


# Insomnia and Alexithymia in Chinese Adolescents with Major Depressive Disorder: A Cross-Sectional Study of Sex Differences and Associations

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**Purpose:** Insomnia is related to alexithymia in adults, but the relationship between insomnia and alexithymia in adolescents with major depressive disorder remains unclear. This study aimed to investigate the sex differences and the association between insomnia and alexithymia in adolescents with major depressive disorder.

**Patients and Methods:** From October 2020 to April 2022, adolescent patients with major depressive disorder were recruited from psychiatric departments of seven hospitals in Anhui Province, China. Their general demographic and clinical information were collected. The 20-item Toronto Alexithymia Scale, the Center for Epidemiologic Studies of Depression Scale, and the Insomnia Severity Index Scale were used to assess their alexithymia, depression, and insomnia symptoms, respectively. The analysis of variance (ANOVA), Student's *t*-test and Mann–Whitney *U*-test were used for continuous variables and chi-square tests for categorical variables. Pearson's correlation analysis and Spearman correlation analysis were used to examine the correlation between ISI and demographic and clinical variables. Multiple binary logistic regression analyses with the “Enter” method were carried out to explore the correlations of insomnia.

**Results:** The prevalence of insomnia in female adolescent patients was similar to that of male patients ( $\chi^2=1.84$ ,  $p = 0.175$ ). Compared with those without insomnia, patients with insomnia had worse family relationships ( $F = 7.71$ ,  $p = 0.021$ ), perceived heavier academic stress ( $F = 6.32$ ,  $p = 0.012$ ), more likely to take sedative-hypnotics ( $F = 5.51$ ,  $p = 0.019$ ), had higher levels of depression ( $F = 81.57$ ,  $p < 0.001$ ) and alexithymia ( $F = 28.57$ ,  $p < 0.001$ ). Correlation analysis showed that alexithymia was significantly associated with insomnia in adolescent patients ( $r = 0.360$ ,  $p < 0.01$ ). Binary logistic regression analyses showed that, alexithymia was significantly associated with insomnia in female patients ( $OR = 1.050$ ,  $p < 0.05$ ) but not male patients.

**Conclusion:** In female adolescent patients, alexithymia is a risk factor of insomnia, which is of great importance in the understanding of the psychopathological mechanisms, treatments and psychological interventions of insomnia in adolescents with major depressive disorder.

**Keywords:** adolescents, major depressive disorder, insomnia, alexithymia

## Introduction

Major depressive disorder (MDD) is a significant mental disease and one of the leading causes of years lived with disability (YLDs).<sup>1</sup> The global point prevalence of MDD in adults (aged 18–99 years) is around 4.7%.<sup>2</sup> Adolescents is vulnerable to mental disorders due to the physiological and psychological changes. Across adolescents aged 10–19 years, the global point prevalence and the lifetime prevalence rate of MDD are 8% and 19%, respectively.<sup>3</sup> Sleep disturbances often occur in patients with MDD and are the most prominent symptom in many circumstances. It is reported that the insomnia rate in patients with a major depressive episode (MDE) is 85.2%.<sup>4</sup> At least two thirds of adolescents with MDD experienced insomnia.<sup>5</sup> Evidence shows that insomnia and depression have a closely two-way relationship.<sup>6</sup> According to a meta-analysis, children and adolescents with sleep disorders are more likely to develop depression.<sup>7</sup> A cohort study showed that compared to healthy controls, the risk of insomnia increased by 2–3 times in adolescents with depression.<sup>8</sup> In

patients with MDD, more severe insomnia symptoms indicate worse health-related outcomes.<sup>9</sup> Thus, it is vital to reveal the risk factors of insomnia in MDD patients.

Current studies have confirmed several insomnia-related factors, such as age, sex, heredity, characteristics, life events, stress, unhealthy sleep behaviors and emotions. A body of researches have investigated the relationship between alexithymia and sleep problems and suggested that alexithymia is also a possible factor that related to sleep disturbances.<sup>10</sup> Alexithymia is a psychological trait including two aspects: difficulty identifying and describing emotions and externally oriented thinking.<sup>11</sup> It is correlated to a series of physical and psychiatric disorders and may be a susceptible factor for a range of symptoms in various diseases.<sup>12</sup> An early survey of a group of Japanese working men showed that sleep characteristics including insomnia are related to high scores of alexithymia.<sup>13</sup> Another study that conducted in a representative Finnish adult population reported independent correlation between alexithymia and sleep disorder symptoms.<sup>14</sup> In a sample of young adults, alexithymia participants scored more on sleep symptoms including insomnia than the non-alexithymia ones.<sup>15</sup> In another sample of college students, alexithymia is positively correlated with insomnia.<sup>16</sup> A research confirmed that in two online-recruited healthy adult groups, alexithymia is associated with poor sleep quality, and the association is dependent from the co-occurring depression or anxiety.<sup>17</sup> There are also studies reaching the same conclusions in the depression participants.<sup>18</sup> While few studies applied objective measurements of sleep, Bazydło et al have reported association between alexithymia with more light sleep and less deep sleep.<sup>19</sup>

Although, among all the legible studies, few researches have been conducted on the underage population. In fact, there is growing evidence that alexithymia may have the same adverse effects on their health as adults.<sup>20</sup> Moreover, patients with MDD may find it challenging to identify and describe emotions subjectively since they usually use emotional inhibition strategies to protect themselves from distress, consequently, patients with MDD experience more severe alexithymia than those with other psychiatric disorders.<sup>21</sup> Therefore, it is necessary to explore the relationship of insomnia and alexithymia in adolescent MDD patients.

It is worth noticing that in adolescent populations, there is sex differences not only in the prevalence rate of MDD but also in the clinical symptoms of MDD. For example, male adolescents are less likely to experience insomnia, and female adolescents display more affective and atypical symptoms.<sup>22</sup> There are also sex differences in alexithymia as well as in insomnia. On the one hand, the risk of alexithymia in men is higher than that of women.<sup>23</sup> Previous study found that alexithymia is related to an imbalance in the noradrenergic and basal activity of the hypothalamic–pituitary–adrenal axis in male MDD patients.<sup>24</sup> Moreover, alexithymia is correlated with deficiencies in right hemisphere function and interhemispheric transfer in men, not women.<sup>25</sup> On the other hand, objective sleep measurements showed different polysomnography (PSG) sleep parameters in early-onset MDD male and female patients.<sup>26</sup> Therefore, in this study, while investigating the association between insomnia and alexithymia in adolescent patients with MDD, we also paid attention to the sex differences in the association.

Taken together, the focus of this study was to (1) investigate the sleep disturbances of adolescents with MDD; (2) explore the association between insomnia and alexithymia in adolescents with MDD. We hypothesized that (1) the prevalence rate of insomnia is high in adolescent MDD patients; (2) insomnia is associated with alexithymia in adolescents with MDD; (3) female MDD adolescents with alexithymia is more likely to experience insomnia symptoms.

## Materials and Methods

### Participants

This study used a cross-sectional design. It was carried out in seven hospitals of seven cities in Anhui Province, from October 2020 to April 2022. Patients were consecutively recruited from the psychiatric outpatients and inpatients of these hospitals. Inclusion criteria: (1) meeting the diagnostic criteria for MDD mentioned in the fifth edition of the diagnostic and statistical manual (DSM-5), two trained psychiatrists made the diagnosis; (2) aged 12–18 years; (3) with an ability of comprehension. Exclusion criteria: (1) meeting the DSM-5 diagnostic criteria of other psychiatric disorders or intellectual disabilities; (2) with severe physical diseases; (3) unable to collaborate.

All patients and their guardians signed consent forms after being informed of the method and purpose of this study. These patients were told that they could terminate the study at any time. Those who are not qualified or comorbid with other disorders were excluded. Finally, 349 patients were initially enrolled, 20 of which were excluded because they did

not complete the questionnaire, and 329 patients were finally included. This study was approved by the Ethics Committee of Chaohu Hospital, Anhui Medical University (202009-kyxm-04).

## Design and Measurements

Participants who met the criteria were given a face-to-face questionnaire by uniformly trained and qualified investigators. Demographic and clinical data were collected using a predesigned questionnaire, supplemented by interviews with their relatives and reviews of their medical records.

Demographic and clinical variables included age, sex, BMI, only child, academic stress, family relationships, exercise, age of onset (years), duration of illness (months), and the use of sedative-hypnotics.

Clinical psychiatric evaluations included the Insomnia Severity Index Scale (ISI), the 20-item Toronto Alexithymia Scale (TAS-20) and the Center for Epidemiologic Studies of Depression Scale (CES-D).

### 1. The Insomnia Severity Index Scale (ISI)

The ISI is a 7 items self-report questionnaire, rated on a Likert-5 point scale. Each item score ranges from 0 to 4. A higher score meant more severe insomnia symptoms. The total score of  $ISI \geq 8$  is defined as insomnia.<sup>27</sup> The Cronbach's  $\alpha$  coefficient for ISI in Chinese adolescents was 0.83, and the 2-week test-retest reliability was 0.79.<sup>28</sup> The item loads of the Chinese version of ISI (0.617–0.797) were rated Good and Excellent in Comrey's Item Load Grading Criteria, supporting good construct validity.<sup>29</sup> It has been verified in adolescents aged 12–19 years in Hong Kong, China and showed good psychometric properties.<sup>28</sup>

### 2. The 20-item Toronto Alexithymia Scale (TAS-20)

The TAS-20 consists of 20 items with a 5-level score (1: completely disagree, 5: agree entirely). It comprises three subfactors: difficulty in identifying feelings (DIF), difficulty in describing feelings (DDF), and externally oriented thinking (EOT).<sup>30</sup> With a total score of 20–100, the higher the score, the more severe the alexithymia. The Cronbach's  $\alpha$  coefficient for TAS-20 in Chinese adolescents is 0.87.<sup>31</sup> The test-retest reliability is 0.87.<sup>32</sup> The Chinese version TAS-20 has good structural validity among teenagers with the values of GFI, NFI, CFI and TLI were all above 0.9.<sup>32</sup> The TAS-20 has shown good validity in Chinese adolescents.<sup>33</sup>

### 3. The Center for Epidemiologic Studies of Depression Scale (CES-D)

The CES-D was used to evaluate depression symptoms. The CES-D contains 20 items, among which 16 items assess negative emotions and 4 measure positive affections.<sup>34</sup> The total score ranges from 0 to 60, reflecting the existence and severity of depression. The Cronbach's  $\alpha$  coefficient for CES-D in Chinese adolescents is 0.88.<sup>35</sup> The test-retest reliability is 0.87.<sup>36</sup> The sensitivity and specificity of CES-D is 95% and 93%, respectively.<sup>36</sup> It has been widely used in Chinese research. Studies have shown that CES-D could effectively evaluate depression symptoms in Chinese adolescents with MDD.<sup>37</sup>

## Statistical Analysis

The SPSS26.0 statistical software was used for statistical analysis. Continuous and categorical variables are presented as mean (SD), Median (interquartile range), and numbers (percentage), respectively. We compared the demographic and clinical variables between male and female patients. The analysis of variance (ANOVA), Student's *t*-test and Mann-Whitney *U*-test were used for continuous variables and chi-square tests for categorical variables. Pearson's correlation analysis was used to examine the correlation among ISI, CES-D, TAS-20 and its subfactors. Pearson's correlation analysis and Spearman correlation analysis was used to examine the correlation between ISI and demographic and clinical variables. Multiple binary logistic regression analyses with the "Enter" method were carried out to explore the correlations of MDD with insomnia in the whole sample and separately by sex.  $P < 0.05$  (two-tailed) was considered statistically significant.

## Results

### Sex Differences in Demographic and Clinical Characters in Adolescents with MDD

The demographic and clinical data of male and female patients are presented in Table 1. In the 329 adolescent patients with MDD, 89 were male and 240 were female. The prevalence of clinically significant levels of insomnia was 78.1% (n = 257) in the whole sample, 80.0% and 73.0% in female and male patients, respectively ( $\chi^2=1.84, p = 0.175$ ). Compared with male patients, female patients were less likely to exercise ( $\chi^2 = 5.94, p = 0.015$ ), had lower rate of being only child ( $\chi^2= 9.47, p = 0.002$ ) and experienced more severe depression (t = 3.12, p = 0.002) and alexithymia (t = 3.20, p = 0.002). There were no significant sex differences in age of onset, duration of illness, BMI, academic stress, family relationships, the use of sedative-hypnotics and ISI scores.

As shown in Table 2, two-way ANOVAs were carried out to explore the interaction between insomnia and sex. Compared with patients without insomnia, those with insomnia had worse family relationships (F = 7.71, p = 0.021), perceived heavier academic stress (F = 6.32, p = 0.012), more likely to take sedative-hypnotics (F = 5.51, p = 0.019), had higher levels of depression (F = 81.57, p < 0.001) and alexithymia (F = 28.57, p < 0.001). These analyses also showed that there were significant sex differences in only-child, exercise and CES-D scores. There was significant insomnia × sex effect in BMI (F = 5.06, p = 0.025).

**Table 1** Demographic and Clinical Characteristics and Sex Differences in Adolescents with MDD

| Variables  | Total Sample (N =329) | Male (N =89) | Female (N =240) | Z/ $\chi^2$ | P            |
|--|-----------------------|--------------|-----------------|-------------|--------------|
| Age (years), mean (SD)                                     | 15.31(1.63)           | 15.69(1.53)  | 15.18(1.64)     | -2.55       | <b>0.011</b> |
| BMI (kg/m <sup>2</sup> ), mean (SD)                        | 20.75(3.63)           | 21.37(4.50)  | 20.52(3.23)     | -1.63       | 0.106        |
| Only-child, n (%)  |                       |              |                 | 9.47        | <b>0.002</b> |
| Yes  | 136(41.30)            | 49(55.10)    | 87(36.30)       |             |              |
| No   | 193(58.70)            | 40(44.90)    | 153(63.70)      |             |              |
| Exercise, n (%)  |                       |              |                 | 5.94        | <b>0.015</b> |
| <1 time/week   | 147(44.70)            | 30(33.70)    | 117(48.80)      |             |              |
| ≥1 time/week   | 182(55.30)            | 59(66.30)    | 123(51.20)      |             |              |
| Heavy academic stress, n (%)                               |                       |              |                 | 0.86        | 0.353        |
| Yes  | 171(52.00)            | 50(56.20)    | 121(50.40)      |             |              |
| No   | 158(48.00)            | 39(43.80)    | 119(49.60)      |             |              |
| Family relationships, n (%)                                |                       |              |                 | 0.34        | 0.844        |
| Good   | 107(32.50)            | 27(30.30)    | 80(33.30)       |             |              |
| Fair   | 178(54.10)            | 49(55.10)    | 129(53.80)      |             |              |
| Poor   | 44(13.40)             | 13(14.60)    | 31(12.90)       |             |              |
| Age of onset (years), mean (SD)                            | 13.63(1.95)           | 13.97(1.88)  | 13.50(1.97)     | -1.92       | 0.056        |
| Duration of illness (months), Median (interquartile range) | 13.00(14.00)          | 15.00(17.50) | 13.00(13.75)    | -0.34       | 0.733        |
| Taking sedative-hypnotics, n (%)                           |                       |              |                 | 2.11        | 0.147        |
| Yes  | 40(12.20)             | 7(7.90)      | 33(13.80)       |             |              |
| No   | 289(87.80)            | 82(92.10)    | 207(86.30)      |             |              |
| CES-D, mean (SD)   | 36.83(12.63)          | 33.31(12.61) | 38.13(12.41)    | 3.12        | <b>0.002</b> |
| TAS-20, mean (SD)  | 67.04(9.75)           | 64.26(8.05)  | 68.08(10.13)    | 3.20        | <b>0.002</b> |
| DIF  | 25.80(5.50)           | 24.44(4.85)  | 26.30(5.64)     | 2.76        | <b>0.006</b> |
| DDF  | 18.10(3.21)           | 17.60(2.71)  | 18.29(3.36)     | 1.75        | 0.080        |
| EOT  | 23.14(3.90)           | 22.22(3.45)  | 23.48(4.00)     | 2.62        | <b>0.009</b> |
| ISI, mean (SD)   | 12.67(5.89)           | 12.02(5.96)  | 12.91(5.86)     | 1.21        | 0.226        |
| Insomnia, n (%)  |                       |              |                 | 1.84        | 0.175        |
| Yes  | 257(78.10)            | 65(73.00)    | 192(80.00)      |             |              |
| No   | 72(21.90)             | 24(27.00)    | 48(20.00)       |             |              |

**Notes:** The bold value is the p-value of less than 0.05. N: number of participants; Z: Statistics for the Student's t-test and Mann-Whitney U-test;  $\chi^2$ : Statistics for the chi-square test; P: p-value.

**Abbreviations:** MDD, major depressive Disorder; BMI, body mass index; CES-D, the Center for Epidemiologic Studies of Depression Scale; TAS-20, the 20-item Toronto Alexithymia Scale; DIF, difficulty in identifying emotions; DDF, difficulty in describing emotions; EOT, externally oriented thinking; ISI, the Insomnia Severity Index Scale.

**Table 2** Comparisons of Male and Female Adolescents with MDD with and without Insomnia

|                                     | Insomnia (N = 257) |               | Without Insomnia (N = 72) |               | Gender $F/\chi^2$ (p-value) | Insomnia $F/\chi^2$ (p-value) | Gender × Insomnia F (p-value) |
|-------------------------------------|--------------------|---------------|---------------------------|---------------|-----------------------------|-------------------------------|-------------------------------|
|                                     | Female (N = 192)   | Male (N = 65) | Female (N = 48)           | Male (N = 24) |                             |                               |                               |
| Age (years), mean (SD)              | 15.10(1.61)        | 15.83(1.41)   | 15.46(1.73)               | 15.29(1.81)   | 1.46(0.228)                 | 0.16(0.690)                   | 3.72(0.055)                   |
| BMI (kg/m <sup>2</sup> ), mean (SD) | 20.40(3.20)        | 21.83(4.70)   | 21.02(3.36)               | 20.12(3.71)   | 0.27(0.607)                 | 1.13(0.290)                   | 5.06( <b>0.025</b> )          |
| Only-child, n (%)                   | 67(34.90)          | 40(61.54)     | 20(41.67)                 | 9(37.50)      | 9.47( <b>0.002</b> )        | 0.04(0.836)                   | –                             |
| Exercise, n (%)                     | 93(48.44)          | 43(66.15)     | 30(62.50)                 | 16(66.67)     | 5.94( <b>0.015</b> )        | 2.74(0.098)                   | –                             |
| Heavy academic stress, n (%)        | 104(54.17)         | 39(60.00)     | 17(35.17)                 | 11(45.83)     | 0.86(0.353)                 | 6.32( <b>0.012</b> )          | –                             |
| Good Family relationships, n (%)    | 55(28.65)          | 19(29.23)     | 25(52.08)                 | 8(33.33)      | 0.34(0.844)                 | 7.71( <b>0.021</b> )          | –                             |
| Age of onset (years), mean (SD)     | 13.40(1.96)        | 14.03(1.79)   | 13.94(1.95)               | 13.79(2.13)   | 0.76(0.383)                 | 0.29(0.589)                   | 1.95(0.164)                   |
| Taking sedative-hypnotics, n (%)    | 30(15.63)          | 7(10.77)      | 3(0.06)                   | 0(0)          | 2.11(0.147)                 | 5.51( <b>0.019</b> )          | –                             |
| CES-D, mean (SD)                    | 41.22(10.26)       | 36.82(10.97)  | 25.79(12.68)              | 23.83(12.06)  | 4.09( <b>0.044</b> )        | 81.57( <b>&lt;0.001</b> )     | 0.60(0.438)                   |
| TAS-20, mean (SD)                   | 69.95(9.20)        | 65.48(7.17)   | 60.56(10.30)              | 60.96(9.45)   | 2.46(0.118)                 | 28.57( <b>&lt;0.001</b> )     | 3.51(0.062)                   |

**Notes:** The bold value is the p-value of less than 0.05. N: number of participants; F: Statistics for the F-test;  $\chi^2$ : Statistics for the chi-square test.

**Abbreviations:** MDD, major depressive disorder; BMI, body mass index; CES-D, the Center for Epidemiologic Studies of Depression Scale; TAS-20, the 20-item Toronto Alexithymia Scale.

## The Correlation Between CES-D, TAS-20 and Its Subfactors in Adolescents with MDD

The correlation analysis of CES-D with TAS-20 and its subfactors was illustrated in Table 3. Irrelevant, weak, moderate and strong correlation( $r$ ) were defined as  $r$  between 0–0.09, 0.10–0.30, 0.30–0.50 and 0.50–1.00, respectively.<sup>38</sup> The correlations between TAS, DIF, DDF, and CES-D were moderate to strong ( $r = 0.434$  to  $0.547$ , all  $p < 0.01$ ). The correlation between EOT and CES-D was weak ( $r = 0.191$ ,  $p < 0.01$ ).

## The Related Factors of Insomnia in MDD Adolescents

In total sample, correlations between ISI scores and heavy academic stress ( $r = 0.185$ ,  $p < 0.01$ ), family relationships ( $r = 0.111$ ,  $p < 0.05$ ), CES-D scores ( $r = 0.602$ ,  $p < 0.01$ ) and TAS-20 scores ( $r = 0.360$ ,  $p < 0.01$ ) were significant (Table 4). Further binary logistic regression showed that only CES-D scores were correlated with insomnia (OR = 1.102, 95% CI: 1.066–1.139,  $p < 0.001$ ),  $R^2=0.355$  (Table 5).

In male patients, correlation between ISI scores and CES-D scores ( $r = 0.524$ ,  $p < 0.01$ ) was significant (Table 4). Further binary logistic regression indicated that insomnia was significantly associated with depression symptom's severity (OR = 1.098, 95% CI: 1.047–1.150,  $p < 0.001$ ),  $R^2 = 0.286$  (Table 5).

In female patients, correlations between ISI scores and heavy academic stress ( $r = 0.229$ ,  $p < 0.01$ ), CES-D scores ( $r = 0.629$ ,  $p < 0.01$ ) and TAS-20 scores ( $r = 0.402$ ,  $p < 0.01$ ) were significant (Table 4). Further binary logistic regression indicated that two factors were significantly associated with insomnia: depression (OR = 1.094, 95% CI: 1.054–1.135), alexithymia (OR = 1.050, 95% CI: 1.003–1.099),  $R^2=0.371$  (Table 5).

**Table 3** Correlations Among CES-D, TAS-20 and Its Subfactors in the Whole Sample

| Variables | CES-D   | TAS-20  | DIF     | DDF     | EOT |
|-----------|---------|---------|---------|---------|-----|
| CES-D     | I       |         |         |         |     |
| TAS-20    | 0.528** | I       |         |         |     |
| DIF       | 0.547** | 0.877** | I       |         |     |
| DDF       | 0.434** | 0.781** | 0.637** | I       |     |
| EOT       | 0.191** | 0.622** | 0.259** | 0.232** | I   |

**Note:** \*\* $p < 0.01$ .

**Abbreviations:** CES-D, the Center for Epidemiologic Studies of Depression Scale; TAS-20, the 20-item Toronto Alexithymia Scale; DIF, difficulty in identifying emotions; DDF, difficulty in describing emotions; EOT, externally oriented thinking.

**Table 4** Correlations Between the ISI Scores and Demographic and Clinical Variable in Adolescents with MDD

| Characteristic               | Total Sample | Male    | Female  |
|------------------------------|--------------|---------|---------|
| Age (years)                  | -0.041       | 0.174   | -0.104  |
| BMI (kg/m <sup>2</sup> )     | 0.014        | 0.157   | -0.049  |
| Only-child                   | -0.033       | 0.013   | -0.025  |
| Exercise                     | -0.079       | -0.106  | -0.054  |
| Heavy academic stress        | 0.185**      | 0.094   | 0.229** |
| Family relationships         | 0.111*       | 0.135   | 0.101   |
| Age of onset (years)         | -0.054       | 0.080   | -0.093  |
| Duration of illness (months) | 0.085        | 0.132   | 0.055   |
| Taking sedative-hypnotics    | 0.073        | 0.12    | 0.052   |
| CES-D                        | 0.602**      | 0.524** | 0.629** |
| TAS-20                       | 0.360**      | 0.203   | 0.402** |

Notes: \*\*p<0.01; \*p<0.05.

Abbreviations: ISI, the Insomnia Severity Index Scale; MDD, major depressive disorder; BMI, body mass index; CES-D, the Center for Epidemiologic Studies of Depression Scale; TAS-20, the 20-item Toronto Alexithymia Scale.

**Table 5** Multiple Binary Logistic Regression Analyses for Associations with Insomnia in the Whole Sample and Separately by Sex

| Characteristic              | OR    | 95% CI      | P      |
|-----------------------------|-------|-------------|--------|
| <b>Total sample (N=329)</b> |       |             |        |
| Heavy academic stress       | 1.261 | 0.671–2.371 | 0.471  |
| Family relationships        | 0.698 | 0.413–1.179 | 0.179  |
| CES-D                       | 1.102 | 1.066–1.139 | <0.001 |
| TAS-20                      | 1.038 | 0.998–1.079 | 0.066  |
| <b>Male (N=89)</b>          |       |             |        |
| CES-D                       | 1.098 | 1.047–1.150 | <0.001 |
| <b>Female (N=240)</b>       |       |             |        |
| Heavy academic stress       | 1.321 | 0.607–2.874 | 0.483  |
| CES-D                       | 1.094 | 1.054–1.135 | <0.001 |
| TAS-20                      | 1.050 | 1.003–1.099 | 0.037  |

Notes: The bold value is the p-value of less than 0.05. N: number of participants; P: p-value.

Abbreviations: OR, odds ratio; CI, confidence interval; CES-D, the Center for Epidemiologic Studies of Depression Scale; TAS-20, the 20-item Toronto Alexithymia Scale.

## Discussion

As far as we know, this is the first study to explore the sex differences in alexithymia severity between adolescent MDD patients with and without insomnia. This study found no significant differences in age, age of onset, BMI, academic stress, family relationships, rate of taking sedative-hypnotics, alexithymia and insomnia between male and female adolescent patients with MDD. Compared with patients without insomnia, those with insomnia experienced more severe alexithymia. Binary logistic regression analyses showed that insomnia was independently correlated with higher level of alexithymia in female patients but not in male patients. This indicated that there might be sex differences in the relationship between insomnia and alexithymia in adolescent MDD patients.

This study found that the insomnia rate in adolescents with MDD was 78.1%, which is slightly higher than that in another study of Chinese adolescents with depression (70.71%).<sup>39</sup> An early survey conducted in 187 adolescents with MDD in the New York State Psychiatric Institute showed that the prevalence of insomnia was 74%.<sup>40</sup> Another study

involving 553 children with MDD from Hungary reported a prevalence of 53.5%.<sup>5</sup> It is worth noting that among these children, 55% of them were male. In fact, the prevalence of insomnia reported in different studies varies due to the different age and sex ratio of the patient samples and various diagnostic and assessment methods. We already know that insomnia rates are higher in older or female adolescents.<sup>6</sup> Moreover, the present study was conducted at the time of the outbreak and epidemic of COVID-19. During the COVID-19 epidemic in China, the prevalence of psychological and sleep problems was higher than usual,<sup>41</sup> and children and adolescents were more affected.<sup>42</sup> The insomnia rates between male and female patients did not show notable difference, which is inconsistent with earlier studies. Previous study showed that insomnia was more common in male adolescent MDD patients.<sup>22</sup> Although the study was carried out in Hungary, more researches need to be performed on adolescent MDD patients in different countries.

In female patients, insomnia is associated with alexithymia after controlling for depressive symptoms, which consisted with earlier studies. The reason for this correlation might be biological, such as hyper arousal. It is demonstrated that higher levels of arousal play a crucial part in the pathophysiology of insomnia. Researchers suggested that internalizing psychic conflicts and being unable to verbalize them may lead to increased neurological arousal and subsequent sleep disturbances.<sup>43</sup> Alexithymia also causes hyperarousal,<sup>44</sup> which indicates that alexithymia may increase the risk of insomnia through hyper arousal.

In this study, the relationship between insomnia and alexithymia existed only in female adolescents. However, a study conducted in university students, mainly female students, showed that after eliminating the contribution of depression, the association between alexithymia and insomnia disappeared.<sup>45</sup> In another study, after adjusting the contribution of depression, the association between alexithymia and insomnia existed only in male patients.<sup>46</sup> The studies of interoception in recent years might provide new insights into this discrepancy. Recently, it has been pointed out that alexithymia is closely related to interoceptive impairment. The multiple psychiatric symptoms that co-occur with alexithymia indicate the impaired interoception among clinical patients.<sup>47</sup> Interoception is the ability of perceiving the body's internal state, which is related to a variety of basic functions, and it may be the reason behind some cross-disorder symptoms, such as sleep disorders.<sup>48</sup> For example, a study measured the interoceptive sensitivity using MAIA (Multidimensional Assessment of Interoceptive Awareness) and found that sleep quality was associated with alexithymia in people with low interoceptive sensitivity, while in people with moderate and high interoceptive sensitivity, sleep quality was associated with negative emotions.<sup>49</sup> Thus, alexithymia may induce varying consequences to the sleep quality of people with different levels of interoception sensitivity. We speculate that the sex differences in the interoceptive sensitivity of adolescents are sophisticated, which explains the discrepancy in the sex differences of the relationship between insomnia and alexithymia. It might be interesting to conduct more studies in this area.

Researchers also used PSG to assess objective sleep quality of alexithymia patients and reported that alexithymia was associated with increased light sleep and decreased deep sleep.<sup>19</sup> However, PSG findings showed that compared with patients' self-report, the objective total sleep time is usually longer.<sup>50</sup> The subjective-objective sleep discrepancy is common and should be considered in sleep studies. It has been suggested that in the study of adolescent MDD, in addition to objective sleep/wake behavior, it may be more critical to evaluate their feelings about sleep.<sup>51</sup>

This study showed that the severity of insomnia in adolescents with MDD is associated with depression. Previous evidence indicated that insomnia is not related to immunologic, neurotrophic and neuroendocrine biomarkers that resemble the pathophysiology of MDD.<sup>52</sup> Studies also showed that the improvements in insomnia symptoms were independent of depression remission.<sup>53</sup> These findings support that insomnia may be a separate disorder rather than a common symptom of mental illness, and it has been suggested that insomnia needs to be conceived as a comorbidity.<sup>54</sup> Thus, insomnia requires effective interventions during the treatment of depression, as a separate focus of therapy, including behavioral, cognitive, and pharmacologic interventions.<sup>55</sup> However, there is inadequate evidence on pharmacological interventions' effectiveness and long-term outcome for adolescent insomnia. Although some drugs are used clinically to treat adolescent insomnia, the American Academy of Sleep Medicine recommends that further studies be conducted to clarify the appropriate dosage, safety, and efficacy of these drugs in adolescents.<sup>56</sup> Therefore, insomnia in adolescent MDD patients needs other treatments, relevant researches has proven cognitive behavioral therapies (CBTs)

effective in treating teenage insomnia.<sup>57</sup> Recent studies suggested that short-term psychoanalytic psychotherapy (STPP) might help reducing sleep disturbances in early-onset MDD.<sup>58</sup>

In this study, insomnia was related to higher BMI in male patients but lower BMI in female patients. But the relationship between insomnia and BMI remains to be controversial. A study showed that obesity assessed by BMI was associated with chronic insomnia only in women, and this revealed sex-specific associations of BMI with different types of insomnia.<sup>59</sup> Another study indicated that lower weight was related to the most severe type of insomnia, which is insomnia associated with physiological hyperarousal.<sup>60</sup> Although limited study investigated the relationship between adolescents' sleep and their eating behaviors, insufficient sleep has been associated with worse health status and irregular eating habits in adolescents.<sup>61</sup> To sum up, the association between insomnia and BMI is affected by multiple factors and more intensive research is needed.

Consistent with previous studies, we found that alexithymia and its subcomponents DIF and DDF were moderately correlated with depressive symptoms, whereas EOT was only weakly correlated with depressive symptoms.<sup>62</sup> EOT is a pragmatic thinking style that does not value emotions and the inner world.<sup>63</sup> Studies showed that high EOT tendency can protect us from traumatic stressful experiences and cause harmful psychosomatic consequences by depriving positive or soothing experiences.<sup>64</sup> Besides, people with high EOT tendency are prone to regulate stress through externalizing behaviors such as substance use.<sup>65</sup>

This study investigated the prevalence of insomnia and the correlation between insomnia and alexithymia in adolescents with MDD. It provided new insight into psychopathological mechanisms, treatments and psychological interventions in adolescents with MDD. However, there are several limitations in this study. First, the current design was cross-sectional, and the causality relationships between insomnia and alexithymia could not be adequately obtained. Second, since this study was conducted in a convenience sample, the sample size was small, and the sex ratio was imbalanced; therefore, the selection bias and sampling bias were inevitable. All patients were recruited from seven hospitals in Anhui Province, China. Thus, the findings might not be generalized to other adolescents with MDD from different regions and cultures. Third, there was no matched healthy control group in this study, so we could not compare the clinical features between MDD and community adolescents. Fourth, the assessment tools used in this study are self-rating scales, which may lead to a certain recall bias. Finally, other relevant factors that may cause insomnia, such as anxiety, somatic diseases and poor sleep hygiene behaviors, were not controlled.

## Conclusion

To sum up, the prevalence of insomnia was high in adolescent MDD patients. There was no sex difference in the insomnia rate in adolescents with MDD. Patients with insomnia experienced more severe alexithymia than those without insomnia. The relationship between insomnia and alexithymia existed only in female patients, but not in male patients. In female adolescent MDD patients, alexithymia is a risk factor for insomnia. Future treatments of insomnia in MDD adolescents need to design programs to improve the ability of emotional regulation.

## Abbreviations

MDD, major depressive disorder; YLDs, years lived with disability; MDE, major depressive episode; PSG, polysomnography; DSM-5, the diagnostic and statistical manual; BMI, body mass index; CES-D, the Center for Epidemiologic Studies of Depression Scale; TAS-20, the 20-item Toronto Alexithymia Scale; DIF, difficulty in identifying emotions; DDF, difficulty in describing emotions; EOT, externally oriented thinking; PSQI, the Pittsburgh Sleep Quality Index; SD, standard deviations; ANOVA, the analysis of variance; CI, confidence interval; OR, odds ratio; MAIA, multidimensional assessment of interoceptive awareness; COVID-19, Corona Virus Disease 2019; CBT, cognitive behavioral therapies; STPP, short-term psychoanalytic psychotherapy.

## Data Sharing Statement

As this study is still ongoing, the raw datasets for the current study will not be available until the end of this research project. Please contact the first author (Xiaoxue Yang, xiaoxueyang07@163.com) for raw data requests.



## Ethical Statement and Consent to Participate

This study received ethical approval from the Ethics Committee of Chaohu Hospital, Anhui Medical University (202009-kyxm-04). This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

## Acknowledgments

We thank all the participants who volunteered to participate in this study.

## Funding

This study was supported by the National Key Clinical Specialty Project Foundation (CN) and the Research Fund Project of Anhui Translational Research Institute (No. 2022zhyx-B01).

## Disclosure

The authors report no conflicts of interest in this work.

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