Introduction

Panic disorder, affecting up to 5% of the population, is one of the most commonly diagnosed mental disorders [1]. It is primarily characterized by extreme fear and a sense of impending death or catastrophe, often accompanied by various physical symptoms including tachycardia, palpitations, dyspnea, sweating, depersonalization, anticipatory anxiety about another attack, and concerns of death from cardiac or respiratory problems [2]. Beyond the diagnostic criteria, panic disorder encompasses various aspects such as agoraphobic avoidance, physical symptoms, anxiety sensitivity, and symptom frequency. Numerous attempts have been made to improve the understanding of panic disorder, with several models, including psychodynamic, cognitive, and biological hypotheses, proposed to better explain the disorder [3,4].

Panic disorder is also known to have a substantially high incidence of psychiatric comorbidity, with 91% of patients reporting an additional psychiatric disorder [2]. Notably, patients with panic disorder have a greater risk of comorbid depressive disorder. This poses significant implications for clinicians [5-7], as the comorbidity of these two psychiatric disorders is associated with less favorable outcomes and a greater clinical burden. This burden includes severity and persistence of the disorders, increased functional impairment, escalated help-seeking behavior, and higher suicidal risks [8-10]. The presence of panic attacks, persistent avoidance, or severe impairment related to anxiety has been found to increase the risk of onset of new episodes of major depressive disorder [11]. Insomnia symptoms, which are extensively related to depression both clinically and epidemiologically [12] have also been reported in patients with panic disorder. Several studies have highlighted the high prevalence of insomnia symptoms in individuals with panic disorder. For instance, up to 68% of those with panic symptoms (endogenous anxiety) were found to have difficulties initiating sleep, and 77% reported sleep disturbances [13].
Singareddy and Uhde [14] also reported that generally around 70%, even up to 98% of patients diagnosed with panic disorder reported experiencing insomnia symptoms, which could be attributed to anxiety, nocturnal panic attack and comorbid depression [15]. Another study by Overbeek et al. [16], who have compared sleep disturbances in 70 panic disorder patients with those in 70 healthy controls, have reported approximately 67% of individuals with panic disorder experiencing sleep disturbances, and the prevalence remained significantly higher in nondepressed patients with panic disorder when compared with the healthy controls. Considering the high comorbidity and frequent complaints of nocturnal panic attacks in the patients diagnosed with panic disorder [14], the burdens of comorbid insomnia in panic disorder patients has become substantial clinical consideration for clinicians. There has been a report that insomnia and the severity of panic symptoms have significant association, stating that insomnia is somewhat related to prolongation of panic symptoms [17]. In addition, it is known that sustained sleep disturbance may exacerbate the depressive symptom, even leading to suicidality [18]. As some studies showed the bidirectional relationship between depression, anxiety and symptoms of insomnia [19–23], questions about effects of managing insomnia on reduction of anxiety symptom has been raised and some has found that managing anxiety may have moderating effect on sleep disturbance [24], even though it has been concluded that the effect of managing anxiety on insomnia still remains to be uncertain, considering the bias included in the study. Although many previous studies have reported the clear associations between depression, anxiety and insomnia stating that anxiety may be a risk factor for occurrence of sleep disturbance while insomnia may be a risk factor for occurrence of anxiety and depression [25–29], the precise etiological relationship between these comorbidities in panic disorder remains unclear.

Therefore, understanding the psychological correlation between comorbidities in panic disorder, including depressive disorder, is critical for the development of more effective treatment strategies that can lead to improved outcomes for these individuals. This study aims to investigate the impact of insomnia symptoms on depression in patients with panic disorder, with a focus on understanding the psychological correlation between these comorbidities. By identifying the relationship between insomnia and depressive symptoms, this study seeks to contribute to the development of more effective treatment strategies for individuals with panic disorder, ultimately improving their clinical outcomes. In this study, it is hypothesized that there is a significant association between insomnia symptoms and depressive symptoms in patients with panic disorder. It is expected that patients with panic disorder accompanied by significant depressive symptoms will exhibit higher levels of insomnia, indicating a potential mediating role of insomnia in the relationship between panic disorder and depression. Furthermore, it is also hypothesized that some specific symptom aspects of panic disorder may have a stronger association with depressive symptoms than the overall severity or other symptom aspects of panic disorder.

**METHODS**

**Study design and participants**

This study is a retrospectively conducted cross-sectional study. We analyzed data from patients diagnosed with panic disorder who visited the outpatient clinic of the psychiatric department at Konkuk University Medical Center between January 1, 2018, and December 31, 2023. Initially, 210 patients were enrolled for analysis, but 18 were excluded due to missing data regarding panic disorder scales including Albany Panic and Phobia Questionnaire (APPQ), Anxiety Sensitivity Index (ASI), and Panic Disorder Severity Scale (PDSS) and insomnia scale including Insomnia Severity Index (ISI), leaving 192 patients for the final analysis. This study was approved by the Institutional Review Board of Konkuk University Hospital (IRB number: KUMC 2023-04-066), and due to retrospective nature of this study, informed consent was waived by the IRB.

**Measures**

Demographic data of the patients including age and sex were collected and clinical features were measured using psychological instruments including PDSS, ASI-revised (ASI-R), APPQ, ISI, and Beck Depression Inventory-II (BDI-II).

**ISI**

The ISI is a self-report scale consisting of 7 items assessing the symptoms of insomnia including its nature, severity, and impact [30]. Each item is rated based on a 5-point Likert scale from 0 indicating “no problem” to 4 indicating “very severe problem” with a total score ranging from 0 to 28 [30,31]. The total score is interpreted as follows: absence of insomnia (0–7); sub-threshold insomnia (8–14); moderate insomnia (15–21); and severe insomnia (22–28). The Korean version of ISI (ISI-K), which was used in this study, has been demonstrated to be reliable and valid [32]. In this study, cases corresponding to the score categories from moderate to severe insomnia were considered to have insomnia, excluding sub-threshold insomnia, which indicate ISI-K scores to be 15 or higher.

**PDSS—self report version**

The PDSS is a measurement scale for severity of 7 symptom dimensions of panic disorder, including frequency of panic attacks, agoraphobic fear and avoidance, and impairment in social functioning [33,34]. The self-report version of the PDSS (PDSS-SR), the adjusted version of scale validated with internal consistency of 0.88 in Korean population, was used in this study [33]. The total score of PDSS-SR was used to indicate overall severity of panic disorder in this study.

**ASI-R**

The ASI-R is a self-reported questionnaire used to measure the
degree of fear arising from the belief that bodily sensations will produce dangerous outcomes. It is measured using a 5-point Likert scale in 4 anxiety sensitivity dimensions including fear of respiratory symptoms, fear of publicly observable anxiety reactions, fear of cardiovascular symptoms, and fear of cognitive dyscontrol. The Korean version of the ASI-R has been validated and shown to have good test–retest reliability (r=0.82) and internal consistency (α=0.92) [35].

APPQ

The APPQ is a scale designed to assess 3 types of fear related to panic disorder. The scale consisted of 27 items categorized into 3 subscales: 1) agoraphobia, 2) social phobia, and 3) interoceptive fear (i.e., fear of activities that cause painful bodily sensation). The Korean version of the APPQ was used in this study, which has shown significant psychometric qualities [36,37].

BDI-II

BDI-II is a self-report scale consisting of 21 items to evaluate the severity of depressive symptoms [38]. The severity of emotional, physiological, and cognitive symptoms of depression is rated with a 4-Likert scale, ranging from 0 to 3. Since the criterion for the BDI-II score cutoff for severity of depressive symptom, which is based on the total score of the scale, has not yet been specifically established with Korean population [39], cutoff for severity of depressive symptom is set as follows according to the manual of original version of BDI-II: minimal (0–13); mild (14–19); moderate (20–28); and severe (29–63) [40]. In this study, cases with moderate to severe degree of depressive symptom were considered to have significant depressive symptoms, which indicates total score of 20 or higher, excluding those with minimal and mild depression. A BDI-II adjusted for the Korean version validated with internal consistency of 0.94 [39,41].

Statistical analysis

The student’s t-test and chi-square test were performed in order to examine whether there are any significant differences in distribution between the groups, comparing the demographic and clinical variables, respectively for continuous variables including age and psychological measurement scores and categorical variables including sex and presence of insomnia. The Pearson’s correlation analysis was conducted to examine correlation between BDI-II scores and other measured clinical scales including PDSS, APPQ, ASI-R, ISI-K, and its subscale scores from the data of included panic disorder patients, determining significant correlations between each subscale of panic disorder and insomnia and severity of depression in panic disorder. Partial correlation analysis was additionally conducted controlling the confounding effects of demographic variables including age and sex on the depressive symptom in patients with panic disorder. Subsequently, the logistic regression analysis was conducted to estimate correlation between significant depressive symptom, defined as BDI-II score measured to be 14 or greater, and other symptom variables including subscales of PDSS, APPQ, ASI-R, and ISI-K. A p-value of 0.05 or lower was considered statistically significant and all statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software version 17 (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 192 patients were included in this study. The mean age of the subjects was 34.71±12.77 years, ranging from 18 to 66, and 54.7% of the subjects were male, while 45.3% were female. There was no significant difference in sex distribution (p=0.911) between patients with panic disorder manifesting significant depressive symptom (PDD) and those not manifesting significant depressive symptom (PD), while significant difference was found in age distribution, with the mean age of the PDD group being greater than that of PD (31.98±12.10 vs. 39.28±12.62 years, p<0.001).

The PDD group had significantly higher proportion of patients with insomnia when compared to that of the PD group (65.0% vs. 12.5%, p<0.001). The PDD group also had significantly higher scores in other clinical symptom scales related to panic disorders including PDSS, APPQ, ASI-R and its subscales, compared to PD group. It was found that the PDD group had significantly higher total PDSS scores than the PD group (14.83±5.89 vs. 9.43±4.68, p<0.001), indicating that panic disorder patients with significant depressive symptoms tend to have more severe panic symptoms. These findings were consistent in all other subscales of PDSS including phobic avoidance of physical sensations, impairment in work functioning, and impairment in social functioning (2.00±1.04 vs. 1.13±0.85, p<0.001; 2.12±1.07 vs. 1.18±0.88, p<0.001; 2.08±1.03 vs. 1.04±0.76, p<0.001; respectively). PDD group was also shown to have higher scores in total scale and other 3 fear subscales in APPQ scores (total score: 64.88±17.27 vs. 48.65±12.36, p<0.001; agoraphobia: 64.23±15.99 vs. 49.80±13.03, p<0.001; social phobia: 63.14±16.13 vs. 45.14±11.40, p<0.001; interoceptive fear: 63.98±16.23 vs. 52.78±13.11; p<0.001). PDD group had higher scores in total and subscales of ASI-R (total score: 77.08±13.16 vs. 60.31±13.17, p<0.001; fear of publicly observable anxiety reactions: 66.32±12.05 vs. 51.22±11.29, p<0.001; fear of cognitive dyscontrol: 76.16±18.47 vs. 51.50±13.05; p<0.001) (Table 1).

In correlation analysis, BDI-II scores of the subjects were found to be positively correlated with ISI-K and all clinical symptom variables related to panic disorder including PDSS, APPQ, and ASI. These tendencies were consistent in partial correlation analysis in which confounding effects of demographic features of subjects including age and sex were controlled. In partial correlation analysis, the total score of PDSS and its subscale had a positive correlation with BDI-II score (R=0.54). For APPQ score, total score and all 3 subscale scores were found to be positively correlated with BDI-II score, with social phobia scores showing the highest correlation coefficient (R) of 0.69. For ASI-R, it is also shown that total score and all subscale scores were positively correlated with...
BDI-II scores, with fear of cognitive dyscontrol being most strongly correlated, followed by total score of ASI-R and fear of publicly observable anxiety reaction in order (R=0.75, R=0.64, R=0.64, respectively, p<0.001) (Table 2).

The logistic regression analysis was performed to examine the magnitude of associations of each clinical symptom subscales related to panic disorder on presence of significant depressive symptoms, stipulated as BDI-II score of 20 or greater. In the analysis, 2 subscales of ASI-R, fear of publicly observable anxiety reactions and fear of cognitive dyscontrol (OR=1.05, 95% CI=1.009–1.092, p=0.017 and OR=1.05, 95% CI=1.014–1.078, p=0.004, respectively), and ISI-K scores were shown to be significantly associated with significant depressive symptom in panic disorder patients (OR=1.24, 95% CI=1.138–1.355, p<0.001) (Table 3). Significant association was found between increase in ASI-R subscale scores, fear of publicly observable anxiety reactions and fear of cognitive dyscontrol, and ISI-K scores and existence of significant depression in panic disorder.

DISCUSSION

In this study, we explored the association between insomnia, sub-symptoms of panic disorder, and depressive symptoms in patients with panic disorder using correlation analysis and logistic regression analysis. Our findings revealed that patients with panic disorder accompanied by significant depressive symptoms were more likely to have insomnia symptoms, were younger, and had more severe panic symptoms than those not accompanied by depressive symptoms. These findings align with previous studies that have demonstrated that panic disorder patients who currently have or once had secondary depression have a longer illness duration, more severe anxiety symptoms, and more extensive phobic avoidance [10].

In our sample, insomnia symptoms were independently associated with depressive symptoms in panic disorder patients, suggesting that irrespective of the severity of panic disorder symptoms, or the related phobia and anxiety sensitivity, depressive
Insomnia and Panic Disorder

Symptoms were related to the severity of insomnia in patients with panic disorder. As previously reported, patients with panic disorder often suffer from insomnia and anxiety, which may play a key role in both disorders [42]. Anxiety, especially that which occurs before bedtime, may play a crucial role in the development of insomnia, and consistent results have been reported in previous mediation studies. This suggests that insomnia may act as a mediating factor in the relationship between panic disorder and depression. Since not all patients with panic disorder complain of insomnia, preventive education for patients without insomnia, sleep hygiene correction for patients with mild symptoms, and cognitive behavioral therapy for insomnia in patients with clinically significant levels of insomnia might help to ameliorate the difficulties faced by the panic disorder patients suffering from burden of comorbid psychiatric symptom including impaired sleep quality, which may induce daytime sleepiness, fatigue, difficulty in concentrating, and impaired cognitive and psychomotor performance and also exacerbate anxiety symptoms leading to heightened levels of worry, fear, and apprehension, contributing to the overall distress and decreased overall functioning.

Among subscales related to panic symptom, the fear of publicly observable anxiety reaction and fear of cognitive dyscontrol were found to have the most significant association with the presence of depressive symptoms in panic disorder patients, even more so than the overall severity of panic symptom itself, which is represented by the total score of PDSS. This finding aligns with a previous network study, demonstrating that cognitive and behavioral symptoms, including fear of cognitive dyscontrol, social dysfunction, phobic avoidance, and anticipatory anxiety about panic attacks, are core symptoms of panic disorder, while distress from panic attacks and attack frequency had no direct effects on other symptoms of panic disorder [43]. This suggests that depressive symptoms experienced by patients with panic disorder may be more significantly correlated with the cognitive and behavioral symptoms of panic disorder than with the physical symptoms of panic disorder.

Table 2. Pearson’s correlation analysis between Beck’s Depression Inventory-II (BDI-II) scores and other symptom variables related to panic disorder

<table>
<thead>
<tr>
<th></th>
<th>R*</th>
<th>R†</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDSS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>0.54</td>
<td>0.51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P1: Panic frequency</td>
<td>0.36</td>
<td>0.35</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P2: Distress during panic</td>
<td>0.32</td>
<td>0.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P3: Panic-focused anticipatory anxiety</td>
<td>0.32</td>
<td>0.30</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P4: Phobic avoidance of situations</td>
<td>0.48</td>
<td>0.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P5: Phobic avoidance of physical sensations</td>
<td>0.50</td>
<td>0.49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P6: Impairment in work functioning</td>
<td>0.54</td>
<td>0.51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P7: Impairment in social functioning</td>
<td>0.54</td>
<td>0.51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>APPQ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>0.60</td>
<td>0.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>0.59</td>
<td>0.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Social phobia</td>
<td>0.69</td>
<td>0.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interoceptive fear</td>
<td>0.50</td>
<td>0.49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASI-R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>0.64</td>
<td>0.62</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fear of respiratory symptoms</td>
<td>0.45</td>
<td>0.40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fear of publicly observable anxiety reactions</td>
<td>0.64</td>
<td>0.61</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fear of cardiovascular symptoms</td>
<td>0.44</td>
<td>0.48</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fear of cognitive dyscontrol</td>
<td>0.75</td>
<td>0.72</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ISI-K score</td>
<td>0.70</td>
<td>0.68</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*correlation coefficient; †partial correlation coefficient excluding demographic factors (age, sex). PDSS, Panic Disorder Severity Scale; APPQ, Albany Panic and Phobia Questionnaire; ASI-R, Anxiety Sensitivity Index-Revised; ISI-K, The Korean version of Insomnia Severity Index

Table 3. Logistic regression analysis on significant depressive symptoms (BDI-II score ≥20) and correlating clinical variables with significant depressive symptoms in patients with panic disorder

<table>
<thead>
<tr>
<th></th>
<th>Coefficient (β)</th>
<th>Standard error</th>
<th>Wald χ²</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASI-R: Fear of publicly observable anxiety reactions</td>
<td>0.048</td>
<td>0.020</td>
<td>5.68</td>
<td>1.05</td>
<td>1.009–1.092</td>
<td>0.017</td>
</tr>
<tr>
<td>ASI-R: Fear of cognitive dyscontrol</td>
<td>0.044</td>
<td>0.016</td>
<td>8.16</td>
<td>1.05</td>
<td>1.014–1.078</td>
<td>0.004</td>
</tr>
<tr>
<td>ISI-K</td>
<td>0.217</td>
<td>0.045</td>
<td>23.72</td>
<td>1.24</td>
<td>1.138–1.355</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

BDI-II, Beck Depression Inventory-II; ASI-R, Anxiety Sensitivity Index-revised; ISI-K, The Korean version of Insomnia Severity Index; CI, confidence interval
Negative cognition in panic disorder—the idea that one might not be able to control their panic symptoms—may be more strongly associated with depression. Therefore, as some researchers have focused their attention on identifying and subsequently modifying negative cognitions involved in the process of panic attacks [44,45], our findings imply that rather than focusing solely on the management of physical symptoms experienced by panic disorder patients, correcting negative cognition could be an essential part of the treatment. Given the higher incidence of depression in patients with panic disorder, and considering the negative outcomes linked with this comorbidity including social dysfunction, a prolonged illness course, and even suicidality, psychological interventions are critical. Cognitive behavioral therapy (CBT), which focuses on cognitive symptoms like catastrophic thinking and the misinterpretation of ordinary bodily sensations or situational cues as life-threatening events, can help individuals manage the feeling of losing control over their thoughts. This approach can potentially prevent and alleviate depressive symptoms in patients suffering from panic disorder. This could, in turn, enhance the overall quality of life for these patients [46,47].

This study has several limitations. First, due to its retrospective and cross-sectional nature and the relatively small sample size, there may be some limitations in generalizing the findings from this study, and selection bias could be a factor. Therefore, further studies with larger sample sizes would be necessary to generalize the findings from this study, and the temporal relationship between panic disorder and depressive symptoms should be considered to ensure the predictive nature of the variables. Second, depressive symptoms and insomnia were evaluated through a questionnaire rather than a direct evaluation, which may impact the precision of the evaluation. Third, considering the bidirectional relationship between insomnia and depression, the effects of insomnia on the occurrence of depressive symptoms in panic disorder patients may be exaggerated.

In conclusion, this study examined the association between insomnia, sub-symptoms of panic disorder, and depressive symptoms in patients with panic disorder using correlation analysis and logistic regression analysis. It is found that insomnia was significantly associated with the presence of depressive symptoms in panic disorder, as well as several sub-symptoms of panic disorder, including fear of social dysfunction and cognitive dyscontrol. These comprehensive results highlight the need for interventions such as cognitive behavioral therapy that may identify and modify maladaptive thoughts, behaviors, and beliefs that contribute to sleep difficulties and the cognitive distortions of catastrophic thinking and interpretation that contribute to the development and maintenance of panic attack in order to prevent and assist with depressive symptoms in panic disorder patients and those suffering from insomnia.

Funding Statement
None
Insomnia and Panic Disorder


