

Gender and Schizophrenia

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Schizophrenia is one of the most serious mental illnesses with about 1 in 100 people developing the disorder over a lifetime. This illness can begin at any age but commonly manifests itself in the late teens through early to mid 20's. It is prevalent in both sexes and the clinicians are now accepting that outcome of schizophrenia is multidimensional across interlinked domains of symptoms severity, social/functional disability, employment and a number of treatment and management variables¹. Although, many modern approaches to diagnose and describe the phenomenology of this illness have been proposed since the original description by Kraepelin², controversy still exists regarding the nosological boundaries of schizophrenia and related disorders. Described at times as one distinct syndrome it is now generally considered a group of syndromes which are phenomenologically heterogeneous.

The difference of opinion varies across a number of parameters ranging from aetiology to treatment, causes to manifestations and sensitivity to response to different management strategies. When it comes to the issues of gender, schizophrenia plays a decidedly different role, not only does it strike men and women at different ages but it follows different course and displays a remarkable gender sensitivity to treatment.

Age at Onset

Schizophrenia has a later onset in females than in males and this difference has been found to be about 5 years in most studies. Considering all measures of onset into account, like earliest sign of mental disorder, first psychotic symptoms and hospitalisation, it is suggested that women, as a group, have a significantly later age of onset. The peak age of onset in males is from 21-25 years whereas in females the peak age of onset is from 25-32 years³.

The difference in age at onset is also consistent across a number of studies carried out in different cultures. A multi-cultural WHO collaborative study confirmed that age of onset was lower in male schizophrenics in different centres⁴. In another study of 392 consecutive first admissions from a defined catchment area with a diagnosis of schizophrenia or paranoid disorder, males showed a single peak in their early 20's while females had an onset at a later age group⁵. Similarly results were reported by others^{6,7}.

Life events precipitating the onset seem to be more commonly reported by women. Schizophrenic women show a significant seasonality of first admissions as compared to the males and season of onset also differs among the different sexes^{8,9}.

Phenomenology

Differences exist in the symptoms of schizophrenia between either sexes¹⁰⁻¹². Overall, women with schizophrenia appear to have a less severe clinical presentation and clinical course. A number of studies and reviews have concluded that male patients are generally prone to express more negative symptoms as well as social withdrawal and blunted or incongruent effects than female patients. Women schizophrenics on the other hand, are more likely to present with mood disturbances, dysphoria, depressive symptoms and atypical affective features. Substance abuse and anti-social behaviours have also been found to be more common in schizophrenic men, than the women^{12,13}. The complexity of the association and overlap between schizophrenia and affective disorders in female schizophrenics are also interesting. Recent reviews suggest that females with schizophrenia are more likely to receive differential diagnosis of affective, atypical or manic psychosis and are over-represented among patients with a diagnosis of schizoaffective disorder. Furthermore, women appear to be more susceptible to acute

reactive psychosis and schizophreniform disorders which present as florid and abrupt onset psychotic states and tend to resolve with good outcome. A study from India published the results of long term course of psychosis and found a better outcome in women than men¹⁴.

Ring et al¹⁵ also found that men and women were not effected equally by schizophrenia. In their study, negative symptoms such as affective flattening, poverty of speech and social withdrawal were more prevalent among males than females both in extent as well as severity.

Pit-Morbid Functions

Abnormalities in pit-morbid functioning particularly in intellectual and social areas have been well documented in schizophrenia. A range of studies and reports are now available which suggest that the pre-morbid deficits are more common and more severe in boys than girls who later on develop schizophrenia^{16,17}. Retrospective reports and follow-up of children presenting to 'mental health services and of those at high risk suggest similar results. The presence of such deficits also predict an early onset of schizophrenic psychopathology, in male gender.

Developmental Phase and Gender

The neurodevelopmental model of schizophrenia is strongly supported by 'evidence that persons, who later develop this disorder, have abnormal developments in early years. Crow et al¹⁸ confirmed this view, point and suggested that developmental abnormalities prior to the onset of psychosis differ by gender. Boys who will later develop schizophrenia tend to be irritable, disagreeable and defiant of authority. In contrast girls are insecure, shy and participate less in groups.

Genetic Vulnerability

There is a convincing evidence about the familiar predisposition and genetic vulnerability to develop schizophrenic illnesses and reports confirm about different models of genetic risks operating at different levels. Although, no specific studies are available about different genetic predisposition to schizophrenia for males and females, there has been some interest to find out whether the families of schizophrenic men and women are at different degrees of moderate risk for this disorder.

Goldstein et al¹⁹ re-analysed the data from the IOWA cohort of schizophrenic patients for whom family interview diagnostic data was obtained. Age corrected life time risk of DSM III schizophrenia, in the first degree relatives of schizophrenic men was 2.2% as compared to 5.2% in relatives of schizophrenic women. This notion also got support from some other work which predicted that relatives of male and female patients seem to be at different risk²⁰. Interestingly, increased risk to the relatives is 'found in some other disorders such as stuttering and epilepsy and if these findings are to be linked to the current aetiological model of schizophrenia being considered as a neuro developmental disorder, such findings can thus have an important and long lasting impact in understanding of this disorder

Oestrogen Hypothesis

Evidence demonstrating modulating effects of oestrogen on the symptoms of schizophrenia provides basis for an association in this regard. Strong support for this hypothesis comes from various findings²¹⁻²³. Variations in the severity of symptoms are found as oestrogen level changes during the menstrual cycle, relapse rate of women with pre-existing schizophrenia is reduced during pregnancy and mental state changes that occur around the time of menopause are related to this hormone.

Brain Structure and Morphological Changes

As sex differences in normal brain functioning and morphology have long been known to exist, there has been some reports to suggest similar differences in the brains of male and female schizophrenic patients²⁴. Castle and Murray²⁵ reviewed the findings in this area and concluded that there is an evidence for this difference. Studies using MRI have also shown reduced coronal brain area, small left hippocampal formation and enlarged lateral ventricles in men with schizophrenia. but not in women²⁶⁻²⁸, Magnetic resonance imaging (MRI) studies also suggest that many of the structural brain

abnormalities in schizophrenia occur in 'areas that are normally sexually dimorphic'²⁶. Compared to men, women have a greater ratio of grey matter in the caudate, hippocampus, frontal cortex and temporal gyrus- all of which are involved in higher functions including language, thinking, sustained attention and working memory. These results may suggest that normal sexual dimorphism may help to protect schizophrenic women from some of the more severe cognitive consequences of brain abnormalities associated with the disorder.

Johnston et al²⁷ re-analysed the post-mortem data on schizophrenic patients in terms of gender differences and found that brains of female patients showed more gliosis and focal damage than males. This work indeed raised the question whether such features represent any specific gender vulnerability, in this disorder.

The association between prenatal exposure to influenza and later onset of schizophrenia is well documented. Regarding the gender differences examined in seven studies, five showed that the effect reached significance only for females²⁸. Re-analysis of Kendel and Kemp's data²⁹ also showed an effect for females, but not males³⁰. Similarly Takei et al³¹ while looking at influenza epidemics over a long time period, demonstrated the significance of this causative factor more in female than male schizophrenics.

Culture and Gender Difference

World Health Organisation conducted a systematic research on the influence of gender factors on age at onset, symptomatology and course of schizophrenia in seven research centres of three different cultures. It was revealed that females did have an early onset and had more nonspecific symptoms like irritability and tiredness than males. Males on the other hand reported to have more maladaptive behaviour like alcohol abuse and social withdrawal³².

Treatment

Many reports strongly suggest that treatment response is faster in women, the duration of psychosis is reduced and the amount of anti-psychotic drugs used even on a milligram per kilogram basis is significantly lower in female schizophrenics^{32,33}. Szymanski et al³, while using the standard doses of anti-psychotic drugs in men and women admitted to hospital with a first episode of schizophrenia, found more rapid and complete remission for women. Overall 95% of women attained full remission from their first episode, compared to 70% for men. Also, differentiating on the basis of the sexes, the response to psychosocial interventions was variable. Studies are also showing that unlike men, women who have intensive 'family intervention in conjunction with psychopharmacological treatment continue to improve significantly after discharge from hospital as compared to the male schizophrenics³⁴.

Course and Outcome

Schizophrenia runs a chronic course. Although, there has been a number of developments in area of treatment, management and rehabilitation, the overall outlook of schizophrenia is not very promising. If we consider the course and outcome of this illness with a special reference to gender the results are again suggestive of a difference between two sexes. Studies carried out during the past few decades are consistent in showing the difference between the sexes and reflect a need to consider this variable more importantly^{35,36}.

Angermeyer³⁷, reviewed the whole literature on the effects of gender on the course of schizophrenia. Out of 102 published studies in this area the findings showed some consensus. Regardless of the precise outcome measures used, either clinical, time spent in hospital, number of relapses, symptoms at follow-up like social functioning, social adaptation or occupational status, more than half of these studies showed statistically significant difference in terms of gender. The conclusion was that the outcome of schizophrenia is better in women at various lengths of follow-up. Men were at greater risk of re-admissions and they spent almost twice as long in hospital as the women.

Part of the outcome studies also showed better premorbid social adjustments of females and long term

outcomes were found to be better than males in terms of social activity, work competence, substance abuse and marital and parental status. Thara et al³⁸ followed ninety, first episode patients fulfilling ICD 9 criteria for schizophrenia prospectively for 10 years. They found that factors like phenomenology and duration of illness were very significant in the outcome of this illness. But being male and presence of self-neglect, religious delusions and hallucinations predicted poorer pattern of the illness.

In terms of treatment there were strong indications of better drug response in females and also of their less liability to develop long term effects of neuroleptic treatment. Reports also showed that significantly more women were married than the men at the follow up and had less disability in social functioning³⁹. Similarly female schizophrenic patients were enjoying a better quality of life than male patients when assessed on different aspects of functioning and quality of life⁴⁰.

Negative Findings

Despite a number of studies showing the gender difference in Schizophrenia, there are some reports which call into question the universality of such differences.

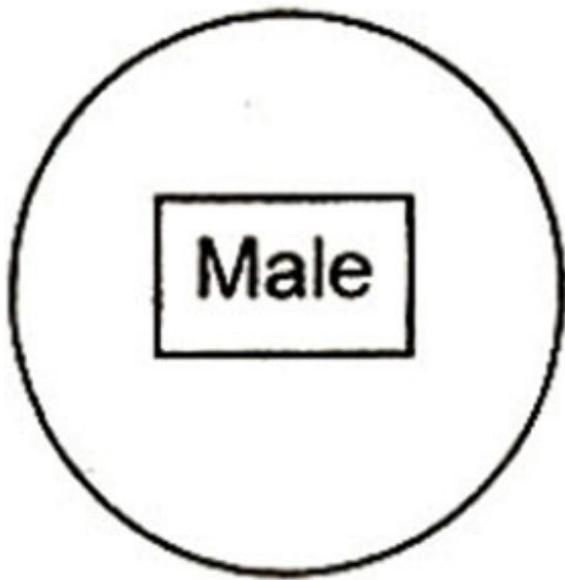
Murthy et al⁴¹ were unable to find an early age of onset in male schizophrenics. Survival analysis of subjects in their study, in fact, documented a female preponderance at younger age. Shankar et al⁴² indicated that females were more disabled than males and there were no differences between the sexes either on mean age or duration of illness.

Lindstrom and Knorrning⁴³ from Sweden correlated syndromes of schizophrenia (positive, negative, excited, anxious/depressive and cognitive factors) with background factors but could not find any significance to age or sex differences. Fenning et al⁴⁴ looked at gender premorbid characteristics and negative symptoms in schizophrenia. Their findings supported the importance of assessing negative symptoms longitudinally but suggested that gender is not strongly associated with these symptoms profile.

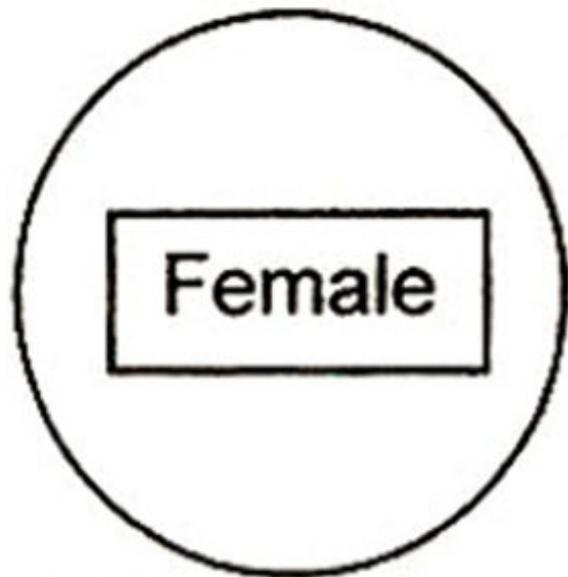
Kendler and Walsh in their epidemiologically based study in Ireland⁴⁵ were unable to show any demonstrable impact of gender on the presentation and course of schizophrenia. Contrary to other reports, no evidence was found in their study that schizophrenia in women, compared to men, is more closely related to affective illness from a symptomatic or familial perspective.

Conclusion

The evidence provided on the whole in this paper generally points towards a different susceptibility of males and females for schizophrenia. Despite few studies to the contrary most of the work consistently show that schizophrenic males as compared to female patients are more likely to have early onset, present with frequent negative symptoms and severe symptomatology and show more structural brain abnormalities and relatively less promising response to neuroleptic medication. The dissimilarities in terms of gender are also evident in, premorbid functioning, social demographic attributes and the overall course and prognosis of this illness. It is true that the differences in expression of this disorder between men and women have long been ignored. but such differences are appearing more significantly and being addressed more precisely in current studies. Along with some genetic vulnerability and other environmental factors it thus may be the case that we are in fact having two types of schizophrenias, one male schizophrenia and the other female schizophrenia, (Figure 1)



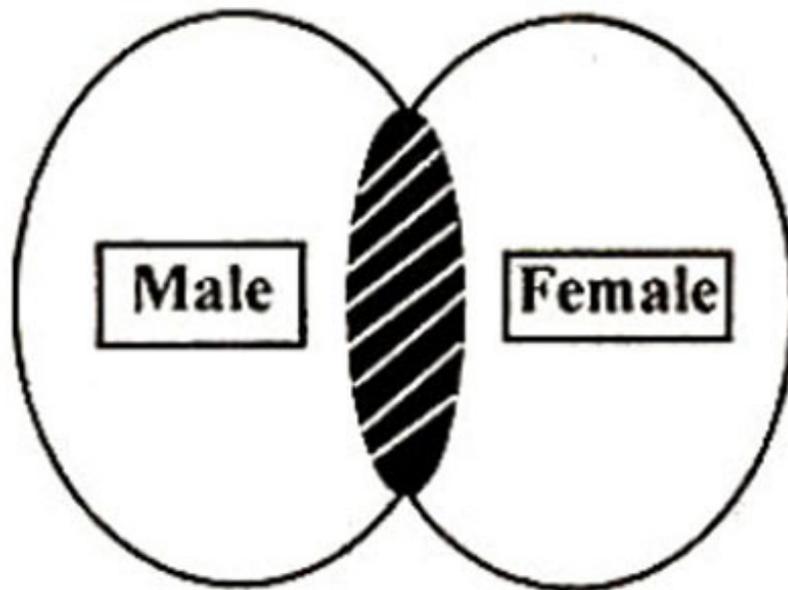
- Severe form
- Susceptibility to neurodevelopmental basis
- Typical features
- Negative symptoms
- Chronic course



- Less severe form
- Less susceptibility to neurodevelopmental basis
- Atypical features
- Depressive symptoms
- Favourable outcome

Figure 1

or we may be dealing with one disorder with overlapping of these two distinct syndromes, but retaining the individual characteristics (Figure 2).



- Severe form
- Susceptibility to neurodevelopmental basis
- Typical features
- Negative symptoms
- Chronic course

- Less severe form
- Less susceptibility to neurodevelopmental basis
- Atypical features
- Depressive symptoms
- Favourable outcome

Figure 2.

The second Option, however, looks more promising and viable.

In present day classifications, we prefer sub-typing of schizophrenia as it is argued that this illness comprises of a group of syndromes. The advantage of using gender as the sub-dividing variable by which to look For heterogeneity of this disorder, will therefore be completely reliable and valid in many ways. Apart from getting a number of advantages by grouping schizophrenia by gender, we may be able to get some more insight to the understanding of this illness. Schizophrenia is currently being explained by a number of psycho-sociobiological factors, the observable gender sensitivity in terms of aetiology presentation, psychopathology and response to the treatment will therefore be of much help in this regard. Such findings will also have implications for treatment and rehabilitation in this illness. Perhaps there may be some hope in certain areas of cognition where we may focus more on women and perhaps there will be the development of some sex specific medication that will alter neurotransmissions differently in different genders.

It is hoped that as these differences get more clarity the understanding of this disorder will become more fascinating, informative, as well as, insightful. It is therefore the appropriate time that physicians should become more aware that schizophrenia, as they know, is different in males and females and that several findings should be taken as further lines of guidance. Of course the observed neurobiological

and psychosocial differences require further explorations. Such differences will also require more critical reviews specially in terms of offering different psychosocial interventions and pharmacological treatments in different gender. But, as sex differences in schizophrenia become better documented, their importance to the understanding of the disorder itself will become clearer. This topic will hopefully assume a paramount importance in future research in schizophrenia and we will enter the next century with more clarification of many concepts which are still unclear and uncertain.

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