Age of Onset and Gender in a Sample of Egyptian Schizophrenic Patients

Omar, A.N.M., Haroun A and Nagy N. E. S.

Abstract

We examined 100 schizophrenic patients diagnosed according to the ICD 10 research diagnostic criteria. We compared clinical presentation and outcome in relation to the age of onset and gender. Female patients showed later age of onset compared with males in all conditions. Gender effect on the age of onset was apparent in the different subtypes of schizophrenia as well, with female patients having onset later 5 years than their male counterparts. Early onset was associated with worse prognosis and poor response to classical neuroleptics.

Introduction

The vulnerability to schizophrenia may be initiated during the second and third trimesters of pregnancy, the prenatal period and later stages of development (Bloom, 1993).

The symptoms of schizophrenia usually emerge in the second and third decades of life. This suggests that pathological processes occur in the brain during that time and play a decisive role in the expression of the biological vulnerability to schizophrenia.

From this point of view, we can conclude that studying the factors that affect the age of onset can help to identify the biological basis of schizophrenia (De Lisi ,1992).

The phenomenon of a gender difference in age at onset of schizophrenia was described by Kraeplin (1909-1915). Since then numerous studies have been conducted which quite consistently have found that age at onset and at first admission is 5-10 higher in females than in males. The importance of this unusual finding had been stressed as well as the lack of valid explanation on several occasions (Hafner1987, 1988; Hafner et al.1989). Angermeyer and Kuhn (1988). reported on 53 studies from a total of 19 countries published by the end of 1983. In 50 of these, the investigators found a higher mean age in females than in males at first hospitalization for schizophrenia. In the majority of studies the difference was 4-5 years.

Harris and Jeste (1988) reviewed over 30 European studies on "late-onset schizophrenia" and found a clear predominance of female patients with first onset of the disease at an age of over 40 years.

Gender effect on the age of onset has been addressed in many more recent studies and was found to be related to clinical subtypes of schizophrenia (Beratis et al, 1994).

These type of studies became of interest for many researchers working in the field of pathophysiology of schizophrenia especially since the development of atypical antipsychotics and its effect on patients with poor outcome and predominant negative symptoms (Buchanan et al ,1990). The purpose of this study was to examine the effect of the age of onset and gender on the

clinical presentation and outcome of schizophrenia in an Egyptian sample of patients.

Subjects and Methods

Subjects

The subjects were 100 schizophrenic patients (64 males and 36 females) recruited from the inpatient department and outpatient clinic in the Institute of Psychiatry, Ain Shams University.

Their age ranged between 20-45 years. They had a diagnosis of schizophrenia and being subtype according to the ICD 10 research diagnostic criteria .All patients gave consent to participate in the study.

Past or present history of organic mental disorders, substance use disorders, other psychiatric disorders and medical illness were considered as exclusion criteria.

Methods

The diagnosis and age of onset were based on clinical interviews of the patients and informants and confirmed by the available data in their medical records .

Interviews were done by two psychiatrists on two separate occasion's blind to the results of each other.

Age of onset was defined as the first report of positive psychotic symptoms, negative symptoms, or disorganized behavior (Haas and Sweeney, 1992).

All patients received the equivalent of 600 mg/day of chlorpromazine for 24 weeks and were reexamined to detect response to treatment and outcome (Nimgaonkar et al ,1988).

Poor outcome and lack of response to treatment (at least three trials of typical neuroleptics) were defined as the presence of: 1) persistent delusions, hallucinations or thought disorder, 2)pervasive negative symptoms as withdrawal, anhedonia, poverty of thought or avolition and 3) social impairment in the most recent psychotic episode (Loebel et al ,1992).

Results

The demographic data and clinical characteristics of schizophrenic patients are presented in table (1).

We examined 100 schizophrenic patients (64 males and 36 females) with mean age about 32.2±8.0. They were diagnosed and subtype according to the (ICD) 10 research diagnostic criteria.

The sample included 25 paranoid schizophrenics as well as 45 hebephrenic and 30 undifferentiated schizophrenics' patients. About 33% of those examined showed persistent thought disorder and poor response on typical antipsychotics.

Table (2) and (3) show the mean age of onset in both males and females for those with good and poor prognosis over duration of 24 weeks respectively. . Early age of onset was associated with poor prognosis in both sexes.

Table (4) compares the age of onset and gender in relation to the subtypes of schizophrenia. We found that female paranoid patients have significant later age of onset than males.

Table (1):
The Demographic and Clinical Characteristics of Schizophrenic Patient's

Number	100
Age	20-45
Mean ± SD	32.2±8.0
Sex:	
M/F	64/36
Subtypes	
Paranoid	25
Hebephrenic	45
Undifferentiated	30
Outcome	
Good prognosis	67
Poor prognosis	33

Table (2):
Age of Onset and Gender in the Group with Good Prognosis

Number	67
Sex:	43/24
M/F	
Mean age of onset *(±SD)*	
Males	*22.8±2.3*
Females	*26.0±3.3*

M = males, F =Females

Table (3):
The Age of Onset and Gender in the Group with Poor Prognosis

Number	33
Sex:	
M/F	18/15
Mean age of onset(±SD)	
Males	16.7±1.1
Females	19.7±1.2

Table (4):
The Age of Onset and Gender in Schizophrenic Subtypes

Subtypes	Males: Age(±SD)	Females: Age(±SD)
Paranoid	23.0±1.6	28.1±1.5
Hebephrenic	22.2±1.4	24.1±0.2
Undifferentiated	20.0±2.0	21.4±1.6

Discussion

Several studies in the pathogenesis and pathophysiology of schizophrenia examined the age of onset, gender, neuroleptic responsivity, clinical subtypes and the interaction between these factors. Some of these studies suggested that neuroleptic resistance might be a distinctive subtype of schizophrenia (Brown and Herz, 1988). The difference in age of onset and gender in schizophrenic patients with good and poor outcome points to biological processes playing role in the onset of psychosis.

However, the question of whether and what age extent at first psychiatric contact truly reflects age at onset which has not yet been addressed sufficiently. A sizeable number of studies have in fact reported a higher mean age at onset in females. However, in none of the studies published so far has "onset of the disease" been clearly defined and assessed by means of an operationalized procedure. So, this higher age at first hospitalization in females- provided it is confirmed- might in fact be accounted for not only by a higher age at true onset, but also by a usually longer interval between onset and first admission. This may be due to gender difference in the individual perception of the disease, coping and help-seeking behavior (Mechanic, 1982,1986; Gove 1984; Leaf et al., 1987), or influencing of sex-specific roles and stereotypes on the tolerance and/or reaction of society to deviant behavior at the beginning of a psychosis (Clausen et al.1982; Warren1983). This, of course, can show transcultural variability.

In our study we found that 30% of the patients shows poor prognosis and resistance to classical neuroleptics over the period of 24 weeks. This coincides with the study of (Loebel et al, 1992), who reported that 18.9% of patients with first episode schizophrenia or schizoaffective disorder failed to respond adequately to typical neuroleptics.

In another study they found that neuroleptic responders would be expected to predominate in most populations of schizophrenic patients, since about 70% are believed to respond to neuroleptic treatment. This response. was defined according to the criteria used in our work (Kane et al, 1988).

The results of our study suggest that younger age of onset in both sexes is associated with poor prognosis. This finding is consistent with those found in the work of Gureje (1991) and Hafner et al (1993). Gender differences in age at onset and in the course of the disease, provided they are confirmed, may be an important clue to a better understanding of the

development of schizophrenia. For an explanation of the gender difference in age at onset, several hypotheses are feasible which may partly also refer to differences in course and outcome.

There are two varieties of Schizophrenia an "early-onset type" with a higher incidence in males and a "late-onset type" with a higher incidence in females (Seeman, 1982). These types might be transmitted genetically and determine age at onset as well as symptomatology and course of the disease.

Males generally have for whatever reasons a higher vulnerability to schizophrenia than females and therefore develop the disease earlier. This higher vulnerability might be transmitted linked to sex chromosomes, for example, or might be due to a higher occurrence of neurodevelopment problems - possibly on account of pre- or prenatal complications, which seem to occur more often in males than in females (Murray and Lewis, 1987).

Apart from the biological causes mentioned, it is feasible that manifold psychological causes may contribute to an earlier onset or more severe course of the disease in males, such as sex differences in coping behavior or in social support received (Riecher et al., 1991).

It is feasible that protective or aggravating factors has different effects on the two sexes at different ages. These include psychosocial as well as biological factors, which either increase the morbid risk in young males or, inversely, decrease the risk in young females. From a biological point of view, there is some indication that female sexual hormones have a protective effect to the advantage of sexually mature young females. This effect is accounted for mainly by the antidopaminergic property of ostrogens, for which there is good evidence (Villeneuve et al .,1980; Di Paolo et al., 1981; Seeman, 1983; Nicoletti et al., 1983; Maggi and Perez, 1985).

Further hypotheses attempting to explain the more negative course in males include worse compliance (Hogarty, 1988) and poorer response to neuroleptics (Seeman, 1986). This latter effect might again be due to the fact that males generally lack the additional antidopaminergic effect of ostrogens (Seeman, 1986).

We found that female schizophrenic patients with paranoid subtypes have later age of onset, about 5 years later than their male counterparts. The significant difference in age of onset, as a function of gender was found in the paranoids but not in the hebephrenic and undifferentiated subtypes.

The differences in age of onset between paranoids and non-paranoids might be due to differences in dopaminergic mechanisms.

Paranoid symptoms have been specifically related to increased dopaminergic activity on the basis of amphetamine-induced psychosis (Snyder, 1973).

However, the hebephrenic and undifferentiated symptoms may be related to glutamatergic neurotransmission because of their similarity to behavioral changes induced by phencyclidine, a non-competitive antagonist of glutamate receptors (Tamminga et al, 1989).

In conclusion, we found that poor response to classical neuroleptics in our sample of Egyptian schizophrenic patients was evidenced in earlier age of onset and that

female paranoid schizophrenics shows later age of onset than males.

However, further studies are needed on larger samples to cover other issue e.g. sociocultural factors playing role in the onset of schizophrenia and how they interact with biological mechanisms .

References:

Angermeyer MC, Kuhn L (1988): Gender differences in age at onset of schizophrenia. An overview. Eur Arch Psychiatry Neurol Sci 237: 351-364.

Beratis S, Gabriel J, Hoidas S.(1994): Age at onset in subtypes of schizophrenic disorders.Schizophrenic Bulletin 20:287-296

Bloom FE. (1993): Advancing a neurodevelopmental origin for schizophrenia. Archives of General Psychiatry 50: 224-227.

Buchanan RW,Kirkpatrick B et al.(1990): Clinical correlates of the deficit syndrome of schizophrenia. American Journal of Psychiatry 147:290-294.

Brown WA and Herz LR. (1988): Neuroleptic response as a nosologic device, in Handbook of Schizophrenia,volume 3. Edited by Tsuang MT and Simpson JG.NewYork,Elsevier,p139-149.

Clausen JA, Pfeffer NG, Huffine CL (1982): Help-seeking in severe mental illness. In: Mechanic D (ed) Symptoms, illness behavior and help-seeking.Watson, New York, pp: 135-155.

De Lisi LE .(1992): The significance of age of onset for schizophrenia. Schizophrenic Bulletin 18:209-215.

Di Paolo T, Poyet P, Labrie F (1981): Effect of chronic estradiol and haloperidol treatment on striatal dopamine receptors.Eur J Pharmacol 73: 105-106.

Gove WR (1984): Gender differences in mental and physical illness: the effects of fixed roles and nurturant roles.Soc Sci Med 19: 77-91.

Gureji O .(1991): Gender and schizophrenia :age of onset and sociodemographic attributes. Acta Psychiatrica Scandinavia 83:402-405.

Haas GL. and Sweeney JA.(1992): Premorbid and onset features of first episode schizophrenia.Schizophrenia Bulletin 18:373-387.

Hafner H (1987): Epidemiology of schizophrenia. In: Hafner H, Gattaz WF, Janzarik W (eds) Search for the causes of schizophrenia.Springer-Verlag, Berlin Heidelberg New York.

Hafner H (1988): What is schizophrenia? Changing perspectives in epidemiology. Eur Arch Psychiatry Neurol Sci 238: 63-72.

Hafner H, Riecher A, Maurer K, Loffler W, Munk-Jorgensen P, Stromgren E (1989): Does gender influence age at first hospitalization for schizophrenia? Psychol Med 19: 903-918.

Hafner H,Maurer K et al.(1993): The influence of age and sex on the onset and early course of schizophrenia.British Journal of Psychiatry 162: 80-86.

Harris MJ and Jeste DV (1988): Late-onset schizophrenia: an overview. Schizophr Bull 14: 39-55.

Hogarty GE (1988): Resistance of schizophrenia patients to social and vocational rehabilitation. In: Dencker SJ and Kuhlanek F (eds) Treatment resistance in schizophrenia.Vieweg, Braunschweig.

ICD-10 Classification of Mental and Behavioral Disorders(1993) : Diagnostic Criteria for Research. WHO, Geneva.

Kane J,Honigfeld G et al .(1988): Clozapine for treatment-resistant schizophrenic : a double-blind comparison with chlorpromazine. Archives of General Psychiatry 45 :789-796.

Kreaplin E (1909-1915): Psychiatrie.Barth, Leipzig.

Leaf PJ and Livingstone Bruce M (1987): Gender difference in the use of mental health-related services : a re-examination. J Health Soc Behav 28: 171-183.

Lewine RR, Gulley LR, Risch SC et al.(1990): Sexual dimorphism, brain morphology, and schizophrenia. Schizophrenic Bulletin 16:195-203.

Loebel AD,Lieberman JA, Alvir JMJ et al.(1992): Duration of psychosis and outcome in first episode schizophrenia. American Journal of Psychiatry 149:1183-1188.

Maggi A and Perez J (1985) : Minireview. Role of female gonadal hormones in the CNS: clinical and experimental aspects. Life Sci 37: 893-906.

Mechanic D (1982): The epidemiology of illness behavior and its relationship *to* physical and psychological distress. In Mechanic D (ed) Symptoms, illness behavior and help-seeking. Prodist, N.York.

Mechanic D (1986): Illness behavior: an overview. In: Mc Hugh S and Vallis TM (eds) Illness behavior. A multidisciplinary model.Plenum, New York.

Murray RM and Lewis SW (1987): Is schizophrenia a neurodevelopmental disorder? Br Med J 295: 681-682.

Nicoletti F, Ferrara N, Patti F, Viglianesi M, Rampello L, Bianchi A, Reggio A, Scapagnini U (1983): Influence of sex steroids and prolactin on haloperidol-induced catalepsy.Brain Res 279:352-358

Nimgaonkar VL,Wesseley S,Tune LE et al.(1988): Response to drugs in schizophrenia: the influence of family history, obstetric complications and ventricular enlargement. Psychological Medicine 18:217-228.

Riecher A, Maurer K, Loffler W et al. (1991): Gender differences in age at onset and course of schizophrenia disorders. **A** contribution to the understanding of the disease? In: Hafner Hand Gattaz WF (eds) Search for the causes of schizophrenia. Springer-Verlag, Berlin Heidelberg New York.

Seeman MV (1982): Gender difference in schizophrenia.Can J Psychiatr 27: 107-112.

Seeman MV (1983): Interaction of sex, age and neuroleptic dose.Compr Psychiatr **24:** 125-128.

Seeman MV (1986): Current outcome in schizophrenia: women vs. men.Acta Psychiatr. Scand 73: 609-617.

Synder S.(1973): Amphetamine psychosis : a model schizophrenia mediated by catecholamines. American Journal of Psychiatry 130: 61-67.

Tamminga CA,Thaker GK, Alphs LD et al.(1989): Limbic system : localization of PCP drug action in rat and schizophrenic manifestations in humans, in Schizophrenia: Scientific Progress.Edited by Schulz SC and Tamminga CA.New York, Oxford University Press, PP 163-172.

Villeneuve A, Cazejust T, Cote M(1980): Estrogens in tardive dyskinesia in male psychiatric patients.Neuropsychobiology 6: 145-151.

Warren CAB (1983): Mental illness in the family: a comparison of husbands` and wives` definitions. J Fam Issues 4:533-558

Authors:

Omar,A.N. M.
Lecturer of Psychiatry
Ain Shams University

Haroun A.
Lecturer of Psychiatry
Ain Shams University

Nagy,, N.E.S
Lecturer ofd Psychiatry
Ain Shams University

Adress of Correspondance
Omar, A.N.M.
Lecturer of Pyshciatry
Ain Shams University

سن بداية المرض و نوعية الجنس
فى عينة من مرضى الفصام المصريين

تم فحص ١٠٠ مريض فصامى وفقا وفقا للتصنيف الدولى العاشر للأمراض النفسية و تمت مقارنة حالتهم الإكلينيكية و تحسنهم بالنسبة لسن بداية المرض و جنسهم. وجد ان المرضى الإناث سن بداية المرض اعلى مقارنة بالذكور فى كـل الحالات.

نوعية الجنس أيضا كان لها تأثيرها على بداية سن الامراض فى مختلف أنواع الفصام كالاتى:

- المرضى الإناث سن بداية المرض فيهم اعلى بخمس سنوات من المرضى الذكور
- كلما كان سن بداية المرض صغيرا كلما كان تحسن الحالة أسوء فى الاستجابة للأدوية النفسية التقليدية.