CME ACTIVITY

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CME Objectives

After completing this CME activity, physicians practicing clinical psychiatry should be able to:
- Discuss the role of gender in the prevalence of bipolar disorder I and II.
- Review the association of gender and comorbidity in bipolar disorder I and II.

Statement of Need and Purpose

Women have higher prevalence rates of anxiety, mood, and eating disorders than men, and they are prescribed the majority of psychotropic medications. Physicians responding to questionnaires in the *Journal* and its related CME activities have requested updated information on psychiatric illness in women. This CME activity was created to address that need. There are no prerequisites for participating in this CME activity.

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None of the authors of this article has significant commercial relationships to disclose relative to the presentation.

Gender and Bipolar Illness

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Background: For major depression and schizophrenia, gender differences have been reported in symptom expression and course of illness. Gender differences in bipolar disorder are becoming increasingly apparent, but have been less studied. Research data on these differences will help determine whether gender is important in influencing illness variables such as course, symptom expression, and likelihood of comorbidity.

Method: Charts of 131 patients (63 women and 68 men) with a DSM-IV diagnosis of bipolar disorder admitted to the University of California Los Angeles Mood Disorders Program over a 3-year period were reviewed to gather data on demographic variables and course of illness and to assess differences in the illness across genders.

Results: No significant gender differences were found in the rate of bipolar I or bipolar II diagnoses, although women were overrepresented in the latter category. Also, no significant gender differences emerged in age at onset, number of depressive or manic episodes, and number of hospitalizations for depression. Women, however, had been hospitalized significantly more often than men for mania. Further, whereas bipolar men were significantly more likely than bipolar women to have a comorbid substance use disorder, women with bipolar disorder had 4 times the rate of alcohol use disorders and 7 times the rate of other substance use disorders than reported in women from community-derived samples.

Conclusion: For bipolar disorder, course of illness variables such as age at onset and number of affective episodes of each polarity do not seem to differ across genders. Women, however, may be more likely than men to be hospitalized for manic episodes. While both men and women with the illness have high rates of comorbidity with alcohol and other substance use disorders, women with bipolar disorder are at a particularly high risk for comorbidity with these conditions.

(J Clin Psychiatry 2000;61:393–396)

Gender differences are becoming increasingly apparent in the prevalence, phenomenology, and course of psychiatric disorders such as unipolar depression and schizophrenia. Although less studied to date, gender differences in bipolar patients have been reported in phenomenology, course, and treatment response.[1–5] Rapid-cycling bipolar disorder, for example, is reported to occur more frequently in female bipolar patients than in male bipolar patients.[1,6] The greater incidence of rapid cycling among female patients may reflect a greater rate of exposure to antidepressants, but this issue remains to be carefully examined. Also, some data show that female bipolar patients are at greater risk for depression than male patients, whereas male patients are at greater risk for manic episodes.[4,7]

Gender differences in bipolar subtype (bipolar I vs. bipolar II) and comorbidity have received little attention to date. In an effort to examine these issues and further explore course-of-illness variables such as age at onset, number of episodes of depression and mania, and number of hospitalizations, we collected and analyzed data from the University of California Los Angeles (UCLA) Mood Disorders Clinic over a 3-year period.

METHOD

Patients admitted consecutively to the UCLA Mood Disorders Clinic between July 1994 and June 1997 with a DSM-IV diagnosis of bipolar disorder (N = 131) were evaluated using a structured questionnaire (developed by the authors and available on request) to obtain data on

Table 1. Gender Distribution Within Bipolar Disorder[a]

Gender	Bipolar Overall (N = 131) N	%	Bipolar I (N = 94) N	%	Bipolar II (N = 37) N	%
Women	63	48	41	44	22	60
Men	68	52	53	56	15	40

[a]$\chi^2 = 2.7$, df = 1, p = .10.

symptoms at admission to the clinic and past psychiatric history. The questionnaire consists of a 1-page form with 35 questions about demographic and clinical variables including gender, number of depressive and manic episodes, number of psychiatric hospitalizations for depression and mania, age at first depressive and manic episodes, and comorbidity of alcohol and other substance use disorders. For patients enrolled prior to July 1996 who were no longer receiving care at the clinic (N = 21), the questionnaires were completed through the use of chart reviews and life-chart data, and patients were contacted to corroborate information drawn from their records. For all patients seen in the clinic after July 1, 1996 (the date of study initiation; N = 110), clinic physicians completed questionnaires during a clinic visit. Diagnoses of mood and substance use disorders were made after these clinical interviews and were based on DSM-IV criteria. Cases in which the questionnaires could not be completed (e.g., patients whose charts were missing data on the variables being examined and who could not be reached to supply the missing information) were not included in the study. The information from the questionnaires was entered into a computer database for analysis.

Statistics

A chi-square test was used to measure gender differences among dichotomous variables such as comorbidity with alcohol and substance use disorders. To demonstrate whether continuous variables such as number of episodes of depression and mania are different across gender groups, t tests were performed. For the t tests, inequality of variances was assumed.

RESULTS

Distribution by gender is seen in Table 1. Data are reported for 63 women and 68 men. The mean ± SD age for women was 43.0 ± 12.17 years; for men, the mean age was 41.2 ± 12.47 years (t = 0.83, p = .41). Data on mean duration of the illness were available for 33 men and 31 women and were not significantly different: mean ± SD

Table 2. Illness History Variables by Gender

Variable[a]	Women N	Mean	SD	Men N	Mean	SD	t Test	p Value
No. of depressive episodes	23	4.30	5.55	29	6.66	9.34	1.127	.265
No. of manic episodes	26	2.34	4.36	38	4.08	4.88	1.489	.142
No. of hospitalizations for depression	26	3.88	9.09	30	2.40	6.46	0.695	.491
No. of hospitalizations for mania	48	8.71	12.67	39	2.18	2.78	3.467	.001
Age at first depressive episode, y	46	21.35	10.64	41	22.46	11.43	0.469	.640
Age at first manic episode, y	44	24.82	11.86	47	24.36	10.24	0.196	.845

[a]Number of manic episodes and number of hospitalizations for mania relate only to bipolar I disorder.

Table 3. Comorbidity With Alcohol and Substance Use Disorders by Gender

Variable	Women N	%	Men N	%	χ^2 (df = 1)	p Value
History of alcohol use disorder	12/59	20.3	31/64	48.4	10.66	.001
History of substance use disorder (nonalcohol)	11/60	18.3	25/62	40.3	7.09	.008

duration of illness for men was 17.8 ± 8.3 years and for women, 19.5 ± 13.7 years (t = 0.59, p = .55). While women were overrepresented in the bipolar II category and underrepresented in the bipolar I category, the gender differences in these diagnoses were not significant ($\chi^2 = 2.7$, p = .10).

Table 2 demonstrates illness history variables by gender. As there were no significant differences between bipolar I and II on these variables, we combined groups for analysis and report on the total (combined) sample in the table. No significant gender differences were found in the total number of depressive or manic episodes, number of hospitalizations for depression, or age at first depressive or manic episode. However, women with bipolar disorder had been hospitalized significantly more often than men for mania.

Table 3 displays a significant gender effect in comorbidity with alcohol and other substance use disorders. The prevalence of alcohol use disorders in men was 48.4%, compared with 20.3% in women ($\chi^2 = 10.66$, p = .001). The prevalence of substance use disorders (other than al-

cohol use disorders) in men and women was 40.3% and 18.3%, respectively (χ^2 = 7.09, p = .008).

The following data show gender effects, analyzed separately by bipolar subtype. For bipolar I, the mean ± SD number of depressive episodes was 3.3 ± 4.9 for women and 4.7 ± 6.3 for men. For bipolar II, mean number of depressive episodes was 6.3 ± 6.5 for women and 16 ± 15.9 for men. For bipolar I, mean age at first depressive episode was 22.6 ± 12.6 years for women and 22.7 ± 11.6 years for men. For bipolar II, mean age at first depressive episode was 19.6 ± 6.9 years for women and 21.8 ± 11.8 years for men. Comorbidity with alcohol use disorders occurred in 24.3% of women and 49% of men with bipolar I disorder, and in 13.6% of women and 46% of men with bipolar II disorder. Comorbidity with substance use disorders occurred in 18.4% of women and 36.7% of men with bipolar I disorder and in 18.2% of women and 53.9% of men with bipolar II disorder.

DISCUSSION

Our finding that the number of lifetime manic and depressive episodes did not vary by gender is in contrast to 2 studies reporting an overrepresentation of hospitalizations for depression in women and for manic episodes in men.[4,7] Like our study, those studies were entirely[7] or mostly[4] retrospective, and therefore subject to the unreliability of patient recall. However, our study results are consistent with a recent prospective 10-year study[5] of 131 patients with bipolar disorder, in which the percentage of manic and depressive episodes was not different between men and women.[5] Age at illness onset was similar between bipolar I and bipolar II patients, but rates of depression doubled in bipolar II women as compared with bipolar I women and were 3 times higher in bipolar II men as compared with bipolar I men. A longitudinal study[8] of bipolar disorder similarly found more numerous depressive episodes among bipolar II versus bipolar I patients.

While there appeared to be an overrepresentation of women in the diagnostic category of bipolar II disorder (60% female), this finding was not statistically significant. Consistent with our finding, 2 previous reports, 1 of 35 bipolar II patients[9] and a second of 94 bipolar II patients,[10] found no significant gender difference in the rate of that diagnosis, although the latter study, like ours, did find an overrepresentation of female patients with the diagnosis.[10] Further community-based studies with larger numbers of patients may be better able to assess whether there is a significant overrepresentation of women in the bipolar II category.

No significant gender differences emerged in the number of depressive episodes or the number of hospitalizations for depression. The number of hospitalizations for mania was significantly greater for women than men, despite no significant difference in the lifetime number of manic episodes. This finding may reflect a greater tendency for women to seek and obtain treatment as compared with men.[11] Alternatively, family members may have been more able or likely to bring ill female relatives rather than ill male relatives to mental health facilities. This may result from different expectations of normative behaviors for men and women and/or from the higher likelihood that women live with their families as compared with men. Family members may be particularly likely to intervene when women experience manic episodes in the postpartum period. Another possibility is that the high comorbidity of alcohol and drug use in male patients may have led to a psychiatric admission diagnosis of substance abuse rather than mania.

As in the general population,[12,13] a significant gender difference emerged in the prevalence of alcohol and other substance use disorders. Men were over twice as likely as women to have a comorbid alcohol or substance abuse diagnosis. Our data are consistent with epidemiologic studies of bipolar disorder demonstrating a rate of comorbidity with an alcohol use disorder of 46% and comorbidity with a substance use (nonalcohol) of 40.7% in men.[14] However, we found that alcohol use disorders in women with bipolar disorder were extraordinarily frequent. The rate of those disorders in our female patients was over 4 times greater than the community rate, estimated at approximately 4.6%.[12] In contrast, the rate of alcohol use in the male patients in our sample was approximately twice the community rate of 23.8%.[12] The rate of other substance use disorders in both our male and female patients was approximately 7 to 9 times the community rate of 2.6% for women and 4.6% for men.[12] Thus, bipolar disorder was associated with high rates of comorbidity with alcohol and other substance use disorders in both genders. Women with bipolar disorder may be at particularly high risk for comorbid substance abuse and dependence.

The prevalence of substance use disorders in the Los Angeles area has been reported to be higher than in other cities and may therefore not reflect general community rates.[15] Also, patients obtaining treatment at a tertiary care center such as the UCLA Mood Disorders Clinic may not be representative of the general population evaluated in epidemiologic studies. However, the very high prevalence of substance use disorders among our bipolar women patients bears further study.

CONCLUSION

In this retrospective review of lifetime characteristics of bipolar illness among men and women, no significant gender differences were found in age at onset, number of manic or depressive episodes, or number of hospitalizations for depression even when duration of illness was controlled. Women were significantly more likely to be hospitalized for mania, were overrepresented in the bipolar II category, had 4 times the community rate of alcohol abuse, and had 7 to 9 times the rate for other substance abuse disorders. Our findings are limited by the retrospective nature of the study and the inclusion of data from chart reviews, but they highlight the need for future prospective research on gender differences in bipolar disorder. Future studies should carefully screen for comorbidity with alcohol and substance use disorders, perhaps especially in women.

Given the relatively small sample sizes in this and another study that reported gender differences in rates of bipolar II disorder,[9] studies with larger samples may be able to further assess the significant overrepresentation of women in this diagnostic category, should it exist. The high rate of alcohol and other substance use disorders in women with bipolar disorder, to our knowledge, has not previously been reported and may have clinical implications for treatment response and compliance.

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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Instructions

Physicians may receive up to 1 hour of Category 1 credit toward the American Medical Association Physician's Recognition Award by reading the article starting on page 393 and correctly answering at least 70% of the questions in the posttest that follows.

1. Read each question carefully and circle the correct corresponding answer on the Registration form.

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1. **In this study, the rate of comorbidity with alcohol and substance use disorders in the men with bipolar disorder was:**
   a. Between 40% and 50%
   b. Between 10% and 20%
   c. Between 80% and 90%
   d. Between 1% and 5%

2. **In this study, the rate of comorbidity with alcohol and substance use disorders in women with bipolar disorder was:**
   a. Approximately 10%
   b. Approximately 20%
   c. Approximately 50%
   d. Approximately 80%

3. **In this study, the rate of alcohol use disorders among the women with bipolar disorder was:**
   a. Approximately 4 times greater than community rates for alcohol use among women
   b. Approximately 10 times greater than community rates for alcohol use among women
   c. Approximately twice as high as community rates for alcohol use among women
   d. Approximately equal to community rates for alcohol use among women

4. **In this study, the rate of alcohol use disorders among the men with bipolar disorder was:**
   a. Approximately 4 times greater than community rates for alcohol use among men
   b. Approximately 10 times greater than community rates for alcohol use among men
   c. Approximately twice as high as community rates for alcohol use among men
   d. Approximately equal to community rates for alcohol use among men

5. **The study found significant gender differences in:**
   a. Number of depressive episodes
   b. Number of hospitalizations for depression
   c. Number of manic episodes
   d. Number of hospitalizations for mania

6. **In this study, patients with a diagnosis of bipolar I disorder differed from patients with a diagnosis of bipolar II disorder in all of the following except:**
   a. Age at onset
   b. Rate of depression among women
   c. Rate of depression among men
   d. Comorbidity with alcohol use disorders among women

7. **Gender differences in rates of hospitalizations may result from:**
   a. Different expectations of normative behaviors for men and women
   b. Gender differences in the likelihood of intervention by family members
   c. Gender differences in the tendency to seek and obtain treatment
   d. All of the above

8. **Compared with bipolar I patients, bipolar II patients were:**
   a. Slightly more likely to be women
   b. Significantly more likely to be women
   c. Slightly more likely to be men
   d. Significantly more likely to be men

Answers to the November 1999 CME posttest

1. a   2. c   3. b   4. c   5. d   6. a   7. d

Circle the one correct answer for each question.

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      ❏ Yes ❏ No

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      ❏ Yes ❏ No

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