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Psychotic disorders and bipolar affective disorder

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1.1 Psychotic disorders in women

If mental health is low in the priority of policy and programmes in many countries, women's mental health issues have been a subject of neglect and indifference for a long time. In women, severe mental illness, even if low in prevalence assumes importance largely on account of the social ramifications and human distress. Feminists often opine that they have not been involved in the complex process of understanding and dealing with the issues around women's mental health [1].

The 1998 World Health report states that 'Women's mental health is inextricably linked to their status in society'. It benefits from equality and suffers from discrimination [2]. Many women with severe mental illness stay outside treatment settings, especially in low income countries with poor and inadequate mental health facilities. Those who do enter treatment settings have varied experiences ranging from humane care to indifference and stigmatisation. This chapter outlines the clinical features of women with schizophrenia and bipolar disorder, BPD, but chooses to place greater emphasis on interpersonal and social ramifications of these disorders and the impact on their lives as a whole.

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1.2 Schizophrenia

Epidemiological indices

Incidence

Incidence of schizophrenia seems to be fairly stable in both genders across reported studies. The diagnostic definitions (broad vs restrictive) used have however determined differences as in the case of the Determinants of Outcome of Severe Mental Disorders DOSMED study [3].

The review of 55 core incidence studies by McGrath *et al.* [4], reported higher incidence rates in males; the male-female rate ratio median was 1.4 (0.9–2.4). Nine studies, which reported higher rates in women were examined in detail, but showed no features distinguishable from the other studies.

The Madras study on a population of 100 000 did not show any gender differences [5]. However, Dube and Kumar [6] in Agra reported a greater incidence in males (1.5 : 1). In the Chandigrah study, the incidence rates of broadly defined schizophrenia were the highest among rural women (0.47/1000) and lowest in urban males (0.37/1000).

Prevalence

Rates for genders have varied greatly across studies, and variations in methodology, sample sizes prevent any definitive conclusions to be drawn. A review of prevalence studies in schizophrenia by Saha *et al.* [7] did not find any striking sex differences.

Mortality

Morbidity risk for schizophrenia over the lifespans seems to be around 1% in both genders. In the 25-year follow-up of the Madras Longitudinal Study of 90 first episode schizophrenia patients, 25 patients have died, of whom males were 15. More males have had physical illnesses, while more women have committed suicide (unpublished data). The suicides in women were largely in response to symptoms as in the case of one woman who had the delusion that she appeared nude to others and resultant social embarrassment. Higher suicide risk in women with schizophrenia was also reported by Mortenesen and Juel [8].

A recent study in rural China by Ran *et al.* [9] found much more mortality and suicide in men than in women and ascribed the higher prevalence found in women to this.

A systematic review of mortality in schizophrenia revealed no sex differences [4]. Augier *et al.* [10] however, report more suicides in young males with schizophrenia.

Course and outcome

Women have a better outcome than men. It is unclear whether this is due to later age of onset, protective nature of hormones such as oestrogens or better drug response.

The Australian Study of Low Prevalence (Psychotic) Disorders looked at gender differences among 1090 cases of psychosis (schizophrenia, schizoaffective disorder, affective psychoses and other psychoses). Results within diagnostic groupings confirmed differences in how men and women experience and express their illness. Within each diagnostic group, women reported better premorbid functioning, a more benign illness course, lower levels of disability and better integration into the community than men. They were also less likely to have a chronic course of illness. There were no significant differences in age at onset. Differences between women across the diagnostic groups were more pronounced than differences between women and men within a diagnostic group. In particular, women with schizophrenia were severely disabled compared to women with other diagnoses [11].

The Madras Longitudinal study found better outcome in women after five years of follow-up, but this did not sustain through the rest of the 15 years of follow-up [12]. It is likely that several mechanisms are needed to explain the differences. Greater social integration and functioning in women across diagnostic groups may well reflect culturally and socially determined gender differences. In contrast, variability and attenuated findings with respect to symptom profiles beg the question of biological mechanisms with some degree of specificity [11, 13].

Psychopathology

It has been documented that women with schizophrenia tend to be more overtly hostile, physically active and dominating, have more sexual delusions and are more emotional than men.

A large sample of Chinese patients with schizophrenia had more paranoid subtype of schizophrenia in females. They also showed a different pattern of ongoing symptoms and severity with more severe positive and affective symptoms, and a greater number of suicide attempts whereas male patients were more likely to show severe deterioration over time [14].

Muller [15] studied gender specific differences in association of depression in persons with schizophrenia. In females, depression was independently associated with higher negative symptom scores ($P < 0.01$) and younger age ($P < 0.05$) whereas in males positive symptoms ($P < 0.05$) and short hospitalisation ($P < 0.05$) were the main factors associated with depression.

Age at onset

A higher mean age at onset of schizophrenia for women has been one of the very consistent findings in the last 20 years. Several independent reviews of many studies have shown that the disorder appeared later in women. Since the time between onset of symptoms and first hospitalisation were the same in both genders, it was evident that women did have a later onset. There have been however a few reports which have not replicated this finding. Some studies from India have not found a gender difference in the age of onset and have questioned the universality of the traditional view of earlier onset in men [16]. The Madras longitudinal study of almost equal numbers of men and women in a sample of 90 cases also did not find a gender difference in onset [12].

Alcohol and drug abuse

Women with chronic mental illness tend to use alcohol and drugs of addiction, especially if they have become victims of sexual abuse. This however may not be the case in some developing countries where almost all women live with families who keep a close watch on them. Besides, these women also do not have the financial independence to acquire these substances. Many studies from the developing world have reported very low rates of drug abuse in women with schizophrenia.

Response to treatment

There is an expanding literature on gender differences in psychopharmacology. It has long been observed that men and women seem to require different dosages of anti-psychotics and have different responses to them. The SOHO (Schizophrenia Outpatient Health Outcomes) study was a three-year, prospective, observational study of health outcomes associated with antipsychotic treatment in 10 European countries that included over 10 000 outpatients initiating or changing their antipsychotic medication in 4529 men (56.68%) and 3461 women (43.32%). Findings showed that gender was a significant predictor for response based on the Clinical Global Impression (CGI) scale and for improvement in quality of life. The highest gender differences were found in typical antipsychotics and clozapine. Olanzapine only showed differences in quality of life, and no differences were found for Risperidone [11].

In the Chinese study of Tang *et al.* [17], males received higher daily doses of antipsychotics and demonstrated a different pattern of antipsychotic usage, being less likely to be treated with second-generation antipsychotics. The clozapine blood level was 35% higher in women than in men.

In general, premenopausal women seem to require lower doses. The role of oestrogens in neuromodulation seems to account for this difference. It has to be kept in mind that the bulk of patients taking part in drug trials are men and much of the knowledge about dosing is therefore more applicable to men.

Side effects of medication

Neuroendocrine effects of antipsychotics, especially those secondary to hyperprolactinaemia can cause a lot of distress to women patients. This is true with all First Generation Antipsychotics and to an extent risperidone and ziprasidone. Clozapine, olanzapine and quetiapine seem to spare prolactin. Amenorrhoea, galactorrhoea, decreased sexual interest and functioning and changes in bone density are the side effects of increased prolactin levels.

Obesity also seems to be more common among women and has its own psychological and medical effects.

Marriage and schizophrenia

While international research has largely dealt with marital rates in schizophrenia the outcome of the marriage itself has received sparse attention. Kreitman [18], Eaton [19], Odegaard [20], Saugstad [21] and Hafner [22] have all examined the relationship between marriage and schizophrenia and most of them have reported low marital rates. The issue of marital status vis àvis outcome of schizophrenia has been examined by few [23–26].

In countries like India, marriage is not just an indicator of social functioning, but is almost a mandatory event in life. Separation and divorce are still stigmatised and even unheard of in rural areas. In this context, we interviewed 75 women with schizophrenia/BPD who were separated/divorced. While 40 women (53%) had been rejected/abandoned by their spouses without going through any formal divorce/separation proceedings, only 16 had been legally divorced, 5 had their marriages annulled by local rural governing bodies (Panchayat), 7 had their cases pending in court. Three (4%) had been granted *talaq* by the Muslim court and four had not been granted divorce by the courts.

Only four of the women received any kind of financial support from their husbands. Thirty-three husbands (44%) had remarried after separation from the ill woman [27, 28]. The women experienced a gamut of emotions starting with denial and shock to deep depression and suicidal thoughts and attempts. Many of them retained their symbol of marriage since being separated was more stigmatising than being mentally ill. When asked about future plans, the characteristic reply was '. . . there is no future for me, so what's the point of thinking about it, this will only lead to more worries, I have enough as it is'.

Concerns of being a burden to their aged parents were widely expressed and many wanted to work to support themselves. Hostile criticisms from parents and siblings that openly ridiculed their uselessness further reinforced their sense of being a burden to their families and were also particularly painful to them. But faced with few options, they felt they had little choice but to carry on with their lives and leave it all to God and fate.

In contrast many of the women had extremely supportive and overly protective families on whom the patient was deeply dependent. These women were quite content to live under the protective umbrella of their parental homes. While

some of them did express concerns about what was to become of them after the death of their loving parents, it was obvious that this was only a fleeting thought and not one which they liked to dwell on much. Avoiding, escaping and shifting the onus of care onto someone else seemed to be markedly present among these women.

This study brought into focus some issues that confront women with chronic mental illness in many developing countries. They are:

1. A lack of awareness of the illness and its disabilities resulting in a widespread belief that marriage is a panacea for all ills. This results in their families arranging their marriages, very often suppressing the fact of mental illness to the husband and his family.
2. Absence of legal protection including maintenance for such women.
3. Once they have a relapse after marriage, they are sent back to the parental home and the responsibility of caring for them falls on the ageing parents.
4. Lack of welfare programmes to offer physical, sexual and financial security for these women.

However, we see this as a priority area of intervention by governments, which should have some national policies and programmes to take of such women whose families are unable to continue caring for them. If not provided with a suitable shelter, these women can land on the streets and become prey to sexual abuse and other high-risk activities.

Homelessness

Homelessness is probably the most visible of all the social sequelae of psychotic disorders in women. It has been estimated that 20–40% of homeless women suffer from psychotic disorders. In many developing countries, family support notwithstanding, the numbers of mentally ill women who become homeless seems to be on the increase. This may well be due to breaking up of joint and extended families, and better transport facilities resulting in such women migrating from one part of the country to the other. In many countries, services for such women are either absent or totally fragmented and inadequate. Homeless mentally ill women have more pregnancy and childbirth related complications.

Though males who are ill are at grater risk of becoming homeless, homeless women seem to be sicker than their male counterparts [29], Goering *et al.* [30] spoke of demoralisation of the female homeless who wanted their rights respected and autonomy maintained.

A comparative study found substance abuse to be less in homeless women than in men. Symptom severity in homeless individuals with schizophrenia appears as an interaction of symptom profiles and risk behaviours that are gender specific [31].

There has been a dearth of systematic research in homelessness, especially in developing countries. As pointed out by Dinesh Bhugra in his book [32], the impact of risk factors such as poverty and poor environmental conditions and their association with ill health needs to be studied in various socio-cultural settings. In large countries like India, where the homeless travel long distances across the length and breadth of the country, the challenge is relocating them in their families. While some families are keen to receive them, others tend to be distinctly hostile or indifferent to them when they are sent back. Planning of care facilities for this group of persons with severe mental illness is hardly a priority in many countries.

Burden and stigma

Stigma faced by patients and families has also evinced a lot of international research interest and efforts are underway to plan major stigma reduction programmes. The WHO's Dare to Care campaign and the WPA's global anti-stigma programmes are foremost among these. Knowledge of mental illness in the relative, the need to seek psychiatric treatment, which is still not looked upon very favourably in many traditional societies, the need for social restraints on account of behaviour problems and above all issues of employment and marriage contribute to the experience of stigma in families. Thara and Srinivasan [33] found that many caregivers felt depression and sorrow, which was more profound if the patient was a woman. Women caregivers reported more stigma than male carers. These feelings probably become even more severe when they have to deal with their daughters with uncertain futures and broken marriages and lack of social support.

Another Indian study [34] observed similar levels of burden among caregivers of patients of schizophrenia and BPD. They used similar types of coping methods to deal with it. Awad and Voruganti [35] in an article on burden of schizophrenia opine that 'there are no reliable estimates of the costs associated with care of persons with schizophrenia'. As there is a lack of reliable cost information about the family burden of care specific to schizophrenia, there is an urgent need to develop reliable approaches that can generate data that can inform in policy making and organisation of services.

Disabilities in women

The 1992 National Health Interview Survey NHIS data from the USA is a comprehensive published data set that contains domains of disabilities associated with health conditions. The survey assessed three domains of disabilities: limitations in activities, work and self-care. A minimally greater proportion of women were more disabled than men in all three domains. However women who were mentally disabled were younger than their physically disabled counterparts. This was especially notable in limitations in personal care. It was pointed out

by the authors that policy makers need to be aware of the special needs of service development and configuration for women disabled by mental disorders. Appropriate coverage for the care of disorders and disabilities would result in better short term and long term outcomes [36].

In the Madras Study, there were no differences in disabilities between genders at five-year follow-up. However, work in the case of men and daily activities in the case of women seemed critical to address and intervene [25].

Psychosocial rehabilitation in women

It has been observed that Psychosocial Rehabilitation programmes by and large have not paid much attention to the special needs of women. Carol Mowbray [37] points out that only 3% of the 127 articles published in the Psychiatric Rehabilitation Journal from 1999 to 2001, focused on women. For women, relationship and basic survival skills take precedence over substance abuse related skills. In many countries in Asia where women live in joint and extended families, there is a constant need to adjust to various emotions, critical comments and expectations of the family members. Married women in the west are often exposed to Psycosocial Rehabilition, PSR programmes with specific focus on motherhood and care of children. While the focus of PSR in the west is on independent living, it is on managing dependent relationships in large families in many Asian countries. Marriage and motherhood are also issues that need to be addressed during rehab.

Ageing women with schizophrenia

Like everybody, women with schizophrenia also age. And like the age, some of their problems can also increase. The gender differences seen in the younger years seem to plateau off as the age increases. Problems of ageing such as cognitive decline and chronic medical conditions may be exacerbated by schizophrenia and the disorder is associated with premature mortality. Older women with schizophrenia are at risk for neglect of psychiatric and other health needs that are further compounded by limited social support and low socioeconomic status.

In countries like India where families are the primary caregivers, older women, especially those widowed, meet with varying reactions from the younger members. As long as they are physically active and able to contribute to the household chores, they are quite welcome. However, a physical illness or relapse of schizophrenia upsets the balance and many women feel ignored and rejected. In the absence of any alternative boarding and care facilities, the families look upon them as a 'burden'.

1.3 Bipolar disorder

Introduction

Bipolar affective disorders are currently classified as illnesses separate from clinical depression. The spectrum of psychopathology under the rubric of 'bipolar disorder' is wide and includes bipolar I, bipolar II and mixed states, which is an admixture of both poles of the illness.

Epidemiology

The lifetime prevalence of bipolar disorders has been reported as 0.5–1.6% [38]. The differences in lifetime prevalence and current (12-month rates) are smaller than in major depression. In contrast to major depression, there are relatively few gender differences in bipolar disorder, a finding supported by large population studies across several countries and cultures, including studies in Asian countries like Hong Kong [39] or Taiwan [40]. There is preliminary evidence to suggest that women may be more likely to be diagnosed as bipolar disorder type II. In a chart review of 131 patients attending a Mood Disorder Clinic in Los Angeles, Hendrick *et al.* [41] found 48% of their clinic population to be women and 60% of the women were diagnosed as BPD II. Contrary to this, similar rates of BPD II in men and women was reported by Szadoczky *et al.* [42] in a Hungarian Epidemiological study.

Age of onset

There has been some suggestion that the onset of illness is later in women with BPD than men [43]. Several other studies have not demonstrated any difference in the age of onset between men and women [41, 44–47]. The findings need to be viewed cautiously, since they did not provide age at the time of first mania or first depression. Hendrick's study, which provided the data, did not show the effect of sex on age of onset. Taylor and Abrams subdivided patients into early and late onset based on a cutoff age of 30. Females accounted for 35% in early onset group versus 22% in late onset, a non-significant finding. More male patients were identified in case records of adolescents with a diagnosis of bipolar disorder over six years in India, indicating that males had an earlier age of onset in this group [48].

Pattern of course and outcome

Several longitudinal studies have shown that bipolar disorders are characterised by frequent recurrences. Only a few longitudinal evaluations have explored the

course of illness in developing countries [40, 49–53]. Few have commented on gender differences. In the studies which have compared the course of illness in men and women [41, 45, 54] differences in the number of hospitalisations and the episodes of mental illness have been inconsistent. These results may be either due to different methodologies used or, it is more likely that sex probably does not impact the course of bipolar illnesses.

Mixed mania

The effect of gender on mixed mania is inconsistent through literature. There is some evidence that women with BPD may be more likely than men to experience mixed episodes. This finding is however not consistent across studies. Definitional and methodological limitations hinder comparisons. Arnold *et al.* [55] in a review of gender effects in mixed mania, suggested that as the definition of mixed mania involves an increasing number of depressive symptoms, the ratio of women to men increases This finding was supported by Akiskal [56]. In a comprehensive review of 17 mixed studies by McElroy *et al.* [57] female patients accounted for 58–90% of subjects with mixed mania in five studies. One study found that male patients accounted for 59% of the subjects with dysphoric mania. The remaining 11 studies did not report the sex of the subjects. Rob *et al.* [54] identified a trend towards females experiencing more mixed episodes in the previous one year.

Rapid cycling

Women are more likely than men to experience a rapid cycling phase in their bipolar illness. This finding has been consistent across several studies. Pooled data from 10 studies showed that women on an average accounted for 71.7% of the cases of rapid cycling, defined as at least four distinct mood episodes in a 12-month period [58]. Similar findings were reported by Wherr *et al.* [59] and Robb *et al.* [54]. In addition to finding more rapid cycling amongst women, Schneck *et al.* [60] also reported that rapid cyclers had a greater severity of illness than those without rapid cycling. Several explanations have been put forth to explain the effects of sex on rapid cycling. These have included higher rates of hypothyroidism in women, more frequent use of antidepressants and the effects of menstrual cycle on mood changes [43]. All these factors however remain speculative [61]. Hormonal fluctuations do not seem to influence rapid cycling in women. The possibility of greater use of antidepressants to explain the higher rates of rapid cycling in women remains untested.

Suicide

People with bipolar disorder are at great risk for suicide if they are not treated. The National Mental Health Association reports that 30–70% of suicide victims have suffered from a form of depression. Women had a significantly higher rate

of suicidal attempt, but men a higher risk of suicide death [62]. The data from a study in an Italian tertiary care centre suggests that females were more likely to report a history of suicidal gestures and a comorbid panic disorder; males were more likely to present with a comorbid obsessive-compulsive disorder, and there was a trend for a more frequent history of alcohol or substance abuse [63].

Phenomenology and bipolar disorder

In a study on gender differences, Kawa *et al.* [64] reported that most gender comparisons showed no differences. Nonetheless, more men than women reported mania at the onset of bipolar I disorder. Men also had higher rates of comorbid alcohol abuse/dependence, cannabis abuse/dependence, pathological gambling and conduct disorder. Men were more likely to report 'behavioural problems' and 'being unable to hold a conversation' during mania. Women reported higher rates of comorbid eating disorders, weight and appetite change and little disorder during depression. Kessing [65] reported that significantly more women were treated as outpatients than as inpatients. Women were treated for longer periods as inpatients but not as outpatients. In both settings, the prevalence of depressive versus manic/mixed episodes was similar for men and women and the severity of manic (hypomanic/manic without psychosis/manic with psychosis) and depressive episodes (mild/moderate/severe without psychosis/severe with psychosis) did not differ between genders. The prevalence of psychotic symptoms at first contact was the same for both genders. Among patients treated in outpatient settings more men than women presented with comorbid substance abuse and among hospitalised patients, more women than men presented with mixed episodes.

The severity of the illness in the developing countries at onset is no less than in the west [66]. Although symptomatology appears not dissimilar to patients from developed countries, more pronounced distractibility and a persistent embarrassing behaviour are more common in the Indian Setting [67]. The same authors also reported a preponderance of mania in Indian patients in a more recent study, Shahul Ameen and Daya Ram [68] reported that there were no significant gender differences in the prevalence of negative symptoms in remitted bipolar disorder.

Cognitive dysfunction and bipolar disorder

Although several reviews of neuropsychological deficits in bipolar disorders have been reported [69, 70] few studies have commented on sex differences in cognitive deficits in bipolar disorders. Sex differences are not found in cognitive functioning of patients with bipolar disorder, both in acute phase as well as when in remission [71].

Substance abuse and bipolar disorder

Several studies have reported an association between alcoholism and mood disorders. Data from both developed and developing countries reveal high levels of comorbidity in bipolar illness [72]. Data collected on bipolar disorder show rates of substance abuse that are five to six times greater than those among general populations [73, 74]. Three studies found the rate of substance misuse in those with bipolar I disorder to be over 60%, and at least 35% of total bipolar disorder cases were complicated by alcohol abuse [75, 76]. A diagnosis of an underlying bipolar illness may be missed because of the high rate of comorbidity and the more conspicuous signs and symptoms of substance abuse [77]. Very little research has addressed the issue of substance abuse and bipolar comorbidity amongst women. Chandra *et al.* [78] reported that areca nut, commonly occurs amongst Indian psychiatric patients. Predictors of current areca nut use included less education, diagnosis of bipolar disorder and current tobacco use. Predictors of severe use were older age, female gender, less education and current tobacco use.

Bipolar disorder and pregnancy

Contrary results have been put forth on the impact of pregnancy on bipolar disorders. Some have suggested that pregnancy may be a time in which women may experience a relief from their mood symptoms. However, Blehar *et al.* [44] closely examined the timing of pregnancy and emotional problems in women with BPD Type 1 and found that 37% reported mood episodes during their pregnancy and 14 reported mood changes in pregnancy and postpartum periods.

Postpartum period and bipolar disorder

Nonacs and Covans [79] reported that women with BPD had a 20–50% risk of relapse during the postpartum period. The risk of postpartum relapse appears to be even higher in women with a past history of postpartum psychoses. Kendal *et al.* [80] provide the strongest evidence supporting these findings. Linking data from the Edinburgh Case Register to the Scottish maternity discharge database, they inferred that a psychiatric admission for psychoses during the first 90 days after childbirth was 14% more likely than before childbirth. Amongst women with a past history of bipolar disorder, 21.4% required admission during the first three months after childbirth. This risk was significantly greater than the risk of women diagnosed as schizophrenia (3.4% risk) or depressive neurosis (1.7% risk). In a study in Turkey, Kisa *et al.* [81] reported 32% patients were diagnosed as bipolar disorder in the postpartum period.

Menopause

The effects of menopause have not received much research attention and the reported findings have been contradictory. In a study of menopausal women, Blehar *et al.* [44] found 13% women with depression and 4% women with mania.

Management of bipolar disorders: Impact of sex on response rates

Possible sex differences in the responses to treatment with mood stabilisers has been an understudied area, although it has been well established that sex differences have been found in absorption, metabolism and excretion of medications. Endogenous hormone cycles have been known to influence the pharmacokinetics of the treatment agents, whatever the life cycle of the woman.

The sex differences in response to treatment with lithium have been extensively studied. Viguera *et al.* [82] reviewed 17 lithium studies comprising of 1548 patients. No significant differences were seen in the response rates. A recent large-scale efficacy study using divalproex [83] did not report efficacy on sex of the participant.

Decisions regarding treatment of bipolar disorder during pregnancy

Evidence base indicates that decision to treat must balance the risks associated with the untreated condition versus teratogenecity.

No treatment

Patients who discontinue mood-stabilising medication after conception increase their risk of relapse [84] either of which could lead to complications and untoward effects on the foetus. Untreated mania may be associated with perinatal risks, as a pregnant patient in a manic state may engage in impulsive, high-risk behaviours that endanger her and the foetus [85]. These effects may be mediated by the illness itself or by other factors that indirectly affect birth outcomes.

Antimanic (mood stabilising) agents

Patients vary in their response to antimanic agents. Therefore, there is no single preferred medication for bipolar disorder, regardless of reproductive status. The preferred medication is what has been effective for and has been tolerated by the individual patient.

Lithium

Lithium is a first line drug for acute and maintenance treatment of bipolar disorder. There is no evidence for an increased risk of miscarriage or intrauterine foetal death in women treated with lithium [86]. Recent controlled epidemiologic studies suggest a real, but modest, teratogenic risk of Ebstein's anomaly following first-trimester lithium exposure. Based on a pooled analysis of the data, Cohen *et al.* [87] estimated the risk of Ebstein's anomaly to between 1/1000 (0.1%) and 2/1000 (0.2%), which is 10–20 times higher than rates in the general

population. Thus, while the relative risk for Ebstein's anomaly is increased, the absolute risk remains small. Pregnant women taking lithium should be evaluated with a high-resolution ultrasound and foetal echocardiography at 16–18 weeks gestation to screen for cardiac anomalies. Still birth was reported in a patient in whom lithium prophylaxis was considered essential for clinical and social reasons in India [88]. The authors suggested avoiding the use of lithium, at least in the first trimester.

Maternal lithium toxicity can occur due to various factors such as vomiting, febrile illness, alteration of sodium intake for treatment of pre-eclampsia or diuretic therapy. Toxicity is most likely to occur during the intrapartum period. Patients are encouraged to have their lithium level monitored every two to four weeks throughout pregnancy, weekly in the last month and every few days shortly before and after delivery [89]. Adverse neonatal outcomes are more extensive in the setting of higher lithium concentrations at delivery. Lithium delivery concentrations can be significantly reduced at delivery without compromising pharmacotherapeutic efficacy by withholding lithium therapy from the onset of labour [90]. While lithium is associated with significant risks in all stages of pregnancy, it arguably remains the safest medication for the pregnant woman with bipolar disorder.

There are no prospective studies to establish the incidence and risk factors for occurrence of lithium toxicity in the foetus and newborns, although this was reported in the mid 1970s [91]. This follow up study showed that attainment of major developmental milestones for 22 lithium-exposed subjects was comparable to controls. In a more recent study, serum lithium levels in nursing infants were reported to be low. No significant adverse clinical or behavioural effects were noted [92]. These findings encourage reassessment of recommendations against lithium during breast-feeding and underscore the importance of close clinical monitoring of nursing infants.

Anticonvulsants

Studies performed through the late 1990s suggest that the risk of morphologic malformations in infants exposed to valproate and carbamazepine is about two to three times higher than in the general population. The most common malformations in exposed offspring are similar to those seen in the general population (e.g. heart defects, hypospadias, club foot and cleft lip or palate). No single malformation has been associated with a specific antiepileptic drug, with the exception of spina bifida, which is more common with exposure to valproic acid (1–5% of exposed infants) and carbamazepine (0.5–1%). Malformations are also more common after exposure to polytherapy than after exposure to a single drug. Additional evidence for a higher teratogenic potential of valproate comes from the North American registry, in which malformations were four times more common among infants exposed to valproic acid than in those exposed to all other antiepileptic monotherapies combined.

The risk of birth defects after Lamitrogine exposure used in first trimester are similar to rates in general population. Intrauterine growth retardation is included in descriptions of the foetal valproate syndrome, but the incidence has not been established. Carbamazepine is associated with reductions in mean birth weight (about 250 g).

Other anticonvulsants, such as oxcarbazepine (Trileptal; Novartis), tiagabine (Gabitril; Cephalon, Inc., Frazer, PA) and topiramate (Topamax; Ortho-McNeil Neurologics, Inc., Titusville, NJ) are occasionally used in clinical practise as antimanic agents or to treat anxiety symptoms. Outcomes of 94 pregnancies in women exposed to oxcarbamazepine found no anomalies related to its use; however, these are too few to rule out adverse effects with confidence. The safety of tiagabine and topiramate for use in pregnancy has not been investigated.

Neurobehavioural teratogenicity

A retrospective survey of British women between the ages of 16 and 40 who were exposed to antiepileptic drugs during pregnancy evaluated the subsequent need for special education for their exposed children. Those exposed to valproate monotherapy had a higher likelihood of needing special education (OR, 3.4; 95% CI 1.63–7.10). In contrast, carbamazepine had no statistically significant effect (OR, 0.26; 95% CI 0.06–1.15). Polytherapy including valproate had similarly high odds ratios for lower academic achievement (OR, 2.51; 95% CI 1.04–6.07) compared with those exposed to polytherapy excluding valproate (OR, 1.51; 95% CI 0.56–4.07). Although these findings should be treated with caution, they suggest that monotherapy or polytherapy with valproate during pregnancy carries particular risks for the neurodevelopment of children exposed in utero.

A prospective study of children's intelligence quotients (IQs; mean age seven years) compared IQs in children of epileptic mothers to the IQs of children in a control group. Again, children exposed to valproate prenatally had a mean IQ that was 11 points lower than those children who were not exposed. The same study found no association between carbamazepine and cognitive dysfunction. A single follow-up of 23 infants exposed to lamotrigine demonstrated no alterations or delays in development at 12 months of age. Data are still inadequate to determine the risks of developmental effects of foetal exposure to lamotrigine. No evidence of growth problems, post-birth discovery of occult malformations, neonatal seizures or deviations in psychomotor development to one year of age were observed in 62 infants exposed to lamotrigine in utero.

Neonatal toxicity

Manifestations of withdrawal, including irritability, jitteriness, abnormal tone, feeding difficulties and seizures have been described in infants whose mothers took valproic acid during pregnancy. The frequency of withdrawal symptoms was significantly related to the dose of valproate given to the mothers in the third trimester, and there was a tendency for both the frequency of the minor

abnormalities and the major malformations to be related to the valproate dosage in the first trimester.

Maternal vitamin supplementation

Maternal folate supplementation reduces the risk of neural tube defects. However, risk reduction has not been confirmed in pregnant women treated with anticonvulsants. Some experts recommend a daily dose of 4–5 mg of folic acid before and during pregnancy, or at least through the first trimester, for all women who take antiepileptic drugs. Pernicious anaemia can be masked by folate supplementation; therefore, a B12 level obtained before beginning folate treatment is a prudent recommendation. Carbamazepine has been associated with vitamin K deficiency. Because adequate levels of vitamin K are necessary for clotting, in utero carbamazepine exposure could increase the risk of neonatal bleeding. Most experts recommend women on carbamazepine take an additional 20 mg of vitamin K supplement daily throughout pregnancy.

Other anticonvulsants

Other anticonvulsants, such as oxcarbazepine (Trileptal; Novartis), tiagabine (Gabitril; Cephalon, Inc., Frazer, PA) and topiramate (Topamax; Ortho-McNeil Neurologics, Inc., Titusville, NJ) are occasionally used in clinical practise as antimanic agents or to treat anxiety symptoms. Outcomes of 94 pregnancies in women exposed to oxcarbazepine found no anomalies related to its use; however, these are too few to rule out adverse effects with confidence. The safety of tiagabine and topiramate for use in pregnancy has not been investigated.

Antipsychotic agents

Antipsychotic drugs are often used as monotherapy or adjunctive medications for patients with bipolar disorder. Antipsychotics are commonly used in the management of acute mania. The largest body of evidence regarding safety for use in pregnancy exists for the older, first-generation antipsychotics.

The best-studied drug in this class is chlorpromazine, in a 1977 survey of more than 50 000 mother-child pairs that identified 142 first trimester exposures and 284 total exposures to chlorpromazine, there was no elevation in the rate of physical malformations. Several case reports have documented transient extrapyramidal symptoms, including motor restlessness, tremor, hypertonicity, dystonia and Parkinsonism in neonates exposed to antipsychotic agents during pregnancy. These problems have typically been of short duration and have been followed by apparently normal subsequent motor development.

In a 2004 review of the management of bipolar disorder in pregnancy, Yonkers [89] supports the role of first-generation antipsychotic agents both in the treatment of acute mania during pregnancy, and as an alternative to selected mood stabilisers. Psychiatric clinicians may elect to switch a patient's medication

from lithium or an anticonvulsant to a first-generation antipsychotic either for the entire pregnancy or for the first trimester. This strategy is particularly recommended for patients who have benefited from mood stabilisation with antipsychotic medications in the past. First-generation antipsychotic medications may also be a choice for women with bipolar disorder who elect to discontinue medication during pregnancy but begin to experience a recurrence of symptoms while pregnant.

Atypical antipsychotic agents

McKenna *et al.* [93] examined 151 pregnancy outcomes from mothers enrolled in the Canadian Motherisk Programme to determine whether atypical antipsychotics increase the rate of major malformations. These included exposures to olanzapine (n = 60), risperidone (n = 49), quetiapine (n = 36) and clozapine (n = 6). The results suggest that atypical antipsychotics are not associated with an increased risk for major malformations; however, the limited numbers are inadequate to determine the risk of foetal exposure.

Olanzapine is associated with serious metabolic side effects that could potentially exacerbate maternal weight gain and gestational diabetes, which is associated with an increased risk for a large for gestational age newborn.

Antidepressants

Monotherapy with antidepressants – that is, use of an antidepressant without concomitant antimanic medication – is not appropriate in the management of bipolar disorder. Use of antidepressants in a patient with bipolar disorder may trigger a mood shift from depression to induction of a manic, hypomanic, mixed episode or rapid cycling.

Psychosocial management

A number of studies have addressed effectiveness of various psychosocial strategies [94–98]. There is limited literature on the role of gender in the effectiveness in these strategies. In an analysis of intensive family intervention, bipolar patients were reported to do better than depressive patients in terms of global ratings, symptoms social role functions and family attitudes. The beneficial effects seen were attributed to improvement in female patients [99].

1.4 Other psychoses

Schizoaffective psychoses

The definition of schizoaffective psychoses has undergone several changes through the years, making it difficult to get reliable epidemiological information. However, pooled data from various clinical studies have estimated that approximately

2–29% patients have been diagnosed as schizoaffective. Levinson *et al.* [100] estimated 19% patients were diagnosed as schizoaffective disorder. Women had a higher prevalence of the disorder. Relatives of women suffering from the disorder had a higher rate of schizophrenia and depression as compared to relatives of male schizophrenia patients [101].

Acute and transient psychoses

Acute and transient psychoses is a relatively new entrant into psychiatric nosology [102]. Female preponderance was noted in the occurrence of this category of psychoses [103–105].

Delusional disorder

Mixed results have been published on the gender differences in patients diagnosed as suffering from delusional disorder. A crude estimate of the condition has been reported to be between 0.7 and 3.0 per 100 000 population [106]. In a retrospective study from China, 0.83% of 10 418 outpatients met DSM IV criteria for delusional disorder, with equal gender distribution. Women were significantly older than men [107]. Yamada and associates [108] reported a 3 : 1 female to male ration in Japan. Hwu and colleagues [40] did not find any sex differences in their studies. In India, rates have varied: from 0.5 to 5% [109, 110]. In a study from North India, 55.7% of the patients diagnosed as delusional disorder were females [111].

Postpartum psychosis

Postpartum psychosis is a term used for all psychoses occurring during the postpartum period. All classic psychoses (i.e. the manic, the depressive or very often the schizoaffective type, but also schizophrenic or 'atypical' psychoses) can occur. In contrast to depressive disorders, risk for psychosis is excessively higher during the postpartum period than at other times of a woman's life – up to 20 times higher in the first month after parturition [80]. Recent evidence suggests that postpartum psychiatric illness is virtually indistinguishable from psychiatric disorders that occur at other times during a woman's life. Postpartum psychosis, a severe form of postpartum psychiatric illness, is a rare condition that typically has a dramatic onset and is characterised by psychotic symptoms including disorientation and disorganised behaviour. Epidemiological studies have reported rates of 1–2 cases per 1000 live births. Most studies have not distinguished postpartum psychosis from bipolar disorder or the proportion of the incidence attributable to pre pregnancy psychiatric morbidity [112]. The incidence of postpartum psychosis was reported as 0.07% from the USA. In a prevalence study of postpartum disorders, in Tamil Nadu, India, the estimate of psychoses was 0.63% [113]. Data from a psychiatric clinic in Hazara district in Pakistan reported 8.6% of the women attending the clinic over three years had

a history of postpartum disorders. Of these, 60% had diagnoses of postpartum psychosis. This high rate was attributed to the selection of specialist clinics for the study, where only gravely ill subjects were brought [114].

1.5 Special issues in women with severe mental illness

Sexuality

Few studies describe sexual disturbance in schizophrenia and only a few of these describe sexual function or dysfunction in women [115]. Whereas men with schizophrenia frequently lose their sexual drive early in the course of illness and are not likely to be sexually active if their illness is severe, this is generally not true for women. They continue to be interested in relationships and to engage in sexual intercourse [116]. The relative passivity and isolation that accompany schizophrenia are fertile ground for sexual victimisation. For these reasons, women with schizophrenia are at special risk not only for unwanted pregnancy but also for sexually transmitted disease [117].

Two studies compared schizophrenia women to normal controls [118, 119]. Schizophrenia women are more likely than normal controls to have low sexual desire and difficulty becoming aroused or reaching orgasm. Several factors contribute to sexual dysfunction amongst women. Amongst women receiving conventional antipsychotic treatment, 50–90% experience menstrual irregularities [120]. Serum Prolactin irregularities are also hypothesised to contribute to sexual dysfunctions. Women may also experience dyspareunia due to vaginal dryness and atrophy.

Social skills deficits in schizophrenia is likely to make a woman vulnerable to sexual exploitation. Social consequences such as homelessness, vulnerability to sexual abuse and exposure to HIV and other infections contribute to the difficulties to rehabilitation of women [121].

Mothers with psychosis as parents

Many women with schizophrenia are mothers. This is particularly true in societies like India when women marry rather early and have children. The later age of onset of illness in women also seems to facilitate this. Research in this area has been sparse and has included some qualitative interviews with women who are mothers [122]. The problems faced by such women also differ across countries and cultures. Issues regarding day to day parenting, custody, foster care and dealing with welfare agencies are important in many western countries. In the east, where joint families provide substitute or supplementary mothering, the problems are lack of social welfare schemes and the additional burden and responsibility on the women's families. In a study on 75 women with schizophrenia who were separated or divorced, 29 women had children [27]. Twenty of these 29 who had children who continued to live with their ill mothers even after separation. When the mother was too ill or had multiple relapses, the

ageing grandparents often had to take on the parental roles. Only six husbands of these 75 women came forward to take care of the children and only two provided financial support to the wife and children.

In a literature review of studies in the last five years [123], it has been pointed out that maternal mental illness can impact negatively on a child's life, especially where an insecure attachment is formed between mother and baby during the important early developmental years. Impaired cognitive development, behavioural difficulties and increased risk of psychiatric disorder seem to be some of the sequelae. Effective parenting skills are suggested to be a protective factor against these sequelae. It therefore becomes imperative to focus on providing parental skills as part of the general psychosocial programmes.

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