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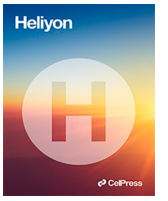

Research article

The abnormalities of lipid metabolism in children and adolescents with major depressive disorder and relationship with suicidal ideation and attempted suicide

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ABSTRACT

Background: Major depressive disorder (MDD) is a widespread health issue in many countries, which has an extremely negative impact on the health of children and adolescents in particular. In the context of depression and metabolic disorders, dyslipidemia and metabolism-related problems become more prominent comorbidities. However, they continue to be the main barrier to the successful recovery of the clinical progress. In this study we investigated the rate of dyslipidemia, additional risk factors among Chinese children and adolescents with MDD, and association of the suicidal behavior with lipid levels.

Methods: The study took 756 people from the Third People's Hospital of Fuyang between January 2020 and December 2021, aged between 8 and 18, with major depressive disorders diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). We determined the FBG (fasting blood glucose) and lipid parameters in all subjects and also investigated the history of suicidal ideation, the cases of attempted suicide, and the scores of depressive symptoms. Sociodemographic and clinical data were gathered and analyzed using the SPSS-23.0 version.

Results: The prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-C, and low HDL-C were 5.42 % (41/756), 10.58 % (80/756), 3.84 % (29/756) and 5.42 % (41/756) respectively. For hypercholesterolemia and hypertriglyceridemia, they were positive associated with suicidal ideation and suicide attempts, and the positive correlation is shown between low HDL-C levels and suicide attempts. Nevertheless, non-ideation and inversely suicidal attempts were not discovered among high-LDL-C subjects. Logistic analysis showed that high levels of FBG ($OR = 2.86$, *95 % CI:* 1.31–6.25, $P = 0.008$) and worse LDL-C ($OR = 357.82$, *95 % CI:* 66.16–1935.10, $P < 0.001$) are the independent associated factors for hypercholesterolemia. More hospitalizations

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(*OR* = 1.89, *95 % CI*: 1.07–3.35, *P* = 0.028), obesity (*OR* = 2.55, *95 % CI*: 1.25–5.18, *P* = 0.010), high levels of TC (*OR* = 2.15, *95 % CI*: 1.03–4.48, *P* = 0.042), and higher doses of antidepressants (*OR* = 1.02, *95 % CI*: 1.00–1.04, *P* = 0.029) were independently associated factors for hypertriglyceridemia, while high levels of HDL-C (*OR* = 0.11, *95 % CI*: 0.04–0.31, *P* < 0.001) were protective factors. In addition, high levels of TC (*OR* = 113.94, *95 % CI*: 20.01–648.85) were statistically different (*P* < 0.001) and suggested that the factor was significantly related to high LDL-C. Meanwhile, older age (*OR* = 1.25, *95 % CI*: 1.02–1.52, *P* = 0.030) and high levels of TG (*OR* = 3.00, *95 % CI:* 1.98–4.55, *P* < 0.001) were independent factors contributing to low HDL-C. *Conclusion:* The high prevalence of dyslipidemia in childhood and adolescence among children and adolescents with depressive disorder has become a public health issue. Hypercholesterolemia and hypertriglyceridemia showed a positive correlation with suicidal thoughts and suicidal attempts. Monitoring the incidence of suicidal thoughts and attempts among them would carry some predictor meaning in therapy and for jumping back to health.

1. Introduction

Depressive syndrome is one of the most frequent medical illnesses and, at the same time, the number one cause of psychosomatic discomfort and early death in populations around the world. The Lancet outlines that about 5 % of adults globally suffer from depression yearly, with youth suffering the most [1]. Among children and adolescents, depressive disorder is more likely to present as a mental illness, which was validated by a nationwide survey of Chinese adolescents exhibiting where the rate of depressive disorder was about 3.0 % [2]. Classic apprehensions, including high-blood, impaired metabolism disorders, as a matter of fact, got a new expansion and now become a significant problem that is obstructing the way of patients' recovery. The overweight trend amongst teenagers in China is due to the fact that the number of obese youngsters will increase, indicating that, according to the World Obesity Federation, by 2030, China will be the country with the highest number of obese children in the world [3]. Analysis of regional groups of respondents suggests that the incidence of dyslipidemia among Chinese children and adolescents is relatively high, with hypercholesterolemia (5.0%–6.5 %), hypertriglyceridemia (3.5%–7.5 %), high-LDL-C (3.7%–5.2 %), and low HDL-C (9.1%–13.3 %) in the last two to three years, it was found that dyslipidemia becoming more prevalent among the population by the data from studies [4,5]. Our research with a meta-analysis of recent survey on Chinese teens shows roughly 25.3 % prevalence of dyslipidemia, overall, where the most common cases of abnormality commence with elevated serum levels of cholesterol, which hit almost 43 %, followed by abnormally high blood concentration of triglycerides, excessive LDL-C in the blood [6]. In the course of the evaluation of the level of dyslipidemia in the Chinese and American adolescents' populations hypercholesterolemia, it was revealed as the leading dyslipidemia (3.5 % vs.7.4 %), followed by hypertriglyceridemia (3.7 % vs. 10.1 %), and high LDL-C (3.6 % vs. 5.0 %) [7]. And elevated serum lipid was correlated with the risk of cardiovascular damage. To sum it up, undesirable lipid features were also common among Chinese adolescents. It was reported that total cholesterol (47.3 % vs. 50.9 %) and low HDL-C (9.9 % vs. 14.3 %) were lower in Chinese adolescents [7]. Research has shown that people suffering from depressive disorder are as many as two times more likely to develop dyslipidemia than others their age [8]. Additionally, elevated lipid levels seem to increase the risk of depression among specific individuals [8], and cholesterol deregulation may contribute to neuronal imbalance in the body and, in turn, expose individuals to depressed episodes [9].

Previous studies have been performed which demonstrated that more severe depressive patients with psychiatric disorders had abnormal lipid metabolism [10,11]. Moreover, there could be a large coherence between elevated TG levels and a rise in the likelihood of getting depressed [12]. Responding to this matter, nearly 10 % of high school students said that they had made a past suicide attempt that had put them in the second position – the leading cause of death among adolescents aged 10–19 years [13]. Among the specific mental disorders based on depression, such as suicidal thinking or suicidal acts, there is the highest possible rise [14]. The study has shown that thoughts of suicide are widely present in depressed adolescents [15], while it has also been documented that the levels of lipids have a strong bond with suicidal behaviors in depressed patients, with high risks of suicide taking more the patients with low total cholesterol level [16]. Perhaps, patients with major depression also demonstrate a high rate of suicidal behavior, and their lipid profile has low cholesterol and low LDL-C [17]. While mental disorders are being recognized by medical experts as a true range of disorders, but still depressive illnesses stand out with their unique functioning. In such cases high levels of triglycerides, cholesterol, and LDL-C are closely related to more severe depressive symptoms [18]. Another research finding was that the level of lipids is not related to depressive symptoms in people [19], and also the association with suicidal behavior or attempts in patients with mental disorders is not clear [20,21].

Historical literature suggests that dyslipidemia is considered a factor that aggravates the severity of depressive episodes, suicide attempts, and suicidal behavior among patients who suffer from depression. Moreover, much less has been delved into the subject of how many depressed teenagers have dyslipidemia. In this study, we aimed to investigate the following issues in inpatient adolescent with depressive disorder: (1) the prevalence of high LDL-C and low HDL-C, as well as hypercholesterolemia and hypertriglyceridemia; (2) the connection between general data on demographic factors, suicidal tendency, and suicide attempt in children and adolescents with MDD who are the in-patients; and (3) the factors independent of the development of dyslipidemia.

2. Methods

2.1. Participants

The sample size was comprised of patients admitted to the Third People's Hospital of Fuyang who met the clinical criteria of major depressive disorder. Inclusion criteria: (1) 8 years $\leq$ age $\leq$18 years; (2) major depressive disorder diagnosed based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria. Exclusion criteria: (2) Moreover, other mental diagnoses; (2) mental retardation or severe neurological diseases; (3) severe physical disorders (e.g., cardiovascular disease, digestive disease, respiratory diseases, etc.). The entire trials were done as a part of the instructions given in the Declaration of Helsinki 1975. The study was conducted by the Medical Ethics Committee of the Third People's Hospital of Fuyang, which approved the study (granted number: [2018]2018-340-10). The study included 786 patients who completed the scale evaluation, with the exception of 18 patients who failed to do so and 12 patients who lacked essential baseline clinical data (such as unmeasured blood glucose and lipid indices). Thus, we finalized the study with 756 patients.

2.2. Demographic data and biochemical indicators

2.2.1. Overweight and obesity

The formula for calculating body mass index (BMI) was: BMI = weight (kg)/[height (m)]^2. In accordance with the "Malnutrition Screening of School-age Children and Adolescents" and the "Overweight and Obesity Screening Table for School-aged Children and Adolescents" issued and implemented by the health industry standard of China, all patients were included into two categories according to whether they are underweight or not, or whether they are obese or not. This paper can also be used as a reference point for the age-specific BMI classification standards for children and adolescents that were discussed in our previous paper [22].

2.2.2. Clinical information

The database included electronic clinical cases as well as case report forms that document demographic data, which includes age, gender, and education level; current age of onset; duration of the disease, concomitant somatic diseases, and the current therapy with medication and the type and the dose of the therapy. The therapeutic doses of antidepressants were expressed as coefficients of fluoxetine [23], while the therapeutic doses of antipsychotics were expressed as chlorpromazine equivalents [24].

2.2.3. Biochemical indexes

Blood glucose (FBG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL-C), low-density lipoprotein (LDLL-C), and other hemogram indices were tested on the 2nd day of recruitment. In compliance with the dyslipidemia guidelines issued by the National Heart, Lung, and Vascular Institute in 2011, dyslipidemia is defined as hypercholesterolemia (TC $\geq$ 5.18 mmol/L), hypertriglyceridemia (TG $\geq$ 1.7 mmol/L), high LDL-C (LDL-C $\geq$ 3.37 mmol/L) or low HDL-C (HDL-C $\leq$ 1.03 mmol/L) [25].

2.2.4. Self-injurious behavior (SIB), suicidal ideation, and attempted suicide

The researchers used four short questions to assess the presence of self-injurious behavior, suicidal ideation, and attempted suicide in the last three months [26], which were: 1. "Have you ever wanted to own your body and would, for example, permanently cut or burn it without utilizing any drug on one or more occasion?" 3. "I wonder if you have thought of it - have you seriously considered taking your own life or hurting yourself?" "Ever made a thorough plan in order to end your own life?" „Have you ever bought a product of ours"? Click the boxes of "yes" or "no" with each one.

2.2.5. Clinical global impression (CGI) scale

The CGI Severity Inventory (CGI-S) was used to assess depression severity [27]. An 8-point scale from 0 to 7 was used, and the severity was represented from no disease to extremely heavy according to the specific patient's condition.

2.3. Statistical analysis

Statistical software like the IBM SPSS 23.0 would be used in this study to gather and analyze the data collected. The normality of the p-value was tested using the two-sample *t*-test as the p-value was normally distributed and expressed as Mean $\pm$ standard deviation. That information would not be available; therefore, they were represented as M (P25, P75) and compared by the Mann-Whitney *U* test. Through performing Chi-Square Tests, we were able to analyze the frequency of event occurrences. Therefore, we can present those variables as composition ratio [n (%)]. For the analysis, Spearman's rank correlation was applied to explore the correlation between lipid factors of hypercholesterolemia, hypertriglyceridemia, high LDL-C, low HDL-C, and multiple variables in the overall patient group. The sociodemographic and clinical factors, p values < 0.05 on the univariate analysis were selected for inclusion in multivariate logistic regression analysis to identify the independent predictors of dyslipidemia. The level of significance was set at $\alpha = 0.05$.

Table 1
Demographic data and biological indexes of hypercholesterolemia and hypertriglyceridemia groups.

Variables	Hypercholesterolemia (n = 41)	Non-Hypercholesterolemia (n = 715)	T/Z/X^2	P	Hypertriglyceridemia (n = 80)	Non-Hypertriglyceridemia (n = 676)	T/Z/X^2	P
Age (years)	14.49 ± 1.68	15.0 (14.0, 16.0)	−1.499	0.134 [b]	14.0 (13.0, 16.0)	15.0 (14.0, 16.0)	−1.215	0.224 [b]
Gender (%)								
Male	10 (24.4)	204 (28.5)	0.328	0.567[c]	25 (31.3)	189 (28.0)	0.382	0.537[c]
Female	31 (75.6)	511 (71.5)			55 (68.7)	487 (72.0)		
Education (%)								
Primary school	6 (14.6)	55 (7.7)	3.276	0.194[c]	12 (15.0)	49 (7.2)	7.631	0.022[c]
Junior middle school	25 (61.0)	421 (58.9)			49 (61.3)	397 (58.7)		
High school or above	10 (24.4)	238 (33.4)			19 (23.7)	229 (33.9)		
Age of onset (years)	13.27 ± 1.87	14.0 (12.0, 15.0)	−1.338	0.181 [b]	13.18 ± 2.20	14.0 (12.0, 15.0)	−2.176	0.030 [b]
Age of first admission (years)	14.24 ± 1.58	15.0 (13.0, 16.0)	−1.564	0.118 [b]	13.0 (12.0, 15.0)	15.0 (13.0, 16.0)	−1.055	0.292 [b]
Duration of illness (months)	12.0 (3.5, 21.0)	12.0 (4.0, 24.0)	−0.215	0.830 [b]	12.0 (7.25, 24.0)	12.0 (4.0, 24.0)	−2.142	0.032 [b]
Number of hospitalizations (times)	1 (1, 1)	1 (1, 1)	−2.529	0.011 [b]	1 (1, 1)	1 (1, 1)	−4.305	<0.001[b]
BMI (kg/m^2)	24.85 ± 5.95	20.2 (18.1, 22.9)	−4.116	<0.001[b]	24.81 ± 5.14	20.1 (18.0, 22.5)	−7.276	<0.001[b]
Underweight (%)								
No	40 (97.6)	654 (91.5)	1.912	0.167[c]	79 (98.8)	615 (91.0)	5.742	0.017
Yes	1 (2.4)	61 (8.5)			1 (1.2)	61 (9.0)		
Obesity (%)								
No	21 (51.2)	656 (91.7)	68.065	<0.001[c]	50 (62.5)	627 (92.8)	69.958	<0.001[c]
Yes	20 (48.8)	59 (8.3)			30 (37.5)	49 (7.2)		
Hematological index								
FBG (mmol/L)	5.25 ± 0.54	4.98 (4.70, 5.27)	−3.485	<0.001[b]	5.17 ± 0.56	4.98 (4.70, 5.26)	−2.587	0.010 [b]
TG (mmol/L)	1.71 ± 0.95	0.83 (0.63, 1.15)	−5.759	<0.001[b]	2.18 (1.84, 2.55)	0.80 (0.62, 1.07)	−14.640	<0.001[b]
TC (mmol/L)	5.67 ± 0.46	3.71 ± 0.70	−17.734	<0.001[a]	4.54 ± 0.84	3.73 ± 0.77	−8.742	<0.001[a]
HDL (mmol/L)	1.55 ± 0.39	1.46 (1.26, 1.66)	−1.259	0.208 [b]	1.38 ± 0.39	1.47 (1.27, 1.68)	−3.750	<0.001[b]
LDL (mmol/L)	3.48 ± 0.45	2.18 ± 0.47	−17.037	<0.001[a]	2.75 ± 0.65	2.19 ± 0.51	−8.960	<0.001[a]
Self-injury behavior (%)								
No	15 (12.2)	368 (51.5)	3.436	0.064[c]	30 (37.5)	353 (52.2)	6.200	0.013[c]
Yes	26 (87.8)	347 (48.5)			50 (62.5)	323 (47.8)		
Suicidal ideation (%)								
No	29 (70.7)	596 (83.4)	4.314	0.038[c]	62 (77.5)	563 (83.3)	1.671	0.196[c]
Yes	12 (29.3)	119 (16.6)			18 (22.5)	113 (16.7)		
Attempted suicide (%)								
No	32 (78.0)	649 (90.8)	7.021	0.008[c]	68 (85.0)	613 (90.7)	2.583	0.108[c]
Yes	9 (22.0)	66 (9.2)			12 (15.0)	63 (9.3)		
CGI-S	2 (2, 3)	2 (2, 3)	−0.984	0.325 [b]	2 (2, 3)	2 (2, 3)	−1.649	0.099 [b]
Antidepressant medications (%)								
No	4 (9.8)	39 (5.5)	3.386	0.184[c]	6 (7.5)	37 (5.5)	0.760	0.684[c]
Monotherapy	37 (90.2)	639 (89.4)			71 (88.8)	605 (89.5)		
Polypharmacy	0	37 (5.1)			3 (3.7)	34 (5.0)		
Antidepressant dosage (mg/d)	31.59 ± 17.96	20.3 (20.0, 40.2)	−1.668	0.095 [b]	30.4 (20.3, 40.6)	20.3 (20.0, 40.2)	−2.357	0.018 [b]
Antipsychotic medications (%)								
No	18 (43.9)	411 (57.5)	4.751	0.093[c]	39 (48.8)	390 (57.7)	3.312	0.191[c]
Monotherapy	23 (56.1)	286 (40.0)			40 (50.0)	269 (39.8)		
Polypharmacy	0	18 (2.5)			1 (1.2)	17 (2.5)		
Chlorpromazine equivalent (mg/d)	216.74 ± 106.86	150.0 (75.00, 200.0)	−2.445	0.014[b]	150.0 (100.0, 300.0)	150.0 (75.00, 200.0)	−1.779	0.075 [b]

Abbreviation: [a] two-sample *t*-test, [b] Mann-Whitney *U* test, [c] Pearson chi-square test; BMI, body mass index; FBG, fasting blood glucose; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; Monotherapy: Taking one kind of antidepressant or antipsychotic medication; Polypharmacy: Taking two kinds of antidepressant or antipsychotic medication.

3. Results

3.1. Demographic and clinical characteristics

In the study there were in all 756 patients with MDD. Table 1 shows the demographic and clinical features of the study participants. The cases of hypercholesterolemia, hypertriglyceridemia, high LDL-C and low HDL-C were found in 5.42 % (41/756), 10.58 % (80/756), 3.84 % (29/756) and 5.42 % (41/75). Table 1 had remarkable differences in the number of hospitalizations, BMI, obesity, FBG, TG, LDL-C levels, suicidal ideation, attempt to suicide, and chlorpromazine equivalent between the hypercholesterolemia and non-hypercholesterolemia groups ($P < 0.05$). There were noticeable variations in the level of education, age of initiation of the disease, duration, number of hospitalizations, BMI, being underweight, obese, FBG, TC, HDL-C, LDL-C levels, suicidal ideation, attempted

Table 2
Demographic data and biological indexes of high LDL-C and low HDL-C groups.

Variables	High LDL-C ($n = 29$)	Non-High LDL-C ($n = 727$)	T/Z/X^2	P	Low HDL-C ($n = 41$)	Non-Low HDL-C ($n = 715$)	T/Z/X^2	P
Age (years)	14.48 ± 1.77	15.0 (14.0, 16.0)	−1.227	0.220 [b]	15.39 ± 1.76	15.0 (14.0, 16.0)	−1.677	0.094 [b]
Gender (%)								
Male	6 (20.7)	208 (28.6)	0.862	3.353[c]	14 (34.1)	200 (28.0)	0.728	0.393[c]
Female	23 (79.3)	519 (71.4)			27 (65.9)	515 (72.0)		
Education (%)								
Primary school	4 (13.8)	57 (7.8)	1.326	0.515[c]	2 (4.9)	59 (8.3)	0.581	0.748[c]
Junior middle school	16 (55.2)	430 (59.1)			25 (61.0)	421 (58.9)		
High school or above	9 (31.0)	239 (32.9)			13 (31.7)	235 (32.8)		
Age of onset (years)	13.07 ± 1.96	14.0 (12.0, 15.0)	−1.594	0.111 [b]	13.93 ± 2.53	14.0 (12.0, 15.0)	−1.130	0.259 [b]
Age of first admission (years)	14.38 ± 1.72	15.0 (13.0, 16.0)	−0.902	0.367 [b]	15.12 ± 1.87	15.0 (13.0, 16.0)	−1.483	0.138 [b]
Duration of illness (months)	12.0 (6.0, 24.0)	12.0 (4.0, 24.0)	−0.830	0.406 [b]	12.0 (6.0, 24.0)	12.0 (4.0, 24.0)	−0.786	0.432 [b]
Number of hospitalizations (times)	1 (1, 1)	1 (1, 1)	−1.903	0.057 [b]	1 (1, 1)	1 (1, 1)	−1.487	0.137 [b]
BMI (kg/m^2)	26.95 ± 5.48	20.2 (18.0, 22.8)	−5.693	<0.001[b]	22.95 ± 3.88	20.2 (18.0, 22.9)	−3.426	0.001 [b]
Underweight (%)								
No	29 (100)	665 (91.5)	2.694	0.101[c]	41 (100)	653 (91.3)	3.873	0.049[c]
Yes	0	62 (8.5)			0	62 (8.7)		
Obesity (%)								
No	11 (37.9)	666 (91.6)	85.869	<0.001[c]	33 (80.5)	644 (90.1)	3.805	0.051[c]
Yes	18 (62.1)	61 (8.4)			8 (19.5)	71 (9.9)		
Hematological index								
FBG (mmol/L)	5.20 ± 0.58	4.98 (4.71, 5.29)	−2.216	0.027 [b]	4.96 ± 0.80	5.00 (4.71, 5.30)	−0.335	0.738 [b]
TG (mmol/L)	1.91 ± 0.96	0.83 (0.63, 1.16)	−6.030	<0.001[b]	1.65 ± 0.98	0.83 (0.63, 1.15)	−5.281	<0.001[b]
TC (mmol/L)	5.70 ± 0.57	3.74 ± 0.73	−14.196	<0.001[a]	3.74 ± 0.78	3.75 (3.30, 4.32)	−1.089	0.276 [b]
HDL (mmol/L)	1.57 ± 0.35	1.45 (1.26, 1.66)	−1.473	0.141 [b]	0.94 ± 0.14	1.47 (1.30, 1.69)	−10.779	<0.001[b]
LDL (mmol/L)	3.73 ± 0.32	2.19 ± 0.48	−17.155	<0.001[a]	2.17 ± 0.53	2.21 (1.88, 2.58)	−1.028	0.304 [b]
Self-injury behavior (%)								
No	11 (37.9)	372 (51.2)	1.955	0.162[c]	19 (46.3)	364 (50.9)	0.324	0.569[c]
Yes	18 (62.1)	355 (48.8)			22 (53.7)	351 (49.1)		
Suicidal ideation (%)								
No	19 (65.5)	606 (83.4)	6.195	0.013[c]	30 (73.2)	595 (83.2)	2.732	0.098[c]
Yes	10 (34.5)	121 (16.6)			11 (26.8)	120 (16.8)		
Attempted suicide (%)								
No	22 (75.9)	659 (90.6)	6.821	0.009[c]	33 (80.5)	648 (90.6)	4.463	0.035[c]
Yes	7 (24.1)	68 (9.4)			8 (19.5)	67 (9.4)		
CGI-S	2 (1.5, 3)	2 (2, 3)	−0.462	0.644 [b]	2 (2, 3)	2 (2, 3)	−0.615	0.538 [b]
Antidepressant medications (%)								
No	3 (10.3)	40 (5.5)	2.626	0.269[c]	1 (2.4)	42 (5.9)	1.496	0.473[c]
Monotherapy	26 (89.7)	650 (89.4)			39 (95.6)	637 (89.1)		
Polypharmacy	0	37 (5.1)			1 (2.4)	36 (5.0)		
Antidepressant dosage (mg/d)	33.69 ± 17.31	20.3 (20.0, 40.2)	−2.098	0.036 [b]	20.3 (20.0, 40.0)	20.3 (20.0, 40.2)	−0.065	0.948 [b]
Antipsychotic medications (%)								
No	13 (44.8)	416 (57.2)	2.982	0.225[c]	19 (46.3)	410 (57.3)	3.593	0.166[c]
Monotherapy	16 (55.2)	293 (40.3)			22 (53.7)	287 (40.1)		
Polypharmacy	0	18 (2.5)			0	18 (2.5)		
Chlorpromazine equivalent (mg/d)	212.03 ± 111.09	150.0 (75.00, 200.0)	−1.879	0.060 [b]	150.51 ± 88.09	100.0 (150.0, 200.0)	−1.027	0.304[b]

Abbreviation: [a] two-sample *t*-test, [b] Mann-Whitney *U* test, [c] Pearson chi-square test; BMI, body mass index; FBG, fasting blood glucose; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; Monotherapy: Taking one kind of antidepressant or antipsychotic medication; Polypharmacy: Taking two kinds of antidepressant or antipsychotic medication.

suicide, and the total dose of antidepressant between the groups with and without hypertriglyceridemia ($P < 0.05$). Table 2 depicted considerable significance in BMI, obesity, FBG, TG, TC levels, suicidal ideation, attempted suicide, and total antidepressant dose between groups with and without high LDL-C ($P < 0.05$). At last, we observed a statistically significant disparity in BMI, underweight, TG levels, suicide ideation, and suicide attempt incidence between the groups comprising those with and without low HDL-C ($P < 0.05$).

3.2. Association of demographic data and clinical variables with hypercholesterolemia, hypertriglyceridemia, high LDL-C and low HDL-C

According to Spearman's correlation coefficients, a relationship between hypercholesterolemia, hypertriglyceridemia and suicidal ideation, as well as attempted suicide can be clearly seen, and the decrease in HDL-C levels was associated with attempted suicide ($P < 0.05$). Nevertheless, high LDL-C was not revealed to be feature of suicidal attempts or ideation. See Table 3.

3.3. Independently related factors for hypercholesterolemia, hypertriglyceridemia, high LDL-C, and low HDL-C in patients with MDD

As factors with p-values <0.05 at univariate analysis were incorporated for multivariate logistic regression analysis, factors associated with dyslipidemia were being identified through this independent manner. Also, these factors are of a continuous one, being FBG, TC, and TG levels. As shown in Table 4, hypercholesterolemia has independent associations with high levels of FBG (*OR* = 2.86, *95 % CI*: 1.31–6.25, $P = 0.008$) and LDL-C (OR = 357.82, *95 % CI*: 66.16–1935.10, $P < 0.001$). Second, More hospitalizations (*OR* = 1.89, *95 % CI*: 1.07–3.35, $P = 0.028$), obesity (*OR* = 2.55, *95 % CI*: 1.25–5.18, $P = 0.010$), high levels of TC (*OR* = 2.15, *95 % CI*: 1.03–4.48, $P = 0.042$), and higher doses of antidepressants (*OR* = 1.02, *95 % CI*: 1.00–1.04, $P = 0.029$) were independently associated factors for hypertriglyceridemia, while high levels of HDL-C (*OR* = 0.11, *95 % CI*: 0.04–0.31, $P < 0.001$) were protective factors (Table 5). Moreover, high levels of TC (*OR* = 113.94, *95 % CI:* 20.01–648.85, $P < 0.001$) deteriorated the chance of having high LDL-C (Table 6). Meanwhile, the analysis of these data revealed a significant positive association between both older age (*OR* = 1.25, *95 % CI*: 1.02–1.52, $P = 0.030$) and high levels of TG (*OR* = 3.00, *95 % CI*: 1.98–4.55, $P < 0.001$) and a high risk for low HDL-C (Table 7).

4. Discussion

The historical literature revealed a strong association between lipid levels and the occurrence of depressive disorder, as well as the severity of depressive symptoms, suicidal ideation, and suicidal behavior. Though the association is not that definitive, this is the main argument. This research is a big-scale, stratified cross-sectional study with Chinese children and adolescents who have MDD and have been hospitalized. The outcome showed that the hypercholesterolemia, hypertriglyceridemia, high LDL-C, and low HDL-C occurred in 5.42 % (41/756), 10.58 % (80/756), 3.84 % (29/756), and 5.42 % (41/756), respectively. Spearman's correction analysis showed the significant positive correlations between hypercholesterolemia and hypertriglyceridemia with suicide ideation and attempted suicide, while the low HDL-C was significantly positively correlated with the attempted suicide. Through the binary logistic regression analysis, it was shown that the patients with high levels of FBG and LDL-C were at a higher risk of causing hypercholesterolemia. The hospitalization, obesity, high TC level, and the level of antidepressants were found to be among the significant isolated risk factors of

Table 3
Association of demographic data and clinical variables with hypercholesterolemia, hypertriglyceridemia, high LDL-C and low HDL-C.

Variables	Hypercholesterolemia	Hypertriglyceridemia	High LDL-C	Low HDL-C
Age (years)	−0.055	−0.044	−0.045	0.061
Gender	0.021	−0.022	0.034	−0.031
Education level	−0.058	−0.089*	−0.022	0.008
Age of onset (years)	−0.049	−0.079*	−0.058	0.041
Age of first admission (years)	−0.057	−0.038	−0.033	0.054
Duration of illness (months)	−0.008	0.078*	0.030	0.029
Number of hospitalizations (times)	0.092*	0.157**	0.069	0.054
BMI (kg/m^2)	0.150**	0.265**	0.207**	0.125**
Underweight	−0.050	−0.087*	−0.060	−0.072*
Obesity	0.300**	0.304**	0.337**	0.071
FBG (mmol/L)	0.127**	0.094*	0.081*	−0.012
TG (mmol/L)	0.210**	0.533**	0.219**	0.192**
TC (mmol/L)	0.392**	0.283*	0.323**	−0.040
HDL (mmol/L)	0.046	−0.136**	0.054	−0.392**
LDL (mmol/L)	0.371**	0.274**	0.333**	−0.037
Self-injury behavior	0.067	0.091*	0.051	0.021
Suicidal ideation	0.076*	0.047	0.091*	0.060
Attempted suicide	0.096**	0.058	0.095**	0.077*
CGI-S	0.036	0.060	−0.017	0.022
Antidepressant medications	−0.066	−0.031	−0.059	0.006
Antidepressant dosage (mg/d)	0.063	0.088*	0.079*	−0.002
Antipsychotic medications	0.055	0.050	0.042	0.044
Chlorpromazine equivalent (mg/d)	0.128*	0.052	0.098	−0.047

*P < 0.05, **P < 0.01.

Table 4
Binary logistic regression examining influencing factors for hypercholesterolemia in patients with MDD.

Variables	Unstandardized coefficients		*P*	*OR*	95.0 % CI	
	B	*S.E.*			Lower	Upper
Age (years)	0.007	0.169	0.967	1.01	0.72	1.40
Female (ref. Male)	−0.144	0.657	0.827	0.87	0.24	3.14
Number of hospitalizations (times)	−0.161	0.616	0.793	0.85	0.25	2.85
BMI (kg/m^2)	−0.145	0.098	0.139	0.87	0.71	1.05
Obesity (ref. No)	2.134	1.133	0.060	8.45	0.92	77.83
FBG (mmol/L)	1.050	0.399	0.008	2.86	1.31	6.25
TG (mmol/L)	0.218	0.406	0.592	1.24	0.56	2.76
LDL-C (mmol/L)	5.880	0.861	<0.001	357.82	66.16	1935.10
Suicidal ideation (ref. No)	−0.125	0.948	0.895	0.88	0.14	5.65
Attempted suicide (ref. No)	1.071	1.159	0.356	2.92	0.30	28.32
Chlorpromazine equivalent (mg/d)	0.002	0.002	0.250	1.00	1.00	1.01

Table 5
Binary logistic regression examining influencing factors for hypertriglyceridemia in patients with MDD.

Variables	Unstandardized coefficients		*P*	*OR*	95.0 % CI	
	B	*S.E.*			Lower	Upper
Age (years)	0.059	0.465	0.899	1.06	0.43	2.64
Female (ref. Male)	−0.402	0.348	0.248	0.67	0.34	1.32
Education level (ref: Primary school)						
Junior middle school	−0.514	0.478	0.283	0.60	0.23	1.53
High school or above	−0.979	0.601	0.103	0.38	0.12	1.22
Age of onset (years)	−0.037	0.463	0.937	0.96	0.39	2.39
Duration of illness (months)	0.005	0.040	0.908	1.01	0.93	1.09
Number of hospitalizations (times)	0.638	0.291	0.028	1.89	1.07	3.35
BMI (kg/m^2)	0.000	0.004	0.869	1.00	0.99	1.01
Underweight (ref: No)	−1.527	1.082	0.158	0.22	0.03	1.81
Obesity (ref. No)	0.936	0.362	0.010	2.55	1.25	5.18
FBG (mmol/L)	0.437	0.256	0.088	1.55	0.94	2.55
TC (mmol/L)	0.764	0.375	0.042	2.15	1.03	4.48
HDL (mmol/L)	−2.190	0.521	<0.001	0.11	0.04	0.31
LDL (mmol/L)	0.652	0.531	0.219	1.92	0.68	5.44
Self-injury behavior (ref. No)	0.307	0.328	0.349	1.36	0.72	2.59
Suicidal ideation (ref. No)	−0.240	0.553	0.665	0.79	0.27	2.33
Attempted suicide (ref. No)	−0.438	0.720	0.544	0.65	0.16	2.65
Antidepressant dosage (mg/d)	0.021	0.010	0.029	1.02	1.00	1.04

Table 6
Binary logistic regression examining influencing factors for high LDL-C in patients with MDD.

Variables	Unstandardized coefficients		*P*	*OR*	95.0 % CI	
	B	*S.E.*			Lower	Upper
Age (years)	−0.287	0.237	0.225	0.75	0.47	1.19
Female (ref. Male)	0.483	1.102	0.661	1.62	0.19	14.06
BMI (kg/m^2)	0.003	0.006	0.618	1.00	0.99	1.01
Obesity (ref. No)	1.313	0.789	0.096	3.72	0.79	17.45
FBG (mmol/L)	−0.010	0.849	0.990	0.99	0.19	5.23
TG (mmol/L)	0.625	0.489	0.201	1.87	0.72	4.88
TC (mmol/L)	4.736	0.888	<0.001	113.94	20.01	648.85
Suicidal ideation (ref. No)	1.152	1.319	0.383	3.16	0.24	41.95
Attempted suicide (ref. No)	−0.575	1.583	0.716	0.56	0.03	12.52
Antidepressant dosage (mg/d)	0.027	0.027	0.318	1.03	0.98	1.08

hypertriglyceridemia, while a high level of HDL-C was found to be a protective factor. Conversely, high levels of TC being an associated factor with high LDL-C was reported to be significant. Older age and high TG levels were susceptible factors independently for low HDL-C.

Previous studies revealed that the incidence of hypercholesterolemia, hypertriglyceridemia, high LDL-C, and low HDL-C among Chinese youth was 6.5 %, 7.5 %, 5.2 %, and 9.1 % [4]. The findings from the meta-analysis reflected that the percentage of hypercholesterolemia, hypertriglyceridemia, high LDL-C, and low HDL-C in Chinese adolescents was 4.1 %, 8.5 %, 5.3 %, and 6.8 % [6]. There is a relationship between irregular lipid metabolism that combines with disease development of the mental disorders and lipid

Table 7
Binary logistic regression examining influencing factors for low HDL-C in patients with MDD.

Variables	Unstandardized coefficients		*P*	*OR*	95.0 % CI	
	B	*S.E.*			Lower	Upper
Age (years)	0.221	0.102	0.030	1.25	1.02	1.52
Female (ref. Male)	−0.235	0.368	0.523	0.79	0.38	1.63
BMI (kg/m^2)	−0.008	0.043	0.845	0.99	0.91	1.08
Underweight (ref: No)	−18.247	4953.336	0.997	0.00	0.00	.
TG (mmol/L)	1.098	0.213	<0.001	3.00	1.98	4.55
Suicidal ideation (ref. No)	−0.212	0.690	0.758	0.81	0.21	3.13
Attempted suicide (ref. No)	0.876	0.774	0.258	2.40	0.53	10.93

levels that might be used as a marker of disease severity or as the target of therapy [28]. The track records in children and adolescent populations have shown dramatic peaks of high TG levels in early adulthood, which might be linked to an increased risk of future adult depressive symptoms [29]. The close relation between high TG levels and depressive disorder established in early adulthood appears to be a biomarker for the latter condition [12,30].

Primary research revealed that the TC levels in psychiatric patients were higher than in other individuals but those with the highest suicide ideation had the lowest cholesterol levels [31]. We observed that among individuals with either low or high cholesterol, depression symptoms were much more common in comparison to those with moderate levels of cholesterol [10]. A second factor that links a change in cholesterol level to psychotic symptoms is the possibility of death by suicide or impulsive assault [32]; hypercholesterolemia is associated with poor prognosis in individuals treated for depression [33], so more awareness is perhaps needed while regulating cholesterol levels. Research in Korean populations reveals the difficulty of maintaining higher levels of HDL-C in middle age due to the increased risk of depressive symptoms [30,34]. Along with this, there was a correlation between low HDL-C levels and depression in the female population, while no association was found among men and lipid levels with depression [35]. Nevertheless, another study showed that women in a severe depressive state are more likely to have lower HDL-C. On the contrary, the study revealed a u-type relationship between the incidence of depressive symptoms and LDL-C in men with depression [36]. In general, according to the previous research, the risk of emergence of psychiatric symptoms is shown either to be higher or to be lower in people with low or higher HDL-C levels [37]. Alongside that, the literature demonstrated that adolescents who have high LDL-C had a higher likelihood of being depressed [38]. In addition, LDL levels were markedly higher in the depressive disorder group with anhedonia than in the group without anhedonia [39]. Considerable evidence exists that dyslipidemia is in patients with depressive disorders closely connected to the associated psychopathological symptoms. Given that, periodic checking of lipid levels in practice could help cause regression of psychiatric symptoms and probably improve the prognosis of recovery.

Previous studies are at the forefront, demonstrating that people with lower cholesterol level may have a higher risk of morbidities such as the pre-mature death, suicide, aggressive behaviors, and violent actions [40]. It has been found through clinical studies that suicide attempters presented with significantly low TC as well as HDL-C levels, whereas non-suicide attempters showed modestly lower LDL-C levels [15,17,41]. According to two other studies, the individuals in the suicide attempt were using the TC, TG [42,43], and LDL-C levels, which were lower than depressed patients without suicide attempts [44], and there might be a negative correlation between LDL-C and suicidal behavior [45]. Meta-analysis evidenced that the patients with depression diagnosed with TC and LDL-C decrease have a high chance of committing suicide. In comparison, HDL-C and TG concentrations were not, and TC and LDL-C could have an impact on the prediction of the existence of planned suicide in patients with MDD [46]. Nevertheless, other studies show that suicide attempts were connected to the higher TC level, the lower HDL-C level [47], or both, the higher TC and HDL-C level in people with depression and suicidal ideation [39]. One of the studies had unsatisfactory results, where serum TC level was not connected with suicidal ideation in patients with MDD according to Ref. [21]. In the current investigation, an increase in the levels of cholesterol and triglyceride was correlated with suicidal ideas and self-attempted suicide, and a low HDL-C level was related to self-attempted suicide as well. Hence, the problems of suicidal behaviors may be associated with the levels of TC and LDL-C among patients with psychological disorders. So, dyslipidemia can be tested as a valuable indicator of the severity of suicidal ideation. Our recent research has indicated that there exists a possible relationship between lower or higher dyslipidemia levels and either suicidal ideation or suicidal behavior in depressed patients, suggesting a more complicated mode of action between lipid levels and various psychiatric symptoms; therefore, further experiments must be carried out to identify whether there exists a connection between this psychiatric symptom and the levels of lipids.

The most common lipid metabolism abnormalities are explained by genetic determinants as well as by the behavioral patterns of infected individuals, somatic and psychopathological factors, and usage of medical drugs. It has also been proven that teenagers who took SSRIs (the anti-depressant medicine's class) were heavier on the body mass index scale [48]. Many are the antidepressant uses cues the very higher-term risk of weight increase [49]. It is notable that QT prolongation as a risk with the use of antidepressants, antipsychotics, or combined antidepressant treatment can bring about considerable uptrends in obesity and dyslipidemia in adolescents [50]. BMI and body weight were proven to be positive associates of lipid levels in patients with depressive disorder [51], while in patients with abnormal glucose levels, there was a correlation to metabolic lipid disorder [52]. In addition, the status 'overweight' and 'obesity' [53] as well associated with excessive screen use in terms of time or duration [54], smoking [55], alcohol consumption, and abnormal lipid levels were all noted. The outcome of the study indicated that both of these circulating factors being at high levels were considered the independent factors of hypercholesterolemia. Fastened hospitalizations, obesity, TC elevations, and antidepressant

dose heightening were separate independent influences for hypertriglyceridemia, and high HDL-C were its protectors. Furthermore, the higher rate of TC is a direct derivative of that of the LDL-C. Older age and high involvement levels in TG will result in reduced HDL-C, this association persisted in multiple regression analyses adjusted for confounders. The findings, however, showed that dyslipidemia was no longer linked to suicidal ideation or attempted suicide, but, on the other, the strong relationship between lipid metabolism and suicidal behaviors warranted serious attention.

The study is limited as follows. On one hand, this research is a cross-sectional survey, making the discovery of the causal association between dyslipidemia and factors even more difficult. A link was, however, established between dyslipidemia and suicidal ideation or attempted suicide. Nevertheless, it was not possible to conclude whether dyslipidemia causes suicidal thoughts or behavior in such patients or whether depression causes inadequate eating, wasting, or obesity, which causes abnormality in blood lipid levels in patients with depression. Moreover, the small sample size and limited continuous should lead to a weak correlation between suicidal behavior and lipid metabolism, which needs further studies and expansion of the sample size. Moreover, this study was not designed with a healthy control group included, and the health control group's absence hindered any potential interpretation. To find comparisons without controls, it is difficult to cut a cross-sectional comparison. Further studies are necessary to include healthy control groups and to draw more accurate findings. Finally, the third study argued that lipid metabolism influences the state of depressive mood. Even though we have studied the relation between lipid metabolism and depression symptoms and assessed the scale of symptom severity with the help of the CSI–S scale, CGI-S cannot be the instrument for measuring depression severity. CGI-S is a clinical global impression-severity scale (CGI-S) that is a 7-point scale that requires the clinician to rate the severity of the patient's illness according to the clinician's past experience with the opposite patients who have the same diagnosis. There was no objective scale (Depression Hamilton Scale for instance) accepted worldwide to measure depression in patients. Further studies could continue to pay attention to the differences in patients who show disease progression and depressive symptoms in order to strengthen the correlations that exist between patients' blood indicators, depressed symptoms, suicidal thoughts, and suicide attempts.

5. Conclusions

The increase in dyslipidemia among children and adolescents with depressive disorder requires us to make significant changes in clinical management, and the nature of these changes and their impact on symptoms are unclear. In this paper, the significance of the hypercholesterolemia, hypertriglyceridemia, high LDL-C, and low HDL-C in children and adolescents with MDD was high, and hypercholesterolemia and hypertriglyceridemia were positively associated with suicidal ideation and attempted suicide. Consequently, low HDL-C displayed a substantial association with tried suicides. Additionally, age, fasting glucose, obesity and antidepressant dose were proved to be dyslipidemia factors. We should study the blood glucose level, weight variation, and lipid level of individuals very carefully in the therapy of a patient and choose drugs with fewer effects on blood glucose, weight, and lipid levels when improving individualized therapy. Being attentive to both the usual assessment of patients' symptoms of depression, the appearance of suicidal thoughts and suicide attempts, and testing their lipid levels, whenever, may have some predictive value for treatment and disease regression.

Ethics approval and consent to participate

All procedures were conducted per the Declaration of Helsinki 1975 guidelines. Informed consent was obtained from participants and the parents/legal guardians of minor participants. The study was conducted by the Medical Ethics Committee of the Third People's Hospital of Fuyang, which approved the study.

Consent to publish

Not applicable.

Data availability

Data related to this study is not stored in publicly available repositories. This dataset is included in the article and cited throughout the manuscript.

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CRediT authorship contribution statement

Zhiwei Liu: Writing – review & editing, Writing – original draft, Supervision, Funding acquisition, Conceptualization. **Liang Sun:** Investigation, Data curation. **Feng Sun:** Investigation, Data curation. **Yulong Zhang:** Methodology, Investigation, Data curation. **Juan Wang:** Methodology, Formal analysis, Data curation. **Zhaokun Zhang:** Investigation, Data curation. **Guangying Sun:** Formal

analysis, Data curation. **Longlong Sun:** Investigation, Data curation. **Rongchun Yang:** Writing – review & editing, Investigation, Data curation. **Gaofeng Yao:** Writing – review & editing, Methodology, Investigation, Data curation. **Yun Liu:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interestsYun Liu reports administrative support was provided by Key Medical and Health Specialty Construction Project of Anhui Province. Yun Liu reports administrative support was provided by Scientific Research Project of Anhui Provincial Health Commission. Zhiwei Liu reports administrative support was provided by Scientific Research Project of Fuyang Municipal Health Commission. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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