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REVIEW ARTICLE

Bipolar Disorder in the Life Span of Females: Treatment Implications

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Abstract

Given the fact that bipolar disease affects both men and women, special care must be taken while treating a woman over the course of her life. Bipolar disorder is a serious and debilitating illness that affects about 5% of women. In most women, the first sign of sickness is a depressive episode. Greater axis-one comorbidity, more depressive episodes, quicker cycling, and mixed affective states have all been linked to female gender. Treatment of bipolar disorder during reproductive events necessitates special consideration. More research is needed to better understand the disorder's course, outcome, and gender-specific treatment options.

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Introduction

Bipolar affective disorder (BPAD) is a severe and debilitating psychiatric condition that emerges in young adulthood and is marked by alternating episodes of depression, hypomania, and/or mania, or mixture of manic & depressive symptoms separated by euthymic intervals.[1,2] The annual incidence rate is between 3 and 10 cases per 1 lakh people. The lifetime prevalence of bipolar I disorder (BD I) has been estimated at 1.3% from epidemiologic catchment area study data.[3] However, recent reports have suggested much higher prevalence rates, 3.7 to 6.4%, for bipolar spectrum disorders.[4,5] Overall, BD I affects women and men equally,[6] but bipolar II disorder (BD II), mixed episodes, bipolar depression, and a rapid-cycling course of illness occur more commonly in women.[7] There are substantial disparities in how this sickness manifests in men and women. Furthermore, women with bipolar disorder face distinct challenges in their management. Except for investigations of bipolar disorder in women during reproductive events, most bipolar disorder research is not gender-specific; nonetheless, specific understanding about bipolar disorder in women comes from comparing data from male and female subgroups. Childbearing, other reproductive difficulties (e.g., menstruation and menopause), phenomenology, disease course, and sexual side effects of drugs must all be taken into account.[8]

Woman-A Life Cycle of Vulnerabilities

Biological

There are various genetic factors that predispose women to increased risk. Life span of changes during puberty, pregnancy, and menopause, as well as after giving birth or experiencing a miscarriage. Differences in communication, handling relationships and stress, and expressions. Mental disorders at times of hormone change, such as perinatal depression, premenstrual dysphoric disorder, and peri menopause-related depression. It has been seen during childbearing years women are more susceptible to mood changes. Inadequate nutrition is also a predisposing factor. More number of hospital admissions and complications of pre-existing mental illness during the perinatal period.[9]

Social

Women are mostly abandoned by marital families, left homeless, working excessively for lower wages, restricted roles, or sexually abused in society. The sexual and physical abuse rates of women with SMI are high compared to healthy females. Further, there are no clear policies for the welfare of severely ill women. A lifetime prevalence rate of violence in females ranges from 16 to 50%. At least one in five women suffers rape or attempted rape in their lifetime.

Social support from family and friends can buffer against the deleterious effects of stress or directly enhance functioning among bipolar individuals which lacks for females whereas high criticism and emotional over-involvement from family members give stress and worsen the course of bipolar disorder. On the work front and capitalism, it is evident that employment inspires confidence, self-worth and financial freedom; however, low pay, unequal pay or forced labor can lead to abuse of human rights and subjugation.[10] Illiteracy, poor educational standards, economic dependency, poverty, domestic isolation and feudalistic oppressions were all found to be related to high prevalence among females.[11] Problems like household violence, locality-related violence, civil conflict, family breakdown, substance abuse and community disintegration are known to have implications on health.[12]

Psychological

Since childhood females face adversity and lack of support from family and care givers, develop poor coping skills and face multiple personality issues.

Traditional

India has a firm patriarchal family system dominated by males. Females are dependent on males for financial and safety purposes and are kept indoors. Women's education is not given importance and they often have to drop off from school to take care of home. Mental illness in women takes a non-significant role and compounded by a poor family support becomes a 'Dual curse'.[12]

Cognitive

Bipolar individuals exhibit dysfunctional cognitive styles similar to those observed among unipolar depressed individuals; and whether these cognitive patterns, alone or in combination with life events, serve as risk factors that predict the expression or course of bipolar disorder.[13]

Comorbidities

BD is associated with increased comorbid axis I illnesses: panic disorder/agoraphobia, social phobia, alcohol use, marijuana use, and, to a lesser degree, bulimia nervosa.[14,15] A past history of sexual abuse is reported twice as often in women as men with BD (43% vs 21%). Early extreme stressors predict early onset of BD, rapid cycling, increased suicide attempts, and post-traumatic stress disorder.[16] Women with BD are at higher risk of alcohol abuse/dependence than are men with BD (odds ratios of 7.35, 2.77, respectively).[17] Biologically, alcohol dehydrogenase activity and first-pass hepatic metabolism are lower in women than men, which result in higher blood alcohol levels and increased risk of alcohol toxicity. Increased physical health problems and pain disorders occur in bipolar women. Hypothyroidism is twice as common in women as men with BD (23%, 12%, respectively) and may contribute to a delayed response to treatment in bipolar depression.[18,19] Lithium treatment and the presence of thyroid antibodies are associated with increased risk of thyroid failure.[20] Although valproate appears to induce menstrual irregularities more frequently than

Table 1: Gender differences in BPAD (8)

S.No.	*Characteristics*	*Female*	*Male*
1.	Onset	Earlier & 5th decade	3 yrs later
2.	Type BPAD II	More (3 times >)	Lesser (2 times)
3.	Episodes	MDD >;mixed >>	Manic >
4.	Seasonality	+++	+
5.	Polarity shift	++++	++
6.	Pattern of episodes	DMI(dep. mania)	MDI (mania Dep.)
7.	Admission	Bimodal peak spring & fall; Hospitalization >>	Unimodal; Hospitalisation <<
8.	Delay in treatment	11yrs from onset	7 yrs from onset
9.	Economical burden	++++	++
10.	Comorbidities	Migraine, obesity, PCOS,Hypothyroidism, eating disorders >>	Substance abuse>>
11.	Hormonal influence	+++++	++
12.	Medications	To be modified under hormonal life cycle	Not needed
13.	Side effects of medication	Obesity>;EPS >; Iatrogenic switch >; PCOD	Sedation >>, Iatrogenic switch lesser
14.	Abuse & life events	43%	21%

lithium therapy, the association between valproate and polycystic ovarian syndrome in BD remains uncertain.[21] Menstrual irregularities may also arise from non-pathological causes, hypothyroidism, hyperprolactinemia (triggered by certain atypical antipsychotics such as risperidone, and eating disorders (Figure 1).[21] An increased susceptibility to obesity and a drug-induced metabolic syndrome may be linked with valproate in bipolar women, who appear to develop hyperandrogenism and elevated leptin levels more frequently with it than with lithium.[22] Bipolar inpatients have an increased prevalence of diabetes, which may be associated with a body mass index (BMI) equal to or greater than 25 when age, sex, and race-matched with the general population.[23,24] The overall prevalence of migraines in BD is 13 to 25.9%.[25,26] Migraines are much more prevalent in BD II (64.7–77%), however,[26,27] and affect more women than men (44%, 31% respectively).[27] Acquired immune deficiency syndrome (AIDS)-related dementia can present as secondary mania, with symptoms of irritability and cognitive slowing, whereas a lowered immune function has been associated with depression in human immunodeficiency virus (HIV)(28). In fact, depressed women with HIV and CD4 counts less than 200 × 106 /L have a significantly higher mortality rate (54%) than non-depressed HIV-positive women (21%) with similar counts (28). More complete reviews on the topic of BD and HIV, coronary artery disease, and cerebrovascular disease have been addressed (29-31).

Gender differences in BPAD (Table 1)

Pregnancy and BPAD: Medication Guidelines

Pregnancy and BPAD: Guidelines

Level 1: Second-generation antipsychotic (SGA) monotherapy, or lamotrigine monotherapy, or lithium monotherapy only in known lithium responders (consider avoidance during the first trimester due to known association with Ebstein's anomaly). Both lithium and lamotrigine are metabolized during the second half of pregnancy at higher than at non-pregnant rates, and with declines in blood levels many women will need higher doses in later pregnancy

Level 2: If Level 1 is ineffective and/or not tolerated. Lithium monotherapy, or Two drug combination – SGA + SGA, or SGA + mood stabilizer.

Table 2: Specific Medications[40,41]

Drug	Potential Risk	Pregnancy recommendation	Breast Feeding
Lithium	1/1000 (1st trimester) to 1/2000 (births) develop Ebstein's anomaly[40] No cognitive or behavioral effects in exposed children Safest mood stabilizer during pregnancy Max recommended dose in pregnancy-400 mg thrice a day	Lithium levels should be followed closely during pregnancy. The dose should be held or reduced with the initiation of labor. Postpartum, the dose should be reduced to pre-pregnancy levels. Fetal echocardiogram in the first trimester is recommended	If close monitoring of infant blood levels available Risk of toxicity in case of dehydration
Valproate	Associated with up to 10% rate of malformations- neural tube defects, effects on cognition and brain volume, craniofacial anomalies, cardiac defects, cleft palate, and Hypospadias. Recently linked to autism	Generally should not be used during pregnancy NICE guidelines-contraindicated in reproductive age group in women High-dose folate (4 mg) supplementation is recommended	Considered safe(41)
Carbamazepine	Increased risk of malformations- spina bifida, other neural tube defects, facial and skeletal abnormalities, hypospadias, and diaphragmatic hernia Increased the risk of neonatal hemorrhage Risk increases-dose dependant pattern- High risk with doses 400mg/day	Generally should not be used during pregnancy High-dose folate (4 mg) supplementationis recommended	Considered safe
SSRI	Modest increased risk of spontaneous abortion, preterm birth and low birth weight but may be secondary to psychiatric illness No confirmed risk of birth defects except for small absolute increased risk of cardiac defects (2/1000 births) with paroxetine with first trimester exposure As per PNAS (proceedings of national academy of science) -- third-trimester exposure in about 30% of cases	Best studied class of Antidepressants High relapse rate in women who stop their antidepressants for pregnancy Avoid use of paroxetine during pregnancy if possible	Generally considered safe
SNRI	Less data available Modest increased risk of spontaneous abortion and preterm birth and low birth weight but may be secondary to psychiatric illness No confirmed risk of birth defects	Most studies are confounded by not controlling for the underlying psychiatric illness	Generally considered safe
TCAs	Less data available Modestly increased risk of spontaneous abortion and risk of preterm birth and low birth weight but may be secondary to psychiatric illness No confirmed risk of birth defects	Most studies are confounded by not controlling for the underlying psychiatric illness	Generally considered safe except for doxepin Monitor the baby for Sedation (TCA)

Typical Antipsychotics	No major congenital malformations have been demonstrated Associated with low birth weight and preterm delivery Exposure in third trimester associated with transient extrapyramidal and withdrawal symptoms in the infant	Most studies are confounded by not controlling for the underlying psychiatric illness High-potency antipsychotics are preferred over low potency due to anti-cholinergic, hypotensive, and anti-histaminergic side effects	Limited to no data on long term outcomes for exposed infants. Considered relatively safe
Atypical Antipsychotics	No major congenital malformations have been demonstrated May increase maternal weight gain May increase risk of gestational diabetes May increase size of the baby	Most studies are confounded by indication. Relatively, less data available for clozapine and lurasidone Glucose monitoring, Routine ultrasound monitoring of foetal size in late pregnancy Clozapine - floppy baby syndrome agranulocytosis monitoring-weekly for 6 months	Monitor for EPS and sedation Avoid clozapine in breastfeeding Aripiprazole-may reduce lactation Risperidone-breast engorgement
Benzodiazepines	May induce perinatal toxicity: temperature dysregulation, apnea, lower APGAR scores, hypotonia, and poor feeding Use just before delivery - floppy baby syndrome Some studies suggest oral cleft palate defects; others are negative	Consider tapering benzodiazepines before delivery. Intermittent use is unlikely to induce withdrawal symptoms in the newborn	Use during breastfeeding may cause sedation or potential infant dependence Shorter-acting agents preferred

Level 3: If Levels 1 and 2 are ineffective and/or not well tolerated, consider electroconvulsive therapy (ECT) if symptom severity is warranted, or carbamazepine or First generation antipsychotic (FGA). On all accounts benefits Vs risks is always taken into consideration.[32]

Mood episodes are found to be more common in first pregnancy and the postpartum period. It has been suggested that this may be due to placental hormones increasing throughout pregnancy, and their abrupt fall after childbirth.[33,34] Women with BD face a complex varieties of problems including: increased libido during episodes of mania, health related risks for the mother and/or the baby, decisions regarding treatment during pregnancy, as well as concerns related to unplanned/undesired pregnancy, and sexually transmitted infections.[35-37] It is important to start mood stabilizers for maintaining stability during pregnancy and preventing relapse. Discontinuation might lead to relapse, particularly in the first trimester.[38] A large meta-analysis and systematic review found that women without prophylactic pharmacotherapy during pregnancy had a postpartum relapse rate of 66%, compared with 23% for women who were taking medications.[39] To best advise patients about using psychotropic medications during pregnancy or lactation, treating doctor should help patients weigh the risks of untreated illness against the risks of teratogenicity, perinatal complications, and neurodevelopmental problems.

Pregnancy and BPAD: Neonate-Specific Concerns

Opt for hospital delivery followed by fetal screening and monitoring of the neonate for adverse effects is mandatory.[39] Involvement of pediatric services for premature or ill babies who are at risk is of utmost requirement. Monitoring the infant for specific drug side effects as well as feeding patterns, growth and development is needed. Additionally cautioning women against sleeping in bed with the infant, if taking sedative drugs is also important.

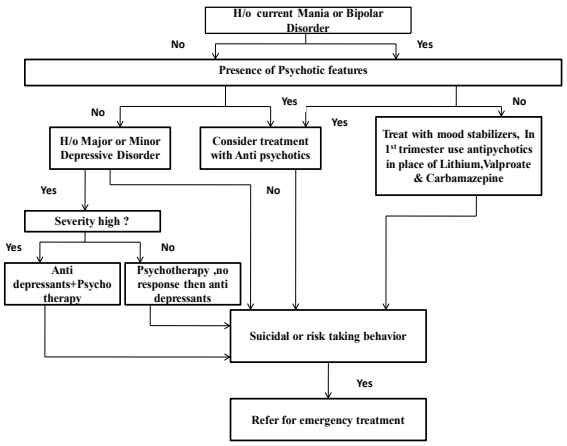

Figure 1: Algorithm for Treatment of BD during pregnancy

Role of ECT[42]

ECT is safe and effective treatment during pregnancy. Complications associated with ECT during pregnancy, include benign fetal arrhythmias; mild vaginal bleeding; abdominal pain; self-limited uterine contractions, increased likelihood of aspiration- without proper preparation, aortocaval compression, and respiratory alkalosis. Preparation for ECT during pregnancy should include adequate hydration, pelvic examination, discontinuation of nonessential anticholinergic medication, uterine tocodynamometry, intravenous hydration, administration of a non-particulate antacid, elevation of the pregnant woman's right hip during ECT, external fetal cardiac monitoring, intubation, and avoidance of excessive hyperventilation.

Specific precautions[43]

FOLIC ACID- prior to conception & during 1st trimester for women receiving anticonvulsants should be administered. In case of treatment with carbamazepine/oxcarbazepine, vitamin K-10 mg/day oral supplement in the last month pregnancy should be prescribed for patients continued and to the newborn- 1 mg Vit K IV /IM on day1 after delivery should be given.

Postpartum Period[41]

The postpartum period is a particularly high-risk period for women with BD. A Danish, population-based, cohort study found a 24-fold increase in the risk of postpartum mental disorders for women who had a first-degree relative diagnosed with BPAD.[44] Postpartum hypomania has been reported in 10–20% of women after childbirth and symptom emergence is rapid and antidepressant manic switch is common .

Lactation[45]

Lithium is contraindicated for breastfeeding. A systematic review of AD and mood stabilizer in lactation reveals that SSRIs, TCAs (except doxepin), Carbamazepine, sodium valproate, low dose short-acting benzodiazepines are relatively safe for the breastfed infant. The American College of Obstetricians and Gynecologists categorized the lactation risk of psychiatric medications as follows (Table 2):

L1 = Safest

L2 = Safer- divalproex , carbamazepine, olanzapine, quetiapine

L3 = Moderately safe - lamotrigine , risperidone, aripiprazole, and clozapine

L4 = Possibly hazardous – ziprasidone

L5 = Contraindicated- Lithium

It is also important to note that breastfeeding can lead to sleep disruption which should be avoided and hence the role of family as care takers is important.

BPAD & Peri-menopause, Menopause, and Late Life

Peri-menopause and menopause have been associated with bipolar exacerbations.[4] 20% of postmenopausal women with BD report worsening of mood symptoms. A protective effect of HRT (hormone replacement therapy) has been noted in menopausal females . Age-related illnesses like CVD (cerebrovascular disorders) and dementia lead to changes in mood and behavior in BD (Bipolar Disorder) and have been noted to complicate the existing illness.[46]

CONCLUSION

Pre pregnancy counseling with the encouragement of patients and family to take an informed decision improves compliance in pregnant females having BPAD. Ensuring continuity of care with active liaison with obstetricians and pediatricians is the need of the hour. The woman with BD will be managed by

close collaboration with all her providers like psychiatrist, psychotherapists, and primary care providers. Management in perinatal period needs a case based application of evidences and knowledge. Explaining the risks benefits is vital to the decision-making of the patients. The complex interplay of socio-cultural factors are important while planning the treatment of such individuals. There is a strong need for clinicians to be updated as and when evidences emerge so as to offer effective management to the patients.

REFERENCES

1. Goodwin FK, Jamison KR. Manic Depressive Illness: Bipolar disorders and Recurrent Depression. 2nd ed. NewYork: Oxford University Press; 2007.
2. Diagnostic criteria from DSM-IV-TR (4th Edition). American Psychiatric Association, Washington, DC, USA (2000).
3. Bebbington P, Ramana P. The epidemiology of bipolar affective disorder. Soc Psychatry Psychiatr Epidemiol. 1995; 30:279–292.
4. Hirschfeld RM, Calabrese JR, Weissman MM. Lifetime prevalence of bipolar I and II disorders in the United States. Paper presented at the 155th Annual Meeting of the American Psychiatric Association; Philadelphia, PA. May, Spring, 2002;
5. Judd LL, Akiskal HS. The prevalence and disability of bipolar spectrum disorders in the US population: Re-analysis of the ECA database taking into account subthreshold cases. J Affect Disord. 2003; 73:123–131.
6. Goodwin FK, Jamison KR. Suicide in Manic-Depressive Disorder. New York, NY: Oxford University Press; 1990. p. 227-244.
7. Benazzi F. Gender differences in bipolar II and unipolar depressed outpatients: A 557-case study. Ann Clin Psychiatry. 1999; 11:55–59.
8. Curtis V: Women are not the same as men: specific clinical issues for female patients with bipolar disorder. Bipolar Disord. 2005; 7(Suppl. 1): 16–24**.**
9. Women's reproductive mental health across the lifespan edition-1,switzerland,Springer charm,2014,Barnes
10. Cohen A. Site Visits. Updates on Global Mental and Social Health. 2007; 2:1
11. Belle D. Poverty and Women's Mental Health. American Psychologist. 2009; 45:385-89
12. Brown G W, Bhrolchain M, Harris T. Social Class and Psychiatric Disturbance among Women in an Urban Population. Sociology. 2005; 9:225-257.
13. Alloy L B, Abramson L Y, Neeren A M, Walshaw P D, Urosevic S, Nusslock R. (in press). Psychosocial risk factors for bipolar disorder: Current and early environment and cognitive styles. In S. Jones, & R. Bentall (Eds.), The psychology of bipolar disorder: New developments and research strategies. Oxford, England: Oxford University Press.
14. Post RM, Leverich GS, Altshuler LL, et al. An overview of recent findings of the Stanley Foundation Bipolar Network (Part I). Bipolar Disorders. 2003; 5:310–19.
15. McElroy SL, Altshuler L, Suppes T, et al. Axis I psychiatric comorbidity and its relationship to historical illness variables in 288 patients with bipolar disorder. Am J Psychiatry. 2001; 158:420– 26.
16. Leverich GS, McElroy SL, Suppes T, et al. Early physical and sexual abuse associated with an adverse course of bipolar illness. Biol Psychiatry. 2002; 51:288–97.
17. Frye MA, Altshuler L, McElroy SL, et al. Gender differences in prevalence, risk, and clinical correlates of alcoholism comorbidity in bipolar disorder. Am J Psychiatry. 2003; 160:883–889.
18. Salloum IM, Cornelius JR, Mezzich JE, Kirisci L, Daley DC, Spotts CR, Zuckoff A. Characterizing female bipolar alcoholic patients presenting for initial evaluation. Addictive Behaviors. 2001; 26:341–8.
19. Cole D, Thase M, Mallinger A, et al. Slower treatment response in bipolar depression predicted by lower pretreatment thyroid function. Am J Psychiatry. 2002; 159:116–21.
20. Kupka RW, Nolen WA, Post RM, et al. High rate of autoimmune thyroiditis in bipolar disorder: Lack of association with lithium exposure. Biol Psychiatry. 2002; 51:305–11
21. Joffe H, Hall JE, Cohen LS, Taylor AE, Baldessarini RJ. A putative relationship between valproic acid and polycystic ovarian syndrome: implications for treatment of women with seizure and bipolar disorders. Harv Rev Psychiatry. 2003; 11:99–108.
22. McIntyre RS, Mancini DA, McCann S, Srinivasan J, Kennedy SH. Valproate, bipolar disorder and polycystic ovarian syndrome. Bipolar Disord. 2003; 5:28–35.
23. Regenold WT, Thapar RK, Marano C, Gavirneni S, Kondapavuluru PV. Increased prevalence of type 2 diabetes mellitus among psychiatric in patients with bipolar I affective and schizoaffective disorders independent of psychotropic drug use. J Affect Disord. 2002; 70:19–26.
24. Cassidy F, Ahearn E, Carroll BJ. Elevated frequency of diabetes mellitus in hospitalized manic depressive patients. Am J Psychiatry. 1999; 156:1417–20.
25. Mahmood T, Roman S, Silverstone T. Prevalence of migraine in bipolar disorder. J Affect Disord. 1999; 52:239–41.
26. Fasmer OB. The prevalence of migraine in patients with bipolar and unipolar affective disorders. Cephalagia. 2001; 21:894–99.
27. Low NCP, DuFort GG, Cervantes P. Prevalence, clinical correlates, and treatment of migraine in bipolar disorder. Headache. 2003; 43:940–49.
28. Ickovics JR, Hamburger ME, Vlahov D, Schoenbaum EE, Schuman P, Boland RJ, Moore J. Mortality, CD4

cell count decline, and depressive symptoms among HIV-seropositive women. HIV Epidemiology Research Study Group. JAMA. 2001; 285:1466–1474.
29. Cruess DG, Evans DL, Repetto MJ, Gettes D, Douglas SD, Petitto JM. Prevalence, diagnosis, and pharmacological treatment of mood disorders in HIV disease. Biol Psychiatry. 2003; 54:307–16.
30. Joynt KE, Whellan DJ, O'Connor CM. Depression and cardiovascular disease: Mechanisms of interactions. Biol Psychiatry. 2003; 54:388–98.
31. Robinson RG. Poststroke depression: prevalence, diagnosis, treatment, and disease progression. Biol Psychiatry. 2003; 54:376–87.
32. British Association for Psychopharmacology consensus guidance on the use of psychotropic medication preconception, in pregnancy and postpartum 2017 https://www.bap.org.uk/pdfs/BAP_Guidelines-Perinatal.pdf
33. Grof P, Robbins W, Alda M. Protective effect of pregnancy in women with lithium-responsive bipolar disorder. Primary Care Companion J Clin Psychiatry. 2001;3(2):8
34. Di Florio A, Forty L, Gordon-Smith K, Heron J, Jones L, Craddock N, Jones I. Perinatal episodes across the mood disorder spectrum. JAMA psychiatry. 2013;70(2):168–75.
35. Di Florio A, Gordon-Smith K, Forty L, et al: Stratification of the risk of bipolar disorder recurrences in pregnancy and postpartum. Br J Psychiatry 2018; 213:542–547.
36. Viguera AC, Whitfield T, Baldessarini RJ, Newport DJ, Stowe Z, Reminick A, Zurick A, Cohen LS. Risk of recurrence in women with bipolar disorder during pregnancy: prospective study of mood stabilizer discontinuation. American Journal of Psychiatry. 2007 Dec;164(12):1817-24.
37. Bodén R, Lundgren M, Brandt L, et al: Risks of adverse pregnancy and birth outcomes in women treated or not treated with mood stabilisers for bipolar disorder: population based cohort study. BMJ 2012; 345:e7085
38. Grof P, Robbins W, Alda M, Berghoefer A, Vojtechovsky M, Nilsson A, Robertson C. Protective effect of pregnancy in women with lithium responsive bipolar disorder. J Affect Disord. 2000;61(1–2):31–9.
39. Nelson AM. Transition to motherhood. J Obstet Gynecol Neonatal Nurs. 2003;32(4):465.
40. Schou M, Goldfield MD, Weinstein MR, et al: Lithium and pregnancy: I. Report from the register of lithium babies. BMJ 1973; 2: 135–136 .
41. Holmes L B,Harvey E A, Coull B A, Hutington K B, Khosbin S, Hayes A M,Ryan L M. The teratogenicity of anticonvulsant drugs. N Engl J Med 2001;344:1132–8.
42. Leinkens K A,Cooke M J,Schweder L J,Harboe I,Hoie B. ECT during pregnancy: A systematic review of case studies. Arch Womens Ment Health.2015;18(1):1-39.
43. Shah N,Grover S, Rao G P.Clinical practice guidelines for management of bipolar disorder. Indian J Psychiatry.2017;59 (Suppl 1):S51-S66.
44. Silverman M E,Reichenberg A, Savitz D A,Cnattinguis S, Lichtenstien P, Hultman C M,Larsson H,Sandi S. The risk factors for post partum depression: A population based study. Depress Anxiety.2017;34(2):178-187.
45. Grover S, Avasthi A. Mood stabilizers in pregnancy and lactation. Indian J Psychiatry.2015 ;Suppl2:S308-S323.
46. Kessing LV,Vradi E,Andersen P A. Life expectancy in bipolar disorder. Bipolar Disord.2015;17(5):543-8.