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Original Article

Epidemiological study on seroprevalence of syphilis in patients with mental diseases

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Abstract

Introduction: The objective of this study was to investigate the seroprevalence of syphilis and its possible influencing factors in patients with mental illness.

Methodology: A total of 24,414 patients with mental illness from 2019 to 2021 were included. Serum syphilis antibody test results and available demographic data were collected. Chi-square test and regression analysis were used to analyze the data.

Results: The seroprevalence of syphilis was 0.59% (95% CI 0.49-0.69%) in patients with mental illness in the study area. There were significant differences in the seroprevalence of syphilis in age, marital status, occupation, urban region, and mental disease classification. The seroprevalence of syphilis increased with age ($p < 0.01$). The seroprevalence of syphilis was higher in patients with "Nonorganic sleep disorders" and "Reaction to severe stress, and adjustment disorders". Adjusted logistic regression analysis showed that the seroprevalence of syphilis in patients with mental illness was associated with age, region, and psychiatric classification. Older age group was a risk factor for syphilis seropositivity. Compared with schizophrenia, "bipolar affective disorder" (OR = 1.707, 95% CI: 1.017-2.864, $p = 0.043$) and "severe stress response and adjustment disorders"(R = 4.912, 95% CI: 1.138-21.204, $p = 0.033$) were risk factors for syphilis antibody positivity.

Conclusions: The patients with "nonorganic sleep disorders" and "reaction to severe stress, and adjustment disorders" had a high seroprevalence of syphilis. Age and psychosis types became the influencing factors of the positive rate of serum syphilis antibody in patients with mental illness.

Key words: *Treponema pallidum*; mental illness; psychosis; risk factor.

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Introduction

Syphilis is a chronic, systemic bacterial infectious disease in untreated cases caused by *Treponema pallidum (TP)*. Sexual contact is the main transmission route of syphilis, accounting for more than 95% of the total infected patients. It can also be transmitted through blood and vertical transmission, and the course of the disease may involve all organs of the body [1]. *TP* can enter the body through sexual contact directly through the mucosa or breaks in the skin resulting from sexual activity. Once inside the epithelium, *TP* multiplies locally and spreads throughout the body through the blood and lymphatic vessels [2,3]. According to the Law of the People's Republic of China on the Prevention and Treatment of Infectious Diseases, syphilis has been listed as a class B disease for prevention and management in China. Class B infectious diseases are also known as strictly managed infectious diseases, including infectious atypical pneumonia, influenza A (H1N1), AIDS, viral hepatitis, polio, and 26 other infectious diseases.

Syphilis infection is a worldwide public health problem. The World Health Organization estimates that 10 to 12 million new syphilis infections occur each year, mainly in developing countries in Africa, South America, and Southeast Asia [4]. Different stages in the clinical course of syphilis include early infectious syphilis: primary, secondary, and early latent syphilis, as well as late latent and tertiary syphilis [5]. At any stage of infection, the brain and the nervous system may be invaded by *TP*, causing neurosyphilis, and producing neurological and psychiatric symptoms [6-8]. Some studies suggest that people with mental health problems may be at higher risk for syphilis [4,6,7,9]. The purpose of this study is to study the epidemiological status of *TP* in patients with mental diseases in this region, provide data support for the prevention and control of syphilis in this region, and provide references for research in the same field.

Methodology

Study design and data collection

This study was approved by the ShanDong Daizhuang hospital ethics committee (Ethics Number: 2023 Research No. 08-202302KS-1). Taking into account the special situation of psychiatric patients, the hospital stipulates that syphilis serum antibody testing is a routine test item for admitted patients to evaluate the physical health of patients. To ensure the privacy of the patients this study did not include the patients' names and contact information instead the admission number was used as the unique identifier to collect the syphilis serum antibody test results and medical record information from Shandong Daizhuang Hospital. The inclusion criteria included: (1) newly admitted inpatients from 2019 to 2021; (2) patients diagnosed by a psychiatrist as having mental illness according to the International Classification of Diseases, 10th Revision (ICD-10); (3) serum test results for syphilis antibodies were available; (4) The medical record information of patients is comprehensive and available, including age, gender, race, diagnosis, marital status, occupation, residence, etc.

Laboratory testing

According to the regulations, psychiatrists prescribe syphilis antibody testing applications for psychiatric patients who need to be hospitalized, and patients with mental illness go to the medical laboratory for testing. Fasting venous blood (5 mL) was extracted and centrifuged at 4000 R/min for 10 minutes, and serum was separated for syphilis antibody detection. The isolated serum was detected for syphilis antibodies using the *TP* antibody detection kit (magnetic particle chemiluminescence method, CMIA. Autobio PRODUCTS, INC. China).

Statistical analysis

SPSS V22 software (IBM, Chicago, USA) was used for statistical analysis of data in this study. Demographic characteristics were analyzed by descriptive analysis, Pearson chi-square test, continuity correction, or Fisher exact test for categorical data. Univariate and multivariate logistic regression were used to analyze the correlation between infection markers and putative risk factors by odds ratio (OR) and 95% confidence interval (95%CI). A p value < 0.05 was considered statistically significant. Stepwise regression strategy was used in multivariate logistic regression analysis.

Results

A total of 24,414 valid samples meeting the requirements were included in this study. The average age was 41.85 ±1 7.19 years (6-93 years). The populations were divided into 4 age groups according to the age difference: 6-17 years age group, 18-44 years age group, 45-59 years age group, and 60-93 years age group. Males accounted for 44.26% and females accounted for 55.74% of the total patients. The Han ethnic population accounted for 99.36% of the included population. According to marital status, the population was divided into four groups: single, married, divorced, and widowed. A majority of patients were residents of Shandong Province; however, patients came from 30 other Chinese provinces including Jiangsu and Henan Provinces, among others. Based on the city of the patients, the top 8 urban areas were listed, which can cover and represent the study area of at least approximately 56 million people and 75,000 square kilometers. Among different regions, Jining accounted for 68.76% patients. Patients were divided into rural and urban groups according to their living location and surrounding environment. According to the different nature of work, the patients were divided into six groups: unemployed persons, farmers, workers, students, retired persons, and other professional personnel, among which the unemployed persons accounted for 55.44%.

According to the severity of the disease, the patients were divided into two groups: general and severe. Severe mental illness refers to six types of serious mental illness defined in the Mental Health Law of the People's Republic of China, including schizophrenia bipolar disorder, persistent delusional disorder (paranoid mental disorder), mental retardation with related mental disorders, mental disorders due to epilepsy, and schizoaffective disorder. According to the *ICD-10* diagnostic criteria, the patients were divided into 17 categories in this study, including schizophrenia, bipolar disorder, depressive episode, recurrent depressive disorder, dissociation [conversion] disorder, and so forth. Schizophrenia, bipolar disorder, depressive episodes, and recurrent depressive disorder accounted for the highest proportion (Table 1).

Seroprevalence of syphilis in patients with mental illness

In the study population, there were 143 cases of syphilis seropositivity in psychiatric patients, the seroprevalence was 0.59%, 95% CI: 0.49-0.69%. The seroprevalence of syphilis in 2019, 2020, and 2021 were 0.61%, 0.54%, and 0.61%, respectively, and there

was no significant difference in the seroprevalence of syphilis in the three years (p = 0.817).

The seroprevalence of syphilis in mental patients showed an increasing trend with age (p for trend < 0.01). The seroprevalence of syphilis was the highest in the 60-93 years old group (1.06%) (Figure 1).

There were significant statistical differences in the seroprevalence of syphilis in mental patients with different types of mental diseases. The seroprevalence of syphilis was the highest in "Reaction to severe stress, adjustment disorders" and "Nonorganic sleep disorders" (1.92% and 1.91%, respectively). Patients with schizophrenia accounted for the highest proportion in the study population, and the positive rate of syphilis antibody was 0.43% (Figure 2).

Figure 1. The seroprevalence of syphilis between the age groups.

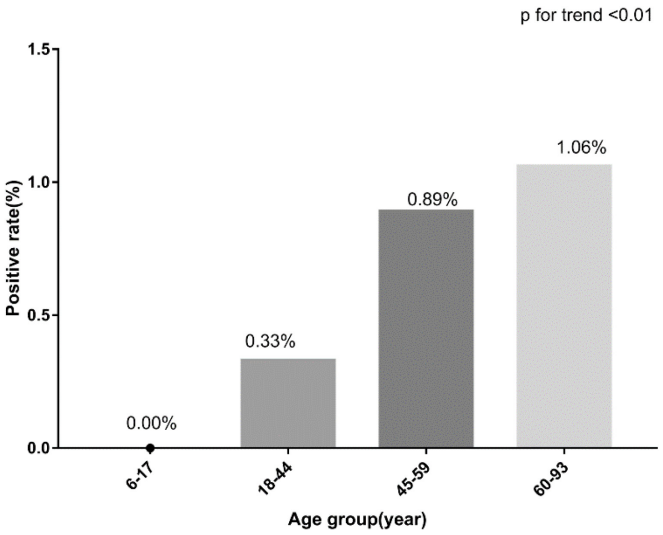

Table 1. Demographic characteristics of psychiatric patients and results of intergroup comparison.

Characteristics	Number	Percentage (%)	Positive	Positive rate (%)	χ^2	p
Sex						
Female	13609	55.74	91	0.67	3.633[a]	0.057
Male	10805	44.26	52	0.48		
Age (years)						
6-17	2208	9.04	0	0.00		
18-44	11053	45.27	37	0.33	51.684[a]	0.000
45-59	7084	29.02	63	0.89		
60-93	4069	16.67	43	1.06		
Ethnicity						
Han	24258	99.36	142	0.59	0.000[b]	1.000
Others	156	0.64	1	0.64		
Marital status						
Single	6581	26.96	14	0.21		
Married	16929	69.34	122	0.72	21.646[a]	0.000
Divorced	801	3.28	6	0.75		
Widowed	103	0.42	1	0.97		
Occupation						
Jobless	13535	55.44	89	0.66		
Farmer	3609	14.78	27	0.75		
Worker	736	3.01	5	0.68	23.441[a]	0.000
Student	3067	12.56	1	0.03		
Retired	1096	4.49	11	1.00		
Other	2371	9.71	10	0.42		
Residence						
Urban	6695	27.42	45	0.67	1.183[a]	0.277
Rural	17719	72.58	98	0.55		
Region						
Jining	16787	68.76	96	0.57		
Heze	3481	14.26	14	0.40		
Zaozhuang	1245	5.10	12	0.96		
Taian	1123	4.60	3	0.27	23.545[a]	0.001
Linyi	668	2.74	7	1.05		
Xuzhou	244	1.00	0	0.00		
Jinan	164	0.67	0	0.00		
Other	702	2.88	11	1.57		

[a]Pearson chi-square test; [c]Fisher's exact probability method.

Chi-square test analysis results

Through the chi-square test, the results showed that there were significant statistical differences in the seroprevalence of syphilis in patients with mental illness in various factors such as age, marital status, occupation, region and type of mental illness. There were no significant differences in gender, residence, ethnicity, and severity (Table 2).

In different age groups, the seroprevalence of syphilis was 0.00% in the age group of 6-17 years, and the highest in the age group of 60-93 years (1.06%) (χ^2 = 51.684, p = 0.000**).** Among different marital status groups, the seroprevalence of syphilis was the lowest in the single group (0.21%), and the highest in the widowed group (0.97%) (χ^2 = 21.646, p = 0.000). Among different occupational groups, the seroprevalence of syphilis was the lowest in the student group (0.03%), and the highest in the retired group (1.00%) (χ^2 = 23.441, p = 0.000) (Table 2).

Logistic regression analysis results

Univariate binary logistic regression analysis and multivariate binary logistic regression analysis were used to analyze the correlation between the seroprevalence of syphilis and potential risk factors. Multivariate analysis of binary logistic regression showed that the seroprevalence of syphilis was associated with age, region, and type of psychosis (Table 3).

Figure 2. The positive rate of serum syphilis antibodies in different types of mental diseases.

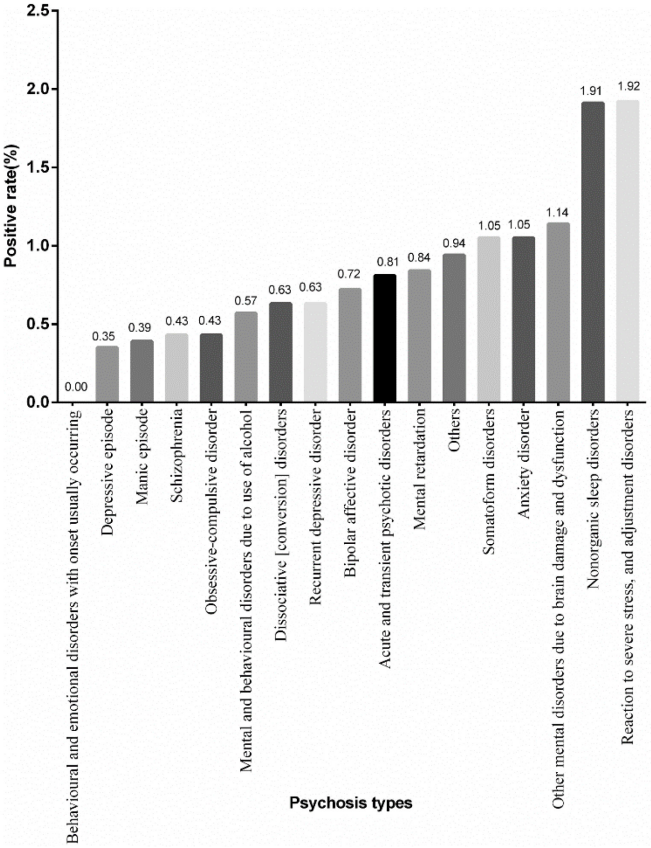

Table 2. Seroprevalence of syphilis according to the severity of mental disorder and psychosis type

Variables	Number	Percentage (%)	Positive	Positive rate (%)	χ^2	p
Severity						
Severe	10869	44.52	59	0.54	0.619[a]	0.431
General	13545	55.48	84	0.62		
Psychosis types						
Schizophrenia	6306	25.83	27	0.43		
Bipolar affective disorder	4436	18.17	32	0.72		
Depressive episode	3732	15.29	13	0.35		
Recurrent depressive disorder	3651	14.95	23	0.63		
Dissociative [conversion] disorders	1434	5.87	9	0.63		
Mental and behavioural disorders due to use of alcohol	1231	5.04	7	0.57		
Other mental disorders due to brain damage and dysfunction and to physical disease	615	2.52	7	1.14		
Somatoform disorders	478	1.96	5	1.05		
anxiety disorder	569	2.33	6	1.05		
Manic episode	254	1.04	1	0.39		
Mental retardation	237	0.97	2	0.84	28.675[a]	0.026
Obsessive-compulsive disorder	231	0.95	1	0.43		
Nonorganic sleep disorders	209	0.86	4	1.91		
Behavioural and emotional disorders with onset usually occurring in childhood and adolescence	484	1.98	0	0.00		
Reaction to severe stress, and adjustment disorders	104	0.43	2	1.92		
Acute and transient psychotic disorders	123	0.50	1	0.81		
Others	320	1.31	3	0.94		

[a]Pearson chi-square test; [c]Fisher's exact probability method.

Compared with the age group of 60-93 years, the age group of 18-44 years was a potential protective factor for the patients with mental illness (OR = 0.336, 95% CI: 0.197-0.575, p = 0.000). Compared with the Jining area, other regions, and the Zaozhuang area may be a potential risk factor for the positive rate of serum syphilis antibody (OR = 01.990, 95% CI: 1.804-3.652, p = 0.026). Compared with schizophrenia, "bipolar affective disorder" and "reaction to severe stress, and adjustment disorders" were potential risk factors for serum antibody positive rate (OR = 1.707, 95% CI: 1.017-2.864, p = 0.043 and OR = 4.912, 95% CI: 1.138-21.204, p = 0.033, respectively) (Table 3).

Discussion

Although *TP* was discovered early on, because *TP* cannot be continuously cultured in vitro, we know much less about the pathogenesis of *TP* than other common bacterial phases [10,11]. It is generally believed that at any stage of syphilis infection, the brain nervous system may be invaded by *TP*, causing neurosyphilis [7,8]. Neurosyphilis is a clinical

Table 3. The results of logistic regression analysis between the seropositivity of syphilis and the influencing factors.

Factors	Number	Positive	Positive rate (%)	OR	95% CI	*p*	OR[a]	95% CI[a]	*p*[a]
Age Group (years)									
6-17	2208	0	0.00			0.984			0.985
18-44	11053	37	0.33	0.314	0.202-0.489	0.000	0.336	0.197-0.575	**0.000**
45-59	7084	63	0.89	0.84	0.569-1.240	0.381	0.903	0.591-1.380	0.638
60-93	4069	43	1.06	ref		0.000	ref		**0.000**
Marital status									
Single	6581	14	0.21	ref		0.000	ref		0.736
Married	16929	122	0.72	3.405	1.957-5.924	0.000	1.037	0.539-1.993	0.914
Divorced	801	6	0.75	3.54	1.357-9.238	0.010	1.664	0.618-4.480	0.313
Widowed	103	1	0.97	4.599	0.599-35.302	0.142	1.084	0.135-8.728	0.939
Occupation									
Jobless	13535	89	0.66	ref		0.019	ref		0.527
Farmer	3609	27	0.75	1.139	0.739-1.754	0.556	1.127	0.729-1.741	0.591
Worker	736	5	0.68	1.033	0.419-2.552	0.943	0.896	0.359-2.235	0.814
Student	3067	1	0.03	0.049	0.007-0.354	0.003	0.267	0.035-2.051	0.204
Retired	1096	11	1.00	1.532	0.816-2.874	0.184	0.925	0.479-1.785	0.816
Other	2371	10	0.42	0.64	0.332-1.232	0.182	0.624	0.320-1.216	0.166
Regions									
Jining	16787	96	0.57	ref		0.008	ref		**0.002**
Heze	3481	14	0.40	0.702	0.400-1.231	0.217	0.863	0.490-1.521	0.611
Zaozhuang	1245	12	0.96	1.692	0.926-3.092	0.087	1.990	1.084-3.652	**0.026**
Taian	1123	3	0.27	0.466	0.147-1.472	0.193	0.522	0.165-1.654	0.269
Linyi	668	7	1.05	1.841	0.851-3.982	0.121	2.031	0.935-4.413	0.073
Xuzhou	244	0	0.00			0.995			0.995
Jinan	164	0	0.00			0.996			0.996
Other	702	11	1.57	2.768	1.476-5.189	0.002	3.347	1.768-6.337	**0.000**
Psychosis types									
Schizophrenia	6306	27	0.43	ref		0.110	ref		0.441
Bipolar affective disorder	4436	32	0.72	1.69	1.011-2.824	0.045	1.707	1.017-2.864	**0.043**
Depressive episode	3732	13	0.35	0.813	0.419-1.577	0.540	0.828	0.422-1.627	0.584
Recurrent depressive disorder	3651	23	0.63	1.474	0.844-2.575	0.172	1.095	0.613-1.957	0.758
Dissociative [conversion] disorders	1434	9	0.63	1.469	0.689-3.130	0.319	1.144	0.530-2.470	0.731
Mental and behavioural disorders due to use of alcohol	1231	7	0.57	1.33	0.578-3.061	0.503	1.069	0.460-2.484	0.877
Other mental disorders due to brain damage and dysfunction and to physical disease	615	7	1.14	2.677	1.161-6.174	0.021	1.565	0.654-3.746	0.315
Somatoform disorders	478	5	1.05	2.458	0.942-6.413	0.066	1.420	0.531-3.796	0.484
anxiety disorder	569	6	1.05	2.478	1.019-6.028	0.045	1.854	0.748-4.594	0.182
Manic episode	254	1	0.39	0.919	0.124-6.791	0.934	1.003	0.135-7.451	0.998
Mental retardation	237	2	0.84	1.979	0.468-8.372	0.354	2.965	0.690-12.747	0.144
Obsessive-compulsive disorder	231	1	0.43	1.011	0.137-7.473	0.991	1.638	0.219-12.221	0.631
Nonorganic sleep disorders	209	4	1.91	4.538	1.573-13.087	0.005	2.577	0.875-7.592	0.086
Behavioural and emotional disorders with onset usually occurring in childhood and adolescence	484	0	0.00			0.993			0.994
Reaction to severe stress, and adjustment disorders	104	2	1.92	4.56	1.070-19.431	0.040	4.912	1.138-21.204	**0.033**
Acute and transient psychotic disorders	123	1	0.81	1.906	0.257-14.141	0.528	1.835	0.245-13.742	0.555
Others	320	3	0.94	2.201	0.664-7.293	0.197	2.030	0.607-6.790	0.250

[a]adjusted; ref: reference.

manifestation of syphilis with central nervous system (CNS) involvement. Although early neurosyphilis mainly involves meningeal and vascular structures, parenchymal effects of the brain and spinal cord appear in the later stages of neurosyphilis. It presents with symptoms of meningitis, meningeal vasculitis, and substantial neurosyphilis (manifested by syncope and general paralysis). Neurosyphilis often begins with psychiatric symptoms [12], Clinically, it can model a variety of psychiatric disorders such as depression, psychosis, mania, delirium, personality change, and dementia [1]. However, the clinical and pathological manifestations of neurosyphilis are diverse and non-specific, such as depressive symptoms, schizophrenia-like symptoms, and anxiety symptoms, and can also lead to cognitive decline [13-18]. It has been suggested that cognitive decline may be one of the main symptoms of neurosyphilis [18]. The clinical manifestations of neurosyphilis are different in different stages, and it needs to be differentiated from a variety of mental disorders [19-22]. Neurosyphilis can occur at any age and should be of great concern to the population [23-25].

Patients with neurosyphilis and psychiatric symptoms were often misdiagnosed as a primary psychiatric disorder such as schizophrenia or bipolar disorder [26,27]. Previous studies have shown that patients with schizophrenia are at increased risk for syphilis. In addition, patients with severe schizophrenia are at higher risk of being infected with sexually transmitted pathogens such as syphilis and HIV compared to other populations [5]. Studies have shown that *TP* infection can aggravate mental symptoms [4]. This study showed that elderly patients with mental disorders have a high positive rate of syphilis antibody. Therefore, it is necessary to improve the understanding of neurosyphilis, especially for elderly patients with mental symptoms as the main manifestation [16].

Studies have shown that globally, there are more than 10 million new cases of syphilis infection every year, and more than 90% of them occur in developing countries [5], several European countries have also seen an increase in syphilis rates in recent years [6,7,28,29]. It has been suggested that the prevalence of syphilis is higher in people with mental illness than in people without mental illness [9,30], patients with mental disorders are at high risk of syphilis infection [31]. According to Friedrich *et al.*, current epidemiological data and difficulties in differential diagnosis of neurosyphilis still recommend routine screening tests in the field of psychiatry, and people with mental health problems may be at higher risk of contracting syphilis [4]. A study in Brazil showed that the point prevalence of HIV, syphilis, hepatitis B, and hepatitis C was higher compared to studies of other non-psychotic population probability samples in Brazil. Severe mental health conditions associated with lower risk perception and cognitive impairment may partially explain these indicators [5,9]. In the study by Lorenza *et al.*, the prevalence of syphilis among persons with mental illness ranged from 1.1% to 7.6% [5]. In recent years, the positive rate of syphilis antibodies in patients with mental disorders in China ranged from 0.64% to 8.71%, with great regional differences [32-36]. Compared with the existing studies, the positive rate of syphilis serum antibodies in patients with mental illness in the study region may be at a low level. Although the incidence of neurosyphilis is very low, it is necessary to suspect neurosyphilis in patients with symptoms of psychiatric disorders [37]. Serological screening for syphilis should be carried out in high-risk groups such as neuropsychiatric disorders to prevent the onset of syphilis and help to eliminate syphilis [38].

A study in Guizhou, China, found that the rate of syphilis infection among local men increased with age [39], similar to the results in the psychiatric population in this study. However, it does not explain why the positive rate of syphilis increases with age. It may be that as people get older, they are sexually active for longer periods and therefore have a higher chance of infection. More relevant research is needed to explore this. A study in Xiamen, China, suggests that people with mental illness are at high risk for *TP* infection. In addition, people with schizophrenia who are infected with syphilis may be more irritable [31]. Therefore, follow-up studies can focus on a specific subtype of mental illness for analysis.

Serological methods have become the main means of syphilis diagnosis, including chemiluminescence immunoassay (CMIA), *TP* particle agglutination test (TPPA), *TP* hemagglutination test (TPHA), and rapid plasma reagin flocculation test (RPR). It is generally accepted that if CMIA and TPPA are positive, the serologic result of syphilis is considered positive regardless of whether the RPR test result is positive or not [40]. The sensitivity and specificity of chemiluminescence immunoassays (CMIA), *TP* hemagglutination tests (TPHA), and others are not affected by infection activity and remain positive throughout the patient's life [41,42]. Therefore, the positive rate of syphilis antibodies may be an additive process with increasing age and could not well reflect the current status of syphilis infection. More precise cohort studies are needed to study the incidence of

syphilis in different age groups to understand the distribution of syphilis in different age groups of patients with mental illness.

Conclusions

The seroprevalence of syphilis was higher in patients with "Nonorganic sleep disorders" and "Reaction to severe stress, and adjustment disorders". The seroprevalence of syphilis in patients with mental illness in this study area may be relatively low. Age and psychosis types became the influencing factors of seroprevalence of syphilis in patients with mental illness. Based on the seroprevalence of *TP* in patients with mental disorders in this study, the available epidemiological data and epidemiological characteristics, and the difficulty in the differential diagnosis of neurosyphilis, routine *TP* screening is still recommended in the field of psychiatry.

Limitations

In recent years, there have not been many studies on the infection rate of syphilis in patients with mental disorders. In this study, the effects of age, region, and different types of mental disorders on the positive rate of serum syphilis antibody in patients with mental disorders were not explained by sufficient references. Subsequent studies should add data on syphilis infection in the general population to better interpret the results of this study.

Acknowledgements

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Authors' contributions

Taixiu Liu analyzed the data and wrote this manuscript, and Peng Gao initiated the study and designed the protocol. Wu Li and Xinhui Lv provided guidance on the study design. Heng Zhang and Zheng Shi conducted the serum concentration test. All authors read and approved the final manuscript.

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