

Insomnia Symptoms in Chinese Patients with Chronic Schizophrenia: Prevalence, Clinical Correlates and Relationship with Inflammation

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Abstract

Background: Sleep disturbances are common in patients with schizophrenia, with serious consequences. The purpose of this study was to investigate the prevalence and clinical correlates of insomnia symptoms, and to explore the relationship between insomnia and inflammatory markers in Chinese patients with chronic schizophrenia.

Methods: A total of 328 inpatients with chronic schizophrenia were recruited. Insomnia Severity Index (ISI), Calgary Depression Scale for Schizophrenia (CDSS), and Positive and Negative Syndrome Scale (PANSS) were used to assess the severity of insomnia, depression, and psychotic symptoms. The plasma levels of several inflammatory markers (CRP, IL-6, and TNF- α) were measured.

Results: The prevalence of insomnia symptoms in patients with schizophrenia was 38.4%. Depressive symptoms were significantly associated with insomnia symptoms (OR = 1.23, 95%CI: 1.13-1.33, $P < 0.001$). Higher CDSS score (beta = 0.55, $t = 8.21$, $P < 0.001$) and older age (beta = 0.06, $t = 3.59$, $P < 0.001$) were significantly associated with higher ISI score, while taking a single SGA (beta = -0.85, $t = -1.99$, $P < 0.05$) was independently associated with lower ISI score. There was no significant association between any inflammatory markers and insomnia or ISI score.

Conclusions: Our results demonstrate that the prevalence of insomnia symptoms is high in Chinese inpatients with chronic schizophrenia. Some demographic and clinical variables, such as depressive symptoms and older age, are risk factors, while others are beneficial factor, such as taking atypical antipsychotic drug for insomnia in schizophrenia patients. No association has been found between insomnia symptoms and inflammation.

Background

Insomnia is a common sleep disorder characterized by dissatisfaction with the quality or quantity of sleep. It usually manifests as having difficulty falling asleep, waking up frequently, and waking up too early [1, 2]. According to different definitions, the prevalence of insomnia varies considerably in different epidemiological studies. In the general population, 6%-9.5% of people meet the insomnia criteria of the 4th edition of Diagnostic and Statistical Manual of Mental Disorder (DSM-IV), while approximately 30% report having insomnia symptoms without strict criteria assessment [2–4]. Individuals with insomnia are more likely to be absent from work, have more accidents in their lives, and take up more medical and health resources than people with good sleep quality [5].

Sleep disturbances usually occur in patients with schizophrenia [6], which may have existed before the onset of the disease and are highly associated with acute exacerbation of psychotic symptoms [7]. A one-year follow-up study [8] of adolescents at high risk for psychiatric disorders found that circadian rhythm disorders predicted the severity of psychotic symptoms and psychosocial damage. Furthermore, in patients with schizophrenia, insomnia may lead to a significant reduction in quality of life [9] and a more

than 10-fold increase in the risk of suicide [10]. There is no doubt that insomnia is very harmful to this group of population and is worthy of attention.

Difficulties in falling asleep and maintaining sleep are the two most common manifestations of insomnia in schizophrenia, which may be due to overactivity of the dopaminergic system and dysfunction of the GABA system [11]. Regarding the effects of antipsychotic administration on sleep architecture, second-generation antipsychotics (SGAs) tend to ameliorate insomnia in patients with schizophrenia [12]. However, antipsychotics act by blocking D₂ receptors, which may exacerbate restless leg syndrome and periodic limb movement disorder, ultimately worsening sleep quality [7].

Sleep plays a homeostatic role in the regulation of inflammatory biology dynamics. Sleep disturbances, including insomnia, can activate the innate immune system at multiple levels and promote the production of proinflammatory cytokines [13]. There has been many studies on the relationship between sleep disturbances (including poor sleep quality, and insomnia complaints) and inflammatory markers [14], but few studies have focused on specific populations [15]. A recent study was considered to be the first report to show an association between sleep quality and inflammatory response in schizophrenia by measuring neutrophil–lymphocyte and platelet–lymphocyte ratios, but not levels of inflammatory cytokines [16]. Another more recent study found that sleep quality was related to CRP and IL-6 levels in outpatients with schizophrenia, but did not use any validated sleep questionnaires [17].

To date, only a few studies [9, 18, 19] have investigated insomnia in Chinese outpatients or community patients with schizophrenia, with inconsistent insomnia rates, ranging from 19.3–36.0%. There is no data on insomnia in Chinese hospitalized patients with chronic schizophrenia. Also, there is no report on the relationship between insomnia and inflammatory cytokines in these patients. Therefore, the main purposes of this study were 1) to examine the prevalence, socio-demographic and clinical correlates of insomnia in patients with chronic schizophrenia, and 2) to explore the relationship between insomnia and inflammatory markers in these patients.

Methods

Study Design and Participants

This cross-sectional study was part of a survey of physical diseases and psychological status in inpatients with schizophrenia (Trial registration: www.chictr.org.cn, ChiCTR1800017044). The survey was conducted in three hospitals: Chaohu Hospital of Anhui Medical University, Hefei Fourth People's Hospital, and Maanshan Fourth People's Hospital, which have a total of 1500 psychiatric beds, and serve more than 5 million people in Anhui Province, China. Patients were recruited consecutively from May 2018 to December 2018, provided that they met the following criteria: 1) aged ≥ 18 years; 2) met diagnosis of schizophrenia based on the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) [20]; 3) with ≥ 5 years of disease course; and 4) no pregnancy or

breastfeeding. People were excluded if they had 1) serious nervous system diseases, mental retardation, or dementia; or 2) immune diseases, or taking anti-inflammatory drugs.

Data collection

Socio-demographic characteristics

Each participant completed a predesigned questionnaire to collect socio-demographic and clinical variables such as age, sex, marital status, education, smoking behavior, antipsychotic (APs) and benzodiazepine (BZDs) use, and detailed hospitalization information. The data of all inpatients were extracted from electronic medical records. The chlorpromazine equivalent (CPZeq) of the APs dose was calculated in the defined daily doses (DDDs) method [21]. In this study, patients with hypertension and diabetes, were considered to have chronic somatic diseases (CSDs) through hospital diagnosis and corresponding medications (antihypertensive, hypoglycemic drugs, etc.).

Insomnia assessment

Under the guidance of the researchers, participants completed some clinical questionnaires through self-assessment, and conducted clinical interviews when necessary. Following the methods of previous studies [22, 23], three sleep items (4, 5, and 6) of the Hamilton Depression Rating Scale (HAM-D) were used to assess sleep disturbances in the previous 2 weeks, and three types of insomnia were identified: early, middle and late insomnia. These items were scored on a 3-point scale, from 0 = no difficulty to 2 = severe difficulty. If a patient was rated as ≥ 1 on any of the three items, he or she was defined as “having insomnia symptom”.

Insomnia Severity Index (ISI) [24] is a 7-item self-rating questionnaire designed to assess the severity of insomnia symptoms in different populations, including patients with schizophrenia. Its seven items are scored on a 4-point scale from 0 to 4, and the higher the total score, the more severe the symptoms of insomnia. Because the optimal cut-off score for ISI is still uncertain [25], in this study, the ISI total score was only used to assess the severity of insomnia symptoms.

Furthermore, the seven items of ISI are divided into three components: Factor 1 is labeled as “Impact” (interference, noticeability, and distress), Factor 2 is labeled as “Severity” (sleep onset, sleep maintenance, and early morning awakening), and Factor 3 is labeled as “Satisfaction” (sleep onset, satisfaction, and distress). The three-factor structure was supported by confirmatory factor analysis in previous studies [26].

Assessments of depressive and psychotic symptoms

Calgary Depression Scale for Schizophrenia (CDSS) is a 9-item scale, which has been proved to be a reliable and effective tool for the assessment of depressive symptoms in Chinese patients with schizophrenia [27]. The total score of the CDSS ranges from 0 to 27. As in the previous study, the 7th item requiring early awakening, was removed from the data analysis [28].

The Positive and Negative Syndrome Scale (PANSS) [29] was used to measure positive symptoms (items P1-7), negative symptoms (items N1-7), and general psychopathology symptoms (items G1-16) in schizophrenia patients with schizophrenia. The subscales were abbreviated as “PANSS-P”, “PANSS-N” and “PANSS-G”, respectively. Four psychiatrists participated in scoring PANSS, and received a training course in the use of PANSS before the the study began. Their inter-rater correlation coefficient was 0.9 for the PANSS total score.

Body Mass Index (BMI), fasting blood glucose (FBG), and inflammatory markers

BMI was calculated by the following formula: weight (kg) / height (meters²). Blood samples were collected from patients with schizophrenia between 06:00 and 08:00 AM after an overnight fast. The plasma was separated and then frozen at – 80°C until analysis. FBG levels were measured by glucose oxidase method (Meikang Biotech, Ningbo, China), high sensitivity CRP levels by immunoturbidimetric method (Leadman Biotech, Beijing, China), and IL-6 and tumor necrosis factor-alpha (TNF-α) levels by cytometric bead array (CBA) method (BD Biosciences, San Diego, USA) in the clinical laboratory in Chaohu Hospital of Anhui Medical University. The detection range for CRP was 0.06-16.0 mg/dL, with inter- and intra-assay variation coefficients of 8% and 6%, respectively. And the detection limits for IL-6 and TNF-α were 1.6 and 0.7 pg/mL, respectively.

Data analysis

Statistical analyses were conducted using SPSS (version 23.0). Kolmogorov-Smirnov test was used to detect the normality of the distribution of variables. Demographic and clinical variables were compared between different groups (patients with and without insomnia symptoms) by using chi-square test, independent sample t-test, and Mann-Whitney U-test, as appropriate. Furthermore, binary logistic regression analysis was performed to examine the related factors of insomnia in patients with schizophrenia by taking insomnia as the dependent variable and potential confounding factors with P-value < 0.10 in univariate analyses as independent variables. Pearson or Spearman coefficients were further performed to explore the association between ISI components and other variables. Stepwise multiple regression was then performed to identify which factors were attributed to ISI. The significance level of all analyses was set at $P < 0.05$ (2- tailed).

Results

Participant characteristics

Of the 331 inpatients with chronic schizophrenia recruited from the three hospitals, 328 patients (including 196 men and 132 women) completed all questionnaires and were included in the analysis. Table 1 shows that the average age was 45.1 ± 11.8 years (range, 19–74 years) and the average education level was 8.1 ± 3.6 years (range, 0–18 years). The proportion of patients taking a single first-generation (FG), second-generation (SG), and mixed antipsychotics was 2.1% (7/328), 41.7% (136/328),

and 56.4% (185/328), respectively. In addition, 16.5% (54/328) of patients had at least one type of CSD, including 39 cases of diabetes and 28 cases of hypertension.

Table 1
Socio-demographic and clinical characteristics of patients

	Whole sample (<i>n</i> = 328)		Insomnia (<i>n</i> = 126)		Non-insomnia (<i>n</i> = 202)		Statistics		
	N	%	N	%	N	%	χ^2	df	P
Male	196	59.8	72	57.1	124	61.4	0.58	1	0.45
Married	96	29.3	38	30.2	58	28.7	0.08	1	0.78
Smoking behavior	98	29.9	31	24.6	67	33.2	2.72	1	0.10
Single FGA	7	2.1	3	2.4	4	2.0	0	1	1.00
Single SGA	136	41.7	49	38.9	87	43.1	0.56	1	0.46
BZDs	62	18.9	28	22.2	34	16.8	1.47	1	0.23
CSDs	54	16.5	24	19.0	30	14.9			
Diabetes	39	11.9	15	11.9	24	11.9	0	1	1.00
Hypertension	28	8.5	16	12.7	12	5.9	4.54	1	0.03
	Mean	SD	Mean	SD	Mean	SD	T / Z	df	P
Age (years)	45.1	11.8	47.0	11.7	43.9	11.7	2.40	326	0.02
Education (years)	8.1	3.6	8.0	3.4	8.2	3.8	-0.24 ^a		0.81
Age of onset (years)	26.0	8.2	26.3	7.9	25.7	8.4	0.66	326	0.51
Duration of illness (years)	19.1	10.4	20.6	11.0	18.1	10.0	-1.97 ^a		0.049
Number of hospitalizations	5.7	4.9	5.7	5.5	5.7	4.6	-0.32 ^a		0.75
CPZeq (mg/day)	455.3	261.7	453.6	237.8	455.0	275.6	-0.65 ^a		0.51
Dose stabilization (weeks)	11.7	10.4	11.0	9.1	12.0	11.1	-0.60 ^a		0.55
BMI (kg/m ²)	24.1	3.8	24.4	3.8	23.9	3.9	1.16	326	0.25

^a Mann-Whitney U-test; Statistical differences are bold.

FGA, first-generation antipsychotic; SGA, second-generation antipsychotic; CSD, chronic somatic diseases; BZD, benzodiazepine; CPZeq, chlorpromazine equivalent; FBG, fasting blood glucose; BMI, Body Mass Index; PANSS-P, Positive subscore of PANSS; PANSS-N, Negative subscore of PANSS; PANSS-G, General psychopathology subscore of PANSS; CDSS, Calgary Depression Scale for Schizophrenics, minus the sleep item.

	Whole sample (<i>n</i> = 328)		Insomnia (<i>n</i> = 126)		Non-insomnia (<i>n</i> = 202)		Statistics		
FBG (mmol/L)	5.3	1.4	5.6	1.6	5.2	1.2	-2.47 ^a		0.01
PANSS-P	17.9	7.3	19.1	6.9	17.1	7.5	-2.66 ^a		0.008
PANSS-N	21.6	7.6	21.7	6.6	21.5	8.2	0.33	326	0.74
PANSS-G	38.3	12.7	40.6	11.6	36.9	13.1	2.65	326	0.009
CDSS	3.0	3.1	4.2	3.3	2.3	2.8	-6.43 ^a		< 0.001
^a Mann-Whitney U-test; Statistical differences are bold.									
FGA, first-generation antipsychotic; SGA, second-generation antipsychotic; CSD, chronic somatic diseases; BZD, benzodiazepine; CPZeq, chlorpromazine equivalent; FBG, fasting blood glucose; BMI, Body Mass Index; PANSS-P, Positive subscore of PANSS; PANSS-N, Negative subscore of PANSS; PANSS-G, General psychopathology subscore of PANSS; CDSS, Calgary Depression Scale for Schizophrenics, minus the sleep item.									

Prevalence of insomnia symptoms

The prevalence rate of ≥ 1 type of insomnia symptoms among all patients was 38.4% (126/328), and the prevalence of early, middle and late insomnia was 26.2% (86/328), 21.6% (71/328), and 17.1% (56/328), respectively. Although the prevalence of insomnia symptoms in females appeared to be higher than that in males (40.9% *versus* 36.7%), the difference was not statistically significant ($\chi^2 = 0.58$, *df* = 1, *P* = 0.45).

Demographic and clinical variables between insomnia and non-insomnia groups

Compared with those without insomnia symptoms, patients with insomnia symptoms had older age, longer duration of illness, higher proportion of hypertension, higher levels of FBG, as well as more positive (PANSS-P), general psychopathology (PANSS-G), and depressive symptoms (CDSS) (Table 1). Further, binary logistic regression analysis showed that only depressive symptoms (CDSS) were still associated with insomnia symptoms (OR = 1.23, 95%CI: 1.13–1.33, *P* < 0.001). In addition, there were no significant differences in CRP, IL-6, or TNF- α levels between the insomnia and non-insomnia groups (Table 2).

Table 2
Inflammatory markers

Inflammatory markers	Insomnia (n = 126)	Non-insomnia (n = 202)	Z ^a	P value
CRP (mg/L)	2.46 ± 4.00 ^b	2.46 ± 8.02 ^c	-0.85	0.40
IL-6 (pg/ml)	1.65 ± 1.59 ^c	1.68 ± 2.14 ^d	-0.89	0.38
TNF-α (pg/ml)	0.39 ± 0.33 ^c	0.48 ± 0.86 ^d	-1.08	0.28
^a Mann-Whitney U-test; Missing information for ^b 2, ^c 3, and ^d 5 patients.				

Associations between ISI and demographic and clinical variables

Compared with patients without insomnia symptoms, patients with insomnia symptoms had higher ISI score (7.5 ± 4.6 versus 1.4 ± 1.4 ; $Z = -13.55$, $P < 0.001$). There was no significant difference in ISI score between male and female, married and non-married, or smoking and non-smoking patients (all $P > 0.05$).

Correlation analysis showed that ISI score was significantly associated with age ($r = 0.13$, $P < 0.05$), blood glucose level ($r = 0.14$, $P < 0.05$), PNASS positive symptoms ($r = 0.19$, $P < 0.001$), general psychopathology ($r = 0.17$, $P < 0.01$), PANSS total score ($r = 0.18$, $P < 0.01$), and depressive symptom shown on CDSS ($r = 0.43$, $P < 0.001$) (Table 3). Further stepwise multiple regression showed that higher CDSS score (beta = 0.55, $t = 8.21$, $P < 0.001$) and older age (beta = 0.06, $t = 3.59$, $P < 0.001$) were significantly associated with higher ISI score, while taking a single SGA (beta = -0.85, $t = -1.99$, $P < 0.05$) was associated with a lower ISI score (Table 4).

Table 3
Correlations between the components of ISI and demographic and clinical measures

	Age	Hypertension	Duration of illness	FBG	PANSS- P	PANSS- N	PANSS- G	CDSS
ISI-1	0.11*	0.11*	0.09	0.09	0.25***	0.13*	0.24***	0.40***
ISI-2	0.16**	0.13*	0.10	0.16**	0.14**	0.07	0.14*	0.37***
ISI-3	0.13*	0.09	0.12*	0.10	0.18**	0.13*	0.18**	0.43***
ISI Total	0.13*	0.10	0.10	0.14*	0.19***	0.11	0.17**	0.43***
FBG, fasting blood glucose; ISI-1, Factor 1 labeled as “Impact” in ISI; ISI-2, Factor 2 labeled as “Severity” in ISI; Factor 3 labeled as “Satisfaction” in ISI; PANSS-P, Positive subscore of PANSS; PANSS-N, Negative subscore of PANSS; PANSS-G, General psychopathology subscore of PANSS; CDSS, Calgary Depression Scale for Schizophrenics, minus the sleep item.								
* $P < 0.05$.								
** $P < 0.01$.								
*** $P < 0.001$.								

Table 4
Factors associated ISI score by Stepwise Multiple Regression

	Coefficients		T	P	95% CI for B	
	B	Std. Error			Lower Bound	Upper Bound
(Constant)	-0.46	0.88	-0.52	0.60	-2.19	1.27
CDSS	0.55	0.07	8.21	< 0.001	0.42	0.68
Age	0.06	0.02	3.59	< 0.001	0.03	0.10
Single SGA	-0.85	0.43	-1.99	0.048	-1.69	-0.01
CI, confidence interval; SGA, second-generation antipsychotic.						

In addition, correlation analysis showed no significant correlation between ISI score and any of inflammatory markers (CRP, IL-6, or TNF- α ; all $P > 0.05$) (Table 5).

Table 5
ISI and Inflammatory markers

	CRP	IL-6	TNF- α
ISI-1	0.04 (0.51)	-0.16 (0.77)	0.03 (0.63)
ISI-2	0.04 (0.46)	0.01(0.81)	-0.08 (0.18)
ISI-3	0.02 (0.74)	0.00 (0.96)	-0.02 (0.78)
ISI Total	0.03 (0.60)	0.00 (0.95)	-0.02 (0.73)
Data are presented as correlation coefficient and P value.			

Discussion

To the best of our knowledge, this was the first study to investigate the prevalence and clinical correlates of insomnia symptoms, and to explore the relationship between insomnia and inflammatory markers in patients with chronic schizophrenia in China. There were several main findings of this study: 1) we found a high rate of insomnia symptoms in patients with chronic schizophrenia; 2) compared with patients without insomnia symptoms, patients with insomnia symptoms had older age, longer duration of illness, higher proportion of hypertension, higher levels of FBG, more psychotic and depressive symptoms; 3) some demographic and clinical variables were found to be risk factors for insomnia in these patients, including more severe depressive symptoms and older age, while taking a single SGA was a beneficial factor; 4) there was no significant correlation between insomnia symptoms and any inflammatory markers.

The prevalence of insomnia symptoms in hospitalized patients with chronic schizophrenia was 38.4%, which was close to the results of previous studies in Chinese outpatients (36.0%) and community patients (28.9%) with schizophrenia [9, 18], but lower than that in a study of 175 outpatients with schizophrenia or schizophrenic affective disorder from the USA (44%), adopting more stringent criteria for insomnia with ISI ≥ 15 [28]. This difference can be considered as a considerable regional difference in the rate and severity of insomnia between Chinese and Western populations [30]. Also, this can be explained by their different hours of work and rest, or their different perception of insomnia, such as sensitivity to insomnia.

Furthermore, the prevalence of early, middle and late insomnia symptoms found in this study were very close to the corresponding 21.1%, 23.6% and 11.9%, as well as 20.5%, 19.6% and 17.7% in the previous two studies [9, 18]. These results confirmed that difficulty falling asleep and maintaining sleep are the two most common manifestations of insomnia in schizophrenia [11]. In a Chinese epidemiologic survey [31] using insomnia criteria similar to this study, the prevalence rates of early, middle, late, and any type of insomnia symptoms in general population were 7.0%, 8.0%, 4.9% and 9.2%, respectively. Therefore, the prevalence of insomnia symptoms in inpatients with schizophrenia is higher than that in normal people.

As a result, hospitalized patients with schizophrenia are prone to insomnia and require more attention, even if they receive regular medical rounds and care.

Our current study found that schizophrenia patients with insomnia symptoms had significantly older age and longer duration of illness than those without insomnia symptoms. Further correlation analysis and showed that the ISI score was positively associated with the patients' age, which was confirmed by stepwise multiple regression. These results confirmed the findings of previous studies [9, 18]. In addition, we found that ISI-3 (Satisfaction) was positively associated with duration of illness, indicating that patients with longer duration of illness had lower satisfaction with sleep in schizophrenia patients. Taken together, these findings suggest that older age and longer duration illness may be risk factors for sleep disturbances in patients with chronic schizophrenia.

Further, we found that FBG level was significantly higher in the insomnia group than that in the non-insomnia group. Moreover, FGB level was positively correlated with ISI score and ISI-2 (Severity). Our results suggest that schizophrenia patients with higher FBG levels were more likely to suffer from insomnia than those with normal FBG levels. In a large epidemiological study, about 25% patients with type 2 diabetes were diagnosed with sleep disorders, and more than 75% reported sleep symptoms [32]. A number of observational studies have shown an association between metabolic disturbance and sleep disorders [33]. These results suggest that abnormal glucose metabolism or diabetes may have a significant impact on sleep in both schizophrenia patients and general population.

In addition, we found that the proportion of hypertension in patients with insomnia symptoms was higher than that in patients without insomnia symptoms, indicating that insomnia is associated with hypertension in schizophrenia. A previous study confirmed that patients with chronic insomnia had an increased cardiovascular risk compared with healthy controls [34]. This may be related to the dysregulation of hypothalamic-pituitary axis, increased activity of sympathetic nervous system, and elevated inflammatory level [35].

Our results showed that patients with insomnia symptoms had more severe positive and general psychopathological symptoms than those without insomnia symptoms, which was consistent with the results of several previous studies. For example, a previous study found that sleep disturbances predicted the greater auditory hallucinations, paranoia and delusions the next day in schizophrenia [36], suggesting that insomnia or poor sleep quality is associated with worse psychotic symptoms in patients with schizophrenia. Moreover, several studies have found that insomnia was associated with positive [9, 18], negative [18], anxiety [9, 18] and depressive symptoms [9, 18, 28] in patients with schizophrenia. Among the schizophrenia patients in this study, the correlation remained significant after removal of the overlapping item with insomnia in CDSS. More severe depressive symptoms were independently associated with a higher risk of insomnia and higher ISI scores, suggesting that they are risk factors for insomnia. Additionally, the multiple regression showed that taking a single SGA was associated with a lower ISI score, which may be a protective factor for insomnia in the patients with schizophrenia.

Of note, we found no significant correlation between inflammatory markers and insomnia or ISI score in patients with chronic schizophrenia. In contrast, two previous studies found higher levels of inflammatory measures (neutrophil-lymphocyte and platelet-lymphocyte ratios) [16] and higher levels of CRP and IL-6 [17] in schizophrenia patients with poor sleep quality. The first study assessed inflammation and sleep quality differently from this study. And the participants in the latter study were outpatients with schizophrenia, whose lifestyles and sleep habits may differ from those of inpatients with chronic schizophrenia. Moreover, although the relationship between schizophrenia and inflammatory abnormalities has been repeatedly confirmed [37], the levels of inflammatory cytokines are easily affected by a variety of confounding factors, such as gender, stress, course of disease and the administration of different antipsychotics [37–39]. Therefore, the relationship between sleep disturbances and inflammation in patients with schizophrenia needs to be further studied.

Several methodological limitations of this study should be noted. First, this was a cross-sectional design that did not identify the direction and causal relationship between demographic or clinical variables and insomnia or ISI score in patients with schizophrenia. Second, all participants were recruited from three hospitals in the same province, which led to a lack of nationwide representation. Third, insomnia was defined by loose criteria rather than an objective measure of sleep, such as recording through polysomnography or actigraphy. Finally, there was no healthy control group in this study, and we were unable to make a direct comparison between schizophrenia and normal populations.

Conclusions

In conclusion, insomnia is common in hospitalized patients with schizophrenia in China, especially those with older age, or more depressive symptoms. Taking a single SGA may be a protective factor for insomnia. In addition, there is no clear correlation between insomnia symptoms and inflammation in schizophrenia. Due to methodological limitations, including a small sample size, chronic inpatients, no matched healthy controls, and no objective measurements for sleep, our results should be considered preliminary. Longitudinal studies with more representative samples will help to further clarify the relationship of insomnia with its risk factors and inflammation in patients with schizophrenia, and provide reasonable prevention and intervention measures for clinical practice.

Abbreviations

AP: antipsychotic; BMI: Body Mass Index; BZD: benzodiazepine; CBA: cytometric bead array; CDSS: Calgary Depression Scale for Schizophrenia; CPZeq, chlorpromazine equivalent; CSDs: chronic somatic diseases; DDDs, defined daily doses; DSM-IV: 4th edition of Diagnostic and Statistical Manual of Mental Disorder; FBG: fasting blood glucose; FGA: first-generation antipsychotic; HAM-D: Hamilton Depression Rating Scale; ICD-10: 10th revision of the International Statistical Classification of Diseases and Related Health Problems; ISI: Insomnia Severity Index; PANSS: Positive and Negative Syndrome Scale; SGA: second-generation antipsychotic; TNF- α : factor-alpha.

Declarations

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Authors' contributions

Study design and funding acquisition: HL. Data collection, analysis and interpretation: LX, YZ, ZL, YZ, KZ. Drafting of the manuscript: LX, YZ. Critical revision of the manuscript: XYZ. Approval of the final version for publication: all co-authors.

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Availability of data and materials

The datasets used and analysed for this study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The Ethics Committee of Chaohu Hospital of Anhui Medical University approved the protocol before the study began. All participants in this study provided written informed consent.

Consent for publication

All participants provided written informed consent for publication.

Competing interests

The authors declare that they have no conflict of interest.

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