INTRODUCTION

There exits a rapidly growing body of knowledge concerning gender differences relevant to the fields of psychiatry. Although gender is commonly used interchangeably with sex, within the social sciences it often refers to specifically social differences known as gender roles in the biological science (*Putnam et al., 1986).*

Putnam et al. (1986) have reported that gender is an interesting example of a complex factor that may influence the development or course of mental illnesses. However, the way a man or woman lives within his or her assigned sex can play out in many different directions. Gender identity is influenced by many things, such as socialization styles suggested by parents or schools or peers, location and quality of housing, the availability of education and the type provided, the kinds of toys that are given to the child, and perhaps even the kind of clothing that a child is allowed to wear. All these factors may also affect differential vulnerability to mental illnesses.

Although gender is a critical determinant of mental health and mental illness, the morbidity

associated with mental illness has received substantially more attention than the gender specific determinant and mechanisms that promote and protect mental health and foster resilience to stress and adversity. Gender determines the differential power and control men and women have over the socioeconomic determinants of their mental health and lives, their social position, status, and treatment in society and their susceptibility and exposure to specific mental health risks. Gender specific risk factors for common mental disorders that disproportionately affect women include gender based violence, socioeconomic disadvantage, low income, low or subordinate social status and unremitting responsibility for the care of others. The high prevalence of sexual violence to which women are exposed and the correspondingly high rate of post traumatic stress disorder following such violence renders women the largest single group of people affected by this disorder *(Häfner et al., 1998).*

Herman et al. (1989) have stated that epidemiologic studies of mental disorders have long shown dramatic difference in the prevalence of different mental disorders in men versus women. According to DSM IV, Alcohol related disorder, other

substance related disorder, paraphilias, gender Identity disorder and pyromania are diagnosed at least twice in men compared to women. While major depressive disorder, dysthmic disorder, agoraphobia, anorexia nervosa and bulimia nervosa are diagnosed at least twice in women compared to men. Also there is gender difference in diseases usually first diagnosed in childhood. Some disorders are more frequent in boys for example, reading disorder, stuttering, autism, attention deficit hyperactivity disorder, conduct disorder, Tourette's disorder and enuresis while Rett's disorder is more frequent in girls.

Reed et al. (1998) also added that men are also more likely to be diagnosed with antisocial personality more than 3 times compared to women. While data from large scale epidemiological surveys suggest that panic disorder is more common in women. They found that panic disorder is 2.5 times more in women than in men. Another study showed that there are no marked gender differences in the rates of severe mental disorders like schizophrenia and bipolar disorder that affect less than 2% of the population.

Piazza et al. (1989) have also suggested that gender difference are not found only in the prevalence

but also in many other aspects of mental disorders. For instance, important gender difference in phenomenology, course, treatment response and outcome have been demonstrated for alcoholism and for schizophrenia. Women with alcoholism have later onset, rapid course, and suffer more physical consequences than do men with alcoholism.

While women with schizophrenia have later onset, on average women are older 3 to 5 years than do men on first contact with a health professional, more affective symptoms, better response to neuroleptic medication and to psychosocial treatment programs and better outcome than do men *(Rossler et al., 2000)*.

Häfner et al. (2000) also report that negative symptoms occur more frequently in men. Also another research suggested that there is a great difference in symptomatolgy in panic disorder for example; shortness of breath, nausea and feeling smothered are more common in women while pain in stomach and sweating are more common men.

There is continued controversy regarding the extent to which gender difference in individual psychology are biologically versus socio- culturally based *(Hanlly et al., 1993)*.

Goldstein et al. (2002) have suggested that gonadal hormones may be important for understanding these differences. Female sex hormones not only have "activational" effects but also "organizational" effects in adult life pre and perinatally which means that they induce alteration in brain during critical periods of development. A well- controlled magnetic resonance imaging study showed that normal patterns of sexual brain dimorphism are disturbed in schizophrenia. Organizational effects of gonadal hormones during the developmental period could be partly responsible for that finding. Also certain brain functions show different alterations in adult women with schizophrenia as compared with men with schizophrenia. it seems that neuropsychological functioning relevant to language, verbal memory, visual-spatial functions, and olfaction is relatively better preserved in women. this could have consequences for rehabilitations.

There is increased evidence presented by both clinical and basic research studies of estrogen protective effects in schizophrenia. Thus recent researches show that estrogens have specific and significant effects not only on dopamine which is probably the most important neurotransmitter regarding schizophrenia but also on

serotonin and other neurotransmitter systems (*Rossler et al., 2003)*.

Kulkarni et al. (2001) also added that using estradiol in treatment of schizophrenic women was studied by Dr. Kulkarni. She found that addition of 100Mcg transdermal estradiol yielded a greater symptom improvement. This finding is in line with a study by Lindamer which showed that hormone replacement therapy in post menopausal women might save neuroleptics and reduce negative symptoms of schizophrenia.

Thus there is considerable knowledge concerning gender differences in prevalence, phenomenology, course, response to treatment and outcome of mental disorders. this makes it clear that any research or clinical endeavour in psychiatry should involve the separate study of men and women.

AIM OF THE WORK

1- To review the literature of gender difference in various aspects of mental disorder.

2- To discuss Biological and psychosocial hypothesis that may explain these gender differences.

3- To clarify the implication of these gender differences for treatment.

Chapter 1

GENDER DIFFERENCE IN SCHIZOPHRENIA

Schizophrenia is psychiatric diagnosis that describes a mental disorder characterized by abnormalities in the perception or expression of reality. It most commonly manifest as auditory hallucinations, paranoid or bizarre delusions or disorganized speech and thinking with significant social or occupational dysfunction with approximately 0.4-0.6% of the population affected. Diagnosis depend on the patient's self reported experience and observed behavior *(Bhugra et al., 2006)*.

Goldstein et al. (1995) have stated that schizophrenia is a heterogeneous disorder. One of the goals of research in this area has been to identify homogeneous subgroups with the assumption that this will lead to the identification of specific etiological risk factors and focused treatment strategies.

Historically, sociodemographic factors, such as one's sex, have not been used to subtype schizophrenia and have been relatively neglected in research on schizophrenia However, over the last 15

years there has been a growing interest in understanding whether, and if so, how one's sex contributes to explaining some of the heterogeneity of the disorder *(Wahl et al., 1992)*.

Bhugra et al. (2006) have reported that the identification of sex differences in schizophrenia is not new, since even Kraepelin described dementia praecox as disorder men and women with schizophrenia differ regarding age at onset, Symptomatology, neurobiological factors, such as brain abnormalities aud cognitive function, course of illness, treatment response, incidence and familial transmission. However, many would also argue that sex effects seen in schizophrenia are the same as seen in the general population, and therefore one's sex does not contribute to our understanding of the illness. Others have argued that sex is a risk factor, i.e. it has etiological consequences, for the illness. So, what is the evidence for sex effects in schizophrenia, and is sex a modifier of phenotypic expression or a risk factor for the illness?

Incidence and prevalence

Castle et al. (1993) have reported that the incidence of schizophrenia ranges from approximately 0.5 to 2.0 per 10000 population, and the prevalence from 1 to 12% in different countries.

Castle et al. (1993) also found that studies on incidence and prevalence of schizophrenia supported the notion that the sex effect on incidence was, in part, highly dependent on the stringency of the diagnostic criteria and the decision of what other related diagnoses were included in the definition of a case. Studies using broader criteria reported no significant sex differences in incidence or prevalence, as did studies that combined schizophrenia with paranoid disorders or other non-affective psychoses i.e. disorders in which women have been shown to have higher rates while studies that used more stringent diagnostic criteria for schizophrenia showed a significant sex effect on incidence, with men experiencing significantly higher rates than women.

These studies showed that males younger than age 45 years had the highest incidence compared to young females. Women older than age 45 years had a significantly higher incidence of schizophrenia than men older than age 45. However, it was demonstrated in a well-designed population-based study that the higher incidence among older women did not offset the higher incidence among younger males, thus still resulting in a significantly higher rate among men

when all ages were combined, e.g. male-to-female risk ratio was 1.34 *(Castle et al., 1993)*.

Okasha and his Coworker, (1990) had studied 200 schizophrenic patients diagnosed according to DMP-1.They found 72% were males (144) and 28% were females (56*)*.

Regarding sex differences in prevalence, studies reported a lower male to female rate ratio than did incidence studies. however, as with incidence, male to female ratios varied from 1,04 to 2,1 based on diagnostic criteria, sampling frame and duration of the reported prevalence (i.e. point and period, ranging from two weeks to life time. higher rates among females were also reported in three studies. however in these studies, either diagnostic criteria were loosely defined or there was poor diagnostic reliability *(Goldstein et al., 1995)*.

A well designed one year prevalence study of DSM-111-R schizophrenia cases in a rural area of Ireland reported a non significant male to female rate ratio of 1.23, which was replicated in a second study. Opposite to the previous study, another recent prevalence study in Ireland, not limited to rural areas, reported a significantly higher prevalence of

DSM 111-R schizophrenia among men than women *(Youseff et al., 1999)*.

Bhugra et al. (2006) have also reported that as with the incidence findings, the prevalence in young men was found to be higher than in young women, and in older women it was higher than in older men. This attenuated the overall prevalence rates by sex.

Age at onset

One of the most replicated finding in the schizophrenia literature is the age-at-onset differences between men and women. The literature consistently demonstrates that men have an earlier onset age than women, which is specific to schizophrenia, not an artifact of admission practices, and similar across cultures. The age of women at first contact with a health professional and first admission to hospital was higher—on average between 3 and 5 years higher—than that of men. This gender difference was already evident at the first onset of the disease and could not attributed to just a delay by these women in seeking help. The cumulative lifetime risk for men and women, on the other hand, seems to be identical. This suggests that the gender difference is modulated by age (*Usall et al., 2001*).

Omar et al. (1998) have examined 100 schizophrenic patients diagnosed according to the lCD-10 research diagnostic criteria, comparing 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.

Castel et al. (1998) have reported that studies on the onset of schizophrenia have revealed that the onset peaks at around age 20-25 years in men, whereas the onset peak is later in women, at around age 25-30 years. In addition, there is a second smaller peak in women after age 45. In early adolescence, the onset ratio of men to women is generally 2:1. However, by age 50 and older, the onset ratio becomes 2:1 female-to-male. Approximately 3-10% of women have onset after age of 40, compared to few, if any men.

Hambrecht et al. (1992) have found that the magnitude of age at onset sex difference varies by geographic region. Although women had a later age at onset than men in developing and developed countries

in the World Health Organization's study of first-episode schizophrenic cases, the difference was smaller in developing countries. This may have been due to the fact that few onsets occurred after age 40, which was presumably a consequence of earlier mortality in developing countries.

Explanations of sex differences in age at onset have ranged from biology to social-role hypothesis it had been hypothesized that sex steroid hormones have a direct effect on age at onset. In rats, estrogens have been found to have a small antidopamincrgic effect. Thus, it has been hypothesized that estrogens may delay the onset in women. The lowering of estrogens in postmenopausal women could also account for the slight increase in the risk for schizo-phrenia after age 45 *(Castle et al., 1998)*.

Hafner and Colleagues, (1992) have found that in a recent experimental study with neonatal and adult rats, neonatal exposure of estrogen caused a downward regulation of D2 receptor numbers, which occurred most frequently in the youngest animals. The impact of estrogen on D2 receptors could contribute to explaining later age at onset in women. An alternative hypothesis is that androgens may

trigger earlier onset in men Finally, from a social role-social expectations viewpoint of sex differences, it has also been suggested that late adolescence may be a more socially demanding developmental period for boys due to the social expectations of independent work and active courting, thus triggering' an earlier onset in men than women.

Hafner et al. (1993) had also suggested that greater likelihood of aggression in males with schizophrenia would bring them to the attention of services earlier than female counterparts. conversely, it has been suggested that females with schizophrenia are more likely to be protected by their families, and that social role expectations would make them less likely to come to the attention of psychiatric services.

Gender differences in disease course

Usall et al. (2003) have reported that women have a more favorable disease course than men. But again, looking at more recent and more reliable studies, it seems that we have to differentiate Do we mean symptom-related course or social course? Do we mean narrowly or broadly defined schizophrenia? Do we mean young or older women? When analyses are restricted to more narrowly defined schizophrenia, the