Review Article

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Gender Differences in Mania

Suprakash Chaudhury[1], Ajay Kumar Bakhla[2], Vijay[3], Subodh Kumar[4], Swaleha Mujawar[5], Chetan Dewan[6]

Abstract

Gender remains an important determinant of psychological fitness and psychiatric disorders. Biological vulnerabilities may be accentuated and exacerbated by interaction of gender and social determinants. Sex differences in age of commencement of psychiatric disorders, their course, symptom presentation, co-morbidity rates and treatment response have been reported consistently in bipolar disorder. Few workers evaluating differences, according to sex, in presenting symptoms of mania have reported men with mania exhibit higher prevalence of problems in behavior and are able to converse with difficulty. In contrast, female patients even during mania show higher amount of symptoms of depression. More recently women with mania were reported to have higher scores on lability of mood, depression, anxiety, guilt and suicidal thoughts while men obtained higher scores on humor, grandiose ideation, psychosis and motor activity. The finding of clinical differences in mania according to gender emphasizes the need for large scale studies on patients with bipolar disorders to firmly establish whether there exist clinical differences in symptomatology according to gender and measures to improve compliance with treatment. There is a pressing requirement to evaluate the safety of different treatment modalities during pregnancy.

Keywords: Gender; Sex; Mania; Bipolar Disorder.

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Introduction

To a great extent gender affects the power males and females have over the social and economic factors that influence their social position, social status and exposure to risk factors for psychiatric disorders. Thus gender has a vital influence on psychological fitness and psychiatric disorders. The genetic difference between women and men alone do not explain differences in vulnerability, prevalence and symptom presentation of illness. The genes and environment interaction is complex; genetic endowment elicits individual environments (the nature of nurture), and experience modulates the expression of genes [1].

Author's Affiliation: [1]Professor, [5]Resident, Dept. of Psychiatry, Dr DY Patil Medical College, Hospital & Research Center, Dr DY Patil Vidyapeeth, Pune, Maharashtra 411018, India. [2]Assistant Professor, Department of Psychiatry, Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand 834009, India. [3]Senior Resident, Dept. of Psychiatry, Ranchi Institute of Neuro-Psychiatry & Allied Sciences (RINPAS), Kanke, Ranchi 834006, Jharkhand, India. [4]Department of Psychiatry, K.C. Roy Hospital, Ranchi 834001, Jharkhand, India. [6]Assistant Professor of Social Work, Karve Institute of Social Service, Pune, Maharashtra 411052, India.

Correspondence and Reprint Requests: Suprakash Chaudhury, Professor, Dept. of Psychiatry, Dr D Y Patil Medical College, Hospital & Research Center, Dr DY Patil Vidyapeeth, Pune, Maharashtra 411018, India.

Email: suprakashch@gmail.com

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In most of the psychiatric disorders, the symptomatology, clinical course and outcome have received greater interest while the influence of gender on symptomatology as also the mechanisms that may prevent psychiatric disorders and promote resilience to stress have not received much attention.

Gender Difference is not synonymous with Sex Difference

The increasing tendency of using "Gender" as a substitute for "Sex" has created confusion since they are not synonyms. Sex indicates specific characteristics that are biologically determined. In contrast, gender denotes culturally-and socially-determined distinctions between males and females [2].

Gender is linked to how we are supposed and projected to feel and behave as males and females because of our social and cultural background, and not because of biology [3]. Gender equality implies evenhandedness and fairness in the allocation of duties and reimbursements between males and females [4].

Gender-based differences may originate from a biological, psychological, social and/or epidemiological (population-based risk) factors. Rarely does biology acts alone in the causation of psychiatric disorders. Usually biological vulnerabilities are affected by interaction of social and psychological factors, including gender [5].

In a number of psychiatric disorders gender based differences have been reported in age of commencement and natural history of the disorder, symptom presentation, co morbidity rates and treatment response. The differences are remarkable during childhood, then the pattern of difference changes at puberty, at adulthood and around old age [6]. Male child are more prone to conduct disorders, hyperactivity syndromes, anxiety and depression, autism and learning disabilities.

However around and after puberty the predominance of psychological illness is taken over by girls except substance abuse, schizophrenia, and impulse control disorders [7]. It has been estimated by the World Health Organization that women and children constitute 80% of 50 million people who are forcibly displaced as a result of violent conflicts, wars, and disasters. In their lifetime one in five women are raped or face a rape attempt while 16% to 50% endure violence [8]. Exposure to such stressful life events may lead to psychiatric disease [9].

Gender Difference in Mania

The prevalence of bipolar disorder (BD) is equal in women and men according to epidemiological studies [10], while females have a higher prevalence of depression. There have been suggestions that women experience more depressive episodes than their male counterparts, but the Systematic Treatment Enhancement Program for Bipolar Disorder study found no gender difference with respect to past episodes of mania or depression [11]. It has been suggested that "hard" or "core" bipolarity, characterized by mania or prominent hypomania, may have an equal gender distribution, and possibly a male predominance when defined by minimal associated depression. By contrast, "soft" bipolarity, particularly when defined by mild hypomania or hypomanic symptoms and prominent associated depression, may have a female predominance [12].

Age of onset

In the Epidemiologic Catchment Area study the mean age at onset of mania was 21.2 years [13], whereas the more recent Systematic Treatment Enhancement Program for Bipolar Disorder (STEP–BD) study reported a mean of 17.37 years [14]. A retrospective analysis of all adult patients suffering from first-episode psychosis, mania, or hypomania and reporting for psychiatric treatment in Camberwell, during 1965-1999 revealed onset of mania in men was earlier as compared to women [15]. Though women have an earlier age at onset than men, [16] but they receive the diagnosis of BD on average 4.4 years later than men [15]. This difference in age of commencement of illness is not only of theoretical interest but also is of clinical significance. Early age at onset is associated with poor prognosis: increased rates of psychosis, increased rates of co morbid substance misuse and co morbid psychiatric disorders, increased suicide risk and neuropsychological dysfunction [17].

Course of illness

First episode in BD is likely to be a manic for males and depressive for females [18,19]. Rapid cycling course in female has been one of the most consistent findings [16,20]. The European Mania in Bipolar longitudinal evaluation of medication (EMBLEM) study found a predominance of females with rapid cycling course [21]. Contrary to this, of the individuals entering the STEP–BD trial, 32%

met rapid cycling criteria in the previous year but no correlation was found with female gender and rapid cycling [11].

In females more episodes of depression or dysphoric mania was noted than pure mania [22,23] the average duration of individual episodes of depression was found to be longer in female [24].

Female patients with BD are more prone than bipolar men to experience a sequence of depression followed by mania (sometimes called the DMI pattern) [25], whereas men with BD are more or equally prone to suffer the episode pattern of manic episode followed by depression (the MDI pattern) [18]. A possible relationship between female bipolarity and seasonality was reported [16]. This was further substantiated by a study that reported increase in psychiatric hospitalizations of female BD patients in the spring and fall as compared to a unimodal peak in the spring in bipolar male patients [26]. An Indian study found that resolution of mania settles faster if they exhibit aggression and sexuality, and females settles later specially if they exhibit anxiety and lability [27].

Clinical feature

Classical symptoms of mania as described with the 10th edition of International Classification of Disease, Diagnostic Criteria for research (ICD -10, DCR) are elevated, expansive or irritable and abnormal mood, increased activity or physical restlessness, talkativeness, self -esteem or grandiosity, sexual energy, thoughts racing, loss of normal social inhibitions, decreased need for sleep, distractibility and foolhardy or reckless behaviors. But clinically other atypical features like depression, anxiety, irritability, and psychosis related aggression, paranoia and disorganization are found in part or even dominates the clinical picture.

Factor analytic studies have extracted five factors: dysphoria (depression), increased psychomotor activity, amplified hedonism, irritation with belligerence and psychotic features as features of atypical mania [28]. There is a paucity of studies evaluating differences in presentation of episodes of mania according to gender. Similar to the pattern reported for BD, studies suggests that female patient even during the episode of mania exhibit higher amount of symptoms of depression (mixed mania) compared to male patients [29,30]. On the other hand men suffering from mania are not able to take part in a discussion and show greater behavioural problems [18]. A recent Indian study on mania observed significantly higher grandiosity, humor, motor activity and psychotic symptoms in men while scored significantly higher on dress, mood lability, depression, anxiety, guilt and suicidal ideation [31].

Comorbid conditions

Overall in BD a higher psychiatric co-morbidity is observed in females [32], but substance use and conduct problems are more frequently encountered in males and sexual trauma in females. [15,33]. Some of the important co-morbidities associated with women with BD are:

Anxiety disorders

Comorbid anxiety disorders are common and there is a lesser association with bipolar I disorder than bipolar II disorder [34]. The presence of high anxiety scores in patients with BD is associated with higher rates of cyclothymia, alcohol use disorder and suicide. BD patients with high anxiety respond poorly to treatment with lithium [35].

Thyroid disease

Thyroid disease is more common in BD populations, especially in women, and this finding is present in populations which have not received lithium therapy [36].

Migraine

Females with Bipolar II disorder have increased likelihood of suffering from migraine. In females the occurrence of migraines with BD is associated increased prevalence of comorbid medical problems, whereas in males the presence of migraine in BD is associated with early onset of the disorder and increased occurrence of anxiety disorders [37].

Eating disorders

Studies have found that females suffering from BD have higher prevalence of eating disorders [18].

Pregnancy

During the course of BD in women, a major risk factor for relapse is the occurrence of pregnancy. Some studies have reported the risk of relapse to be

50% [38]. In a small prospective observational cohort study of pregnant women with BD pregnancy was associated with relapse in 71% patients. These episodes were depressive in nature in the majority of cases and nearly half had occurred within the first trimester. Recurrence was more likely if a woman had discontinued medication.[39]. Studies on the consequences of taking antipsychotics and mood stabilizers in pregnant BD women are of small sample size/case reports and have given contradictory results. Lithium use in pregnancy is associated with occurrence of Ebstein's anomaly of the heart [40]. The use of antipsychotics and anticonvulsants during pregnancy is associated with higher occurrence of complication of pregnancy, birth defects, complications during neonatal period, and long term adverse developmental outcomes during childhood [40–45]. In women who were treated with multiple anticonvulsants during the first three months of pregnancy, the risk of fetal malformation was significantly higher when lamotrigine or carbamazepine was used together with valproate, but not when either anticonvulsant was used alone [46]. Treatment with clozapine, olanzapine, risperidone, and quitapine are not reported to cause major fetal malformations. There is limited information on aripiprazole and ziprasidone. Due to its association with cleft lip and palate benzodiazepines should be avoided during pregnancy. Similarly antiparkinsonian drugs should be avoided in pregnant women. Electroconvulsive therapy is safe and effective in pregnant women [32].

Therapeutic issues

The pharmacotherapy of bipolar in female patient is complicated due to its atypical and mixed presentation, associated medical and psychiatric comorbidities, and distinct side effect profile. The salient therapeutic issues restricted to gender variation are summarized here. Gender does not affect pharmacodynamic response of bipolarity to lithium. [47]. Possible gender differences in the pharmacodynamic response of bipolarity to valproate, carbamazepine and atypical antipsychotics have been less systematically evaluated. No data exist, however, to suggest that gender produces clinically relevant changes in the response to these agents. Though reproductive-aged women with BD being treated with valproate (and other mood stabilizers associated with weight gain) should be monitored for menstrual irregularities and hyperandrogenism [48]. Lithium-associated hypothyroidism and weight gain is more common in women, whereas men are more likely to develop tremor [49]. Typical antipsychotic medications and the novel antipsychotic risperidone are associated with increased risk as well as more distressing presentation of hyperprolactinemia in females [50].

Adherence to treatment

In BD patients high rates of nonadherence to treatment of up to 32.9% have been reported in a study in United States of America [51]. A 10 year naturalistic follow up study in Span reported nonadherence to be 6.7% in women versus 39.39% in men. Treatment nonadherence in BD patients is associated with comorbid substance use disorders, marital status, hospitalization, suicide attempts, age at disease onset, family history, health status, functional level, residual cognitive dysfunction, lower level of education and gender [52–54]. Most of the studies have evaluated gender differences in clinical features and there is a dearth of knowledge about the effects, if any, on occupational and social functioning. A few studies have observed that among patients with acute mania lesser number of men than women lived with a partner of resided alone. However, as regards working or taking part in social activities no gender differences have been reported [55].

Conclusion

From the review it is evident that there are clear gender differences in mania. This emphasizes the need for large scale studies to evaluate the various aspects of gender differences in mania and measures to improve compliance with treatment. There is a pressing need to evaluate the safety of different modalities during pregnancy.

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