

The Effect of Premorbid Functions on Symptoms Severity in First-Episode of Schizophrenia: An Egyptian Study

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By

Jihan Abdel Salam Abdel Maksod

M.Sc. of Neuropsychiatry

Supervision BY

Professor / Safeya Mahmuod Effat

Professor of Psychiatry

Faculty of Medicine

Ain Shams University

Ass. Professor / Heba Ibrahim Essaway

Assistant Professor of Psychiatry

Faculty of Medicine

Ain Shams University

Ass. Professor / Ghada Abdel Razeq Mohamed

Assistant Professor of Psychiatry

Faculty of Medicine

Ain Shams University

Faculty of Medicine

Ain Shams University

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LIST OF ABBREVIATION

APA	: American psychiatric association's
CAS	: Comprehensive assessment of symptoms and history
CT	: Computed tomography
CIDI	: Composite international diagnostic interview
DALY	: Disability adjusted life year
DIS	: Diagnostic interview schedule
DSH	: Deliberate self-harm
DSM	: Diagnostic and statistical manual of mental disorders
DUP	: Duration of untreated psychosis
EF	: Executive function
ECT	: Electroconvulsive therapy
EPQ	: Eysenck personality questioner
ICD	: International classification of diseases and causes of death
IM	: Impulsivity
LCU	: Life change unit
M	: Mean (arithmetic average)
MINI	: The mini international neuropsychiatric interview
MS	: Motor speed
MPAS	: Modified premorbid adjustment scale
PANSS	: Positive and negative syndrome scale
PAS	: The Premorbid adjustment scale
PTSD	: Posttraumatic stress disorder

RDC	: Research diagnostic criteria
SCID	: The structured clinical interview for DSM-III-R
SD	: Standard deviation
SDDS-PC	: The Symptom-driven diagnostic system for primary care
VL	: Verbal learning
WAIS	: Wechsler adult intelligence scale
WHO	: The World health organization
WM	: Working memory
YLL	: Years of life lost because of premature death
YLD	: Years of life lived with disability

Introduction

Mental health is an important component of overall health. Mental disorders cause suffering, disability, and, more rarely, death (*Pratt et al., 2007*).

Recent data on the burden of mental disorders worldwide demonstrates a major public health problem that affects patients, society, and nations as a whole (*Ustun, 1999*). As for example in 2002, there were an estimated 17.5 million adults aged 18 years or older with serious mental illness. This represents 8.3 percent of all adults. According to the National Survey on Drug Use and Health; the rates of serious mental illness were highest for individuals aged 18 to 25 years (13.2 percent) and lowest for those aged 50 years or older (4.9 percent). The percentage of females vs. males was 10.5 percent vs. 6.0 percent, and, in general, rates were higher for women than men in all age groups (**Figure i**) (*NSDUH Survey, 2002*).

Schizophrenia as a mental disorder is the most common chronic psychosis in Egypt that accounts for the majority of inpatients in our mental hospitals (*Okasha, 2004*).

At the same time evidence from nearly a century of epidemiological research indicates that schizophrenia occurs in all populations with prevalence in the range of 1.4 to 4.6 per 1000 and incidence rates in the range of 0.16-0.42 per 1000 population (*Jablensky, 2000*).

In addition geographically, schizophrenia appears to be evenly distributed throughout the world. A country's stage of economic development, degree of urbanization, or climate seems to have little influence on schizophrenia prevalence. However, the course of the illness has been more favorable in developing countries than in developed countries. This may reflect the tendency for developing countries to have sociocentric cultures and for developed countries to have egocentric cultures. Sociocentric cultures may be more supportive of marginal function than egocentric cultures, in which demands for autonomous function may be particularly challenging for persons with schizophrenia (*Carpenter and Thaker, 2002*).

On the other hand, the incidence of first episode psychosis is estimated to be 15-20 cases per 100,000. The overwhelming majority of first episodes of psychosis will occur among young people between the ages of 15 and 34.4 thus intervening in a comprehensive way as quickly as

possible following the onset of psychosis is of significant importance (*Edwards and McGorry, 2002; Milliken, 2003*).

At the same time, the incidence of relapse in patients who have experienced one or more psychotic episodes is high and ranges between 50 and 80 percent in the year following an episode of psychosis without treatment (*Fitzgerald, 2001*).

As, schizophrenia is a severe mental disorder, it is characterized by fundamental disturbances in thinking, perception and emotions. More than 100 years of research have not been able to fully resolve the puzzle that schizophrenia represents. Even if schizophrenia is not a very frequent disease, it is among the most burdensome and costly illnesses worldwide (*Rassler et al., 2005*).

As known Persons with schizophrenia have shorter life expectancies than the general population. Premature deaths in schizophrenia are due to infections and disorders of the cardiac, endocrine, and respiratory systems. Studies from different countries have shown an increased mortality due to “natural causes”. It can be concluded that on an average, schizophrenia reduces the life span by about 10 years (*Harris and Barraclough, 1998; Thara, 2005a, b*).

Meanwhile, according to the global burden of disease study, schizophrenia causes a high degree of disability, which accounts for 1.1 percent of the total disability-adjusted life years (DALYs) and 2.8 percent of years lived with disability (YLDs). Schizophrenia is listed as the eighth leading cause of DALYs worldwide in the age group 15-44 years (*Rassler et al., 2005*).

On the other hand, like leprosy, schizophrenia has been heavily stigmatized. While the stigma attached to leprosy has been reduced in many developing countries, largely due to effective treatment and early detection as a result of massive awareness and educational programs, schizophrenia remains a stigmatizing affliction. There are several reasons for this. A host of stereotypes such as aggression, contagion, unpredictability, and inevitable heritability exist. This is compounded by the reality that a small percentage of persons with schizophrenia do not improve and remain considerably disabled all through their lives, despite treatment. The consequences of stigma were severe and included differential treatment by society; a paucity of marriage proposals, discrimination at work and by family; and feelings of shame, sexual harassment, and social exploitation (*Thara, 2005 a, b*).

In addition, an estimated 50 to 80 percent of persons with schizophrenia and related psychotic disorders live with or have regular contact with a family caregiver. These caregivers report high levels of burden related to caring for their family members (*McDonnell et al., 2003*).

However, despite many years of research, the clinical and economic effects of schizophrenia are staggering. The resulting economic burden of schizophrenia is substantial. These include direct, indirect costs and additional costs. Additional costs include unemployment, homelessness (11 percent of homeless individuals suffer from schizophrenia) and substance abuse (schizophrenia have a 10.1 percent higher risk of substance abuse than the average population) (*Perkins, 2005*). So, the excess of low socio-economic status among people with schizophrenia was reported (*Murali and Oyeboode, 2004*).

On the other hand, the treatment goals for the moment are to identify the illness as early as possible, treat the symptoms, provide skills to patients and their families, maintain the improvement over a period of time, prevent relapses and reintegrate the ill persons into the community (*Rassler et al., 2005*).

In addition, several concurrent strategies aimed at reducing disability were recommended, including early

intervention programs, assertive evidence-based rehabilitation and supported employment programs. The cost-effectiveness of these approaches needs to be evaluated from the perspectives of both government and society (*Carr et al., 2004*).

Recently, in the last few years there has been a great deal of interest in early detection and intervention in schizophrenia and related disorders generating enthusiasm (in some countries) and hope in both clinicians and the public (*Malla and Norman, 2002*).

Meanwhile, early detection studies fall into two groups. **Firstly**, operational criteria now exist for prodromal or at risk mental states which predict transition to psychosis of 20-40 percent over 1 year. **Secondly**, duration of untreated psychosis (DUP) in the first episode seems genuinely to be associated with clinical outcome but how much of the association is truly causal remains disputed (*Drake and Lewis, 2005*).

In addition, during the past decade, many studies on first-episode schizophrenia have revealed that the duration of untreated psychosis (DUP) is between one and two years on average. Moreover, findings from these studies suggested that a long duration of untreated psychosis might lead to neurotoxic processes, manifested as

persistent morbidity, treatment resistance, and clinical deterioration. These findings have resulted in a growing interest in the early detection and treatment of psychotic disorders (*Bottlender and Moller, 2003*).

Lastly, by studying events preceding the first episode of schizophrenia and the multiple domains of psychosocial and educational functioning, it may be possible to detect protective or vulnerability factors and perhaps to advise interventions aiming at secondary prevention such as supplementary educational and vocational programs, and other supportive measures (*Rabinowitz et al., 2002*). Such preventive measures may be needed to achieve an ideal outcome for schizophrenic patients and those predisposed to the disorder (*Faraone et al., 2002*).

The Rationale for the Study

The need for these study stems from two important observations.

First, males and females between the age 18-60 years constitute 28,606,000 i.e. 47% of total population in Egypt as shown in the statistical year book for census (central Agency for public Mobilization and statistics, 1996). Since the life-time prevalence of schizophrenia is 0.55%- 1% in a recent review of studies from around world (*Golden et al., 2002*), it is expected that at least (143,040 - 286,080) individuals will experience this disorder; that leads to enormous direct and indirect costs. Studies that shed light on vulnerability factors and predictors of severe episodes of schizophrenia, and help to develop better prevention strategies are needed especially in developing countries with limited resources such as Egypt.

Second, this study has not been performed in any Egyptian work and it might help in comparing between Egyptian patients and western patients.

Subjects and Methods

I- Study design:

This study was observational, descriptive, analytical and longitudinal. Part of the study was retrospective and part was prospective.

II- Site of the study:

The cases were selected as a random sample from inpatients, and those attending outpatient clinic and emergency room of Psychiatric Institute - Ain Shams University Hospital. The Psychiatric Institute is characterized by:-

- It is located in East Cairo.
- It serves as a catchments area of about 1/3 rd of Cairo population.
- It serves both urban and rural areas.
- It is subdivided into private and free sections so the patients would represent all social strata.

That's why it was selected as site of the study

III- Subjects:

Fifty patients participated in this study. All patients were selected during a two year interval starting from June 2005 to June 2007.

A. The patients group:

A constrictive selective sample of 50 patients attended outpatient clinic, emergency room and inpatients who were admitted to the hospital before receiving treatment for first episode schizophrenia in the psychiatric institute, Ain Shams University.

1- Selection of sample:

i. Inclusion criteria:

The study included Egyptian patients with the following criteria:

- Fulfilling the diagnosis of first episode schizophrenia according to International Classification of Diseases (ICD-10).
- Age range: 18 – 40 years old.
- Sexes: both male and female.
- Time of first assessment: before the patients starting Electroconvulsive therapy (ECT) or they have just received first two session's maximum.

ii. Exclusion criteria:

- Organic, including symptomatic, mental disorders.
- Mental and behavioral disorders due to psychoactive substance use.
- Mental retardation with IQ less than 70.
- Comorbidity either with other psychiatric disorders or chronic physical diseases.

2. Choice of cases:

The cases were selected from new cases, who attending outpatient clinic, emergency room or were recently admitted to the psychiatric institute from outpatient clinic and emergency room.

They were selected according to the inclusion criteria and the exclusion criteria.

All cases had the selection criteria were included in the study.

B. The control group:

Thirty normal control group subjects volunteered to undergo the procedures. They were selected to match the patients group for age, sex and years of education. They were selected among employees and mates working in psychiatric institute, Ain Shams University Hospital. All subjects had a negative past, present and family records of significant medical, neurological, psychiatric or drug use disorders.

I- Procedure

A. Operational definitions:

1. Schizophrenic disorders

The schizophrenic disorders are characterized in general by fundamental and characteristic distortions of thinking and perception, and by inappropriate or blunted affect (ICD-10).

2. First episode schizophrenia

Diagnosis of schizophrenia is clearly present for most of the time during a period of one month or more and for less than 12 month (*Addington and van Mastrigt, 2002*).

3. Premorbid adjustment (function)

It represents function of the patients during the period of time ending 12 months before evidence of characteristic florid psychotic symptomatology (*Addington and van Mastrigt, 2002*).

4. Short-Term degree of improvement

Operationally, it represents improvement of symptoms during period of 6 weeks after starting management according to PANSS score.

B. Pilot study

Time

- A pilot study was done from June to September 2005.

Objectives:

1. To determine the size of the sample to be studied.
2. To assess the reliability, validity and applicability of the chosen tools.

Results of the pilot study:

i. It determined the size of the sample to be included in the study.

According to the pilot study that was carried out in 2005 in the institute of psychiatry, Ain Shams University, Cairo:-

- 682 new out patients and 338 emergency room patients came to services within 4 month period (some of them were sever cases, so they were admitted to the department).
- 5% (n=51) of patients presented for the first time for psychiatric consultation.
- Out of 10 patients contacted for the study (diagnosed as first episode schizophrenia and had inclusion inclusion

criteria for study) 7 patients responded positively and agreed to participate in the study.

- Accordingly, our study sample included about 50 patients within the period of two years.

ii. Regarding the study tools, reliability and validity of the study

- Tools were performed, and kappa coefficient yielded: 0.8.
- Remodulation of life change unites value of the Social Readjustment Rating Scale according to *Okasha et al., (1981)* to suit the Egyptian patients.

C. Study proper

All patients chosen to be included in the study were subjected to the following:

1. First interview:

- This interview was done for clinical assessment.
- Interviewers were the researcher and one of the supervisors.
- Interviewers introduce themselves to the patient and his / her relatives.
- Verbal consent was taken from the patient or one of his / her relatives that he / she accepts to be included in the research after detailed explanation of the study aim and procedures, that the patient followed.

- Clinical interview to fulfill the items of the sheet designed by the researcher that include all relevant demographic data
- Diagnosis was carried out according to ICD-10 criteria using *The Mini International Neuropsychiatric Interview (M.I.N.I.)* which is a structured interview schedule was tested as regard reliability and validity on Egyptian patients (*Ghanem et al., 2002*).
- Severity and pattern of symptoms were assessed by using *Positive and Negative Syndrome Scale (PANSS)* (*Kay and Singh, 1989*). It was done independently by the researcher and one of the supervisors. Then it was rated jointly to achieve a consensus between the two clinicians.
- Premorbid function was assessed using *Modified premorbid adjustment scale (MPAS)*. It was tested as regard reliability and validity on Egyptian schizophrenic patients (*Ryaad, 1990*). It was applied independently by the researcher and one of the supervisors. Then it was rated jointly to achieve a consensus between the two clinicians. Information was gained from patient and his / her relatives.
- Psychosocial stressor that was experienced by patient within the last 12 months was assessed using *Social Readjustment Rating Scale (Okasha et al., 1981)*.

2. The second meeting

- It was done for psychometric assessment.
- It was done by psychologist.
- Evaluation of IQ (verbal, performance and total) using *Wechsler Intelligence Scale (Wechsler, 1987)*.
- Assessment of executive functions of the patients using *Wisconsin Card Sorting Test (Heaton et al., 1993)*.
- Detection of personality dimensions in the domains of extroversion, neuroticism, psychoticism and criminality by *Eysenck Personality Questionnaire (EPQ) (Eysenck and Eysenck, 1985)*.

3. The third interview

- It was done six weeks after initial assessment by the researcher.
- It was done for reevaluation of symptom severity using *Positive and Negative Syndrome Scale (PANSS)*.

D. Tools

1. Mini International Neuropsychiatric Interview (M.I.N.I) (*Lecrubier et al., 1997; Sheehan et al., 1998*).

The Mini International Neuropsychiatric Interview (M.I.N.I.) is a short structured diagnostic interview developed by psychiatrists and clinicians in the United States and Europe (*Lecrubier et al., 1997; Sheehan et al., 1998*). It can be easily incorporated into routine clinical interviews and it has good acceptance by patients (*Pinninti et al., 2003*).

Sheehan and Lecrubier, when designed the MINI, their central goals for it were:-

- Short and inexpensive tool.
- Simple, Clear, and easy to administer.
- Highly sensitive i.e., a high proportion of patients with a disorder should be detected by the instrument.
- Specific, i.e., have the ability to screen out-patients without disorders.
- Compatible with international diagnostic criteria, including the International Classification of Diseases (ICD-10) as well as the Diagnostic and statistical Manual of Mental Disorders. Third Edition, Revised (DSM-III-R) and later the Diagnostic and statistical Manual of Mental Disorders. Fourth Edition (DSM-IV).

- Able to capture important sub-syndromal variants (*Sheehan et al., 1998*).

The liability and validity of this interview procedure have been investigated in some clinical groups (*Jones et al., 2005*). It has been validated against the much longer Structured Clinical Interview for DSM diagnoses (SCID-P) in English and French and against the Composite International Diagnostic Interview for ICD-10 (CIDI) in English, French and Arabic. It has also been validated against expert opinion in a large sample in four European countries (France, United Kingdom, Italy and Spain) (*Lecrubier et al., 1997; Sheehan et al., 1998*).

Study was set out to validate and test the inter-rater and test-retest reliability of MINI as a diagnostic tool for psychotic disorders in Arabic language on 108 Egyptian patients and 60 controls. All patients had a primary diagnosis of a psychotic disorder (43 schizophrenia, 41 schizoaffective disorder and 34 mood disorders with psychotic features) as diagnosed by ICD-10 and DSM-IV diagnostic criteria. It was concluded that MINI-Arabic can serve as a valid and reliable structured diagnostic interview for psychotic disorders. It can provide satisfactory diagnoses in Arabic language and culture as MINI and MINI-plus had a very good Kappa values for

most diagnoses ($=0.75$) when compared with CIDI (*Ghanem et al., 2002*).

Research has shown that the MINI can be used successfully as a gold standard of psychiatric diagnosis in multi-centre clinical trials and epidemiology studies (*Gabarron et al., 2002; Wojnar et al., 2003*).

MINI consists of standardized, structured, closed-end questions throughout its diagnostic procedure. The DSM-IV and ICD-10 criteria were reframed into standardized questions in MINI. The interviewers read literally these close-ended questions as verbatim as possible to the interviewers. Psychiatric diagnosis was made according to the number of affirmative replies to the specific questions (*Lecrubier et al., 1997; Sheehan et al., 1998*).

As a general rule, in structured diagnostic interviews, there are two screening questions. In the negative, no further questions are asked in that disorder module, and the patient is identified as not having the disorder. If the patient responds positively, to one or both of the screening questions, more detailed symptom questions are asked. If these symptoms are endorsed further branching tree logic leads to questions about any associated disability, and additional questions are used to rule out illness and acute

bereavement as possible causes of the disorder. If these questions suggest the presence of a typical case, then further branching leads to question on the chronology and time frame (*Sheehan et al., 1998*).

Administration time of MINI ranges from approximately 15–20 minutes for individuals with few positively endorsed symptoms to 20–30 minutes for individuals who meet criteria for current diagnoses (*Jones et al., 2005*). The M.I.N.I. screen (for the primary care setting) should not exceed 5 minutes if they are to be widely adopted. In designing these instruments they tried to adhere to these guidelines, and the results of the validation studies suggest that they succeeded in doing so (*Sheehan et al., 1998*).

2. Positive and Negative Syndrome Scale (PANSS) (*Kay and Singh, 1989*).

Despite the importance of the positive-negative distinction in schizophrenia, efforts at measurement have been hampered by inadequately standardized methods. For example, the available techniques have been criticized for their lack of construct validity, longitudinal reliability, and detailed operational criteria for psychiatric interview and ratings of symptom severity. The Positive and Negative syndrome scale (PANSS) was developed to meet

these objections and provide a well researched psychometric instrument for evaluating these syndromes in schizophrenia (*Peralta and Cuesta , 1994*).

Depression exists as an independent domain, differentiated from negative symptoms, in the structure of schizophrenia symptomatology (*Lee et al., 2003*) and PANSS evaluation itself may be sufficient to give a correct approximation of the depression in patients with schizophrenia (*El Yazaji et al., 2002*). Also cognitive component of the PANSS is a valid measure of cognitive deficits in schizophrenia, and they support the hypothesis that cognitive impairment is a distinctive feature of schizophrenia independent of positive and negative syndromes (*Bell et al., 1994*).

The objective in developing the PANSS was to provide a well-defined, standardized technique for positive-negative evaluation. At the same time, we recognized the importance of a procedure which can be applied in relatively brief time, with minimal training and reorientation for the clinician and which can be used repeatedly for longitudinal assessment. We have reported on studies with the PANSS that support its reliability, stability in unremitting chronic schizophrenics, and

various aspects of its validity (*Kay et al., 1987; 1988; Kay and Opler, 1987; Opler et al., 1987*).

The PANSS initially was formulated as a special adaptation of two psychiatric rating instruments, the Brief Psychiatric Rating Scale (*Overall and Gorham, 1962*) and the Psychopathology Rating Schedule (*Singh and Kay, 1975*). The PANSS selected items that best represented the positive and negative features of schizophrenia. As it evolved, however, the authors recognized the need for greater psychometric sophistication to successfully standardize the technique, including more rigorous guidelines for eliciting and evaluating psychiatric symptoms. Accordingly, the interview procedure and all rating items have been modified and expanded to provide precise instructions for conduct of the PANSS interview, clear-cut definition for each parameter to be rated distinct criteria for all seven levels of psychopathology, and what we judge as equivalent distance between rating points on each item (*Kay et al., 1987; 1988*).

Comprehensive tool - PANSS includes 30 items, necessitating a long interview with the patient (30-40 minutes). Seven are grouped to form a Positive Scale, measuring symptoms that are superadded to a normal mental status. And another seven items constitute a

Negative Scale, assessing features absent from a normal mental status. Based on the differential between these scales, a bipolar Composite Scale specifies the degree of preponderance of one syndrome over the other. Finally, a fourth index, the General Psychopathology Scale, gauges the overall severity of schizophrenic disorder by summation of the remaining 16 items (*Kay et al., 1987*).

3. Modified Premorbid Adjustment Scale (MPAS) (Addington and Van Mastrigt, 2002) (*Appendix*)

During Andreasen and colleagues at the University of Iowa worked on first episode schizophrenia they have developed a modified version of a premorbid scale, the Modified Premorbid Adjustment Scale (MPAS), it is 24-item scale. It is designed to measure only premorbid functioning, where “premorbid” is defined as the period ending 12 months before evidence of characteristic florid psychotic symptomatology. They report good inter-rater reliability and test-retest reliability (*Andreasen et al., 1992; Addington and Van Mastrigt, 2002*).

The scale examines 4 areas of development; sociability and withdrawal; peer relationships; ability to function outside of the nuclear family and capacity to form intimate socio-sexual ties at each of 4 developmental stages (i.e., childhood [up to age 11], early adolescence [12–15 years],

late adolescence [16–18 years] and adulthood [19 years of age and older]) (*Andreasen et al., 1992*).

Validation and reliability of PAS was set as a tool for premorbid adjustment in Arabic language on Egyptian patients (*Reyad, 1990*). A modified Arabic version of a premorbid scale was used in this study (*Appendix*).

Only those life periods that are premorbid by this definition should be rated on this scale, regardless of the present age of the subject (e.g., a 39-year-old who had his first psychotic episode at age 17 would not be rated on the adult section, but would be rated on all other sections (*Addington and Van Mastrigt, 2002*).

In order to determine if a particular section should be scored, the onset date recorded in the chart should be consulted. If the individual showed signs of psychotic symptoms less than 12 months prior to this date, the section corresponding to this time frame should not be scored because it does not fall under the “premorbid period” (*Addington and Van Mastrigt, 2002*).

All MPAS is rated retrospectively and ratings are based on interviews with the patients, their family members or both and each item is scored on a Liker type

scale of 0–6, where lower numbers indicate normal, healthy functioning and higher numbers suggest pathologic development. Phrased anchor points are given for each item to aid in scoring. Insinuations where, for any reason, there is insufficient information to complete an item, it is not scored and the item is excluded in the calculation of the overall score. Scores for each of the subscales are calculated by dividing the obtained score by the total possible score for that section. The overall MPAS score is calculated by averaging the scores obtained on each of the developmental subscales. Ratings for both the subscales and the overall PAS score are expressed as decimal point numbers ranging from 0.0 to 1.0, where lower numbers represent the “healthiest” level of functioning (*Cannon-Spoor et al., 1982*).

The MPAS has been used in several studies, yet there is no consensus as to how to present the data. Studies report overall mean scores (*Levitt et al., 1996*), and others like *Haas and Sweeney in 1992* defined three patterns of PAS in the following manner: deteriorating PAS was defined as ‘a pattern of worsening scores from childhood over the remaining premorbid periods and the equivalent of a two-point change over four premorbid stages’. The remaining cases were divided into ‘stable good’ and ‘stable poor’, split by the median score (*Larsen et al., 2004*).

In our study we calculated overall mean scores of MPAS. We calculated change scores as the difference between the mean score of one period and the mean score for the previous period (early adolescence minus childhood; late adolescence minus early adolescence; adulthood minus late adolescence; essence. We thus identified a subgroup with deteriorating course. Like *Haas et al. (1998)*, we used the median scores divide the remaining patients into 'stable good' and 'stable poor' subgroups.

The identification of deteriorated group would be important, because a substantial neuroregressive element in schizophrenia imply a deteriorating course, whereas a predominantly neurodevelopment element dominantly would probably be expressed as a stable course, even if poor (*Larsen et al., 2004*).

4. Social Readjustment Rating Scale (Holmes and Rahe, 1967) (Appendix)

An effort to systemically catalogue many different kinds of life occurrences and to assign stress or threat ratings have been done by several investigators. One of them is stress-rating scale. In 1967 *Holmes and Rahe*, have developed a so-called SRS Questionnaire (Schedule of Recent Experience) to quantify the degree of adaptation required by diverse life events. A certain number of scores of LCU value (life change unit) has been in this way

secured for each event, with the highest value=100 for “death of the spouse” and divorce (score 73). The total life events were 43 ranked in order according to the degree of adaptation required by these events (*Holmes and Rahe, 1967*).

If a person experienced total stress within the last twelve months of 300 or greater, even with normal stress tolerance, he may be overstressed Person. Levels, as low as, 150 denote no stressors.

In 1981, cross culture comparison between the Egyptian sample and American subjects as regard the degree of adaptation required by diverse life events was done.

It was found that there is difference between scores of LCU value (life change unite) in Egyptian sample. Accordingly we reviewed scores obtained by the patients according to Egyptian scores (*Okasha et al., 1981*).

5. Psychometric assessment

i. Wechsler Adult Intelligence Scale (WAIS) (*Wechsler, 1987*).

The WAIS is an extensively standardized instrument for the measurement of intelligence. It is applied on individual age range from 15 to 60 years.

The WAIS was translated to Arabic language by prof, Lwess Kamel Meleka, Prof. of psychology in 1996.

The WAIS defined the intelligence as the total ability of the individual to work for certain task or to think and effectively deal with the environment.

The WAIS consists of eleven subtests. Six of them are *Verbal subtests, which include:-*

- General information.
- Comprehension.
- Arithmetic.
- Similarity.
- Digit span.
- Vocabulary.

The other five subtests are performance subtest

- Digit symbol.
- Picture completion.
- Block design.
- Picture arrangement.
- Object assembly.

The raw score on each subtest is transmuted into a standard score (scaled score), which represents the individual's distance from the mean in terms of the distribution for that particular subtest. By this procedure

all subtest scores are expressed in units which can be compared one with another (*Crawford et al., 1992*).

ii. Wisconsin Card Sorting Test (*Heaton et al., 1993*).

It is a measure of executive functioning e.g., cognitive flexibility, maintenance of a cognitive set, working memory.

The WCST was administered to all subjects enrolled in the study with standard instruction described by *Heaton* in *1981*, using a computerized version implemented with micro experimental laboratory (*Schneider, 1990*). The test consists of 128 cards, each of which contains geometric figures that may vary along three dimensions (color, form, number).

Subjects are instructed to place each card below one of four target or key cards and to use some principle to guide them. They are not informed of correct principle, but are told whether they are correct or incorrect after their placement of each card. The initial sorting principle is to match according to color. Once a criterion of 10 correctly sorted cards is attained, the principle is changed, although the subject is not informed of their change. The test proceeds until the subject has completed six sorting categories, each consisting of 10 consecutive cards

matching the sorting principle, until patient has sorted all 128 cards (*Rossi et al., 2002*).

The computer automatically score performances, following Heaton's rules, with the exception that the first unambiguous error repeating the previously correct principle was not scored as preservation because the subject had not received feedback indicating that the previously correct principle was incorrect. This scoring rule resulted in negligible changes in the perseverative error score. The performance on the WCST was based on the number of categories achieved, number and percentage of perseverative errors, failure to maintain set and number and percentage of unique errors (*Rossi et al., 2002*).

iii- Eysenck Personality Questionnaire (E.P.Q): (*Eysenck and Eysenck, 1985*).

This is simple self-report test. It has 101 questions (of which 11 questions were omitted) on the right side of the page the patient has to answer Yes or No to these questions, which are phrased in formal Arabic and can be understood by all those people who can read simple Arabic. The E.P.Q. was translated to Arabic language by Prof. Ahmed Mohamed Abdel Khalic, Prof. of Psychology, Faculty of Arts, Alexandria University in 1991. For illiterate people the test was read in colloquial formal Arabic.

The E.P.Q. was designed to measure two major dimensions of personality, psychoticism (P) which is related to odd cruel, antisocial behavior, suspicion and a lack of feeling towards even those close to one, for females $P = 2 \pm 2$, neuroticism (N) is defined as emotional lability, over-responsiveness and liability to neurotic breakdown under stress, $N = 12 \pm 4$, and extraversion – introversion (E) which implies the presence of an outgoing personality with uninhibited social tendencies, $E = 12 \pm 5$, it includes also lie scale (L) which is regarded by Eysenck as a measure of "faking good".

Normal values

	Male	Female
Psychoticism (P)	3.95 ± 3.28	2.27 ± 2.54
Neuroticism (N)	9 ± 5	12 ± 5
Criminality (c)	9 ± 4	9 ± 4
Extraversion – introversion (E)	13 ± 4	12 ± 4
Lie scale (L)	7 ± 4	8 ± 4

6- Other tools:

Designed sheet

We have devised sheet in the form of yes / no or multiple choice to assess the following domains:

- Personal data.
- Marital status.
- Family history of neuropsychiatric disorders.

E. Statistical methods

Statistical results were done by the Statistical Package for Social Sciences (SPSS), version 13.2, Echo soft Corp., USA, 2003.

The following statistical procedures have been employed:

1. Descriptive statistics

Data were expressed as Mean $\pm$ SD for quantitative measures and both number and percentage for categorized data.

i. Mean (arithmetic average) (M)

The sum of the scores, or values divided by their number. M is a “point of balance” between the highest and lowest scores or values in a distribution.

$$\bar{X} = \frac{\sum X}{N}$$

Where $\sum$ = the sum, X = individual values, N = number of cases.

ii. Standard deviation ($\pm$ SD)

It is the square root of the variance. It gives an estimate of the average deviation around the mean.

$$SD = \sqrt{\frac{\sum X^2 - \frac{(\sum X)^2}{n}}{n}}$$

Where $\sum X^2$: the sum of squares of individual values

$(\sum X)^2$: the square of the sum of the individual variance

2. Analytical statistics

i. Student's-t-test:

Differences between the mean of groups were assessed by Student's t-test adopted for either equal or unequal variances.

$$t = \frac{M_1 - M_2}{\sqrt{\frac{(SD_1)^2 + (SD_2)^2}{N_1 + N_2}}}$$

M_1 = mean of first group.

M_2 = mean of second group.

SD_1 = SD of first group.

SD_2 = SD of second group.

N_1 = number of cases of first group.

N_2 = number of cases of second group.

ii. Ranked Sperman Correlation test

Ranked Sperman Correlation test to study the association between each 2 variables among each studied group.

The probability (p) value was then obtained from all these tests with (n_1+n_2-2) degrees of freedom. P-values less than 0.05 were considered significant, while at 0.01 or 0.001 were highly significant.

iii. Wilcoxon Rank Sum Test.

Comparison between 2 groups for non-parametric data, using Wilcoxon Rank Sum Test.

iv. Analysis of variance (ANOVA):

Allows, using sample data, to test whether the values of two or more unknown population means are likely to be equal.

F ratio is computed by the following equation.

$$F = \frac{\sigma^2 \text{ between}}{\sigma^2 \text{ within}}$$

The One-way analysis of variance (ANOVA) is employed when three or more values are involved.

v. Multi-Regression analysis

Multi-Regression estimates the coefficients of the linear equation, involving one or more independent variables that best predict the value of the dependent variable.

Statistics for each variable: number of valid cases, mean and standard deviation. For each model: regression coefficients, correlation matrix, part and partial correlations, multiple R, R squared, change in R squared, standard error of the estimate, analysis of variance table, predicted values and residuals. Also 95% confidence intervals for each regression coefficient, variance-

covariance matrix, variance inflation factor, tolerance, Durbin-Watson test, distance measures (Mahalanobis, Cook and Leverage values), Df Beta, Df Fit, prediction intervals and casewise diagnostics.

N.B.: - P. value (probability) means level of significance

- $P > 0.05$ not significant
- $P < 0.05$ significant

vi. Calculated Delta Change

Degree of changes in values was calculated by, the difference between values before and after the change divided by the value before that change.

$$\text{Calculated Delta Change} = (\text{After} - \text{Before}) / \text{before}$$

Hypothesis and Aim of the Work

The present study is designed to test the hypothesis that poor premorbid function that include; sociality, peer relationship, socio-sexual relation, work and education; leads to sever symptom of first episode of schizophrenia.

The aims of the study are:-

1. Assessment of premorbid functioning during the first episode of schizophrenia.
2. Assessment of relation between premorbid function and symptom severity at first episode of schizophrenia.
3. Assessment of the effect of stressor on symptom severity at first episode of schizophrenia.
4. To asses the relation between short term degree of improvement (6th weeks of starting either pharmacotherapy, ECT or both) and premorbid function.

RESULTS

Interest in studying the relation between premorbid adjustment and symptoms severity in first episode schizophrenia patients reflects the persistence interest in clinical aspects of the disorders.

The present study investigates symptoms severity and the premorbid adjustment among 50 patients. MINI which is a reliable valid standardized diagnostic instrument was used to identify schizophrenia disorder at the time of the interview. MPAS which is a reliable valid scale was used to investigate premorbid adjustment in retrospective manner.

Results in this chapter were grouped to answer the following questions:

- What are pattern of premorbid functioning in the first episode of schizophrenic patients?
- What are the effects of premorbid function on symptoms severity at first episode of schizophrenia?
- Does the premorbid function have an effect on short term degree of improvement?
- Does the group of medication have an effect on short term degree of improvement?
- What are the effects of stressor on symptoms severity at first episode of schizophrenia?

SECTION (I)

- What are pattern of premorbid functioning in the first episode of schizophrenic patients?

Description of Demographic Data

A total of 50 patients were selected attending outpatient clinic, emergency room and inpatients admitted to the hospital who are receiving treatment for first episode schizophrenia in psychiatric institute, Ain Shams University.

A. Demographic variables:

Table (1) shows that sample consists of 41 male and 9 female in a percentage of 82% and 18% respectively; patient age mean $\pm$ standard deviation = 24.86 ± 5.5 years, range =18-38 years with 80% (n=40) of sample are unmarried and 18% (n=9) are married .

As regard the level of education 44% (n=22) of the sample graduated from university, 30% (n=15), postgraduate 2% (n=1), from secondary or technical school, 14% (n=7) from preparatory school, 8% (n=4) from primary school and 2% (n=1) read and write.

It is found that 82% (n=41) of sample have family support from there parents, 16% (n=8) from there partner (wife), while 2% (n=1) from other relatives

B. Family history

As regard family history of suicide and psychiatric disorder among patients group, the majority of sample have no family history that represent 68% (n= 34) as shown in table (2), while 26% (n=13) have family history of psychiatric disorder and 6% (n=3) have family history of mood disorders.

Aggressive Behavior and Suicidal Behavior at Presentation and During Inpatients Treatment

A. At presentations

Figure (1): Presenting symptoms in first episode schizophrenic patients

B. During inpatient treatment

Table (3) demonstrates that 84% (n=42) of the sample were inpatient and 14% (n=7) are outpatients. There were certain types of behavior that occurred during inpatient treatment. It was found that 36%, (n=18) of sample experienced aggressive behavior in the form of 12%, (n=6) non-physical injury, 18%, (n=9) damage to property and 6%, (n=3) only threaten behavior.

In addition to suicidal behavior that represents 8%, (n=4) of sample, 22%, (n=11) trial of escape during inpatients management and 32% (n=16) of sample exposed to restrain/isolation out of aggressive behavior.

Symptoms of the First Episode Schizophrenia

A. Personality diminutions and IQ

Table (4) shows that the main traits of schizophrenic patients were characterized by high percentage of psychoticism, neuroticism and criminality and low scores on extroversion. Also it shows most of the patients were of average intelligence.

B. Executive function in first episode schizophrenia

Table (5)

This table shows that (mean) for some items of WCST had low score especially percent of conceptual level responses and categories completed that reflect impairment in concept formation in the patients. In addition to higher levels in percent of errors and percent of preservative errors that reflect difficulty in cognitive flexibility of the patients. And high score in failure to maintain set that reflect impaired attention.

Table (6)

This table show highly significant difference between patients and healthy control in trials administered, total errors, percent of errors, percent of conceptual level responses and learning to learn. In addition to significant difference in failure to maintain set. That reflects impaired executive function in first episode schizophrenic patients.

Figure (2): Comparison between first episode schizophrenic patients and controls as regards mean scores of WCST

C. Symptoms severity of first episode schizophrenia

Table (7)

This table shows that general psychopathology symptom score is the highest score at first week. Also shows that activation symptom and aggression have the best short degree of improvement.

Premorbid Adjustment in First Episode Schizophrenic Patients

A- Difference between males and females

Table (8)

No significant difference was found between males and females in premorbid adjustment.

Figure (3): Modified Premorbid adjustment scale (MPAS) among males and females

B. Pattern of premorbid adjustment among first episode schizophrenic patients

In **figure (4)** 38% (n=19) of patients had deteriorating premorbid functioning. Deteriorating premorbid functioning, in terms of the premorbid adjustment scale, was defined as "a pattern of worsening scores from childhood over the remaining premorbid periods and the equivalent of a 2-point change over four premorbid stages (childhood, early adolescence, late adolescence, and adulthood) or a proportional decline for cases in which illness onset was before late adolescence or adulthood."

The remaining patients were regarded as stable premorbid functioning. The median value (0.3896) of the premorbid adjustment scale total score was used as a cutoff point to assign these patients to stable-good 30% (n=15), or stable-poor groups 32% (n=16).

SECTION II

- What are the effects of premorbid function on symptoms severity at first episode of schizophrenia?
- Does the premorbid function have an effect on short term degree of improvement?
- Does the group of medication have an effect on short term degree of improvement?

Correlation between Premorbid Adjustment and symptoms in First Episode Schizophrenic Patients

A. Correlation between symptoms severity of first episode schizophrenic patients and overall score of MPAS

Table (9)

This table shows that negative symptoms, general psychopathology and total positive and negative scale score have highly significant positive correlation with overall score of premorbid adjustment scale. Thought disturbance symptoms and anergia symptoms show significant positive correlation with overall score.

B. Correlation between WCST items and overall score of MPAS

Table (10)

Total correct shows a highly significant negative correlation with over all score of premorbid adjustment score.

C. Correlation between overall score of MPAS and personality dimension- overall score of MPAS and IQ

Table (11)

There is negative, yet non significant correlation between the overall score of modified premorbid adjustment scale and all dimensions of personality except

extroversion. As well there is highly significant and negative correlation with IQ.

D. Correlation between symptom severity of first episode schizophrenic patients and IQ

Table (12)

This table shows that there is a highly significant negative correlation between negative symptoms and IQ. Also, there is significant negative correlation between anergia symptoms, total positive and negative score and IQ.

E. Difference between every two groups of premorbid adjustment and Symptom severity of first episode schizophrenic patients

Table (13)

This table shows that there is significant and negative difference between the stable good and stable poor patterns (categories) of modified premorbid adjustment scale as regard negative symptoms, thought disturbance symptoms and total positive and negative scale score. Also it shows a highly significant and negative difference between them as regard general psychopathology symptoms score.

F. Correlation between WCST items and symptom severity of first episode schizophrenia

Table (14) and (15)

This table shows that there is significant negative correlation between general psychopathology symptoms, paranoid symptoms and total positive and negative symptoms scores with total correct score of WCST. Also it shows significant negative correlation between paranoid

symptoms and supplemental symptoms scores with learning to learn score of WCST.

G. Correlation between symptom severity of first episode schizophrenia and personality dimensions

Table (16)

This table shows that there is a significant negative correlation between psychoticism with general psychopathology and a total positive and negative scale score. Also, it shows a significant negative correlation between psychoticism and criminality with thought disturbance. Other scores of PANSS subscales show non significant correlation with personality dimensions.

Correlation between Premorbid Adjustment and Short Term Degree of Improvement in First Episode Schizophrenic Patients

A. Correlation between overall score of MPAS and short term degrees of symptom improvement of first episode schizophrenic patients

Table (17)

This table shows that all score shows non significant correlation with overall score of modified premorbid adjustment scale.

B. Correlation between short term degrees of improvement of symptoms and IQ

Table (18)

This table shows that there is a highly significant and positive correlation between short term degree of improvement of anergia symptoms and IQ.

C. Correlation between IQ and WCST items

Table (19)

This table shows that there is a highly significant positive correlation between total correct, percent of conceptual level responses and learning to learn with IQ. As well there is significant positive correlation between categories completed and IQ. Also it shows highly significant and negative correlation between total errors and percent of errors with IQ.

D. Difference between every two groups of premorbid adjustment and Short term degree of improvement of symptoms

Table (20)

This table shows that there is significant and negative difference between the stable poor and deteriorating patterns (categories) of modified premorbid adjustment scale as regard general psychopathology short degree of improvement score.

E. Correlation between short term degree of improvement and WCST items

[Table \(21\)](#)

This table shows that there is significant and negative correlation between short degree of improvement of anergia symptoms and learning to learn. Also it shows a highly significant and negative between short degrees of improvement of anergia symptoms and total correct of WCST.

F. Correlation between short-term degree of improvement symptoms of first episode schizophrenia and personality dimensions

[Table \(22\)](#)

This table shows that there is a significant and positive correlation between psychoticism and short degree of improvement of supplemental score (aggression).

G. Correlation between the type of treatment and short term degree of improvement

[Table \(23\)](#)

This table shows a non significant difference between group that was treated with typical antipsychotic with or without ECT and the other group that was treated with atypical antipsychotic with or without ECT as a regard to the short degree improvement of symptoms.

H. Correlation between short term degree of improvement and symptom severity of first episode

Table (24)

This table shows that there is a non significant correlation between symptom severity and short degree of improvement of first episode symptoms.

I. Multiple Regression Analysis of Variables (PANSS at first week) against total short term degree of improvement score.

Multi-Regression analysis was used to search for symptoms of first episode (independent parameters) that can predict total score of short term degree of improvement (dependant variable). By using stepwise multi-regression analysis, parameters among these symptoms can sorted according to their sensitivity to discriminate.

Table (25) & (26)

These tables show that PANSS scores of first episode schizophrenia have non significant predictability to short degree of improvement. This was confirmed on testing the predictive ability of gen psychopathology symptoms and activation symptoms subscale scores.

J. Multiple regression analysis of variables (WCST items) against total short term degree of improvement score.

Multi-Regression analysis was used to search for WCST items (independent parameters) that can predict total score of short term degree of improvement (dependant variable). By using stepwise multi-regression analysis, parameters among these symptoms can sorted according to their sensitivity to discriminate.

Table (27) & (28)

These tables show that WCST items (executive function) have non significant predictability to short degree of improvement. This was confirmed on testing the predictive ability of total correct and trial administration items of WSCT.

SECTION III

1- What are the effects of stressor on symptoms severity at first episode of schizophrenia?

A. Frequency and percentage of patients exposed to stressors before the onset of illness

Table (29)

This table shows that most of patients were not exposed to any stressors before the onset of the psychiatric illness.

B. Correlation between stress and premorbid adjustment

Table (30)

C. Correlation between stress and symptoms of first episode schizophrenic patients

Table (31)

This table shows that there is negative but non significant correlation between all subscales of PANSS and the total score of social readjustment scale.

D. Correlation between Stress and Short Term Degrees of Improvement of Symptoms

Table (32)

This table shows that only total short degree of improvement show significant and negative correlation with social readjustment scale score.

Discussion

Males and females between the ages 18-60 years constitute 47 percent of total population in Egypt as shown in the statistical year book for census (central Agency for public Mobilization and statistics, 1996). Since the life-time prevalence of schizophrenia is 0.55- 1 percent in a recent review of studies from around world (*Golden et al., 2002*). It is expected that at least (143,040 - 286,080) individuals will experience this disorder, which leads to enormous direct and indirect costs.

Although the lifetime prevalence of schizophrenia is about 1 percent, but the associated social disability and cost are disproportionately large. According to the World Health Organization, schizophrenia is among the leading causes of disability worldwide (*Frangou and Byrne, 2000*).

A growing body of evidence suggests that the early stages of schizophrenia are critical in forming and predicting the course and outcome of the disorder. Accordingly, clinical and research interest is now focused on the early stages of the illness because early detection and treatment may result in a better prognosis and functional outcome (*Frangou and Byrne, 2000*).

Studies that shed light on vulnerability factors and predictors of severe episodes of schizophrenia are needed. They help to develop better prevention strategies, which are needed especially in developing countries with limited resources such as Egypt.

There is consistent evidence that many, but not all, persons affected by schizophrenia manifest poor social adjustment and subtle deviations from cognitive norms much before the illness is formally diagnosed. However, despite the many studies on this topic (*Mohamed et al., 1999 and Rabinowitz et al., 2002*), the prevalence, course, characteristics, and correlates of the premorbid and prodromal impairments are far from clear.

By studying the events preceding the first episode of psychosis and the multiple domains of psychosocial and educational functioning, it may be possible to detect protective or vulnerability factors and perhaps to devise interventions. They aimed at secondary prevention such as supplementary educational and vocational programs and other supportive measures.

Therefore the present study was specifically designed to investigate premorbid adjustment of first episode schizophrenic patients and its effect on symptoms severity, executive functions and short-term degree of

improvement. *Positive and negative syndrome scale*, *Modified Premorbid Adjustment scale (MPAS)*, *Wisconsin Card Sorting Test (WCST)* were used as standard tests for evaluation of patients.

Demographic variables

The mean age of subjects selected for this study was 24.86 years. 82 percent of subjects were males and only 18 percent were females. Gender difference in presentation of cases is very apparent. It has been noted since Kraepelin (1919/1971) that dementia praecox seemed to be primarily a disorder of young men.

Although previous epidemiological data suggested that schizophrenia occurs equally among both sexes (*Lewine et al., 1984*), results of a large community-based first-episode study suggested that the incidence of schizophrenia is roughly twice as high for men than for women. The results were regardless of the particular diagnostic criteria used (*Iacono and Beiser, 1992*).

The difference between the previous epidemiological data and our findings emerges from that:- **(1)** these studies focused on the first-hospital-admission statistics, as earlier incidence studies found equal prevalence rates of schizophrenia among men and women; **(2)** also, these

studies were affected by regional differences in hospitalization policies, lack of consistency in diagnostic rules across hospitals, omission of non hospitalized schizophrenic patients, and inclusion of patients with delusional disorders.

In our study, we overcame those limitations by selecting hospitalized and non hospitalized schizophrenic patients. We applied the same diagnostic system (ICD 10) on all patients. That is why our findings agreed with *Iacono and Beiser (1992)* and differed from previous epidemiological data of *Lewine et al. (1984)*.

One of the factors that contribute to the gender difference in the present study is that in our culture male subjects usually come to psychiatric services faster and more frequent than female subjects. That's because of the belief in our community that treated females are stigmatized and their chances for marriage will decrease as well as their risk of being divorced will increase.

The other factors, the majority of our sample were inpatients in psychiatric institute, where numbers of male beds are more than number of female beds.

It was found that 82 percent of the patients in our study were unmarried. This high incidence of unmarried

patients explained by the fact that schizophrenia may limit their chances of getting married

Also, it was found that 82 percent of the patients live with their parents. Parents are the main caregiver for them. These findings are in agreement with most of the studies. Studies reported an estimated 50 to 80 percent of persons with schizophrenia live with or have regular contact with a family caregiver (*McDonell et al., 2003*).

The family caregivers were suffering from three types of stresses:-

First: the stress of caring of the patients as dressing, bathing, toileting, cleaning the house and making meals, which are certainly taxing.

Second: research on the stress of giving care to ill family members has shown that it's emotional component can be the most draining. The emotional component varies by the disease, the individual suffering and the suffering of caregiver.

Third: As a result of misunderstanding and stigma, people don't discuss a family member's schizophrenia or other serious mental illnesses. These are resulting in a greater sense of social isolation for the caregiver.

Regarding behavior of patient at presentation, there was clearly a high prevalence of suicidal behavior in individuals suffering from schizophrenia. 28 percent of them presented with suicidality at their first presentation. Suicidality included suicidal and homicidal acts or trials.

The renaissance in psychiatric epidemiology of violence suggests that individuals with mental disorders may be two or three times more likely to behave violently than control (*Brennan et al., 2000*).

In this study 46 percent of the patients presented with violence. About 50 percent of patients developed aggressive behavior during inpatient treatment. Aggressive behavior include: - **(1)** 12 percent physical injures; **(2)** 18 percent damage to property; and **(3)** 6 percent only threatening behavior.

Our results confirmed some previously reported studies with aggression in first episode psychosis, where it was found that 9.6 percent demonstrated at least one act of serious aggression during at least one psychotic episode. 23.5 percent demonstrated lesser acts of aggression among inpatients with a first episode psychosis. Those were ascertained from a catchments area (Nottingham, UK). They

were assessed using clinical interview; informant and health care record (*Milton et al., 2001*).

Also, *Foley et al. (2005)* prospectively recruited subjects with a first episode of DSM-psychosis. Subjects were presenting from a geographically defined catchment's areas to a secondary referral psychiatric service over a four-year period (n = 157). They used the *Modified Overt Aggression Scale* to retrospectively assess aggression. They operationally defined aggression as a hostile or destructive mental attitude, including verbal aggression, physical aggression and/or violence. Also, they assessed violence. That was defined as the exercise of physical force. The assessment was blind to diagnosis. They found that, one in three patients with psychosis was aggressive at the time of presentation. One patient in 14 engaged in violence that caused, or was likely to cause, injury to other people.

The difference between results of these studies and our study may be explained by the following:-

- (1) We use "static" predictor variables (socio-demographic variables) rather than dynamic (symptom profile) variable that was used in *Foley et al. (2005)* study.
- (2) Data sets in *Milton et al. (2001)* study restricted to hospitalized patients. Yet in our study include hospitalized and non hospitalized patients.

(3) *Foley et al. (2005)* and *Milton et al. (2001)* sought to use a representative first episode community based sample and broad diagnostic range of psychotic disorder. Yet our study restricted to first episode schizophrenia patients.

As regard smoking, in our study, patients with first episode schizophrenia had higher rate (60 percent) than general population (25-30 percent).

As the same as *Mcevoy and Brown (1999)* reported that 50 percent of first episode schizophrenic patients were smokers.

In addition, *Goff et al. (1992)* reported that patients with chronic schizophrenia smoke at substantially higher prevalence rates (70–80 percent) than first episode patient and the general population (25–30 percent).

The increased smoking rate in schizophrenia patients could be explained by that smoking lowers antipsychotic blood levels and it lowers extra pyramidal side effects of antipsychotic drugs via stimulating hepatic microsomal enzymes (*Goff et al., 1992; Miller et al., 1990*). Also, nicotine reverses antipsychotic-induced cognitive slowing (*Levin et al., 1996*).

If patients with schizophrenia smoke primarily to reverse the effects of antipsychotic drugs, those with chronic schizophrenia should smoke at substantially higher prevalence rates than first-episode patients. However, there is also evidence that smoking produces direct "therapeutic" effects (i.e., independent of its interactions with antipsychotics) for patients with schizophrenia. For example, nicotine corrects abnormalities in sensory gating seen in many patients with schizophrenia (*Griffith et al., 1998*).

Another suggestion is that patients smoke as a form of self-medication with nicotine, which may help regulate a dysfunctional mesolimbic dopamine system. It may increase dopamine release in the pre-frontal cortex and alleviate positive and negative symptoms. Worsening of psychotic symptoms on nicotine withdrawal has been reported (*Kelly and McCreadie, 2000*).

Recently, it was found that genetic and/or environmental factors might predispose individuals to develop both schizophrenia and nicotine addiction yet much work in the genetics of both schizophrenia and nicotine addiction is needed (*Kelly and McCreadie, 2000*).

Regarding vulnerability factors for schizophrenia, which are family history of psychiatric disorders and stress level. It was found that schizophrenia and affective disorders co-occur in some families. It is interesting that indirect evidence suggests that family members of schizophrenic women in particular may have an increased morbid risk of affective disorder. In addition to increased morbid risk of schizophrenia.

Specifically, studies have consistently reported that good-prognosis schizophrenia with affective features (which is more common in women than men) is associated with an increased risk of affective disorder in family members.

By one estimate, good-prognosis schizophrenic patients, regardless of gender, have two to three times as much affective disorder as schizophrenia in their families. This suggesting that good-prognosis of schizophrenia is genetically related to affective disorder.

The reverse is true for poor-prognosis schizophrenic patients, who have two to three times, as much schizophrenia as affective disorder in their families (*Salem and Kring, 1998*).

In our study we found that 26 percent of patients had family history of psychosis. 6 percent has family history of mood disorders. Further studies are needed to evaluate the effect of family history on prognosis of schizophrenia.

There is a growing body of evidence supporting the idea that stress and schizophrenia are closely linked. One groundbreaking study found that 46 percent of patients who experienced their first bout of schizophrenia underwent some stressful life event in the preceding three months (*Ventura et al., 1989; Norman and Malla, 1993*).

In our study we found that 26 percent underwent stressful events in preceding 12 month. 12 percent of them exposed to mild stress based on *Social Readjustment Scale score*. And 14 percent exposed to moderate degree stress, based on *Social Readjustment Scale score*.

Premorbid function in first episode schizophrenia patients

By studying premorbid function in first episode schizophrenia. It was found that all patients had onset of schizophrenia after age of 18 (young age), with 70 percent showed a disturbance in functioning (*Rabinowitz et al., 2002*).

In our study there are different pattern of premorbid function in the patients according to *Modified Premorbid Adjustment Scale* score. 38 percent (n=19) had deteriorating premorbid function, 32 percent (n=16) had stable poor premorbid function and 30 percent (n=15) had stable good function.

We postulate that these patterns might be the product of two different but developmentally linked neurobiological processes. Levels of functioning in childhood may be determined early in life, largely by

neurodevelopmental processes related to genetics and perinatal forces (*Murray and Lewis, 1987*).

Also, levels of functioning that decline later on, especially in adolescence, may be determined by neuroregressive processes such as developmentally determined reductions in cortical synaptic connectivity (*McGlashan and Hoffman, 2000*).

As many as 30 percent reported 'good stable' social functioning. There was an argument against seeing schizophrenia as an entirely neurodevelopmental disorder with social dysfunction being an obligatory early manifestation (*Weinberger and McClure, 2002*).

A particular subgroup of schizophrenic disorders may be defined by an early pathophysiological process that manifests as poor social adjustment during childhood and adolescence. This process may then evolve into more severe negative and general symptoms, as well as poorer cognitive performance in early adulthood and at the onset of psychosis. A number of scenarios could be responsible for these pathophysiological processes. An accumulation of genetic and environmental risk factors (or lack of environmental protective factors), consistent with a "multiple-hit" hypothesis, may lead to the premorbid

manifestations, and an environmental insult or a gene expressed later in life may be necessary for the full syndrome of schizophrenia to develop. Depending on the nature of the additional, later insults, the same early-life manifestations (e.g., marginal social adjustment) might remain stable through life, evolve into milder mental disorders such as schizotypal personality disorder, or lead to schizophrenia. If indeed the phenotype of schizophrenia reflects the consequences of an accumulation of genetic and environmental risk factors, research examining the course of the disease from birth through the age of risk may be required to identify specific etiological patterns (*Rabinowitz et al., 2002*).

Many studies tried to describe the pattern of premorbid function in schizophrenic patients. For example in 2002, *Rabinowitz et al.* conducted trial on eleven countries and have enrolled psychotic patients between the ages of 16 and 45 years. Patients who have had a DSM-IV diagnosis, based on the Structured Clinical Interview for DSM-IV, of schizophrenia, schizophreniform disorder, or schizoaffective disorder for less than 12 months. They have had a maximum of two lifetime psychiatric hospitalizations for psychosis. The cumulative exposure to neuroleptics could not have exceeded 12 weeks.

Subjects' scores on the Premorbid Adjustment Scale were used to assign them to groups according to whether their premorbid functioning was stable-good, stable-poor, or deteriorating using the method of Haas and Sweeney. It was found that 47.5 percent of the subjects (n=252) were categorized as having stable-good premorbid functioning; 37.3 percent (n=198) as having stable-poor functioning; and 15.3 percent (n=81) as having deteriorating premorbid functioning.

Also, they found that female subjects had significantly better premorbid functioning (stable-good: 57 percent, n=88; stable-poor: 34 percent, n=53; deteriorating: 9 percent, n=14) than male subjects (stable-good: 44 percent, n=164; stable-poor: 18 percent, n=67; deteriorating 39 percent, n=145) ($F=10.1$, $df=2$, $p=0.006$).

In the study by *Addington and Addington (2005)*, 194 patients with first episode psychosis (FEP) were assessed using the Premorbid Adjustment Scale (PAS). Cluster analysis was used to detect patterns of premorbid functioning. Twenty nine percent of the sample had stable good premorbid functioning.

Stable good premorbid functioning indicated that, they had no marked problems in social or school

functioning at all, even though they developed psychosis later in life. A group of people with deteriorating premorbid function was identified and this group had more symptoms at 1 year (positive and negative symptoms) and 2 year follow up (negative symptoms) compared with the stable-good premorbid functioning group.

In 2004 *Larsen et al.* identified and validated patterns of premorbid functioning in first-episode psychosis (n=335) using The Structured Clinical Interview for DSM-IV for diagnostic purposes. First-episode psychosis includes non-affective psychosis, i.e. schizophrenia, schizophreniform psychosis, schizoaffective psychosis, delusional disorder, brief psychosis, affective disorder with mood-incongruent delusions and psychosis not otherwise specified. They carried out separate *K*-mean cluster analyses for the social and academic domain. Within each domain they identified similar patterns of premorbid function as described by Addington and Addington.

For social and academic dimensions the analyses suggested four or five clusters. They chose the four-cluster solutions as they seemed to give the clearest picture for both dimensions they defined a starting level as good (<1.50), intermediate ($1.50-2.99$) or poor (≥ 3.00). The courses were defined by change scores over the time

periods as clearly stable (<1.00), slightly deteriorating ($1.00-1.99$) and clearly deteriorating (≥ 2.00). Clusters were labeled according to this definition, but as none of them occupied the 'slightly deteriorating' category, only the terms 'stable' and 'deteriorating' are used to describe course.

The Premorbid Adjustment Scale scores for social dimension clusters were good stable ($n=133$), good deteriorating ($n=96$), intermediate stable ($n=58$) and intermediate deteriorating ($n=48$). And The Premorbid Adjustment Scale scores for academic dimension clusters were good stable ($n=136$), good deteriorating ($n=77$), intermediate stable ($n=66$) and poor stable ($n=56$).

The difference between our study and these studies emerges from: **(1)** we used different diagnostic system as they used DSM IV and we use ICD 10 systems; **(2)** we were restricted to first episode schizophrenia yet they include all first episode psychotic disorder (broad rang); and **(3)** we used Modified Premorbid Adjustment Scale (MPAS) in contrast to premorbid adjustment scale (PAS) that they used.

We need more studies in Arab countries that share the same cultural background, using the same tools for more confirmation and comparison

Gender difference between male and female in premorbid function

In addition our study showed that there was no significant gender difference between male and female in premorbid function based on Modified Premorbid Adjustment Scale (MPAS) scores. This finding agreed with study that found, men and women had relatively similar ratings relatively similar on most of the indicators of premorbid functioning (*Fennig et al., 1995*).

Recently, *Schmael et al. (2007)* found that there was no difference in Premorbid Adjustment Scale (PAS) ratings between males and females in patients with schizophrenia. On the other hand, females showed significantly better PAS scores than males among the control probands at the same study.

Our study results were different from some previous reports. They found that men have poorer premorbid function and more deterioration close to onset of schizophrenia (Table 8) (*Rabinowitz et al., 2002; Addington and Van Mastrigt, 2002; Preston et al., 2002*).

In addition to *Strous et al. (2004)* who examined retrospectively the premorbid status of patients in their first episode of psychosis. Their aims were determination of the correlation between premorbid status and (1) baseline symptoms; (2) treatment response; and (3) medication side effects. They found that, males and females had comparable overall PAS scores during childhood. However, males became progressively worse over subsequent stages, as indicated by a significant stage-by-sex interaction in mixed models analysis ($t = 2.41$, $df=286$, $p = 0.016$). The rate of change among men was three times greater than among women, increasing by 0.22 (95% CI = 0.04, 0.40) above the female rate of 0.11 (95 percent CI = -0.14, 0.24).

The difference between our results and *Strous et al* results may be explained by: (1) cultural difference especially for gender role; or (2) small sample size of our study that affect statistical data especially numerical data relative to large sample size of *Strous et al.* study.

The effect of premorbid function on symptoms severity of first episode schizophrenic patients

One of our aims was to study the effect of premorbid function on symptoms of first episode schizophrenic patients ($n=50$). The results of this study are consistent with previous reports about first episode schizophrenia. These reports have found that individuals with poorer (as

opposed to better) premorbid function have more severe symptoms. The correlation was reflected by negative syndrome scale, general psychopathology and thought disturbance subscale of positive and negative syndrome scale (*Table 9*).

On studying the difference between the three patterns of premorbid function (stable-good, stable -poor and deteriorating) against symptom severity of first episode there was significant difference between them in general psychopathology symptom subscale of PANSS.

Studying the difference between every two pattern of premorbid function was done. It was found that stable poor group, had significant relation to high score in some subscales of PANSS than stable good group.

That subscales include negative syndrome scale, general psychopathology, thought disturbance subscale of positive and negative syndrome scale and in total score of scale. These results reflected that more severe symptoms are related to poor premorbid function in comparison to good premorbid function (*Table 13*).

At the same time there is no significant difference between scores of stable poor group versus deteriorated group with subscale of PANSS. At the same time, stable good group versus deteriorated group with subscale of PANSS.

Thus, our findings revealed significant negative correlation between overall score of MPAS and some PANSS subscales. These subscales include negative syndrome scale, general psychopathology, thought disturbance subscale and in total score of scale. Thus, poor premorbid function is related to these symptoms.

Many previous reports were in agreement with our results. For example, in 1993, *Addington* and *Addington* found significant association between premorbid function of schizophrenic patients and their negative symptoms. Their finding was applied to at both the acute phase and the remitted phase of the illness six months later.

And in 1995 *Gupta et al.* were using the Modified Premorbid Adjustment Scale in a large sample (n = 131) of schizophrenic patients. Subjects were evaluated with the Comprehensive Assessment of Symptoms and History (CASH) and magnetic resonance imaging. Multiple correlations indicated that poor premorbid adjustment was significantly associated with prominence of negative symptoms, early age of onset, educational problems, chronicity, and neurological soft signs, but not with any MRI measures.

These results confirm poor premorbid adjustment as an important predictor of a malignant form of schizophrenia as evidenced by an earlier age of onset, poorer educational performance, prominent negative symptoms, presence of soft signs, and chronicity of course.

Also, in 2003 *Addington et al.* studied premorbid functioning in a sample of 306 subjects newly admitted to an early-psychosis program. Using cluster analyses, they identified four patterns: stable-good, stable-moderate, deteriorating and poor-deteriorating. Results were that relative to the stable-good group, the deteriorating and the poor-deteriorating groups had more negative symptoms, poorer social functioning and some evidence of poorer

cognitive functioning. The deteriorating group had increased positive symptoms compared to the stable-good group.

These results suggest that prior to the onset of the acute psychosis those who have poor social and interpersonal functioning premorbidly present initially with increased social impairment and negative symptoms compared to those who have better premorbid functioning.

Recently, *Schmael et al. (2007)* investigated the possible correlations of premorbid morbid adjustment, measured with the Cannon-Spoor Premorbid Adjustment Scale (PAS) and symptoms of 316 inpatients with schizophrenia and 137 population based controls using the Structured Clinical Interview for DSM. Controls demonstrated better PAS scores than inpatients with schizophrenia. Earlier age at onset and negative symptoms were found to be associated with poorer PAS scores.

Executive functions in first episode schizophrenia

Executive functions assessment in first episode schizophrenia represent an important item in our study.

Executive functions encompass a group of cognitive processes, that include planning, strategy-use, set-shifting, divided attention, and working memory. The results of studies measuring executive functions in first-episode schizophrenia are inconsistent.

In our study executive function values (mean) for some items of WCST were clearly below the levels found for normative healthy comparison sample. 30 control subjects, matched to patients according to age and education were included in the study. The WCST was administered. Patients with first episode schizophrenia showed low values especially in percent of conceptual level responses and categories completed, that reflect impairment in concept formation in patient with first episode. Also, higher values for percent errors and percent of preservative errors that reflect difficulty in cognitive flexibility of patient.

On the other hand, impaired attention reflected by significant difference between the patients and control in failure to maintain set ($t=-2.21$, $p < 0.05$) and in learning ability ($t=-4.34$, $p < 0.001$). And there was no significant difference between the patients and control as regard total correct ($t=-1.21$, $p > 0.05$) (Table 5, 6).

Therefore, our results replicate the original finding that patients with first episode schizophrenia are impaired on executive tasks (*Hutton et al., 1998*).

In 2002 *Addington and Addington* studied cognitive functioning in first-episode schizophrenia. They suggested that first-episode patients demonstrate cognitive impairments that were similar to those of patients with an established schizophrenic illness. Also, they supported the previous findings in studies of chronic schizophrenia (*Goldberg et al., 1990; Braff et al., 1991; Hoff et al., 1992; Blanchard and Neale, 1994; Mohamed et al., 1999*)

Also in 2003 *Ludewig et al.* reported that schizophrenic patients at the beginning of their illness exhibit deficiency in executive functions. Furthermore, decision-making dysfunctions are not due to a deficient attention resource allocation, but related to set-shifting and planning dysfunctions.

In 2001 *Everett et al.* started prospective cross-sectional study in psychiatry department in a university-affiliated hospital. 30 patients with schizophrenia, diagnosed according to DSM-IV criteria. 30 control subjects, matched to patients according to age and education were included in the study. The WCST was administered. Patients with schizophrenia succeeded on fewer categories ($t = 23.3$, $p < 0.001$), committed more preservative errors ($t = 15.6$, $p < 0.001$), made more preservative responses ($t = 14.6$, $p < 0.001$), needed more trials to succeed at the first category ($t = 9.2$, $p < 0.003$) and gave significantly lower conceptual level responses ($t = 4.1$, $p < 0.001$) than the controls.

There is accumulating evidence that executive dysfunction is a pervasive abnormality, intrinsic to schizophrenia. It is not account for by illness chronicity, antipsychotic treatment or antipsychotic type. It is present in first episode patient even before management started.

Relationships between symptoms severity, premorbid adjustment and executive functions in first episode schizophrenia

In the last years, the era of interest is studying relationships between clinical, neurocognitive indices in first episode psychosis.

It was found that psychosis and neurocognitive indices are two independent domains, when psychosis is treated (*Rund et al., 2007*).

In our study there were significant negative correlations between total correct with some PANSS subscales. These subscales include paranoid, general psychopathology subscale and total positive and negative scale score in the first week. Total correct was not affected significantly in first episode schizophrenia. In addition to significant negative correlation between learning to learn with paranoid, supplemental symptoms score (aggression) at first week.

This indicates that the more severe psychopathology and paranoid symptoms the lower the score of total correct. Also, the decreased ability to learn in the patients with high paranoid and supplemental symptom scores.

Other important aspect of cognitive function is IQ. IQ of patients negatively correlates with anergia symptom, negative symptoms and total symptom severity score at first week of presentation.

As regard correlation between premorbid adjustment and executive functions. We found that poorer (as opposed

to better) premorbid function are related to executive function impairment (especially total correct). That was consistent with previous reports about first episode schizophrenia.

For example *Silverstein et al. (2002)* examined the relationship between premorbid adjustment and neuropsychological deficit in schizophrenia, in 61 outpatients with diagnoses of chronic schizophrenia ($n=53$) or schizoaffective disorder (depressive subtype: $n=6$, bipolar type: $n=2$) based on the Structured Clinical Interview for *DSM-III-R*. The specific tests included measures of the attention, executive functions/problem solving (WCST) and memory. Premorbid adjustment was rated using the Premorbid Adjustment Scale (*Cannon-Spoor et al., 1982*). It was found that Poor neuropsychological performance was associated with poor premorbid adjustment. And a multiple regression analysis was performed in which the five neuropsychological variables were treated as predictors of the overall PAS rating. This analysis was statistically significant ($F = 2.567$, $df = 5, 55$, $p < 0.037$), and it accounted for nearly 19 percent of the variance among the PAS and the cognitive measures ($R^2 = 0.189$).

Addington and Addington (1993) examined the relationship between premorbid functioning, outcome, cognitive functioning, positive and negative symptoms of schizophrenia in a sample of 39 subjects with schizophrenia. Subjects were diagnosed according to the DSM-III criteria. Subjects were assessed at admission to hospital and six months later. Deficits on cognitive tests of verbal reasoning and concept formation were significantly associated with poor premorbid functioning and outcome.

As regard the correlation of premorbid function with IQ it was found that premorbid function has direct correlation with IQ. As higher IQ accompanied by good premorbid function and lower IQ patient have poorer premorbid function.

We were in agreement with the result of the previously mentioned study, as we used almost the same tools for assessment of executive function and IQ and the same age group of the patients.

In our study, executive functions in the first episode schizophrenia have direct correlation with IQ. That was reflected by WCST items especially percent of conceptual level, learning to learn and total correct. In addition, there was negative correlation between IQ and both percent of errors and total errors in the patients.

Relationships between symptoms severity, premorbid adjustment, executive functions and short term degree of improvement in first episode schizophrenia

Studying the pattern of short term improvement of symptoms after six weeks was done. The maximum degree of improvement was associated with total score of positive and negative syndrome scale. There were different degrees of improvement in the subscales. The best improvement was with supplemental symptoms. The least improvement was with thought disturbance symptoms

As regard the relation between short term degree of improvement of symptoms and executive functions it was

found that learning to learn has negative correlation with short term degree of improvement of paranoid symptoms and aggression.

When executive functions were tested as predictors of short term degree of improvement, they failed to prove this point.

On studying the effect of clinical variables on short term improvement of symptoms, a multiple regression analysis was performed in which symptom severity of the first episode was treated as predictor of the short term degree of improvement. This analysis was statistically insignificant.

Therefore both symptom severity at first week of presentation and short term degree of improvement after six weeks are independent domains.

That was inconsonance with many studies, which suggested that premorbid social functioning is a crucial variable with regard to therapeutic outcome in first-episode psychosis (*Amminger et al., 1997*).

Also *Strous et al. (2004)* examined retrospectively the premorbid status of patients in their first episode of psychosis in order to determine the relationships with treatment response. They found that, females have better

treatment response than males. And the sociability and withdrawal significantly predicted worse treatment response during early adolescence (hazard ratio = 0.85 percent, 95 percent CI = 0.73, 0.99).

In addition to *Rachel, et al. (2006)* examined the relationship of premorbid functioning using the Premorbid Adjustment Scale and outcomes in first admission psychoses (schizophrenia, n = 177; bipolar disorder, n = 106; major depression, n = 68) in the Suffolk County-wide mental health project. Poor premorbid functioning was associated with worse outcomes in all the three diagnostic groups. Specifically, it was associated with more negative symptoms early in the course of illness, less improvement in negative symptoms, poorer overall clinical functioning, and poorer social functioning. Consistent with new the epidemiological research, early assessment of premorbid functioning could provide an avenue for targeted interventions that might improve outcomes.

Thus, clinical observation and most of the previous studies suggested that better premorbid functioning is associated with better outcomes in first episode and chronic schizophrenia. In our sample we couldn't prove that. It may be due to smaller number of the sample or short duration of follow up (six weeks).

Group of medication and short term degree of improvement

In our study we compare short term degree of improvement in two groups of patients. One group received conventional antipsychotic with or without ECT. The other group received new (atypical) antipsychotic with or without ECT. It was found that there is no significant difference in short term degree of improvement between both groups. That indicates that both types of management almost have the same efficacy on symptoms management.

Our results agree with Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS 1) done in fourteen community psychiatric services in the English National Health Service. Two hundred twenty-seven people aged 18 to 65 years with *DSM-IV* schizophrenia and related disorders assessed for medication review because of inadequate response or adverse effects. It was found that the primary hypothesis of significant improvement in Quality of Life Scale scores during the year after commencement of second generation antipsychotic (SGAs) vs First-generation antipsychotic (FGAs) was excluded. Participants in the FGA arm showed a trend toward greater improvements in Quality of Life Scale and symptom scores. Participants reported no clear

preference for either drug group; costs were similar (*Jones et al., 2006*).

We explain that agreements by the fact that the patients who are at the beginning of their illness may be extremely sensitive to treatment. That sensitivity makes them very responsive to the therapeutic effects of anti-psychotic drugs.

They respond to all treatment including the newer and older type of treatments. However, they're also more sensitive to side effects. This sensitivity can become a real problem in terms of their willingness to continue their medication and the likelihood of them to stop their medication.

Effect of stressors and personality dimensions on symptom severity of first episode schizophrenia

As regard other variables effect on .On studying the effect of stressors on symptom severity of first episode schizophrenia, it was found that all scores showed non significant correlation with the degree of stress. Yet there was significant negative correlation with the short term degree of improvement of symptoms. Thus, stressful life events have bad impact on the degree of improvement of symptoms and bad prognosis. Yet stress doesn't affect severity of symptoms in the first episode patients.

As regard the effect of personality dimensions on symptoms of first episode. It was found that lower scores of psychotism and criminality are related to sever thought disturbance. Yet, low scores of psychotism only is related severe negative symptoms and sever general psychopathology symptom. Also, it was related to low short term degree of improvement of aggressive symptom.

Taken together, our study and other studies emphasized the importance of measuring premorbid adjustment. They were showing associations between premorbid adjustment and the severity of symptoms. They strengthen the evidence for the predictive value of premorbid adjustment in schizophrenia.

Seen from the premorbid point of view, the syndrome of schizophrenia is not only heterogeneous regarding symptom formation at baseline and outcome, but also on its precursors.

Our findings emphasize the importance of considering the possibility of psychotic development in people with long-lasting dysfunction. Our study also supports the idea that schizophrenia is a heterogeneous disorder with neurodevelopmental and neuroregressive pathways to psychosis. Processes that may be qualitatively distinct in their neurobiological origins but interactive in their contribution to the pathophysiology of schizophrenia

Strength and limitations

A clear strength of this study is that it has not been performed in any Egyptian work. It might help in comparing between Egyptian patients and western patients.

Although the main component of mental health care costs for schizophrenia is hospitalization, there are also substantial indirect or time-loss costs. If factors that are predictive of higher-treatment and/or indirect costs can be identified, they may be useful as foci for interventions aimed at reducing costs (*Carr et al., 2004*).

One of such factors is poor premorbid adjustment that is related to severe symptoms of schizophrenia. Therefore poor premorbid adjustment increases the need for hospitalization because of severe symptoms that lead to increase the cost of treatment.

This study emphasises the importance of measuring premorbid adjustment for planning the early detection service for high risk individuals of developing schizophrenia especially, those with deteriorating premorbid function and early intervention of those cases.

The goal of early intervention is to improve outcomes by promoting a full recovery if possible thereby reducing the long term disability and costs (both human and economic) associated with schizophrenia.

The study carried the limitations of assessment of premorbid function, these were:

- As assessment of premorbid function was done retrospectively.
- The patients recall may be unreliable because of cognitive impairment associated with this illness that led to high possibility of bias; thus more than one source of information had to be used aiming to avoid the "hindsight bias" in asking about all aspects of premorbid function. And an informant from among the

reliable family members was also interviewed for more accurate assessment of premorbid function.

- Also, the study showed the limitation arising out of the relatively small sample size, that limited the statistical power of analysis and clinically important associations may not have been detected.
- Absence of control group representative of the population from which our subjects were taken especially for assessment of their premorbid adjustment, IQ and for conclusion about prevalence of violence, suicidality and smoking as alert symptoms of schizophrenia.

Recommendations

Recommendations of social policy

- Long-term psychosocial interventions are necessary to minimize functional impairments, to strengthen existing cognitive coping strategies, to increase environmental and intrapsychic adaptability and to promote self-sufficiency. The provision of mental health services addressed to schizophrenic patients should be reviewed and re evaluated to cope with the burden of schizophrenia which is still a devastating disorder of the productive years of the affected subjects.
- This calls for a comprehensive policy of mental health providers and the allocation of more resources both human and financial to cope with the problem. Further studies in different epidemiological catchment areas and studies of different age groups are needed. A National Central Register for all psychiatric patients is called for.
- We need to alleviate the burden on the patients and their families resulting from the stigma and the rejecting attitudes towards patients with schizophrenia. We need a national program involving mental health policy makers and mass media for the coordination of

knowledge and efforts to fight the stigma of schizophrenia.

Management recommendation

- Focusing on early detection and intervention in schizophrenia offers the opportunity to make a real difference to the lives of our patients and their families.
- During their first episode of schizophrenia patients need specific services that provide rapid and easy access to specialist assessments, swift initiation of treatment in a setting which does not have stigma attached to it, and comprehensive psychosocial interventions and support.
- Programs of management of first episode patients should be planned including
 - Stress management program for patients with stressful life events that impair their improvement.
 - Family psychoeducation to decrease burden on family caregivers.
 - Regular follow up for early detection of symptoms in high risk apparently healthy individuals.
 - Early relapse prevention programs.

Research recommendation

- Future research in the premorbid adjustment in schizophrenia should be prospective to high risk people and in longitudinal study, assessment of premorbid adjustment in other psychotic episodes, objective markers of psychotic episodes, enabling the clinician to detect more precisely the earliest, even sub clinical stages of illness exacerbation or for relapse in Egyptian patient for early prevention of psychiatric illness.
- Research should be directed to detection of factors affecting short term degree of improvement and outcome of first episode schizophrenia on Egyptian patient.

Summary

Recent data on burden of mental disorders world wide demonstrates a major public health problem that affects patients, society, and nations as a whole. Mental disorders contribute significantly to the global burden of disease, as four out of the ten diseases with the highest burden are psychiatric disorders.

Schizophrenia as a mental disorder is the most common chronic psychosis in Egypt and accounts for the majority of inpatients in our mental hospitals.

Although the main component of mental health care costs for schizophrenia is hospitalization, there are also substantial indirect or time-loss costs. If factors that are predictive of higher-treatment and/or indirect costs can be identified, they may be useful as foci for interventions aimed at reducing costs.

By studying the events preceding the first episode of psychosis and schizophrenia and the multiple domains of psychosocial and educational functioning, it may be possible to detect protective or vulnerability factors and perhaps to advice interventions aimed at secondary prevention such as supplementary educational and

vocational programs, and other supportive measures. Such preventive measures may be needed to achieve an ideal outcome for schizophrenia patient and those predisposed to the disorder.

Premorbid adjustment in schizophrenia may have predictive value. So a number of scales have been developed to describe the premorbid phase. For example, The Modified Premorbid Adjustment Scale (MPAS), which defined the premorbid phase as the time from birth until 12 months before onset of psychosis. It is probably the widely used premorbid scale for the first episode psychosis.

The present study is designed to test the hypothesis that poor premorbid function that include; sociality, peer relationship, socio-sexual relation, work and education; leads to severe symptom of first episode of schizophrenia.

The aim of this study was to assess premorbid functioning during the first episode of schizophrenia, relation between premorbid function and symptom severity, correlation with short term degree of improvement. In addition, it examined the effect of stressor on symptom severity and short term degree of improvement.

The cases were selected as a random sample from inpatients, and those attending outpatient clinic and emergency room of Psychiatric Institute, Ain Shams University Hospital. This serves as a catchment area of about one third of Cairo population, serves both urban and rural areas and subdivided into private and free sections so the patients would represent all social strata.

The study included Egyptian patients, who were diagnosed according to ICD-10 criteria using *The Mini International Neuropsychiatric Interview (M.I.N.I.)*. Also, severity and pattern of symptoms were assessed by using *Positive and Negative Syndrome Scale (PANAS)* and premorbid function was assessed by *Modified premorbid adjustment scale*.

In addition, psychosocial stressors faced the patients prior to his illness were assessed by *Social Readjustment Scale*.

The Patients subjected to cognitive function evaluation including assessment of IQ using *Wechsler Adult Intelligence Scale* and using *Wisconsin Card Sorting Test* for executive function assessment.

Eysenck Personality Questioner (EPQ) was used for detection of personality traits in domains of introversion, extroversion, neuroticism and psychoticism.

Reevaluation of symptom severity after six weeks using *Positive and Negative Syndrome Scale (PANSS)*.

Many statistical methods were used for analysis of data. Data were expressed as mean and standard deviation (SD) for quantitative measures and both number and percentage for categorized data and differences between groups were assessed by Student's t-test adopted for either equal or unequal variances.

Ranked Sperman Correlation test was used to study the association between each 2 variables among each studied group allows using sample data to test whether the values of two or more unknown population means are likely to be equal. Also multiple regression analysis was applied to some the variables, to find factors that may affect the total short term degree of improvement.

Our study showed that the socio-demographic characteristics of the sample pointed at a male preponderance (n=41, 82 percent), with the majority of subjects having never married (n=41, 82 percent) and most of the patients live with their parents so family is the main caregiver.

As regard family history, it was found that 26 percent of patient has family history of psychosis and 6 percent of the patients have family history of mood disorders.

Also, it was found that 12 percent had exposed to mild stress and 14 percent had moderate stress during the year preceding the illness.

As regard the clinical characteristics of the sample it is found that 46 percent of the patients presented with violence and 28 percent of them presented with suicidality and about 60 percent of the patients are smokers.

On studying premorbid function of the patients, it was found that it was characterized by disturbance in functioning (38 percent have deteriorating premorbid function and 32 percent have stable poor premorbid function) with no significant gender difference between male and female in premorbid function.

It was found that executive function values of the first episode schizophrenic patients were impaired in relation to normative healthy comparison sample especially, percent of conceptual level responses and categories completed that reflect impairment in concept formation and there were higher levels for percent errors and percent of preservative errors that reflect difficulty in cognitive flexibility of the patients. In addition, patients had impaired attention reflected by significant difference between patients and control in failure to maintain set and learning ability.

On the other hand, executive function impairment was related to more severe symptoms (as decreased ability to learn was related to severe paranoid symptom and aggression--- and decreased total correct was related to severe paranoid, general psychopathology and total score of positive and negative syndrome scale). Also Low IQ was related to severe negative symptom, anergia total score of positive and negative syndrome scale score.

The results of this study were consistent with previous reports about first episode schizophrenia, which have found that individuals with poor premorbid function have more severe symptoms, as reflected by negative,

general psychopathology and thought disturbance subscales of positive and negative syndrome scale. Also, they have executive function impairment (especially total correct).

Also, It was found that symptoms differs in there short degree of improvement with best degree of improvement to supplemental symptoms and activation symptoms and lest degree of improvement was thought disturbance symptoms degree of improvement.

And there was impairment of short degree of improvement of symptoms by stressful life events and executive function impairment.

It was found that the degree of improvement was not affected by group of medication which used. As there is no significant deference in short term degree of improvement between patient received conventional antipsychotics with or without ECT and patient received new (atypical) antipsychotics with or without ECT. Also, neither symptom severity nor executive function could predict short term degree of improvement of symptoms.

Although clinical observation and most of the previous studies suggest that better premorbid functioning

is associated with better outcomes in first episode and chronic schizophrenic but in our sample we couldn't prove it may be due to smaller number of the sample or short duration of follow up.

Taken together, our study and other studies emphasized the importance of measuring premorbid adjustment, showing associations between premorbid adjustment and the severity of symptoms strengthens the evidence for the predictive value of premorbid adjustment in schizophrenia. Seen from the premorbid point of view, the syndrome of schizophrenia is not only heterogeneous regarding symptom formation at baseline and outcome, but also on its precursors. Our findings emphasized the importance of considering the possibility of psychotic development in people with long-lasting dysfunction.

A clear strength of this study was that it had not been performed in any Egyptian work and it might help in comparing between Egyptian patients and western patients.

On the other hand, the study carried some limitations for example:

- As assessment of premorbid function was done retrospectively.

- The patients recall may be unreliable because of cognitive impairment associated with this illness That led to high possibility of bias; thus more than one source of information had to be used aiming to avoid the “hindsight bias” in asking about all aspects of premorbid function. And an informant from among the reliable family members was also interviewed for more accurate assessment of premorbid function.
- Also, the study showed the limitation arising out of the relatively small sample size, that limited the statistical power of analysis and clinically important associations may not have been detected.
- Absence of control group representative of the population from which our subjects were taken especially for assessment of their premorbid adjustment, IQ

Future research in the premorbid adjustment in schizophrenia should be prospective to people at risk and in longitudinal study, assessment of premorbid adjustment in other psychotic episodes, objective markers of psychotic episodes, enabling the clinician to detect more precisely the earliest, even sub clinical stages of illness exacerbation or for relapse in Egyptian patient for early prevention of psychiatric illness.

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تأثير أداء الفرد في مرحلة ما قبل المرض على شدة الأعراض في النوبة الأولى من مرض الفصام: دراسة مصرية

لقد أوضحت البيانات الحديثة العبء الذي تمثله الاضطرابات العقلية على مستوى العالم، حيث أنها تمثل مشكلة صحية كبيرة ذات تأثير قوى على المرضى، والمجتمع والأمم بشكل عام.

وقد وجد أن الفصام هو الاضطراب العقلي المزمن الأكثر انتشارا فهو يتسبب في معظم حالات الحجز في مستشفيات الطب النفسي في مصر.

وعلى الرغم من أن الجزء الأكبر من تكلفة الرعاية الصحية لمرضى الفصام هو تكلفة العلاج في المستشفيات، إلا أن نسبة الخسائر غير المباشرة الناتجة عن الإعاقة وضياع ساعات العمل تمثل نسبة كبيرة لا يستهان بها من التكلفة. وإذا أمكن التعرف على العوامل التي نستطيع من خلالها التنبؤ بالحاجة إلى رعاية طبية مكلفة و تقييم حجم الخسائر غير المباشرة المتوقعة، فمن الممكن توظيف هذه العوامل في الخطط العلاجية التي تهدف لخفض الخسائر الناتجة عن المرض.

وبدراسة الأحداث التي تسبق النوبة الأولى من مرضى الفصام والاضطرابات العقلية ، وتقييم مستوى الأداء في العملية التعليمية والتفاعل النفسي الاجتماعي ، يمكن تحديد العوامل التي تحمي من المرض والتي تزيد احتمال حدوث ، وبالتالي توجيه برامج التدخل العلاجي التي تهدف للوقاية الثانوية مثل برامج التعليم الإضافي والتوظيف ، وبرامج الرعاية الإضافية الأخرى. هذه البرامج الوقائية مطلوبة من أجل

الوصول إلى أفضل نتيجة ممكنة في علاج مرضى الفصام والأفراد المعرضين للإصابة به.

يمثل أداء الفرد في مرحلة ما قبل المرض في مرض الفصام قيمة في توقع حدوث مواصفات معينة في صورة المرض.

وقد تم وضع العديد من الاختبارات لقياس أداء الفرد في مرحلة ما قبل المرض ومن هذه الاختبارات "مقياس التكيف في مرحلة ما قبل المرض المعدل" والذي يقوم بقياس القدرة على التأقلم قبل بداية المرض. وهو يعتبر من أوسع الاختبارات انتشاراً من حيث استخدامه مع مرضى الفصام.

وقد صممت هذه الدراسة لاختبار الافتراض الآتي "ضعف أداء الفرد في مرحلة ما قبل النوبة الأولى للفصام تؤدي إلى ظهور أعراض شديدة في أثناء النوبة الأولى للمرض".

تهدف هذه الدراسة إلى تقييم مستوى أداء الفرد قبل بداية النوبة الأولى للفصام وتقييم العلاقة بين مستوى أداء الفرد في مرحلة ما قبل المرض ، وشدة الأعراض المرضية أثناء النوبة الأولى لمرض الفصام وكذلك مستوى الاستجابة للعلاج (درجة التحسن) بعد ٦ أسابيع من بدايته بالإضافة إلى تقييم العلاقة بين وجود الضغوط النفسية في مرحلة ما قبل المرض وشدة الأعراض المرضية أثناء النوبة الأولى لمرض الفصام.

وتضمنت الدراسة مجموعة عشوائية من المرضى الذين يتم علاجهم داخل المستشفى أو المرضى المترددين على العيادات الخارجية وغرفة الاستقبال في مركز الطب النفسي بمستشفيات جامعة عين شمس. حيث يقع مركز الطب النفسي في شرق

مدينة القاهرة ، وتغطي خدماته حوالي ثلث مدينة القاهرة ويخدم كل من المناطق الحضرية والريفية ويوجد بالمركز أقسام داخلية مجانية وخاصة وبذلك يمثل المرضى كل طبقات المجتمع.

تضمنت الدراسة ٥٠ مريض مصري تنطبق عليهم الشروط التشخيصية لمرض الفصام وفقاً للتقسيم العالمي للأمراض (ICD-10) النوبة الأولى وليس لديه أي أمراض مصاحبة أو سبب عضوي للفصام ويتم تحديد شدة الأعراض وفقاً لمقياس " مقياس الأعراض السلبية والإيجابية " ويتم تقييم القدرة على التأقلم قبل بداية المرض عن طريق مقياس "مقياس التكيف في مرحلة ما قبل المرض المعدل"

وبالنسبة إلى تقييم شدة الضغوط النفسية التي تعرض لها المريض قبل بداية المرض تمت باستخدام مقياس " مقياس إعادة التكيف للضغوط الاجتماعية"

خضع المريض لاختبار ويسكونسون لترتيب الكروت لتقييم الوظائف التنفيذية للمخ ويتم استخدام مقياس ويكسلر لمقياس درجة الذكاء.

تم استخدام مقياس ايزينك (EPQ) لتقييم سمات الشخصية والتي تشمل على الإنطوائية والإنبساطية والعصابية والذهانية.

تم إعادة تقييم شدة الأعراض مرة أخرى بعد ٦ أسابيع باستخدام " مقياس الأعراض السلبية والإيجابية " لتحديد درجة تحسن المريض والاستجابة العلاجية قصيرة المدى.

تم استخدام المتوسط والانحراف المعياري لتمثيل البيانات الخاصة بكلاً من المقاييس العددية والأرقام والنسب للتقسيمات البيانية. ولمعرفة الاختلافات بين المجموعات ثم استخدام اختبار (T) لمعرفة التباينات المتساوية والغير متساوية لكل

منهم. بينما تم استخدام اختبار (Ranked Spermam Correlation) لدراسة مدى الارتباط لكل متغيرين لكل مجموعة تحت الدراسة.

فى حين تم تطبيق (Multiple Regression analysis) على مجموعة من المتغيرات لإيجاد معاملات الاحتمال التي تؤثر على درجة التحسن قصيرة المدى. مثل شدة الأعراض فى النوبة الأولى والوظائف التنفيذية للمخ وكذلك مجموعة العلاج المستخدمة فى علاج الأعراض المرضية.

أظهرت الدراسة أن معظم المرضى المشاركين بالدراسة كانوا رجال (٨٢%) وأغلبية الأفراد غير متزوجين (٨٢%) ومعظم المرضى يعيشون مع كلا الوالدين أو أحدهما.

بالنسبة للتاريخ العائلى المرضى لمرضى الفصام وقد وجد أن حوالي ٢٦% منهم لديه تاريخ مرضى للاضطراب الذهاني و٦% لديهم تاريخ مرضى للاضطراب المزاجى.

وقد تعرض ١٢ % من المرضى لضغوط نفسية بسيطة فى حين تعرض حوالي ١٤% لضغوط نفسية متوسطة فى مرحلة ما قبل المرض.

بالنسبة للأعراض الأولى التي يتقدم بها مريض النوبة الأولى للفصام وجد أن ٤٦% يشكو من أعراض عدوانية و ٢٨% أعراض انتحارية.

وبدراسة أداء الفرد فى مرحلة ما قبل المرض وجد انه يتميز بالاضطراب (حيث أن ٣٨% أداء متدهور و ٣٢% أداء متواضع مستقر) مع عدم وجود اختلاف بين الرجال والنساء من حيث الأداء فى مرحلة ما قبل المرض.

وبدراسة الوظائف التنفيذية للمخ فى مرضى الفصام ومقارنتها بالوظائف التنفيذية للمخ لأشخاص غير مرضى وجد أن مرضى النوبة الأولى يعانون من تدهور شديد فى الوظائف التنفيذية وخاصة تكوين المفاهيم ، المرونة المعرفية، الانتباه و كذلك القدرة على التعلم.

وقد وجد أن الأداء المتواضع فى مرحلة ما قبل المرض يرتبط بأعراض مرضية شديدة وخصوصاً الأعراض السلبية و أعراض اضطراب التفكير وكذلك يرتبط بتدهور الوظائف التنفيذية للمخ.

وبدراسة شدة الأعراض بعد ٦ أسابيع لمعرفة درجة التحسن بها وجد تفاوت فى درجات التحسن حيث أن الأعراض العدوانية هي الأفضل فى درجة التحسن يليها أعراض الإضطهاد ثم الأعراض الإيجابية يليها الأعراض السلبية والأقل فى درجة التحسن هي أعراض اضطراب التفكير.

من الجدير بالذكر أن درجة التحسن تقل فى وجود ضغوط نفسية شديدة وبالتالي تقل فرصة التعافي وتزيد فرص الانتكاس المرضى.

فى حين أن درجة الذكاء المرتفعة تزيد فرصة تحسن بعض الأعراض السلبية (Anergia).

وقد وجد أن درجة التحسن لا تعتمد على شدة الأعراض أو نوعها فى الأسبوع الأول وكذلك لا تعتمد على الوظائف التنفيذية للمخ ولا تختلف باختلاف مجموعة العلاج المستخدمة.

بالرغم من أن الملاحظات الإكلينيكية وكذلك معظم الدراسات السابقة فى هذا المجال تشير إلى أن هناك ارتباط بين الأداء الجيد للفرد فى مرحلة ما قبل المرض

والنتائج العلاجية لمرض الفصام سواء فى النوبة الأولى أو فى الحالات المزمنة إلا أن هذه الدراسة لم تستطع إثبات ذلك وهناك احتمال أن السبب وراء هذه النتيجة هو صغر حجم عينة الدراسة وكذلك قصر مدة المتابعة للمرضى فى هذه الدراسة.

أوضحت هذه الدراسة والدراسات الأخرى فى هذا المجال أهمية قياس أداء الفرد فى مرحلة ما قبل المرض وكذلك الارتباط بين هذا الأداء وشدة الأعراض.

وقد ألفت الضوء أيضا على أن متلازمة الفصام ليست متعددة الأوجه بالنسبة للأعراض والنتائج العلاجية فقط وإنما فى أداء الأفراد فى مرحلة ما قبل المرض

وتبرز قوة هذه الدراسة فى أنها سوف تمكنا من المقارنة بين النوبة الأولى لمرض الفصام فى المرضى المصريين ونفس المرض فى بلاد الغرب.

وكذلك دراسة الأداء فى مرحلة ما قبل المرض سوف تمكنا من وضع خطط تهدف الى التحديد المبكر للأفراد المعرضين للإصابة بمرض الفصام وخاصة الذين يتميزون بأداء متدهور فى هذه المرحلة بالإضافة إلى التدخل العلاجى المبكر مع هذه الحالات وبالتالي تحقيق التحسن الكامل لها وتقليل نسبة الإعاقة طويلة المدى لهم وتقليل التكاليف الناتجة عن الإصابة بالمرض.

تحمل هذه الدراسة بعض القصور منه أن تقييم أداء الفرد يتم باثر رجعى معتمدين فى هذا التقييم على ذاكرة المريض والمعلومات المتاحة من بعض أفراد العائلة مما يزيد نسبة الأخطاء فى جمع هذه المعلومات وكذلك فان صغر حجم عينة الدراسة يحدد القدرة الإحصائية لها وأخيرا عدم وجود عينة ضابطه لمقارنة نتائجهم مع مجموعة الدراسة.

وأخيراً, نوصى بالاهتمام بدراسة أداء الفرد في مرحلة ما قبل المرض
خصوصاً في دراسات طويلة المدى (مستقبلية) نظراً لأهمية هذه المرحلة في برامج
الاكتشاف المبكر للمرض في الأشخاص المعرضين للإصابة بالفصام أو غيره من
الاضطرابات العقلية.

Okasha et al. SRRS Compared with Holmes & Rahe SRRS

Items	Egyptians		Americans	
	Rank	Mean	Rank	Mean
Death of spouse	1	100	1	100
Divorce	2	81	2	73
Death of close Family member	3	76	5	60
Marital separation	4	75	3	65
Detention in prison	5	74	4	63
Change in health or behaviour of family member	6	62	11	44
Major Personal illness or injury	7	60	6	53
Marital reconciliation	8	59	10	45
Major change in living conditions	9	58	27	25
Being fired from work	10	56	8	47
Major business readjustment	11	52	15	38
Son/daughter leaving home	12	51	23	27
Pregnancy	13	51	12	40
Sexual difficulties	14	50	13	39
Gain new family member	15	50	14	39
Marriage	16	48	7	50
Out standing personal achievement	17	47	24	28
Change in financial state	18	45	16	38
Change in arguments with spouse	19	45	19	35
Death of a close friend	20	44	17	37
Retirement from work	21	42	9	46
Change in residence	22	42	31	20
Begin/end of formal Schooling	23	41	25	26
Change in work- responsibilities	24	40	21	29
Change to a different line of work	25	40	18	36

Items	Egyptians		Americans	
	Rank	Mean	Rank	Mean
Change in family gatherings	26	40	38	15
Wife begins/ends work	27	39	26	26
Morgage greater than £1000	28	34	20	31
Trouble with in-laws	29	33	22	29
Change in work conditions	30	33	30	20
Change in schools	31	30	32	20
Vacations	32	29	40	13
Changes in religious activities	33	28	34	19
Feasts	34	26	41	11
Change in recreation	35	25	33	19
Troubles with boss	36	25	29	23
Change in Social activities	37	24	35	18
Change in sleeping habits	38	22	37	16
Change in eating habits	39	21	39	15
Change in personal habits	40	18	28	24
Morgage less than £1000	41	17	36	17
Change in friends gatherings	42	17	42	11
Minor violations of law	43	15	43	11

مقياس التنكيف لمرحلة ما قبل المرض

تأليف : كانون سبور (١٩٨٢م)

ترجمة وإعداد : د/ مصطفى رسلان

أولاً : مرحلة الطفولة حتم سن ١١ عام :

١- الكفاءة الاجتماعية والميول الإنسحابية

الدرجة	الوصف
صفر	يسعى بنشاط إلى الاحتكاك الاجتماعي
٢	يسعى أحياناً إلى الاحتكاك الاجتماعي ويستمتع بها حينما تتاح له الفرصة
٤	يستجيب سلباً لدعوة الآخرين ويكثر من أحلام اليقظة
٦	شديد الانطواء ويتجنب الاحتكاك بالآخرين

٢- العلاقة بالقرناء

الدرجة	الوصف
صفر	كثير الأصدقاء وله علاقات وطيدة متعددة
٢	له علاقات وطيدة مع واحد أو اثنين كما قد يكون له علاقة صداقة عابرة وبالصدفة
٤	له علاقات ذات طابع غير عادي مثلاً مع سن أصغر أو أكبر بدرجة ملحوظة أو مع الأقارب فقط أو علاقات عابرة وبالصدفة
٦	في عزلة كاملة وليس له أصدقاء البتة ولا حتى علاقات عابرة وبالصدفة.

٣- الأداء الدراسي

الدرجة	الوصف
صفر	ممتاز دراسياً
٢	جيد دراسياً
٤	مقبول دراسياً
٦	راسب في الأداء الدراسي

٤- التكيف في المدرسة

الدرجة	الوصف
صفر	متكيف في المدرسة ويألف الزملاء ويحترم نظام المدرسة
٢	يتقبل المدرسة بالكاد وله أصدقاء وليس له نشاطاً مدرسياً غير المقرر المفروض
٤	لا يتقبل المدرسة إلا بصعوبة ويزوغ منها كثيراً وله مشاكل مع نظامها
٦	يرفض أي علاقة بالمدرسة وسلوكه يصل إلى درجة الانحراف أو تخريف أشيائها

ثانياً : مرحلة المراهقة الأولى (سن ١٢ - ١٥ عاماً) :

١- الكفاءة الاجتماعية والميول الانسحابية

الدرجة	الوصف
صفر	يسعى بنشاط إلى الاحتكاك الاجتماعي
٢	يسعى أحياناً إلى الاحتكاك الاجتماعي ويستمتع بها حينما تتاح له الفرصة
٤	يستجيب سلبياً لدعوة الآخرين ويكثر من أحلام اليقظة
٦	شديد الانطواء وتجنب الاحتكاك بالآخرين

٢- العلاقة بالقرناء

الدرجة	الوصف
صفر	كثير الأصدقاء وله علاقات وطيدة ومتعددة
٢	له علاقات وطيدة مع واحد أو اثنين كما قد يكون له علاقة صداقة عابرة وبالصدفة
٤	له علاقات ذات طابع غير عادي مثلاً مع سن أصغر أو أكبر بدرجة ملحوظة أو مع الأقارب فقط أو علاقات عابرة وبالصدفة
٦	في عزلة كاملة وليس له أصدقاء البتة ولا حتى علاقات عابرة بالصدفة

٣- الأداء الدراسي

الدرجة	الوصف
صفر	ممتاز دراسياً
٢	جيد دراسياً
٤	مقبول دراسياً
٦	راسب في الأداء الدراسي

٤- التكيف في المدرسة

الدرجة	الوصف
صفر	متكيف في المدرسة ويألف الزملاء ويحترم نظام المدرسة
٢	يتقبل المدرسة بالكاد وله أصدقاء وليس له نشاطاً مدرسياً غير المقرر المفروض
٤	لا يتقبل المدرسة إلا بصعوبة ويزوغ منها كثيراً وله مشاكل مع نظامها
٦	يرفض أي علاقة بالمدرسة وسلوكه يصل إلى درجة الانحراف أو تخريف أشيائها

٥- النشاط الجنسي

الدرجة	الوصف
صفر	يشعر برغبة جنسية تجاه الجنس الآخر ومصحوبة بخيال جنسي مع العادة السرية أو بدونها
١	يشعر برغبة جنسية تجاه الجنس الآخر ولكنها غير مصحوبة بخيال جنسي
٤	لا يشعر بأية أحاسيس جنسية
٥	يميل جنسياً إلى نفس الجنس ولكنه لا يمارس الجنس فعلاً
٦	يمارس الجنس مع نفس الجنس

ثالثاً : مرحلة المراهقة الثانية (١٦ - ١٨ سنة) :

١- الكفاءة الاجتماعية والميول الإنشائية

الدرجة	الوصف
صفر	يسعى بنشاط إلى الاحتكام الاجتماعي
٢	يسعى أحياناً إلى الاحتكاك الاجتماعي ويستمتع بها حينما تتاح له الفرصة
٤	يستجيب سلباً لدعوة الآخرين ويكثر من أحلام اليقظة
٦	شديد الانطواء وتجنب الاحتكاك بالآخرين

٢- العلاقة بالقرناء

الدرجة	الوصف
صفر	كثير الأصدقاء وله علاقات وطيدة ومتعددة
٢	له علاقات وطيدة مع واحد أو اثنين كما قد يكون له علاقة صداقة عابرة وبالصدفة
٤	له علاقات ذات طابع غير عادي مثلاً مع سن أصغر أو أكبر بدرجة ملحوظة أو مع الأقارب فقط أو علاقات عابرة وبالصدفة
٦	في عزلة كاملة وليس له أصدقاء البتة ولا حتى علاقات عابرة بالصدفة

٣- الأداء الدراسي

الدرجة	الوصف
صفر	ممتاز دراسياً
٢	جيد دراسياً
٤	مقبول دراسياً
٦	راسب في الأداء الدراسي

٤- التكيف في المدرسة

الدرجة	الوصف
صفر	متكيف في المدرسة وبألف الزملاء ويحترم نظام المدرسة
٢	يتقبل المدرسة بالكاد وله أصدقاء وليس له نشاطاً مدرسياً غير المقرر المنروض
٤	لا يتقبل المدرسة إلا بصعوبة ويزوغ منها كثيراً وله مشاكل مع نظامها
٦	يرفض أي علاقة بالمدرسة وسلوكه يصل إلى درجة الانحراف أو تخريف أشيائها

٥- النشاط الجنسي

الدرجة	الوصف
صفر	يشعر برغبة جنسية تجاه الجنس الآخر ومصحوبة بخيال جنسي مع العادة السرية أو بدونها
١	يشعر برغبة جنسية تجاه الجنس الآخر ولكنها غير مصحوبة بخيال جنسي
٤	لا يشعر بأية أحاسيس جنسية
٥	يميل جنسياً إلى نفس الجنس ولكنه لا يمارس الجنس فعلاً
٦	يمارس الجنس مع نفس الجنس

رابعاً : مرحلة الرجولة (عمر ١٩ سنة فما فوق) :

١- الكفاءة الاجتماعية والميول الإنسحابية

الدرجة	الوصف
صفر	يسعى بنشاط إلى الاحتكاك الاجتماعي
٢	يسعى أحياناً إلى الاحتكاك الاجتماعي ويستمتع بها حينما تتاح له الفرصة
٤	يستجيب سلبياً لدعوة الآخرين ويكثر من أحلام اليقظة
٦	شديد الإنطواء وتجنب الاحتكاك بالآخرين

٢- العلاقة بالقرناء

الدرجة	الوصف
صفر	كثير الأصدقاء وله علاقات وطيدة ومتعددة
٢	له علاقات وطيدة مع واحد أو اثنين كما قد يكون له علاقة صداقة عابرة وبالصدفة
٤	له علاقات ذات طابع غير عادي مثلاً مع سن أصغر أو أكبر بدرجة ملحوظة أو مع الأقارب فقط أو علاقات عابرة وبالصدفة
٦	في عزلة كاملة وليس له أصدقاء البتة ولا حتى علاقات عابرة بالصدفة

٣- الأداء الدرسي

[أ] متزوج حالياً أو سابقاً ،

الدرجة	الوصف
صفر	تزوج مرة واحدة أو تزوج مرة أخرى نتيجة وفاة الزوجة الأولى ومتوافق مع شريك العمر والعلاقة الجنسية جيدة.
١	تزوج مرة ثانية نتيجة الطلاق الأول أو متعدد الزوجات مع وجود تكيف جنسي جيد في إحدى الزوجتين على الأقل
٢	متزوج ويعاني من مشاكل جنسية مختلفة أو مطلق ولكنه استمر ثلاث سنوات على الأقل متزوجاً.
٣	تزوج بعد طلاقه الأول ويعاني من مشاكل جنسية من الزوجتين
٤	أ (مطلق منذ أكثر من ٣ سنوات وكان يعاني من مشاكل جنسية أثناء الزواج ب) متزوج وله علاقات جنسية أخرى خارج نطاق الزواج

[ب] لم يتزوج وتعدى سن الخامسة والثلاثين ،

الدرجة	الوصف
٢	خطوبة أو أكثر أو ارتباط عاطفي مع الجنس الآخر واستمر الارتباط لفترة معقولة مع وجود دلائل على وجود ظروف قهرية عاقت الزواج
٣	علاقة حب أو خطوبة ولكن لفترة قصيرة
٤	علاقات سطحية قصيرة الفترة ولا توجد دلائل على وجود العاطفة والارتباط
٥	علاقات طارئة ونادرة
٦	لا يرغب إطلاقاً في الجنس الآخر والارتباط به

[جأ لم يتزوج ولم يتعدى سن الخامسة والثلاثين

الدرجة	الوصف
صفر	علاقة حب أو خطوبة إختيارية ودامت فترة معقولة
٣	صداقات متعددة مع الجنس الآخر ولكنها سطحية بدون حب أو إرتباط
٤	علاقات سطحية قصيرة المدى (بضع أسابيع) مع الجنس الآخر ولا تصل لدرجة الصداقة
٥	علاقات عارضة ونادرة مع الجنس الآخر
٦	لا توجد رغبة بتأناً تجاه الجنس الآخر

الاسم: جيهان عبد السلام عبد المقصود مصطفى

Cellular: 0105373378

E-mail: jina7s91@yahoo.com

Jihanmostafa@okashahospital.com

CHAPTER (I)

Historical Background of Schizophrenia

Symptoms relating to schizophrenia have been noted since the age of antiquity. A popular belief was that strange behavior was a result of possession by the devil or assaults from the gods for immoral behavior (a kind of punishment). Ethnographic studies have demonstrated that schizophrenia is present in all existing cultures (*Kyziridis, 2005*).

History of schizophrenia passes in different steps as follow

Benedict A. Morel

Morel coined the term *démence précoce* to refer to mental state and behavior of young patients with *stupidité* (stupor). By dementia he meant any state of psychosocial incompetence related to a mental disorder and occurring at any age, the criterion of irreversibility did not yet exist. In this sense, the term *démence précoce* has little relationship to the work of Kraepelin or Bleuler (*Berrios, 2005*).

Emil Kraepelin

A nonspecific concept of "madness" has been around for many thousands of years, but schizophrenia was only classified as a distinct mental disorder by Kraepelin in 1893 (*Kraepelin, 1907*).

Emil Kraepelin delineate two major pattern of insanity-manic-depressive psychosis and dementia praecox (or dementia of the young) (*Buchananand Carpenter, 2005*), thus he was the first to make a distinction in the psychotic disorders between what he called *dementia praecox* (a term first used by psychiatrist Benedict A. Morel) and manic depression(*Kraepelin, 1907*).

Kraepelin believed that dementia praecox was primarily a disease of the brain (*Kraepelin, 1907*), that described patients who showed a global disruption of perceptual and cognitive processes (dementia) and an early onset (praecox) (*Tsuang et al., 2000*).

Kraepelin named the disorder 'dementia praecox' (early dementia) to distinguish it from other forms of dementia (such as Alzheimer's disease) which typically occur late in life. He used this term because his studies focused on young adults with dementia (*Hansen and Atchison, 2000*).

Kraepelin's dementia praecox patients usually had an illness onset in early adulthood and a progressively

deteriorating course with no return to premorbid levels of function. These features contrasted with the relatively intact thinking, later onset, and episodic nature of illness in patients with manic-depressive psychoses, whose episodes of psychopathology alternated with periods of normal function (*Tsuang et al., 2000*). In addition to relatively non deteriorating course of manic-depressive illness (*Buchanan and Carpenter, 2005*).

Kraepelin went on to describe the two principals pathophysiological or disease processes occurring in dementia praecox, those were:-

- Destruction of the personality provides a conceptual framework for the a volitional or negative symptom component of the illness
- The loss of the inner unity of activities” process provides a conceptual frame work for the positive symptoms of schizophrenia (*Buchanan and Carpenter, 2005*).

He divided dementia praecox into 4 subtypes: paranoid, hebephrenic, catatonic, and simple. The paranoid patient primarily exhibited persecutory delusions. The hebephrenic individual presented with silly and facetious behaviors. The hallmarks of the catatonic patient were motor symptoms such as increased muscle tone and

sustained postures. The simple subtype exhibited apathy as well as social withdrawal and decline rather than florid psychotic symptoms (*Krieger, 1971*).

Eugen Bleuler

Eugen Bleuler (1857-1959) was the director of Burghlozli clinic and professor of psychiatry in Zurich. He based his work on that of Kraepelin, and in his own book wrote the whole idea of dementia praecox originates with Kraepelin (*Gelder et al., 2005*).

Bleuler proposed the name schizophrenia to denote "a splitting of psychic function, which he thought to be of central importance (*Gelder et al., 2005*).

In 1908 *Eugen Bleuler* coined the term *schizophrenia* to refer to the lack of interaction between thought processes and perception. He was also the first to describe the symptoms as "positive" or "negative." (*Kraepelin, 1907*). He suggested the name schizophrenia, as it was obvious that Kraepelin's name was misleading. The word "praecox" implied precocious or early onset, hence premature dementia, as opposed to senile dementia from old age. Bleuler realized that the illness was not a dementia as some of his patients improved rather than following a deteriorating course (*Stotz-Ingenlath, 2000; Hansen and Atchison, 2000*).

Compared with Kraepelin, Bleuler was concerned less with prognosis and more with the mechanisms of symptom formation. Since Bleuler was preoccupied more with psychopathological mechanisms than with symptoms themselves, his approach to diagnosis was less precise than that of Kraepelin (*Gelder et al., 2005*).

Bleuler introduced the concept of primary and secondary schizophrenic symptoms; his four primary symptoms (the four as) were abnormal associations, autistic behavior and thinking, abnormal affect, and ambivalence (*Buchanan and Carpenter, 2005*).

Eugen Bleuler, in 1915, wrote about the etiology of schizophrenia: “One must acknowledge that, at least the great majority of clinical pictures, which are now collected under the name of *dementia praecox*, rests on some toxic action or anatomical process, which arises independently of psychic influences . . . The principal group is, in my opinion, certainly caused by organic changes” (*Lehmann and Ban, 1997*).

Bleuler's view that a dissociative processes is fundamental to schizophrenia and that this process underlies a wide variety of the symptom manifestations of schizophrenia has provided a major paradigm for conceptualizing the illness, that is, that in spite of its various manifestations, schizophrenia is a single disease

entity in which there is extensive similarity in etiology (cause) and pathophysiology (mechanism) across all patients with the disorder. In this view, a neurophysiologic disturbance of indeterminate origin and nature occurs that is manifested as dissociative processes adversely influencing the development of mental capacities in the areas of thought, emotion, and behavior. Depending on the individual's adaptive capacity and environmental circumstances, this fundamental process could lead to secondary disease manifestations, such as hallucinations, delusions, social withdrawal, and diminished drive (*Buchanan and Carpenter, 2005*).

Splitting

Splitting were originating in early nineteenth century romantic psychology and the work of Herbat, the mechanism of separating, dividing, breaking, dissociating, divorcing, or splitting of mental functions was a common explanation for any unpredictable or strange human behavior. For example, it is present in Wigan's two-brains model, Stevenson's, Dr Jekyll and Mr. Hyde, Hartmann's model of the unconscious, Jackson's hierarchical model of the brain, Azam's dissociation, Charcot's hysteria and Freud's splitting of the ego. The mechanism of splitting was popular in German psychiatry at the time when Bleuler coined the term of schizophrenia (*Berrios, 2005*).

Adolph Meyer

Adolph Meyer, an American theorist was founder of the psychobiological school of psychiatry. He contended that psychological symptoms emanated directly from the patient's past social, physical and psychological issues. He believed that each individual's psychiatric disorder was unique and therefore was unable to accept the classificatory schemas of either Kraepelin or Bleuler. He also rejected Freudian assertions of the presence of hidden psychodynamic factors causing the mental madness (*Meyer, 1952*).

German psychiatrists

Several German psychiatrists tried to define sub groupings within schizophrenia.

Karl Kleist, looked for associations between brain pathology and different subtypes of psychotic illness, he used careful clinical observation in an attempt to distinguish various subdivisions within schizophrenia and other atypical disorders. His attempt to match these subtypes to specific kind of brain pathology was ingenious but not successful (*Kleist 1928; Gelder et al., 2005*).

Also *Leonhard* divided schizophrenia in to two groups. **The first group** is characterized by a progressive

course, and is divided into catatonias, hebephrenias, and paraphremas. Leonhard gave this group a name which is often translated as *systematic* and **the second group**, called *non-systematic*, is divided into affect-laden paraphrenia, schizophasia, and periodic catatonia. Affect-laden paraphrenia is characterized by paranoid delusions and the expression of strong emotion about their content. In schizophasia, speech is grossly disordered and difficult to understand. Periodic catatonia is a condition with regular remissions; during an episode, kinetic symptoms are sometimes interrupted by hyperkinetic symptoms (Leonhard, 1957; Gelder et al., 2005).

Scandinavian psychiatrist “Langfeldt”

In the late 1930s, Scandinavian psychiatrist Langfeldt, using follow-up data on patients in Oslo, proposed a distinction between true schizophrenia, which had a poor prognosis and schizophreniform states, which had a good prognosis (Langfeldt, 1961; Gelder et al., 2005).

True schizophrenia was characterized by emotional blunting, lack of initiative, paranoid symptoms, and primary delusions. Schizophreniform states were described as often precipitated by stress and frequently accompanied by confusional and affective symptoms. According to modern diagnostic criteria, most of Langfeldt's cases or

schizophreniform psychosis would, in fact, be classified as mood disorder (*Bergen et al., 1990; Gelder et al., 2005*).

Denmark and Norway psychiatrists

In Denmark and Norway, cases of psychosis arising after stressful events have received much attention. The term reactive psychosis or psychogenic psychosis are commonly applied to conditions which appear to be precipitated by stress, are to some extent understandable in their symptoms, and have good prognosis. In current diagnostic scheme such disorders would be classified as brief psychotic disorder or schizophreniform disorder (*Pitta and Blay, 1997*).

Kurt Schneider

Other clinicians also advocated a hierarchical system of symptom classification like Bleuler's. In 1959, Kurt Schneider termed the core features "first-rank" symptoms (*Schneider, 1959*) these symptoms included:

- Hearing one's thoughts spoken aloud
- Auditory hallucinations commenting on one's own behavior
- Thought withdrawal, insertion and broadcasting
- Somatic hallucinations, or the experience of one's thoughts as being controlled or influenced from the outside

Manifestation of one of the first-rank symptoms in the absence of organic disease, persistent affective disorder, or drug intoxication, was sufficient for a diagnosis of schizophrenia (*Schneider, 1959*).

Second-rank symptoms included other forms of hallucinations, depressive or euphoric mood changes, emotional blunting, perplexity, and sudden delusional ideas (*Schneider, 1959*).

When first-rank symptoms were absent, schizophrenia might still be diagnosed if a sufficient number of second-rank symptoms was present (*Schneider, 1959*).

For Schneider, the first-rank symptoms were not

pathognomonic but suggested a diagnosis of schizophrenia only if there was no evidence of any other organic psychosis. The eleven first-rank symptoms only gain meaning when sought in the context of three diagnostic perspectives which were, course, symptomatology and interaction (*Berrios, 2005*).

Although the schneiderian criteria have been criticized as being nonspecific, they have been incorporated into clinical diagnostic tools such as the Research Diagnostic Criteria (RDC) and Diagnostic and Statistical Manual of Mental Disorders (DSM) classificatory systems (*Schneider, 1959*).

There is no continuity between Schneider's notion of schizophrenia and earlier views; hence it is nonsense to choose some criteria from Kraepelin (i.e. course and duration), others from Bleuler (formal thought disorder), and yet others from Schneider (First rank symptoms). It is nonsense because each of these alienists has a different (and non-additive) definition of schizophrenia, and hence the clinical features that each described only make sense in terms of their own conception (*Berrios, 2005*).

Diagnostic and Statistical Manual of Mental Disorders (DSM)

In 1949, the American Psychiatric Association in collaboration with the New York Academy of Medicine began to standardize the diagnostic system throughout the United States. The result was the Diagnostic and Statistical Manual of Mental Disorders (DSM-I), which was published in 1952. The classification was influenced by the theories of Adolf Meyer. And psychiatric disorders were viewed as reactions of the personality to psychological, social, and biological factors (*American Psychiatric Association, 1994*).

The manual has gone through several major revisions. The *DSM-II* was published in 1968, but did not differ significantly from its predecessor. The *DSM-III* was published in 1980, the *DSM-IV* in 1994, (*American Psychiatric Association, 1994*) and *DSM-IV-TR* in 2000 (*American Psychiatric Association, 2000*).

Attempts were made to make the manual theoretically neutral and based on a descriptive lists or clusters of symptoms. Previous editions of the manual contained categories that was vague and often based on unobservable processes that could not be agreed upon by different practitioners. The *DSM-IV* outlines seventeen different categories of mental disorders. Schizophrenia and other related disorders include schizophrenia, delusional

disorder, and schizoaffective disorder. Schizophrenia is divided into five subtypes including paranoid, disorganized, catatonic, undifferentiated, and residual.

The Diagnostic and Statistical Manual (DSM-IV) is considered the most authoritative resource for the characterization of mental health disorders. The Manual divides the symptomology of the disease into two broad categories: positive symptoms and negative symptoms.

Positive symptoms are behavioral abnormalities that include “hallucinations, delusions, impaired perception, impaired inferential thinking, incoherence, illogical thought progression, irrational behavior,” and unregulated emotions (DSM-IV 273-278). The “negative symptoms” are behavioral deficits that may include a lack of energy, drive, initiative, and interest, in addition to poor concentration and attention, social withdrawal, emotional unresponsiveness, and impaired social and daily living skills (*American Psychiatric Association, 1994*).

Most afflicted individuals are young male adults and episodes typically peak between the ages of 19 and 25, with a later and broader peak for women between the ages of 26 and 45.

Although there is controversy concerning the degree to which symptoms are treatable, there is agreement that while these symptoms are manifest, they are substantial obstacles to self-fulfillment that may render afflicted persons totally incapable of self-care because many affected persons are hesitant to seek help.

The disease is further complicated by the unwillingness of those affected by the disease to report the symptoms of their illness. In addition to the costs of treatment and lack of productivity, the devastating consequences on an individual's family life, social relations, and productive cognitive capacities affect his or her future employment prospects (*Andreasen and Schultz, 1996*).

International Classification of Diseases (ICD)

In 1948, the World Health Organization (WHO) published the first International Classification of Diseases (ICD). This coding system was developed by (WHO) to provide international consistency for reporting mortality statistics only. Numbers were added with subsequent revisions to identify the new "version". Thus the nomenclature became ICD-2, ICD-3 and so forth. ICD-9 and ICD-10, the most current versions, are copyrighted by the World Health Organization (WHO). ICD-10 is the latest

version. Effective January 1, 1999, ICD-10 officially was implemented in the United States for reporting the cause of death on death certificates (*World Health Organization, 1993*).

A tenth version of the International Classification of Diseases (ICD-10) is currently being prepared by the World Health Organization, who called for field trials of suggested guidelines. A field trial of the guidelines for the diagnosis of schizophrenia is presented. There is a consistency with ICD-9-based diagnosis. Schneider's first-rank symptoms acquire special importance in the suggested guidelines, but caution is necessary in detecting these symptoms in cultures in which socioculturally shared beliefs bear a resemblance to first-rank symptoms (*World Health Organization, 1993*).

The clinical discovery of antipsychotic drugs

This somatic perception of schizophrenia, which was certainly not shared by North American Psychiatry in the 1930s and 1940s, was proved to be correct only with the introduction of clinically effective pharmacotherapy in the 1950s. It is not often mentioned that the clinical discovery of antipsychotic drugs served as important, albeit indirect, evidence of schizophrenia's physical substrate which, in turn, led to essential new insights into the neuroscientific

dynamics of schizophrenia (*Lehmann and Ban, 1997*).

The Japanese classification

Concerns about potential stigma associated with having a serious mental illness have resulted in proposals to change the name of schizophrenia. "Integration disorder" and "dopamine dysregulation disorder" have been suggested as possible alternatives (*Lieberman and First, 2007*).

The Japanese classification has renamed schizophrenia as "integration disorder" in 2004. The change appears understandable in the light of translation of the word "schizophrenia" in to Japanese, as "Seishin Bunretsu Byo" means "mind-split-disease". It is not difficult to see as to how the term would seem pejorative to the patients and their families. The new term "Togo Shitcho Sho", with the meaning of "integration disorder", seems therefore more positive to the patients and their families (*Sugiura et al., 2001; Sato, 2006*).

DSM- V and ICD-11

The development of DSM-V and ICD-11, due for publication in 2011, provides an opportunity now to develop more accurate, specific and acceptable terminology as part of broader efforts to reduce stigmatization.

Vulnerability to schizophrenia

In the first half of the twentieth century schizophrenia was considered by many to be a "hereditary defect", and individuals affected by schizophrenia became subject to eugenics in many countries (*Read and Masson, 2004*).

Compared with normal controls, people with schizophrenia have abnormalities in brain structure and function seen on neuroimaging and electrophysiological tests. In addition, the evidence that vulnerability to schizophrenia is at least partly genetic is indisputable (*Lieberman and First, 2007*).

CHAPTER (II)

Symptoms of First Episode Schizophrenia

Schizophrenia is the commonest chronic variety of psychosis in psychiatric service places. It represents the bulk of inpatients in mental hospitals. 7.44 to 15.3 percent of the total newly examined cases in university hospitals in Egypt were labeled with the diagnosis of schizophrenia (*Okasha 1967, 1977; Rakhawy et al., 1978*).

In the year 2000, a study done to evaluate the capacity of emergency room service in Ain Shams university hospital as well as the diagnostic characteristics of patients attending this service, it was found that schizophrenic patients represent 25 percent of patients attending emergency room (*Effat, 2000*).

First-episode schizophrenia represents a diagnostic challenge because of symptomatic overlap between the various causes of psychosis. An early and accurate diagnosis is important for the implementation of appropriate treatment, for determining the prognosis and for identifying research participants (*Gelber et al., 2004*).

Thus, over the past decade, there has been a great upsurge in interest in studies focusing on the first episode

of schizophrenia.

It has also become clear that the early course of schizophrenia is punctuated by:-

I. *The premorbid phase:*

It is characterized by subtle cognitive and social difficulties.

II. *The prodromal phase:*

It is characterized by gradual beginning of subtle psychotic-like symptoms, social withdrawal and functional decline.

The term "prodrome" is derived from the Greek word *prodromos* meaning the forerunner of an event (*Fava and Kellne, 1991*).

It is defined as "a heterogeneous group of behaviors temporally related to the onset of psychosis" (*Keith and Matthews, 1991*).

And the definition used by *Loebel et al. (1992)* was the time interval from onset of unusual behavioral symptoms to the onset of psychotic symptoms.

Also, *Beiser et al. (1993)* defined it as the period from first noticeable symptoms to first prominent psychotic symptoms.

In schizophrenia, the prodrome may be thought of in two ways: **(1)** as the earliest, prepsychotic form of a psychotic disorder (an attenuated form of a psychotic process), or **(2)** as a syndrome that confers a heightened

vulnerability to developing psychosis, though psychosis is not inevitable (*Yung and McGorry, 1996*).

As in clinical medicine, prodrome is a retrospective concept, diagnosed only after the development of definitive symptoms and signs (*Yung and McGorry, 1996*) and the term "prodrome" has been used by some authors to denote the prepsychotic period before a relapse in those patients with established psychotic illnesses (*Birchwood et al., 1989; Malla and Norman, 1994*).

More accurate characterization of the prodrome can help identifying high-risk individuals when they first manifest subtle changes in mental state suggestive of impending psychosis (*Fenton and McGlashan, 1987; Yung and McGorry, 1996*).

Recently, it was found that the early adolescent patients presented with a number of symptoms consistent with a schizophrenia prodrome, including a long-standing history of difficulties with attention, a recent history of cognitive decline, social withdrawal, and what appears to be psychotic symptoms and these symptoms explained in terms of major depression with psychotic features, bipolar affective disorder, substance use disorder, posttraumatic stress disorder (PTSD), or even an aberration in the

maturation and solidification of personality structure (*White et al., 2006*).

The presence and duration of prodromal symptoms may predict outcome in schizophrenia, that is, long duration of prodromal symptoms may be indicative of poor prognosis (*Fenton and McGlashan, 1987; Yung and McGorry, 1996*).

Prodromal symptoms and signs have different presentations for example:-

- *Neurotic symptoms.....*Anxiety, restlessness, anger and irritability (*Hafner et al., 1992; Hambrecht et al., 1994*).
- *Mood-related symptoms.....* Depression, anhedonia, guilt, suicidal ideas (*Hafner et al., 1992; Hambrecht et al., 1994*) and mood swings (*Bowers and Freedman, 1966; Bowers, 1968*).
- *Changes in volition.....* Apathy, loss of drive, boredom, loss of interest, fatigue and loss of energy (*Hafner et al., 1992; Hambrecht et al., 1994*).
- *Cognitive changes.....* Disturbance of attention, inability to concentrate, preoccupation, daydreaming, thought blocking (*Hafner et al., 1992; Hambrecht et al., 1994*) and reduced abstraction (*Meares, 1959*).

- *Physical symptoms.....* Somatic complaints, loss of weight, poor appetite and sleep disturbance (*Hafner et al., 1992; Hambrecht et al., 1994*).
- *Other symptoms.....* Obsessive compulsive phenomena, dissociative phenomena (*Docherty et al., 1978*), increased interpersonal sensitivity, change in sense of self, others, or the world, change in motility Speech abnormalities, perceptual abnormalities (*Hafner et al., 1992; Hambrecht et al., 1994*), suspiciousness (*Birchwood et al., 1989*), and change in affect (*Varsamis and Adamson, 1971*).
- *Behavioral changes.....* Deterioration in school, work, or other role functioning, social withdrawal, impulsivity (*Docherty et al., 1978*), odd behavior, and aggressive disruptive behavior (*Hafner et al., 1992; Hambrecht et al., 1994*) .

III. *The psychotic phase:*

It is characterized by florid symptoms such as hallucinations and delusions.

The psychotic phase diagnosed according to currently two main diagnostic systems which are the ICD and DSM.

International classification of diseases (ICD) that diagnose schizophrenia by at least one month of delusions,

hallucinations, disorganized speech, grossly disorganized or catatonic behavior, or negative symptoms according to criteria listed in [table \(i\)](#)

And the American Psychiatric Association's (APA) Diagnostic and Statistical Manual for Mental Disorders (DSM) that diagnose schizophrenia by at least six month of delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, or negative symptoms according to criteria listed in [table \(ii\)](#)

Numerous studies subcategorize the symptoms of this illness (as well as symptoms of some other disorders) into five dimensions:

1. Positive symptoms.
2. Negative symptoms.
3. Cognitive symptoms.
4. Aggressive/hostile symptoms.
5. Depressive/anxious symptoms (*Stahl, 2002*).

1- Positive symptoms

Positive symptoms seem to reflect an *excess* of normal functions and typically include delusions and hallucinations; they may also include distortions or exaggerations in language and communication (disorganized speech), as well as in behavioral monitoring (grossly disorganized or catatonic or agitated behavior)

(*Stahl, 2002*).

Delusions usually involve a misinterpretation of perceptions or experiences. The most common type of delusion in schizophrenia is persecutory, but the delusions may include variety of other themes, including referential (i.e., erroneously thinking that something refers to oneself), somatic, religious, or grandiose.

Hallucinations may occur in any sensory modality (e.g., auditory, visual, olfactory, gustatory, and tactile), but auditory hallucinations are by far the most common and characteristic hallucinations in schizophrenia (*Stahl, 2002*).

2- Negative symptoms

Negative symptoms represent an intractable and disabling feature for patients, often amounting to a severe burden on families, careers and the patients themselves. It refers to a reduction in normal functioning (*Winograd-Gurvich et al., 2006*).

Negative symptoms include:

- *Affective flattening* is a common negative symptom that is characterized by a marked decrease in the range and intensity of emotional expression.

- *Alogia* is a decrease in the amount and content of speech. Patients experiencing alogia show less spontaneous speech and speak less fluently. In conversations, their answers are brief and often lack original content and ideas
- *Avolition* is a decreased ability to initiate activities. These symptoms can severely restrict a patient's experiences and opportunities for social development.
- *Social/occupational dysfunction* for a significant portion of time since the onset of a disturbance, one or more areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset of the disturbance (*American Psychiatric Association, 2000*).

Negative symptoms are heterogeneous, consists of primary and secondary negative symptoms (*Brazo et al., 2005*). Primary negative symptoms are considered to be a core to primary deficits of schizophrenia itself. Yet, secondary negative symptoms are that the deficits thought to be secondary to the positive symptoms of psychosis (*Stahl, 2002*).

In addition, in 2005, a study supported the view that primary and secondary negative symptoms could be associated with different levels of executive/ attentional dysfunctions was done and it was found that these

functions are significantly more impaired in patients with primary than in patients with secondary negative symptoms independently of their IQ (*Brazo et al., 2005*).

3- Cognitive symptoms

Neurocognitive function in first-episode psychosis is described by at least five independent dimensions these are, working memory (WM); verbal learning (VL); executive function (EF); impulsivity (Im); and motor speed (MS) (*Friis et al., 2002*).

Multiple areas of cognitive functioning are often impaired in patients with schizophrenia (*Harvey and Keefe, 1997*) as 75 percent of patients have significant cognitive impairment. That pre-dates the illness onset and considered as an intrinsic part of the illness that is observed in young, drug-naïve patients (*O'Carroll, 2000*).

4- Aggressive/hostile symptoms

Aggressive and hostile symptoms can overlap with positive symptoms but specifically emphasize problems in impulse control. They include overt hostility, such as verbal or physical abusiveness or even assault. Such symptoms also include self-injurious behaviors, including suicide and other property damage. Other types of impulsiveness, such as sexual acting out, are also in this category of aggressive and hostile symptoms

(*Stahl, 2002*).

Aggressive behavior against self and others is a frequent symptom of schizophrenia especially in the first two years of illness and plays a major role in rehospitalization (*Steinert et al., 1999*).

Yet recent study reported that physical violence towards other people is uncommon in individuals presenting with first episode psychosis (*Foley et al., 2005*).

There is a fairly specific relationship between violence on one hand and paranoid ideas and perceptions on the other, with the latter expressed on a continuum ranging from cognitive personality style and referential thinking to malignant, encapsulated delusions (*Nestor, 2002*).

Patients with schizophrenia have increased mortality risk due to physical illness, accidents, and other causes of violent death, especially suicide and some evidence supports that being unmarried, socially isolated, and unemployed are risk factors for suicide among schizophrenics as well (*Conwell et al., 1998*).

In terms of studying the association between schizophrenia and suicide, reports over the past two years

have described studies of both (1) the occurrence of suicide in populations of schizophrenia patients, and (2) the presence of schizophrenia in individuals who have attempted or completed suicide.

The cohort studies in schizophrenia confirm prior observations of increased attempted and completed suicide in schizophrenia, but yield discrepant findings with regard to whether only males or both males and females suffering from schizophrenia exhibit this increase in suicidal behavior.

In a recent 1-year follow-up study of first-episode psychosis, 11 percent of individuals attempted suicide, with hallucinations and a history of prior suicidal attempts being the strongest predictors of suicidal behavior.

On the other hand studies of the prevalence of the diagnosis of schizophrenia in individuals exhibiting suicidal behavior document the fact that a higher proportion of individuals exhibiting suicidal behavior suffer from schizophrenia, this association is more pronounced in individuals who utilize more violent methods (*Tandon and Jibson, 2003*).

In addition, deliberate self-harm (DSH) is a strong predictor of suicide in schizophrenia as past depressive episode, drug abuse or dependence. Higher mean number of psychiatric admissions was associated with an increased risk of deliberate self-harm. So, schizophrenic patients, with these risk factors, need careful follow-up and monitoring. Together with treatment of any associated comorbid depression or drug abuse (*Haw et al., 2005*).

According to the previous data, effectively treating positive symptoms and depression, reducing substance abuse, avoiding akathisia, addressing demoralization and instilling hope are important elements in the treatment approach. The newer generation of antipsychotics and developing psychological approaches (particularly cognitive-behavioral therapy) appear to be useful in reducing suicidality in schizophrenia (*Tandon and Jibson, 2003*).

5- Depressive and anxious symptoms

Depressive and anxious symptoms are frequently associated with schizophrenia, but this does not necessarily mean that they fulfill the diagnostic criteria for a comorbid anxiety or affective disorder. Nevertheless, depressed mood, anxious mood, guilt, tension, irritability, and worry frequently accompany schizophrenia (*Stahl, 2002*).

Also, depressive symptoms often precede psychosis, in two senses: **(1)**: before the first episode of clear-cut psychosis, most patients have a period of nonpsychotic symptoms that lasts weeks to months and that frequently include depressive symptoms, and **(2)**: in patients with a previous history of psychotic symptoms, a subsequent psychotic exacerbation may be preceded by symptoms that include depressive mood, anxiety, irritability, and increasing psychotic like experience. As is the case in other disorders, anxiety is associated with depression in schizophrenia (*Kirkpatrick and Tek, 2005*).

IV. *The transitional or recovery phase:*

It is characterized by a return to functioning but with increased proneness to relapses and co morbid difficulties.

It is the period in which the patient returns to functioning but with increased proneness to relapses and comorbid difficulties (*Keshavan, 2005*).

Prospective studies have shown that psychotic relapse can be predicted with a sensitivity of 50 to 79 percent and a specificity of 75 to 81 percent when standardized measures of 'neurotic' or 'dysphoric' symptoms are combined with those of low-level psychotic symptoms and ratings are conducted at least fortnightly

(Birchwood et al., 2000).

Changes in thought, affect and behavior for example 'Dysphoric' symptoms (depressed mood, withdrawal, sleep and appetite problems) are conceptualized as 'early warning signs' of psychotic relapse *(Birchwood et al., 2000).*

However, there is a considerable variability between individuals in the nature and timing of their early warning signs and predictors of relapse. It would be more accurate if the changes in early warning scores are evaluated against individuals' own baseline scores rather than compared with those of other patients. Thus, to be clinically useful, methods of identifying early warning signs of psychotic relapse must take into account this individual variation.

Research attention has recently been directed towards identifying and managing each patient's 'relapses signature' (his or her unique pattern of early warning signs most likely to indicate impending psychotic relapse *(Birchwood et al., 2000).*

V. *The stable or residual phase:*

It is characterized by persistent cognitive and social deficits *(Keshavan, 2005).*

CHAPTER (III)

Cognitive Functions in Schizophrenia

Schizophrenia implicates disturbances in several cognitive domains (*Joyce et al, 2005*) including deficits in executive function, attention, memory and language (*Kuperberg and Heckers, 2000*).

Patients with schizophrenia, exhibit wide-ranging impairments on neuropsychological tasks, compared to healthy subjects, including tasks measuring memory, attention, and executive function (*Rund et al, 2004*).

Several studies show that patients with schizophrenia perform poorly in the WCST categories and commit more errors on the test than normal subjects (*Everett J et al., 2001*).

A further delineation of dysfunctional cognitive processes would provide information about the neurobiology of the disorder as well as contribute to its rehabilitation. Abnormalities detected earlier in development are more likely to be etiological (*Rund et al, 2004*).

First-episode psychosis is an optimal disorder for

examining the neurobiology of the illness since confounds such as hospitalizations, long-term medication, and chronicity can be avoided (*Bilder et al, 2000*).

Some studies suggested that the cognitive impairment in first-episode psychosis differs from that in chronic schizophrenia only in terms of degree of severity (*Saykin et al., 1994*). In the West London study, *Joyce et al. (2002)* identified a profile of executive impairment in first-episode psychosis that they suggested to differ from their previous findings in chronic schizophrenia.

Numerous studies have reported deficits in attention, memory and executive functioning (*Bilder et al., 1996; Heinrichs and Zakzanis, 1998*). Recently, these deficits are thought to be strongly related to clinical outcome, perhaps more than are positive and negative symptoms (*Hoff and Kremen, 2003*).

Problem solving considered an important category of cognitive function. And there are numerous tests of reasoning and problem solving, the most well-known and most frequently utilized in schizophrenia research is the Wisconsin Card Sorting Test (*Heaton, 1981*). Patients in their first episode also appear to have severe impairments in sequencing, organizational flexibility (*Mohamed et al.,*

1999), planning ability and strategy use (*Hutton et al., 1998*).

There is increasing evidence of structural and functional brain impairments in schizophrenia. Although these impairments are controversial, several neurological structures are at the heart of a certain consensus (*Everett J et al, 2001*).

In fact, the very poor performance of patients with schizophrenia on the Wisconsin Card Sorting Test (*Goldberg et al., 1987*), and the reduced activity of the dorsolateral prefrontal cortex during performance of this test led to widespread pursuit of the hypothesis of frontal hypoactivation in schizophrenia (*Weinberger, 1987*) .

As it was discovered that neural circuitry underlying these cognitive functions primarily involves the frontal lobes and front limbic or paralimbic regions with presence of cellular abnormalities in the frontal lobe suggest abnormal connectivity between local cortical circuits and cortico-cortical and cortico-subcortical connectivity (*Selemon and Goldman-Rakic, 1999*).

One popular hypothesis postulates a dysfunction of the dorsolateral prefrontal cortex. The prefrontal cortex plays an important role in the processing and integration of

internal and external information, in abstraction and problem solving and in the planning, execution and evaluation of behaviour. Frontal dysfunctions may lead to distortions in planning and execution and to perseverative and rigid behaviour (*Everett J et al., 2001*).

Weinberger et al. (1986) have shown lower regional cerebral blood flow (RCBF) in the dorsolateral prefrontal cortex of patients with schizophrenia compared with healthy controls while performing the WCST. In the patients tested, RCBF in the dorsolateral prefrontal cortex correlated positively with cognitive performance.

Other regions of the brain have also been associated with performance of the WCST, however (*Anderson et al., 1991*).

The relationship between neurocognitive deficits and premorbid adjustment in schizophrenia has been studied to a limited degree. *Binder et al. (1998)* reported no difference in neuropsychological performance between patients with short and long prodromal periods, suggesting that neuropsychological deficits in first-episode schizophrenia are independent of the early course of the illness.

DeQuardo et al. (1994) associated premorbid asociality with adult neuropsychological dysfunction, and *Levitt et al. (1996)* reported an association of poor premorbid adjustment with perseverative errors on the Wisconsin Card Sorting Test and poor visual memory span performance.

Bilder et al. (2000) found that neuropsychological measures correlated with childhood adjustment. *Silverstein et al. (2002)* reported greater cognitive deficits when premorbid adjustment was unfavorable, particularly for measures of attention and executive functions.

Collectively, these studies indicate a relationship between premorbid social adjustment and neurocognitive deficits after onset of the disorder, but methodological shortcomings, especially the small numbers of subjects, make the results inconclusive.

The relationship between neurocognitive deficits and symptoms of schizophrenia is also an area with inconsistent findings. Some have found an association of neurocognitive deficits with negative symptoms (*Bilder et al., 2000*) others have not (*Bilder et al., 1998*).

In addition, findings indicating that first-episode patients perform less well on free recall than on verbal memory tests have led to the suggestion that difficulty with free recall is possibly secondary to impaired executive functioning (*Hutton et al., 1998*).

Yet a later study reported that executive and motor dysfunctions were relatively less impaired than memory and attention in first episode patients (*Bilder et al., 2000*).

CHAPTER (VI)

Premorbid Function in Schizophrenia

Psychiatric research focusing on development of psychosis, first-episode psychosis, early detection and early intervention has begun to identify and define different phases in the development of the illness.

Researchers describe the premorbid period, the prodromal period and the period of untreated psychosis before adequate treatment begins. Understanding and distinguishing between these periods is crucial to future research, early detection and illness management. Thus, an appropriate measure that supports these goals and is both valid and reliable for first-episode samples is required (*Addington and van Mastrigt, 2002*).

Premorbid adjustment in schizophrenia is of interest because it may help reduce the heterogeneity of the disorder and it may have predictive value (*Levitt et al., 1994*).

A number of scales have been developed to describe the premorbid phase. The premorbid adjustment scale (PAS), which defines the premorbid phase as the time from birth until 6 months before onset of psychosis, is probably

the most widely used premorbid scale for psychosis (*Cannon-Spoor et al., 1982*).

(I) Studies of Premorbid Functioning in Individuals with Established Schizophrenia

The premorbid adjustment scale (PAS) provides reliable and consistent data on premorbid functioning (*Rabinowitz et al., 2007*). It was found that PAS scores are worse in individuals who eventually develop schizophrenia (*Schamael et al., 2007*).

It was found that studies comparing non psychiatric subjects, subjects with schizophrenia and those who exhibit schizoaffective and major affective disorders show that those with schizophrenia exhibit the poorest premorbid adjustment overall. This adjustment is characterized by early and progressive deterioration in social functioning, which rarely improves over time (*Gupta et al., 1995; Krauss et al., 1998; Vocisano et al., 1996*).

Research has shown premorbid functioning in individuals with schizophrenia. Research covered the *following fields:-*

- A.** Premorbid function, season of birth and family history.
- B.** Premorbid function and sex differences among affected individual.

- C. Premorbid function and age of onset of illness.
- D. Premorbid function, symptoms and subtypes of Schizophrenia.
- E. Premorbid function and cognitive function.
- F. Premorbid function, outcome and quality of life.
- G. Premorbid function and neurophysiological finding.

A. Premorbid function and onset

Good premorbid adjustment was strongly associated with an acute onset of the illness, and poor premorbid adjustment with an insidious onset (*Bailer et al., 1996*).

Recently it was found that premorbid abnormalities are common features of early-onset psychotic disorders. The social withdrawal and peer problems specific to youths with schizophrenia likely represent early manifestations of negative symptoms (*McClellan et al., 2003*).

B. Premorbid function and sex differences

Sex differences have emerged in research examining premorbid functioning in patients with schizophrenia.

It has been clearly illustrated that males experience poor premorbid social adjustment (*Larsen et al., 1996*) and female subjects showed better premorbid functioning (*Bailer et al., 1996*).

Males have earlier age of onset and a greater degree of deterioration across both the premorbid functioning that became progressively worse over time and morbid period, than do Females (*Vazquez-Barquero et al., 1995, Strous et al., 2004*).

In addition male patients, who show a higher frequency of poor premorbid functioning, have a longer delay in seeking treatment that conditions a longer duration of untreated psychosis (*Fresan et al., 2003*).

Recently the widely reported association of poor premorbid adjustment (PMA) with male sex, if genuinely present, does not appear to be disease specific (*Schamael et al., 2007*).

C. Premorbid function, symptoms and subtypes of schizophrenia

In the 1989 a study showed that poor premorbid sociosexual functioning was associated with greater severity of negative symptoms, fewer positive symptoms, and worse current social functioning. These data suggested that factors associated with severe social deterioration in the end stage of schizophrenia are also associated with premorbid sociosexual impairment (*Keefe et al., 1989*).

In 1992, *Kelley et al.* found that patients with negative symptoms had significantly lower levels of premorbid functioning during late adolescence and significantly greater premorbid deterioration between childhood and early adolescence. Also there were significant positive relationships between premorbid variables and negative symptoms.

In 1995 that correlation was confirmed by *Gupta et al.* as he reported that poor premorbid adjustment was significantly associated with prominence of negative symptoms, early age of onset, educational problems, chronicity, and neurological soft signs, but not with any MRI measures.

In addition, in 1996 *Bailer et al.* reported that premorbid functioning showed a stronger correlation with the course of negative symptoms and social disability than

with the course of positive symptoms. Poor premorbid social functioning implies a poor social course of the illness.

In 2002 *Guerra et al.* studied correlation between premorbid function especially in childhood period and other symptoms and it was found that delusions and hallucinations, negative symptoms and paranoia all appeared to have a developmental origin though they were associated with different childhood problems.

In 2003 *Addington et al.* divided schizophrenia patient into three groups according to there premorbid function. They found that relative to the stable-good group, the deteriorating and the poor-deteriorating groups had more negative symptoms, poorer social functioning and some evidence of poorer cognitive functioning.

The deteriorating group had increased positive symptoms compared to the stable-good group. These results suggest that prior to the onset of the acute psychosis those who have poor social and interpersonal functioning premorbidly present initially with increased social impairment and negative symptoms compared to those who have better premorbid functioning.

Also in 2003 *Kulhara and Avasthi* suggested that

apathy and anhedonia seem to be linked to premorbid adjustment.

On the other hand, in 2003 *Fresan et al.* found that violent schizophrenic patients showed an overall worse premorbid adjustment during childhood. In addition, the area of "peer relationships" was significantly diminished in several life period sections such as childhood, early and late adolescence in violent patients. That data indicate that difficulties in social relationships during early stages of life may increase the risk of future violent behavior among schizophrenic patients.

Also, level of premorbid functioning has also been used to distinguish between possible subtypes of schizophrenia including process versus reaction (*Guy et al., 1986*), paranoid versus non paranoid (*Burack et al., 1989*), deficit versus non deficit (*Gureje et al., 1994*) and deteriorating versus non deteriorating types (*Haas and Sweeney, 1992*).

D. Premorbid function and cognitive function

It is suggested that childhood onset of premorbid deficits in selective areas of social and academic adjustment appears to influence the cognitive performance seen in adult schizophrenia (*Silverstein et al., 2002*).

For example worse Premorbid Adjustment Scale scores were significantly associated with more perseverative errors on the Wisconsin Card Sorting Test and worse performance on the visual memory span task of the Wechsler Memory Scale (*Levitt et al., 1996*).

E. Premorbid function, season of birth and family history

Patients with schizophrenia are more likely to be born in the winter and early spring than at any other time of the year. Some studies have reported that winter-born patients differ from non-winter-born patients in terms of risk factors, symptoms, sensory abnormalities and brain morphology (*St-Hilaire et al., 2005*).

Associations between season of birth and premorbid adjustment, however, are still unclear until it was founded that Non-winter-birth and a positive family history of schizophrenia-spectrum disorders were associated with worse premorbid adjustment (*St-Hilaire et al., 2005*).

Also it was found that poor premorbid function was related to lower quartile birth weight and height (*Nopoulos et al., 1998*).

F. Premorbid function, outcome and quality of life

Schizophrenic patient who demonstrated poor or deteriorating functioning prior to the onset of acute psychosis have a poor outcome up to at least 2 years (*Addington and Addington, 2005*). Specifically, poor premorbid was associated with more negative symptoms early in the course of illness, less improvement in negative symptoms, poorer overall clinical functioning, and poorer social functioning (*Haim et al., 2006*).

Also, in 2005 *Czernikiewicz et al.* found that poor premorbid adjustment can be manifested by poorer quality of Life among schizophrenic patients, especially, the lower adjustment in adolescence, the poorer quality of Life.

G. Premorbid function and neurophysiologic finding

1. Magnetic Resonance Imaging (MRI)

Premorbid adjustment, rigorously measured, is poorer in schizophrenics than in normal controls and correlates with psychosocial and ventricular pathology in schizophrenia. Also, worse premorbid adjustment in schizophrenia was associated with larger Magnetic Resonance (MR) Ventricular Brain Ratio (VBR) in an exploratory analysis using a subset of schizophrenia patients (*Levitt et al., 1994*).

2. Computerized Brain Topography

It was found that patients with CT evidence

suggestive of brain atrophy had significantly worse premorbid scores, particularly during childhood, than did the patients with normal scans (*Weinberger et al., 1980*).

3. Positron Emission Tomographic (PET)

Positron emission tomographic (PET) scans are also related to poor premorbid functioning (*Cannon et al., 1997; Gur et al., 1995*).

4. Electro Dermal Nonresponding

In addition, poor premorbid adjustment appears to be more common in patients with schizophrenia who exhibit electro dermal nonresponding (*Ohman and Ohlund, 1989*).

5. Event Potentials

Decreased event potentials are related to poor premorbid function (*Levitt et al., 1996*).

H. Premorbid function and personality

In the 2005 a study examined the correlation between premorbid function personality trait and disorders .It was found that premorbid adjustment correlates with avoidant, schizotypal and schizoid personality disorders. And the more personality pathology found, the poorer is the

premorbid psychosocial adjustment. Premorbid adjustment positively correlates with histrionic personality traits. The pathological traits of schizotypal and schizoid personalities account for up to 77 percent of the variance of the total premorbid adjustment in schizophrenic patients (*José Juan and Manuel, 2005*).

II- Studies of Premorbid Functioning in Patients Experiencing a First Episode of Schizophrenia

Research covered the following fields:

- A. Premorbid function and gender difference.
- B. Premorbid function and symptoms.
- C. Premorbid function and cognitive impairment.
- D. Premorbid function and remission of positive symptoms.
- E. Treatment response.
- F. Resting cerebral glucose metabolism.

A. Premorbid function and gender difference

Results of studies conducted with individuals' experiencing a first episode of psychosis are similar to those with individuals who have a chronic course of illness. As regard gender difference it was found that women tend to display better premorbid adjustment than men (*Larsen et al., 1996; Amminger et al., 1997; Vazquez-*

Barquero et al., 1995).

The results suggested that in comparison with their female counterparts, males who developed a psychotic illness had significantly poorer premorbid adjustment at the late adolescent stage and that this may contribute to higher levels of negative symptoms (*Preston et al., 2002*).

B. Premorbid Function and Symptoms

In first episode schizophrenia studies it was reported that poor premorbid functioning appears to be associated with cognitive impairment (*Fannon et al., 2000*), poor adaptation to school (*Robinson et al., 1999*), poor social, sexual and occupational functioning (*Gupta et al., 1995*), long duration of untreated psychosis (*Larsen et al., 2000*), negative symptoms (*Larsen et al., 2000*).

C. Premorbid function and cognitive impairment

It was found that milder Working Memory (WM), deficits are associated with higher premorbid academic functioning (*Rund et al., 2007*).

D. Premorbid function and remission of positive symptoms

Patients with complete remission of positive symptoms after eight weeks of therapy had experienced far better premorbid adjustment in early adolescence and in

childhood (*Amminger et al., 1997*).

E. Treatment response

In first-episode psychosis good premorbid functioning is associated with better response to treatment and fewer extra pyramidal symptoms.

In the 2006 a study done on first episode schizophrenia found that there were significant differences between the premorbid groups on change on the Positive and Negative Syndrome Scale, Clinical Global Impression severity and cognitive functioning and Extrapyramidal Symptoms Rating Scale. Patients in the stable-good' premorbid group improved more than those in the 'stable-poor' and 'declining' groups. The stable-good' group received the lowest doses of antipsychotic and had the least extrapyramidal symptoms. Patients in the 'declining' group had the highest dosages and the most extrapyramidal symptoms (*Rabinowitz et al., 2006*).

F. Resting cerebral glucose metabolism

In the 1995 a study examining the relation between premorbid functioning and resting cerebral glucose metabolism levels in first-episode and previously treated patients with schizophrenia, higher metabolism and lower left hemispheric values were related to better premorbid

adjustment and outcome (*Gur et al., 1995*).

[Table \(iii\)](#)

[Table \(iv\)](#)

CHAPTER(V)

Factors Affecting Outcome of Schizophrenia

In general, outcome includes all changes in a person's health that are the consequences of dealing with the health problem (*Last, 2001*).

There are several descriptions for good and poor outcome are presented. For example, good outcome can be seen as improvement of functioning and lack of symptoms, but also, more broadly, as a stable, non-deteriorating course of illness (*Ruggeri et al., 2004*).

According to meta-analysis of 320 studies published during the period of 1895-1992, approximately 40 percent of the patients were considered as having a good outcome (*Hegarty et al., 1994*).

Until recent decades, the outcome studies of schizophrenia focused mainly on two dimensions which were serving utilization (e.g. the number of hospital episodes) and psychopathology.

Although during the 1980s a few large outcome studies with multiple outcome measures were presented.

Nowadays the multidimensional viewpoint in measuring outcome in schizophrenia is getting stronger (*McGlashan, 1984, Harding et al., 1987b, Leff et al., 1992*).

In addition to psychopathology and social and occupational functioning, met and unmet needs for treatment, quality of life and satisfaction with services are considered important (*Ruggeri et al., 2004*) and different dimensions of outcomes. And it may be specific predictors of outcome (*Ruggeri et al., 2004; Hofer et al., 2006*).

The World Health Organization's studies of relapse in the 1960s and 1970s showed better outcomes of schizophrenia surprisingly in developing countries than in industrialized ones. As the percentage of patients, with a good outcome tends to be higher in developing nations than in developed countries. In a review of transcultural outcome studies, it was found that the course and outcome of schizophrenia in developing and non-western countries is remarkably better than that seen in developed countries (*Kulhara, 1994*).

The reason for the better outcome in the developing world is not completely understood (*Khalil, 2001*). It may be due to the fact that many people with mental illness in villages in the developing world are better accepted, less

stigmatized, and more likely to find work in the subsistence agricultural economy or to engage in meaningful labor (*Al Assraand Amin, 1988*).

Also the influence of family support in the course of schizophrenia in Arab cultures is important and remains a significant area for research and for psychosocial interventions (*Khalil, 2001*).

Schizophrenia is associated with a significant amount of stigma and discrimination, which further increase the burden on patients and their families. A variety of studies in Arab countries have illustrated the general negative and rejecting attitudes towards patients with schizophrenia (*Owaida et al., 1990; Kamel et al., 1991*).

And it was found that strategies that reduce criticism and hostility from family members improve outcome (*Okasha et al., 2000 - a*).

Therefore the idea of better outcome in developing countries and the favorable effect of socio-cultural factors on outcome in these countries has been questioned (*Patel et al., 2006*) and still remains unclear (*Kurihara et al., 2000*).

Existing data on outcome prediction in schizophrenia suggests several dimensions.

It was recommended that dividing predictors into three chronologically ordered components: **(1)** premorbid characteristics, **(2)** type of psychopathology, **(3)** course. They further subdivided the first component into the perinatal period, infancy, childhood, adolescence and adulthood. And a fourth now added to reflect background dimensions external to the patient (*Mc Glashan, 1986*).

In general, a good outcome has been predicted by later age at illness onset as *Suvisaari et al.* found in 1998.

Also studies showed that gender play an important role in outcome as in 1998 *Suvisaari et al.* found better outcome in female than male among schizophrenia patient. Yet in 2003 *Kua et al.* reported better outcome in men.

In addition, being married (*Harding et al., 1987a*), well educated (*Johnstone et al., 1995*) and belonging to higher social class at inception are also related to good prognosis (*Jonsson and Nyman, 1991*).

Conversely, poor outcome of schizophrenia was related to many variables as male sex (*Suvisaari et al.,*

1998), early age at illness onset (*Harrison et al., 2001*), poor premorbid functioning (*Hofer et al., 2006*), premorbid alcohol use (*Häfner and an der Heiden, 2003*), long duration of untreated psychosis (*Marshall et al., 2005*) and cannabis use (*Linszen et al., 1994*).

III- Studies of Factors Affecting Outcome of Schizophrenic Patients

Studies involved the following factors that affect outcome:-

- A.** Early development.
- B.** Environmental factors.
- C.** Premorbid adjustment.
- D.** Duration of illness.
- E.** Type and severity of symptoms.
- F.** Type of medication (pharmacotherapy).

A. Early development and outcome

Although there is convincing evidence that children who have delays in neurocognitive and motor development have a small but significantly increased risk of developing schizophrenia, once illness develops, the association between these markers and the subsequent course of the illness remains poorly understood (*Isohanni et al., 2004; Cannon et al., 2002; Niemi et al.,*

2003).

It was found that schizophrenia cases with poor outcome had significantly more neurological symptoms (e.g. bad coordination of muscles or speech, difficulties in reading and writing) during childhood and adolescence when compared to good outcome cases. Surprisingly, birth trauma has also been suggested to predict a favorable course of illness (*Johnstone et al., 1995*).

B. Environmental factors, outcome and relapse

Environmental factors also seem to have an effect, for example: - stressful life events have been associated with increased risk of relapse in schizophrenia and poor outcome (*Bebbington and Kuipers, 2003*).

Also, family members play an important role in the survival of psychotic patients in the community (*Freeman and Simmons, 1963*).

However, schizophrenic patients are more likely to relapse if their family members express intrusive, negative or hostile emotions (high level of expressed emotions) in dealing with them (*Brown et al., 1962*).

In the 2003 a study showed that high expressed

emotion in the families of patients (i.e. poor emotional environment) correlated to poor outcome among schizophrenia patient (*Bebbington and Kuipers, 2003*).

In this respect, the concept of expressed emotions has gained respectable ground in the field of Psychiatry. It includes many components: criticism, hostility, emotional over-involvement (*Okasha et al., 1994*).

A series of studies have demonstrated that family expressed emotions predict a patient's symptomatic relapse, both in Anglo and American settings (*Wig et al., 1987*).

In 1993 and 1995, two Egyptian studies unexpectedly reported that there was no association between emotional over-involvement and relapse in Egyptian schizophrenic patients (*Abol Magd, 1993; Kamal, 1995*). Moreover they proved that family expressed emotions, mainly criticism and hostility, seem to be an independent risk factor for relapse of their patients. Their results seem to be similar to those found by study done in Chinese culture (*Moasheng and Zaijn Hand Mengze, 1998*).

In 2000 *Okasha et al.* postulated that schizophrenic patients and family members often retrospectively report

having a number of non – psychotic symptoms and/or certain alterations in behavior that they believed to precede any psychotic symptoms and behavior.

The identification of possible relapse before its actual occurrence and the timely intervention in management were expected to spare both patient and family suffering and pain of a full schizophrenic episode.

They concluded from their study on a sample of Egyptian schizophrenic patients that clusters of non-specific prodromal symptoms existed, that significantly differentiated between relapsing, non-relapsing and healthy controls (*Okasha et al., 2000 - b*).

C. Premorbid adjustment and outcome

Premorbid adjustment in schizophrenia has attracted great interest as a potential predictor of clinical course and outcome (*Levitt et al., 1994*).

In first-episode psychosis good premorbid functioning is associated with better response to treatment and fewer extra pyramidal symptoms (*Rabinowitz et al., 2006*).

In 2006, a team of researchers concluded that "Premorbid functioning is thus of both clinical and theoretical importance and may suggest the need to

consider aggressive intervention, either pharmacologic or psychosocial, at the time of the first episode of illness," (*Czernikiewicz et al., 2006*).

Both poor and/or deteriorating social, interpersonal, school, and work functioning predict poor outcome for people with first episode psychosis (*Larsen, 2006*), and those who demonstrated poor or deteriorating functioning prior to the onset of acute psychosis have a poorer outcome up to at least 2 years in terms of negative symptoms and social functioning (*Addington and Addington, 2005*).

On the other hand, A higher level of premorbid functioning has been associated with a better course, particularly if there is greater social contact with friends and family (*Carpenter and Strauss, 1991*).

In addition to that having obtained a higher level of education has also been correlated with better outcome in patients with schizophrenia; this may be related to higher premorbid functioning (*Geddes et al., 1994*).

D. Duration of illness and outcome

The duration of untreated psychosis (DUP) is defined as the interval from first psychotic symptoms to first psychiatric hospitalization (*Craig et al., 2000*).

Many studies have suggested that there may be an association between longer duration of untreated psychosis and poor outcome in schizophrenia. These studies have been interpreted as providing evidence that untreated psychosis may constitute an “active morbid process” that is “toxic” to the brain. If untreated psychosis is neurotoxic, this would form a strong basis for early intervention in schizophrenia (*Ho et al., 2000*).

As in other studies, the longer the duration of untreated psychosis (DUP), the more severe the baseline symptoms. Thus, it appears that with sufficient resource it is possible to reduce DUP to half its usual value; and by doing so, patients will start treatment at lower symptom levels (*Marshall et al., 2004*).

In the 2005, a study found that longer duration of untreated psychosis is associated with worse symptoms and functioning, and less chance of remission in people with first episode psychosis (*Marshall et al., 2005*).

Also other studies showed that longer duration of untreated psychosis is associated with more severe positive symptoms at two years, poorer social and occupational

functioning prior to presentation, and poorer outcome at one and three years (*Larsen et al., 1996*) and on outcome at fifteen years (*Bottlender et al., 2003*).

On the other hand, better prognosis has also been associated with a shorter duration of untreated psychosis (*Harrison et al., 1996; Drake et al., 2000*).

Accordingly, factors that affect DUP indirectly will influence outcome of schizophrenia. It was found that social isolation or avoidance has predicted long DUP in two studies. And abnormal premorbid function that might lead to both long DUP and poor outcome (*Drake et al., 2000; Larssen et al., 2001*).

Studies examining this have indeed found that it explained some of the association between DUP and outcome (*Keshavan et al., 2003; Addington et al., 2004; Perkins et al., 2004*).

Yet in 2000, *Drake et al.* found that good insight, reduced daily living skills or hostile behavior are linked to short DUP.

Two large studies from the UK and Australia showed a curvilinear relationship between DUP and one year outcome, such that the improvement in outcome is much greater if one moves from six down to three weeks

compared with from six down to three months.

This implies that the maximum benefit of early intervention services will be gained only by shifting patients into the shortest part of the DUP range. Lastly, and potentially the most important issue, is what the mechanism by which long DUP might confer a poor outcome. In broad terms, the mechanism might be biological, with active psychosis leading to treatment refractoriness perhaps through dopaminergic or glutamatergic processes; or it might be primarily psychosocial, with prolonged untreated psychosis progressively leading to psychological and social dysfunction (*Drake et al., 2000; Harrigan et al., 2003*).

Recent in-vivo magnetic resonance imaging spectroscopy studies have shown evidence of reduction in neuronal membrane integrity during the prodrome and perhaps DUP (*Theberge et al., 2004; Wood et al., 2003*).

Most studies of first-episode schizophrenia have suggested that treatment delay is a serious problem because the beneficial effects of treatment may be strongest in the earliest phases of the illness. It was assumed that people with schizophrenia who had a long duration of untreated psychosis would have poorer premorbid functioning and more negative symptoms at onset, and

that the main obstacles to receiving treatment would be social withdrawal, a poorly functioning social network, and the misinterpretation of early symptoms of psychosis by primary health services (*Larsen et al., 1998*).

E. Type, severity of symptoms and outcome of schizophrenia

The symptoms of schizophrenia have been divided into the positive and negative categories. Although negative symptoms have been associated with poor outcome, the relationship between positive symptoms and subsequent outcome has been less clear (*Ho et al., 1998*).

Some studies reported that symptom severity at presentation correlates quality-of-life outcomes in first episode patients (*Browne et al., 2000; Robinson et al., 1999*) however; others have failed to find such relationships (*Lastra et al., 2000*).

Furthermore lower levels of positive, negative, and depressive symptoms at presentation predicted a higher overall level of functioning at follow up. That was reflected in the better occupational and social interactions of the patients that were studied. Thus, patients who present with

higher levels of positive, negative, or depressive symptoms at presentation may be expected to have a poorer prognosis than those with lower levels of symptoms. Also it was found that the type of symptoms at presentation appears to be less important than the intensity of symptoms in predicting the later level of functioning (*Siegel et al., 2006*).

For instance, severity of positive symptoms has been correlated with poor outcome at 1 year and better long-term outcome at 23 years, but there was no correlation found at 2 to 8 years (*Robinson et al., 1999; Jonsson and Nyman, 1984*).

On the other hand negative symptoms have been correlated with poor functioning at intake and at 2 years, but not at 1-year follow-up (*Robinson et al., 1999; Addington, 1998*) and depressive symptoms have been correlated with 1-year outcome (*Eaton et al., 1998; Robinson et al., 1999*).

In addition, it was found that insight into illness is a primary factor related to good versus poor outcome in schizophrenia. That is, awareness of having a mental disorder may have significant relevance to prognosis and treatment interventions.

In a study that was concerning insight and outcome

in schizophrenia, it was found that greater insight was shown to be significantly related to both higher global and specific functioning after long-term treatment.

Insight was also found to account for a substantial amount of the variance in global and specific functional rating scores.

In addition, a higher degree of insight was significantly correlated with increased participation in treatment (*Schwartz, 1998*).

This finding supports a previous report that good insight is related to better psychosocial treatment compliance. Moreover results suggest that poor insight is related to reduce psychosocial functioning before and after treatment, less compliance with medication and treatment regimens, and impediments to the treatment process (*Lysaker et al., 1994*).

F. Type of medication and outcome

Many studies showed that the class of antipsychotic medication used was not associated with functional outcomes.

Specifically, there was no higher level of functioning with newer antipsychotic medications than with older ones. This is consistent with several recent studies

suggesting that there is no distinction in terms of efficacy between older and newer antipsychotic; rather, they appear to have equal efficacy across several domains (*Rosenheck et al., 2003; Lieberman et al., 2005*).

Yet poor compliance with treatment is considered to be a significant preventable cause of poor outcome and is in turn likely to be influenced by the patient's experience of drug treatment (*Gerlach , 2002*).

In addition recent study of first episode schizophrenia suggested that treatment compliance and early premorbid adjustment level seem to be important predictors of relapse rate (*Üçok et al., 2006*).