

ORIGINAL RESEARCH

Nightmare Distress as a Risk Factor for Suicide Among Adolescents with Major Depressive Disorder

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Purpose: Nightmare is common and is also independently implicated in suicide risk among the adolescent population. Adolescents with major depressive disorder (MDD) are at an increased risk of suicide. Therefore, comorbid nightmares may amplify suicide risk among this clinical population. This study aimed to explore the effects of nightmares on suicide risk among adolescents with MDD. **Patients and Methods:** Subjects were 499 outpatients aged 12–18 in four large psychiatric hospitals clinic of China, from January 1 to October 31, 2021. Simultaneously, we matched 499 healthy controls according to gender and age. All participants underwent affective state (depressive and anxiety symptoms) and sleep variable (nightmare frequency/distress, insomnia symptoms, and daytime sleepiness) evaluation as well as MDD diagnoses and determination of suicide risk by a fully structured diagnostic clinical interview. **Results:** Adolescents with MDD reported a higher incidence of frequent nightmares (at least one night per week) and level of nightmare distress than healthy controls (22.0% vs 6.1%; 28.85 \pm 11.92 vs 17.30 \pm 5.61). Over half of the patients with suicide risk (51.6%) experienced frequent nightmares compared with approximately one-third of those at a risk for suicide (30.7%). Patients with suicide risk scored scientifically higher on sleep variables, depressive and anxiety symptoms than those without the risk. Further logistic regression analysis indicated that female gender, junior grade, recurrent depressive episode, severe nightmare distress and severe depressive symptoms were independently and significantly associated with suicide risk.

Conclusion: Our study provided evidence that adolescents with MDD experienced a higher prevalence of frequent nightmares and suffered more nightmare distress. Nightmare distress is an independent risk factor for suicide risk.

Keywords: major depressive disorder, sleep problems, nightmare, suicide risk, adolescent

Introduction

Major depressive disorder (MDD) is a significant public health concern worldwide; approximately 264 million individuals are affected by MDD. Adolescents are a population group at a high risk of experiencing MDD, and the prevalence is increasing. A meta-analysis suggests that the global prevalence of any depressive disorder is 2.6% and 1.3% major depression. There is strong evidence on the relationship between MDD and severe consequences, including suicide, which is the third leading cause of death among adolescents. Therefore, it is critical to identify the risk factors related to increased suicide risk among adolescents with MDD to develop effective interventions accordingly.

Sleep is a physiological phenomenon that occupies up to one-third of the human lifespan and is believed to be a pivotal operating state of the central nervous system.⁶ Adequate sleep among adolescents is essential owing to its significant effects on the development of vital psychophysiological functions.⁷ The findings of several previous studies in the adolescent population, which showed that sleep problems, such as insomnia, are closely linked to depression and other psychiatric disorders and are major risk factors for developing suicidal thoughts and behaviors, supported this

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notion.⁸⁻¹⁰ Sleep problems are common among patients with MDD and have been formerly regarded as the core secondary symptoms of a depressive episode. 11-13 Furthermore, patients with sleep problems are often implicated with adverse outcomes, including elevated symptom severity, increased suicide risk, ¹⁴ and greater recurrence risk. ^{15,16} Therefore, sleep problems warrant attention as a public health concern. It is a particularly important step to prevent and identify these problems as accurately as possible and develop effective strategies of sleep improvement interventions to reduce suicide risk.^{8,9}

Nightmare is one of the most common and specific types of sleep problems, typically characterized by dysphoric, frightening, or disturbing dreams that cause extreme irritability and often lead to awakening. 17,18 According to several epidemiological studies on the general adolescent population, nightmares are prevalent. 17,19,20 For example, Liu et al reported that 45.2% of the participants experience at least one nightmare episode per month, and 8% experience frequent nightmares (at least one episode per week). 19 Nightmares have been linked to a variety of mental health consequences, such as insomnia, daytime sleepiness, anxiety and depressive symptoms, post-traumatic stress disorder, behavioral problems, and impaired psychosocial function. 19,21,22 Furthermore, studies have demonstrated that nightmares are associated with an increased risk of suicide risk in the past few years. 17,21,23

However, several issues have been left open by the previous literature, which warrant to be addressed in the current study. First, in adult psychiatric patients with MDD, bipolar disorders, and schizophrenia, nightmares occur at a higher rate than in the general population, ranging from 29.9% to 62.3%. 18,24,25 However, to date, no evidence for the prevalence of nightmares among adolescent patients with MDD exists. Second, although a growing number of studies have focused on the sleep-suicide relationship, only two studies have specifically been designed to examine this issue using adolescent samples with MDD.^{26,27} Moreover, sleep variables in these studies only include insomnia and sleepiness, but not nightmares. Third, no studies have attempted to identify which specific sleep problems are associated with suicide risk independently from other sleep variables since they are probably highly correlated or overlap. For example, nightmares frequently lead to insomnia and excessive daytime sleepiness.

Therefore, using valid measures of a wide range of different sleep disturbances and suicide risk in adolescent patients with MDD, we mainly sought to investigate the following research questions: (1) determine the prevalence of nightmares among the clinical population and whether it is higher than in healthy controls and (2) whether nightmares are associated with suicide risk after controlling for demographics, psychopathology (eg. anxiety and depressive symptoms), and other sleep variables.

Methods

Participants **Participants**

This study was conducted at the outpatient clinics of four large psychiatric hospitals in China between January 1 and October 31, 2021. The following were the inclusion criteria: participants 12–18 years old, those who met the diagnostic criteria of MDD according to the DSM-IV, and those not receiving any treatment during the current depressive episode (The participants include first episode and recurrence of depression). The DSM-IV diagnosis of MDD was established by a trained psychiatrist using a face-to-face structured clinical interview using the Mini-International Neuropsychiatric Interview (MINI) Version 5.0.²⁸ Patients with any of the following conditions were excluded from this study: significant physical illnesses, such as cardiovascular disease and organic brain disorder; another mental illness, such as Post traumatic stress disorder (PTSD) and bipolar depression; pregnant or lactating; alcohol, drug and cigarette dependence or abuse and mental retardation; and those who have undergone treatment with electroconvulsive therapy within the last month.

Gender and age matched controls were also included as controls in this study. The following were the inclusion criteria: participants 12-18 years old, those without a personal or family history of mental illness. They also received a face-to-face clinical interview to determine that they without a personal or family history of mental illness. Other exclusion criteria were the same as those in the experimental group. There were recruited from volunteers in the community near the hospital between January 1 and October 31, 2021. All participants and their guardians provided written informed consent to indicate their willingness to participate.

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Measures

Insomina

Insomnia symptoms were measured using the Chinese version of the Insomnia Severity Index (ISI), a brief self-reported questionnaire with seven items.²⁹ A five-point Likert scale was used (total score range: 0–28). The severity level is divided into four grades (normal, 0–7; subthreshold [mild], 8–14; moderate, 15–21; and severe, \geq 22).³⁰ In one adolescent validation study, reliability was strong (Cronbach's α =0.83), and test-retest reliability was acceptable (r=0.79).³¹

Daytime Sleepiness

Daytime sleepiness was assessed using the Chinese Adolescent Daytime Sleepiness Scale (CADSS).³² The CADSS consists of seven items, and all items are rated using a five-point scale, with a total score ranging from 7 to 35. Higher scores indicated more daytime sleepiness. The scale has better reliability and validity than other scales among Chinese adolescents, with a Cronbach's alpha coefficient of 0.89.³²

Nightmare Frequency

Nightmare frequency was measured by the first question from the Nightmare Disorder Index,³³ "How many nights a week did you have nightmares in the past 1 month (ie, disturbing, extended, and well-remembered dreams)?" Participants were offered a range of five response options, from "0 nights per week" to "7 nights per week".

Nightmare Distress

Nightmare distress was measured using the Nightmare Distress Questionnaire-Chinese version (NDQ-CV).²⁰ The questionnaire consists of 14 items, and each item is rated using a five-point scale, with a total score ranging from 14 to 70. The higher the score obtained from the NDQ-CV, the higher the degree of nightmare distress. This scale has good reliability and validity among Chinese adolescents, with a Cronbach's alpha coefficient of 0.88.²⁰

Depression Severity

The 17-item Hamilton Rating Scale (HAMD-17) was used to assess the depression severity. The total HAMD-17 score ranges from 0 to 52 and is divided into four grades (normal, 0–7; mild, 8–16; moderate, 17–23; and severe, \geq 24). In this study, the raters from each clinical site were trained, and the average between-rater intraclass correlation coefficient was 0.87.

Anxiety Severity

Anxiety severity was measured using the seven-item Generalized Anxiety Disorder (GAD-7). GAD-7 is a seven-item self-report scale with a four-point Likert scale (from 0 to 3), and the total score ranges from 0 to 21. The severity level is categorized as none (0–4 points), mild (5–9 points), moderate (10–14 points), and severe (\geq 15 points). This scale has good reliability and validity among Chinese adolescents, with a Cronbach's alpha coefficient of 0.90–0.92.

Suicide Risk

Suicide risk was evaluated using the suicidal module of the MINI.²⁸ The suicidal module consists of six screening questions, with a total score ranging from 0 to 33. The suicide risk is divided into four groups: none (0), low (1–5), moderate (6–9), and high (\geq 10) risk. Based on previous studies, we stratified all participants into two groups: absence (low or none) or presence of suicide risk (moderate or high).^{8,37}

Statistical Analyses

Statistical analyses were performed using SPSS 25.0 (IBM SPSS, IBM Corp., Armonk, NY). Continuous variables were expressed as means and standard deviations and categorical variables as raw numbers and percentages (%). The *t*-test was employed for parametric continuous variables and the Mann–Whitney *U*-test for continuous nonparametric variables. The Chi-square test was used for categorical variable analyses. Correlation analysis among the scores of each scale

was performed by determining the Pearson correlation coefficients with Bonferroni correction. Binary multivariate logistic regression analyses were used to explore the association between the predictors of suicide risk. Suicide risk (no = 0; yes = 1) was used as a dependent variable. Gender, grade, depressive episode, insomnia symptoms, daytime sleepiness, frequency of nightmare distress, and anxiety and depressive symptoms were the independent variables. Backward stepwise binary logistic regression analysis was performed to determine the factors providing independent prediction of suicide risk. P values <0.05 (two-sided) were considered statistically significant.

Results

A total of 523 outpatients with MDD participated in this survey, and 24 patients were excluded from the analysis owing to missing data that precluded assessment. No significant differences in age, gender, and grade between outpatients (n = 499) and healthy participants were noted (n = 499) (p > 0.05). The demographic and clinical characteristics of the participants are outlined in Table 1. In the participants with MDD, the proportion of insomnia and suicide risk was higher than in the healthy ones (all p < 0.001). Patients with MDD showed higher total ISI, CADSS, and NDQ-CV scores than healthy controls (all p < 0.001). Moreover, patients with MDD reported more nightmare frequency than healthy controls (p < 0.001). Up to 67.5% (339/499) of the patients had experienced nightmares in the past month, and 38.7% (193/499) reported frequency nightmare at least once a week, and 28.7% (143/499) and 6.0% (30/499), respectively, among the controls. Significant differences in the abovementioned two indexes between patients and controls were noted (all p < 0.001).

Of all adolescents with MDD, 190 (38.1%) presented a risk of suicide (Table 2). Between patients with or without suicide risk, significant differences were observed in terms of gender, grade, and insomnia prevalence (all p < 0.001). One in two patients with suicide risk (51.6%) experienced frequency nightmares, which was significantly higher than those without suicide risk (30.7%). Moreover, patients with recurrence were at a higher risk of suicide than those with first episodes (p < 0.001). To compare the effects of different degrees of daytime sleepiness and nightmare distress on patients, the total scores of CADSS and NDQ-CV were categorized into three levels ("low", "medium", and "severe") using terciles as cutoff points. A significant difference in the severity of insomnia symptoms, daytime sleepiness,

Table I Demographic and Clinical Characteristics of All Participants

Variable	Total	Adolescent with MDD	Adolescent with MDD Controls		Þ
	(n = 998)	(n = 499)	(n = 499)		
Gender, n (%)				0.000	1.000
Male	352(35.3)	176(50.0)	176(50.0)		
Female	646(64.7)	323(50.0)	323(50.0)		
Age (years), mean ± SD	15.95 ± 1.61	16.01 ± 1.58	15.89 ± 1.63	1.081	0.280
ISI scores, mean ± SD	6.42 ± 6.41	10.76 ± 6.01	2.08 ± 2.86	-22.159	<0.001
Insomnia, n (%)				357.475	<0.001
No	677 (67.8)	199(29.4)	478(70.6)		
Yes	321 (32.2)	300(93.5)	21(6.5)		
Suicide risk, n (%)				193.738	<0.001
No	795(79.7)	309(38.9)	486(61.1)		
Yes	203(20.3)	190(93.6)	13(6.4)		
CADSS scores, mean ± SD	14.26 ± 10.60	22.73 ± 6.81	12.78 ± 5.88	-22.150	<0.001
Nightmare frequency				199.343	<0.001
None	516(51.7)	160(31.0)	356(69.0)		
<i night="" td="" week<=""><td>259(26.0)</td><td>146(56.4)</td><td>113(44.6)</td><td></td><td></td></i>	259(26.0)	146(56.4)	113(44.6)		
I-3 nights/week	163(16.3)	137(84.0)	26(16.0)		
4–6 nights/week	40(4.0)	37(92.5)	3(7.5)		
7 nights/week	20(2.0)	19(95.0)	I (5.0)		
NDQ-CV scores, mean ± SD	23.07 ± 10.96	28.85 ± 11.92	17.30 ± 5.61	-18.425	<0.001

Abbreviations: ISI, Insomnia Severity Index; CADSS, Chinese Adolescent Daytime Sleepiness Scale; NDQ-CV, Nightmare Distress Questionnaire-Chinese Version.

Table 2 Demographic and Clinical Characteristics of Participants with Depression in Relation to Suicide Risk

Variable	All Patients (n = 499)		With Suicide Risk (n = 190)		Without Suicide Risk (n = 309)		χ²	P
	n	%	n	%	n	%		
Gender							29.216	<0.001
Male	176	35.3	39	22.2	137	77.8		
Female	323	64.7	151	46.7	172	53.3		
Grade							22.289	<0.001
JHS	198	39.7	101	51.0	97	49.0		
SHS	301	60.3	89	29.6	212	70.4		
Depressive episode							24.845	<0.001
First	407	81.6	134	32.9	273	67.1		
Recurrence	92	18.4	56	60.9	36	19.1		
Insomnia symptoms							14.091	0.003
None	169	33.9	49	29.0	120	71.0		
Subthreshold	198	39.7	75	37.9	123	62.1		
Medium	108	21.6	55	50.9	53	49.1		
Severe	24	4.8	11	45.8	13	54.2		
Daytime sleepiness							7.658	0.022
Low	163	32.7	48	29.4	115	70.6		
Medium	174	34.9	73	42.0	101	58.0		
Severe	162	32.5	69	42.6	93	57.4		
Nightmare frequency							35.677	<0.001
None	160	32.1	35	21.9	125	78.1		
< I night/week	146	29.3	57	39.0	89	61.0		
I-3 nights/week	137	27.5	63	46.0	74	54.0		
4–6 nights/week	37	7.4	23	62.2	14	37.8		
7 nights/week	19	3.8	12	63.2	7	36.8		
Nightmare distress							48.680	<0.001
Low	163	32.7	37	22.7	126	77.3		
Medium	158	31.7	50	31.6	108	68.4		
Severe	178	35.7	103	57.9	75	42.1		
Depressive symptoms							80.692	<0.001
Mild	84	16.8	12	14.3	72	85.7		
Moderate	184	36.9	42	22.8	142	77.2		
Severe	231	46.3	136	58.9	95	41.1		
Anxiety symptoms							56.055	<0.001
None	51	11.3	9	17.6	42	82.4		
Low	182	40.4	40	22.0	142	78.0		
Moderate	108	23.9	44	40.7	64	59.3		
Severe	110	24.4	68	61.8	42	38.2		

Abbreviations: JHS, junior high school; SHS, senior high school.

nightmare distress, and anxiety and depressive symptoms between patients with and without suicide risk was noted (all p < 0.05). Notably, the percentage of severe nightmare distress among patients with suicide risk was 54.2%, whereas that without suicide risk was 24.3%.

The results of correlation analysis are shown in Table 3 and Figure 1. Positive Correlations among suicide risk, nightmare frequency NDQ-CV, CADSS, ISI and PHQ-9 scores ranged from r = 0.141 to 0.669 and all of their coefficients were significantly correlated (P < 0.001).

Binary logistic regression analyses were conducted to explore the relationships between suicide risk and demographic and clinical characteristics significant in univariable analyses (Table 4). Female gender (odds ratio [OR] = 2.722, 95% confidence interval [CI]: 1.64–4.52), junior grade (OR = 2.758, 95% CI: 1.73–4.41), recurrent

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Table 3 Correlations Among Suicide Risk, Sleep Disorders, and Depressive Symptoms in Participants with MDD

Variable	Suicide Risk	NDQ-CV Scores	CADSS Scores	ISI Scores	PHQ-9 Scores	Nightmare Frequency	GAD-7 Scores
Suicide risk scores	1						
NDQ-CV scores	0.367**	1					
CADSS scores	0.115**	0.229**	1				
ISI scores	0.255**	0.509**	0.340**	1			
PHQ-9 scores	0.520**	0.470**	0.272**	0.484**	1		
Nightmare frequency	0.281**	0.674**	0.188**	0.427**	0.392**	1	
GAD-7 scores	0.419**	0.489**	0.238**	0.522**	0.740**	0.391**	1

Note: **p < 0.001.

depressive episode (OR = 2.525, 95% CI: 1.73–4.71), severe nightmare distress (OR= 2429, 95% CI: 1.38–4.29) and severe depressive symptoms (OR = 7.065, 95% CI: 3.36–14.86) were independently and significantly associated with suicide risk.

Discussion

Most of the previous studies on nightmares and suicide risk were conducted in schools. We have extended the current knowledge about the impact of nightmares on the risk of suicidality in this particular population. This large-scale, cross-sectional investigation has shown that nightmares are frequent among adolescents with MDD: 67.5% and 38.7% of the patients reported at least one nightmare episode per month and at least one nightmare episode per week, respectively, both were observed to be higher than those of controls (27.7% and 8.0%). Furthermore, the prevalence of frequent nightmares in our patient group (51.6%) was significantly higher than those of previous studies (8.9%). The results were compatible with other studies. ^{39,40} Consistent with the higher nightmare frequency among adolescents with MDD,

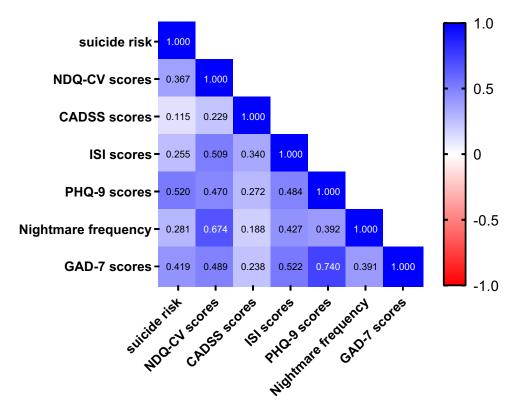


Figure I Pearson rho correlation coefficients.

Table 4 Logistic Regression of Demographic and Clinical Characteristics of Depressive Patients and Suicide Risk in Participants with MDD

Variable	OR	95% CI	Þ
Gender			
Male	1		
Female	2.722	1.64-4.52	0.001
Grade			
Senior	1		
Junior	2.758	1.73-4.41	0.001
Depressive episode			
First	1		
Recurrence	2.525	1.73–4.71	0.004
Nightmare distress			
Low	1		
Medium	1.206	0.68–2.14	0.523
Severe	2.429	1.38-4.29	0.002
Depressive symptoms			
Low	1		
Medium	1.742	0.81-0.3.75	0.156
Severe	7.065	3.36–14.86	<0.001

Abbreviations: CI, confidence interval; OR, odds ratio.

these patients experienced more severe nightmare distress than healthy ones. Moreover, compared with normal individuals, adolescents with MDD may be predisposed to insomnia symptoms, daytime drowsiness, and suicide risk, which were concordant with several previous studies. 41–43

This study represents one of the exploring sleep disorders associated with suicide risk in a sample of adolescents with MDD. Consistent with most previous studies, ^{9,44,45} our results indicated significant correlations between suicide risk and multiple sleep disorders, including nightmare frequency, nightmare distress, insomnia symptoms, and daytime sleepiness. Considering that the pairwise comparisons of sleep disorders were significantly correlated, it would be important to examine the shared and specific effects of sleep disorders on suicide risk. However, we performed a logistic regression analysis and demonstrated that only nightmare distress was an independent risk factor for increased suicide risk after adjusting for grade, gender, emotional symptoms, and other sleep variables. Such information may help us to better understand the role of sleep problems in the pathogenesis of suicide and design effective prevention and intervention strategies for suicide by improving nightmare distress.

Over the past decades, several researchers investigating nightmares have long been interested in nightmare frequency and have provided some evidence to support it as an independent risk factor for suicide. Notably, most individuals who experienced nightmares may have only mild negative effects on psychosocial functioning, and distress caused by nightmares is the most important clinical indicator of nightmare severity because it is more highly correlated with psychological disturbances. In this context, the study of nightmares needs to include frequency and distress, which can be potentially overlapping and interconnected. A recent prospective longitudinal survey with a large general population of adolescents found that both nightmare frequency and distress significantly increased suicidal thoughts, plans, and attempts. In our study on adolescents with MDD, we identified and validated that more than half of the patients with suicide risk were accompanied by frequent nightmares and severe nightmare distress. However, it is not the frequency of nightmares but the self-reported distress related to the nightmare experience that may be the critical variable in predicting suicide risk.

Several studies have investigated the psychological mechanisms underlying the association between nightmares and suicide; however, the association remains unclear. The promising preliminary evidence suggests that difficulties with affect/emotion regulation and negative cognitive appraisals may play a pivotal role in nightmares leading to suicide.⁴⁷ For example, Littlewood et al⁴⁸ found that the experience of nightmares initially resulted in defeat, which in turn leads to perceptions of entrapment and hopelessness, and ultimately suicidal behaviors. Neuroimaging argue that nightmare

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severity was associated with reduced activity in the limbic-prefrontal emotion regulation network, particularly the right medial prefrontal cortex and bilateral anterior cingulate cortex, and these areas are believed to play a significant role in suicide. ⁴⁹ In addition, nightmares may cause sleep disruption and nighttime wakefulness, thereby increasing the likelihood of suicidal ideations. ⁵⁰

Several studies in various countries have suggested that females with MDD were more likely to be affected by the occurrence of suicidal ideation. Si,52 Similarly, we found that adolescent patients with MDD had a relative risk that was 2.67 times higher than male patients, possibly owing to gender differences in neuroendocrine responses under stress and different emotional responses during adolescence. In the general adolescent population, suicide risk increases with age. However, our study on MDD showed that junior students had a higher suicide risk than senior ones. There are similar results in some domestic studies, and the suicide risk of adolescents is negatively correlated with age. Some studies show that suicidal behavior is related to impulse control. The reason for the high suicide risk of junior high school students may be related to their younger age and relatively insufficient ability to control impulsive behavior. The brain function of patients with relatively young age is relatively weak, so the risk of suicide is relatively high. S8,59

We found that patients with severe depressive episodes had a seven-fold increased risk of suicide compared with those with mild depressive episodes. A strong and robust relationship between depressive symptom severity and suicide has been confirmed by several cross-sectional and longitudinal studies. The possible cause may be related to depressed mood, hopelessness, self-blame, and feelings of worthlessness that could influence patients to commit suicide to end their suffering. Furthermore, consistent with some previous studies, the present study indicated that suicide risk in patients with recurrent episodes was significantly higher than that in patients with first-episode MDD. Anxiety is one of the most common psychological comorbidities among patients with MDD. Of the overall depressive adolescents, the majority with suicide risk had moderate to severe anxiety symptoms, which were significantly higher than those without suicide risk. However, further analysis found that the coexistence of anxiety was not an independent predictor of suicide risk. This result is consistent with that of a recent study, which showed no statistically significant correlation between MDD with comorbid anxiety and suicidal behavior.

Although the results of our study add to the understanding of suicide risk in adolescent patients with MDD, several limitations need to be considered. First, the data were collected using a cross-sectional study design, making it impossible to determine the direction of a causal relationship between nightmare stress and suicide risk. Further study with a longitudinal or retrospective cohort design should be employed to establish the relationships among these variables. Second, sleep variables were measured by self-report questionnaires, which may have led to biased reporting of the sleep variables. Therefore, studies must include personal interviews and appropriate objective measures, such as electroence-phalography and actigraphy, to overcome the limitations from exclusive use of self-report data. Third, Some studies have shown that the age of onset, life stress, and previous suicide risk of MDD patients are risk factors for their current suicide risk. However, these variables were not included them in the analysis. Future studies of the relationship between nightmares and suicide will need to include more possible factors influencing suicide risk.

Conclusion

In conclusion, the current study, which included a large clinical population, provides evidence that nightmares occur frequently among adolescent patients with MDD. Furthermore, the results of this study demonstrate that nightmare distress is independently associated with an increased risk of suicide. These findings may have important implications for further research on night-suicide mechanisms and for identifying individuals who are at a risk of suicide by asking about nightmare distress. Since nightmares are potentially modifiable, and the clinical efficacy of psychotherapy is well documented, intervention programs aimed at addressing nightmare-related distress may play an important role in preventing suicide among adolescents with MDD.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Ethics Approval and Informed Consent

Formal approval for the study was obtained from the Ethics Committees of the four participating hospitals (ie, Peking University HuiLongGuan Clinical Medical School, Dongying People's Hospital, Jining Psychiatric Hospital, and The Third Hospital of Longyan). All participants and their guardians provided written informed consent to indicate their willingness to participate. The study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2008.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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