

Insomnia Associated with Depressive Disorder: Primary, Secondary, or Mixed?

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ABSTRACT

Background: Insomnia is a common problem that is known to occur during depression. However, literature still debates whether insomnia is part of depression or a separate entity. **Materials and Methods:** Subjects presenting with depressive disorder according to DSM-IV-Text Revision criteria were recruited after seeking informed consent. Clinical interview was performed with the help of Mini International Neuropsychiatric Interview Plus. Their demographic data and depression related history were recorded. Depression severity was assessed by using Hamilton Rating Scale for Depression. Diagnosis of insomnia was made with the help of International Classification of Sleep Disorders-2 criteria. Type of insomnia, its duration, and its relationship with depressive illness were specifically asked. If any subject fulfilled criteria for more than one type of insomnia, both were recorded. Statistical analysis was done with the help of statistical package for social sciences (SPSS) version 17.0. χ^2 test, independent sample *t* test, and Pearson's correlation were performed. **Results:** A total of 54 subjects were enrolled in this study. Primary insomnia was seen in 40.7% cases and secondary insomnia in 58.8% cases; 27.3% subjects did not experience insomnia along with depressive disorder. In the primary insomnia category, adjustment insomnia was most prevalent (63.6%), and in secondary insomnia group, insomnia due to depressive disorder was most frequent (59.3%). Interestingly, primary insomnia often followed an onset of depressive illness ($P=0.04$), while secondary insomnia preceded it ($\chi^2=11.1$; $P=0.004$). The presence of either type of insomnias was not influenced by duration of depressive illness, number of depressive episodes, and duration of current depressive episode. On the other hand, duration of insomnia was positively correlated with total duration of depressive illness ($P=0.003$), number of episodes ($P=0.04$), and duration of current depressive episode ($P<0.001$). **Conclusion:** Primary insomnia is common in subjects with depression, and it usually follows depressive illness. On the other hand, secondary insomnia often precedes the onset of depressive illness. Duration of insomnia positively correlates with duration and frequency of depressive episodes.

Key words: Major depressive disorder, primary insomnia, secondary insomnia

INTRODUCTION

Insomnia is a common problem and affects nearly 10%

of individuals.^[1] The relationship between insomnia and depression is complex, and our knowledge has changed substantially in the past decade regarding the relationship between these two entities. Earlier, an epidemiological study has shown that persons with insomnia are at a higher risk of developing depression and anxiety disorders.^[2] This is not a one-way relationship, as Buysee *et al.*^[3] have shown that depression also predicts future insomnia. It was further shown that depression has not only qualitative but also quantitative effect on the sleep; severely depressed people have the worse sleep pattern as compared with

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those with mild-to-moderate depression.^[4] Furthermore, insomnia with depression can be considered as an intermediate subtype between pure depression and isolated insomnia.^[3] Thus, it appears that these two disorders are independent entities but they co-occur more than by chance.

A number of factors may contribute to their co-occurrence: Hyperarousal and stress are common in both disorders; depressed persons may engage in poor sleep hygiene practices. They may be due to an effect of some untreated illness or emerges because of drugs. In addition, in substance abusers, addictive substance may be responsible for either of them. However, sleep hygiene practices and hyperarousal do not differ between depressed and psychophysiological insomniac patients.^[5] In addition, symptoms of chronic insomnia and depression frequently overlap and it may sometimes be difficult to differentiate between them. However, the 'preoccupation with sleep' and other features of depression may be considered while differentiating between these two groups.^[5] Another report suggested that treatment of insomnia improves depression by an unknown mechanism.^[6]

It has also been reported that when the depression is treated, some of its symptoms remain unresolved and manifest as residual symptoms of depression, with sleep problems forming a major chunk.^[7] Moreover, addition of behavioral therapy for insomnia to pharmacotherapy for depression resulted in improvement of sleep.^[8]

Although recent literature talks about comorbid insomnia and blurred the boundaries between primary and secondary insomnia, International Classification of Sleep Disorders-2 (ICSD-2) still keeps primary insomnia and secondary insomnia to psychiatric illness categories.^[9,10] We could not find any study that has attempted to diagnose primary insomnia in subjects with depressive illness. Thus, this study was planned with the aim of finding the type of insomnia (primary or secondary) in patients suffering from depression; ascertaining the onset of insomnia relative to the onset of depressive illness; and lastly measuring the effect of insomnia on the course of depressive disorder.

MATERIALS AND METHODS

This study was conducted after seeking ethical approval from the ethics committee of our institution. All consecutive subjects attending the psychiatry outpatient department of a tertiary care teaching hospital between January 2011 and March 2011 and complaining of depressive illness were included in the present study. Depressive illness was defined as the presence of either major depressive disorder (MDD) or

dysthymia or recurrent depressive disorder according to DSM-IV-TR criteria.^[11] All patients were subjected to structured clinical interview using Mini International Neuropsychiatric Interview Plus.^[12] However, the following subjects were excluded from the study: Those developing depression or insomnia after the onset of any medical or neurological disorder (i.e., having a temporal relationship); those ever suffered from any kind of psychotic disorder; those presently meeting the criteria of substance abuse, dependence, or withdrawal; those consuming any medicine that is known to induce depression, sleep disturbances, or movement disorders; those not willing to participate; those having history suggestive of any other sleep disorder (e.g., sleep apnea and parasomnia). Similarly, pregnant women, those within postpartum period (12 months since last childbirth) and having symptoms of postmenopausal syndrome, were also excluded from the study.

All included subjects were explained about the rationale of the study in detail, and their written informed consent was taken. Thereafter, their demographic data were recorded and clinical history regarding course of their illness, treatment history, and family history of psychiatric illness was sought. Two independent episodes of depression were diagnosed when the subject was asymptomatic for at least 2 months in between consequent episodes.^[11] If somebody reported reemergence of symptoms of depression within this period, he was considered as continuing the previous episode of MDD or dysthymia.

Diagnosis of insomnia

Similarly, they were asked regarding insomnia. Diagnosis of insomnia was made when the subjects complained of either difficulty falling asleep, staying asleep, or early morning awakening (at least 2 h before their usual wake time) on most of the days for at least 1 month.^[10] The temporal relationship of the onset of insomnia symptoms was specifically asked from the patients in relation to the onset of depressive illness. Insomnia was further classified according to ICSD-2 criteria.^[10] ICSD-2 also allows diagnosis of primary insomnias in the presence of mental disorders, provided insomnia is a cause of clinical concern and runs an independent course.^[10] Adjustment insomnia was diagnosed when it followed any significant stressor and the subject conveyed preoccupation with that stressful event; in other words, he reported that 'thoughts related to stressor keep coming in my mind and do not allow me to fall asleep'. Psychophysiological insomnia was diagnosed when the person reported 'feeling nervous before bedtime', 'fear that I would not be able to fall asleep', 'racing thoughts whenever I wake up in night, especially regarding my sleep problem' or 'I sleep better away from my home'. Poor sleep hygiene

and paradoxical insomnia were also diagnosed as per standard criteria.^[10]

In some cases, where a person was suffering from both primary and secondary insomnias, both were diagnosed independently. Only insomnia due to depressive disorder (IDD) was diagnosed when the person had complained of significant insomnia but person was not fulfilling criteria for any of the primary insomnias.^[10] Diagnosis of both primary insomnia and IDD was made in the following circumstances: (1) adjustment insomnia: Person was exposed to a stressor that had an increased importance for the person, so much that the already existing insomnia in the person worsened; (b) psychophysiological insomnia: Poor sleep became a primary focus after the subject has a learned behavior that was sleep defeating, lead to hyperarousal and hence insomnia exacerbated; (c) paradoxical insomnia: There was a huge mismatch between insomnia reported by the patient and bed partner and daytime symptoms that accompanied insomnia; (d) insomnia due to poor sleep hygiene: Person developed practices that are counterproductive to sleep with an increase in severity of insomnia during depression.

Severity of depressive episode

After making clinical diagnosis of depressive disorder, severity of depressive episode was assessed by using the Hamilton Rating Scale for Depression (HAM-D).^[13]

Statistical analysis

Analysis was performed by using SPSS version 17.0. Descriptive statistics analysis was done. χ^2 analysis was done for the nonparametric variables. An independent sample *t* test was used to find out the difference between the means in two groups. Pearson's correlation was performed to assess the correlation between parametric variables.

RESULTS

This study included 54 subjects. Among them, 42.6% were males and 57.4% were females. The mean age of the subjects was 37.13 years (± 11.54 years; range=17-62 years). The mean duration of the depressive episode was 40.9 months ± 50.5 months). Some of the episodes were as long as 10 years since the subjects did not report complete remission between them. In this study sample, number of episodes of depression ranged from 1 to 10.

Insomnia was not reported by 27.3% subjects, whereas 33.3% complained of both types of insomnias occurring together [Figure 1]. Primary insomnia was seen in 40.7% cases, and secondary insomnia was evident in 58.8% cases. In the primary insomnia group, 63.6%

subjects reported adjustment insomnia, 22.7% met criteria for psychophysiological insomnia, and 13.6% were suffering from paradoxical insomnia. Table 1 depicts the distribution of depression-related variables in subjects with and without primary insomnia. Of note is the fact that primary insomnia often followed the depressive episodes.

Table 1: Comparison of MDD-related variables between primary insomnia and other subjects

Variable	Primary insomnia (n=21)	No primary insomnia (n=33)	P
Age (years)	40.75 \pm 9.6	34.93 \pm 12.19	0.75
Gender			
Male	9 (42.85)	14 (42.4)	0.59
Female	12 (57.15)	19 (57.6)	
Interepisodic remission			
Complete	6 (28.6)	5 (15.2)	0.1
On drugs only	1 (4.8)	2 (6.1)	
No remission with therapy	5 (23.8)	2 (6.1)	
Not applicable*	9 (42.9)	24 (72.7)	
Relation to MDD episode			
Precede	7 (33.3)	8 (24.2)	0.04
Followed	14 (66.7)	16 (48.5)	
Not applicable**	–	9 (27.3)	
Family history of insomnia			
Present	2 (9.5)	1 (3)	0.33
Absent	19 (91.5)	32 (97)	
Family history of psychiatry illness			
No history	21 (100)	28 (84.8)	0.17
MDD	0	3 (9.1)	
Other	0	2 (6.1)	
Duration of depressive episode (months)	49.95 \pm 49.52	35.19 \pm 51.03	0.29
Number of depressive episodes	1.85 \pm 2.03	1.39 \pm 0.93	0.26
HAM-D score	19.07 \pm 4.26	18.86 \pm 5.0	0.91

*First episode of depression, drug naïve; **Primary insomnia not reported; Figures in parenthesis are in percentage; MDD – Major depressive disorder; HAM-D – Hamilton Rating Scale for Depression

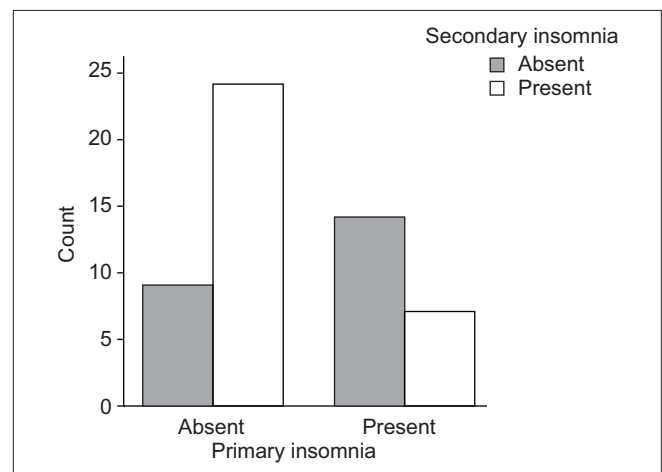


Figure 1: Relationship between primary and secondary insomnias during depression

In the secondary insomnia group, insomnia secondary to poor sleep hygiene was evident in 7.4%, insomnia due to restless leg syndrome was evident in 33.3%, and IDD was reported by 59.3%. Secondary insomnia was not associated with gender difference ($\chi^2=0.19$; $P=0.43$) and interepisodic recovery of depressive disorder ($\chi^2=3.54$; $P=0.31$). Prevalence of secondary insomnia was not different between subjects with and without family history of insomnia ($\chi^2=4.28$; $P=0.71$) or family history of psychiatric illness ($\chi^2=2.86$; $P=0.23$). However, in a significantly higher proportions of subjects, secondary insomnia preceded depressive episode ($\chi^2=11.1$; $P=0.004$). Similar to primary insomnia, age, duration of depressive episode, number of episodes, and HAM-D scores were not different between subjects with and without secondary insomnia. Figure 1 shows the relationship between primary and secondary insomnias.

The duration of insomnia positively correlated with the total duration of depressive episodes ($r^2=0.40$; $P=0.003$), number of depressive episodes ($r^2=0.27$; $P=0.04$), and duration of current depressive episode ($r^2=0.73$; $P<0.001$).

DISCUSSION

This study showed that a proportion of subjects with depressive disorder do not suffer from insomnia. On the other hand, a number of subjects with depressive disorder showed symptoms of primary insomnia and some had met criteria for both primary and secondary insomnias. It must also be noted that while primary insomnia frequently follows a depressive episode, secondary insomnia often precedes it. Importantly, age, total duration of depressive illness, number of depressive episodes, and HAM-D scores were not different between subjects with and without insomnias, irrespective of their nature – primary or secondary. Similarly, family history of person with primary or secondary insomnia did not affect the development of insomnia in that group. However, duration of insomnia – whether primary or secondary or combined – was positively correlated with total duration of depressive illness, number of depressive episodes, and duration of current depressive episode.

Primary insomnia has never been examined in depression, and hence we do not have any comparable study. Therefore, in present discussion we will focus on issues related to independent diagnosis of depression and insomnia, factors that can provide a seed for the development of primary insomnia in depression, and so on.

Whether sleep disturbance is an integral part of a depressive episode is questionable. A large

epidemiological study had shown that all subjects with depression do not develop insomnia.^[2] Functional imaging of the brain during a depressive episode provides the biological basis of sleep disturbance during depression and suggests that discrete brain areas are responsible for different symptoms in a depressed patient.^[14] This is one reason why insomnia is not considered merely as a symptom of depression but considered comorbid.^[9] A number of studies support the fact that insomnia is an independent illness that co-occurs with depression. First, insomnia is known to worsen dramatically when depression reaches a critical limit, further supporting the notion that they are in fact two disorders.^[4] Second, insomnia had either preceded a depressive episode or led to a depressive episode or seen a residual symptom after treatment of depression.^[2,7,8,15,16] This is possible only when insomnia occur independently of depression; otherwise, one would have expected it to start with depression and to remit with the antidepressant therapy. Third, when depressed patients are subjected to psychological therapies for insomnia in addition to pharmacotherapy for depression, response is often better as compared with antidepressant therapy alone.^[8,17] This is another reason why insomnia is now considered to be a separate entity.

It is also possible that depressed subjects with primary insomnia have heightened arousal and they have behaviors that are counterproductive to sleep as compared with depressed subjects without primary insomnia. Although a direct evidence in this context is not available, but an indirect evidence may give us a clue. Earlier, it has been reported that sleep-related behavior does not differ among subjects with psychophysiological insomnia and insomnia secondary to depression and control group.^[5] In addition, subjects with psychophysiological insomnia and insomnia with depression have comparable cognitive arousal and dysfunctional beliefs regarding sleep.^[5] However, in that study, diagnostic criteria for psychophysiological insomnia and insomnia associated with depression appear to be loose and hence conclusion cannot be reached. Moreover, the sample was small, which precludes from generalization of results. On the contrary, subjects with insomnia – whether psychophysiological or ‘insomnia with depression’ often have difficulties with sleep hygiene.^[5] This perpetuates insomnia in these persons as we have seen in the present study and they suffer from combined insomnia (primary and secondary occurring together). Furthermore, depressed patients often develop cognitive distortions and their perception regarding their health, future, and relationships are negatively shaded. This has been shown in patients with myocardial infarction.^[18,19] We assume that some of the individuals with depressive disorder perceive their

existing insomnia or depressive symptoms negatively and consequently develop primary insomnias. We have not examined sleep-related cognitive mechanisms of these patients, and this is clearly an area for further research.

Taylor *et al.*^[2] had shown that depression severity was related to the number of nocturnal awakenings and the frequency of insomnia was associated with both depression and anxiety. Another study suggested that severe insomnia in depressed patients was associated with long duration of current depressive episode and higher HAM-D scores.^[20] We have not measured insomnia severity directly. However, duration of insomnia is a surrogate marker of severity and we have found its positive correlation with total duration of depressive illness, number of depressive episodes, and length of the current depressive episode.

However, this study had some methodological limitations. First, the sample size was small due to strict inclusion criteria followed in this study. In future, a study with a larger sample may be planned to unravel this issue. Second, as already mentioned, we did not assess the insomnia severity owing to absence of a rating scale in Hindi language. Third, duration of depressive episode had a large variance. A number of factors might be responsible for it: Recall bias, poor treatment compliance and consequently incomplete remission in the included subjects, inaccessibility of specialized services soon after the onset of illness, and so on. Fourth, we could not divide the insomnia subjects into three groups – those with primary insomnia, those with IDD, and a combined insomnia group – owing to the small sample size. This kind of grouping could have thrown more light on the issues addressed in the present study. Fifth, the HAM-D scores do not represent the longitudinal severity, and considering the long duration of depressive episodes in the present study, HAM-D scores do not adequately represent the magnitude of depression. Sixth, this was a cross-sectional study and we could not examine the effect of the antidepressant therapy on either of the insomnia groups. An adequate treatment of depression is thought to clarify the diagnostic confusion between primary insomnia and depression-related insomnia.^[10]

Nevertheless, despite limitations, to best of our knowledge, this is the first study to examine the presence of primary insomnias during depressive disorders. This may help in choosing an appropriate psychological treatment for primary insomnias early in the course of treatment of depression, and we may expect a better outcome.

In conclusion, primary insomnias are frequent during depressive disorders. They usually follow depressive

symptoms. On the other hand, secondary insomnias often precede depressive illness. If insomnia remains untreated for a long time, it can lengthen the depressive illness as well as the current depressive episode and increases frequency of depressive disorders.

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