. In addition, the majority of women caring for patients with nonpsychiatric disorders were illiterate (66.7%) compared with 15.3% women caring for patients with psychiatric disorders, and there was a significant difference between both groups with regard to distribution of women (mother or wife), their age, residence, and educational level, whereas no significant difference with regard to their job (the majority in both groups were housewives) was observed (Table 1).

In this study, there was a statistically significant increase in objective burden in group 2 (caring for nonpsychiatric patient; 146 cases had high objective burden) in comparison with group 1 (89 cases had high burden). Similarly, the subjective burden was statically high in women caring for nonpsychiatric disorders in comparison with those caring for psychiatric disorders (Table 2).

In this study, the objective burden was high in cases with poststroke disabilities, schizophrenia, chronic renal failure, chronic liver cell failure, and in those with bipolar disorder (Table 3). Similar distribution was observed in the subjective burden (Table 4).

Table 1 Characteristics of caregivers

Parameter	Group 1 (psychiatric)	Group 2 (physical)	*P* value
Who (*N*, %)			
Mother	121 (80.7%)	19 (12.7%)	<0.001(S)
Wife	29 (19.3%)	131 (87.3%)	
Age (mean ± SD)	37.20 ± 10.17	47.36 ± 6.91	<0.001(S)
Residence			
Rural	79 (52.7%)	98 (65.3%)	0.026 (S)
Urban	71 (47.3%)	52 (34.7%)	
Educational level			
Illiterate	23 (15.3%)	100 (66.7%)	<0.001(S)
Middle	75 (50.0%)	36 (24.0%)	
Higher	52 (34.7%)	14 (9.3%)	
Job			
Employee	25 (16.7%)	17 (11.3%)	0.18 (NS)
Housewife	125 (83.3%)	133 (88.7%)	

NS, not significant.

Table 2 The objective and subjective burden exerted on caregivers

	Group 1 (psychiatric)	Group 2 (physical)	*P* value
Objective burden (*N*, %)			
Low	61 (41)	4 (0.03)	<0.001(S)
High	89 (59)	146 (0.97)	
Subjective burden (*N*, %)			
No or mild	16 (10.7)	0 (0.0)	<0.001(S)
Moderate	47 (31.3)	18 (12.0)	
Severe	56 (37.3)	71 (47.3)	
Extreme	31 (20.7)	61 (40.7)	

S, significant.

With regard to psychiatric disorders in caregivers, major depression was observed in 102 cases (34.0%), adjustment disorder with depressed mood in 32 cases (10.7%), adjustment disorder with anxious mood in 34 women (11.3%), adjustment disorder with mixed depressive and anxious mood in 15 women (5.0%), mixed anxiety and depression in 31 cases (10.3%), generalized anxiety disorders in 67 cases (22.3%), and no psychiatric disorders in 19 cases (6.3%). There was statistically significant difference between mothers and wives with regard to distribution of psychiatric disorders (Table 5).

Discussion

In this study, there is a significant statistical difference between the number of mothers and wives in the two groups ($P < 0.001$). The number of mothers in the first group was 121 (80.7%), whereas the number of wives in the same group was 29 (19.3%). These results are in accordance with other studies, for example, Pim and Heleen [16] who found that more than 50% of cases were mothers and only 25% were wives who are caring for patients with psychiatric disorders. In addition, Lakishika *et al.* [19] reported that 70% were mothers and only 5% were wives, whereas in the study of Eija *et al.* [20], mothers as caregivers were 49% and wives as caregivers were 15%. These differences could be explained by the fact that psychotic disorders (schizophrenia and bipolar) included in this study start at a younger age, drug abuse usually starts in adolescence, and ADHD in childhood, and thus, the original family (mothers) cares for their children.

In the second group, the number of wives caring for patients with nonpsychiatric disease (e.g. chronic kidney or liver failure) was 131 (87.3%) compared with 19 (12.7%) mothers, and these results are in agreement with the study of Lois [21] where most of the caregivers

Table 3 Objective burden according to the type of disorder

	Low (%)	High (%)	*P* value
Schizophrenia	0 (0.0)	38 (100.0)	<0.001(S)
Bipolar disorder	11 (28.9)	27 (71.1)	
ADHD	22 (59.5)	15 (40.5)	
Drug abuse	28 (75.7)	9 (24.3)	
Chronic liver cell failure	2 (4.0)	48 (96)	
Chronic renal failure	2 (4.0)	48 (96.0)	
Poststroke disabilities	0 (0.0)	50 (100.0)	

ADHD, attention-deficit hyperactivity disorder.

Table 4 Subjective burden according to the type of disorder

	No or mild (%)	Moderate (%)	Severe (%)	Extreme (%)	*P* value
Schizophrenia	0 (0.0)	2 (5.3)	9 (23.6)	27 (71.1)	<0.001(S)
Bipolar disorder	1 (2.6)	12 (31.6)	22 (57.8)	3 (7.8)	
ADHD	14 (37.8)	12 (32.4)	11 (29.7)	0 (0.0)	
Drug abuse	1 (2.7)	21 (56.7)	14 (37.8)	1(2.7)	
Chronic liver cell failure	0 (0.0)	9 (18.0)	25 (50.0)	16 (32.0)	
Chronic renal failure	0 (0.0)	6 (12.0)	22 (44.0)	22 (44.0)	
Poststroke disabilities	0 (0.0)	3 (6.0)	24 (48.0)	23 (46.0)	

ADHD, attention-deficit hyperactivity disorder.

were wives. These findings may be explained by the fact that these chronic diseases are most prominent in old age; thus, wives care for their husbands.

In this study, results show that the mean age of the caregivers in the first group (37.20 years) is significantly lesser than the mean age of the caregivers in the second group (47.36 years; $P < 0.001$), and this is attributed mainly to the younger age where psychotic disorders start to represent itself. These ages are slightly younger than those reported in the studies of Pim and Heleen [16] and Lakshika *et al.* [19] where it was 49.6 and 49.04 years, respectively, and this may be explained by the fact that these studies were carried out on caregivers for schizophrenia, bipolar disorders, and depression only, but this study included caregivers for ADHD who are cared for by younger mothers.

In addition, the mean age of mothers caring for patients with nonpsychiatric disorders was in agreement with that reported by Lois [21] where it was 48 years.

With regard to residency, there is no statistical difference between mothers and wives, whereas there is significant statistical difference between the caregivers in the two groups, as most of the caregivers in the psychiatric patients' group (52.7%) were living in urban areas, whereas most of the caregivers in the nonpsychiatric patients' group (65.3%) were living in rural areas.

These findings could be explained by the fact that nonpsychiatric disorders were prevalent in rural areas. In addition, the inhabitants of urban areas were more oriented by psychiatric disorders and asked for treatment, whereas the culture of rural inhabitants prevents them from asking treatment for their psychological suffering, or denies the disease at all [22].

With regard to the level of education, there is no significant statistical difference between mothers and wives as most of them are illiterate or have middle level education. However, there is a significant statistical difference between the caregivers in the psychiatric and nonpsychiatric patients' groups, as the percentage of illiterates in the caregivers of the nonpsychiatric patients' group is 66.7%, whereas the percentage of illiterates in the caregivers of the psychiatric patients' groups is 15.3%. This may be explained by the increased prevalence of illiteracy in rural areas in comparison with urban areas.

In this study, there is no significant statistical difference between the caregivers in the study groups regarding occupation as most of the caregivers are housewives. These results are in contradiction to other studies that found that caregivers were working full time [23–25]. In contrast, these results are in agreement with Egyptian studies, for example, Abou El Magd *et al.* [26] who reported that 60% of caregivers for substance abusers were housewives. These results could be explained by the fact that the society in Damietta Governorate tends to keep women at home.

With regard to objective burden, there is no significant statistical difference in the level of the objective burden between mothers and wives, whereas the level of objective burden in the caregivers of patients with nonpsychiatric disorders is significantly higher when compared with the level of objective burden in the caregivers of patients with psychiatric disorders. However, when we study the level of objective burden in the caregivers for patients with each disease individually, we find that the level of objective burden does not depend on whether the disease is psychiatric or nonpsychiatric, but it depends on the level of disability caused by the care recepient's disease, where there is a high level of objective burden in all caregivers of patients with schizophrenia and patients with poststroke disabilities and most caregivers of patients with chronic liver disease, chronic renal disease, and patients with bipolar mood disorder, and the level of objective burden was low in most caregivers of children with ADHD and substance abuse patients.

Table 5 Psychiatric disorders in caregivers (mother and wife)

	Mother (%)	Wife (%)	Total (%)	*P* value
Major depression	33 (23.6)	69 (43.1)	102 (34.0)	<0.001(S)
Adjustment disorder with depressed mood	20 (14.3)	12 (7.5)	32 (10.7)	
Adjustment disorder with anxious mood	20 (14.3)	14 (8.8)	34 (11.3)	
Adjustment disorder with mixed anxious and depressed mood	12 (8.6)	3 (1.9)	15 (5.0)	
Mixed anxiety and depression	13 (9.3)	18 (11.3)	31 (10.3)	
Generalized anxiety disorder	26 (18.6)	41 (25.6)	67 (22.3)	
No psychic disorder	16 (11.4)	3 (1.9)	19 (6.3)	

The poststroke disabilities interfere with the patients' ability to walk and care for themselves, and these facts are true for patients with chronic liver cell failure and chronic renal failure as they lead to several disabilities that represent a major burden on the caregiver; besides, these diseases have poor prognosis and continuously deteriorate, and the patients' need for caregiving increases day by day [27].

In contrast, the bipolar disorder is accompanied by free periods where the patient can care for his or her self, thus leading to a decrease of the burden of caregiving [16]. These facts are also true for ADHD as it needs slight adaptation and the nature of the Damietta governorate provides the child with a wide place to play and thus the burden on the family is less in comparison with other diseases.

In this study, the level of subjective burden was significantly higher in the wives when compared with the mothers. In addition, the level of subjective burden was significantly higher in the caregivers of patients with nonpsychiatric disorders when compared with the caregivers of patients with psychiatric disorders. But as in objective burden, the level of subjective burden does not depend on whether the disease of the care recipient is psychiatric or nonpsychiatric because when we study the subjective burden caused by each disease separately we find that the subjective burden was significantly high in the caregivers for patients with schizophrenia than the caregivers of patients with poststroke disabilities, and it was significantly low in the caregivers of children with ADHD and substance abuse patients.

In fact, no sufficient studies were found comparing wives with mothers as caregivers, but Lois [21] reported that the relation between the subjective burden and the degree of relativity is unclear. Some studies reported that the level of subjective burden is higher in wives in comparison with any other relative [28,16]. Other studies have not found any difference in the level of subjective burden between wives and other female caregivers [29], whereas other studies found that the levels of subjective burden were higher in other women compared with wives [30].

The increased level of subjective burden in wives in comparison with mothers may be explained by the difference between both wives and mothers in their understanding of caregiving; for example, Kurz and Cavanaugh [31] reported that the fundamental characters of a marriage relationship are that it is optional and it can be ended at any time, whereas the relation between the mother and her child is more powerful. In addition, it is noted that the majority of wives in this study care for patients with chronic nonpsychological disorders that need higher level of caring and that affects the husband's sexual power, thus, increasing the burden on wives [27].

The results of this study showed that there is a significant statistical difference between mothers and wives with regard to the prevalence of psychiatric disorders, which are more prevalent in the wives compared with mothers, especially major depressive disorder, generalized anxiety disorder, and mixed anxiety and depression, whereas adjustment disorders are more prevalent in the mothers compared with wives. The results also showed that there is a significant statistical difference between caregivers of patients with psychiatric and nonpsychiatric disorders with regard to the prevalence of psychiatric disorders, which are more prevalent in the caregivers of patients with nonpsychiatric disorders compared with caregivers of patients with psychiatric disorders. However, when we study the prevalence of psychiatric disorders in the caregivers for patients with each disease, we find that the prevalence of psychiatric disorders does not depend on whether the disease is psychiatric or nonpsychiatric but it depends on the nature of the disease of the care recipient and its impact on the functional level of the patient, as the depressive disorders were more prevalent in the caregivers of patients with schizophrenia and patients with poststroke disabilities. However, anxiety disorders are more prevalent in the caregivers of substance abuse patients, and psychiatric disorders are less prevalent in the caregivers of children with ADHD.

These results are compared with that of Beason *et al.* [32] and Berg *et al.* [33] who reported that depression is more prevalent in wives caring for their husband in comparison with other relatives (sons).

The increased prevalence of psychiatric disorders in wives can be explained by the increased subjective burden in wives in comparison with mothers. Previous studies showed that the relation between subjective burden and the prevalence of psychiatric disorders is proportional [34,35]. In addition, wives are younger than mothers, and some studies found that depression is less in older caregivers in comparison with younger caregivers [33,36]. Increased prevalence of psychiatric disorders in caregivers of nonpsychiatric disorders in this study is in agreement with Dennis *et al.* [37] and with Kotila *et al.* [38] who reported that the degree of depression in caregivers of patients with poststroke disabilities increased significantly with the degree of disability.

Conclusion

The study results may indicate that caregiver burden (objective and subjective) and prevalence of psychiatric disorders in caregivers do not seem to depend on whether the disease of the care recipient is psychiatric or physical, but seem to depend on the impact of the disease on the functional level of the patient. No difference exists between mothers and wives in the level of objective burden, which does not depend on the relation between the caregiver and the care recipient; however, the level of subjective burden and prevalence of psychiatric disorders are higher in wives compared with mothers, which could be attributed to the difference in their view and appreciation of the caregiving situation.

Limitations of the study

(1) There was a significant difference between both groups 1 and 2 with regard to age and relation to the patient, which may cause bias for the study, but this factor

could not be avoided because of the uneven distribution of mothers and wives as caregivers in both groups.
(2) Age of the patients, level of education, residence (rural or urban), and occupation were not considered as factors, which could affect the burden level.

There is no conflict of interest to declare.

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الملخص العربى

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الخلفية : هناك أعداد متزايدة من مقدمات الرعاية لذوي الأمراض المزمنة . وتقديم الرعاية يمثل عبئا , وهو يقع غالبا على النساء (أمهات أو زوجات) , ولا نعرف على وجه التحديد مدى وتأثير ذلك العبء .
هدف البحث: دراسة العبء الذي تتعرض له مانحات الرعاية(أمهات ، زوجات) للمرضي المزمنين (نفسيين أو غير نفسيين) , وأثر ذلك على حالتهن النفسية.
العينة وأدوات البحث: تمت هذه الدراسة على عينة مكونة من 300 سيدة (أمهات ،زوجات) ممن يتردد أزواجهن أو أبناؤهم على عيادة الطب النفسي وبعض التخصصات الأخري بالمستشفى الجامعي بمدينة دمياط الجديدة والتابع لجامعة الأزهر في الفترة من يونيو 2007 م إلى مارس 2008 م ، وذلك من خلال استخدام المقابلة الإكلينيكية شبه المقننة حسب الخصائص التشخيصية للدليل الأمريكي الرابع المراجع نصيا (DSM IV- TR) , ودليل انضغاط مانح الرعاية (C.S.I) , ومقابلة زاريت للعبء (Zarit burden interview) .
النتائج: مانحات الرعاية للمرضي النفسيين كن أمهات في 121 حالة (80,7%) وزوجات في 29 حالة (19,3%) بينما العكس في الاضطرابات العضوية حيث مثلت الزوجات131(87,3%) بينما الأمهات مثلن 19 فقط (12,7%) . ووجدت فروق ذات دلالة احصائية كبيرة في السن والبيئة الجغرافية والمستوي التعليمي بين السيدات في المجموعتين ، بينما لم تجد الدراسة فروقا ذات دلالة احصائية في وظيفة السيدات (الغالبية ربات منازل)، كما وجدت الدراسة أن العبء (الذاتي والموضوعي) كان ذا دلالة احصائية كبيرة في مانحات الرعاية لمرضي عجز ما بعد الجلطة المخية ، الفصام ، الإضطراب الوجداني ثنائي القطب ، فشل الكلي والكبد المزمنين (0.001.) . كما وجدت الدراسة أن 102 (34%) من مانحات الرعاية لديهن اضطراب الاكتئاب الجسيم ، وعانت 67 (22,3%) منهن اضطراب القلق العام ، كما وجدت اضطرابات نفسية أخري حسب نوع وشدة مرض من يرعونهم.
الخلاصة : يعتمد الشعور بعبء رعاية المرضي (الذاتي والموضوعي) ومعدل انتشار الاضطرابات النفسية بين مانحات الرعاية علي طبيعة المرض ومدي تأثيره علي كفاءة المريض الشخصية والوظيفية ، كما أن العبء الذاتي ووجود الاضطرابات النفسية كان أعلي بين الزوجات مقارنة بالامهات اعتمادا علي إدراك كل منهن لموقف الرعاية .

Coping with stress and quality of life among patients with schizophrenia in Egypt and Saudi Arabia: effect of sociodemographic factors

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Introduction
In Arab countries, epidemiological data about the ways of coping with general day stresses in schizophrenic patients and their quality of life are scarce. This study sought to determine whether there was a difference in ways of coping with stress and quality of life of schizophrenic patients attending the Baljurashi Psychiatric Hospital, AlBaha region, Saudi Arabia compared with schizophrenic patients at the Mansoura University Hospital, Egypt.

Materials and methods
A sample of 140 schizophrenic patients in Saudi Arabia and 140 schizophrenic patients in Egypt was enrolled. Data on sociodemographical and clinical variables were recorded. The following scales were utilized: Scale for Assessment of Positive Symptoms, Scale for Assessment of Negative Symptoms, Brief COPE Scale, and Self Report Quality of Life for Schizophrenia (SQLS).

Results
Saudi patients used less number of coping skills than Egyptian patients and were higher on self-distraction and acceptance; they were better on most items of SQLS. The duration of illness correlated positively with affection of motivation and energy subscale of SQLS in Egyptian patients ($r=0.259$, $P=0.002$), whereas in Saudi patients it showed no correlation.

Conclusion
Social factors are the most important determinants of quality of life rather than the symptoms. Long duration of illness has a negative influence on motivation and energy among Egyptian schizophrenic patients.

Keywords:
Arab, coping with stress, quality of life, schizophrenia

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Introduction

Globally, the incidence of schizophrenia is 1% of the population [1,2]. Schizophrenia is a chronic disorder with a heterogeneous presentation, which is marked by an array of symptomatology, variations in outcome, and responses to treatment [1–4]. Schizophrenia causes many disturbances, which have the propensity to have a pervasive impact on many areas of life functioning and subsequently on the quality of life (QOL) [1]. Sullivan *et al.* [5] noted that long-term psychotics are more vulnerable to stress, more dependent, and have greater deficits in living skills and in relationship with their social environment. Patients often report chronic difficulty coping effectively with both major and minor stresses [6,7]. They may possess a relatively limited repertoire of coping strategies and tend to avoid rather than actively attempt to solve problems [8–11]. Different coping strategies may reduce the negative influence of specific symptoms and distress on the subjective QOL of schizophrenic patients [12,13]. Maladaptive coping patterns are of larger importance because they have been linked to symptom exacerbation and failure to sustain community tenure [14,15]. Studies identify QOL as an important (if not the most important) measure of the impact of schizophrenia and its respective treatment [16]. QOL of chronic patients is impoverished especially in the domains of housing conditions, family environment, social network, financial circumstances, and safety and practical skills [5]. In Arab countries, epidemiologic data about the ways of coping and QOL among schizophrenic patients are scarce. Egypt and Saudi Arabia share common life profiles, including language and religion, but are different with regard to cultural, historical, and financial aspects of life. Thus, there is a good reason to hypothesize that there would be a significant difference between the two samples in the QOL, and in the way they cope with stress and to propose that the Saudi sample might attain a better QOL and level of functioning than their Egyptian counterparts. The aim of this study was to explore the difference between Egyptian and Saudi schizophrenic patients regarding the patterns of cope employed in the face of general day-to-day stressors and its correlates and the difference in the QOL.

Materials and methods

This was a comparative study of schizophrenic patients at the Psychiatric Department of Mansoura University Hospital, Egypt and the Baljurashi Psychiatric Hospital, Al Baha region in the Kingdom of Saudi Arabia, conducted simultaneously in both groups from 1 January 2009 to 1 July 2009. After approval from the ethics board, patients were recruited after they gave a written informed consent to accept joining the study to carry out some scales and more investigations for the patient to measure the effect of illness over their living environment; no financial or extramedication benefit would be received by the patients from joining the study. Diagnosis was made according to the criteria described by *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* (DSM-IV). The age range was from 18–45 years, for a duration of more than 2 years. The stability of illness was for at least 3 months before assessment (stability of illness was defined as a clinical and functional stability as judged by the treating physician, reflected by the criterion of absence of exacerbation of illness requiring increase in drug dosages by 50%, as mentioned by Gupta *et al.* [17]) excluding patients who were changing their antipsychotic medication, which would suggest the absence of stability. Excluding patients with all axis 1 comorbidity or personality disorder or evidence of organic pathology that could explain the presenting symptomatology. This information was clarified from patient notes. All the patients who were included were subjected to physical examination and special questionnaire; the questionnaire was designed by the authors to tap into different sociodemographic variables. Socioeconomic status in Egypt was measured by the Fahmy and El-Sherbiny's Scale whereas in Saudi they are measured by some question, which determines the income, water, and electricity supply nearly similar to that of the Fahmy and El-Shirbiny's Scale, duration of illness, and medications received. Psychometric assessment was made by using the following tools:

(1) SAPS and SANS [18,19] was developed by Andreason to measure positive and negative symptoms in schizophrenia; it was rated by the treating psychiatrist.
(2) The Brief COPE [20] is a validated short form of the COPE inventory [21], which is a widely used measurement of coping in health-related research. The Brief COPE consists of 14 scales of two items each. Both cognitive and behavioral strategies of coping are included.
(3) Self report on Quality of Life for Schizophrenia (SQLS) [22] have 30 items incorporated in three scales: (i) psychosocial (15 items), (ii) motivation and energy (seven items), and (iii) symptoms and side effects (eight items). Both Brief COPE and self-report on Quality of Life scales were translated by the research team and are subjects of translation in another study.

At the Baljurashi Psychiatric Hospital in Al-Baha, the total number of patients received from January 2009 till July 2009 (6 months) was 450; only 140 of them accepted to join the study and completed the questionnaires. An equal number of schizophrenic patients in Egypt were targeted.

Statistical analysis was conducted using the statistical package for the social sciences (SPSS version 12, IBM, Chicago, USA). For quantitative data, the unpaired *t*-test was used for group comparisons. For categorical data, the χ^2-test was used for comparison between the groups. *P* value of less than 0.05 was considered to be statistically significant. Correlation studies were also conducted.

Results

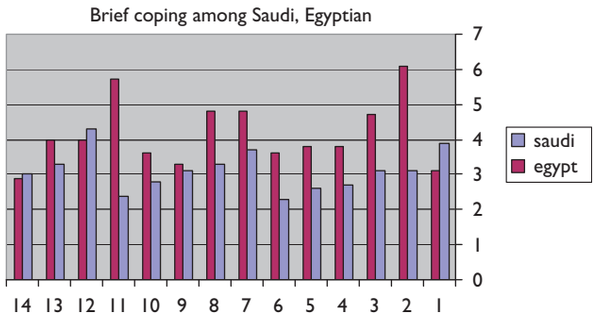
Table 1 shows that the patients of the Saudi group were relatively old, 43.6% of them were female patients, 42.3% were single, 32.9% were married, and 24.3% were divorced, nearly more than half of them having lower level of education, 75.7% of them came from rural areas and were nomads with relatively longer duration of illness, and 55.5% of them had a positive family history of psychiatric illness. A major proportion of them (70%) were on atypical antipsychotics with their scores on global assessment of functioning (GAF; 32.6 ± 7.1), SAPS (9.2 ± 2.3), and SANS (11.4 ± 2.5). Although Egyptians were observed to be relatively young, more male patients were included, more likely to be single or divorced, 85.5% were on typical antipsychotics, scored 28.5 ± 7 on GAF, scored 9.3 ± 2.4 on SAPS, and scored 12.8 ± 2.4 on SANS.

As evident from the graph on the Brief COPE Scale, it was observed that Saudi patients were higher on self distraction, acceptance, and self blame subscales, whereas

Table 1 Sociodemographic variables in Saudi and Egyptian schizophrenic patients

Variables	Saudi patients *N* % (140)	Egyptian patients *N* % (140)
Age (mean ± SD) (years)	32.7 ± 8	30.7 ± 7.2
Sex		
Male	79 (56.4)	88 (62.9)
Female	61 (43.6)	52 (37.1)
Education		
Primary	44 (31.4)	12 (8.6)
Preparatory	51 (36.4)	20 (14.3)
Secondary	31 (22.2)	84 (60)
College	14 (10)	24 (17.6)
Occupation		
Employed	20 (14.3)	34 (24.3)
Unemployed	31 (22.1)	34 (24.3)
Student	11 (7.9)	12 (8.6)
Retired	21 (15)	20 (14.3)
Housewives	57 (40.7)	40 (17.1)
Marital status		
Single	60 (42.3)	88 (62.9)
Married	46 (32.9)	36 (25.6)
Divorced	34 (24.3)	16 (11.5)
Socioeconomic status		
Low	28 (20)	72 (51.4)
Middle	79 (56.4)	57 (40.7)
High	33 (23.6)	11 (7.9)
Residence		
Urban	34 (24.3)	57 (40.7)
Rural	106 (75.7)	83 (59.3)
Type of family		
Nuclear	21 (15)	105 (75)
Extended	119 (85)	35 (25)
Duration of illness	10.8 ± 6.8	9.7 ± 8.1
Positive family history		
Present	78 (55.5)	35 (25)
Absent	62 (44.5)	105 (75)

Figure 1



Brief COPE Scale among Saudi and Egyptian schizophrenic patients.

the Egyptians were higher on using most subscales of Brief Coping (Fig. 1).

Results on the QOL showed that Saudi patients were better on most items of the scale except for the Motivation and Energy Scale (Table 2).

Correlation studies revealed that, on coping with general stress, the SAPS score among Saudi patients was negatively correlated with self blame ($r = -0.202$, $P = 0.017$), whereas in Egyptians it was positively correlated with denial ($r = 0.240$, $P = 0.004$), behavioral disengagement ($r = 0.294$, $P < 0.001$), venting ($r = 0.24$, $P = 0.004$), and humor ($r = 0.284$, $P = 0.001$). SANS score had no correlation in Saudi patients, whereas in Egyptians it was negatively correlated with planning ($r = -0.232$, $P = 0.006$) and active coping ($r = -0.207$, $P = 0.014$).

Table 3 shows that in Egyptian schizophrenic patients, long duration of illness was correlated with poor motivation and energy, whereas it showed no correlation in the Saudi group of patients.

Table 3 Correlation between duration of illness and quality of life in Egyptians versus Saudi schizophrenic patients

	Egyptians (*r*)	Saudis (*r*)
Psychosocial Scale	0.033	−0.116
Motivation and Energy Scale	0.259[a]	−0.115
Symptoms and Side Effects Scale	0.122	−0.154

[a]Highly significant at $P<0.01$.

Discussion

Schizophrenia is a severe and debilitating disorder, which affects general health, functioning, autonomy, subjective well being, and life satisfaction of those who suffer from it [23]. As evident from the results, compared with Egyptian patients, it was clinically observed that there were more Saudi female patients in the study although both authors were females which explains the fact that Saudi patients prefer a female psychiatrist to deal with their female patients and are encouraged to get their female patients when they encounter with a female doctor whom they believe is more understanding and appreciative of female problems, and can uncover their face and speak openly (clinical observation, not a fact).

Higher percentage of the patients were married; as the Saudi patients are more dependent on their families regarding the expenses of marriage, they tend to marry early and live in extended families. This was supported by Abdullah Al-Sabaie [24] who explained that culturally, the large family enhances the sense of collective strength and influence in the community. High rates of divorce may be related to the effects of illness [24]. Saudi patients were of higher socioeconomic status relative to Egyptians, and they mostly belonged to middle class from rural and nomadic areas, whereas those of higher class were few. This could be explained by the fact that in the southern area of Saudi there are limited resources, less job opportunity, less level of education, and less contact with civilization than other Saudi areas. However, a high percentage of them were maintained on atypical antipsychotics, which are offered to patients by governmental hospitals because of high country resources. As Egyptian patients tend to live in nuclear families and only the typical antipsychotics were provided by governmental hospitals, it was evident that Saudi patients had relatively less negative symptoms and got higher scores on GAF probably due to the use of atypical antipsychotics.

There was a large percentage of Saudi patients having a positive family history of psychiatric illness, more commonly schizophrenia that was supported by Chaleby and Tuma [25] who observed that schizophrenia tends to cluster in families in Saudi Arabia due to high consanguinity supporting the genetic hypothesis of the disorder.

With regard to the results on Brief COPE Scale, as evident from the graph, Egyptians were more ready to use several strategies including problem centered and neutral strategies, whereas Saudi patients relatively used less number of coping skills and were higher on self distraction and acceptance. Carter *et al.* [12] have shown that effectiveness improves if participants use several strategies at the same time, whereas other researchers have argued the converse [26]. Contradictory findings may

Table 2 Self report quality of life in Egyptian and Saudi schizophrenic patients

SQLS	Egyptian patients (140)	Saudi patients (140)	Statistical test results d.f.=139
Psychosocial Scale	40.98±10.5	38.7±9.2	$t=2.540$, $P=0.012$
Motivation and Energy Scale	41.99±10.2	40.26±8.5	$t=1.788$, $P=0.076$
Symptoms and Side Effects Scale	30.17±11.2	22.63±9.4	$t=8.107$, $P<0.001$

Significant at $P<0.05$.
d.f., degrees of freedom; SQLS, self report quality of life for schizophrenia.

be related to different ways of measuring effectiveness just as Farhall and Gehrke [9] considered effectiveness as a multidimensional construct including a degree of control, anxiety level, and overall coping effectiveness. This was supported by a previous study done by Boschi *et al.* [27] on patients with nonfirst episode psychosis which explained that patients with severe symptomatology tended to endorse a greater number of coping strategies, suggesting that use of more strategies is a response to symptoms [26]. High self distraction observed among Saudi patients could be of value when it seemed inappropriate to include maladaptive strategies such as acting violently or using alcohol [28]. Certain distraction efforts that are actively pursued to eliminate a symptom are categorized as problem-centered strategy. Although acceptance is considered from the neutral defense that is commonly described by psychotics, this is in accordance with McGorry's suggestion that the trauma associated with psychosis may result in people believing that most situations exceed their coping skills [29].

From correlation studies, Egyptian patients with more negative symptoms were related to less use of problem focusing coping as planning and active coping, which is consistent with previous studies [26]. Those with high positive symptoms were correlated more with dysfunctional coping as denial and behavioral disengagement, whereas venting and emotion focused coping as humor. This could be explained, as patients with positive symptoms had denial as a part of lost insight and they were more likely to have behavioral disengagement. In addition, venting coping strategy is considered as part of acceptance that is commonly seen in psychotics. In Saudi schizophrenic patients, those who had high positive symptoms were correlated with less self blame probably due to impaired insight.

As evident from results, Saudi patients had better QOL as they scored less on most items of the scale except for Motivation and Energy Scale, which could be due to the previous factors explained such as early marriage and living in extended families; these factors carry most of the burden of psychosis that mental health system rely on them for post discharge care by the family [24]. Among the factors of good prognosis which were observed in Saudi schizophrenic patients are being married and having adequate psychosocial functioning before illness [30]. Together with availability of most recent medications with very few side effects, which are supplied freely to patients, and families of psychotics do not carry any expenses for medications together with rising awareness about psychiatric illness. It was evident that pharmacological therapies that result in symptom reduction can produce important improvements in health-related QoL [16]. In addition, lower level of education seen among Saudi patients could be predictor of better prognosis as it was found that in underdeveloped countries, patients with higher educational levels appear to have a worse evolution in the disease due to the higher social demands and expectations compared with patients with low schooling [30]. Although motivation and energy not significantly differ as impaired motivation and energy are considered to be a corner-stone effect of schizophrenic illness.

Long duration of illness in Egyptian schizophrenic patients was associated with poorer motivation and energy, this may be due to the influential effect of schizophrenia on motivation together with the role played by typical antipsychotics with high side effects and negative influence on motivation and energy. This could explain the contrary, as in Saudi patients no correlation was observed, this may be due to the use of atypical antipsychotics by a large proportion of them.

Conclusion

It was concluded that Egyptian schizophrenic patients used more number of coping strategies, whereas Saudi schizophrenic patients were better on coping with stress and on most domains of QOL. Social factors are the most important determinant on the QOL, rather than the symptoms. This was in accordance with recent studies addressing QOL for individuals with schizophrenia and other severe mental illnesses that identified a number of important influential factors, such as social support, unmet need, and medication side effects [16]. However, most of the research examining factors affecting QOL has primarily focused on the impact of psychiatric symptoms, especially negative symptoms [16]. It is also known that the progress of schizophrenic patients is better in developing countries because of more handling of patients in families and in society and less institutionalization [23].

Clinical implications and recommendation

(1) Progress of patients is better in developing countries such as Egypt and Saudi Arabia because of better handling in families and in society, and less institutionalization.
(2) Careful management of negative symptoms of schizophrenia because of its negative effects on QOL.

Limitations

(1) Some of the findings are based on self-reported information, and thus some reporting bias might have occurred.
(2) The study took place at only two sites with small number of patients, which will affect the generalizability of results.
(3) The results of this study shouldn't be generalized to all schizophrenic patients as severe, unstable, and disturbed patients with active symptoms were excluded from the study.

There is no conflict of interest to declare.

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الملخص العربي

دراسة مواجهة الضغوط وجودة الحياة بين مرضي الفصام السعوديين والمصريين:

تأثير العوامل الاجتماعية والديموجرافية

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**قسم الطب النفسى- كلية الطب –جامعة المنصورة

تهدف هذه الدراسة إلي استكشاف الفرق في طرق التعامل مع الضغوط وجودة الحياة بين مرضى الفصام السعوديين والمصريين، ومعرفة مدى تأثرها بالعوامل الاجتماعية والديموجرافية..

وقد أجريت الدراسة على عينة تشمل مائة وأربعين (140) مريضا بالفصام تم اختيارهم من بين المترددين على العيادة الخارجية النفسية ومرضى القسم الداخلي بمستشفى بلجرشى للصحة النفسية بمنطقة الباحة بالمملكة العربية السعودية،ومائة وأربعين(140) مريضا بالفصام من بين المترددين على العيادة النفسية بمستشفى المنصورة الجامعي بجمهورية مصر العربية وكانت حالتهم مستقرة بالعلاج. وقد تم اختيار المرضى طبقاً للتقسيم الأمريكي الرابع لمرضى الفصام . وقد تم لهم جميعاً إجراء:

1- تجميع بيانات خاصة بالمتغيرات الاجتماعية والديموجرافية من سجلات المرضى
2- فحص اكلينيكى ونفسي شامل
3- مقياس تقييم للأعراض الموجبة والسالبة لمرضى الفصام
4- مقياس المواجهة المختصر
5- التقرير الذاتي لجودة الحياة لمرضي الفصام

ولقد أظهرت النتائج أن المرضى السعوديين قد استخدموا عددا اقل من استراتيجيات المواجهة بالنسبة للمرضي المصريين ولكنهم كانوا أكثر استخداما للقبول والإلهاء، في حين أنهم كانوا أفضل في معظم نتائج جودة الحياة. ولقد كان لطول مدة المرض تأثير سلبي على الحافز والنشاط بين المرضى المصريين في حين انه لم يظهر له تأثير واضح بالنسبة للمرضى السعوديين.

ومن هنا نستنتج أن العوامل الاجتماعية تلعب دورا أساسيا في التأثير علي جودة الحياة بالمقارنة بالأعراض المرضية، وذلك يعضض من أهمية التدرب علي استراتيجيات المواجهة ضمن التأهيل الاجتماعي النفسي لمرضي الفصام

Comorbid psychiatric symptoms in patients with psoriasis

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Introduction
Psoriasis is a chronic inflammatory skin disease. Generally, approximately one in four patients experiences significant psychological distress. Depression and anxiety are the most common disorders that are associated with psoriasis. This study was carried out to assess the psychiatric comorbidities in patients suffering from psoriasis, such as depression, and their effects on the quality of life and the personality characteristics of patients suffering from psoriasis.

Materials and methods
This study is a comparative case–control cross-sectional study. The sample of this study included two groups: cases and controls. The cases consisted of 30 patients with the diagnosis of psoriasis recruited from the outpatient clinic of the Dermatology Department of the Kasr El Aini Hospitals. They represent consecutive referrals of patients fulfiling the criteria for inclusion in the study. The controls consisted of 30 individuals free of any psychiatric and physical disorders; the relatives of the patients were excluded to avoid genetic factors. Controls were age-matched and sex-matched with the psoriasis group. Both groups were subjected to the following: Beck Depression Inventory, Arabic version; Eysenck's Personality Questionnaire, Arabic version; Body Image Scale, Rating Scales for Psychopathological Health Status, and Quality of life Scale, Arabic version.

Results
Twenty-six percent of the patients had major depressive disorder, 23.3% had adjustment disorder with depressed mood, and 13.3% had dythymic disorder. Forty-three percent of the psoriatic patients had severe depression on Beck Depression Inventory, 16.7% had moderate depression, and 16.7% also had mild depression, whereas in 23.3% patients depression was absent. There were statistically significant differences between the two groups ($\chi^2 = 21.2$, $P = 0.000$) regarding the Beck Depression Inventory. There was statistically significant difference between the psoriasis group and controls regarding Neuroticism, Introversion, and Lie, whereas there was no statistical significance difference between the two groups regarding Psychoticism and Criminality. There were statistically significant differences between the two groups ($P = 0.000$) regarding the mean of Body Image Scale.

Conclusion
There is high frequency of psychiatric comorbidities in psoriatic patients especially depression, which represents the most frequent psychiatric symptom in psoriasis. The presence of psychiatric comorbidities increases the impairment in quality of life in psoriatic patients. There were no specific personality characteristics for psoriatic patients.

Keywords:
body image, depression, psoriasis

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Introduction

Psoriasis is a chronic inflammatory skin disease that is characterized by thick, red, scaly lesions that may appear on any part of the body. Generally, approximately one in four patients experiences significant psychological distress. In fact, one of the most persuasive indications of a link between stress and psoriasis comes from patients themselves, with studies illustrating that the majority of patients believe that stress or psychological distress is a factor in the manifestations of their condition [1,2]. Depression and anxiety are the most common disorders that are associated with psoriasis, but the proportion of patients meeting criteria for an anxiety disorder is notably higher than that for depression in patients with psoriasis [3]. Psychiatric disturbance and psychosocial impairment are reported in at least 30% of patients who have dermatologic disorders. Major depressive disorder is the most frequently encountered psychiatric disorder in

dermatology and is often associated with suicidal risk. Other psychiatric syndromes comorbid with dermatological disorders include obsessive–compulsive disorder, social phobia, posttraumatic stress disorder, dissociation, conversion disorder, body image pathologies, delusional disorder, and a wide range of personality disorders [4]. Moreover, symptoms of psoriasis, especially pruritus, are related to depression. Similarly, there is evidence that patients who report high levels of stress experience pruritus more frequently than patients with lower stress levels [5,6]. In contrast, patients with psoriasis have significant impairment in their quality of life (QOL). Psoriasis usually does not take lives, but it does ruin them. The impact of psoriasis on QOL is similar to that of other major medical diseases, and it is not only limited to the patients but psoriasis also has a major secondary impact on the lives of family members and partners [7].

The aim of the study was to assess the psychiatric comorbidities in patients suffering from psoriasis such as depression, anxiety, and disturbed body image and their effects on QOL and to assess the personality characteristics of patients suffering from psoriasis.

Patients and methods

This study is a comparative case–control study.

Patients

The sample of this study included two groups: cases and controls.

Cases

Thirty patients with psoriasis were diagnosed by the lecturer and assistant lecturer of dermatology, and were recruited from the outpatient clinic of the Dermatology Department of Kasr El Aini Hospitals. Both sexes were included. Patients' ages ranged from 15 to 45 years, and they were diagnosed with psoriasis vulgaris. The general exclusion criteria were patients suffering from other dermatological diseases, medical condition that would interfere with the assessment, mental subnormality suspected on clinical interview and intelligent quitent assessment by psychometric testing, past history of psychiatric disorders and substance use disorders (before psoriases), comorbidity with other active major medical problems (e.g. renal and hepatic failure), and patients under oral or systemic corticosteroid medication.

Controls

Thirty individuals were selected who were completely free of any psychiatric and physical disorders, and we excluded the relatives of the patients to avoid genetic factors. They have been age-matched and sex-matched with the psoriasis group. Informed oral and written consent were taken from all patients who participated in this study.

Methodology

Both the groups were subjected to the following assessment:

Psychiatric examination

This examination was applied by using the modified clinical sheet of the Psychiatry Department of Cairo University (Kasr El Aini) to diagnose psychiatric disorders according to *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* (DSM-IV) criteria [8] using the Structured Clinical Interview for DSM Axis of Disorders (SCID-I): SCID-I provides a broad coverage of Axis I psychiatric diagnosis according to DSM-IV [9]. Relevant data include sociodemographic data, family history, past history, dermatological history, and screening of psychiatric symptoms.

Psychometric tools

Beck Depression Inventory (BDI), [10] *Arabic version*: this inventory used for measuring depression, which is translated to Arabic by Gharib Abdel Fattah, is a self-reported scale designed to assess DSM-IV-defined symptoms of depression. The inventory consists of 21 groups of statements on a four-point scale with the subject selecting the one that best matches the patient's current state. Each statement group corresponding to a specific behavioral manifestation response is scored as 0–3, corresponding to no, mild, moderate, or severe depressive symptomatology in the response. The score range varies from 0 to 63, where higher scores indicate greater depression severity. Scores in the range of 0–13 indicate no or minimal depression; 14–19, mild depression; 20–28, moderate depression; and 29–63, severe depression.

Eysenck's Personality Questionnaire (EPQ), [11] *Arabic version*: it was translated to Arabic by Ahmed Mohamed Abdel Khalek in 1991. It is used to assess Neuroticism, Psychoticism, Introversion/Extroversion, Criminality, and Lie scale. Extraversion is characterized by being outgoing, talkative, high on positive affect (feeling good), and in need of external stimulation. Introverts, in contrast, are chronically overaroused and jittery, and are therefore in need of peace and quiet to bring them up to an optimal level of performance. Neuroticism or Emotionality is characterized by high levels of negative effects such as depression and anxiety. Psychoticism is associated not only with the liability to have a psychotic episode (or break with reality), but also with aggression. Psychotic behavior is rooted in the characteristics of tough mindedness, nonconformity, inconsideration, recklessness, hostility, anger, and impulsiveness. The questionnaire is formed of 99 questions to be answered by yes or no. Each one of the five dimensions has certain questions and each question takes a score; then the total score for each dimension is calculated.

Body Image Scale [12]: this scale is based on the phenomena that body image is the mental picture or presentation of the body at times of rest and movement or either. It is derived from the internal perception of external appearance and internal body, and also from accompanied emotional experiences and its reflection on interactions with self and others. This scale is self rated, formed of 26 items and every patient answers in three grades from totally accepting to totally not accepting with a score from 0 to 2 for each item. The normal range for

male patients is 14 ± 6 and for female patients is 16 ± 6, above which the body image is considered as disturbed.

Rating Scales for Psychopathological Health Status and Quality of Life Scale (PCASEE) [13] *Arabic version*: it is a self-rated scale. Clarify the subjective expression of the QOL of the patients. It consists of six domains to estimate the degree of impairment in the QOL of the patients. These domains are physical, cognitive, affective, social, economic, and ego.

Scoring of the scale was done for each item from 0 to 2, where 0 stands for bad response, 1 for moderate response, and 2 for good response. The results were calculated by multiplying the sum of each domain with 4 to obtain the percentage for QOL. Therefore, 100% means the best QOL.

Statistical analysis

All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, New York, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, Illinois, USA) version 15 for Microsoft Windows. Descriptive statistics was used for illustrating the mean and standard deviation of quantitative data. Statistical tests were used to find out the significant differences between the two groups. The student *t*-test was used for quantitative variables, for example, age, BDI, Beck Anxiety Inventory, Quality of Life Scale, and Body Image Scale. The χ^2-test was used for qualitative variables, for example, sex, education, occupation, marital status, socioeconomic level, and EPQ. Correlation coefficient test was used for correlation between depression (BDI) and Quality –of Life Scale. Probability level (P value < 0.05) was considered to be statistically significant [14].

Results

Sociodemographic data

There were no statistically significant differences regarding age, sex, marital status, education, and occupation.

Clinical profile of the psoriasis group

The age of onset of psoriasis ranges from 14 to 44 years, with a mean of 28.93 years and a standard deviation of + 9.4 years. The duration of illness in psoriatic patients ranges from 1 to 28 years, with a mean of 9.3 years and a standard deviation of + 7.97 years. Twenty psoriatic patients had lesions on their face and hands (66.7%), which were absent in 10 patients (33.3%). In contrast, eight patients had nail involvement (26.7%), which was absent in 22 patients (73.3%). Four psoriatic patients had joint involvement (13.3%), which was absent in 26 patients (86.7%).

Table 1 Distribution of psychiatric symptoms in patients with psoriasis

	Psoriasis patients $n=30$	
Psychiatric symptoms	*N*	Percentage
Depressed mood	20	66.7
Suicidal ideation	2	6.7
Suicidal attempt	1	3.3
Obsessions	4	13.3
Panic attacks	4	13.3
Worry from chronicity	17	56.7
Worry from recurrence	18	60.0
Sexual dysfunctions	18	60.0

N, numbers.

Table 2 Psychiatric diagnosis in patients with psoriases

Psychiatric diagnosis in psoriasis group ($n=30$)	*N*	Percentage
Major depressive disorder	8	26.7
Adjustment disorder with depressed mood	7	23.3
Dythymic disorder	4	13.3
Mixed anxiety and depression	1	3.3
Bipolar I disorder	1	3.3
No psychiatric diagnosis	9	30.0
Total	30	100

N, numbers.

Table 1 shows that depression is the most presenting psychiatric symptoms in patients with psoriasis and as shown in table 3 the score of depression in Beck depression inventory was higher in patients than control and the difference was statistically significant. Table 4 also shows that 43% of patients with psoriasis has severe depression.

Table 2 shows that 21 psoriatic patients (70%) had psychiatric diagnoses according to the DSM-IV and SCID-I [8,9].

Table 5 shows that there is a statistically significant difference between the psoriasis group and controls regarding Neuroticism, Introversion, and Lie Scales.

Table 6 shows that there is a statistical significant deference between the two groups as regards the disturbed body image

Table 7 shows that there is a statistically significant difference between the two groups regarding the physical, cognitive, affective, social, economic, and ego problems.

As regards depression and site of the lesion, patients with psoriatic lesions on their hand and face had a higher score on BDI, with a mean of 32.2 and standard deviation of ± 15.5 compared with those without lesions on their hand and face, with a mean of 19.9 and standard deviation of ± 15.4. There were statistically significant differences between the two groups ($P = 0.04$).

There is a statistically significant difference between the psoriasis group with disturbed body image and the

Table 3 Beck depression inventory in the psoriasis group and the control group

Beck depression inventory	Psoriasis group $n=30$	Control group $n=30$	*P*
Mean	28.1	10.03	
Standard deviation	± 16.3	± 7.1	0.000*

N, numbers.
$P<0.05$ is statistically significant.

Table 4 The severity of beck depression inventory (BDI) in the patients group and controls

	Psoriasis group $n=30$		Control group $n=30$			
Beck depression inventory	*N*	%	*N*	%	χ^2	*P*
Absent	7	23.3	20	66.7		
Mild	5	16.7	10	33.3		
Moderate	5	16.7	0	0.0	21.2	0.000*
Severe	13	43.3	0	0.0		
Total	30	100.0	30	100.0		

N, numbers.
*$P<0.05$ is statistically significant.

psoriasis group without disturbed body image as regards Neuroticism and Introversion, whereas there is no statistically significanct difference between the two groups regarding Psychoticism, Criminality, and Lie.

There are statistically significant negative correlations between BDI and Quality of Life Scale in all its subscales: physical ($P=0.000$), cognitive ($P=0.000$), affective ($P=0.000$), social ($P=0.001$), economic ($P=0.037$), and ego problems ($P=0.000$). This means that the increase in severity of depression is associated with decrease in QOL.

Discussion

In viewing the demographic data of the sample it can be noticed that there were no statistically significant differences between the psoriasis and the control group as regards all the sociodemographic data including age, sex, marital status, education, and occupation. This indicated that the samples were well matched and fit for the study and comparison. Our study indicates that

Table 6 Body image scale in the psoriasis group and the control group

Body image scale	Psoriasis group $n=30$	Control group $n=30$	*P*
Mean	23.03	8.3	
Standard deviation	±10.7	±7.03	0.000*

*$P<0.05$ is statistically significant.

the average age of onset in the psoriasis vulgaris group was 28.9 ± 9.4 years, with a range of 14–44 years and the average duration of illness in patients with psoriasis vulgaris was 9.3 ± 7.9 years. These results correspond with another recent study carried out on 50 consecutive patients with psoriasis in which the average age of onset was 31.1 ± 12.7 years and the duration of illness was 6.7 ± 5.7 years [15].

As regards the psychiatric morbidity, a study of 149 patients referred to liaison psychiatrist from a dermatology clinic reported that 95% warranted psychiatric diagnosis. Of these, depressive illness accounted for 44% and anxiety disorders for 35%, less common psychiatric disorders included social phobia, somatization disorder, alcohol dependence syndrome, obsessive–convulsive disorder, post-traumatic stress disorder, anorexia nervosa, and schizophrenia [16]. Our study revealed that 70% of patients with psoriasis have a psychiatric diagnosis according to DSM-IV, SCID-I [8,9]. Our findings could be compared with another study that found psychiatric comorbidity in 47.6% of the patients with psoriasis vulgaris [17]. Our findings also could be compared with another Egyptian study done on 50 patients with psoriasis identified psychiatric co-morbidity in 38% of them [18]. These differences in the prevalence of psychiatric disorders in psoriasis in the different studies could be explained by the diversity of psychiatric morbidity in psoriasis, which may be related to the sample size, the difference in patient

Table 5 Eysenck personality questionnaire (EPQ) in the psoriasis patients and the control group

	Psoriasis group $n=30$		Control group $n=30$		
Eysenck personality questionnaire (EPQ)	*N*	%	*N*	%	*P*
Psychoticism					
Normal	15	50.0	20	66.7	
Significant	15	50.0	10	33.3	0.295
Total	30	100.0	30	100.0	
Neuroticism					
Normal	9	30.0	21	70.0	
Significant	21	70.0	9	30.0	0.004*
Total	30	100.0	30	100.0	
Introversion					
Normal	12	40.0	26	86.7	
Significant	18	60.0	4	13.3	0.000*
Total	30	100.0	30	100.0	
Lie					
Normal	12	40.0	21	70.0	
Significant	18	60.0	9	30.0	0.018*
Total	30	100.0	30	100.0	
Criminality					
Normal	20	66.7	23	76.7	
Significant	10	33.3	7	23.3	0.567
Total	30	100.0	30	100.0	

N, numbers.
*$P<0.05$ is statistically significant.

Table 7 Quality of life scale in the psoriasis patients and the control group

	Psoriasis group $n=30$		Control group $n=30$		
Quality of life scale	Mean	SD	Mean	SD	*P*
Physical problems	36.7	±23.5	85.0	±12.5	0.000*
Cognitive problems	65.7	±26.5	86.7	±13.7	0.000*
Affective problems	52.0	±26.6	79.3	±15.7	0.000*
Social problems	58.0	±23.1	79.7	±14.7	0.000*
Economic problems	42.0	±27.1	69.7	±16.9	0.000*
Ego problems	51.0	±19.0	71.3	±12.2	0.000*

*$P<0.05$ is statistically significant.

selection, the duration of illness, and the different psychometric measures used with different cutoff scores used. Even studies that used standardized diagnostic criteria do not allow us to come to a conclusion about the relative prevalence of the psychiatric disorders in psoriasis.

In our study, the most common diagnosis was major depressive disorder (26.7%) followed by adjustment disorder with depressed mood (23.3%) then Dythymic disorder (13.3%), and only 3.3% have diagnosis of mixed anxiety and depression and 3.3% have diagnosis of bipolar I disorder. These findings were compared with the results of the study carried out using Mini International Neuro-Psychiatric Interview, and it was found that the most common psychiatric comorbidity in patients with psoriasis vulgaris was depression (28%) followed by suicidality (6%), alcohol abuse and dependence (6%), psychotic disorder and mood disorder with psychotic features (4%), generalized anxiety disorder (4%), social phobia (2%), and dysthymia (2%) [16]. The difference in the prevalence of different psychiatric comorbidities especially anxiety and depression in our study and this study could be due to the difference in the diagnostic systems used. In addition, different methodologies such as difference in population characters could also be the reason (for example the percentage of male patients in this study were 86% which is much higher than that of our study 53.3%, also our study showed higher illiteracy and unemployment than this study). All these factors make the comparison between both studies difficult. Suicidal ideation is a serious problem among sufferers of psoriasis. In our study, the rate of suicidal ideation was 6.7 and 3.3% had attempted suicide. This finding is consistent with that reported in another study carried out by Gupta *et al.* [19] who found that 9.7% of patients with psoriasis expressed a wish to die and 5.5% were experiencing active suicidal ideation at the time of the study. These rates are up to greater than two-folds that are found in the general community [20]. The rate of suicidal ideation among 79 outpatients being treated for psoriasis was 2.5%, consistent with figures seen in other populations with chronic illness [21]. However, among the 138 inpatients in the study, the rate was 7.2%. The difference in percentage of suicidal ideation between the outpatient and the inpatient groups could be explained by the degree of severity of psoriasis, which was extensive in the inpatient group with higher body surface area involved compared with the outpatient group [21]. In a more recent study who found suicidal ideation in 6% of patient with psoriasis and this could be related to the chronic nature of the disease and the limited life style associated with the disease [15]. In contrast, sexual problems and sexual dysfunction are common symptoms that are associated with psoriatic patients. Sixty percent of the psoriatic patients reported had sexual dysfunctions. This finding is consistent with another survey that found that more than 40% of sufferers felt that psoriasis had an adverse effect on their sexual functioning. In this study, joint involvement, more scaling, more pruritus, and higher depression scores were all significantly associated with impaired sexual functioning [22].

Beck Depression Inventory

This study showed that there were statistically significant differences between the group of psoriatic patients and normal control as regards BDI, with a mean of 28.1 ± 16.3 for the psoriasis group compared with 10.03 ± 7.1 for the control group. Many studies support this result; one of the studies found average BDI scores to be 17.96 ± 9.49 for the psoriatic patients and 8.15 ± 6.69 for the controls [23]. This could be explained by the possibility that people with skin diseases, especially psoriasis, suffer limitations in their social and interpersonal relations; they show signs of shame related to their appearance and sense of insecurity with a decreased possibility of finding any job. All these factors have a great impact on the self-esteem of psoriatic patients, which make them more vulnerable to develop depression.

When the BDI scores were assessed on the basis of mild, moderate, and severe depression, we found that overall 16.7% of the patients with psoriasis had scores corresponding to mild depression, 16.7% to moderate depression, and 43.3% to severe depression. Although there are few studies that quantify the level of depression scores, our findings are to be compared with that of another study [23] carried out on 50 patients with psoriases, which did not agree with our results and found that the majority of the patients had scores corresponding to moderate depression (32%) whereas 26% corresponded to severe depression [23]. The difference between the two studies may be interpreted by the different social, educational, and economic factors in addition to the different medical care and the early diagnosis of depression due to the good screening and effective referral system.

Eysenck Personality Questionnaire

Generally, there is no specific personality for psoriasis and the suggestion that patients with psoriasis have an underlying personality style needs further researches. This is why we tried to assess the personality characteristics of the psoriatic patients in our study, and we found that most of the patients in the psoriasis group showed significant higher score in the Neuroticism Scale, Introversion Scale, and Lie Scale. These results are consistent with the findings of another study [24] carried out on 50 Egyptian patients suffering from psoriasis and proved psoriatic patients to score significantly higher than normal regarding Introversion Scale, Neuroticism Scale, and Lie Scale [24].

Body Image Scale

Our study showed that there were statistically significant differences between the group of psoriatic patients and controls as regards the Body Image Scale, with a mean of 23.03 ± 10.7 in the psoriasis group and 8.3 ± 7.03 in the control group, which conclude that psoriatic patients showed more disturbed body image than normal. This could be explained by the idea that psoriasis has a great impact on the patients' appearance and perception of their own body, which make a great discrepancy between their perceived body and their ideal body. This finding agrees with the results of another study, which conclude that one of the most common psychiatric symptoms attributed to psoriasis include disturbance in body image, which in turn affect social and occupational functioning [25].

Quality of Life Scale (PCASEE)

In our study, we tried not only to examine the QOL of the patient with psoriasis in general but also to specify the degree of impairment in the QOL in each domain (physical, cognitive, affective, social, economic, and ego problems). We found that the group of patients with psoriasis showed lower score in every domain (physical, cognitive, affective, social, economic, and ego problems) when compared with the control group with a statistically significant difference. This result is consistent with the results of a study carried out on Egyptian patients suffering from psoriasis using the same Quality of Life Scale (PCASEE) and found that Psoriasis had the worst QOL compared with Vitiligo and Alopecia areata [18]. Moreover, the degree of psychosocial disability tended to be disproportionate with the degree of physical disability resulting from psoriasis [26]. In addition, the low score on the economic subscale of the Quality of Life Scale in our results is consistent with the finding that psoriasis also adversely affects patients' occupational capability, which can lead to significant financial difficulty [27].

Relationship between depression and site of lesions

In this study, we found a strong relationship between the presence of psoriatic lesions on the exposed sites, such as hand and face, in addition to nail involvement and depression. The mean BDI in the patients with psoriatic lesions on the hand and face was 32.2 ± 15.5 and on the nails was 39.4 ± 12.6, whereas those without lesions on the hand and face was 19.9 ± 15.4 and on nails was 24 ± 15.7 with a statistically significant difference. The above findings are confirmed by the study by Krueger *et al.* [28], who found that the visible area of involvement resulted in more impact on patients' life than involvement of the same size in other invisible areas. It was reported that nail involvement contributed to restrictions in daily activities in almost two-thirds of individuals, who have their impact on the QOL [29].

Relationship between personality characteristics of psoriatic patients and body image

In our study, we also tried to examine the relationship between the body image and the personality characteristics of patients with psoriasis, which to our knowledge is the first study that has investigated such a relationship. We found that there is statistically significant difference between the psoriasis group who had a disturbed body image and the psoriasis group without a disturbed body image regarding Neuroticism and Introversion. This finding supports the idea that the perception of psoriatic patients to their body influences their emotional experience and interaction with others. This idea is consistent with the findings of Jowett and Ryan's [30] study who reported that 89% of patients with psoriasis felt shame and embarrassment over their appearance, 58% suffered from anxiety, and 42% suffered from lack of confidence.

Correlation between depression, anxiety, and QOL

Currently, there is convincing evidence that depression plays an important role in the QOL in patients with psoriasis. Our study found that there is a statistically significant negative correlation between BDI and Quality of Life Scale in all its subscales: physical, cognitive, affective, social, economic, and ego problems. This means that the increase in severity of depression is associated with decrease in QOL and the same for Beck Anxiety Inventory and QOL. These findings are consistent with the study [18] carried out on 50 Egyptian psoriatic patients using the same Quality of Life Scale (PCASEE) and found that there is strong association between psychiatric morbidity and poorer QOL in psoriasis [18]. This is in agreement with the findings of another study that concurrent depression affects health related QOL of patients suffering from psoriasis at least as much as the clinical severity of their psoriasis [31]. The above results appear to be a strong support for the argument that the subjective experience of psoriasis is a more powerful determinant of QOL than is the degree of objective severity [32].

Limitations

(1) The patients were recruited from dermatology clinic and may therefore not be representative of all patients with psoriasis.
(2) Small sample size lead to smaller subgroups.
(3) We did not compare our results with another skin disease.

Conclusion

Findings of the study and other studies reported in the literature indicate that there is a high frequency of psychiatric comorbidities in patients with psoriasis especially depression, which represents the most frequent psychiatric disorder in psoriasis. The presence of psychiatric comorbidities increases the impairment in QOL in psoriatic patients. Although there are no specific personality characteristics for patients with psoriasis, our study found that the patients with psoriasis showed more neuroticism, introversion, and lie than controls. In addition, the disturbed body image perceived by patients about themselves plays an important role in shaping their personality.

There is no conflict of interest to declare.

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الملخص العربى

الاعراض النفسيه المصاحبه لمرضي الصدفيه

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يعتبر مرض الصدفية من الأمراض الجلدية الشائعة حيث يصيب ما يقرب من ٢ % من السكان. ومن المعروف أن الصدفية القشرية هى أكثر الأنواع شيوعاً وهى التهاب جلدي غالباً ما يكون مزمناً وتتميز بطبقة محمرة من الجلد تغطيها القشور وقد تكون مصحوبة بألم أو حكة. وقد يصاحب الصدفية التهابات مفصلية شديدة تؤدي إلى تغيرات مزمنة في المفصل فيما يقرب من ٣٠% من المرضى . و تشير أحدث الدراسات أن ما يقرب من ٣٠ % من المرضى المترددين على عيادات الأمراض الجلدية يعانون من أمراض نفسية قد تؤثر على إستجابتهم للعلاج. ويعد مرض الصدفية من أكثر الأمراض الجلدية التى تصاحبها أمراض نفسية .وقد تزايدت فى السنوات الاخيرة الدلائل على وجود العديد من الأعراض النفسية والمشاكل الإجتماعية المصاحبة لداء الصدفية كثيرة و متنوعة منها: الإكتئاب القلق،الأنطواء و الأنعزال الأجتماعى، المشاكل الجنسية و زيادة الميول الإنتحارية مما يكون له بالغ الأثر على نوعية الحياة للمريض. ولقد كانت أهداف البحث هى تحديد نسبة وانواع الأمراض النفسية المصاحبة لمرض الصدفية مثل الأكتئاب والقلق ومدى تأثيرها على نوعية الحياة للمريض . وكذلك دراسة السمات الشخصية لمرضى الصدفية. وقد خضع جميع الأشخاص الذين شملتهم الدراسة إلى: جمع البيانات الديمجرافية مثل : السن والنوع و المهنة و الحالة الإجتماعية .فحص الحالات فحصاً نفسياً اكلينكياً دقيقاً مقياس بيك للإكتئاب .إختبار صورة الجسم.إختبار أيزنك للشخصية . إختبار نوعية الحياة للمريض النفسى. وجد من خلال البحث مايلى: لا توجد إختلافات إيجابية بين مرضى الصدفية والعينة الضابطة من حيث السن والنوع و المهنة و الحالة الإجتماعية والإقتصادية و المستوى التعليمى . وجد أن ٧٠ % من مرضى الصدفية يعانون من أمراض نفسية حيث يمثل الإكتئاب المرض الأكثر شيوعاً . توجد إختلافات إيجابية بين مرضى الصدفية والعينة الضابطة من حيث مقياس بيك للإكتئاب حيث وجد أن نسبة الإكتئاب أعلى عند مرضى الصدفية وذو دلالة إحصائية . توجد إختلافات إيجابية بين مرضى الصدفية والعينة الضابطة من حيث مقياس بيك للقلق حيث وجد أن نسبة القلق أعلى عند مرضى الصدفية وذو دلالة إحصائية .توجد إختلافات إيجابية بين مرضى الصدفية والعينة الضابطة من حيث إختبار صورة الجسم حيث وجد أن نسبة التشوه فى صورةالجسم أعلى عند مرضى الصدفية وذو دلالة إحصائية . توجد إختلافات إيجابية بين مرضى الصدفية والعينة الضابطة من حيث إختبار نوعية الحياة للمريض النفسى حيث وجد أن نوعية الحياة عند مرضى الصدفية اقل مستوى وذو دلالة إحصائية من جميع النواحى المادية و الإجتماعية و المعرفية و الجسدية و المزاجية و الذاتية . فيما يتعلق بالسمات الشخصية بتطبيق إختبار أيزنك للشخصية وجد أن مرضى الصدفية يميلون أكثر إلى الإنطوائية و الكذب وهم أكثر عصابية من العينة الضابطة وذو دلالة إحصائية . توجد علاقة عكسية وذو دلالة إحصائية بين الإكتئاب ونوعية الحياة لمرضى الصدفية .كما توجد أيضاً علاقة عكسية وذو دلالة إحصائية بين القلق ونوعية الحياة لمرضى الصدفية .وأخيراً توجد علاقة طردية إيجابية بين مدة المرض و درجة تشوه صورة الجسم لدى مرضى الصدفية .

Psychiatric morbidity across perinatal period in a sample of Egyptian women

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Introduction

Pregnancy and puerperium are universal events that face the majority of women in the reproductive age all around the world, during which major biological, hormonal, and psychological events occur. This study was conducted to verify the hypothesis and investigate (i) psychiatric morbidity in the perinatal period and its comparison with controls. (ii) Is there difference in the psychiatric state across the four perinatal periods?

Patients and methods

Accordingly, a study was conducted on 105 women who were pregnant or in the postpartum period. They were selected from the outpatient clinic of Obstetrics and Gynecology Hospital in the Ain Shams University. Control nonpregnant women were also selected. They were subjected to Mini International Neuropsychiatric Interview-Plus, Beck Depression Inventory, State-Trait Anxiety Inventory, and Edinburgh Postnatal Depression Scale.

Results

Our study revealed that the prevalence of psychiatric disorders during the first and second trimesters of pregnancy was not significantly different in comparison with controls. However, it is much higher than controls during the third trimester with slight decrease in the postpartum period. The most common diagnosis that was found is adjustment disorder all through pregnancy. There were no significant differences between psychiatric morbidity across the perinatal period.

Conclusion

We can conclude that women are vulnerable to psychiatric morbidity in the perinatal period especially in the third trimester and they have high depressive and anxiety states.

Keywords:
anxiety, depression, perinatal, postpartum, pregnancy, psychiatric morbidity

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Introduction

The miracle of pregnancy and the transformation of women into mothers have fascinated people from antiquity to the present. However, it is only during the past century that mental health professionals have begun to contribute to our understanding of the psychological aspects of pregnancy and the psychological phases that the women pass through their journey to motherhood [1].

The past decade has witnessed the emergence of an increased interest in women's reproductive health and development-related programs to improve reproductive health across the globe. This phenomenon was primarily catalyzed by the 1994 International Conference on Population and Development in Cairo. This conference solidified a new, comprehensive understanding of reproductive health, largely owing to the efforts of participating policymakers, researchers, health service providers, scholars, feminists, and health advocates from developed and developing countries [2].

Pregnancy is a time of profound biological, psychological, and interpersonal changes in the lives of many women, and as the stages of psychological adaptation to the event are not well understood, yet a stage of ambivalence develops as a normal response to a major life transition for which some women may fail to adapt, hence psychological state develops [3].

Several psychiatric disorders may occur during the perinatal period, such as anxiety, mood symptoms especially depression, obsessive–compulsive disorder, post-traumatic stress disorder, sleep disorders forgetfulness, and postpartum blues, depression, or psychosis postnatally as well [3].

The aims of the study was

(1) To verify that women are more prone to psychiatric morbidity during the perinatal period;
(2) Is psychiatric morbidity more common during pregnancy and postpartum period, in comparison with control group?

(3) Attempt to predict any specific risk factor that could predispose psychiatric morbidity during the perinatal period;
(4) Is there difference in the psychiatric state across the four perinatal periods?

Patients and methods

Study design

This study is a quantitative, cross-sectional case–control, observational study at the Department of Obstetrics and Gynecology, Ain Shams University Hospitals.

One hundred and sixty women participated in this study. They were organized into five groups.

The case group represented pregnant women and was divided into four groups; three groups represented three trimesters of pregnancy (each group for a trimester) and the fourth group represented the postpartum period.

A stratified random sample of 115 women who were attending the outpatient clinic for obstetric antenatal follow-up of pregnancy and the gynecology clinic and family planning clinic for postpartum period follow-up or for postpartum contraception were chosen.

Women who had a medical history and those with a positive psychiatric history were excluded; they were nine in number.

(1) Pregnant women were selected from the obstetric clinic on Sundays on a weekly basis.
(2) We chose the seventh and the 14th names of each clinic, and according to the patient's gestational age she was placed in her group.
(3) The first group included women who were pregnant and their gestational age ranged from first week to 13th week, which represented the first trimester interval. It consisted of 25 women.
(4) The second group included women who were pregnant and their gestational age ranged from 14th week to 27th week, which represented the second trimester interval. It consisted of 25 women.
(5) The third group included women who were pregnant and their gestational age ranged from 28th week to 40th week or term, which represented the third trimester interval. It consisted of 28 women.
(6) The fourth group represented women in the postpartum period ranging from fourth week to 24th week postpartum.

The control group (group 5) consisted of 50 Egyptian married women in the child-bearing period who were not pregnant and a minimum of 2 years had passed since the previous postpartum period. They were matched for age and other demographic variables. An informed verbal consent was obtained from all participants.

All patients were subjected to:

(1) Complete personal, family, past history for both medical and psychiatric histories were obtained.
(2) Full obstetric history of the current pregnancy and previous pregnancies.
(3) General and neurological examinations.
(4) The Mini International Neuropsychiatric Interview (M.I.N.I.-Plus).
(5) Then, all were requested to answer all questions of all used questionnaires:
    (a) Beck Depression Inventory (BDI).
    (b) State-Trait Anxiety Inventory (STAI).
    (c) Edinburgh Postnatal Depression Scale (EPDS).

Mini International Neuropsychiatric Interview-Plus [4]

M.I.N.I.-Plus was designed to provide a structured, standardized, and summarized tool for axis 1 diagnoses by *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* (DSM-IV) and WHO international classification of diseases, tenth revision (ICD-10) either in the past or currently. It is divided into sections from A–Z, and each has an English letter that represents different diagnostic groups, major depression, dysthymia, bipolar affective disorder, panic disorder, agoraphobia, social phobia, obsessive–compulsive disorder, posttraumatic stress disorder, substance and alcohol abuse, psychotic disorders, premenstrual syndrome, and so on. Both required and optional probes are provided, and skip outs are subjected when no further questioning is warranted. Validity and reliability studies were carried out to M.I.N.I.-Plus, and revealed high validity and reliability values. In addition, it has a benefit that it needs less time for application. M.I.N.I.-Plus has been translated by Ghanem *et al.* [5], and this Arabic version was used in this study.

Beck Depression Inventory [6]

It is often used in a self-rating form. It screens and measures the depth and behavioral manifestations of depression and consists of 21 items, each of which has four responses of increasing severity.

Numerical values from 0–3 are assigned to each statement to indicate the degree of severity. The total score is then interpreted; a score from 0 to 20 is considered normal, a score from 31 to 40 is considered mild, a score from 31 to 41 is considered moderate, and a score from 42 to 63 or above is considered severe depression.

It is a widely used standardized, consistent instrument with proven validity and reliability and has been used in several studies. It has been translated to Arabic.

State-Trait Anxiety Inventory

The State-Trait Anxiety Inventory is a self-rating scale that is composed of two parts, and is used to assess both anxiety state and anxiety trait separately in adults whether healthy, physically ill, or mentally ill [7]. Anxiety state assessment reveals the degree of anxiety experienced by the patient currently. In contrast, anxiety trait assessment reveals the degree of anxiety generally and is used to differentiate individual responses to stressors. Each part of the scale is composed of 20 statements, and the answers are graded into four degrees (never, little

amount, sometimes, always). Numerical scores from 1 to 4 are graded according to severity for each statement; these values are summed up to give the total scale ranging from 20 to 80 for each part. The scale has been translated and validated, and this Arabic version El beheery [8] was used in this study.

Edinburgh Postnatal Depression Scale [9]

It is a self-rating screening scale for depressive symptoms during pregnancy and postpartum period. It is composed of 10 items; each item is scored on a four-point scale 0–3, the score ranges from 0 to 30. The scale rates the intensity of depressive symptoms. Five items are concerned with dysphoric mood, two with anxiety, and three with guilt, and one each for not coping and suicidal ideas. A validated Arabic version is used in this study.

Statistical analysis

All data were recorded and entered in a statistical package on a compatible computer and varied. Analysis was carried out using an SPSS version 15 (SPSS, IBM, Chicago, Illinois, USA), 2007.

Results

As regards sociodemographic data:

(1) We found that the mean age for group 1 was 28.1 ± 5.473 standard deviation (SD) years, for group 2 was 28.48 ± 5.471 SD years, for group 3 was 27.27 ± 5.023 SD years, and for group 4 was 28.44 ± 6.216 SD years, with a quite comparable mean age for the control group (29.54 ± 0.186 SD years; $P = 0.381$). In addition, there were no significant differences between the four groups as regards other data, that is, educational level, social class, and occupations when they were compared with the control group.

(2) Marriage duration showed a mean of 4.73 ± 4.221 SD years in the first four groups and a mean of 5.86 ± 3.608 SD years in the control group ($P = 0.232$). In addition, on comparing the four groups with the controls as regards obstetric history (number of parity, history of abortion) there was no difference between them.

Part 1

Group 1 ($n = 25$) represents pregnant women in the first trimester recruited from the obstetric clinic for antenatal follow-up.

Table 1 shows no significant difference between the two groups as regards past history or family history of psychiatric morbidity, but there were significant differences between them in having a history of premenstrual dysphoric disorder (PMDD).

At the same time, current psychiatric morbidity assessed using M.I.N.I.-Plus revealed that 32% of women in the first trimester had an axis-I diagnosis; adjustment disorder was the main diagnosis and this was of no statistical difference when compared with the control group as shown in Table 2.

On assessment of the depressive state in both groups using BDI, there were very high significant differences between both the groups (Table 3); moreover, using EPDS 20% ($n = 5$) of women in the first trimester were found to be depressed.

Table 3, on assessment of anxiety state and trait shows that the women who were in their first trimester showed

Table 1 Psychiatric morbidity among women in the first trimester in comparison with the control group

	Group 1 ($n=25$)		Group 5 ($n=50$)				
	N	Percentage	*N*	Percentage	Chi-square value	*P* value	Significance
Family history							
Yes	1	4	3	6	1.563	0.211	NS
No	24	96	47	94			
Past history							
Yes	3	12	2	4	0.315	0.575	NS
No	22	88	48	96			
PMDD							
Yes	10	40	33	66	4.606	0.032	SIG
No	15	60	17	34			

N, number of patients; NS, not significant; PMDD, premenstrual dysphoric disorder; SIG, significant.

Table 2 Current psychiatric morbidity among women in the first trimester in comparison with the control group

	Group 1 first trimester ($n=25$)		Group 5 controls ($n=50$)				
Psychiatric morbidity	*N*	Percentage	*N*	Percentage	Chi-square value	*P* value	Significance
None	17	68	43	86			
Axis-I diagnosis	8	32	7	14			
Adjustment disorder-mixed type	4	16	3	6	4.061	0.255	NS
Adjustment disorder-depressive type	3	12	2	4			
Major depressive disorders	1	4	2	4			

N, number of patients; NS, not significant.

Table 3 Assessment of depressive state, anxiety state, and trait in women in the first trimester in comparison with the control group

Assessment tool	Group 1 ($n=25$)	Group 5 ($n=50$)	*t* value	*P* value	Significance
BDI					
Mean	14.04	7.14	4.501	0.000	VHS
SD	8.193	5.047			
Anxiety state					
Mean	48.56	35.78	4.986	0.000	VHS
SD	11.023	10.179			
Anxiety trait					
Mean	47.00	38.00	4.389	0.000	VHS
SD	9.587	7.706			

BDI, Beck Depression Inventory; VHS, very high significance.

Table 4 Psychiatric morbidity among women in the second trimester in comparison with the control group

	Group 2 ($n=25$)		Group 5 ($n=50$)				
	N	Percentage	*N*	Percentage	Chi-square value	*P* value	Significance
Family history							
Yes	1	4	3	6	0.132	0.716	NS
No	24	96	47	94			
Past history							
Yes	2	8	2	4	2.027	0.155	NS
No	23	92	48	96			
PMDD							
Yes	14	56	33	66	0.712	0.399	NS
No	11	44	17	34			

N, number of patients; NS, not significant; PMDD, premenstrual dysphoric disorder.

Table 5 Current psychiatric morbidity among women in the second trimester in comparison with the control group

	Group 2 second trimester ($n=25$)		Group 5 controls ($n=50$)			
Psychiatric morbidity	*N*	Percentage	*N*	Percentage	Chi-square value	*P* value
None	21	84	43	86		
Axis-I diagnosis	4	16	7	14		
Adjustment disorder-mixed type	2	8	3	6	4.758	0.313
Adjustment disorder-depressive type	0	0	2	4		
Major depressive disorders	1	4	2	4		
Somatization	1	4	0	0		
Specific phobia	1	4	0	0		

N, number of patients.

Table 6 Assessment of depressive state, anxiety state, and trait in women in the second trimester in comparison with the control group

Assessment tool	Group 2 ($n=25$)	Group 5 ($n=50$)	*t* value	*P* value	Significance
BDI					
Mean	11.16	7.14	2.855	0.006	HS
SD	6.962	5.047			
EPDS					
Mean	7.52	0			
SD	5.277				
Anxiety state					
Mean	46.52	35.78	4.482	0.000	VHS
SD	8.922	10.179			
Anxiety trait					
Mean	47.08	38.00	4.650	0.000	VHS
SD	8.490	7.706			

BDI, Beck Depression Inventory; EPDS, Edinburgh Postnatal Depression Scale.

Table 7 Psychiatric morbidity among women in the third trimester in comparison with the control group

	Group 3 ($n=28$)		Group 5 ($n=50$)				
	N	Percentage	*N*	Percentage	Chi-square value	*P* value	Significance
Family history							
Yes	1	3.6	3	6	0.218	0.641	NS
No	27	96.4	47	94			
Past history							
Yes	2	7.15	2	4	0.770	0.380	NS
No	26	92.85	48	96			
PMDD							
Yes	16	57.1	33	66	0.603	0.437	NS
No	12	42.9	17	34			

N, number of patients; NS, not significant; PMDD, premenstrual dysphoric disorder.

Table 8 Current psychiatric morbidity among women in the third trimester in comparison with the control group

	Group 3 third trimester ($n=28$)		Group 5 controls ($n=50$)				
Psychiatric morbidity	*N*	Percentage	*N*	Percentage	Chi-square value	*P* value	Significance
None	16	57.1	43	86	26.305	0.000	VHS
Axis-I diagnosis	12	42.9	7	14			
Adjustment disorder-mixed type	4	14.2	3	6			
Anxiety disorder	3	10.7	0	0			
Major depressive disorders	2	7.2	2	4			
Post-traumatic stress disorder	2	7.2	0	0			
Specific phobia	2	7.2	0	0			
Social phobia	1	3.6	0	0			
Adjustment disorder anxiety type	0	0.0	2	4			

N, number of patients.

Table 9 Assessment of depressive state, anxiety state, and trait in women in the third trimester in comparison with the control group

Assessment tool	Group 3 ($n=28$)	Group 5 ($n=50$)	*t* value	*P* value	Significance
BDI					
Mean	15.36	7.14			
SD	10.962	5.047	4.528	0.000	VHS
EPDS					
Mean	10.79				
SD	6.713				
Anxiety state					
Mean	50.61	35.78			
SD	12.974	10.179	5.583	0.000	VHS
Anxiety trait					
Mean	48.86	38.00			
SD	12.385	7.706	4.775	0.000	VHS

BDI, Beck Depression Inventory; EPDS, Edinburgh Postnatal Depression Scale.

a mean score of 48.56 ± 11.023 SD compared with a mean score of 35.78 ± 10.179 SD in the control group, and this difference was statistically of high significance ($P = 0.000$).

Part 2

Group 2 represents pregnant women in their second trimester; there were 25 women. They were compared with the control group (group 5, $n = 50$).

Table 4 shows no significant difference between the two groups as regards past history or family history of psychiatric morbidity, but there were significant differences between them in having a history of PMDD.

At the same time, the current psychiatric morbidity that was assessed using M.I.N.I.-Plus revealed that 16% of women in the second trimester had an axis-I diagnosis; adjustment disorder was the main diagnosis and this was of no statistical difference when compared with the control group as shown in Table 5.

On BDI, the scores showed a mean value of 11.16 ± 6.962 SD compared with the controls' mean score (7.14 ± 5.047 SD); this was statistically highly significant ($P = 0.006$) as shown in Table 6. There were 16% ($n = 4$) of women having scores greater than 20 according to the cutoff score of BDI, and they were considered to be depressed.

Table 10 Psychiatric morbidity among women in the postpartum period in comparison with the control group

	Group 4 ($n=27$)		Group 5 ($n=50$)				
	N	Percentage	*N*	Percentage	Chi-square value	*P* value	Significance
Family history							
Yes	2	7.4	3	6			
No	25	92.6	47	94	0.057	0.811	NS
Past history							
Yes	1	3.7	2	4			
No	26	92.85	48	96	0.770	0.380	NS
PMDD							
Yes	14	51.9	33	66			
No	13	48.1	17	34	1.476	0.224	NS
Postpartum blues							
Yes	10	37.0					
No	17	63.0					

N, number of patients; NS, not significant; PMDD, premenstrual dysphoric disorder.

Table 11 Current psychiatric morbidity among women in the postpartum period in comparison with the control group

	Group 4 postpartum ($n=27$)		Group 5 controls ($n=50$)			
Psychiatric morbidity	*N*	Percentage	*N*	Percentage	Chi-square value	*P* value
None	17	63.0	43	86	11.049	0.087
Axis-I diagnosis	10	37.0	7	14		
Adjustment disorder-mixed type	3	11.1	3	6		
Anxiety disorder	1	3.7	0	0		
Major depressive disorders	1	3.7	2	4		
Post-traumatic stress disorder	2	7.4	0	0		
Specific phobia	2	7.4	0	0		
Social phobia	1	3.7	0	0		
Adjustment disorder anxiety type	0	0.0	2	4		
Postpartum depression	1	3.7	0	0		
Postpartum depression with psychotic features	1	3.7	0	0		
Postpartum psychosis	1	3.7	0	0		

N, number of patients.

Table 12 Assessment of depressive state, anxiety state, and trait in females in the postpartum period in comparison with the control group

Assessment tool	Group 4 ($n=27$)	Group 5 ($n=50$)	*t* value	*P* value	Significance
BDI					
Mean	17.52	7.14	6.101	0.000	VHS
SD	9.916	5.047			
EPDS					
Mean	9.37				
SD	6.840				
Anxiety state					
Mean	47.78	35.78	4.711	0.000	VHS
SD	11.524	10.179			
Anxiety trait					
Mean	48.19	38.00	4.443	0.000	VHS
SD	12.404	7.706			

BDI, Beck Depression Inventory; EPDS, Edinburgh Postnatal Depression Scale.

Table 6, on assessment of anxiety state shows that the women who were in their second trimester showed a mean score of 46.52 ± 8.922 SD compared with a mean score of 35.78 ± 10.179 SD in the control group, and this difference was statistically of high significance ($P = 0.000$). As regards anxiety trait, the women in their second trimester showed a mean score of 47.08 ± 8.490 SD compared with a mean score of 38.00 ± 7.706 SD in the control group, and this difference was statistically highly significant ($P = 0.000$).

Part 3

Group 3 represents pregnant women in their third trimester; there were 28 women. They were compared with the control group (group 5), and they were 50 in number.

Table 13 Shows comparison between the four groups as regards depressive state, anxiety state, and trait scores, it showed no statistical difference between different groups

Scores	Group 1 ($n=25$)	Group 2 ($n=25$)	Group 3 ($n=28$)	Group 4 ($n=27$)	*F* value ANOVA	*P* value	Significance
EPDS							
Mean	8.08	7.52	10.79	9.37	1.403	0.246	NS
SD	6.298	5.2777	6.713	6.840			
BDI							
Mean	14.04	11.16	15.36	17.52	2.158	0.098	NS
SD	8.193	6.962	10.962	9.916			
Anxiety state							
Mean	48.56	46.52	50.61	47.78	0.619	0.604	NS
SD	11.023	8.922	12.974	11.524			
Anxiety trait							
Mean	47.00	47.08	48.86	48.19	0.179	0.910	NS
SD	9.587	8.490	12.385	12.404			

ANOVA, analysis of variance; BDI, Beck Depression Inventory; EPDS, Edinburgh Postnatal Depression Scale; NS, not significant.

Table 7 shows no significant difference between the two groups as regards past history or family history of psychiatric morbidity, but there were significant differences between them in having a history of PMDD.

At the same time, the current psychiatric morbidity assessed using M.I.N.I.-Plus revealed that 42.9% of women in the third trimester had an axis-I diagnosis; adjustment disorder was the common diagnosis, and when compared with the control group there were significant statistical differences as shown in Table 8.

On BDI, the scores showed a mean value of 15.36 ± 10.962 SD compared with the controls' mean score (7.14 ± 5.047 SD), this was statistically highly significant ($P = 0.006$) as shown in Table 9. There were 32.1% ($n = 9$) of women having scores greater than 20 according to the cutoff score of BDI, and they were considered to be depressed.

Table 9, on assessment of anxiety state, the women who were in their third trimester showed a mean score of 50.61 ± 12.974 SD compared with the mean score in the control group (35.78 ± 10.179 SD), and this difference was statistically of high significance ($P = 0.000$). As regards anxiety trait, the women in their third trimester showed a mean score of 48.86 ± 12.385 SD compared with a mean score of 38.00 ± 7.706 SD in the control group, and this difference was statistically highly significant ($P = 0.000$).

Part 4

Group 4 represents women in the postpartum period from 2 weeks to 24 weeks postpartum; there were 27 women. They were compared with the control group (group 5); they were 50 in number.

Table 10 shows no significant difference between the two groups as regards past history or family history of psychiatric morbidity, but there were significant differences between them in having a history of PMDD.

At the same time, current psychiatric morbidity assessed using M.I.N.I.-Plus revealed that 37% of women in the postpartum period had an axis-I diagnosis; adjustment disorder was the common diagnosis, and when compared with the control group there were no significant statistical difference as shown in Table 11.

On BDI, the scores showed a mean value of 17.52 ± 9.916 SD compared with the controls' mean score (7.14 ± 5.047 SD); this was statistically highly significant ($P = 0.006$) as shown in Table 12. Of all the women, 40.7% ($n = 11$) had scores greater than 20 according to the cutoff score of BDI, and they were considered to be depressed.

Table 12, on assessment of anxiety state shows that the women who were in their postpartum period showed a mean score of 47.78 ± 11.524 SD compared with a mean score of 35.78 ± 10.179 SD in the control group, and this difference was statistically of high significance ($P = 0.000$). As regards anxiety trait, they showed a mean score of 48.19 ± 12.404 SD compared with a mean score of 38.00 ± 7.706 SD in the control group; this difference was statistically highly significant ($P = 0.000$).

Part 5

In this part, we try to answer the question whether there is any difference between different groups (three trimesters and the postpartum period) in the depressive state, anxiety state, and trait.

It is shown that the highest prevalence of depression and psychiatric morbidity is in the third trimester, followed by the postpartum period, and the least in prevalence is the second trimester as shown in Table 13.

Discussion

Although pregnancy is a common event for reproductive-age women, surprisingly little has been published about the physical and emotional changes that typically occur during pregnancy and the postpartum period in the literature [10,11].

Perinatal mental health refers to the emotional well being of a mother, her partner, and her infant, from conception until 24 months postpartum. Transitional life stages also represent times of increased vulnerability, and a degree of anxiety and a labile mood can be expected at these times. However, they are also associated with increased vulnerability to more severe mental health disturbances.

During this time, women (and their partners) may experience difficulties ranging from mild, transient anxiety, or depression to more severe psychiatric illness [12].

Our results were divided into four parts; each part addresses one trimester of the three trimesters of pregnancy and the postpartum period. These partitions were considered in a trial to associate the results of each part to the nature of changes of each stage of pregnancy and postpartum period.

Psychiatric morbidity in the first trimester

Our results revealed that 32% of female patients in the first trimester had an axis-I diagnosis, but that was not significantly higher than controls. The most frequent diagnosis was adjustment disorder mixed anxiety and depression type (16%), depressive type (12%), major depressive disorder (4%), and one case of double depression (4%). These findings suggest that there is no difference between prevalence of psychiatric disorders among women in the first trimester and the women in the general population, and this agrees with the opinion of literature [13].

During the first trimester, it can be particularly difficult to diagnose depression because of the overlap between symptoms of pregnancy and somatic symptoms of depression. Bennett *et al.* [13] reported a rate of depression during the first trimester was found by Birndorf *et al.* [14] to be 24.6% using BDI, and this agrees with our findings.

When assessing the anxiety state and trait, it was found that there were very high significant differences between women in the first trimester in comparison with controls. There were no researches found assessing anxiety symptomatology. The available researches only assessed specific anxiety disorders such as obsessive–compulsive disorder or panic disorder course during pregnancy in well-known patients with these disorders.

In a trial to find sociodemographic correlates with depression and anxiety states, we found that the depressive state was positively correlated with occupational differences; women who had professional occupations had higher levels of depressive state. Similar finding was found by Felice *et al.* [15], and postulated it as it is due to the trial of the women to adjust with her new condition.

Psychiatric morbidity in the second trimester

In addition, in our study we found that 16% of women in the second trimester had axis-I diagnosis, approximately half of the patients (8%) had adjustment disorder, major depressive disorder (4%), somatization (4%), specific phobia (4%), and this rate was not statistically significant different from controls. The most common diagnosis was adjustment disorder. Nearly the same findings were reported by Andersson *et al.* [16].

Evaluation of the depression state revealed statistically higher scores in women in the second trimester than controls. In addition, depressive symptomatology rates were 16% when assessed by both EPDS and BDI, and those 16% were only having a mild degree of depression according to the severity degrees of BDI. The same rate was found by Salamero *et al.* [17].

Gavin *et al.* [18] in a systematic review of perinatal depression prevalence and incidence reported that prevalence of both minor and major depressions in the first trimester is 11%, which drops to 8.5% in the second trimester. We also found the same drop of the depressive symptomatology from the first trimester 20–25%, which dropped to 16% in the second trimester, but the difference in our rates is postulated to the different study populations and the different assessment tools that were used.

When assessing anxiety state and trait, it was found that there were very high significant differences between women in the second trimester in comparison with controls.

On studying socidemographic correlates, there was significantly positive correlation between low socioeconomic class and severity of depression. This was in agreement with all studies assessing depression in the perinatal period, as they considered that low socioeconomic status is a risk factor for depression in the perinatal period, and those of low socioeconomic status were considered to be a high-risk group and rates of depression may reach 50% [13,19].

Psychiatric morbidity in the third trimester

In the third trimester, we found that the psychiatric morbidity rate increased and reached 42.9% of the sample having axis-I diagnosis, and this rate was significantly higher than controls. With adjustment disorder being the most common diagnosis 14.2%, anxiety disorder 10.7%, the rate of major depressive disorder increased to 7.2% including patients who were having comorbidity (having both depression and anxiety).

Meanwhile, the rate of depressive symptoms increased as well; it reached 32.1–42.9% when assessed by BDI and EPDS, respectively. The mean score of BDI was significantly higher than controls. These findings suggest that the progression of pregnancy may have an impact on the status of depression, and this agrees with Bennett *et al's* findings. [13]. In addition, we suggest that the mechanism of depression progression in the third trimester is related to the high levels of corticotropin-releasing hormone, which reaches its highest levels in the third trimester [13].

When assessing the anxiety state and trait, it was found that there were very high significant differences between women in the third trimester in comparison with controls. Unfortunately, there were no researches found assessing anxiety symptomatology for comparative results. This high anxiety state can be explained by the well-known high comorbidity between depression and anxiety, and also by the high level of cortisol hormonal level during pregnancy specifically during the third trimester, and this hormone increases the sense of stress and stress reaction.

Meanwhile, we found that the BDI score was directly correlated with a history of PMDD. This agrees with the literature and other researchers' findings, as they reported that history of PMDD is considered to be a risk factor for depression during pregnancy [20].

Psychiatric morbidity in the postpartum period

We found that the rate of postpartum blues in our sample is 37%; the universal ranges of postpartum blues is approximately 29–80% [21]. This wide range of variation can be attributed to cultural factors and the presence of high social and familial support after childbirth that may ameliorate the symptoms rapidly. The same percentage of postpartum blues in Egypt was reported by El Akabawi *et al.* [22]; another study in Egypt found lower rates (8%) of postpartum blues, which was explained by methodological differences [23].

Okasha *et al.* [23], in a descriptive, epidemiological study of the postpartum psychiatric disorders in Egypt, found that the incidence of postpartum psychiatric disorders was 4.3%. Most of these findings are in accordance to our findings.

Using the self-report tools, we found that the rate of depressive symptomatology in the postpartum period was 40.7% according to the cutoff scores of both BDI and EPDS. In addition, the mean scores in both the questionnaires were statistically very highly significant than those of the controls.

In a recent study in Brazil, researchers found that the rate of postpartum depression is 20.7%, which as they reported is considered higher than rates recorded in developed countries, and they deduced that low income is a risk for the development of postpartum depression in developing countries [24].

In addition, researchers suggested that postpartum depression is a continuum with prenatal depression, which needs further investigation with longitudinal cohort study to follow these variations.

However, the finding of an increased risk commencing shortly after delivery suggests that childbirth and its immediate psychosocial sequelae are likely to be important causal factors for nonpsychotic depression [25].

On the assessment of anxiety state and trait postpartum, we found very high significant levels in comparison with controls; this finding agrees with Ahmed *et al's.* [26] findings.

Furthermore, obstetric variables as regards parity or way of labor were not significantly correlated to the severity of the depressive state and anxiety state and trait; this agrees with the findings of Ahmed *et al.* [26], and Felice *et al.* [15].

On comparing the four periods of the perinatal period, we did not find any significant difference between them as regards severity of depressive or anxiety state and trait despite being significantly higher than controls. However, we observed that the highest mean scores were in the third trimester, followed by the postpartum period and the lower scores were in the second trimester. Furthermore, the rate of depressed patients and patients with axis-I diagnosis was highest in the third trimester, followed by the postpartum period, and the least percentages were in the second trimester. So we deduced that third trimester is the most critical period in pregnancy where vulnerability to develop depression, anxiety or other psychiatric disorder reaches its peak during the third trimester, with slight decrease of this vulnerability in the postpartum period. The least vulnerability is during the second trimester, which is considered as an interval for emotional, physical, and psychological stability during pregnancy. Therefore, we suggest that longitudinal prospective study on a larger number of patients will show the onset and course of symptomatology more clearly. Similar findings were reported by Evans *et al.* [27] and Josefsson *et al.* [28] in their longitudinal studies, and they recommended that early screening during pregnancy and intervention when needed may decrease the incidence of postpartum psychiatric disorders.

Conclusion

From our research, we concluded that the prevalence of psychiatric disorders during the first and second trimesters of pregnancy is as common as in the general population. However, it is much higher during the third trimester with a slight decrease in the postpartum period. The most common diagnosis that was found is adjustment disorder. Therefore, we suggest that social support may improve their condition.

All through the perinatal period there was high prevalence of depressive and anxiety symptomatology.

In addition, we found that depressed patients had higher harm avoidance, lower persistence, self directedness, and cooperativeness.

Thus, we agree with regard to increased rate of psychiatric morbidity in the perinatal period and how personality affects their presentation.

There is no conflict of interest to declare.

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الملخص العربى

الامراض النفسية المصاحبة لفترة الحمل و ما بعد الولادة فى عينة من السيدات المصريات

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كلية الطب- جامعة عين شمس

إن معجزة الحمل و الولادة و تحول المرأة إلي أم قد شغلت الناس منذ الأزل حتى ألآن، و لكن حديثا فقط بدأ الاهتمام بالجوانب النفسية للمرأة الحامل، في محاولة لفهم التغيرات النفسية التي تحدث لها في هذه المرحلة الهامة لكي تصبح أماً.

الهدف من العمل :

- إثبات ما تتعرض له السيدات أثناء الحمل من مشاكل نفسية .
- مراجعة الأبحاث السابقة التي لها علاقة بالبحث .
- دراسة مدي انتشار الاضطرابات النفسية في النساء.

تم عمل الدراسة في قسم إمراض النساء و التوليد بمستشفيات جامعة عين شمس .

- وقد تم تقسيم هذه العينة الى اربعة أقسام :

القسم الاول : وهو يمثل السيدات اللاتى فى الشهور الثلاث الاولى من الحمل وهن 25 سيدة .

القسم الثانى : وهو يمثل السيدات اللاتى فى الشهور الثلاث الثانية من الحمل وهن 25 سيدة .

القسم الثالث : وهو يمثل السيدات اللاتى فى الشهور الثلاث الاخيرة من الحمل وهن 28 سيدة .

خيراً القسم الرابع : وهو للسيداتفى فترة ما بعد الولادة وعددهن 27 سيدة.

العينة الضابطة : وتتكون من 50 سيدة من العاملات فى المستشفى.

الاختبارات و الأدوات :

1. مقياس ميني بلس الإكلينيكي لتشخيص الأمراض النفسية.
2. مقياس المستوى الاجتماعى لفهمى والشربينى .
3. مقياس ادنبرج لأكتئاب ما بعد الولادة .
4. مقياس بيك الأكتئاب .
5. مقياس حالة وسمة القلق.

زمن العينة : بدأت الدراسة الفعلية فى اغسطس 2006 وحتى أغسطس 2007

نتائج البحث :

1- توصلت الدراسة الى مدى انتشار الامراض النفسية ولكنها كانت مرتفعة جداً فى المرحلة الثالثة للحمل مع تحسن طفيف فى فترة ما بعد الولادة.

2- كانت اكثر التشخيصات شيوعاً فى فترة الحمل هو مرض عدم التكيف

3- وجد أن السيدات فى فترة الحمل وما بعد الولادة يصبن باعراض اكتئابية شديدة بالمقارنة بالعينة الضابطة .

Change in quality of life after cognitive behavior therapy for anxiety disorders: an Egyptian prospective study

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Introduction
Despite increased prevalence, chronic course, and high morbidity rate of anxiety disorders, little is known about the effectiveness of various therapeutic approaches especially cognitive behavior therapy (CBT) in improving the quality of life of anxiety patients. This study aimed at quantifying the impact of CBT in anxiety disorder patients on quality of life (QOL), and to address the question of its long-term effect.

Methods
Forty patients diagnosed with anxiety disorders according to the standard Structured Clinical Interview (SCID-I) of *DSM-IV* were asked to complete the *DSM-IV* semi-Structured Clinical Interview for diagnosis section for anxiety and depression, sociodemographic sheet, medical history sheet, and Beck Depression Inventory. A structured and manual CBT protocol was applied to all participants. An assessment battery tapping QOL issues and the major clinical dimensions of the anxiety disorders was administered at baseline pretreatment (week 0), posttreatment (week 9), and at 6-month follow-up (week 35) to evaluate treatment outcomes on QOL and test its durability. Two male patients dropped from continuing their CBT protocol.

Results
CBT had a positive clinical outcome on anxiety disorders, which was significantly evident in changes in clinical diagnosis, changes in used doses of medications, and changes in outcome tools' scores. With regard to QOL, CBT made statistical significant improvement in the QOL questionnaire score for both anxiety disorders as a whole and subtypes of anxiety disorders posttreatment and at 6-month follow-up. There was a statistically significant difference in improvement between pretreatment and posttreatment, pretreatment and follow-up, but not between posttreatment and follow-up. QOL in anxiety patients was negatively correlated with pretreatment duration of anxiety symptoms and Beck Depression Inventory scores.

Conclusion
We concluded that CBT is effective for the management of anxiety disorders with short term (8 weeks) and long term (35 weeks), with positive impact on QOL. Considering the limited number of studies in this area, it is recommendable to set studies designed to evaluate a diverse range of QOL indicators across different interventions in anxiety disorder patients.

Keywords:
anxiety, cognitive behavior therapy, depression, obsessive–compulsive disorder, quality of life

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Introduction

Lifetime prevalence of anxiety disorders is 16.6% all over the world [1]. In Arab, we lack such global data; however, in Lebanon, the Evaluation of the Burden of Ailments and Needs of the Nation study was carried out on a nationally representative sample of the Lebanese population and anxiety disorders were found in 16.7% of their sample [2]. In Morocco [3], we found that 25.5% met criteria of at least one current anxiety disorder distributed as 2% panic disorder (PD)_, 7.6% agoraphobia, 3.4% social phobia, 6.1% obsessive–compulsive disorder (OCD), 3.4% posttraumatic stress disorder, and 4.3% generalized anxiety disorder in the studied sample.

In Egypt, anxiety states are common [4], and were diagnosed in 36% of university students [5], and represented approximately 22.6% of diagnoses made in a psychiatric outpatient clinic in a selective Egyptian sample [6]. The most common symptoms were worrying (82%), irritability (73%), free-floating anxiety (70%), depressed mood (65%), tiredness (64%), restlessness (63%), and anergia and retardation (61%). Panic attacks were present in 30%, situational anxiety in 35%, specific

phobias in 37%, and avoidance in 53% of the sample [7]. In a recent initial study for the National Survey of Prevalence of Mental Disorders in Egypt conducted by Ghanem *et al.* [8], anxiety disorders were the second most prevalent psychiatric disorders after mood disorders diagnosed in 4.75% of the surveyed sample. PDs were present in 0.68%, agoraphobia in 0.50%, social anxiety disorders (SAD) in 0.23%, specific phobia in 1.35%, OCD in 0.68%, posttraumatic disorder in 0.11%, generalized anxiety disorder (GAD) in 0.91%, and mixed anxiety depression in 0.29% of sample.

Anxiety disorders are usually chronic disorders that are associated with enduring symptoms with significant disability, distress, and impairment in social functioning often many years after disease onset [9]. Onset is frequently early in life, between the age of 20 and 30 years with large health-care costs for the individual and the community [10]. Comorbidity with depression is high and an important predictor of the outcome of anxiety disorders [11].

Despite increased prevalence, chronic course of anxiety disorders, and the associated high rate of morbidity, little is known about quality of life (QOL) in anxiety disorders. The effectiveness of various therapeutic approaches to improve the QOL in anxiety patients is not well understood.

QOL, including a patient's sense of well being and function, can be affected by thoughts, behavior, and poor coping skills and associated depressive symptoms in different anxiety disorders. A major limitation of treating anxiety disorders with medication alone is that patients do not come to evaluate their conditioned dysfunctional patterns of behavior or their unhealthy coping strategies, which may be the root of maintenance of their suffering with poorer QOL [12].

CBT is predicated on the philosophy of the ancient Greeks, which stipulates that 'Nothing in life is actually bad, lest we perceive it to be so'. Fundamentally, it is based on the assumption that behavior develops and is maintained according to the principles of learning. On the basis of this, a model of the causes of each anxiety disorder could be formulated in terms of dysfunctionally learned cognitions and behaviors [13,14].

CBT is a directive form of counseling that uses a collaborative process, which is termed 'guided discovery' [15]; this makes the individual aware of his/her own thinking style, its strengths and limitations, thus acquiring him/her new ways of thinking and alternative ways of behaving. By using this newly acquired knowledge, the individual develops more effective and satisfying ways of dealing with challenges with a positive impact on QOL [16].

Few studies have compared the impact of different anxiety disorders on different domains of QOL; however, instruments generally used to assess QOL in this population have varying specificity, considerable redundancy, and, occasionally, inappropriate content [17]. Although the assessment of therapeutic outcome in the published literature has been of high quality, including multiple symptom indices and composite measures of end-state functioning, the impact of CBT on anxiety patients' QOL is yet to be evaluated in practice [18].

The purpose of this study was to quantify the impact of CBT in anxiety disorder patients on QOL and to address the question of its duration. We hypothesized that treatment would have a significant beneficial impact on QOL, and that these gains would be maintained at follow-up.

Patients and methods

Participants

All anxiety disorder patients presenting to the general outpatient clinics of the Institute of psychiatry, Ain Shams University hospital during April 2008 were invited to participate in our study after obtaining a written informed consent. Patients were excluded if age was less than 18 years, were uncooperative, had secondary anxiety disorder either due to general medical condition and/or substance abuse, had a current diagnosis of substance abuse within the past 6 months, was a mentally subnormal patient as clinically judged, had a current/history of acute fulminating physical disorder, change in psychotropic medication type or dose during the 12 weeks before treatment, unwillingness to keep medication status stable all over the duration of the study, evidence of other primary Axis I psychiatric disorder, and/or previous CBT treatments and no any other additional structured psychosocial therapies during the treatment period.

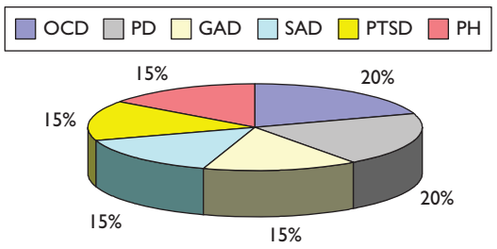
The mean age of participants was 33.6 ± 10.2 years ranging between 20 and 54 years. Twenty patients (50%) were in the 20s group of age, 10 patients (25%) were in the 30s group of age, seven (17.5%) were in the 40s group of age, and three (7.5%) were in the 50s group of age. Of the participants, 57.5% (23 of 40) were female patients and 42.5% (17 of 40) were male patients; 80% (32 of 40) passed a college degree of education and 20% (eight of 40) passed diploma degree; however all finished their high school. Of the participants, 52.5% (21 of 40) were married, 40% (16 of 40) were single, and 7.5% (three of 40) were divorced; 60% (24 of 40) were employed and 40% (16 of 40) were unemployed.

With regard to their clinical diagnoses, distribution of subtypes of anxiety disorder as assessed by SCID-I described as eight (20%) had OCD with a male-to-female ratio (4 : 4), eight (20%) had PD with a male-to-female ratio (3 : 5), six (15%) had GAD with a male-to-female ratio (2 : 4), six (15%) had SAD with a male-to-female ratio (4 : 2), six (15%) had posttraumatic stress disorder (PTSD) with a male-to-female ratio (2 : 4), and six (15%) had phobias with a male-to-female ratio (2 : 4) (Fig. 1).

The duration of anxiety symptoms ranged from 1 month to 17 years, with a mean of 7.8 ± 5.1 years; 27.5% (11 of 40) had a duration of less than 5 years, 50% (20 of 40) had a duration ranged between 5 and 10 years, and 22.5% (nine of 40) had a duration of more than 10 years.

Of the participants, 87.5% (35 of 40) were maintained on psychotropic drugs before participating in the study,

Figure 1



Distribution of diagnoses of subtypes of anxiety disorders among the sample of the study. GAD, generalized anxiety disorder; OCD, obsessive–compulsive disorder; PD, panic disorder; PH, phobic disorder; PTSD, posttraumatic stress disorder; SAD, social anxiety disorder.

including benzodiazepines in 57.5% (23 of 40), antidepressants in 67.5% (27 of 40), and/or antipsychotics in 35% (14 of 40), either individually or in combination. All patients (100%) with OCD, PD, GAD, and PTSD, 66.7% (four of six) of SAD patients, and 50% (three of six) of phobia patients were on psychotropic treatment.

The duration of receiving treatment ranged from 1 month to 10 years, with a mean of 3.3 ± 3.3 years. The benzodiazepines dose used by participants ranged between 3 and 5 mg/day of bromazepam equivalents [19], with a mean of 1.78 ± 1.8 mg/day. The antidepressants dose used by participants ranged between 20 and 60 mg/day of fluoxetine equivalents [20], with a mean of 22.6 ± 21.9 mg/day. The antipsychotics dose used by participants ranged between 0 and 400 mg/day chlorpromazine equivalents [21], with a mean of 94.7 ± 150 mg/day.

Procedure

Forty patients diagnosed as anxiety disorders according to the standard clinical SCID-I [22] of *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* (*DSM-IV*) [23] met the study inclusion criteria and agreed to participate. All participants were asked to complete the semi-Structured Clinical Interview for Diagnosis based on *DSM-IV*, section for anxiety and depression, to validate the diagnosis. Several participants in the study had concurrent depressive symptoms not mounting to clinical depression diagnosis as defined by Yemi and Jeffery [24]. Hence, Beck Depression Inventory (BDI) was applied to measure the severity of coexisting depression with the studied anxiety disorders, and to illuminate the correlation of the depressive symptoms and QOL in anxiety disorders.

The study started at the beginning of April and completed by the end of December 2008. This period was distributed in four phases: (i) case recruitment and pretreatment assessment phase that lasted for 4 weeks during April 2008, (ii) treatment phases that lasted for 8 weeks during May and June 2008, (iii) posttreatment phase immediately after treatment during the first week of July 2008, (iii) follow-up phase was done 6 months later at December 2008.

Cognitive behavior therapy

A structured and manualized CBT protocol was applied to all participants (40 anxiety patients). Our CBT program was deigned based on published evidence-based protocols for CBT in subtypes of anxiety disorders [25–30]. Each treatment protocol was divided into assigned eight weekly sessions; each session lasted for 60 min and used specified techniques and exercises accordingly (Table 1).

Generally, the elements of a CBT session were an initial mood check, an update from the previous session, setting an agenda for the session, reviewing homework, discussing agenda items, summarizing the session content, assigning homework, and finally, obtaining patients' feedback about the session. The final session was devoted to a discussion of what the patients had learned and what they needed to exercise more in the future. A maintenance program should be written down for the patient to consult. Rehearsal of cognitive restructuring techniques, maintaining exposure exercises, and elaborating the concept of self therapist were all addressed. At the end, participants were handed over into their own care, but were also instructed to send in reports on how

Table 1 Different cognitive behavior therapy techniques used for subtypes of anxiety disorders

Sessions	PD	OCD	PTSD	SAD	Phobia	GAD
First	Aimed generally for socialization, information gathering, and psycho education In PTSD trauma education was added					
Second	Aimed generally for behavioral analysis (daily recording of dysfunctional thoughts) and identification of faulty appraisals					
Third	Cognitive restructuring techniques					
Fourth	Relaxation training BE and PMR	Hierarchy of fears Behavioral experiments	Imaginable exposure		Relaxation training BE and PMR	
Fifth	Interoceptive exposure exercises	ERP	In-vivo exposure exercises	Role play	Imaginable exposure	Worry time Worry free zone Short relaxation
Sixth	In-vivo exposure therapy	ERP	In-vivo exposure exercises	Imaginable exposure role play	In-vivo exposure	Applied relaxation imaginable exposure
Seventh	In-vivo exposure	ERP	In-vivo exposure exercises	Social skills training In-vivo exposure Self love	Continue exposure exercises	Fast relaxation In-vivo exposure
Eighth	Relapse prevention					

BE, breathing exercises; ERP, exposure and response prevention; GAD, generalized anxiety disorder; PD, panic disorder; PMR, progressive muscular relaxation; PTSD, posttraumatic stress disorder; OCD, obsessive–compulsive disorder; SAD, social anxiety disorder.

well they were able to keep to their maintenance program.

Treatment integrity

Treatment integrity was rated by the senior researchers on a random sample of sessions using a checklist for assessing compliance with the treatment manual. Compliance was high (i.e. more than 95% of exercises rated as completed and consistent with manual description) across all sessions that were assessed ($n = 32$). In addition, we considered the competencies that are required to deliver effective CBT as proposed by Roth and Pilling [31].

Assessment

The sociodemographic sheet includes information about age, sex, level of education, marital status, and occupation, and the medical history sheet includes information about clinical diagnosis of anxiety disorder, duration of symptoms, and current history of psychotropic drugs, both type and dose.

An assessment battery tapping QOL issues and the major clinical dimensions of the anxiety disorders was administered at baseline pretreatment (week 0), posttreatment (week 9) and at 6-month follow-up (week 35) to evaluate treatment outcomes on QOL and test its durability. Participants who did not meet the specified deadline were reminded through e-mail and/or telephone.

Assessment battery

The assessment battery consisted of seven tools (self-rating/therapist rating); one for QOL questionnaire, five for measuring the anxiety outcome namely Hamilton Anxiety Rating Scale (HAM-A), Beck Anxiety Inventory (BAI), Penn State Worry Questionnaire (PSWQ), Liebowitz Social Anxiety Scale (LSAS), and Yale-Brown Obsessive Compulsive Scale (YBOCS), and one for assessing the severity of associated depression namely BDI-II. Along with these tools, results of the semi-structured clinical interview were obtained and used as indicators of change on the dependent variables.

All the study tools were translated and proved to be a good interrater reliability with relative ease of administration as shown in a pilot study that lasted for 3 months (January to March 2008).

HAM-A is a 14-item test measuring severity of anxiety symptoms with a cutoff score of 15 [32,33]; BAI is a 21-item self-reporting instrument used to measure severity of anxiety symptoms especially the panic ones with a cutoff score 18.4 for female patients and 15.3 for male patients [34–36]; PSWQ is a 16-item self-reporting questionnaire designed to measure trait worry with a cutoff score of 50 [37,38]; LSAS is a 24-item inventory assessing fear and avoidance in several social situations with a cutoff score of 30 [39,40]; and YBOCS is a 10-item semistructured interview that yields symptom severity scores separately for obsessions and compulsions with a cutoff score of 16 [41].

BDI-II is a 21-item commonly used self-reporting questionnaire for assessing the severity of depression with cutoff scores 10, 19, higher than or equal to 30 indicative of mild-to-moderate, moderate-to-severe, and very severe depression, respectively [42,43].

QOL questionnaire/interview [44] is a 7-item clinical tool assessing the degree of efficiency and patient's satisfaction in several domains of life, such as general health, social life, and work. Patients were instructed to rate the personal importance of these domains. Patients were asked to rate their satisfaction with these domains on a scale ranging from 1 (very dissatisfied/very affected) to 5 (very satisfied/not at all affected). The QOL has been validated on clinical samples and had good internal consistency (> 0.82) and test–retest reliability (70–0.80). In addition, it possesses good convergent, discriminate, and criterion-related validity [45]. The instrument is sensitive enough to discriminate between mental health and nonmental health community residents, and has been used in several treatment evaluation studies. The cutoff score of this questionnaire was calculated according to Jacobson and Truax [46] to be 30 points.

Statistical analysis

Data coded and revised were introduced to an EXCEL database to be later manipulated and analyzed using the SPSS version 16 (SPSS, Inc., Chicago, IL, USA). Results were analyzed for the whole sample except for dropped out participants. For the sake of description, categorical data were presented as frequency and percentage, and continuous data as means, standard deviation, and 95% confidence limit. This was followed by a graphic representation whenever needed to assess the distribution of the data and determine an appropriate statistical test for inferential statistical analysis. Independent sample *t*-test (Student's *t*-test), χ^2 test, one-way repeated measures analysis of variance (ANOVA), and two-factor repeated measures (ANOVA) were used in inferential statistical analysis of our results. An effect size (ES) is a measure of the strength of the relationship between two variables in a statistical population. It estimates the strength of an apparent relationship, rather than assigning a significance level reflecting whether the relationship could be due to chance. The ES was computed using Cohen's *d*-tests [47]. Pearson's correlation coefficient was calculated to determine the strength of correlation. Statistical significance level was set at a value of less than 0.05; highly significant level at a value of less than 0.01; and very highly significant at value of less than 0.001.

Results will be presented through changes in outcome tools and changes in clinical diagnosis according to the clinical significant improvement 'change' proposed by Jacobson and Truax [46] who described a broadly and widely applicable method to investigate the clinically significant change in psychotherapy research. Accordingly, patients will be classified in three groups; (i) cured patients with clinically significant (CS) improvement, patients with improvement that is above measurement error but still unresolved (statistically significant changes, SS), and patients with no improvement (NS).

Results

Treatment compliance

This study started with 40 patients in the pretreatment phase, and decreased to 38 in the posttreatment phase. Two male patients dropped out; one had OCD and the other had GAD. Drop out was defined as failing to receive at least three sessions of CBT.

Pretreatment assessment

Means and standard deviations of the used assessing tools at the pretreatment baseline assessment were as follows: HAM-A scored in the range of 25–45, with a mean of 30.5 ± 6.3 and BAI scored in the range of 22–40, with a mean of 28.2 ± 6.7. For patients with a primary diagnosis of PD, the range was 35–40 with a mean of 38.2 ± 2.6. PSWQ scored in the range of 40–69 with a mean of 55.2 ± 9.9. For patients with a primary diagnosis of GAD, the range was 60–69 with a mean of 64.6 ± 2.6. LSAS scored in the range of 40–65 with a mean of 47.4 ± 11.1. For patients with a primary diagnosis of SAD, the range was 55–65 with a mean of 61.3 ± 3.6. YBOCS scored in the range of 0–21 with a mean of 6.1 ± 7.1. For patients with a primary diagnosis of OCD, the range was 10–21 with a mean of 14.3 ± 5.6. QOL scored in the range of 23–29 with a mean of 24.8 ± 1.3.

BDI-II revealed that all participants (40 patients) were suffering from comorbid depression with a mean 17.1 ± 3.3, 70% (28 of 40) had mild degree, and 30% (12 of 40) had moderate degree.

Outcome of cognitive behavior therapy on anxiety disorders

For the purpose of assessing the outcome of CBT on anxiety disorders, ANOVA analysis was reapplied to examine differences from pretreatment to posttreatment for the assessment of the outcome of CBT, and from posttreatment to follow-up and from pretreatment to follow-up to assess whether outcome gained at posttreatment will be maintained or not.

Positive clinical outcome of CBT on anxiety disorders was SS in several domains: (i) changes in clinical diagnosis, changes in used doses of medications, and changes in outcome tools' scores, for all participants and in-between subtypes of anxiety disorders.

With regard to clinical diagnosis, there was posttreatment clinical improvement of 55% (21 of 38) participants who did not fulfill the diagnostic criteria of anxiety disorders anymore as measured by SCID-I. However, follow-up assessment 6 months later revealed no significant changes from posttreatment results.

With regard to medications, 55.2% (21 of 35) of participants were still continuing using psychotropic medications with reduction in doses of all psychotropic drugs compared with the pretreatment phase ($P < 0.001$); in benzodiazepines, the daily intake was reduced to a mean of 0.17 ± 0.47; in antidepressants, the daily intake was reduced to a mean of 6.2 ± 8.37; in antipsychotics, the daily intake was reduced to a mean of 12.2 ± 37.2 (Table 2).

Table 2 Comparing used tools and medications intake in precognitive behavior therapy and postcognitive behavior therapy

Item	Pre-CBT	Post-CBT	*P* value
BZPS intake	1.7 ± 1.8	0.17 ± 0.47	<0.001
AD intake	22.6 ± 11.9	6.2 ± 8.37	<0.001
AP intake	94.7 ± 150	12.2 ± 37.2	<0.001
HAM-A	30.5 ± 6.3	17.6 ± 2.7	0.001
BAI	28.2 ± 6.7	16.5 ± 7.7	<0.001
PSWQ	55.2 ± 9.9	44.4 ± 6.1	<0.001
LSAS	47.4 ± 11.1	41.3 ± 1.8	<0.001
YBOCS	6.1 ± 7.1	5.4 ± 3.1	<0.001
BDI-II	17.1 ± 3.3	9.6 ± 1.6	<0.001
QOL	24.8 ± 1.3	39.8 ± 1.7	0.006

Statistical significance level was set at <0.05; highly significant level at <0.01; and very highly significant at <0.001.
AD, antidepressants; AP, antipsychotics; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-second edition; BZPS, benzodiazepines; CBT, cognitive behavior therapy; HAM-A, Hamilton Anxiety Scale; LSAS, Liebowitz Social Anxiety Scale; PSWQ, Penn State Worry Questionnaire; QOL, quality of life scale; YBOCS, Yale-Brown Obsessive Compulsive Scale.

Follow-up assessment shows no changes in the total number of patients using medications, but with nonsignificant reduction in the dose of benzodiazepines to a mean of 0.09 ± 1.2, antidepressants to a mean of 5.9 ± 9.5, and antipsychotics to mean of 11.9 ± 38.6 ($P = 0.56$) (Table 3).

With regard to anxiety clinical tools, ANOVA results proved that participants had improved significantly on posttreatment tools; HAM-A (0.001), BAI (< 0.001), PSWQ (< 0.001), LSAS (< 0.001), and YBOCS (< 0.001), that is, the mean scores reduced posttreatment. The improvement remained SS after 6 months in the follow-up phase (Tables 2 and 3).

ANOVA tests showed that participants had improved significantly between pretreatment and follow-up; HAM-A (0.001), BAI (< 0.001), PSWQ (< 0.001), LSAS (< 0.001), and YBOCS (< 0.001), but no significant improvement was shown between posttreatment and

Table 3 Comparing used tools and medications intake immediately postcognitive behavior therapy and at 6-month follow-up

Item	Post-CBT	At follow-up	Value
BZPS intake	0.17 ± 0.47	0.09 ± 1.2	0.56
AD intake	6.2 ± 8.37	5.9 ± 9.5	0.56
AP intake	12.2 ± 37.2	11.9 ± 38.6	0.56
HAM-A	17.6 ± 2.7	16.4 ± 3.1	0.37
BAI	16.5 ± 7.7	15.2 ± 8.3	0.23
PSWQ	44.4 ± 6.1	43.7 ± 7.5	0.24
LSAS	41.3 ± 1.8	39.9 ± 2.6	0.38
YBOCS	5.4 ± 3.1	5.1 ± 2.9	0.27
BDI-II	9.6 ± 1.6	8.5 ± 2.4	0.17
QOL	39.8 ± 1.7	40.1 ± 2.5	0.19

Statistical significance level was set at <0.05; highly significant level at <0.01; and very highly significant at <0.001.
AD, antidepressants; AP, antipsychotics; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-second edition; BZPS, benzodiazepines; CBT, cognitive behavior therapy; HAM-A, Hamilton Anxiety Scale; LSAS, Liebowitz Social Anxiety Scale; PSWQ, Penn State Worry Questionnaire; QOL, quality of life; YBOCS, Yale-Brown Obsessive Compulsive Scale.

Table 4 Showed the mean ± standard deviation changes and effect sizes (Cohen's *d*) for the used tools precognitive behavior therapy, postcognitive behavior therapy and 6-month follow-up

Tool	Pre-CBT (M ± SD)	Post-CBT (M ± SD)	At follow-up (M ± SD)	Effect size within (M ± SD)
HAM-A	30.5 ± 6.3	17.6 ± 2.7	16.4 ± 3.1	2.66 ± 0.79
BAI	28.2 ± 6.7	16.5 ± 7.7	15.2 ± 8.3	1.62 ± 0.63
PSWQ	55.2 ± 9.9	44.4 ± 6.1	43.7 ± 7.5	1.3 ± 0.55
LSAS	47.4 ± 11.1	41.3 ± 1.8	39.9 ± 2.6	0.77 ± 0.36
YBOCS	6.1 ± 7.1	5.4 ± 3.1	5.1 ± 2.9	0.13 ± 0.06
BDI-II	17.1 ± 3.3	9.6 ± 1.6	8.5 ± 2.4	2.9 ± 0.82
QOL	24.8 ± 1.3	39.8 ± 1.7	40.1 ± 2.5	− 0.9 ± 0.98

BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-second edition; CBT, cognitive behavior therapy; HAM-A, Hamilton Anxiety Scale; LSAS, Liebowitz Social Anxiety Scale; PSWQ, Penn State Worry Questionnaire; QOL, quality of life; YBOCS, Yale-Brown Obsessive Compulsive Scale.

follow-up; HAM-A (0.37), BAI (0.23), PSWQ (0.24), LSAS (0.38), and YBOCS (0.27) (Table 3).

BDI-II score had improved significantly between pretreatment and posttreatment ($P \leq 001$), that is, the mean score was reduced posttreatment. The improvement remained SS after 6 months follow-up. ANOVA tests showed SS improvement between pretreatment and follow-up ($P \leq 0.001$), but NS was shown between posttreatment and follow-up ($P = 0.17$) (Tables 2 and 3).

There was a large ES for all participants in the study. An ES of Cohen's test value ($d = 1.3$) was calculated at posttreatment and ($d = 1.5$) at follow-up of participants. The within-group ES was large for all tools at posttreatment, with the highest value found for the BDI-II score (Cohen's $d = 2.9$) and the lowest value found for YBOCS scores (Cohen's $d = 0.13$) (Table 4).

Table 5 explores outcome differences achieved by subtypes of anxiety disorders individually as measured by ANOVA and Student's *t*-tests. Differential analysis for outcome changes revealed that all subtypes of anxiety disorders improved significantly from pretreatment to posttreatment in all tools of the study. These changes were found to be constant on follow-up assessment.

Analysis of patients in the study was categorized according to reliable change index into CS, SS, and NS as shown in Table 6.

Outcome of cognitive behavior therapy on quality of life

There was SS improvement in the QOL questionnaire posttreatment (P value = 0.006), such that participants had higher scores posttherapy. The improvement remained SS in the follow-up phase 6 months after treatment. ANOVA tests showed SS improvement between pretreatment and follow-up ($P = 0.005$), but NS was shown between posttreatment and follow-up ($P = 0.19$) (Tables 2 and 3, Fig. 2).

Table 7 explores QOL outcome differences achieved by subtypes of anxiety disorders individually as measured by ANOVA and Student's *t*-tests. Differential analysis for outcome changes revealed that all subtypes of anxiety disorders improved significantly from pretreatment to

Table 5 Showed precognitive behavior therapy, postcognitive behavior therapy and at 6-month follow-up changes in mean ± standard deviation of used tools broken down by subtypes of anxiety disorders

Disorder	BDI-II	HAM-A	BAI	PSWQ	LSAS	YBOCS
Obsessive–compulsive disorder						
Pretreatment	14.7 ± 0.5	27 ± 1.7	24 ± 4	46.4 ± 1.5	37 ± 2.6	14.2 ± 1.5
Posttreatment	11 ± 1	19.6 ± 0.5	23.6 ± 2.3	46 ± 2.6	37 ± 2.6	11.4 ± 2.5
Follow-up	10.2 ± 2.1	18.3 ± 1.6	21.9 ± 3.4	45.5 ± 2.9	36.8 ± 2.9	10.7 ± 3.1
P value	**0.007**	**<0.001**	–	–	–	**<0.001**
Panic disorder						
Pretreatment	19.5 ± 4.7	39.2 ± 4.5	38.2 ± 2.1	56.7 ± 2.2	46.5 ± 4.5	4 ± 2.1
Posttreatment	8.3 ± 1.7	13.5 ± 1.2	8.8 ± 1	43 ± 2.9	4.3 ± 2.1	4 ± 2.1
Follow-up	7.4 ± 2.6	11.9 ± 2.1	7.2 ± 2.7	4.6 ± 3.1	41.8 ± 3.3	3.9 ± 2.9
P value	**<0.001**	**<0.001**	**<0.001**	–	–	–
Phobia						
Pretreatment	13.7 ± 1.5	25.7 ± 2.1	25.7 ± 3.2	52 ± 3.4	43.4 ± 2.5	4 ± 2
Posttreatment	9 ± 1.7	15.6 ± 1.1	9 ± 1	38.4 ± 1.5	42.3 ± 2.5	4.4 ± 2.5
Follow-up	8.1 ± 2.2	14.3 ± 2.4	8.3 ± 2	37.2 ± 2.7	42 ± 2.2	4.1 ± 2.1
P value	**<0.001**	**<0.001**	**<0.001**	–	–	–
Social anxiety disorder						
Pretreatment	18.7 ± 1.5	8.4 ± 2.3	24 ± 2	58.4 ± 0.5	62.7 ± 2.3	4 ± 1
Posttreatment	9 ± 1	18.3 ± 1.5	10.6 ± 1.1	44.4 ± 3.2	41.7 ± 1.2	4.4 ± 1.1
Follow-up	7.9 ± 2.1	17.3 ± 2.2	9.8 ± 2.7	43.4 ± 4.1	39.9 ± 2.8	4 ± 0.3
P value	**<0.001**	**<0.001**	–	–	**<0.001**	–
Generalized anxiety disorder						
Pretreatment	18.7 ± 7.2	34.4 ± 1.1	28.4 ± 1.5	65 ± 3.6	53 ± 1	3.4 ± 1.1
Posttreatment	11 ± 1	20 ± 1	25.6 ± 0.5	55.6 ± 2.5	42.3 ± 0.6	3.7 ± 1.5
Follow-up	10.2 ± 1.9	18.9 ± 2.1	24.3 ± 1.5	45.3 ± 3.1	41.8 ± 1.5	3.6 ± 1.7
P value	**<0.001**	**<0.001**	–	–	**<0.001**	–
Posttraumatic stress disorder						
Pretreatment	16.7 ± 0.5	25.7 ± 1.5	25 ± 1	52.4 ± 1.5	42.4 ± 3.7	5 ± 1
Posttreatment	9.3 ± 1.5	19.6 ± 0.5	23.6 ± 1.5	39.4 ± 2.3	41.7 ± 1.2	5 ± 1
Follow-up	8.1 ± 2.1	18.5 ± 1.2	22.2 ± 2.1	38.5 ± 3.1	40.8 ± 2	4.9 ± 1.8
P value	**<0.001**	**<0.001**	**0.13**	**<0.001**	–	–

Statistical significance level was set at <0.05; highly significant level at <0.01; and very highly significant at <0.001.
BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-second edition; HAM-A, Hamilton Anxiety Scale; LSAS, Liebowitz Social Anxiety Scale; PSWQ, Penn State Worry Questionnaire; YBOCS, Yale-Brown Obsessive Compulsive Scale.

Table 6 Showed clinical improvement in our sample according to reliable change index

	CS		SS		NS		
Tool	*n*	Percentage	*n*	Percentage	*n*	Percentage	χ^2
HAM-A	22	83.4	11	16.7	5	13.2	0.47 (P=0.79)
BAI	7	87.5	1	12.5	0	0	1.14 (P=0.28)
PSWQ	1	20	2	40	2	40	1.33 (P=0.51)
LSAS	3	50	2	33.4	1	16.7	1.33 (P=0.51)
YBOCS	1	14.2	5	71.4	1	14.2	0.88 (P=0.65)
BDI-II	19	50	12	31.6	7	18.4	0.95 (P=0.62)
QOL	23	60.5	11	28.9	4	10.5	1.48 (P=0.48)

Statistical significance level was set at <0.05; highly significant level at <0.01; and very highly significant at <0.001. χ^2 observed time two (posttest) score.
BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-second edition; CS, clinically significant; HAM-A, Hamilton Anxiety Scale; LSAS, Liebowitz Social Anxiety Scale; NS, not improved; PSWQ, Penn State Worry Questionnaire; QOL, quality of life; SS, statistically significant; YBOCS, Yale-Brown Obsessive Compulsive Scale.

posttreatment in QOL. This gain was found to be constant on follow-up assessment.

Does the duration of anxiety symptoms at baseline predict changes in quality of life?

In the whole sample of participants, a SS correlation was found between the duration of symptoms and posttreatment improvement in HAM-A ($r = 0.67$, $P = 0.02$) and QOL ($r = -0.68$, $P = 0.02$).

Analysis of posttreatment outcome of the HAM-A among participants in the study revealed a negative correlation with the duration of symptoms, that is, the longer the duration of the symptoms the higher the posttreatment outcome of HAM-A; in other terms, poorer improvement in anxiety symptoms.

Analysis of posttreatment outcome of the QOL among participants in the study revealed a negative correlation with the duration of symptoms, that is, the longer the duration of the symptoms the poorer the posttreatment outcome of the QOL; in other terms, poorer improvement in the QOL (Fig. 3).

Does severity of comorbid depression in anxiety disorders predict changes in quality of life?

In the whole sample of participants, a SS correlation was found between pretreatment BDI-II scores and posttreatment improvement in HAM-A ($r = 0.57$, $P = 0.04$) and QOL ($r = -0.62$, $P = 0.03$).

Analysis of pretreatment outcome of the BDI-II among participants in the study revealed a negative correlation with the posttreatment outcome of HAM-A, that is, the higher the pretreatment score of the BDI-II the higher the posttreatment outcome of HAM-A; in other terms, poorer improvement in anxiety symptoms.

Analysis of pretreatment outcome of the BDI-II among participants in the study revealed a negative correlation with the posttreatment outcome of QOL, that is, the higher the pretreatment score of the BDI-II the lower the posttreatment outcome of QOL; in other terms, poorer improvement in the QOL (Fig. 4).

Figure 2

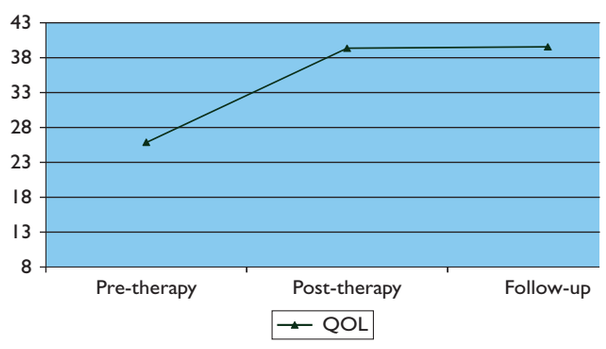


Figure shows precognitive to postcognitive behavior therapy (CBT) and at 6 months follow-up changes in quality of life.

Discussion

In general, most CBT research studies of anxiety disorders tend to focus on symptom measurement at the expense of measurement of functional impairment as QOL. This study examined the effect of CBT on QOL in anxiety disorder patients, and indicates that CBT is effective for the management of anxiety disorders with a short-term (8 weeks) and long-term (35 weeks) positive impact on QOL.

In this study, the positive impact of CBT on QOL was confirmed by the quite uniform indication that an outcome of CBT in our anxiety patients was good. This was detected through several domains; (i) pretreatment to posttreatment overall SS improvement in the scores of all tools, (ii) approximately half of the participants achieved CS changes, sustained by the large ES detected among outcome of tools, and (iii) reduction in the number of participants using psychotropic medications. Some studies lacked this wide range of evidence confirming the effectiveness of CBT in anxiety patients just as Watanabe *et al.* [48] who did not collect information about changes in medication dosing after CBT course. In contrast, our patients' decreased their benzodiazepines daily intake to a mean of 0.17 ± 0.47; antidepressants daily intake to a mean of 6.2 ± 8.37; and antipsychotics daily intake was reduced to a mean of 12.2 ± 37.2 with a SS difference from the pretreatment level.

Table 7 Precognitive behavior therapy, postcognitive behavior therapy and follow-up quality of life in different diagnostic categories of anxiety disorders

Disorder	Pre-CBT	Post-CBT	At follow-up	*P* value
Obsessive–compulsive disorder	26.4 ± 1.5	39.3 ± 2.1	41 ± 3.2	<0.001
Panic disorder	23.2 ± 0.5	41.5 ± 1.2	42.8 ± 2.2	<0.001
Phobia	23.4 ± 0.5	39.6 ± 0.5	41.2 ± 2.1	<0.001
Generalized anxiety disorder	25.7 ± 0.5	38.3 ± 1.5	39.5 ± 2.2	<0.001
Social anxiety disorder	25.7 ± 0.5	41 ± 1	42.5 ± 2.5	<0.001
Posttraumatic stress disorder	25 ± 1	38.6 ± 2.1	39.2 ± 3	<0.001

CBT, cognitive behavior therapy.

This significant reduction of outcome of tools for anxiety disorders treated with a course of CBT was in concordance with results attained by several studies. For example, a controlled clinical trial was conducted by Linden *et al.* [49] to evaluate the efficacy of CBT treatment in outpatients with pure GAD; the reduction in the score on the HAM-A was 6.4% (1.5 points). In addition, results of study by Praško *et al.* [50] study indicated that all patients who completed at least 5 weeks of intensive CBT program showed significant improvement on YBOCS and BDI scales. Moreover, at the end of the treatment, 40.4% of the patients achieved clinical remission. This was agreed with our 55% posttreatment remission rate.

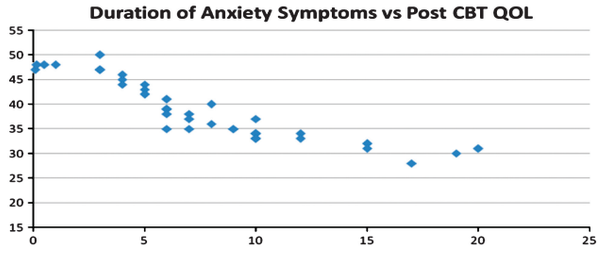
In addition, the long-term effect of CBT on anxiety disorders found in our study was congruent with Prasko *et al.* [51] who aimed to assess the 6-month treatment efficacy and 24-month follow-up of CBT in patients with a generalized form of social phobia. CBT was found to be the best choice for long-term reduction of avoidant behavior with a significant reduction identified on the subjective general anxiety as indicated by LSAS. In addition, this long-term effect increased our confidence that the observed improvements were a result of CBT and not extraneous factors such as the passage of time [52].

Pretreatment assessment of patients concluded that 35 patients (87.5%) from a total of 40 patients were receiving medications; this goes with the recent guidelines for treatment of anxiety disorders provided by the National Guideline Clearinghouse, which necessitates combination of pharmacotherapy and CBT in all subtypes of anxiety disorder [23].

Few researches were regarding the effectiveness of different therapeutic interventions on QOL in anxiety disorders especially CBT. However, a recent study conducted by May *et al.* [53] compared the effect of a CBT on QOL over a 1-year period as measured before and immediately after the intervention and at 3 and 9 months postintervention. QOL and physical activity were significantly and clinically relevantly improved immediately after the intervention and also at 3 and 9 months postintervention compared with preintervention.

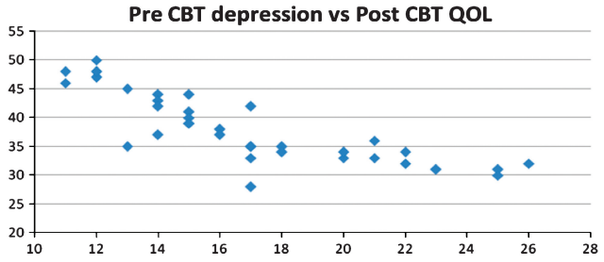
Consistent with other reports, our findings suggest that subtypes of anxiety disorder patients show QOL improvement after CBT. Rapaport *et al.* [18] reported two or more standard deviations below the community norm in QOL in 20% of patients diagnosed as PD, 26% in OCD, 21% in social phobia, and 59% in PTSD. This is accord with Lochner *et al.* [12] who stated that the infrequency and transient nature of panic attacks lead to less impairment than the more chronic and pervasive symptoms of anxiety and/or agoraphobic avoidance. Our results stated a SS improvement in the QOL in OCD from 26.4 ± 1.5 to 39.3 ± 2.1, PD from 23.2 ± 0.5 to 41.5 ± 1.2, phobic disorder from 23.4 ± 0.5 to 39.6 ± 0.5, GAD from 25.7 ± 0.5 to 38.3 ± 1.5, SAD from 25.7 ± 0.5 to 41 ± 1, and PTSD from 25 ± 1 to 38.6 ± 2.1. However, these means showed different order of anxiety subtypes in which PD had the maximum change in QOL followed by phobic disorder and SAD with the same value of change and lastly by OCD, GAD, and PTSD with the same value of change. This was in agreement with Simon *et al.* [54] who found that patients with SAD who do not have significant comorbid depression or anxiety are substantially impaired in QOL, but to a lesser extent than patients with PD, who suffer from both mental and physical impairments in QOL.

Figure 3



Correlation between duration of anxiety symptoms and postcognitive behavior therapy (CBT) outcome of quality of life (QOL).

Figure 4



Correlation between pretreatment depression as measured by beck depression inventory second edition and postcognitive behavior therapy (CBT) outcome of quality of life (QOL).

Assessment instruments used for assessing QOL in both clinical and research settings are numerous; however, no agreement as to which ones are the 'gold standards' remains elusive [55]. In this study, we used Bigelow *et al.* [44] QOL scale, which considered the personal importance and satisfaction with several life domains and had been validated on clinical samples and being sensitive enough to discriminate between residents of mental health hospitals and residents of community [45]. The use of such a standardized scale allows for QOL comparisons across different samples and different populations. Subjective QOL scales are more sensitive to the individual's perception of QOL, which is an additional factor that should be part of a complete assessment of significant QOL impairment [18].

Change in QOL observed for our CBT-treated anxiety patients were not only SS, but were also clinically meaningful. The clinical significance of treatment gains was examined by the reliable change index, which found that 60.5% of our patients had clinical significant improvement, 28.9% had statistical significant improvement, and 18.4% were insignificantly changed after CBT. This was true in relation to all scales used in this study, in which BAI showed the highest ratio of CS change (83.4%), followed in order by HAM-A, QOL, BDI-II, LSAS, PSWQ, and YBOCS. This confirmed that CBT improves clinically both symptom impairment (as measured by scales) and functional impairment of (QOL) anxiety disorders [14].

To examine the extent to which treated anxiety patients' QOL scores move into the range of normal populations' scores, the posttreatment and 6-month follow-up overall QOL index for our treated patients [$M = 39.8$, standard deviation (SD) = 1.3 and 40.1, SD = 2.9, respectively] could not be compared with that reported by Weissman *et al.* [56] for a community sample of control participants ($M = 1.6$, SD = 0.3), because the latter used a different scale for assessing QOL 'Social Adjustment Scale–Self-Report'. However, normative comparisons based on meta-analytic procedures can be expressed as ESs [57]. The comparisons between our sample and the community control participants at posttreatment and follow-up are described by relatively small ESs (i.e. 0.9 at posttreatment and 0.98 at follow-up in our sample and 0.30 at posttreatment and 0.31 at follow-up, respectively).

The pretreatment duration of anxiety symptoms was a potent predictor of QOL at posttreatment and follow-up. In the whole sample of participants, a SS correlation was found between the duration of symptoms and posttreatment improvement in HAM-A ($r = 0.67$, $P = 0.02$) and QOL ($r = -0.68$, $P = 0.02$). The longer the duration of the anxiety symptoms, the poorer the improvement in anxiety symptoms and the poorer the improvement in the QOL was found. To our knowledge, this correlation was not reported before especially in anxiety disorders as a whole diagnosis. However, Telch *et al.* [58] found baseline severity of panic-related symptoms; anxiety and agoraphobic avoidance was related to pretreatment QOL but not to QOL at posttreatment or follow-up. This supported our results that, duration of anxiety symptoms are more powerful predictors of QOL than the severity of symptoms.

Moreover, pretreatment outcome of BDI-II was a potent predictor of QOL at posttreatment and follow-up. In the whole sample of participants, a SS correlation was found between pretreatment BDI-II scores and posttreatment improvement in HAM-A ($r = 0.57$, $P = 0.04$) and QOL ($r = -0.62$, $P = 0.03$). The higher the pretreatment score of the BDI-II, the poorer the improvement in anxiety symptoms and QOL. This is accord with Yemi and Jeffery [24] who stated that comorbidity is the rule with anxiety and depressive disorders and found that HAM-A was correlated significantly with BDI ($r = 0.39$).

Our patients were on combined pharmacological and psychological treatments; this is accord with Osborn *et al.* [14] and Telch *et al.* [58] who supported the encouraging evidence that CBT alone could not lead to CS improvement in patients' QOL; it would be premature to conclude that CBT is uniquely effective in this regard. He also suggested that alternative treatments should lead to enhanced QOL to the extent that they produce meaningful improvements in patients' anxiety. In addition, Eng *et al.* [59] questioned the limited effects of CBT on social functioning domain of QOL.

This study has methodological strengths especially when comparing with other studies; (i) the used outcome measures were similar to those used in pharmacotherapy in contrary to other research studies that tended to use a broader range and/or less sophisticated measures than did pharmacotherapy researchers [58], (ii) all used tools and interview instrument SCID are highly validated and reliable measures for screening and assessing anxiety disorders [17], (iii) the number of tools used to assess outcome changes pretreatment to posttreatment and at follow-up, we used six tools in addition to the QOL one, (iv) we tried to be clear about the integrity of CBT and how it was delivered as reported. In addition, the 95% compliance of participants to CBT program might be regarded as an indicator of patient's approval and satisfaction with the study, (v) we followed the empirical evidence that suggests that assessment of the complete impact of various treatment approaches should involve long-term follow-up. The follow-up duration in our study was 6 months; other studies had follow-up durations ranging from 60 days, 12 weeks, 3 months, 1 month, 10 weeks, and 16 weeks, (vi) some of our assessing instruments are designed for use by (clinical) assessors and others by patients. Patient assessments may result in different results than clinician assessments, as patients may assign more weight to certain domains being measured than clinicians [60], (vii) CBT protocol used in this study followed Lazarus [61] broad-spectrum multimodal CBT who expanded the scope of CBT to include physical sensations, visual images, interpersonal relationships, and biological factors.

However, this study had some limitations: (i) the used QOL battery did not assess other relevant QOL domains such as health-care use, alcohol and substance abuse, or suicide attempts, (ii) our results did not reveal the

association between the characteristic symptoms of each anxiety disorder and differential impairment of various domains of function that guided specifically tailored interventions [12], (iii) no control group was used to avoid the threat of maturation that involves spontaneous recovery over time. However, it should be noticed that anxiety disorders are considered to be chronic disorders and spontaneous recovery is rare, (iv) the high level of education in our sample (80% with a college degree and 20% had a diploma certificate) may lead to selection bias, (v) our sample was a heterogeneous sample of anxiety disorder patients, both in terms of diagnosis and stage of disease. Despite those limitations, the study design is appropriate for its purpose of measuring the change found in QOL after CBT in a typical clinical setting.

Although the limited number of studies in this area necessitated this approach, it is recommendable to set studies designed to evaluate diverse range of QOL indicators across different interventions in anxiety disorders patients.

There is no conflict of interest to declare.

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الملخص العربي

تغير نوعية الحياة بعد العلاج المعرفى السلوكى لاضطرابات القلق: دراسة مصرية من منظور مستقبلي

محمد غانم- منى منصور- محمد فكرى- هشام حتاته- غادة الخولى- ريهام على

هدف البحث: على الرغم من الانتشار الزائد و المسار المزمن و المعدل العالى للتأثير المرضى فى اضطرابات القلق , الا أنه لم يعرف إلا القليل عن تأثير الطرق المختلفة لعلاج القلق على نوعية حياة المرضي. و يهدف هذا البحث إلى دراسة كم التأثير الناتج عن العلاج المعرفي السلوكى لمرضي القلق على نوعية حياتهم' وكذلك التعريف بالتأثير طويل المدى لهذا العلاج. **طريقة البحث:** تناول البحث دراسة أربعين مريضا باضطرابات القلق (تبعا للمناظرة المقننة للتشخيص الأمريكي الرابع)' استكملوا المقابلة الإكلينيكية شبه المقننة للقسم الخاص بالقلق والاكتئاب. و قد خضعوا لاستيفاء تاريخ الجوانب الاجتماعية الديموجرافية' والتاريخ الطبى, ومقياس بك للاكتئاب. كذلك تم تطبيق بروتوكول مقنن للعلاج العقلى السلوكى علي كل الأفراد المشاركين فى البحث. و قد تم تقويم نوعية الحياة , و كذلك الأبعاد المختلفة للقلق قبل العلاج (الأسبوع صفر), و أعيد التقويم بعد العلاج (الأسبوع 9)'و كذلك الشهر السادس من المتابعة (الأسبوع 35) لمتابعة مآل العلاج' وتأثيره على نوعية الحياة' وكذلك مدى بقاء تحسنها. **نتائج البحث:** و قد أظهر البحث التأثير الإيجابى للعلاج العقلي السلوكى' والذى إنعكس على التغير في التشخيص, وجرعات الدواء ,و نتائج مقاييس تقويم المآل. كذلك أظهرت الدراسة تحسن نتائج مقاييس جودة الحياة' سواء على مستوى القلق العام أو التقسيمات الأصغر للقلق' وذلك في تقييمات ما بعد العلاج أو المتابعة بعد 6 شهور و اللتان لم تسجلا إختلافا إحصائيا. و كذلك ظهر إرتباط سلبى بين نوعية الحياة وطول مدة اضطراب القلق قبل العلاج. **الاستنتاج:** و قد خلص البحث إلي أن العلاج السلوكى المعرفى يعالج اضطرابات القلق على المستويين القريب والبعيد' كما أن له تاثيرا علي تحسين جودة الحياة. و مع ندرة الأبحاث في هدا المجال' فإنه ينصح بعمل دراسات تصمم لتقييم المدى المتسع لدلالات جودة الحياة فى الطرق المختلفة لعلاج اضطرابات القلق.

Prevalence of metabolic syndrome in patients with schizophrenia

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Introduction
This study was conducted to assess the prevalence of metabolic syndrome (MetS) and its association with sociodemographic and clinical variables among schizophrenic inpatients in Kuwait. In recent years, especially after the introduction of new generation antipsychotics, researchers have frequently discussed on the metabolic problems seen in patients with schizophrenia.

Methods
This was a cross-sectional observational study; 181 adult patients aged 18 years and above, admitted to Psychological Medicine Hospital, Kuwait in July, 2009, with a diagnosis of schizophrenia according to the *Diagnostic and Statistical manual of Mental disorders – text revised (DSM -IV-TR)* were invited to participate until 30 December 2009. The Third Adult Treatment Panel (ATP III) of The National Cholesterol Education Program, the American Heart Association (ATP-III-A), and International Diabetes Federation criteria were used to define MetS.

Results
The prevalence of MetS among schizophrenic patients is high. The prevalence rate by different definition was 27.1% ($n=49$) (three definitions of MetS were used), and the prevalence was 18.8, 23.2, and 24.9% according to The Third Adult Treatment Panel of The National Cholesterol Education Program, the ATP III-A, and International Diabetes Federation criteria, respectively. The prevalence of MetS increased with age, duration of illness and illness severity.

Conclusion
The prevalence of the MetS among schizophrenic patients is high (27.1%). Although this study found that the prevalence of MetS in schizophrenic patients was lower according to ATP III (18.8%), in comparison with similar studies, it is increased when ATP III-A (23.2%) and IDF (24.9%) were taken into account. Robust correlation of MetS with age, duration of illness, and illness severity were noted.

Keywords:
diabetes, metabolic syndrome, obesity, schizophrenia

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Introduction

During the last several years, there has been a growing interest in metabolic abnormalities in the general population and in schizophrenic patients [1]. The metabolic syndrome (MetS), a cluster of metabolic risk factors (central obesity, dyslipidemia, raised blood pressure, and fasting blood glucose) for type 2 diabetes mellitus and cardiovascular disease (CVD), is a commonly observed phenomenon in psychiatric practice all over the world [2]. In the absence of CVD or diabetes, the MetS is a predictor of these conditions. Once CVD or diabetes develops, the MetS is often present and the number of components of the syndrome contributes to disease progression and risk [3].

In recent years, especially after the introduction of new generation antipsychotics, researchers have frequently discussed on metabolic problems seen in patients with schizophrenia [4]. These metabolic abnormalities are of major clinical concern, not only because of their direct, somatic effects on morbidity and mortality, but also because of their association with psychiatric outcome, such as a higher prevalence of psychotic and depressive symptoms also a worse perceived physical health [5], has a small but measurable impact on psychiatric outcomes and associated with prolongation in length of hospital stay [6]. Body mass index (BMI) status and subjective distress from weight gain were predictors of noncompliance. Obese individuals were more than twice as likely as those with a normal BMI to report missing their medication [7].

MetS is associated with a four times higher risk of developing diabetes [8], three times higher risk of dying from coronary heart disease [9], three times higher risk of stroke, and six times more likely to be at risk of cardiovascular-related mortality [10].

There has been a number of MetS definitions presented over the last decade. The widely accepted ones are those proposed by (i) National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III)

[11]; (ii) American Heart Association/National Heart, Lung, and Blood Institute, AHA (updated ATP III) [12]; and (iii) International Diabetes Federation (IDF) [13]. Table 1 shows the similarities and differences among these definitions.

A major difference between the ATP and IDF diagnostic systems is the necessity of central obesity for making a diagnosis. The updated ATP III definition requires any three of five criteria for a diagnosis, whereas the IDF definition needs central obesity plus any other two abnormalities. Despite this difference, updated ATP III and IDF criteria still identify essentially the same individuals as having MetS. In addition, recommendations for clinical management are virtually identical in the updated ATP III and IDF reports [12]. Depending on the various definitions used, prevalent studies of MetS in large sample sizes of schizophrenic patients showed rates of MetS between 28.4 and 44.7%. In 240 Canadian patients with schizophrenia or schizoaffective disorder, 45.5% (42.6% of men and 48.5% of women) of them met the ATP III diagnosis of MetS [14].

Both the original and updated ATP III definitions were applied in 689 Americans with schizophrenia, who participated in the Clinical Antipsychotic Trials of Intervention Effectiveness Schizophrenia Trial. The prevalence rates of MetS in the Clinical Antipsychotic Trials of Intervention Effectiveness study were 40.9% (ATP III) and 42.7% (updated ATP III) [15]. A more recent study in 430 Belgian patients with schizophrenia showed a prevalence of 28.4% (ATP III), 32.3% (updated ATP III), and 36% (IDF) [16]. In Egypt, the prevalence of MetS in schizophrenic patients was 38.09% [17]. In Turkey, MetS in schizophrenic patients was 21% according to ATP III, 34% according to ATP III-A, and 41% based on IDF [18].

The higher prevalence of MetS in patients with schizophrenia may be explained by medication-related, disease-related, and lifestyle-related factors. Second-generation antipsychotic drugs cause, to a varying extent, dyslipidemia, weight gain, and diabetes [19]. Lifestyle factors such as smoking, unhealthy food intake, and little physical exercise contribute to the development of cardiovascular and metabolic diseases in patients with schizophrenia [9].

Hypothesis and aim of the studywas to assess the prevalence of MetS and its association with sociodemographic and clinical variables in a sample of patients with schizophrenia admitted to Psychological Medicine Hospital in Kuwait.

Patients and methods

This is a cross-sectional observational study; 181 adult patients aged 18 years and above, admitted at the acute admission wards of the Psychological Medicine Hospital, Kuwait over a period of 6 months (July 2009 till end of December 2009, inclusive), who fulfilled the study's inclusion criteria were invited to participate.

The exclusion criteria were being currently pregnant or a history of pregnancy in the past 6 months (to avoid metabolic disturbance), substance use disorder, dementia, mental retardation, and lack of capacity to give written informed consent. The study was approved by the hospital's research and ethics committee. A written informed consent (included study title, different measurement, and investigations) was taken from the patients and their families after discussing the aim of the study with them.

The psychiatric diagnosis considered for each patient was the primary diagnosis, confirmed by their assisting physician, according to the *Diagnostic and Statistical manual of Mental disorders Text Revised*. Sociodemographic variables, details of illness (psychiatric and medical), and a list of all past and current medications were collected systematically through patient interview and from available medical records. MetS was diagnosed using three sets of criteria (definitions of MetS are presented in Table 1).

The IDF lists the following ethnic group-specific thresholds for waist circumference to define central adiposity: Europid, sub-Saharan African men, and Eastern and Middle-Eastern men, more than or equal to 94 cm; South Asian, Chinese, and ethnic South American and Central American men, more than or equal to 90 cm; Japanese men, more than or equal to 85 cm; women except Japanese women, more than or equal to 80 cm; and Japanese women, more than or equal to 90 cm. In this analysis, the following thresholds for waist circumference were used: white men, more than or equal to 94 cm;

Table 1 Definitions of the metabolic syndrome

Criteria	ATP III[a] (NCEP)	ATP III A[a] (AHA)	IDF[b]
Waist (cm)	M>102, F>88	M>102, F>88	M ≥ 94, F ≥ 80
BP[c] (mmHg)			Obligatory criterion
HDL (mg/dl)	≥ 130/85	≥ 130/85	≥ 130/85
TG (≥ 150 mg/dl) or ≥ 1.695(mmol/l)	M<40, F<50	M<40, F<50	M<40, F<50
Glucose (mg/dl) or (mmol/l)[d]	≥ 150 or ≥ 1.695 ≥ 110 or ≥ 6.1	≥ 150 ≥ or ≥ 1.695 ≥ 100 or ≥ 5.6	≥ 150 or ≥ 1.695 ≥ 100 or 5.6

AHA, the American Heart Association; BP, blood pressure; F, female; HDL, high-density lipoprotein; IDF, International Diabetes Federation; M, male; MetS, metabolic syndrome; NCEP ATP III, The Third Adult Treatment Panel of The National Cholesterol Education Program; TG, triglycerides.
[a]MetS if three of five criteria are met.
[b]MetS if additional two criteria are met (waist is obligatory).
[c]Or if treated with antihypertensive medication.
[d]Or if treated with insulin or hypoglycemic medication.

African–American men, more than or equal to 94 cm; Mexican–American men, more than or equal to 90 cm; white women, more than or equal to 80 cm; African–American women, more than or equal to 80 cm; and Mexican–American women, more than or equal to 80 cm. For participants whose designation was 'other race–including multiracial', thresholds that were once based on Europid cut-points ($\geq$ 94 cm for men and $\geq$ 80 cm for women) and once based on South Asian cut-points ($\geq$ 90 cm for men and $\geq$ 80 cm for women) were used.

The participants' height was measured using a wall-mounted standiometer, and the weight was measured using calibrated electronic scales with the patient wearing light clothes. Waist circumference was measured at the midpoint between the upper border of the iliac crest and the lower rib, with a tape measuring horizontally circling the body. Blood pressure was measured with the patient seated, after a minimum of 10 min rest.

Fasting blood samples (blood was sampled after a minimum of 10 h of fasting) were collected to assess glucose, triglycerides, and high-density lipoprotein (HDL) levels. Glucose was measured by the oxidative glucose colorimetric method, with dry chemistry readings with reflectometry. The triglycerides were measured by the enzymatic and colorimetric methods. HDL was measured by the homogenic or direct method.

The statistical analysis consisted initially of descriptive measures for the variables under study. For this purpose, frequencies and percentages were used for category variables, and means and standard deviations were used for quantitative variables. Independent sample *t*-test (*t*) was used when there were two groups of patients compared regarding different variables. Paired samples *t*-test (*t*) was used when same patients (one group) were compared regarding different variables. Pearson χ^2 tests were used to detect whether there is a significant association between two categorical variables. One way analysis of variance (*F*) was applied when comparing several means to see how several independent variables interact with each other and what effects these interactions have on a dependent variable. The statistical significance level was accepted as *P* value of less than 0.05. The analyses were conducted with the software SPSS (version) 15.0 Inc. (Statistical Package for Social Sciences, Chicago, Illinois, USA).

Table 2 Frequencies of distribution of age and duration of illness of patients and indices of metabolic syndrome (*N*=181)

Variable	Number of patient	Percentage
Age (years)		
18–30	42	23.2
31–45	97	53.6
46–68	42	23.2
Mean (SD)	38.5 (10.3)	
Duration of illness (years)		
1–5	39	21.5
6–10	41	22.7
11–20	60	33.1
21–40	41	22.7
Mean (SD)	13.6 ± 8.5	
Height of patients (cm)		
140–160	83	45.8
161–170	57	31.5
171–193	41	22.7
Mean (SD)	163.0 ± 8.8	
Weight of patients (kg)		
43–70	61	33.7
71–90	87	48.1
91–110	27	14.9
111–156	6	3.3
Mean (SD)	77.0 ± 18.5	
Waist circumference of patients (cm)		
43–80	38	21.0
81–90	36	19.9
91–100	40	22.1
101–120	56	30.9
121–150	11	6.1
Mean (SD)	94.5 ± 16.7	
Hip circumference of patients (cm)		
42–90	44	24.3
91–110	97	53.6
111–138	40	22.1
Mean (SD)	100.7 ± 16.0	
Triglycerides level (mmol/l)		
0.24–1.68	148	81.8
1.69–5.10	33	18.2
Mean (SD)	1.3 ± .8	
HDL level (mmol/l)		
0.40–1.00	75	41.4
1.1–1.50	87	48.1
1.51–2.08	19	10.5
Mean (SD)	1.1 ± .28	
Systolic BP of patients (mmHg)		
100–120	110	60.8
125–140	57	31.5
145–190	14	7.7
Mean (SD)	124.6 ± 14	
Diastolic BP of patients (mmHg)		
65–70	53	29.3
75–90	116	64.1
95–110	12	6.6
Mean (SD)	79.9 ± 8.6	
Fasting blood glucose level (mmol/l)		
2.0–5.5	116	64.1
5.6–6.1	30	16.6
6.2–8.00	21	11.6
8.1–18.2	14	7.7
Mean (SD)	5.8 ± 2.3	

BP, blood pressure; HDL, high-density lipoprotein; SD, standard deviation.

Results

Of all the inpatients in the psychological medicine hospital during the study period, we enrolled 181 patients who met the inclusion criteria to participate in the study. Frequencies of distribution of age and the duration of illness of patients and indices of MetS are summarized in Table 2. The mean age of the patients was 38.5 ± 10.3 years, the mean duration of illness was 13.6 ± 8.5 years, the mean height of patients was 163.0 ± 8.8 cm, the mean weight of the patients was 77.0 ± 18.5 kg, the mean waist circumference of the patients was 94.5 ± 16.7 cm, the mean hip circumference of the patients was 100.7 ± 16.0 cm, the mean triglyceride level of the patients was 1.3 ± 0.81 mmol/l, the mean HDL level of the patients was 1.1 ± 0.28 mmol/l, the mean systolic blood pressure of the patients was 124.6 ± 14.5 mmHg, the mean diastolic BP of the patients was 79.9 ± 8.6 mmHg, and the mean fasting blood glucose level of the patients was 5.8 ± 2.3 mmol/l.

Table 3 Demographic and clinical characteristics of the patients (*N*=181)

Variable	*n*	Percentage
Age (years, mean ± SD)	38.5 ± 10.3	–
Sex		
Male	128	70.7
Female	53	29.3
Marital state		
Single	105	58
Married	38	21
Other (widowed, divorced)	38	21
Education level		
No formal education	78	43.1
Primary school	19	10.5
Secondary/intermediate	58	32
School university	26	14.4
Occupation		
Unemployed	161	88.9
Student	2	1.1
House wife only	7	3.9
Junior work	8	4.4
Senior level	3	1.7
Nationality		
Kuwaiti	138	76.2
Non Kuwaiti	23	12.7
Other Arabs	20	11
Diagnosis		
Schizophrenia	165	91.2
Schizoaffective	16	8.8
Illness duration (years, mean ± SD)	13.6 ± 8.5	–
Drug type		
Typical antipsychotic	42	23.2
Atypical antipsychotic	81	44.8
Combined typical and atypical antipsychotic	58	32.8
Smoking		
Present	92	50.8
Not present	89	49.2
Hypertension in family		
Present	88	48.6
Not present	93	51.4
Diabetes in family		
Present	67	37
Not present	114	63

SD, standard deviation.

Demographic and clinical characteristics of the patients are given in Table 3. The mean age of the patients was 38.5 ± 10.3 years; the study cases were 128 (70.7%) male patients and 53 (29.3%) female patients, 105 (58%) single, 38 (21%) married, and 38 (21%) others (divorced, widowed). In addition, there were 138 (76.2%) patients Kuwaiti, 23 (12.7%) patients nonKuwaiti, and 20 (11%) patients of other Arab nationalities.

As regards the occupational status, two patients (1.1%) were students, seven (3.9%) patients were housewives only, eight (4.4%) patients were junior-level workers, three (1.7%) patients were senior-level workers, and 161 (88.9%) patients were unemployed. Considering the educational level, 78 (43.1%) patients received no formal education, 19 (10.5%) patients went to primary school, 58 (32%) patients went to secondary/intermediate school, and 26 (14.4%) patients were university graduates.

Mean duration of illness was 13.6 ± 8.5 years. As regards the antipsychotics used, 81 patients (44.8%) used atypical antipsychotics, 42 (23.2%) patients used typical antipsychotics, and 58 (32.8%) patients used combined typical and atypical antipsychotics. As regards the diagnosis, 165 patients (91.2%) were diagnosed with schizophrenia and 16 (8.8%) patients were diagnosed as schizoaffective.

Overall, 91 patients (50.8%) were smokers, 88 (48.6%) patients had family members with hypertension, and 67 (37%) patients had family members with diabetes.

The sex differences in age and indices of MetS are shown in Table 4. Of the 181 participants, 128 patients (70.7%) were men and 53 were women (29.3%). The mean age of the patients was 38.5 ± 10.3 years; 39.5 ± 11.05 years for men and 36.35 ± 7.7 for women. There was no significant difference among both men and women. As regards the duration of illness, there was no significant difference between men and women, when the mean duration of illness was 13.54 ± 8.8 years for men and 13.9 ± 7.6 years for women.

The mean waist circumference of patients was 94.2 ± 17.8 cm for men and 95.2 ± 13.8 cm for women, with no significant difference between them. The mean triglyceride level was 1.4 ± 0.91 mmol/l for men and 1.03 ± 0.6 mmol/l for women, with no significant difference between them. The mean HDL level was 1.09 ± 0.3 mmol/l for men and 1.1 ± 0.3 mmol/l for women, with no significant difference between them.

The mean systolic BP of the patients was 126.9 ± 15.3 mmHg for men and 119.2 ± 10.9 mmHg for women, with statistically significant difference between them. The mean diastolic BP of the patients was 81.25 ± 8.8 mmHg for men and 76.8 ± 7.2 mmHg for women, with significant difference between them.

The mean fasting blood glucose level was 5.9 ± 2.5 mmol/l for men and 5.8 ± 1.9 mmol/l for women, with no significant difference between them.

Metabolic syndrome types are shown in Table 5. Of the 181 patients, the total prevalence in the population

Table 4 Sex differences in age and indices of metabolic syndrome

Variable	Male (*N*=128)	Female (*N*=53)	*t*	d.f.	Significance: *P* (two-tailed)
Age (years)	39.5 ± 11.05	36.35 ± 7.7	1.86	179	0.069
Illness duration	13.54 ± 8.8	13.9 ± 7.6	0.24	179	0.033
Waist circumference of patients (cm)	94.2 ± 17.8	95.2 ± 13.8	0.34	179	0.73
Triglycerides level (mmol/l)	1.4 ± 0.91	1.03 ± 0.6	2.51	179	0.13
HDL level (mmol/l)	1.09 ± 0.3	1.1 ± 0.3	1.07	179	0.29
Systolic BP of patients (mmHg)	126.9 ± 15.3	119.2 ± 10.9	3.3	179	0.001
Diastolic BP of patients (mmHg)	81.25 ± 8.8	76.8 ± 7.2	3.25	179	0.001
Fasting blood glucose level (mmol/l)	5.9 ± 2.50	5.8 ± 1.9	0.20	179	0.07

BP, blood pressure; d.f., degrees of freedom; HDL, high-density lipoprotein.
Significant=$P<0.05$.

Table 5 Prevalence of metabolic syndrome types (*N*=181)

Metabolic syndrome category	*n*	Percentage
Only two criteria of MetS	43	23.8
Fulfilled MetS	49	27.1
Fulfilled MetS by NCEP ATP III	34	18.8
Fulfilled MetS by AHA	42	23.2
Fulfilled MetS by IDF	45	24.9
No MetS	89	49.2

AHA, the American Heart Association; IDF, International Diabetes Federation; MetS, metabolic Syndrome; NCEP ATP III, The Third Adult Treatment Panel of The National Cholesterol Education Program.

studied is 27.1% ($N=49$), 23.8% of patients ($N=43$) met only two criteria of metabolic syndrome but not diagnosed metabolic syndrome, and 49.2% of patients ($N=89$) had no metabolic syndrome as yet defined. Of the 181 patients 34 (18.8%) fulfilled the NCEP criteria for metabolic syndrome, 42 patients (23.2%) fulfilled AHA criteria, and 45 (24.9%) patients fulfilled IDF criteria. There was considerable overlap between the groups who fulfilled the different sets of criteria. With 69.4% ($N=34$) fulfilled NCEP, 85.7% ($N=42$) fulfilled AHA and 91.8% ($N=45$) fulfilled IDF of all those who fulfilled metabolic syndrome ($N=49$).

The relationship between MetS and sociodemographic and also the clinical characteristics are shown in Table 6. We present the comparison of demographic and clinical characteristics of the patients with or without a diagnosis of MetS. None of the sociodemographic variables were significantly associated with the presence of the syndrome, except marital status in which significant difference between the patients with and without a diagnosis of MetS ($P=0.01$) exists. Those married were found to be more in the category of fulfilled MetS than those without MetS, in which 36.8% ($N=14$) fulfilled MetS, 31.6% ($N=12$) fulfilled only two criteria of MetS, and 31.6% ($N=12$) fulfilled no MetS.

As regards sex, 25% ($N=32$) of men fulfilled MetS, 23.4% ($N=30$) met only two criteria of MetS and 51.6% ($N=66$) met no criteria of MetS. In women, 32.1% ($N=17$) fulfilled MetS, 24.5% ($N=13$) met only two criteria of MetS, and 43.4% ($N=23$) met no criteria of MetS.

Table 6 Relationship between metabolic syndrome and sociodemographic and clinical characteristics

Subject	Fulfilled MetS *n*=49 (%)	Only two criteria of MetS *n*=43 (%)	No MetS *n*=89 (%)	Statistics
Sex				
Men	32 (25)	30 (23.4)	66 (51.6)	$\chi^2=1.8$
Women	17 (32.1)	13 (24.5)	23(43.4)	d.f.=2
				Significance=0.41
Marital state				
Single	20 (19.0)	27 (25.7)	58 (55.3)	$\chi^2=13.1$
Married	14 (36.8)	12 (31.6)	12 (31.6)	d.f.=4
				Significance=0.011
Other (widowed, divorced)	15 (39.5)	4 (10.5)	19 (50)	
Education level				
No formal education	15 (19.2)	25 (32.0)	38 (48.8)	$\chi^2=1.1$
Primary school	5 (26.3)	2 (10.5)	12 (63.2)	d.f.=6
Secondary/intermediate	19 (32.8)	12 (20.7)	27 (46.5)	Significance=0.160
University	10 (38.5)	4 (15.4)	12 (46.1)	
Nationality				
Kuwaiti	38 (27.5)	31 (22.5)	69 (50.0)	$\chi^2=1.1$
Non Kuwaiti	7 (30.4)	6 (26.1)	10 (43.5)	df=4
Other Arabs	4 (20.0%	6 (30.0)	10 (50.0)	Significance=0.89
Occupation				
Unemployed	45 (27.9)	39 (24.2)	77 (47.9)	$\chi^2=7.52$
Student	0 (0)	0 (0)	2 (100.0)	d.f.=8
House wife only	3 (42.8)	2 (28.6)	2 (28.6)	Significance=0.481
Junior work	1 (12.5)	2 (25.0)	5 (62.5)	
Senior level	0 (0)	0 (0)	3 (100)	
Diagnosis				
Schizophrenia	45 (27.3)	39 (23.6)	81 (49.1)	$\chi^2=0.042$
Schizoaffective	4 (25.0)	4 (25.0)	8 (50.0)	d.f.=2
				Significance=0.098
Smoking				
Present	25 (27.2)	26 (28.3)	41 (44.5)	$\chi^2=2.40$
Not present	24 (27.0)	17 (19.1)	48 (53.9)	d.f.=2
				Significance=0.30
Hypertension in family				
Present	27 (30.7)	19 (21.6)	42 (47.7)	$\chi^2=1.23$
Not present	22 (23.6)	24 (25.8)	47 (50.6)	d.f.=2
				Significance=0.54
Diabetes in family				
Present	19 (28.3)	13 (19.4)	35 (52.3)	$\chi^2=1.1$
Not present	30 (26.3)	30 (26.3)	54 (47.4)	d.f.=2
				Significance=0.57

d.f., degrees of freedom; MetS, metabolic Syndroma.
Significant=$P<0.05$.

As regards MetS and psychiatric diagnosis, there were 165 patients diagnosed with schizophrenia [45 (27.3%) fulfilled MetS, 39 (23.6%) met only two criteria of MetS, and 81 (49.1%) met no criteria of MetS] and 16 patients with a diagnosis of schizoaffective disorder [four (25%) fulfilled MetS, four (25%) met only two criteria of MetS, and eight (50%) met no criteria of MetS].

As regards smoking state and family history of diabetes and hypertension, no significant differences exist between those with or without MetS [($P = 0.3$), ($P = 54$), ($P = 54$), respectively].

The relationship between MetS and age of patient and duration of illness is shown in Table 7. There was significant difference in mean age between those with and without MetS. The patients with MetS were found to be older than patients without MetS. The mean age of the patients diagnosed with MetS was 43.4 ± 9.5 years, mean age of patients who met only two criteria of MetS was 39.7 ± 11.3 years and mean age of patients who met no MetS was 35.3 ± 9.0 years.

With regard to the duration of illness, the mean duration of illness was 16.5 ± 8.6 years in the patients diagnosed with MetS, 16.6 ± 8.9 years in inpatients who met only two criteria of MetS, and 10.6 ± 7.1 years in patients who met no criteria of MetS, with statistically significant difference between both with and without MetS.

Table 8 shows the relationship between MetS and Brief Psychiatric Rating Scale (BPRS). The BPRS score range was 39–82, with a mean of 58.2 ± 6.9; there was significant relationship between MetS and BPRS severity ($f = 4.4$, d.f. = two of 181, $P > 0.05$).

The relationship between MetS and antipsychotic treatment is given in Table 9. There were no significant differences in the type of antipsychotic drugs used between the patients with and without MetS.

Discussion

In this sample of schizophrenic patients, 27.1% fulfilled criteria for the MetS as defined by MetS guidelines. This rate is elevated, compared with the rate of 18% found among healthy Kuwaiti adults [20], and 21.4% were found among the United States general population during the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) [12]. In this study, the MetS prevalence in schizophrenic patients was 18.8% ($N = 34$) according to NCEP-ATP III, 23.2% ($N = 42$) according to AHA (ATP III-A), and 24.9% ($N = 45$) according to IDF. This result was lower than the result of Cerit *et al.* [18] who found that MetS prevalence in schizophrenic patients was 21% according to ATP III, 34% according to ATP III-A, and 41% according to IDF. It was also lower than Rezaei *et al.* [21] who found that the prevalence of the MetS according to the different definitions were 27.4% (ATP-III), 37.6% (ATP-III A), and 38.7% (IDF). It was also lower than the result of El Tayebani [22] who found that the prevalence of the MetS in old chronic schizophrenic patients in Kuwait was 52.5% and was lower than that of the values between 42.4 and 62.5% found in North America, [23,24] and than the values of 34.6 and 37.1% found in Sweden [25] and in Finland [26]. A study in Egypt found a prevalence of 38.09% (IDF), [17] and one study in Belgium found a prevalence of 28.4%, which was slightly higher than the value found in this study [27]. An other study in Finland only assessed patients at the age of 30–32 years and found a prevalence of 19.4% [28]. One study in Taiwan found a 22% prevalence rate in the Taiwanese inpatient cohort [29]. One study in turkey found a prevalence of MetS was 18.9% (IDF) [30].

There might be several reasons for the low prevalence rate of MetS in our study: The first might be the low mean age of our patients (38.5 ± 10.3 years). Another reason might be that 23.8% of our patients met only two positive criteria for a diagnosis of MetS and, thus, were not diagnosed with MetS. Moreover, difference in lifestyle factors and balanced hospital diets and optimal medical care provided in the hospital setting could contribute to our finding.

Demographic characteristics

When we compared patients with MetS with those without MetS, according to sociodemographic data, we found that the MetS was not associated with sex difference, educational level, and occupational states. But we found increase prevalence of the MetS according Marital states, ($P = 0.01$) in which those married were found to be more in fulfilled MetS group than those without metabolic syndrome, in which 36.8% ($N = 14$) fulfilled metabolic syndrome, 31.6% ($N = 12$) met two criteria of metabolic syndrome and 31.6% ($N = 12$) met no criteria of MetS.

Table 7 Relation between metabolic syndrome and age of patient and duration of illness

Variable	*N*	Mean (SD)	Statistics
Age of patient			
Fulfilled MetS	49	43.4 ± 9.5	$f = 11.2$
Only two criteria of MetS	43	39.7 ± 11.3	d.f. = 2
			Significance = 0.000
No MetS	89	35.3 ± 9.0	
Duration of illness of patients			
Fulfilled MetS	49	16.5 ± 8.6	$f = 12.3$
Only two criteria of MetS	43	16.6 ± 8.9	d.f. = 2
			Significance = 0.000
No MetS	89	10.6 ± 7.1	

d.f., degrees of freedom; MetS, metabolic syndrome; SD, standard deviation.
Significant = $P < 0.05$.

Table 8 Relation between metabolic syndrome and Brief Psychiatric Rating Scale

Variable	*N*	Mean (SD)	Statistics
BPRS			
MetS categorization			
Fulfilled MetS	49	60.0 (6.2)	$f = 4.4$
Only two criteria of MetS	39	55.5 (8.6)	d.f. = 2/181
			Significance = 0.01
No MetS	71	53.0 (8.2)	

BPRS, Brief Psychiatric Rating Scale; d.f., degrees of freedom; MetS, metabolic syndrome.
Significant = $P < 0.05$.

Table 9 Relation between metabolic syndrome and antipsychotic treatment

Variable	Fulfilled MetS	Only two criteria of MetS	No MetS	*n*	Statistics
Typical antipsychotic	12	6	24	42	*f*=3.9 d.f.=2 Significance=0.21
Atypical antipsychotic	22	21	15	81	*f*=0.89 d.f.=2 Significance=0.41
Combined typical and atypical antipsychotic	15	16	27	58	*f*=1.09 d.f.=2 Significance=0.33

d.f., degrees of freedom; MetS, metabolic syndrome.
Significant=$P<0.05$.

Age

When we compared patients with metabolic syndrome with those without MetS, according to the age, we found that the patients with MetS had higher mean age, (43.4 ± 9.5 years) and that the frequency of MetS increased consistently with age. This is in agreement with results of Cerit *et al.* [18], who found that the patients with MetS had higher mean age and that the frequency of MetS increased consistently with age. This is also in agreement with Moreno *et al.* [31] and Yazici *et al.* [32], who found an association of the syndrome with older age that was statistically significant. Hägg *et al.* [25] did not find a coherent relationship between age and MetS frequency.

Clinical characteristics

Duration of illness

In this study, durations of illness in patients with MetS were longer than in patients without MetS ($P = 0.000$). This is in agreement with the result of Cerit *et al.* [18], who found that illness and treatment durations of patients with MetS were longer than in patients without MetS.

Psychotropic medication

There is an assumption that atypical antipsychotics can trigger weight gain and related metabolic changes; however, in this study there was no statistically significant relationship between the type of drugs used (whether typical or atypical) and MetS diagnoses, which is similar to what was reported by Kato *et al.* [33], Heiskanen *et al.* [26], and Cerit *et al.* [18]. The differential metabolic side effects of atypical antipsychotics should also be considered. For instance, Meyer *et al.* [34] reported that within the 20-week period when there was a shift from olanzapine treatment to risperidone, they observed a significant decrease in the frequency of MetS among patients.

Smoking

In this study, we examined smoking and metabolic problems, but could not find any significant relationship between them, which is in line with the findings of Hägg *et al.* [25], Kato *et al.* [33], Cerit *et al.* [18], and Littrell *et al.* [29]. A family history of diabetes and hypertension has been questioned in limited studies investigating MetS in schizophrenia. In this study, it was found that there is no significant difference between family history of diabetes and hypertension in schizophrenia patients with and without MetS. This is similar to the findings of Kato *et al.* [33], Cerit *et al.* [18], and Yazici *et al.* [32] who did not find a relationship between MetS and a family history of hypertension or diabetes.

Illness severity, we found association between patients fulfilled MetS and illness severity which was those (BPRS) main score was more in patients fulfilled MetS than those met no criteria of MetS.

The main values for MetS criteria in both men and women revealed that waist circumference was more indicators in men and women. The main waist circumference in female (95.2 ± 13.8 cm) met MetS by ATP11, AHA, and IDF definitions, whereas main waist circumference in male (94.2 ± 17.8) met MetS by IDF definitions only. Waist circumference measurement indicates central obesity. Kato *et al.* [33] posited that the relationship between MetS and central obesity was stronger than the relationship between MetS and obesity (as determined by BMI), that is, fat level was less important than the distribution of fat in the body. Therefore, Kato *et al.* [33] pointed out that waist circumference measurement alone was a good indicator of MetS.

Furthermore, an important finding of this study was the mean fasting blood glucose level of the male and female patients was higher than normal levels, whereas the mean fasting blood sugar level in female (5.8 ± 1.9), and male (5.9 ± 2.50), both fulfilled MetS by AHA and IDF definitions, which is in line with the results of McEvoy *et al.* [15], who reported that prediabetes and type II diabetes were frequent among people with schizophrenia. All other main values for MetS parameters did not fulfilled MetS by any definitions.

There are limitations to this study. First, is the type of study which was a cross-sectional (data collection is limited to a single time point. Therefore, changes in relation between MetS and schizophrenia over time cannot be assessed, give no indication of the sequence and difficult to make causal inference). Second, lack of data on the dietary habits, sedentary life, family history of obesity, and other limitations include lack of a control group. On the other hand, the fact that the population studied is made up of hospitalized patients impedes the

results obtained from being generalizable to the rest of the outpatient of psychiatric illnesses. Despite these limitations, our findings are consistent with high rates of the MetS found in other psychiatric populations.

Conclusion

The prevalence of MetS among patients hospitalized in a ward of a psychological medicine hospital in Kuwait was 27.1%. Although this study found that the prevalence of MetS in patients was lower according to NCEP ATP III, (18.8%) in comparison with similar studies, it is increased when AHA (ATP III-A) (23.2%) and IDF (24.1%) were taken into account. The factors related to MetS were age, durations of illness, and illness severity.

We recommend further studies with larger samples involving both inpatients and outpatients to be able to generalize the results. In the light of the findings in this study and other studies, psychiatrists should consider measuring BP and waist circumference, two components of the MetS, and also monitoring of the weight; these are easily assessed in the clinic setting in addition to measuring fasting glucose and lipids. This is important for early intervention to reduce the high rates of the MetS and cardiovascular morbidity in severely mentally ill patients.

There is no conflict of interest to declare.

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الملخص العربى

معدل انتشار المتلازمة الأيضية في مرضى الفصام

رضا رشدى

قسم الطب النفسى- كلية الطب - جامعة الازهر

الهدف من هذه الدراسة هو دراسة معدل انتشار المتلازمة الأيضية في عينة من مرضى الفصام

تم اختيار عينة البحث من مرضى الأقسام الداخلية بمستشفى الطب النفسي بدولة الكويت في الفترة من يوليو ٢٠٠٩ إلى ٣٠ ديسمبر ٢٠٠٩ وكان العدد المشارك هو ١٨١مريض.

وتم تشخيص المرض النفسي طبقاً للدليل التشخيصي والإحصائي للأمراض النفسية الرابع المراجع .وطبق على جميع المرضى ، الدلائل (المو).ات) التشخيصية للمتلازمة الأيضية طبقاً لما يلي:

١- البرنامج الوطني لتعليم الكولسترول – المبادئ التوجيهية للممارسة السريرية لإدارة الكولسترول في البالغين.

٢- جمعية القلب الأمريكية - المبادئ التوجيهية للممارسة السريرية لإدارة الكولسترول في البالغين المعدل.

٣- الإتحاد العالمي لمرضى السكرى.

و أظهرت نتائج العينة أن متوسط الأعمار كان٣٨,٥ ±١٠,٣ عام وكانت نسبة الرجال٧٠,٧ ٪ (العدد = ١٢٨) ونسبة الإناث٢٩,٣٪ (العدد = ٥٣) .وكان معدل انتشار المتلازمة الأيضية طبقاً للدلائل التشخيصية المختلفة ١ ,٢٧ ٪. وكان معدل الانتشار طبقاً للدليل التشخيصي للبرنامج الوطني لتعليم الكولسترول ١٨,٨ ٪ و طبقاً للدليل التشخيصي لجمعية القلب الأمريكية ٢ ,٢٣ ٪ والإتحاد العالمي لمرضى السكري ٩, ٢٤ ٪ . ولوحظ ارتفاع معدل انتشار المتلازمة الأيضية مع كل من ارتفاع سن المريض وزيادة فترة المرض وشدته.

وخلصت الدراسة إلى ارتفاع معدل انتشار المتلازمة الأيضية لدى مرضى الفصام. كما لوحظ الارتباط الوثيق بين المتلازمة الأيضية وكل من سن المريض و فترة المرض وشدته. وتكمن أهمية هذه النتائج في أهمية التدخل المبكر لخفض معدل انتشار المتلازمة الأيضية وأمراض القلب والأوعية الدموية لدى المرضى بمرض نفسي شديد.

Methyltetrahydrofolate reductase polymorphism, folic acid, and B12 in a sample of patients with depressive and anxiety symptoms

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Introduction
Both anxiety and depression are common symptoms or disorders with a major impact on public health. There are several theories regarding potential associations between depression and levels of vitamin B12 and folate. Vitamin B12 and folate are associated with the synthesis of monoamines and are involved in single carbon transfer methylation reactions associated with the production of monoamine neurotransmitters. This study was conducted to investigate the relationship between depression and other components of 1-carbon metabolism, such as vitamin B12, folate, and the methylenetetrahydrofolate reductase 677C→T polymorphism, and to compare the associations among folate, vitamin B12, and the methylenetetrahydrofolate reductase C677T polymorphism, in anxiety and depression.

Methods
After obtaining approval from the ethics committee in Kasr El Aini hospital, 90 participants were randomly selected in a comparative cross-sectional study. The sample consists of three groups: a group of depressive disorders without psychotic symptoms ($n=30$), a group of anxiety disorders ($n=30$), and a control group ($n=30$). The patients were recruited from the psychiatric out-patient clinic. Patients were diagnosed by a lecturer of psychiatry according to *DSM-IV* criteria. Psychometric procedure: Beck depression Inventory for severity of depression, Hamilton rating scale of depression, and Hamilton rating scale of anxiety. Laboratory: simultaneous assay of vitamin B12 and folic acid by radioimmune assay technique and analysis of methylenetetrahydrofolate reductase (C677T) by means of PCR and RFLP.

Results
Both anxiety and depression groups have the same percentage of gene mutation (33.3%). Folic acid and vitamin B12 mean values were the highest in the control group, followed by the anxiety group; the least was in the depression group. Within the depression group, there is a negative correlation between the severity of depression and folic acid. Within the depression group, patients with mutant gene have lower levels of both folic acid and vitamin B12 than patients with nonmutant gene. Within the anxiety group, patients with mutant gene have lower levels of both folic acid and vitamin B12 than patients with nonmutant gene.

Conclusion
Folic acid and vitamin B12 were lower than normal in both patients with anxiety and with depression and this was combined with gene mutation.

Keywords:
anxiety, depression, folic acid, vitamin B12

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Introduction

Both anxiety and depression are common symptoms or disorders with a major impact on public health [1]. A possible role of nutritional factors in the pathogenesis of neuropsychiatric disorders has long been debated [2]. There are several theories regarding potential associations between depression and levels of vitamin B12 and folate. Vitamin B12 and folate are associated with the synthesis of monoamines and are involved in single carbon transfer methylation reactions associated with the production of monoamine neurotransmitters. Low levels of 5-hydroxyindole acetic acid in cerebrospinal fluid have been found in patients with depression with folate deficiency [3]. Clinical studies have shown an inverse relationship between folate status and depression [4]. Such a relationship has been inferred from studies showing an increased frequency of folate deficiency among patients with depression [5]. More severe and

prolonged depressive episodes and weaker treatment response to antidepressants in patients with low folate status and enhanced antidepressant response with folic acid supplementation have been observed [6]. In contrast, the possible role of vitamin B12 status in neuropsychiatric disorders has been motivated by the central nervous system damage caused by overt or subtle vitamin B12 deficiency. Data regarding the association between vitamin B12 status and depression are scarce [7]. Vitamin B12 is also required in the synthesis of S-adenosylmethionine, which is needed as a methyl donor in many methylation reactions in the brain. It has also been suggested to have antidepressant properties. The action of methyltetrahydrofolate reductase (MTHFR) is associated with the formation of tetrahydrobiopterin. This compound is an important enzyme cofactor for tryptophan hydroxylase, the rate-limiting enzyme for the synthesis of 5-hydroxytryptamine (serotonin). Similarly, tetrahydrobiopterin is a cofactor for the rate-limiting enzyme tyrosine hydroxylase (tyrosine 3-monooxygenase) for the synthesis of dopamine and norepinephrine. The three monoamines, dopamine, norepinephrine, and serotonin are neurotransmitters. It is generally accepted that boosting the synthesis or the availability of these compounds results in an antidepressant effect. Thus, MTHFR plays a crucial role in neurotransmitter biosynthesis and in the concentration of monoamines in the synaptic cleft [8]. Single nucleotide polymorphisms in MTHFR have been reported, including a C→T transition at nucleotide 677 in exon 4. For the C677T polymorphism, homozygote variants have 30% enzyme activity in comparison with homozygotes for the wild-type C allele, whereas heterozygotes retain 65% of wild-type MTHFR enzyme activity. Both of these polymorphisms are functional and result in diminished enzyme activity. The consequences of the C677T polymorphism have been demonstrated in population studies, in which lower levels of red blood cell folate, plasma folate, and vitamin B12 have been reported among nondiseased individuals with the 677 TT genotype in comparison with individuals with other genotypes [9].

The aim of this study is to examine the associations among folate, vitamin B12, and the MTHFR C677T polymorphism in anxiety and depression.

Patients and methods

After obtaining approval from Research Ethics Committee Review in Kasr El Aini hospital, 90 patients were randomly selected in a comparative cross-sectional study. All patients gave consent to participate in the study after full explanation of procedures was provided. The sample consists of three groups: a group of major depressive disorders (MDDs) without psychotic symptoms ($n = 30$), a group of generalized anxiety disorders ($n = 30$), and a control group ($n = 30$). The patients were recruited from a psychiatric outpatient clinic. Control cases (healthy volunteers among medical and paramedical personnel staff of Kasr El Aini university hospital) were chosen from an alphabetical computer list of employees of the hospital. All the scales showed an absence of psychopathology in the control group. They were matched in age and sex. This was conducted over 6 months. Patients were diagnosed by a lecturer of psychiatry according to *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* (*DSM-IV*) [10] criteria. Both sexes were included and the age limit was 20–50 years. We excluded patients with other psychiatric disorders such as mixed anxiety–depressive disorder, mental retardation, organic brain disorders, and substance-induced psychiatric disorders, in addition to general medical condition (any condition affecting folic acid or vitamin B12 levels).

Psychometric tools

Semi-structured interview

A specially designed semi-structural interview derived from the Kasr El Aini psychiatric sheet was used to cover demographic data, personal data, history, and family history.

Structured Clinical Interview for DSM Axis of Disorders: it provides broad coverage of axis-I psychiatric diagnosis according to DSM-IV [11].

Hamilton depression rating scale [12]

This scale was designed by Hamilton [12,13]. The original version consisted of 17 items and was later increased to 24 items by Klerman *et al.* [14]. The scale is not meant to be a diagnostic instrument [15]. Hamilton depression rating scale was found to distinguish between different groups of patients drawn from general practice, day-patient care, and in-patients [16]. The concurrent validity is high [17]. The interrater reliability of Hamilton depression rating scale is also consistently high [12]. This is an objective test.

Hamilton anxiety rating scale [18]

Similar to the depression rating scale by the same investigator, the anxiety rating scale was specially developed to rate clinical anxiety in patients already diagnosed as suffering from an anxiety state (it is for use by a trained rater after an ordinary clinical interview). Hamilton took 12 groups of symptoms that were regularly observed in anxiety states as his starting point. The addition of a rating of behavior at an interview made 13 items. Each was rated on a five-point scale from 0 to 4 in an ascending order of severity [16].

Beck depression inventory [19] (Arabic version)

It is a self-report scale designed to assess DSM-IV-defined symptoms of depression such as sadness, guilt, loss of interest, social withdrawal, increase and decrease in appetite or sleep, suicidal ideation, and other behavioral manifestations of depression over the previous 2 weeks. It can also be used over time to monitor symptoms and to assess response to therapeutic interventions. The inventory is composed of 21 groups of statements on a 4-point scale with the patient selecting the one that best matches his or her current state. Each statement group corresponds to specific behavioral manifestation responses and is scored 0–3, corresponding to no, mild, moderate, or severe depressive symptoms. The score range varies from 0 to 63 in which higher score indicates greater depression severity. Score in the range of

0–13 indicates no or minimal depression; 14–19, mild depression; 20–28, moderate depression; and 29–63 indicates severe depression. It is translated into Arabic by Gharib Abdel Fattah and is used in many studies. We used this test for severity ranking and it is a subjective test.

Laboratory

(1) Fasting samples were collected on plain tubes for the assay of serum vitamin B12 and folic acid. Serum was separated and frozen at −20°C until time of analysis. Simultaneous assay of vitamin B12 and folic acid by the radioimmune assay technique was carried out using SimulTRAC-SNB supplied by MP Biomedicals (Diagnostics Division Orangeburg, New York, USA) [20].

(2) Three milliliter of blood was collected using sterile EDTA vaccutainer tubes for DNA extraction and analysis. Samples were stored at −70°C until the assay date. Genomic DNA for MTHFR C677T gene polymorphism was analyzed using PCR, followed by restriction fragment length polymorphism analysis [21].

Genomic DNA was extracted from whole blood by the standard salting-out technique [22].

In brief, the forward and reverse primers supplied by (Fermentas, USA) were used in the following sequence:

5′-TGAAGGAGAAGGTGTCTGCGGGA- 3′ (forward)
5′-AGGACGGTGCGGTGAGAGTG-3′ (reverse).

Amplification was performed using Master Taq polymerase enzyme and a hybaid thermal cycler (Promega Corporation, USA). The mixture was denatured at 95°C for 10 min, and the PCR reaction was performed for 35 cycles under the following conditions: denaturation at 95°C for 1 min, annealing at 65°C for 30 s, and extension at 72°C for 1 min and a final extension cycle of 72°C was for 7 min. Amplified bands were detected by electrophoresis on 1.5% agarose gel containing ethidium bromide. Amplified PCR products were digested with HinfI (Fermentas, USA) and analyzed on agarose gel (3.5%) for the identification of the point mutation in the MTHFR gene. A single fragment of 198 bp was identified as homozygous (CC); a single fragment of 175 bp was identified as homozygous (TT) genotype, and two fragments of 198 and 175 bp were identified as heterozygous (CT).

Statistical methods

Data were statistically described in terms of range, mean ± standard deviation, median, frequencies (number of cases), and percentages when appropriate. Comparison of quantitative variables between the study groups was carried out using the Student *t*-test for independent samples for comparing two groups when normally distributed and using the Mann–Whitney *U*-test for independent samples when not normally distributed. Comparison of quantitative variables between more than two groups of normally distributed data was carried out using the one-way analysis of variance test with posthoc multiple two-group comparisons, whereas non-normal data were compared using the Kruskal–Wallis analysis of variance test with the Mann–Whitney *U*-test for independent samples as posthoc multiple two-group comparisons. For comparing categorical data, the χ^2 test was performed; the exact test was used instead when the expected frequency is less than 5. Correlation between various variables was carried out using the Spearman rank correlation equation for non-normal. A probability value (*P* value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, New York, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, Illinois, USA) version 15 for Microsoft Windows.

Results

Sociodemographic data (Tables 1 and 2)

Table 1 Mean age in the three groups

	Depression (*N*=30)		Anxiety (*N*=30)		Control (*N*=30)	
Age	Mean	SD	Mean	SD	Mean	SD
	32.1	7.7	32.33	7.7	31.2	5.7

SD, standard deviation.

Table 2 Sex and family history of depression or anxiety disorders

	Depression		Anxiety		Control		
	N	Percentage	*N*	Percentage	*N*	Percentage	*P*
Sex							
Male	13	43.3	15	50	17	56.7	0.587
Female	17	56.7	15	50	13	43.3	
Total	30	100	30	100	30	100	
Family history of depression or anxiety disorder							
Positive	9	30	8	26.7	4	13.3	0.271
Negative	21	70	22	73.3	26	86.7	
Total	30	100	30	100	30	100	

N, number.
P<0.05 is statistically significant.

Beck depression inventory (Table 3)

Table 3 Severity of depression in the three groups

	Depression		Anxiety		Control		
	N	Percentage	*N*	Percentage	*N*	Percentage	*P*
Beck depression inventory							
No	0	0	19	63.3	30	100	0.000
Minimum-to-mild	17	56.7	11	36.7	0	0	
Moderate-to-severe	13	43.3	0	0	0	0	
Total	30	100	30	100	30	100	

N, number; No, no depression.
P<0.05 is statistically significant.

Methylenetetrahydrofolate reductase *C677T* polymorphism (Table 4)

Table 4 Methylenetetrahydrofolate reductase *C677T* polymorphism

	Depression		Anxiety		Control		
	N	Percentage	*N*	Percentage	*N*	Percentage	*P*
Gene							
Mutant	10	33.3	10	33.3	6	20	0.42
Nonmutant	20	66.6	20	66.7	24	80	
Total	30	100	30	100	30	100	

N, number.
$P<0.05$ is statistically significant.

Clinical variables among depression, anxiety, and control groups (Table 5–7)

Table 5 Clinical variables between depression and control groups

	Depression (30)		Control (30)		
	Mean	SD	Mean	SD	*P*
Folic acid	5.8	4.5	9.8	4.9	0.003
Vit B12	439.5	189.2	512.4	216.2	0.189
Hamilton depression	27.2	6.9	1.07	1.4	0.000
Hamilton anxiety	4.9	4.1	0.5	0.8	0.000

SD, standard deviation; Vit, vitamin.

Table 6 Clinical variables between anxiety and control groups

	Anxiety (30)		Control (30)		
	Mean	SD	Mean	SD	*P*
Folic acid	8	5.5	9.8	4.9	0.166
Vit B12	504.9	231.9	512.4	216.2	0.89
Hamilton depression	15	5.1	1.07	1.4	0.000
Hamilton anxiety	34	4	0.5	0.8	0.000

SD, standard deviation; Vit, vitamin.

Table 7 Clinical variables between depression and anxiety groups

	Depression (30)		Anxiety (30)		
	Mean	SD	Mean	SD	*P*
Folic acid	5.8	4.5	8	5.5	0.09
Vit B12	439.5	189.2	504.9	231.9	0.23
Hamilton depression	27.2	6.9	15	5.1	0.000
Hamilton anxiety	4.9	4.1	34	4	0.000

SD, standard deviation; Vit, vitamin.
$P<0.05$ is statistically significant.

Correlations within the depression group

Within the depression group (Table 8), there is a negative correlation between the severity of depression and folic acid, which was just statistically significant. There is also a negative correlation between depression severity and vitamin B12, which was statistically significant. Furthermore, there is a positive correlation between the level of folic acid and vitamin B12, which was statistically significant.

Table 8 Correlation between folic acid and vitamin B12 with depression and anxiety

	Beck depression		Vit B12		Hamilton depression		Hamilton anxiety	
	P	*R*	*P*	*R*	*P*	*R*	*P*	*R*
Folic acid	0.05	−0.35	0.02	0.3	0.11	−0.29	0.92	0.019
Vit B12	0.03	−0.38			0.104	−0.302	0.87	−0.03

R, correlation coefficient; Vit, vitamin.
$P<0.05$ is statistically significant.

Within the depression group (Table 9), patients with mutant gene have lower levels of both folic acid and vitamin B12 than patients with nonmutant gene and this difference was statistically significant.

Table 9 Correlation between the folic acid and vitamin B12 and gene mutation within the depression group

	Mutant gene		Nonmutant		
	Mean	SD	Mean	SD	*P*
Folic acid	2	1.8	7.7	4.2	0.000
Vit B12	310	150	504	175	0.002

SD, standard deviation; Vit, vitamin.
$P<0.05$ is statistically significant.

Within the depression group (Table 10), patients with more severe depression have lower levels of folic acid and vitamin B12 than patients with minimal-to-mild depression. This was statistically significant with the vitamin B12 level and did not reach a statistically significant difference with the folic acid level (Table 11).

Table 10 Correlation between the folic acid and vitamin B12 and severity of depression within the depression group

	Minimum-to-mild		Moderate-to-severe		
	Mean	SD	Mean	SD	*P*
Folic acid	6.8	3.9	4.5	5	0.06
Vit B12	484.9	174.4	504	175	0.04

SD, standard deviation; Vit, vitamin.
$P<0.05$ is statistically significant.

Table 11 Correlation between gene mutation and family history in depression group

	Positive FH		Negative FH		Total		
	N	Percentage	*N*	Percentage	*N*	Percentage	*P*
Gene mutation							
Mutant	7	77.8	3	14.3	10	33.3	0.001
Nonmutant	2	22.2	18	85.7	20	66.7	
Total	9	100	21	100	30	100	

FH, family history; *N*, number.
$P<0.05$ is statistically significant.

Correlations within the anxiety group (Tables 12–14)

Table 12 Correlation between folic acid and vitamin B12 with depression and anxiety

	Beck depression		Vit B12		Hamilton depression		Hamilton anxiety	
	P	*R*	*P*	*R*	*P*	*R*	*P*	*R*
Folic acid	0.02	−0.399	0.001	0.57	0.15	−0.026	0.76	−0.05
Vit B12	0.33	−0.181			0.56	−0.11	0.59	0.100

R, correlation coefficient; Vit, vitamin.

Table 13 Correlation between the folic acid and vitamin B12 and gene mutation within the anxiety group

	Mutant gene		Non mutant		
	Mean	SD	Mean	SD	*P*
Folic acid	3.4	3.7	10.3	4.9	0.000
Vit B12	421.3	205	546.7	238	0.183

SD, standard deviation; Vit, vitamin.
$P < 0.05$ is statistically significant.

Table 14 Correlation between gene mutation and family history in anxiety group

	Positive FH		Negative FH		Total		
	N	Percentage	*N*	Percentage	*N*	Percentage	*P*
Gene mutation							
Mutant	7	87.5	3	13.6	10	33.3	0.000
Nonmutant	1	12.5	19	86.4	20	66.7	
Total	8	100	22	100	30	100	

FH, family history; *N*, number.

Discussion

An association between depression and folate status has been demonstrated in clinical studies, whereas data are sparse on the relationship between depression and other components of 1-carbon metabolism, such as vitamin B12, homocysteine, and the MTHFR 677C→T polymorphism. The relationship between anxiety and these components is less well known [6]. Hence, this study was conducted to examine the associations among folate, vitamin B12, and the MTHFR 677C→T polymorphism, and anxiety and depression in a case–control comparative study.

As regards vitamin B12, mean value was highest in the control group followed by the anxiety group; the least was in the depression group and the difference did not reach statistical significance between all groups. As regards folic acid, mean value was highest in the control group followed by the anxiety group; the least was in the depression group and the difference did not reach statistical significance, except between the depression and the control group.

Our finding was proved by the finding of Coppen and Bolander Gouaille [23] who reported that both low folate and low vitamin B12 have been found in studies of patients with depressive disorders. An association between depression and low levels of the two vitamins is found in studies of the general population. Low plasma or serum folate has also been found in patients with recurrent mood disorders treated by lithium. A link between depression and low folate has similarly been found in patients with alcoholism.

Our results were consistent with the results of Alpert and Fava [24], who reported that a low folate level was relatively common (18%) among patients with MDD. Recently, it was reported that low dietary folate and depressive symptoms are associated in middle-aged Finnish men [25].

Nevertheless, a low folate level was not detected in German or Chinese patients with major depression. Hong Kong and Taiwan populations with traditional Chinese diets (rich in folate), including patients with major depression, have high serum folate concentrations. However, these countries have very low life-time rates of major depression and the low folate levels are linked [23]. This contradiction in the previous results could be explained by the fact that culturally defined dietary habits influence the relationship between the folate status and depression in different societies [26]. In addition, sex, smoking, and creatinine could cause this contradiction [27].

We also detected that both anxiety and depression groups have the same percentage of gene mutation (33.3%), whereas the control group reported 20% mutation, and the differences were not significant.

Absence of significant differences between both groups of depression and anxiety may be explained by the high degree of comorbidity between both disorders. Physicians often attempt to separate depression from anxiety. Unfortunately, such distinctions are often challenging and artificial as anxiety symptoms are common in patients with major depression. Moreover, the National Comorbidity Survey indicates that comorbid depression and anxiety is the rule rather than the exception in up to 60% of patients with MDD [28].

In addition, in our study the control group reported 20% with gene mutation; this can be explained by the fact that approximately 10% of the population is homozygous for the 677 C→T polymorphism of the MTHFR gene. In a meta-analysis of studies investigating the association between depression and MTHFR genotype, overall TT carriers had a 22% increase in the odds of depression compared with CC carriers [29]. Another study conducted by Bjelland *et al.* [6] from 1996 to 1997 on a large population group found a strong relationship between the T/T MTHFR genotype and depression, and the association was present for both cutoff levels of depression. Associations were observed between the lowest level of vitamin B12 [< 230.0 pmol/l (< 312 pg/ml)] and depression with high cutoff (HADS-D score ≥11).

Our results show that within the depression group there is a negative correlation between the severity of depression and

folic acid and this was just statistically significant. Moreover, there is a negative correlation between depression severity and vitamin B12, which was statistically significant. There is also a negative correlation between Hamilton depression and both folic acid and vitamin B12, which was statistically significant. Our findings agree with Penninx *et al.* [30] who found that older, physically disabled women with metabolically significant vitamin B12 deficiency have been found to have a two-fold higher risk of depression than women with normal plasma levels of vitamin B12.

However, our study disagrees with the finding of Hintikka *et al.* [3] who detected no correlation between the severity of depression and the level of vitamin B12 at baseline. Furthermore, Bjelland *et al.* [6] failed to detect a relationship between depression and folate.

Only a weak relationship or no relationship was seen between anxiety disorder and folate or vitamin B12 level or MTHFR genotype. In contrast, an inverse relationship between the level of folate and severity of depression has been reported in some other studies [31].

Finally, one of the important factors to be considered is that, whether the deficiencies in B12 and folate are primary and have a role in depression and anxiety or are secondary because both depression and anxiety affect the diet intake through loss of appetite, it is possible that safe augmentation strategies for antidepressive treatments could be advised. It is proved by Hintikka *et al.* [3] who applied his study by the determination of hematological indices, erythrocyte folate, and serum vitamin B12 levels at baseline and again at the 6-month follow-up in 115 outpatients with *DSM third edition, revised* MDD. They found that higher vitamin B12 levels were significantly associated with a better outcome. Finally, increasing dietary intake of B12 and folic acid is a simple, safe, and inexpensive method to improve mood, to fight stress, and to increase mental energy [7]. It is hypothesized that folate augmentation can be used to boost antidepressant efficacy, although further studies are necessary [8].

Conclusion

There is a negative correlation between serum level of vitamin B12, folic acid, and severity of depression in depression and anxiety groups. The levels of folate and vitamin B12 were lower in the depression group than the anxiety group, but the differences were not statistically significant. We detected gene mutation in 33.3% of both anxiety and depression groups. It was found that patients with mutant gene have lower levels of both folic acid and vitamin B12 in both depression and anxiety groups. From the above, we concluded that correction in the level of vitamin B12 and folic acid may lead to improvement of the severity of depression.

Study limitation

(1) The research was financed by the researcher, which limited the size of the sample.
(2) We did not investigate different types of depressive disorders and anxiety disorders.
(3) The sample size was small.

There is no conflict of interest to declare.

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الملخص العربى

دراسة مقارنة لفيتامين ب وحمض الفوليك وتعدد الشكل لجين الميثيلين تيتراهيدرو فولات

في عينة من مرضى الاكتئاب والقلق

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الهدف

دراسة دور نقص فيتامين ب وحمض الفوليك **وتعدد الشكل لجين الميثيلين تيتراهيدرو فولات** فى عينة من مرضى الاكتئاب والقلق في مقارنة لمعرفة اذا كان لهم دور فى مسببات المرض ا لاستفادة من ذلك فى الخطة العلاجية.

طريقة وأدوات البحث

طبقت هذه الدراسة على30 من مرضى الاكتئاب و من 30 من مرضى القلق المترددين على العيادة النفسية بكلية طب القصر العينى وعلى المرضى المحجوزين فى القسم الداخلى. ومقارنتهم30 من عينة قياسية. وقد تم تطبيق مقياس بك للاكتئاب ومقياس هاملتون للاكتئاب والقلق. كما تم قياس مستوى فيتامين ب وحمض الفوليك فى الدم . ودرجة **تعدد الشكل لجين الميثيلين تيتراهيدرو فولات في** مرضى الاكتئاب والقلق كل على حدى.

وجد أن مستوى فيتامين ب وحمض الفوليك اكثر فى العينة الضابطة يليه مرضى القلق ثم أقل مستوى فى مرضى الاكتئاب ولا توجد دلالات احصائية ايجابية الا بين مرضى الاكتئاب والعينة الضابطة . كما وجد أن هناك علاقة عكسية ايجابية بين شدة الاكتئاب والقلق ومستوى فيتامين ب وحمض الفوليك فى كل من مرضى الاكتئاب و مرضى القلق . وهذه العلاقة تبدو اكثر فى مرضى الاكتئاب يليه القلق يليه العينة الضابطة.

وبالنسبة الي **تعدد الشكل لجين الميثيلين تيتراهيدرو فولات** وجد أن هناك تحور عند 33.5 % من مرضى الاكتئاب والقلق كلا على حدة مقارنة ب 20% من العينة الضابطة. و لايوجد اى فروق ايجابية بين القلق والاكتئاب و العينة الضابطة.

الخلاصة:

ان هناك نقص فى مستوي نقص فيتامين ب وحمض الفوليك و **وتعدد الشكل لجين الميثيلين تيتراهيدرو فولات** فى مرضى الاكتئاب يليه القلق يليه العينة الضابطة وان هذه العلاقة عكسية بمعنى نقص فيتامين ب وحمض الفوليك يصاحبه زيادة فى شدة الاكتئاب والقلق. وهذا يدفعنا الى ضرورة اضافة فيتامين ب وحمض الفوليك مع مضادات الاكتئاب والقلق .كما يتطرق بنا الى مزيد من الابحاث فى مجال الجينات لفتح مجال العلاج بالجينات.