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Gender differences, family size and fertility rate among patients with bipolar disorder: A study from India

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ABSTRACT

This study aimed to estimate the gender differences, family size and fertility rate among patients with Bipolar disorder (BD). 219 patients diagnosed with BD, who were married for at least 3 years and aged more than 25 years were assessed clinically for the course of illness as per the NIMH-life chart. Fertility and infertility were assessed based on the information on number of living children, abortions and medical termination of pregnancies. Significantly higher proportion of male patients had comorbid substance dependence while females had significantly higher prevalence of physical comorbidity. Additionally, female participants reported significantly higher mean number of depressive episodes per year of illness and suicidal attempts. When marriage was considered as a life event and its association with onset or relapse of illness was evaluated, about one-fourth (23.3%) of the study sample reported relapse of illness at the time of marriage or immediately following the marriage. About one-fourth (24.7%) of the couple with one of the partner having bipolar disorder had no living children even after four years of their marriage. To conclude, this study suggests that there are certain gender differences with regard to the clinical profile and longitudinal course of illness of BD.

1. Introduction

Bipolar disorder (BD) is a complex mental disorder which usually starts during adolescence or young adulthood and is considered to have an episodic course (Haldipur, 1999). There is enough evidence to suggest that gender plays an important role in the clinical manifestation of unipolar depressive disorder, with significantly higher prevalence of depression among females(Diflorio and Jones, 2010). However, in general, it is reported that there is lack of difference in incidence and prevalence of bipolar disorder across the two genders (Diflorio and Jones, 2010). Some of the studies suggest that compared to females, males with BD have a relatively earlier age of onset (Arnold, 2003) and comorbid substance use disorders (Kawa et al., 2005). In comparison to males, females with BD have higher number of depressive episodes, mixed mania, rapid cycling course, seasonal pattern of relapses and have high physical and psychiatric co-morbidity (Arnold, 2003; Diflorio and Jones, 2010). No gender differences have been reported for variables like polarity of onset, symptoms, severity of illness, treatment response and suicidality. However, many of these findings have not been reported consistently (Diflorio and Jones, 2010).

Other gender related issues which has been investigated in some of the studies is the relationship of BD with marital rates, divorce rates and rate of infertility. Available data suggests high rate of divorce and lower marital rate among patients with BD-I (Nambi, 2005). However, this association is not very clear, i.e., whether the higher divorce rates and lower marital rates are due to psychosocial dysfunction or it is due to some other social factors like stigma, marital discord, etc (Bebbington and Ramana, 1995).

There is lack of consensus with regard to the association of infertility and BD. Some of the studies have reported lower fertility rates among persons with BD, particularly females (Baron et al., 1982; Jönsson, 1991; Odegård, 1980). However, these studies have been limited to married hospitalized persons (Jönsson, 1991; Odegård, 1980) or those subjects with BD seeking treatment for infertility (Alosaimi et al., 2015). Other studies have reported the opposite i.e., fertility rates were lower for men, when compared to women (Alosaimi et al., 2015). The studies which have compared the fertility rates of patients with BD with fertility rates in general population using national census data have been inconclusive with some suggesting reduced fertility rates in both gender (Baron et al., 1982), while others suggest no definite difference in fertility rates between patients with BD and general population (Odegård, 1980). Only one study so far has

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evaluated the association of fertility and onset of illness and have reported that fertility is reduced both before and after the onset of the illness (Baron et al., 1982). Additionally, this study found that while in females lower fertility rates remain constant, whereas in men fertility rates reduce further after the onset of the illness (Baron et al., 1982). Studies which have compared fertility rates in patients with BD with other psychiatric disorders (mainly schizophrenia and major depressive disorder) have found that patients with BD have fewer children/low fertility rates when compared with patients with major depressive disorder (Mansour et al., 2011; Tondo et al., 2011) but almost similar fertility rates when compared with patients with schizophrenia (Mansour et al., 2011; Williams et al., 2007).

Overall it can be said that the association of the longitudinal course of BD with gender and marriage related issues is less researched area and there are many unsettled questions which requires further investigation. Although some of the studies have evaluated the association of BD with marital functioning from India, in general studies have not compared the course of BD between the subjects of either gender. Similarly, there is lack of data from India on fertility rates among patients with BD. It is well known that the family size and fertility can be influenced by the socio-cultural context. Hence, it is important to evaluate the family size in the cultural context of the patients.

2. Aim of the study

The present study aimed to estimate the gender differences, family size and fertility rate among patients with BD.

3. Methods

This was a cross-sectional study conducted from July 2016 to February 2017 and all the patients were assessed only once. Married patients diagnosed with BD were recruited from the patient population attending the outpatient department of psychiatric services of PGIMER, Chandigarh. The study was approved by the Ethics Committee of the Institute.

To be included in the study, the patients were required to be married for at least 3 years, having children or having attempted to conceive, of both genders, diagnosed with BD [confirmed by using Mini International Neuropsychiatric Interview (MINI PLUS)] and aged more than 25 years. We restricted our study sample to those aged 25 or more and married for at least 3 years because we intended to recruit married subjects, who had enough time to conceive as one of the aims of the study was to evaluate infertility rates. Patients with comorbid organic brain syndrome, intellectual disability, those not willing to participate in the study and those uncooperative for interview were excluded from the study. Patients were selected by purposive sampling.

The patients were assessed on the following instruments:

3.1. Instruments

3.1.1. Mini international neuropsychiatric interview (MINI PLUS) (Sheehan et al., 1998)

The MINI-PLUS is a brief structured interview for diagnosis of psychiatric disorders in DSM-IV and ICD-10. The MINI-PLUS is divided into different modules corresponding to diagnostic categories. It elicits all the symptoms listed in the symptom criteria for DSM-IV and ICD-10 for 15 major Axis I diagnostic categories, one Axis II disorder and for suicidality.

3.1.2. Retrospective life chart form of the NIMH (Roy-Byrne et al., 1985)

The LCM-S/R is an easy to follow self- reported method of constructing a clear picture of the longitudinal course of BD. The life chart provides an overview of the number and type of past episodes, their duration, frequency, and response to treatment. Retrospective life chart ratings are recorded by month and year in the form of a graph, with episodes recorded at four well-defined levels of severity. Information was obtained from patient, primary caregivers and review of treatment records. Information was extracted from the NIMH-LCM of each individual patient for duration of illness, number of episodes in the life chart (mania, depression, hypomania and mixed affective state) and severity of episodes. For the present study, marriage was taken as a landmark to divide the course of the illness prior to the marriage and after the marriage.

3.1.3. Clinical profile sheet

A clinical profile sheet especially designed for the study was used to collect data for age at onset of illness, details of current treatment, marital details including number of marriage (s), number of live children, number of abortion(s) and number of deceased children, infertility and contraceptive measures. Strict confidentially was maintained and written informed consent was taken prior to recruitment of patients for the study.

Statistical Package for the Social Sciences Windows version 14 (SPSS version 14, SPSS Inc., Chicago) was used to analyze the data. Analysis included calculating frequency/percentage for categorical variables and mean and standard deviation for continuous variables. Comparisons were done by using Student's t tests, Mann-Whitney-U tests, Chi-square test and Fisher's exact test.

Fertility rate (defined as the average number of children that would be born to a woman over her lifetime if she were to experience the exact age specific fertility) was estimated as number of living children per woman (per patient in our study sample) and this was compared with the National data.

4. Results

4.1. Socio-demographic and clinical profile of study sample

The study included 219 patients. The socio-demographic profile of the study sample is shown in Table 1. The mean age of the study sample was 45.45 (SD = 11.87) years and mean duration of education was 9.68

Table 1
Socio-demographic profile of the study sample.

Socio-demographic variables	Whole sample mean (S.D) (range)/ *N* (%) *N* = 219	Male Mean (S.D) (range)/ *N* (%) *N* = 154	Females Mean (S.D) (range)/ *N* (%) *N* = 65	Comparison statistics *t*-test/Chi-square test (*p*-value)
Age in years	45.45(11.87); 26–75	45.78(11.76);26–75	44.67(12.20);29–74	*t* = 0.63(0.86)
Gender: Male/Female	154(70.3%)/65(29.7%)	–	–	–
Current marital status:				
Married	214 (97.7%)	152(98.7%)	62(95.4%)	*F* = 0.156
Widowed	5 (2.3%)	2(1.3%)	3(4.6%)	
Education – number of years	9.68(4.39);0–17	10.18(4.06);0–17	8.5(4.94);0–17	*t* = 2.6(0.035)*

(SD-4.39) years. The majority of the patients were male, currently married, employed (59.4%), Hindu by religion (59.4%), and from urban locality (56.2%). Less than half of the patients (n = 98;44.7%) were the sole earning member of the family and slightly more than half of the patients (n = 117;53.4%) were head of the family. When the demographic variables of participants of both the genders were compared, significant differences were noted in terms of duration of education, current paid employment (more male subjects were employed; $p < 0.001$), religion (males more often Hindu by religion and females being more often of Sikh religion; $p = 0.001$), being the sole earning member of the family (males > females; $p < 0.001$) and head of the family (males > females; $p < 0.001$) (Table 1).

The mean age of onset of illness for the study sample was 27.59 (SD-8.87) years and the mean duration of illness was 17.86 (SD-11.29) years. The mean duration of treatment for the study sample was 10.2 (SD-8.3) years. About three-fourth of the patients were euthymic at the time of assessment and rest of them were recovering from a recent mood episode. Very few patients had axis-I comorbid psychiatric disorder. Comorbid substance dependence was seen in about one-fourth of the patients, with alcohol dependence being the most common substance dependence. More than one-fourth of the patients also had comorbid physical illness, with hypertension being the most common physical comorbidity, followed by diabetes mellitus and hypothyroidism. About one-fourth (23.3%) of the study participants reported having attempted at least one suicide attempt in their lifetime. The mean number of suicide attempts for the study sample were 0.45 (SD-0.98). Significantly higher proportion of female patients reported suicidal attempt in the lifetime and females also had significantly higher number of suicide attempts in the lifetime, when compared to males (Table 2).

The mean number of lifetime episodes of any polarity were 5.45 (4.05) and the mean number of lifetime episodes per year of illness were 0.76 (SD-1.44). The mean number of lifetime manic episodes was higher than the mean number of lifetime depressive episodes. Very few patients had hypomanic and mixed episodes. When the numbers of episodes were compared between subjects of both the genders, females reported significantly higher number of depressive episodes per year of illness. The severity of various episodes was rated as (1-mild, 2-moderate and 3-severe) and the mean severity of manic episodes was slightly more than the mean severity of depressive episodes. However, no significant difference emerged between the participants of either gender.

The majority (57.5%) of the patients reported the first episode to be of manic polarity and the illness followed a manic-depressive inter-episodic pattern (MDI). When the illness pattern was compared for both the genders, significantly higher proportion of females had first episode of illness as depressive episode and the illness followed a depressive-manic-inter-episodic (DMI) course.

When the clinical profile of male and female patients was compared, males had significantly higher prevalence of comorbid substance dependence and females had significantly higher prevalence of comorbid physical illness. When the prevalence of individual physical comorbidities was compared, females had significantly higher prevalence of hypothyroidism and hypertension (Table 2).

The majority of the patients were only on mood stabiliser at the time of assessment, with lithium being the most common mood stabilizer, closely followed by valproate. About one-third of the study participants were also receiving antipsychotics along with the mood stabilizers. However, no significant difference was seen between the subjects of both genders (Table 2).

4.2. Marital profile and family size of patient with bipolar disorder

As depicted in Table 3, the mean duration of marriage was 23.19 (SD-12.66) years with a range of 4 to 57 years. Almost all (97.3%) had arranged marriage and 95.4% of the patients had married once. The mean number of living children for the couple with one of the partner having bipolar disorder were 1.81 (SD-1.34) and about three-fourth (75.3%) of the couples had at least one living child. About two-third of the couples with one of the partner having BD had 2 or more children. About one-fourth (24.7%) of the couple with one of the partner having BD had no living children even after four years of their marriage. However, only 6.8% of the couples were currently trying for pregnancy/to conceive but were still unable to conceive. Two-third of the patients (or their spouse) did not report any spontaneous abortion and the mean number of spontaneous abortions in patient (or their spouse) was 0.43 (SD-0.72). Medical termination of pregnancy (MTP) was reported in about one-tenth of the patients (or their spouse) and the mean number of MTPs was 0.10 (SD-0.36). In terms of limiting the family size, only two-third of the couple used one or the other method to limit their family size, with use of barrier being most commonly used method.

When marriage was considered as a life event and its association with onset or relapse of illness was evaluated, about one-fourth (23.3%) of the study sample reported relapse of illness at the time of marriage or immediately following the marriage, i.e., onset of at least one lifetime episode 2 weeks prior to the marriage or after the marriage. When childbirth in self (or in spouse) was considered as a life event, about one-third of the sample (31.5%) reported a relapse associated with childbirth, i.e., onset of episode within 6 weeks of childbirth. When the participants of male and female gender were compared, no significant difference was seen between the two genders on any of the marriage and family size related variables.

4.3. Comparison of course of BD in relation to the onset of illness with marriage

When those with onset of illness before and after marriage were compared with regard to number of episodes, significant differences were noted between the two groups only in the variable of total mean number of episodes after marriage, with significantly lower among patients who had onset of illness after marriage (Table 4).

When the number of episodes and suicidal attempts of participants of both the genders with onset of illness after marriage were compared, no significant difference was noted between both genders except for number of suicidal attempts and proportion of patients attempting suicide being more often females (Table 5).

5. Discussion

This study aimed to evaluate the association of gender, marriage and fertility rates with the longitudinal course of BD. In the present study, the majority of the patients were males and the mean age of onset of illness was 27.6 years. Many previous studies from India have also found a male preponderance in the study samples of BD (Grover et al., 2014; Malhotra et al., 2013; Neogi et al., 2016). Some of the studies from this centre, have reported the mean age of onset of BD, to be around 26 years (Grover et al., 2014; Malhotra et al., 2013; Neogi et al., 2016) and the findings of the present study is comparable to the existing literature. This suggests that despite limiting our study sample to those aged 25 or above and being married, our study sample was largely comparable with the existing literature. Participants of both the gender differed on many of the demographic variables. Compared to females, males were significantly more educated and significantly higher proportion of males were employed, were the sole earning member of the family, were head of the family and Hindu by religion. These significant demographic differences were in the expected lines, considering the Indian cultural context. Although in recent times, increasing proportion of females are joining the work force in India, traditionally males have the responsibility of earning and heading the family, whereas females have the responsibility of running the household (Malik, 1993; Sharma et al., 2016).

Table 2
Clinical profile of the study sample.

Clinical variables	Whole sample mean (S.D) (range)/ *N* (%) *N* = 219	Male mean (S.D) (range)/ *N* (%) *N* = 154	Females mean (S.D) (range)/ *N* (%) *N* = 65	Comparison statistics (*p*-value)
Age of onset (years)	27.59(8.87);14–60	27.36(8.85); 14–60	28.13(8.98); 14–50	$t = -0.589$ (0.982)
Duration of illness (years)	17.86(11.29); 5–52	18.42(11.10);5–52	16.54(11.70);5–45	$t = 1.12$ (0.78)
Current episode				
In remission	166 (75.8%)	111(72.1%)	55(84.6%)	$\chi^2 = 6.514$ (0.089)
Mania	16(7.3%)	15(9.7%)	1(1.5%)	
Hypomania	8 (3.7%)	23(14.9%)	6(9.2%)	
Depression	29(13.2%)	5(3.2%)	3(4.6%)	
Comorbid axis-I				
Psychiatric disorders[a](excluding substance abuse disorder)				$\chi^2 = 1.72$ (0.787)
Yes	4(1.8%)	4 (2.6%)	0 (0)	
Substance use disorder:				
Alcohol dependence	14(6.2%)	14(21.2%)	0(0)	$\chi^2 = 19.986$
Opioid dependence	6 (2.7%)	6 (9.09%)	0(0)	(< 0.001)***
Cannabis dependence	4(1.8%)	4(6.06%)	0(0)	
Tobacco dependence	30(13.3%)	27(17.5%)	3(4.61%)	
Comorbid physical Illness				
Present	66(30.13%)	38(24.7%)	28(43.1%)	**$\chi^2 = 12.49$ (0.05)***
None	153 (69.9%)	116(75.3%)	37 (56.9%)	
Diabetes mellitus	25(11.4%)	19(12.3%)	6(9.2%)	$\chi^2 = 0.43$ (0.509)
Hypothyroidism	13(5.9%)	4(2.6%)	9(13.8%)	$\chi^2 = 4.05$ (0.044)*
Hypertension	23(10.5%)	12(7.8%)	11(16.9%)	$\chi^2 = 10.35$ (0.001)***
Glaucoma	1(0.5%)	1(0.6%)	0(0%)	$F = 1.00$
Migraine	2(0.9%)	0(0%)	2(3.1%)	$F = 0.087$
Seizure disorder	1(0.5%)	1(0.6%)	0(0%)	$F = 1.00$
Bronchial asthma	1(0.5%)	1(0.6%)	0(0%)	$F = 1.00$
Number of participants with at least one life time suicide attempt	**51 (23.3%)**	**28 (18.2%)**	**23(35.4%)**	**$\chi^2 = 7.57$ (0.006)***
Number of suicide attempts	0.45 (0.98);0–5	0.29(0.71)	0.81(1.37)	$U = 4066.5$ (0.003)**
Polarity of the first episode				
Depression	**93 (42.5%)**	**54(35.1%)**	**26(40%)**	**$\chi^2 = 11.63$**
Mania	**126(57.5%)**	**100(64.9%)**	**39 (60%)**	**(0.001)*****
Mean number of manic episodes in the lifetime	5.45(4.05);0–20	5.71(4.2)	4.84(3.64)	$t = 1.45$ (0.288)
Mean number of depressive episodes in the lifetime	3.91(3.33);0–18	3.75(3.33)	4.29(3.31)	$t = -1.09$ (0.79)
Mean number of hypomanic episodes in the lifetime	0.41(1.07);0–6	0.49(1.21)	0.23(0.63)	$U = 4681.0$ (0.257)
Mean number of mixed episodes in the lifetime	0.01(0.11);0–1	0.01(0.11)	0.01(0.12)	$U = 4961.0$ (0.894)
Mean number of episodes in the lifetime	9.81(6.49);3–36	10.0(6.82)	9.38(5.68)	$t = 0.639$ (0.199)
Mean number of manic episodes per year of illness	0.42 (0.75);0–7.5	0.38(0.33)	0.52(1.27)	$U = 4450.5$ (0.195)
Mean number of depressive episodes per year of illness	0.31 (0.72); 0–7.5	0.23(0.21)	0.49(1.27)	$U = 4109.5$ (0.036)*
Mean number of hypomanic episodes per year of illness	0.02(1.07);0–5	0.02(0.07)	0.02(0.07)	$t = -0.304$ (0.434)
Mean number of mixed episodes per year of illness	0.0009 (0.008);0- 0.1	0.001 (0.009)	0.0005 (0.004)	$U = 4962.0$ (0.903)
Total number of episodes per year of illness	0.76(1.44);0.05–15	0.64(0.44)	1.02(2.53)	$U = 4805.5$ (0.695)
Average severity of depressive episodes	1.97 (0.82)	1.86(0.87)	2.23(0.63)	$t = -1.679$ (0.776)
Average severity of manic episodes	2.36 (0.55)	2.32(0.57)	2.46(0.50)	$t = -3.072$ (0.364)
Duration of treatment (years)	10.19(8.30);0.4–37	10.76(8.44)	8.44(7.41)	$t = 1.91$(0.33)
Current treatment profile				
MS only	101(46.1%)	71(46.1%)	30(46.2%)	**$\chi^2 = 3.79$ (0.58)**
MS + AP	72(32.9%)	54(35.1%)	18(27.7%)	
MS + AD	27(12.3%)	17(11.0%)	10(15.4%)	
MS + AP + AD	5(2.3%)	4(2.6%)	1(1.5%)	
AP only	13(5.9%)	7(4.5%)	6(9.2%)	
AP + AD	1(0.5%)	1(0.6%)	0(0%)	
Mood stabilizer (MS)				**$\chi^2 = 2.809$ (0.246)**
Lithium	108 (49.3%)	77 (50.0%)	31(47.7%)	
Valproate	92(42.0%)	61(39.6%)	31 (47.7%)	
Carbamazepine	5(2.2%)	5 (3.2%)	0 (0%)	
Benzodiazepines	5 (1.8%)	4 (2.59%)	1(1.53%)	**$\chi^2 = 1.24$ (0.743)**

MS, Mood stabilizer; AP, Antipsychotics; AD, Antidepressants.

[a] Comorbid psychiatric disorders included: Agoraphobia ($n = 1$), Generalized anxiety disorder ($n = 1$), social phobia ($n = 2$).

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$

Table 3
Marital profile and family size of patient with bipolar disorder.

Variables	Mean (S.D) (range)/*N* (%) *N* = 219	Male Mean (S.D) (range)/ *N* (%) *N* = 154	Females Mean (S.D) (range)/ N (%) *N* = 65	Comparison statistics *t*-test/ Chi-square test
Duration of marriage(in years)	23.19(12.66);4–57	22.34(12.41)	25.2(13.10)	$t = -1.529(0.792)$
Type of marriage(with current spouse)				
Arrange	213(97.3%)	149(96.8%)5(3.	64(98.5%)	$F = 0.672$
Love	6 (2.7%)	2%)	1(1.5%)	
Number of marriages				
1	209 (95.4%)	149(96.8%)	60(92.3%)	$\chi^2 = 2.073$ (0.15)
2	10(4.6%)	5(3.2%)	5(7.7%)	
Total number of conceptions (by patient or their spouse)	2.41 (1.46);0–7 Median −2.00	2.40(1.51);0–7 Median −2.00	2.41(1.36);0–6 Median −2.00	$t = -0.029$ (0.58)
Mean number of living children	1.81 (1.34);0–6 Median: 2.00	1.92(1.32)	1.72(1.35)	$t = 1.009$ (0.519)
Number of living children				
None	54 (24.7%)	35(22.7%)	19(29.2%)	$\chi^2 = 1.04(0.308)$
At least one	165(75.3%)	119(77.3%)	46(70.8%)	
Number of children				
0	54(24.7%)	35(22.7%)	19(29.2%)	$\chi^2 = 2.77(0.83)$
1	16(7.3%)	12(7.8%)	4(6.25)	
2	80(36.5%)	55(35.7%)	25(38.5%)	
>2	69(31.5%)	52(33.7%)	17(26.15%)	
Mean number of spontaneous abortions (by patient or their spouse)	0.43(0.72);0–4	0.38(0.67)	0.55(0.82)	$t = -1.527(0.073)$
Number of spontaneous abortions(by patient or their spouse)				
0	148(67.6%)	109(70.8%)	39(60%)	$\chi^2 = 4.59(0.33)$
1	51(23.3%)	32(20.8%)	19(29.2%)	
2	16 (7.3%)	11(7.1%)	5(7.7%)	
>2	4(1.9%)	2(1.3%)	2(3%)	
Number of spontaneous abortions				
0	148(67.6%)	109(70.8%)	39(60%)	$\chi^2 = 2.42(0.119)$
≥1	71(32.4%)	45(29.2%)	26(40%)	
Mean number of abortions in those who had no living children (n = 54)	0.685(0.72);0–2	0.57(0.69)	0.89(0.73)	$U = 251.0$ (0.107)
No abortion	25(11.4%)	19 (12.3%)	6 (9.2%)	
At least one abortion	29 (13.2%)	16 (10.4%)	13 (20.0%)	$\chi^2 = 2.55$ (0.11)
Trying for pregnancy currently but unable to conceive				
Yes	15 (6.8%)	13(8.4%)	2(3.1%)	$F = 0.241$
No	204 (93.2%)	141(91.6%)	63(96.9%)	
Number of medical termination of pregnancy (by patient or their spouse)				
0	199(90.9%)	142(92.2%)	57(87.7%)	$\chi^2 = 1.66(0.43)$
1	16(7.3%)	9(5.8%)	7(10.8%)	
>1	4 (1.8%)	3(1.9%)	1(1.5%)	
Mean number of medical termination of pregnancy	0.10(0.36);0–2 Median:0.00001	0.09(0.35)	0.13(0.39)	$t = -0.756(0.166)$
Any attempt to limit family size				
None	72 (32.9%)	55 (35.7%)	17(26.2%)	
Barrier methods	98 (44.7%)	69(44.8%)	29(44.6%)	$\chi^2 = 7.25(0.203)$
Bilateral tubectomy	39 (17.8%)	22(14.3%)	17(26.2%)	
Vasectomy	2(0.9%)	2(1.3%)	0(0)	
Oral contraceptive pills	3(1.4%)	3(1.9%)	0(0)	
Others	5(2.3%)	3(1.9%)	2(3.1%)	
Number of subjects with relapse of illness with marriage as a precipitating life event (i.e., onset of episode within 2 weeks prior to or after marriage)	51(23.3%)	40(26%)	11(16.9%)	$\chi^2 = 12.09(0.14)$
Number of subjects with relapse of illness with childbirth in (self or in spouse) as a precipitating life event	69 (31.5%)	47(30.5%)	22(33.8%)	$\chi^2 = 0.23(0.62)$

Previous studies which have focussed on the gender differences in patients with BD suggest that males have earlier age of onset(Arnold, 2003; Diflorio and Jones, 2010; Kawa et al., 2005).The present study does not support this finding. Findings of the present study support the existing literature with respect to the higher prevalence of comorbid substance use disorders and higher prevalence of comorbid physical comorbidity in females with BD (Arnold, 2003; Diflorio and Jones, 2010; Kawa et al., 2005). In the present study, compared to males, females had higher number of lifetime suicide attempts and depressive episodes per year. There is lack of consensus in the literature, with some of the studies supporting the findings of the present study (Arnold, 2003; Diflorio and Jones, 2010; Kawa et al., 2005) whereas others suggest that married women have fewer episodes of depression during a 2 year period and marital status had no effect on the course of illness in males (Lieberman et al., 2010).

The relationship of marriage and mental illness has always been hotly debated topic, especially in developing country like India, where there is a general public assumption that marriage can treat/cure certain mental illnesses (Srivastava, 2013). The mean duration of marriage in the present study sample was 23 years which possibly suggest stability of marriage, despite one of the partner having BD. Previous studies from India, involving patients with schizophrenia have also reported low rates of failed marriages/divorces in our country (Srivastava, 2013; Thara and Srinivasan, 1997). However, this finding

Table 4
Association of marriage and course of illness of bipolar disorder.

Variables	Those with onset of illness before marriage $N = 17$	Those with onset of illness after marriage $N = 202$	Comparison statistics t-test)/Mann-Whitney(U)
Mean number of depressive episodes before marriage per year of illness	0.01(0.048)	0.01(0.043)	$U = 1574.5(0.34)$
Mean number of depressive episodes after marriage per year of illness	0.18(0.12)	0.19(0.17)	$t = -0.22(0.35)$
Mean number of manic/ hypomanic/ mixed episodes before marriage per year of illness	0.01(0.04)	0.02(0.07)	$U = 1523.5(0.23)$
Mean number of manic/ hypomanic/mixed episodes after marriage per year of illness	0.23(0.16)	0.24(0.30)	$U = 1434(0.25)$
Total Mean number of episodes before marriage per year of illness	0.02(0.09)	0.03(0.09)	$U = 1489(0.18)$
Total Mean number of episodes after marriage per year of illness	0.419(0.18)	0.412(0.38)	$t = 0.068(0.04)$*
Mean number of suicide attempts	0.23(0.56)	0.47(1.01)	$U = 1591(0.497)$

* $p < 0.05$

must be interpreted in the background of the fact that in the majority of the participants of the present study, the illness started after marriage. Hence, it is quite possible that, this fact in itself could have contributed to continuation of the marriage, as the couple would have developed some bonding between them. Second, in the present study overwhelming proportion of patients with BD were male. Considering the fact that, the Indian society is a male dominated society, if a male develops mental illness after marriage, the female partners easily accept their partner and continue to remain in the marital relationship, in view of their financial dependence on the male partner. Third, it is also quite possible that those with failed marriages could not have been recruited into the study, as the inclusion criteria required minimum duration of marriage to be 3 years.

However, it is well known that marriage demands a continual level of adaptation and may induce more stress in an individual with pre-existing mental illness or can precipitate mental illness in a vulnerable individual. It has also been regarded as a stressful life event and many previous studies from India and abroad suggest marriage to be a stressful life event associated with relapse or onset of BD (Dohrenwend, 2006; Holmes and Rahe, 1967; Kendler et al., 2001; Maiera, 2012; Singh et al., 1984). In the present study, when marriage was evaluated as a precipitating factor or stressful life event for relapse of illness, about one fourth of patients (23.3%) reported experiencing a relapse very close to their marriage (i.e., onset of episode within 2 weeks prior to or after marriage), with no significant difference between the both genders. When the impact of marriage on longitudinal course of illness was evaluated by comparing those with onset of illness before to marriage and those with onset of illness after marriage, significant difference was noted between the two groups in terms of only total number of episodes per year of illness, with those with onset of illness before marriage had a significantly higher mean total number of episodes. However, overall there was no difference between the two groups in terms of polarity of episodes. The higher number of episodes among those with onset of illness prior to marriage may be related to early age of onset, which itself predicts severe course of BD (Perlis et al., 2004).

In terms of marital profile, no significant difference emerged between subjects of both the genders in terms of type of marriage (arranged or love), number of marriages, mean number of living children, proportion of patients having at least one child, mean number of abortions (in patient or spouse in case patient was male) and medical termination of pregnancy. In terms of fertility, mean number of living children per patient were 1.81, with no significant difference between the 2 genders. About one-fourth (24.7%) of the participants had infertility and a small proportion (6.8%) of the couples with one of the partner having BD, were still considering a pregnancy and actively trying for the same. According to National Family Health Survey (NFHS) − 4, total fertility rate is calculated as number of children per women in the age range of 15 to 49 (International Institute for Population Sciences, 2017). According to this data, national total fertility rate is 2.2 and that in the main catchment states (for the study population included in the present study), i.e., Haryana is 2.05, Himachal is 1.88, Punjab is 1.62 and Chandigarh is 1.57. When the findings of the present study are compared with this data, it is evident that fertility rates of patients with BD are comparable to healthy population in the community from which these came from.

In the present study, 24.7% of the study sample with one of the partner having bipolar disorder did not have children despite being married for 3 years and about 6.8% of the sample were currently still attempting to have children but were unable to conceive. These participants can be said to have infertility, i.e., failure to achieve clinical pregnancy after 12 months or more of regular unprotected sexual intercourse (WHO-ICMART, 2009). National Family Health Survey-3 (NFHS-3) estimated the infertility rate in Indian population to be 1.85% (Ganguly and Unisa, 2010).When the infertility rate of the study sample was compared with that reported in NFHS-3 data, it is evident that patients with BD have about 13 times higher prevalence of infertility when compared to national data. Studies from the western countries have also reported low fertility rates in patients with BD (Baron et al., 1982; Jönsson, 1991; Mansour et al., 2011; Odegård, 1980; Tondo

Table 5
Gender differences in the course of illness of bipolar disorder in those who had onset of illness after marriage ($N = 202$).

Variables	Male Mean (S.D) (range)/ N (%) $N = 143$	Females mean (S.D) (range)/ N (%) $N = 59$	Comparison statistics t-test/Mann-Whitney U value
Mean number of depressive episodes per year of illness	0.18(0.16)	0.22(0.19)	$t = -0.833(0.53)$
Mean number of manic/ hypomanic/mixed episodes per year of illness	0.24(0.31)	0.25(0.30)	$U = 3847.5(0.326)$
Total Mean number of episodes per year of illness	0.39(0.37)	0.44(0.40)	$t = -0.29(0.641)$
Mean number of suicide attempts	0.30(0.72)	0.88(1.42)	$U = 3335.5(0.002)$**
Number of patients with at least one suicide attempt	26 (18.2%)	22 (37.3%)	$\chi^2 = 8.41(0.004)$**

** $p < 0.01$

et al., 2011). A recent large multi-generation register Swedish study which estimated fecundity rates of individuals with 6 psychiatric disorders (Schizophrenia, BD, autism, depression, anorexia nervosa and substance abuse), reported that both males and females with BD had fewer children than general population (male fertility ratio −0.75 and female fertility ratio −0.85). Additionally, when any co-morbid conditions were corrected/controlled, there was a slight increase in the fecundity but still it was less than the general population fertility ratio (corrected male fertility ratio −0.94 and corrected female fertility ratio −0.95)(Power et al., 2013).

The present study has certain limitations. The study sample was relatively small to evaluate the gender differences and was limited to the treating seeking population visiting our centre. The course of illness was determined based on the retrospective review of patient's course of illness. It is quite possible that findings of the present study could have been coloured by retrospective recall bias. Further the study was limited to subjects aged more than 25 years and married for at least 3 years. This could have led to elimination of many of those patients with onset of illness prior to marriage with more severe course and unable to marry. Accordingly, the findings of gender difference must be interpreted in the light of this limitation. The present study did not evaluate the possible etiological causes of infertility. The present study also did not evaluate the association of psychotropics with infertility. Further, the present study did not evaluate the association of sexual dysfunction with fertility. The study included patients who were on psychotropic medications for long and were clinically stable. Use of psychotropics could have influenced the fertility rates and family size. Future studies must attempt to overcome the limitations of the present study.

6. Conclusions

The present study suggest that compared to females with BD, male patients have higher prevalence of substance use disorders, whereas females have higher prevalence of co-morbid physical illnesses, higher prevalence of number of suicide attempts and mean number of depressive episodes per year of illness. Compared to those with onset of illness after marriage, those with onset of illness before marriage have higher mean total number of episodes per year of illness. Married patients with BD have higher rates of infertility (24.7%). However, overall number of children for patients with BD is comparable to National fertility rate of India.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2018.12.156.

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