Sleep patterns among bipolar disorder patients
Hussien El Olemy El Sheikh, Hisham Mohammed El Said, Shewikar Tawfik El Bakry, Asmaa Abd El Gafar Abd El Hamed

Background
Bipolar disorder (BD) is a lifelong, potentially treatable psychiatric disorder with substantial morbidity and mortality. Sleep is a very important factor for the quality of life, risk for relapse, affective functioning, cognitive functioning, impulsivity, and general health. It is important to note that a bidirectional relationship likely exists between sleep disturbance and mood disorders, as symptoms of mood disorders may disrupt sleep, and disrupted sleep can increase symptoms of mood disorders. Moreover, the sources of inflammation and immune activation, which play a role in depression, may contribute to the inflammatory burden in patients with mania.

Aim
The aim of this study was to study the nature of sleep disturbance in bipolar patients and to detect the correlation between the severity of BD and sleep disturbance.

Patients and methods; and results
In this case–control study, fifty BD patients (28 male patients and 22 female patients) and 20 age-matched controls were recruited for this study. Structured Clinical Interview for DSM-IV Axis I Disorders for diagnosis of BD; Beck Depression Inventory-II and Young Mania Rating Scale (YMRS) were used to assess the severity of BD. Assessment of sleep pattern was carried out by Pittsburgh Sleep Quality Index (PSQI), and C-reactive protein (CRP) was measured in the current study, with regard to Beck scores before medication, there were inverse relations with YMRS and PSQI. These relations become direct after medication. As regards YMRS scores before medication, there was an inverse relation with Beck, direct relations with PSQI, which did not show any change after medication, except for sleep disturbance, which become an inverse relation. As regards PSQI's total scores before medication, it showed an inverse relation with Beck, direct relations with YMRS and the relation with Beck scores became direct after medication. As regards CRP levels, there was a significant difference between cases before and after medication and significant difference between the case and control groups.

Conclusion
PSQI is a cheap valid test that can be used in Egypt to report sleep profile and abnormalities, to follow-up the patients and prevent relapse. Hence, bipolar patients with depressive symptoms improved and responded better on treatment, with better improvement in sleep profile than patients with manic symptoms. Moreover, a definite correlation between sleep disturbance and CRP levels could not be concluded.

Keywords:
bipolar disorder, C-reactive protein, Pittsburgh Sleep Quality Index, sleep disturbance

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Introduction
Bipolar disorder (BD) is a severe disorder characterized by mood episodes, namely, periods of elevated or irritable mood, referred to as mania, periods of depression, and mixed manic and depressed states (American Psychiatric Association, 2013).

The clinical symptoms of BD do not appear to be correlated to changes in the function or structure of specific brain areas. Rather, bipolar symptoms manifesting as emotional, cognitive, behavioral, autonomic, neuroendocrine, immune, and circadian disturbances better correspond to the dysfunction of interconnected brain networks (Strakowski et al., 2012).

Sleep is a reversible behavioral state of perceptual disengagement and unresponsiveness to the environment (Carskadon and Dement, 2011).

The brain circuitry that regulates sleep and produces wakefulness includes cell groups in the brainstem, hypothalamus, and basal forebrain that are crucial for arousing the cerebral cortex and thalamus (Sinton and McCarley, 2004). 

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Reduced need for sleep is a symptom of manic and hypomanic episodes, and insomnia or hypersomnia are listed as symptoms of a major depressive episode (Baum et al., 2013).

Altered sleep duration is associated with more severe BD symptoms and worse functioning and quality of life (Murray and Harvey, 2010).

Changes in sleep pattern predict new episodes and are a prognostic marker for episode outcomes for all polarities of BD (Gruber et al., 2009).

C-reactive protein (CRP) is a substance produced by the liver and is also indicative of increased inflammation (Subramaniapillai et al., 2017).

The serum concentration of CRP in the normal human population has a median of 0.8 mg/l [interquartile range (IQR): 0.3–1.7 mg/l] and is below 10 mg/l in 99% of normal samples. Levels above these values are abnormal and indicate the presence of a disease process (Vigushin et al., 1993).

As levels of this protein are easily detected through nonfasting blood analysis, it is a commonly used indicator of inflammation in both research and clinical settings (Ockene et al., 2001).

It is evident that the sources of inflammation and immune activation, which play a role in depression, may contribute to the inflammatory burden in patients with mania (Anderson and Maes, 2013).

The pathophysiology of inflammation in mood disorders includes changes in the bioavailability and metabolism of neurotransmitters, increased activation of the hypothalamic–pituitary–adrenal axis, increased levels of oxidative stress, increased activation of microglia, and decreased neural plasticity (Postal and Appenzeller, 2015).

This study has been conducted to evaluate the correlation between BD and sleep disturbance before and after a short-term treatment, and to detect the relation between the CRP levels and the bipolar outcome in Shebeen El-Kom, Egypt.

**Patients and methods**

This was a case–control study; the field work was conducted from January 2017 to April 2017 in Shebeen El-Kom Mental Hospital. Study participants were informed of the possibility of using the data obtained for academic purpose. Confidentiality was assured to all participants, and data used for this study were stripped of personally identifiable information.

**Patients**

Study participants were in the age group of 21–50 years. BD patients (n=50) and controls (n=25) were selected by considering strict inclusion and exclusion criteria. Patients were randomly selected from inpatients and outpatients in Shebeen El-Kom mental hospital, and controls were matched for age and sex with bipolar participants and recruited from the general population and employees in the hospital of the study. Patients with substance abuse, comorbid psychiatric disorders and any concurrent medical condition were excluded.

**Methods**

All patients were subjected to the following: a semistructured interview, including age, sex, occupation, marital status, duration of the disease, number of episodes, medication, and consanguinity and family history of a similar condition. Moreover, general medical and neurological examination were performed to exclude any medical condition: Structured Clinical Interview for DSM-IV Axis I Disorders for diagnosis of BD, Beck Depression Inventory (BDI)-II and Young Mania Rating Scale (YMRS) to assess the severity of BD, Pittsburgh Sleep Quality Index (PSQI) to assess sleep pattern and a blood analysis to measure the CRP levels.

**Statistical analysis**

The collected data were tabulated and analyzed using SPSS version 20 software (SPSS Inc., Chicago, Illinois, USA). Categorical data were presented as number and percentages while quantitative data were expressed as mean±SD and range. χ²-test, or Fisher’s exact test, was used to analyze categorical variables. Quantitative data were tested for normality using the Shapiro–Wilks test, assuming normality at P greater than 0.05; some variables were proved to be nonparametric, and hence the Student’s t’, Mann–Whitney, Paired t, and Wilcoxon tests were used. The accepted level of significance in this work was stated at 0.05 (P<0.05 was considered significant).

**Results**

In this study, 57.3% of the sample consisted of male individuals while 42.7% were female individuals, with a mean age of 33.83±6.35; ages ranged from 23 to 49 years. An overall 48% of the patients’ group working while 52% were not. An overall 52% were
single in cases and 16% in the control group; 28% of cases were married while in the control group 84% were married; in the case group, 20% were divorced, while there were none divorced in the control group, as shown in Table 1.

As regards medications of the case group, 1 month after each patient’s first visit, 38% were on lithium and sedative hypnotics, 36% on lithium and antipsychotics, 22% on sodium valproate and antipsychotic, while 4% were on sodium valproate and sedative hypnotics. An overall 2% of fathers, 2% of mothers, 4% of brothers and 4% of sisters had a similar condition.

The mean±SD of duration of disease was 9.06±6.82 and that of number of episodes was 6.22±4.79 as revealed in Table 2.

An overall 28% of patients presented with a manic episode (35.7% male individuals, 18.1% female individuals), depressive episodes were presented in 34% (28.5% male individuals, 40.9% female individuals) and 38% of the patients had a mixed episode (35.7% male individuals, 18.1% female individuals), as shown in Table 3.

There was a significant difference between cases before and after medication with regard to YMRS scores, as demonstrated in Table 7.

As regards CRP levels, there was significant difference between cases before and after medication and significant difference between cases and the control group. These results were highly significant with \( P \) less than 0.001, as demonstrated in Table 7. 

There was a significant difference between cases, before and after medication, with regard to psychometric tests, as demonstrated in Table 6. These results were highly significant with \( P \) less than 0.001.

As regards CRP levels, there was significant difference between cases before and after medication and significant difference between cases and the control group. These results were highly significant with \( P \) less than 0.001.
Table 4 Comparison between cases before and after medication with regard to Beck scores

<table>
<thead>
<tr>
<th></th>
<th>Case group before medication (n=50)</th>
<th>Case group after medication (n=50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beck</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Borderline clinical depression</td>
<td>16 (32.0)</td>
<td>16 (32.0)</td>
<td>0.006**</td>
</tr>
<tr>
<td>Mild mood disturbance</td>
<td>10 (20.0)</td>
<td>18 (36.0)</td>
<td></td>
</tr>
<tr>
<td>Moderate mood depression</td>
<td>10 (20.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>14 (28.0)</td>
<td>16 (32.0)</td>
<td></td>
</tr>
</tbody>
</table>

Table 5 Comparison between cases before and after medication with regard to Young Mania Rating Scale scores

<table>
<thead>
<tr>
<th></th>
<th>Case group before medication (n=50)</th>
<th>Case group after medication (n=50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>YMRS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Few or no mania</td>
<td>17 (34.0)</td>
<td>17 (34.0)</td>
<td>0.028*</td>
</tr>
<tr>
<td>Hypomania</td>
<td>5 (10.0)</td>
<td>15 (30.0)</td>
<td></td>
</tr>
<tr>
<td>Mania</td>
<td>28 (56.0)</td>
<td>18 (36.0)</td>
<td></td>
</tr>
</tbody>
</table>

YMRS, Young Mania Rating Scale.

Table 6 Comparison between case group before and after medication with regard to Beck, Young Mania Rating Scale and Pittsburgh Sleep Quality Index scores

<table>
<thead>
<tr>
<th></th>
<th>Case group before medication (n=50) (mean±SD)</th>
<th>Case group after medication (n=50) (mean±SD)</th>
<th>Paired t-test</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beck</td>
<td>18.82±3.19</td>
<td>16.41±2.64</td>
<td>9.78</td>
<td>0.001**</td>
</tr>
<tr>
<td>YMRS</td>
<td>29.76±9.04</td>
<td>26.15±8.31</td>
<td>10.13</td>
<td>0.001**</td>
</tr>
<tr>
<td>PSQI total</td>
<td>14.46±2.71</td>
<td>11.56±2.59</td>
<td>13.53</td>
<td>0.001**</td>
</tr>
<tr>
<td>Subjective sleep quality</td>
<td>2.44±0.61</td>
<td>1.64±0.63</td>
<td>10.58</td>
<td>0.001**</td>
</tr>
<tr>
<td>Sleep latency</td>
<td>2.18±0.69</td>
<td>1.72±0.67</td>
<td>6.0</td>
<td>0.001**</td>
</tr>
<tr>
<td>Sleep duration</td>
<td>2.14±0.76</td>
<td>1.32±0.65</td>
<td>11.1</td>
<td>0.001**</td>
</tr>
<tr>
<td>Habitual sleep efficiency</td>
<td>2.32±0.59</td>
<td>1.76±0.69</td>
<td>6.48</td>
<td>0.001**</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>2.2±0.64</td>
<td>1.98±0.65</td>
<td>3.35</td>
<td>0.002**</td>
</tr>
<tr>
<td>Use of sleeping medication</td>
<td>1.58±0.76</td>
<td>2.34±0.66</td>
<td>7.22</td>
<td>0.001**</td>
</tr>
<tr>
<td>Daytime dysfunction</td>
<td>1.6±0.57</td>
<td>0.80±0.57</td>
<td>9.9</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

PSQI, Pittsburgh Sleep Quality Index; YMRS, Young Mania Rating Scale.

Table 7 Comparison of C-reactive protein levels before and after treatment in case group with control group

<table>
<thead>
<tr>
<th></th>
<th>CRP level in case group before medication (n=50) (mean±SD)</th>
<th>CRP level in case group after medication (n=50) (mean±SD)</th>
<th>Control group (n=25) (mean±SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mania</td>
<td>265 (5.3)</td>
<td>125 (2.5)</td>
<td>19 (0.76)</td>
<td>0.001**</td>
</tr>
<tr>
<td>Depression</td>
<td>259 (5.18)</td>
<td>118 (2.36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed episode</td>
<td>245 (4.9)</td>
<td>105 (2.1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CRP, C-reactive protein.

decreased habitual sleep efficiency, sleep disturbance, use of sleeping medication and daytime dysfunction. These relations become direct after medication.

As regards YMRS scores before medication, there is an inverse relation with Beck, direct relations with PSQI total, bad subjective sleep quality, increased sleep latency, duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication, and daytime dysfunction, which did not show any change after medication, except for sleep disturbance, which become an inverse relation.

As regards PSQI total scores before medication, there is an inverse relation with Beck, direct relations with other psychometric tests, which show change in Beck scores, which have a direct relation after medication, as shown in Tables 8 and 9 (Figs 1–4).

Discussion

Sleep disturbance is among the most prominent correlates of mood episodes and inadequate recovery. Reduced need for sleep is a symptom of mania. During episodes of depression, insomnia or hypersomnia are common (American Psychiatric Association, 2013).

Sleep disturbance escalates just before and worsens during episodes (Scott et al., 2003) and does not always resolve with medication (Gruber et al., 2011).

Studying variable sleep profiles among different BDs might help in understanding differences in sleep abnormalities. In addition, treating sleep disturbances in those patients might also serve better therapeutic outcome.

This is a short-term case–control study wherein the questionnaires are used at the beginning of the study and 1 month later.

The study was carried out in inpatients and outpatients in Shebeen El-Kom mental hospital located in
Shebeen El-Kom, El-Monofyia, on 50 bipolar patients and 25 controls.

In this study, the mean age of the studied sample was 33.76±7.44 versus 32.76±6.52 years for bipolar patients and controls, respectively, with no significant difference between these two groups.

These numbers came in accordance with the median and IQR (IQR: 25th–75th percentiles) of age of onset of mood disorders (25–45, IQR: 17–65) recorded by Ronald et al. (2007). In addition, Boland et al. (2015) detected that the mean age of the study participants was 32.63±11.61 years.

The number of female patients with BD was 22 (44%) compared with 28 (56%) male patients, with no significant difference with the control group, wherein female patients were 10 (40%) in number versus 15 (60%) male patients.

These findings come in accordance with that of Kawa et al. (2005) who made a study on sex differences in BD, and found that most sex comparisons showed no evidence of differences. However, these results were contradicted with Lewis et al. (2017) who found that more than half of the patients were women 68% (n=2146).

As regards the occupational status, it was presently revealed that more than half of the case group was unemployed (52%; n=26).

These findings are in accordance with that of Boland et al. (2015) who found that the lifetime

Table 8 Correlation between psychometric tests' scores used in case group before medication

<table>
<thead>
<tr>
<th>Before (r)</th>
<th>Beck</th>
<th>YMRS</th>
<th>PSQI</th>
<th>Subjective sleep Q</th>
<th>Sleep latency</th>
<th>Sleep duration</th>
<th>Habitual sleep efficiency</th>
<th>Sleep disturbance</th>
<th>Use of sleeping medication</th>
<th>Daytime dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beck</td>
<td>–0.60*</td>
<td>–0.02</td>
<td>–0.11</td>
<td>–0.003</td>
<td>–0.23</td>
<td>–0.13</td>
<td>–0.06</td>
<td>–0.06</td>
<td>–0.13</td>
<td>–0.13</td>
</tr>
<tr>
<td>YMRS</td>
<td>–0.60*</td>
<td>0.59*</td>
<td>0.71*</td>
<td>0.50*</td>
<td>0.63*</td>
<td>0.20</td>
<td>0.06</td>
<td>0.38*</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>PSQI total</td>
<td>–0.02</td>
<td>0.64*</td>
<td>0.71*</td>
<td>0.72*</td>
<td>0.68*</td>
<td>0.40*</td>
<td>0.37*</td>
<td>0.67*</td>
<td>0.51*</td>
<td></td>
</tr>
<tr>
<td>Subjective sleep Q</td>
<td>–0.11</td>
<td>0.71*</td>
<td>0.71*</td>
<td>0.44*</td>
<td>0.66*</td>
<td>0.08</td>
<td>0.45*</td>
<td>0.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep latency</td>
<td>–0.003</td>
<td>0.50*</td>
<td>0.72*</td>
<td>0.44*</td>
<td>0.50*</td>
<td>0.26</td>
<td>0.15</td>
<td>0.30*</td>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>Sleep duration</td>
<td>–0.23</td>
<td>0.63*</td>
<td>0.68*</td>
<td>0.66*</td>
<td>0.50*</td>
<td>–0.06</td>
<td>0.07</td>
<td>0.25</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>Habitual sleep efficiency</td>
<td>–0.13</td>
<td>0.20</td>
<td>0.30*</td>
<td>0.06</td>
<td>0.26</td>
<td>–0.06</td>
<td>–0.12</td>
<td>0.17</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>–0.06</td>
<td>0.06</td>
<td>0.37*</td>
<td>0.08</td>
<td>0.15</td>
<td>0.07</td>
<td>–0.12</td>
<td>0.18</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>Use of sleeping medication</td>
<td>–0.06</td>
<td>0.38*</td>
<td>0.67*</td>
<td>0.45*</td>
<td>0.30*</td>
<td>0.25</td>
<td>0.17</td>
<td>0.18</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td>Daytime dysfunction</td>
<td>–0.13</td>
<td>0.07</td>
<td>0.51*</td>
<td>0.14</td>
<td>0.20</td>
<td>0.23</td>
<td>0.02</td>
<td>0.14</td>
<td>0.27</td>
<td></td>
</tr>
</tbody>
</table>

PSQI, Pittsburgh Sleep Quality Index; YMRS, Young Mania Rating Scale. *Significant results. **Highly significant results.

Table 9 Correlation between psychometric tests' scores used in the case group after medication

<table>
<thead>
<tr>
<th>After (r)</th>
<th>Beck</th>
<th>YMRS</th>
<th>PSQI</th>
<th>Subjective sleep Q</th>
<th>Sleep latency</th>
<th>Sleep duration</th>
<th>Habitual sleep efficiency</th>
<th>Sleep disturbance</th>
<th>Use of sleeping medication</th>
<th>Daytime dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beck</td>
<td>–0.67*</td>
<td>0.74*</td>
<td>0.59*</td>
<td>0.65*</td>
<td>0.05</td>
<td>0.67*</td>
<td>0.17</td>
<td>0.79*</td>
<td>0.60*</td>
<td></td>
</tr>
<tr>
<td>YMRS</td>
<td>–0.67*</td>
<td>0.36*</td>
<td>0.02</td>
<td>0.27</td>
<td>0.22</td>
<td>0.15</td>
<td>0.45*</td>
<td>–0.04</td>
<td>0.23</td>
<td>0.09</td>
</tr>
<tr>
<td>PSQI total</td>
<td>0.74*</td>
<td>0.36*</td>
<td>0.68*</td>
<td>0.66*</td>
<td>0.69*</td>
<td>0.47*</td>
<td>0.51*</td>
<td>0.57*</td>
<td>0.42*</td>
<td></td>
</tr>
<tr>
<td>Subjective sleep Q</td>
<td>0.59*</td>
<td>0.27</td>
<td>0.68*</td>
<td>0.34*</td>
<td>0.53*</td>
<td>0.22</td>
<td>0.18</td>
<td>0.25</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>Sleep latency</td>
<td>0.65*</td>
<td>0.22</td>
<td>0.66*</td>
<td>0.34*</td>
<td>0.44*</td>
<td>0.07</td>
<td>0.27</td>
<td>0.22</td>
<td>0.277</td>
<td></td>
</tr>
<tr>
<td>Sleep duration</td>
<td>0.05</td>
<td>0.15</td>
<td>0.69*</td>
<td>0.53*</td>
<td>0.44*</td>
<td>0.08</td>
<td>0.30*</td>
<td>0.17</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>Habitual sleep efficiency</td>
<td>0.67*</td>
<td>0.45*</td>
<td>0.47*</td>
<td>0.22</td>
<td>0.07</td>
<td>0.08</td>
<td>–0.01</td>
<td>0.32*</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>0.17</td>
<td>–0.04</td>
<td>0.51*</td>
<td>0.18</td>
<td>0.27</td>
<td>0.30*</td>
<td>–0.01</td>
<td>0.30*</td>
<td>–0.03</td>
<td></td>
</tr>
<tr>
<td>Use of sleeping medication</td>
<td>0.79*</td>
<td>0.23</td>
<td>0.57*</td>
<td>0.25</td>
<td>0.22</td>
<td>0.17</td>
<td>0.32*</td>
<td>0.30*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daytime dysfunction</td>
<td>0.60*</td>
<td>0.09</td>
<td>0.42*</td>
<td>0.19</td>
<td>0.277</td>
<td>0.23</td>
<td>0.14</td>
<td>–0.01</td>
<td>–0.03</td>
<td></td>
</tr>
</tbody>
</table>

PSQI, Pittsburgh Sleep Quality Index; YMRS, Young Mania Rating Scale. *Significant results. **Highly significant results.
unemployment mean in BD patients is 48.66±31.50, which implies that BD participants had greater lifetime histories of unemployment and greater incidence of being fired from their jobs. The concurrent findings disagreed with Salvatore et al. (2008), who found that most of the studied patients were employed (96.0%). Moreover, Kaplan et al. (2015) reported that 56.9% were employed.
An overall 52% of cases were single, 28% were married and 20% were divorced, with a statistically significant difference, compared with the control group.

Such findings might be expected and explained by the social difficulties and problems that usually come as a consequence of BD.

This result was similar to the study carried out by Sylvia et al. (2017) who found that the majority of BD patients were single (47%; n=225).

Furthermore, Kaplan et al. (2015) reported that 62% of cases were single, 20.9% were married and 17.1% were divorced.

These results came in disagreement with the study carried out by Nga et al. (2016), who detected that the majority of BD patients were married (46.43%; n=39).

As regards consanguinity, there was a 38% positive consanguinity in the case group, and that is culturally accepted in Egypt, as there are many families that marry within the relatives, especially in rural areas.

Mansour et al. (2009) confirmed that the rate of consanguinity is 36.5% among Egyptian bipolar patients, and that was close to the results of the current study.

With regard to the patients in the present research, most were prescribed psychotropic medications during their first visit in the following combinations: 38% received lithium and sedative hypnotics, 36% were on lithium and antipsychotics, 22% on sodium valproate and antipsychotics, while 4% were on sodium valproate and sedative hypnotics, whereas those on lithium represented 74%.
Salvatore et al. (2008), in their research, confirmed that patients were on more than one drug (87.9%). Moreover, Kaplan et al. (2015) reported that 71.7% of their patients were on polytherapy.

Moreover, lithium is the treatment standard for BDs, as presented by Okasha (2004); thus, these results agree with the current results, and the patients reported better response on polytherapy, as it is unusual for them to be on monotherapy.

In the current research, 2% of the fathers and mothers, while 4% of the brothers and sisters, respectively, suffered from the same condition; as there was positive consanguinity and genetic basis of BD, and more than one patient participated from the same family, the rates of BD were high among family members.

This conclusion was in disagreement with the study carried out by Kupfer et al. (2002), who showed that more than 50% of the participants reported having at least one family member with BD.

The mean±SD of the duration of the disorder was 9.06±6.82; in the study by Grandner et al. (2014), the mean ±SD of the disorder was 16.4±13.1, while it was 20.71±13.63 in the study carried out Gruber et al. (2011).

Moreover, the mean±SD of the number of episodes is 6.22±4.79, and the patients in the study were not on a regular treatment.

Rosa et al. (2011) noticed that the mean±SD of the duration of disease was 12.60±11.26, while it was 13.2±16.5 in the Grandner et al. (2014) research study, as the BD tends to be episodic and recurrent.

With regard to the type of episode, male patients presented more with manic episodes (35.7%) than female patients, who presented more with depressive episodes (40.9%). This comes in agreement with Scott et al. (2017), who elicited that male patients presented more with manic episodes (47%), while female patients presented more with depressive episodes (37%).

The Beck scores revealed that 32% of the cases had borderline clinical depression, 20% showed mild mood disturbance, another 20% showed moderate depression, and 28% were normal.

These results are the cases that clinically were diagnosed with either a mixed or a depressive episode. An overall 28% of the control group complained from having mild mood disturbance; this may be due to the economical and family stressors some were facing.

There was a statistically significant difference between cases and controls with regard to the presence of depression. As agreed by Kessler et al. (1994), depression can affect approximately one in six male individuals and one out of four female individuals within their lifetimes.

Manic episodes were present in 56% of the cases and hypomanic in 10%, while the entire control group was free of any symptoms. Thus, there was a statistical difference between patients and the control group (0.001). There was a statistically significant improvement (0.025) with regard to the manic and hypomanic symptoms among the cases before and after medication.

Furthermore, the mean score was 18.82±3.19 and recuperated to 16.41±2.64 in BDI scores, 29.76±9.04–26.15±8.31 in the YMRS scores and 14.46±2.71–11.56±2.59 in the PSQI total score.

In disagreement with the present numbers were those of Jones et al. (2005), who reported 11.68±7.86 for BDI while the YMRS score was 4.74±3.83. Furthermore, Samalin et al. (2016) recorded 7.09±3.94 for PSQI.

Probably the results are different because of the difference in the therapeutic regimens.

Concerning the different criteria of the PSQI, while sleep quality scored 0.44±2.58 in the controls, it scored 2.44±0.61 and 1.64±0.63 before and after medication, respectively. Thus, significant improvement was detected, and this could be due to the impact of the medications for a month of therapy.

In accordance with Harvey (2011), who found that antipsychotics, lithium and valproate regulate sleep and circadian rhythms and stabilize mood, interpersonal and social rhythm therapy is associated with delayed recurrences, when social and circadian rhythms are regulated.

As regards the second criteria of the PSQI, which is the sleep latency, the control group recorded a mean of 0.6±0.58. Before and after medication scores were 2.18±0.69 and 1.72±0.67, respectively. The amount of time that the patient took to fall asleep decreased, and that might have happened because of the regularity of the treatment undergone by the patients.
Sleep duration is the third criteria in the PSQI; its mean value was 1.0±0.58 for the controls. 2.14±0.76 and 1.32±0.65 were the records for the cases before and after medication, respectively. There was a statistical difference between the control and cases, and also between the cases before and 1 month after receiving treatment.

Several patients were hospitalized during that time, and the quiet atmosphere plus the role of nurses in regulating sleep hours, might have played a role in modifying the hours of sleep.

Perlman et al. (2006), study found that shorter sleep duration predicted greater depressive, but not manic, symptoms over 6 months in patients with bipolar I disorder.

Moreover, the Nga et al. (2016) study showed that irregularity in total sleep time was associated with a greater number of depressive episodes in the past 5 years, while irregularity in wake after sleep onset predicted the onset of major depressive episodes over the 2-year follow-up. In addition, sleep irregularity was not associated with the number of manic episodes in the past 5 years.

As regards habitual sleep efficiency, which is the fourth item of the PSQI, a mean score of 0.28±0.46 was detected. A high significant difference was present between the controls and patients, either before or after medication, which proves the disturbed efficiency of sleep in bipolar patients, whether depressed, manic or mixed. Nga et al. (2016), revealed a similar relation between sleep efficiency and BD.

Sleep efficiency score was 2.32±0.59, and, after a month of therapy, it improved to 1.76±0.69 with a high significant value of 0.001.

Sleep efficiency considers the total sleep duration and the time at which the person goes to bed at night and wakes in the morning. Probably this improvement was due to several factors including the regularity and proper medications, the presence of a usual sleep routine in the hospitalized patients, or the minimized symptoms of the disorder after a little treatment.

St-Amand et al. (2013) agree with the current results that sleep disturbance is associated with both depression and manic episodes in BD patients.

The fifth item of the PSQI was questioning the sleep disturbances; this measures several items such as waking in the middle of night or early in the morning, coughing, snoring, bad dreams, inability to breathe comfortably, pain, using the bathroom during sleep and feeling too cold or hot.

The mean scores of sleep disturbance were 1.44±1.00 in the control group, 2.2±0.65 and 1.98±0.65 in the cases, before after medications, respectively. A statistical significance was present between the cases and controls, and again between the cases before and after medications. These results prove the presence of sleep disturbance among bipolar patients.

Moreover, after the therapy, there was still a significant difference between the patients treated for 1 month and the controls (0.017). This also indicates that the disorder itself affects sleep.

This comes in agreement with Perlman et al. (2006) who believed that sleep disturbances are a hallmark symptom of mood disorders, and some disturbances persist after remission from the episodes.

The use of sleep medications is the sixth item in PSQI and has also shown a significant difference between the control and bipolar patients.

The control group did not report using any sleep medications on a regular basis. This is expected, as usually people do not use hypnotics, because of the stigma of using psychiatric medications, and the fear of its dependence.

As regards the patients, they reported higher rates on PSQI with regard to the use of sleep medications, as this could be part of the therapeutic regimen and the medications needed for treating the sleep problems accompanying the BD.

The seventh and last item of the PSQI is the daytime dysfunction. The control group again showed better results with a mean value of 0.08±0.28. There was also a statistically significant difference between cases, before and after medications, although both showed a dysfunction.

Several studies reported that daytime sleepiness and the inability to stay focused on the following day's work was present as mentioned in Murray and Harvey (2010).

Therefore, it can be hypothesized from the present work that there is an inverse significant difference
between the depression seen by the results of BDI and the PSQI.

This can be due to the use of psychotherapy, which helps the patients to sleep well or enjoy long hours of sleep.

This came in agreement with the study carried out by Harvey (2011), who stated the relation between psychotropic medications, sleep and mood, as previously discussed.

As regards the YMRS in the patients before medication, direct significant difference with regard to sleep quality, latency, duration, and the use of medications was seen, as mania affects different aspects of sleep.

Moreover, these relations did not change after 1 month of medication, except for sleep disturbance, which became an inverse relation.

This can be due to the items involved in this fifth element of the PSQI, wherein the used medications do not work in improving coughing, snoring, bad dreams, inability to breathe comfortably, pain, using the bathroom during sleep and feeling too cold or hot.

Soreca et al. (2012), study stated that individuals with BD are at greater risk for sleep disorders such as sleep apnea.

Moreover, Barbini et al. (1996) monitored 34 patients with mania over 3 days for sleep duration and manic symptoms and found significant correlations between decreased sleep duration and increased manic symptoms on the subsequent day.

The studies carried out by Perlman et al. (2006), Barbini et al. (1996), and Bauer et al. (2006) have found longitudinal associations between sleep disturbance and mood changes in BD, although the nature of the association – whether sleep disturbance is more related to manic or depressive symptoms – is less consistent.

Moreover, concerning the results obtained after 1 month of therapy, they validate the presence of a direct significant difference between depression symptoms shown by the BDI, and most of the sleep items obtained from the PSQI.

In agreement with the present work, Bauer et al. (2006) and Gruber et al. (2009) stated similar findings, wherein shortened total sleep duration was associated with increased depressive and manic symptoms severity.

Similar findings were previously narrated concerning the sleep quality in bipolar patients by the PSQI in all criteria. Nevertheless, the difference between the current study and that by Geoffroy et al. (2014), was in the sleep disturbance item.

The current results suggest that total sleep quality in bipolar patients, whether depression or mania, was worse than that of the general population.

As expected, irregularity in sleep scheduling and timing was found to be related to sleep irregularity in patients with BD, as stated by Nga et al. (2016).

Therefore, studies are needed to assess the role of sleep in bipolar patients, as several researches were contradictory.

Although, the patients received medical treatment for only 1 month, yet, the total PSQI scores and hence the total quality of sleep were improved. This further increases the value of the regular sleep routine and the role of sleep hygiene and the dark atmosphere at night that helps sleep.

A possible explanation for these findings is that perhaps within the same month, BD participants are experiencing a decrease in sleep need and try to compensate for this sleep loss by spending an excessive amount of time in bed.

Moreover, having a steady bed time helped them to regulate their sleep, plus being on a regular treatment.

Cases were away from the regular life stressors, being in a comfortable quiet environment, and nurses, doctors and psychologists were taking care of them.

As expected, irregularity in sleep scheduling and timing was found to be related to sleep irregularity in our sample of patients with BD. The overall findings suggest that maladaptive cognitions and behaviors about sleep may play an important role in the development of sleep irregularities.

In the current study, there was a significant difference between cases before and after medication, and significant difference between cases and the control group with regard to CRP levels, which showed a
decrease after treatment, but the correlation between its decrease and improvement of sleep is doubtful.

This is in accordance with Irwin et al. (1996), who demonstrated that acute sleep deprivation results in impairments in immune functioning, characterized by increased levels of the proinflammatory cytokines and CRP.

Furthermore, a recent meta-analysis confirmed that mania and BD are accompanied by activation of inflammatory, cell-mediated and negative immunoregulatory cytokines (Modabbernia et al., 2013).

Patel et al. (2009) study found that improved nocturnal sleep and successful pharmacological treatment of depression are associated with decreased levels of inflammatory mechanisms, and appear to contribute to the pathogenesis of depression and expression of illness in chronic sleep-disordered patients; adaptive sleep habits may, therefore, act as a protective factor against poorer mental health outcomes.

Some limitations met while conducting this study are as follows. (a) Sample size is relatively small. (b) The use of subjective measures of sleep disturbances and other psychometric tests instead of using objective measures such as actigraphy and polysomnography represents another limitation and points to the need to interpret the results with caution. (c) The insight and judgment of the patients, or how much they understand the questionnaires could not be fully assessed, and that might have led to some misinterpretations. (d) The short duration of the study and a month of medical treatment were not enough to give accurate results.

**Conclusion and recommendation**

This case–control study demonstrates the presence of subjective disturbance of sleep in patients with BD. These findings indicate that future studies should examine both the mean scores and the variability over extended periods of time using objective measures such as actigraphy and polysomnography. In addition, a combination of subjective and objective measures (quantity and variability) may be a better circadian biosignature of BD than any single measure on its own.

The PSQI may offer some advantages for routine practice and can provide reasonable approximations of sleep profile as well as daytime dysfunction.

The present results revealed that (a) as regards Beck scores before medication, there were inverse relations with YMRS, PSQI total, subjective sleep quality, sleep latency, duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication and daytime dysfunction. These relations become direct after medication. (b) With regard to YMRS scores before medication, there was an inverse relation with Beck, direct relations with PSQI total, subjective sleep quality, sleep latency, duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication, and daytime dysfunction, which did not show any change after medication, except for sleep disturbance, which became an inverse relation. (c) As regards PSQI total scores before medication, there was an inverse relation with Beck, direct relations with other tests, which show change in Beck scores, which became direct relations after medication. (d) There was a decreased level of CRP after medication.

The overall findings suggest that maladaptive cognitions and behaviors about sleep may play an important role in the development of sleep irregularity in patients with BD.

Hence, by using self-report measures such as PSQI and clinical interviewing, it is possible that we can understand the nature of sleep disturbance across the course of BD, identify sleep disturbance early in bipolar patients and intervene to prevent relapse into a mood episode and improve the quality of life for these patients.

Moreover, PSQI is a cheap valid test that can be used in Egypt in the presence of economic difficulties to report the sleep profile and abnormalities to follow-up patients and prevent relapse.

Hence, bipolar patients with depressive symptoms improve and respond better on treatment, with better improvement in sleep profile than patients with manic symptoms. A definite correlation between sleep disturbance and CRP levels was not proven.

Taking into account, all the limitations of the study, it is recommended that (a) people with BD are more likely to seek help when they are depressed rather than when experiencing mania or hypomania. Therefore, a careful medical history is needed to ensure that BD is not mistakenly diagnosed as major depression. (b) Sleep disorders should be assessed when taking history of BD. (c) Further research about sleep disorders and CRP level in BD needs to be carried
out, with more patients and longer duration of the study, to state its correlation to each other. (d) Prospective longitudinal studies with more accurate and repeated objective assessments to document sleep disorders are needed, such as using polysomnography, actigraphy, or cortisol serum level. (e) Stabilizing social rhythms may be another important strategy in reducing sleep irregularity in BD.

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Conflicts of interest
None declared.

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