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ORIGINAL RESEARCH

Prevalence and Clinically Related Factors of Hypertriglyceridemia in Patients with Bipolar Disorder in Anhui Province, China

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Purpose: The prevalence of comorbid hypertriglyceridemia in patients with bipolar disorder has received international attention. This study aims to explore the prevalence and clinical factors of comorbid hypertriglyceridemia in patients with bipolar disorder (BD) in Anhui, China.

Patients and Methods: A total of 1072 patients with bipolar disorder were recruited from a large specialized hospital in Anhui, China. Demographic and clinical data were collected. Univariate and multivariate regression analyses were performed to assess the association between hypertriglyceridemia and various clinical variables.

Results: The prevalence of hypertriglyceridemia in patients with bipolar disorder in Anhui Province was 22.6%. Compared with patients without hypertriglyceridemia, patients with hypertriglyceridemia were older, and had higher body mass index (BMI), blood glucose, total cholesterol, alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT) and uric acid levels, and lower high-density lipoprotein level. Multiple Logistic regression analysis showed that BMI (OR=1.51, p<0.001, 95% CI=1.23–1.84), blood glucose (OR=1.21, p<0.001, 95% CI=1.09–1.33), total cholesterol (OR=2.88, p<0.001, 95% CI=2.34–3.55) were positively associated with the risk of hypertriglyceridemia, while high-density lipoprotein cholesterol (OR=0.07, p<0.001, 95% CI=0.03–0.15) showed the opposite association. The nomogram developed from these findings demonstrates an area under the curve (AUC) of 0.803 (95% CI: 0.772–0.834), with a sensitivity of 0.770 and a specificity of 0.727. Consequently, it serves as an effective instrument for assessing the risk of hypertriglyceridemia.

Conclusion: The prevalence of hypertriglyceridemia in patients with bipolar disorder is higher than that in the general population in Anhui, China, and its prevalence is related to BMI, blood glucose and other factors, which needs to be paid attention to and relevant measures should be taken.

Keywords: metabolic syndrome, body mass index, fasting blood glucose, total cholesterol, high-density lipoprotein cholesterol, cross-sectional study

Introduction

Bipolar disorder (BD) is a persistent mental health condition characterized by recurrent episodes of depression interspersed with periods of mania or hypomania.[1] According to findings from the Global Burden of Disease (GBD) study, bipolar disorder is ranked as the sixth leading cause of illness burden attributable to mental and substance use disorders, as measured by disability-adjusted life-years (DALYs).[2] The implications of bipolar disorder extend beyond the individual, significantly affecting both the physical and mental well-being of patients, while also imposing substantial economic burdens on families and society at large.[3–5] In the clinical management of bipolar disorder, mood stabilizers and antipsychotic medications, including lithium (Li), valproate (VPA), and quetiapine, are predominantly utilized.

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Research has indicated that patients with bipolar disorder are at an increased risk of developing metabolic disorders following pharmacological treatment, with hypertriglyceridemia being particularly pronounced among these conditions.[6,7]

Patients diagnosed with bipolar disorder who also present with comorbid metabolic diseases exhibit more complex clinical manifestations, face greater challenges in treatment, experience poorer prognoses, and have an increased risk of depressive episodes.[8] Triglycerides serve as a critical lipid marker in the context of metabolic diseases,[9] and elevated triglyceride levels can not only precipitate metabolic disturbances but also heighten the risk of atherosclerosis, diabetes, and pancreatitis.[10–15] Recent research indicates a correlation between elevated triglyceride levels in individuals with bipolar disorder and increased left ventricular wall thickness, which subsequently raises the risk of heart failure.[16] Furthermore, it is noteworthy that the mortality rate associated with vascular diseases stemming from hypertriglyceridemia in this patient population is approximately double that of the general population,[17] marking it as a significant contributor to mortality among individuals with bipolar disorder.

Research conducted across various countries and regions has consistently demonstrated that the prevalence of hypertriglyceridemia among individuals diagnosed with bipolar disorder is significantly higher than that observed in the general population, with notable variations in prevalence rates. For instance, a study in the Netherlands reported a comorbidity rate of hypertriglyceridemia of 35.3% among patients with bipolar disorder, in stark contrast to a rate of 20.1% in the control group.[18] Similarly, in Spain, the prevalence was found to be 36.1%,[19] while in Taiwan, a study of outpatients with bipolar disorder indicated a prevalence rate as high as 36.8%.[20] Furthermore, in Pennsylvania, United States, 41% of patients with bipolar disorder met the diagnostic criteria for hypertriglyceridemia.[21] These discrepancies in prevalence rates may be attributed to a multitude of factors, including geographical location, ethnicity, lifestyle choices, and healthcare standards. Consequently, there is a pressing need for further research to explore these variations across different regions.

In addition to pharmacological influences, researchers have identified several potential factors that may account for the elevated prevalence of comorbid hypertriglyceridemia among individuals diagnosed with bipolar disorder. From a lifestyle perspective, individuals with bipolar disorder frequently exhibit poor dietary and exercise habits, which can predispose them to hypertriglyceridemia.[22] Regarding physiological mechanisms, studies indicate that the levels of peroxisome proliferator-activated receptor gamma (PPARγ) in patients with bipolar disorder are significantly lower than those observed in control groups. PPARγ functions as a critical regulator of immune and metabolic processes, and its diminished levels may facilitate an increase in triglyceride concentrations.[23] Furthermore, external factors such as substance use, including alcohol and nicotine, are more prevalent among patients with bipolar disorder, which can substantially elevate the risk of developing hypertriglyceridemia.[24]

Moreover, the sample sizes reported in the existing literature are typically constrained. This comprehensive cross-sectional study aimed to investigate the prevalence of hypertriglyceridemia and its related clinical factors in patients diagnosed with bipolar disorder in Anhui Province, China. The goal was to provide substantial scientific evidence that could enhance the prevention and management strategies for both mental health disorders and cardiovascular diseases by conducting a thorough analysis of the clinical characteristics associated with these two conditions.

Material and Methods

Participants

This extensive cross-sectional study involved patients diagnosed with bipolar disorder (male/female ratio = 552/520, depressive episode/manic episode ratio = 375/697) who were admitted to the Affiliated Psychological Hospital of Anhui Medical University. The demographic information and test results of the patients were collected anonymously from the electronic health record system. The inclusion criteria for the study were as follows: 1) patients diagnosed with bipolar disorder according to the ICD-10 criteria, confirmed by two or more attending psychiatrists; 2) patients aged between 18 and 60 years; 3) no history of antidepressant, antipsychotic, or other medication use within three months prior to enrollment; 4) absence of alcohol, tobacco, or other substance dependence; and 5) no history of convulsive electroconvulsive therapy in the preceding three months. The exclusion criteria included: 1) pregnant or

lactating women; 2) individuals with neurodegenerative diseases, such as congenital neurodevelopmental delay or Alzheimer's disease; and 3) patients with organic brain diseases or severe physical illnesses. To mitigate confounding factors, the study adhered strictly to these criteria, resulting in the inclusion of 1,072 patients with bipolar disorder. This study was performed in line with the principles of the Declaration of Helsinki. The study was approved by the Medical Ethics Committee (AMHC) of Anhui Mental Health Center. Because of the retrospective nature of the study and the fact that all data (including basic personal information and detailed medical records) were collected anonymously and encrypted, the Ethics Committee waived the requirement to obtain informed consent.

Demographic Variables

Comprehensive demographic data were gathered from patients diagnosed with bipolar disorder who satisfied the specified inclusion criteria. The variables assessed included sex, age, educational attainment, age at onset of the disorder, duration of the illness, marital status, height, and weight. Body Mass Index (BMI) was computed using the formula weight in kilograms divided by height in meters squared. In accordance with the "Guidelines for the Prevention and Control of Overweight and Obesity in Chinese Adults", body weight was categorized into four classifications based on BMI, with corresponding numerical values assigned for analytical purposes: a BMI of less than 18.5 was classified as underweight (0), a BMI ranging from 18.5 to less than 24 was categorized as normal weight (1), a BMI from 24 to less than 28 was designated as overweight (2), and a BMI of 28 or greater was classified as obesity (3).

Clinical Assessment

Blood samples were obtained from each patient between 6 a.m. and 8 a.m. following an overnight fast of 8 to 12 hours. The samples were promptly transported to the hospital's laboratory department for analysis within one hour of collection. Plasma biochemical parameters were assessed using a commercial automatic biochemical analyzer. The parameters measured included blood glucose, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), apolipoprotein A1 (ApoA1), apolipoprotein B (ApoB), and uric acid levels. According to the Chinese Blood Lipid Management Guidelines 2023, hypertriglyceridemia is defined as a fasting blood triglyceride concentration of 150 mg/dL (1.7 mmol/L) or higher.[25]

Statistical Analysis

The analysis was performed using the R programming language. To evaluate the normality of continuous independent variables, the Shapiro–Wilk test and QQ plot were utilized. For continuous variables that conformed to a normal distribution, a *t*-test was conducted, while the Wilcoxon rank-sum test was applied to continuous variables that exhibited a skewed distribution. Categorical variables were assessed using the Chi-square test. Following this, a multivariate analysis was carried out on independent variables that demonstrated statistical significance ($p<0.05$) in the univariate analysis. The variance inflation factor (VIF) was calculated to detect multicollinearity among the independent variables, with a VIF threshold exceeding 5 indicating the presence of multicollinearity. After excluding independent variables that contributed to multicollinearity, logistic regression was employed to investigate their association with hypertriglyceridemia. The Akaike information criterion (AIC) was used to determine the combination of independent variables that minimized the AIC value. In this study, a significance level of $p<0.05$ was established.

Results

Sociodemographic Data

This study encompassed a total of 1,072 eligible patients diagnosed with bipolar disorder, comprising 829 individuals in the non-hypertriglyceridemia cohort and 243 individuals in the hypertriglyceridemia cohort. The observed prevalence of hypertriglyceridemia among patients with bipolar disorder was determined to be 22.6%. The median age of participants in the hypertriglyceridemia group was 33.4 years, which was significantly older than the median age of 30 years in the non-hypertriglyceridemia group. Furthermore, the prevalence of overweight (38.3%)

and obesity (30.0%) was markedly higher in the hypertriglyceridemia group compared to the non-hypertriglyceridemia group. Conversely, the incidence of underweight (1.6%) and normal weight (30.0%) individuals was considerably lower in the hypertriglyceridemia group than in the non-hypertriglyceridemia group. Statistical analysis revealed no significant differences in the type of bipolar episode, gender, height, systolic blood pressure, or educational attainment between the two groups ($p>0.05$). However, both age and weight were significantly greater in the hypertriglyceridemia group compared to the non-hypertriglyceridemia group ($p<0.001$). (Refer to Table 1 for additional details).

Table 1 Demographic and Clinical Characteristics of Patients with Bipolar Disorder with or Without Hypertriglyceridemia

Parameter	Overall (n=1072)	Without HTG (n=829)	With HTG (n=243)	t/z/X^2	p
Age, years	31.00 [24.00, 42.00]	30.00 [23.00, 41.00]	33.40 [27.00, 45.00]	16.6	<0.001
Age of onset, years	22.00 [17.90, 29.21]	22.00 [17.00, 28.75]	24.00 [19.00, 32.50]	16.8	<0.001
Course of disease, years	6.00 [3.00, 12.00]	6.00 [3.00, 12.00]	8.00 [3.21, 13.00]	17.4	0.015
Height, m	1.68 (0.08)	1.68 (0.08)	1.68 (0.08)	0.991	0.315
Weight, kg	68.24 (13.58)	66.46 (12.73)	74.31 (14.64)	7.56	<0.001
BMI, n(%)				67	<0.001
Low weight	62 (5.8)	58 (7.0)	4 (1.6)		
Normal weight	503 (46.9)	430 (51.9)	73 (30.0)		
Overweight	326 (30.4)	233 (28.1)	93 (38.3)		
Obesity	181 (16.9)	108 (13.0)	73 (30.0)		
Education, years	12.00 [9.00, 15.00]	12.00 [9.00, 15.00]	12.00 [9.00, 15.00]	18.5	0.876
Sex, n(%)				2.76	0.093
Female	520 (48.5)	414 (49.9)	106 (43.6)		
Male	552 (51.5)	415 (50.1)	137 (56.4)		
Marital status, n(%)				10.2	0.006
Unmarried	422 (39.4)	344 (41.5)	78 (32.1)		
Married	479 (44.7)	349 (42.1)	130 (53.5)		
Other	171 (16.0)	136 (16.4)	35 (14.4)		
Systolic pressure, mmHg	120.00 [118.00, 126.00]	120.00 [118.00, 126.00]	120.00 [120.00, 129.00]	17.6	0.054
Diastolic pressure, mmHg	80.00 [72.00, 80.00]	80.00 [71.00, 80.00]	80.00 [76.00, 80.00]	17	0.001
Type of onset, n(%)				1.69	0.17
Depression	375 (35.0)	281 (33.9)	94 (38.7)		
Mania	697 (65.0)	548 (66.1)	149 (61.3)		
Psychotic symptoms, n(%)				4.18	0.038
No	753 (70.2)	569 (68.6)	184 (75.7)		
Yes	319 (29.8)	260 (31.4)	59 (24.3)		

(*Continued*)

Table 1 (Continued).

Parameter	Overall (n=1072)	Without HTG (n=829)	With HTG (n=243)	t/z/X^2	p
Diabetes, n(%)				11.4	0.001
No	1033 (96.4)	808 (97.5)	225 (92.6)		
Yes	39 (3.6)	21 (2.5)	18 (7.4)		
Fasting blood glucose, mmol/L	4.84 [4.47, 5.35]	4.78 [4.42, 5.25]	5.05 [4.72, 5.73]	15.8	<0.001
ALT, U/L	16.00 [10.00, 27.00]	14.00 [10.00, 23.00]	23.00 [14.00, 38.00]	15.2	<0.001
AST, U/L	18.00 [14.00, 26.00]	18.00 [14.00, 25.00]	20.00 [15.50, 30.00]	17	0.001
ALP, U/L	66.00 [54.00, 81.00]	65.00 [53.00, 79.00]	72.00 [58.00, 88.00]	16.7	<0.001
GGT, U/L	18.00 [13.00, 29.00]	16.00 [12.00, 24.00]	28.00 [17.00, 43.50]	14.3	<0.001
TC, mmol/L	4.10 (0.94)	3.94 (0.87)	4.65 (0.95)	10.4	<0.001
HDL-C, mmol/L	1.17 [1.01, 1.36]	1.20 [1.03, 1.38]	1.09 [0.93, 1.26]	20.7	<0.001
Uric acid, μmol/L	360.26 (110.21)	353.31 (108.89)	383.97 (111.59)	3.79	<0.001
Apo A1, g/L	1.19 [1.04, 1.41]	1.19 [1.04, 1.40]	1.19 [1.01, 1.41]	18.5	0.93
Apo B, g/L	0.78 (0.24)	0.74 (0.22)	0.92 (0.25)	10.7	<0.001

Notes: Data are presented as mean ± standard deviation, median (interquartile range), or percentage.
Abbreviations: HTG, hypertriglyceridemia; BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate transaminase; ALP, alkaline phosphatase; GGT, glutamyltransferase; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; Apo A1, apolipoprotein A1; Apo B, apolipoprotein B.

Clinical Symptoms and Metabolic Parameters

In comparison to the non-hypertriglyceridemia cohort, the hypertriglyceridemia cohort exhibited a significantly greater prevalence of diabetes (p=0.002). Furthermore, the hypertriglyceridemia group demonstrated markedly elevated levels of blood glucose, ALT, AST, ALP, GGT, TC, uric acid, and apolipoprotein B, all of which were significantly higher than those observed in the non-hypertriglyceridemia group (p<0.001). Conversely, the high-density lipoprotein (HDL) levels in the hypertriglyceridemia group were significantly lower than those in the non-hypertriglyceridemia group (p<0.001). No significant difference was found in the levels of apolipoprotein A1 between the two groups (p>0.05) (see Table 1).

Risk Factors

In order to investigate the risk factors associated with comorbid hypertriglyceridemia in individuals diagnosed with bipolar disorder, the variance inflation factor was employed to assess multicollinearity among the independent variables. Subsequently, multivariate logistic regression analysis was conducted to identify the risk factors for comorbid hypertriglyceridemia in this patient population (refer to Table 2). The results of the logistic regression analysis indicated that

Table 2 Analysis of Risk Factors Associated with Hypertriglyceridemia in Patients with Bipolar Disorder

Parameter	B	Wald	p	OR	95% CI
BMI	0.41	16	<0.001	1.51	1.23–1.84
Glu	0.19	13.3	<0.001	1.21	1.09–1.33
TC	1.1	100	<0.001	2.88	2.34–3.55
HDL-C	−2.66	50	<0.001	0.07	0.03–0.15

Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index; Glu, fasting blood glucose; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol.

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BMI (OR = 1.51, p < 0.001, 95% CI = 1.23–1.84), blood glucose levels (OR = 1.51, p < 0.001, 95% CI = 1.23–1.84), and TC (OR = 2.88, p < 0.001, 95% CI = 2.34–3.55) were identified as significant risk factors for comorbid hypertriglyceridemia in patients with bipolar disorder. Conversely, HDL-C was found to be a protective factor against comorbid hypertriglyceridemia, with an odds ratio of 0.07 (p < 0.001, 95% CI = 0.03–0.15).

In light of the aforementioned findings, we have successfully developed a clinically applicable nomogram designed to accurately assess the individualized risk of hypertriglyceridemia among patients with bipolar disorder in Anhui Province, China (refer to Figure 1). This model integrates four independent risk factors: BMI, fasting blood glucose (Glu), TC, and HDL, thereby establishing a multi-dimensional risk assessment framework. The classification of BMI is as follows: a BMI of less than 18.5 is categorized as underweight (0), a BMI between 18.5 and 24 is classified as normal weight (1), a BMI between 24 and 28 is considered overweight (2), and a BMI of 28 or greater is classified as obesity (3). Each predictor variable is assigned a corresponding scale within the nomogram's coordinate system, allowing clinicians to swiftly ascertain the risk score associated with each indicator through a vertical mapping method (for instance, a BMI of 28 kg/m² yields a maximum score of 13 points, while a Glu level of 18 mmol/L corresponds to 35 points). By summing the scores of all variables (with a total score range of 0–180 points), clinicians can directly interpret the risk of hypertriglyceridemia for patients with bipolar disorder in Anhui Province on the risk probability axis. The nomogram demonstrates robust predictive performance and clinical utility, effectively differentiating between high-risk and low-risk patients. It serves as an intuitive visualization tool for clinicians, facilitating the development of personalized prevention and intervention strategies, thereby enhancing treatment outcomes and the quality of life for patients.

The model's capacity to differentiate between patients diagnosed with bipolar disorder and those exhibiting hypertriglyceridemia in Anhui Province, China, was assessed utilizing Receiver Operating Characteristic (ROC) plots (refer to Figure 2). The area under the curve (AUC) for models employing individual independent variables—namely BMI, blood glucose, total cholesterol, and high-density lipoprotein—was recorded at 0.659 (95% CI: 0.623–0.696), 0.632 (95% CI: 0.623–0.696), 0.716 (95% CI: 0.623–0.696), and 0.616 (95% CI: 0.623–0.696), respectively. The AUC serves as a critical metric for evaluating the model's discriminative ability, with values approaching 1 indicating enhanced

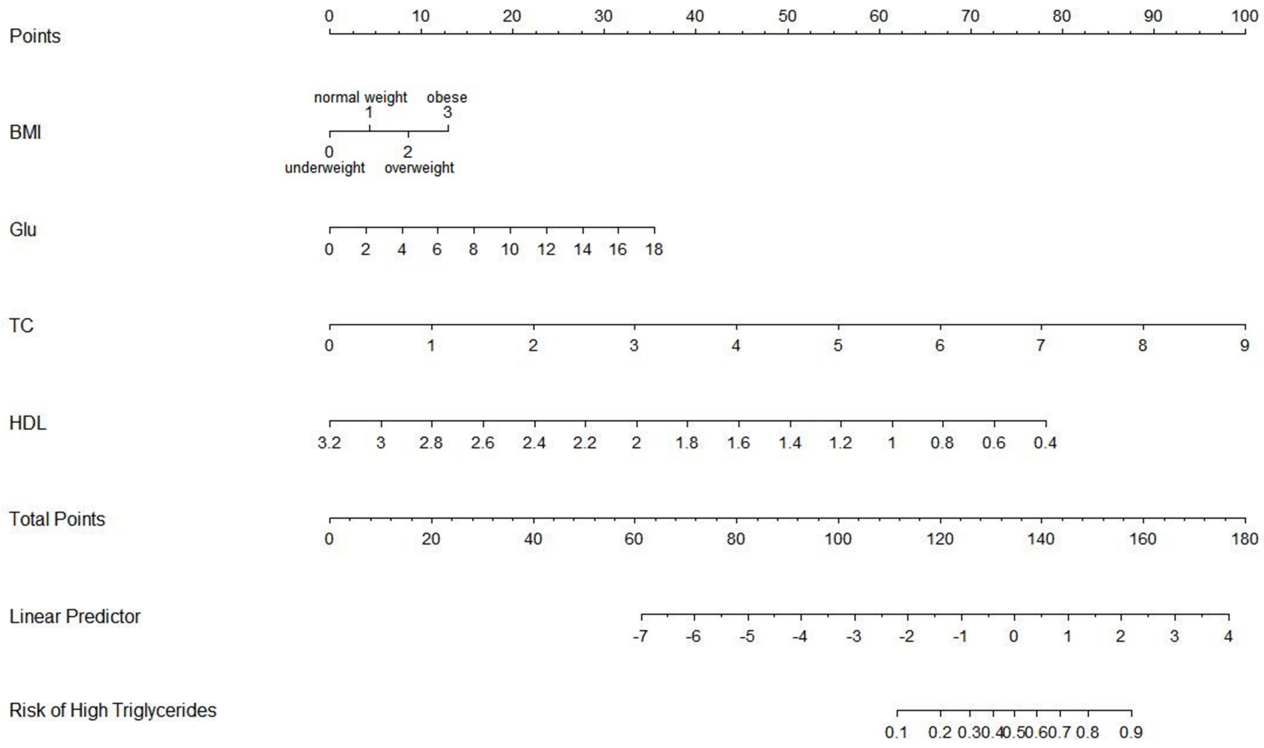

Figure 1 Nomogram to evaluate hypertriglyceridemia in patients with bipolar disorder in Anhui, China.
Abbreviations: BMI, body mass index; Glu, fasting blood glucose; TC, total cholesterol; HDL, high-density lipoprotein.

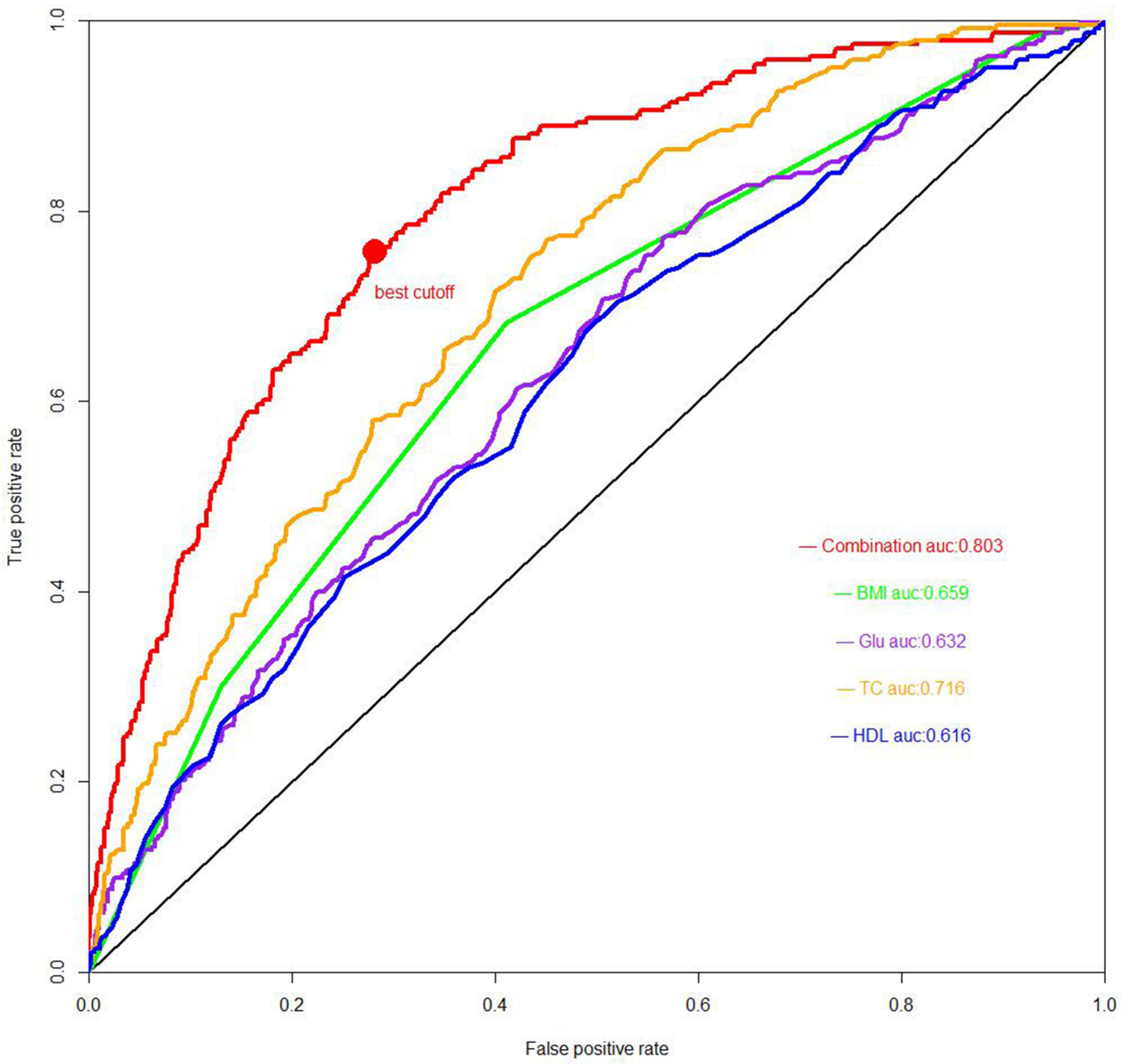

Figure 2 Ability of related factors to discriminate between bipolar disorder patients with and without hypertriglyceridemia. The area under the curve (AUC) of BMI, Glu, TC, HDL and their combination were 0.659 (95% CI: 0.623–0.696), 0.632 (95% CI: 0.623–0.696), 0.716 (95% CI: 0.623–0.696), 0.616 (95% CI: 0.623–0.696) and 0.803 (95% CI: 0.772–0.834), respectively. Best cutoff means a specific value on the abscisce and ordinate, which represents the optimal combination of sensitivity and specificity of the test: specificity: 0.727, sensitivity:0.770.

Abbreviations: BMI, body mass index; Glu, fasting blood glucose; TC, total cholesterol; HDL, high-density lipoprotein.

discrimination. Importantly, the AUC for the composite model incorporating all four variables reached 0.803 (95% CI: 0.772–0.834), significantly surpassing the AUC values of any individual variable. This finding underscores the efficacy of our multivariate integration in augmenting the model's ability to discern whether patients with bipolar disorder also present with hypertriglyceridemia. Furthermore, the optimal cutoff point for the combined model demonstrated a sensitivity of 0.770 and a specificity of 0.727, indicating that this threshold effectively balances high sensitivity with adequate specificity for the identification of patients at elevated risk for hypertriglyceridemia.

Discussion

This study, for the first time, investigated the prevalence of hypertriglyceridemia among individuals diagnosed with bipolar disorder in Anhui, China, revealing a rate of 22.6%. In contrast, a prevalence rate of 12.2% was recorded within

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the general population of Anhui, China.[26] Additionally, the study identified BMI, blood glucose levels, and TC as significant risk factors for hypertriglyceridemia in this patient population, while HDL was identified as a protective factor. The logistic regression model developed in this study, incorporating these four variables, effectively estimated the risk of comorbid hypertriglyceridemia in Chinese patients with bipolar disorder residing in Anhui province.

The incidence of hypertriglyceridemia among Chinese patients diagnosed with bipolar disorder in Anhui Province is reported to be 22.6%. In comparison, the reported international statistics indicate that the prevalence is 41% in Pennsylvania,[21] 35.3% in the Netherlands,[18] 36.1% in Spain,[19] and 36.8% in Taiwan.[20] The current study benefits from a substantial inpatient sample size, in contrast to other investigations that either employed smaller sample sizes or included outpatient populations, which may account for the observed discrepancies in prevalence rates. Furthermore, variations in lifestyle factors, food safety regulations, dietary customs, exercise patterns, and other regional characteristics may also contribute to these differences. For instance, dietary habits characterized by high saturated fat, carbohydrate intake, or elevated glycemic index, alongside the prevalence of physical activities such as walking or cycling, as well as patterns of excessive alcohol consumption, could significantly influence lipid profiles. Additionally, regional disparities in the selection and utilization of pharmacological treatments for bipolar disorder may be influenced by local healthcare systems, the rigor of monitoring adverse drug reactions, and practices regarding the timely adjustment of medication dosages or substitutions.

Further investigation indicated that the BMI of patients diagnosed with bipolar disorder in the hypertriglyceridemia cohort was significantly elevated compared to those in the non-hypertriglyceridemia cohort, a finding that aligns with the outcomes of the Spanish study.[19] This phenomenon may be attributed to various underlying mechanisms. In individuals with bipolar disorder, elevated triglyceride levels can adversely affect cognitive functioning, resulting not only in diminished cognitive flexibility[27] but also heightening the risk of executive function impairment.[3] Executive function encompasses several critical domains, including action planning, inhibition, and impulse control, all of which are vital for the long-term objective of sustaining a healthy weight.[28] When executive function is compromised, adherence to a regular dietary regimen becomes challenging, thereby predisposing the individual to an increase in BMI. Furthermore, an elevated BMI contributes to the accumulation of body fat, particularly in the abdominal region, which subsequently enhances the liver's synthesis of very low-density lipoprotein (VLDL), leading to a direct rise in plasma triglyceride levels and perpetuating a detrimental cycle. Consequently, it is imperative for clinicians to implement weight management strategies for patients with bipolar disorder who present with a BMI above the normal range.

The present study identified a significant positive correlation between triglyceride levels and total cholesterol in individuals diagnosed with bipolar disorder. Research conducted by Patel et al further substantiates this finding, indicating that patients exhibiting hypertriglyceridemia are at an increased risk for elevated total cholesterol levels.[29] This relationship may be attributed to the unhealthy dietary patterns frequently observed in individuals with bipolar disorder, which often include high sugar and high fat consumption. Elevated sugar intake is a primary contributor to increased triglyceride levels, while a diet rich in fats is associated with heightened total cholesterol levels.[30] Both triglycerides and cholesterol are critical components of blood lipids, and their abnormal concentrations are not only closely linked but can also lead to mixed hyperlipidemia when both are elevated, posing significant health risks.

Furthermore, individuals diagnosed with bipolar disorder who also present with elevated triglyceride levels exhibit a markedly heightened risk of abnormal blood glucose levels, a finding that aligns with the research conducted by Calkin CV et al[31,32] This association may be attributable to the administration of atypical antipsychotic medications.[33] Additionally, functional genetic variants in the MTNR1B gene have been shown to impede insulin secretion in patients with bipolar disorder, resulting in increased fasting blood glucose levels.[34] Moreover, the characteristic sleep disturbances associated with bipolar disorder not only elevate inflammatory markers but also contribute to heightened levels of stress hormones, such as cortisol, which can further exacerbate blood glucose levels. Conversely, certain studies have indicated that elevated triglyceride levels may independently induce insulin resistance and compromise β-cell functionality, thereby leading to impaired fasting glucose.[35] Given the cumulative impact of these various risk factors, patients with bipolar disorder who also experience hypertriglyceridemia are at an increased risk for abnormal blood glucose levels. Consequently, it is imperative to closely monitor blood glucose abnormalities in this patient population.

The aforementioned variables, including BMI, TC, and blood glucose levels, exhibit a positive correlation with triglyceride levels. Notably, patients with bipolar disorder who present with hypertriglyceridemia demonstrate significantly lower levels of HDL compared to those without hypertriglyceridemia, a finding that aligns with the research conducted by Langsted et al[36,37] Firstly, cognitive impairments in individuals with bipolar disorder may lead to dietary preferences that are high in sugars and fats, which can subsequently lower serum HDL levels. This reduction in HDL levels diminishes its anti-inflammatory and antioxidant functions, thereby exacerbating the cognitive deficits experienced by these patients and creating a detrimental feedback loop.[38,39] Secondly, from a lipoprotein metabolism perspective, cholesteryl ester transfer protein (CETP) facilitates the transfer of cholesteryl esters (CE) from HDL to apolipoprotein B-containing lipoproteins (VLDL and low-density lipoprotein [LDL]) in exchange for TG when triglyceride levels are elevated. This exchange results in the production of smaller, denser HDL particles that are enriched with triglycerides and metabolized more rapidly, leading to decreased HDL levels.[40] Furthermore, research by Chatterjee et al indicates that HDL engages in component exchange with triglyceride-rich lipoproteins to lower TG levels, suggesting that higher concentrations of HDL facilitate the normalization of TG levels, thereby highlighting the interaction between TG and HDL.[41] Previous investigations have demonstrated that managing sugar and carbohydrate intake,[29] as well as increasing the consumption of Omega-3 fatty acids,[42] can effectively reduce TG levels and enhance HDL levels. Consequently, it is imperative for clinicians to consider the dietary and lifestyle habits of patients with bipolar disorder and to implement proactive interventions aimed at improving lipid management and preventing cardiovascular diseases.

Several limitations of this study merit consideration. Firstly, the cross-sectional design utilized does not allow for the clarification of causal relationships between the variables and comorbid hypertriglyceridemia, nor does it capture the dynamic fluctuations of these variables among individuals with bipolar disorder. Secondly, the sample was confined to hospitalized patients with severe mental disorders, thereby excluding outpatients with less severe conditions, which may introduce a potential bias in the statistical analysis. Thirdly, the study did not address the lifestyle habits of patients with bipolar disorder, such as smoking, dietary choices, and physical activity, which could be critical factors in the assessment of comorbid hypertriglyceridemia. Fourthly, although the study population consisted of individuals who had not received medication in the three months prior to the study, the possible impact of previous medication on the findings cannot be overlooked. Lastly, despite the relatively large sample size, the data were collected from a single-center study, which may restrict the generalizability of the results to the wider population in Anhui, China. Given these limitations, future research should consider employing time series analysis to investigate the prevalence and clinical significance of hypertriglyceridemia in patients with bipolar disorder, including both outpatients and healthy controls, thereby expanding the study's scope and accounting for lifestyle factors and psychiatric medication history. This approach would provide more comprehensive and accurate evidence to guide clinical diagnosis and treatment.

Conclusion

This study presents, for the first time, the prevalence of hypertriglyceridemia among patients diagnosed with bipolar disorder in Anhui Province, China, and elucidates its significant correlation with various clinical indicators. This study contributes novel epidemiological data and clinical relevance to the existing literature in this domain, although the results may not be applicable to the broader population of patients with bipolar disorder in China, given that the sample was obtained from a single inpatient facility. Our findings indicate that the prevalence of hypertriglyceridemia in this population is 22.6%. Multivariate analysis identified BMI, blood glucose levels, and TC as critical risk factors for hypertriglyceridemia, while HDL emerged as a significant protective factor. Consequently, it is imperative for clinical practitioners to routinely monitor serum HDL and TC levels in patients with bipolar disorder and to closely observe trends in these parameters to facilitate the timely identification of dyslipidemia. Additionally, given the elevated rates of overweight and obesity among this patient population, it is essential to implement screening for these conditions. Encouraging patients who are overweight or obese to manage their body weight through appropriate dietary modifications, increased physical activity, and other lifestyle changes may not only enhance their lipid profiles and mitigate the risk of hypertriglyceridemia but could also positively influence the overall prognosis of bipolar disorder and decrease the likelihood of cardiovascular diseases and other related complications. Future research should consider employing multicenter longitudinal cohort studies in conjunction with genomics, metabolomics, and other omics technologies to further

investigate the molecular mechanisms underlying comorbid hypertriglyceridemia in patients with bipolar disorder, as well as the impact of various treatment strategies on lipid levels and disease outcomes.

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Disclosure

The authors report no conflicts of interest in this work.

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