Metabolic Indexes of Obesity in Major Depressive Disorders

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Abstract

Background Major depressive disorder (MDD) is a chronic common mental disorder. Long-term medication may lead to abnormalities in vivo factors, which cause obesity.

Aim To find out the related factors of obesity by analyzing the metabolic indexes of patients with major depressive disorders of all ages in stable stage.

Methods Subjects with major depressive disorder (MDD) were treated with fixed dose drugs and conventional drugs for 2 years or more. Venous blood was collected and blood metabolic indexes were analyzed.

Results Among MDD, with the increase of age, the risk of obesity increases. Body mass index (BMI) was positively correlated with age, total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), uric acid (UA), alanine aminotransferase (ALT), glycosylated hemoglobin (HbA1c) and high sensitivity C-reactive protein (HsCRP), and high density lipoprotein (HDL). But creative kinase isoenzyme (CK-MB), urea, serum creatinine (SCr) and homocysteine (Hcy) were not correlated with BMI. Multiple linear regression analysis showed that the value of BMI increased with the increase of age ($B = 0.050$, $p = 0.002$), AST ($B = 0.094$, $p = 0.049$), ALT ($B = 0.055$, $p = 0.016$), UA ($B = 0.006$, $p < 0.021$), HbA1c ($B = 0.702$, $p = 0.004$) and hsCRP ($B = 0.101$, $p < 0.001$).

Discussion We should pay more attention to the monitoring of blood metabolism indicators with the increase of age in MDD, and timely adjust the use of drugs timely adjust the use of drugs refer to their liver and kidney function, so as to reduce the risk of obesity and improve their quality of life.

1. Introduction

Major depressive disorder (MDD) is a chronic common mental disorder characterized by continuous depression, lack of motivation to do things and loss of appetite. According to the China mental health survey, its annual prevalence rate was about 4.1%[1]. Regular and continuous use of drug treatment can help alleviate the condition of MDD patients, but long-term drug treatment may lead to obesity, whether it's teenagers, adults or the elderly[2] [3] [4]. Previous studies[5] [6] [7] [8]and our previous research[9]showed that after long-term medication, patients with MDD would have abnormalities in vivo factors, which might cause obesity, increased the risk of other complications, such as circulatory system diseases[2], endocrine system diseases[10] and so on.

Some studies suggested that age, education, drinking, smoking and living habits were related to obesity[11]. In terms of blood metabolic indexes, total cholesterol (TC)[12], uric acid (UA)[13], glycosylated hemoglobin (HbA1c)[14], low density lipoprotein (LDL)[15] and so on were also related to obesity. However, as clinicians, this is not enough. We hope to refine these indicators and monitor targeted

indicators for patients with MDD of different ages, so as to achieve the purpose of early intervention, reduce complications, improve prognosis and promote their health.

Therefore, we collected blood samples from patients in order to find out the blood metabolism indicators affecting obesity in MDD.

2. Method

2.1 Participants

The outpatients and inpatients with MDD were included, who met the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) from July 2016 to May 2021 in the Department of Psychiatry, The Third People's Hospital of Foshan, Guangdong, People's Republic of China. They were divided into adolescent depressive depression (ADD, 14 ≤ age < 18), adult depressive depression (DD, 18 ≤ age < 60) and late-life depression (LLD, 60 ≤ age), according to their age. Meanwhile they were required to maintain a fixed drug dose pattern for 2 years or more (in the stable period) before blood testing.

Exclusion criteria: Comorbidity other mental disorders, including mental retardation or other cognitive impairment; Patients with severe and unstable physical diseases, including severe kidney or liver function damage, cardiac insufficiency, etc; Those who didn't cooperate with venous blood drawing, such as phobia, etc; Smoking habits (≥ 1 cigarette per day) or drinking habits (≥ 1 unit alcohol per week); 1 unit alcohol = 480 ~ 600 ml of beer = 350 ml of low alcohol liquor or red wine, yellow wine = 50 ml of high spirits (40 degrees or more).

2.2 Assessments

The subjects who met the above conditions and were willing to participate, after signed the informed consent form, were collected their names, gender and the age through the interviews. Then, the weight, height and BMI of them were measured with Automatic Measuring Stadiometer BSM370 (smitechasia.com).

According to the diagnostic criteria of overweight and obesity proposed by the China Obesity working group, "24 kg/m^2 ≤ BMI < 28 kg/m^2" was defined as overweight, "BMI ≥ 28 kg/m^2 as obesity" was obesity, and "BMI < 24 kg/m^2" was non obesity[16]. The next step was to draw venous blood. Subjects were required to be fasting for more than 8 hours before drawing the venous blood and the night before blood drawing, were needed to maintain a normal diet, without exercise violently and didn't drink any alcohol or coffee after dinner. Finally, TC, TG, HDL, LDL, AST, ALT, LDH, CK-MB, SCr, UA, HbA1c, HsCRP and Hcy would be recorded in the subject's clinical data sheet for subsequent data analysis.

2.3 Data analyses

We used Statistical Product and Service Solutions 19 software (https://www. ibm.com/analytics/spss-statistics-software) to analyze the data. Chi square test was used to compare the differences of general demographic. The blood metabolic indexes of ADD, DD and LLD were compared by one-way ANOVA. The relationships of BMI and variable indexes were analyzed by Pearson correlation. Multiple linear regression was used to analyze the effects of blood index components on BMI.

3. Result

3.1 Comparison of demographic characteristics and metabolic indexes in MDD of different ages level

There were 205 participants in this study, including ADD (n = 57), DD (n = 98) and LDD (n = 50), while 12 subjects were excluded because of eating breakfast before blood drawing or refusing blood test.

There were no significant differences in gender, height, weight, HDL, AST, ALT, LDH, CK-MB, Hcy among ADD, DD and LDD ($p > 0.05$). And there were significant differences in BMI, TC, TG, LDL, ALT, urea, SCr, UA, HbA1c and HsCRP ($p < 0.05$). The incidence of obesity in ADD, DD and LDD was 8.77%, 9.18% and 14.28% respectively. Overweight was 12.28%, 27.55% and 46.43%.(Table 1)

Table 1
Comparison of demographic characteristics and metabolic indexes

	ADD (n = 57)	DD (n = 98)	LDD (n = 50)	F	p
Age (year)	16.07 ± 1.59	31.70 ± 9.98	64.75 ± 4.87	-	-
Gender (male/female)	17/40	32/66	21/29	1.94	0.379
Height (cm)	162.22 ± 8.02	163.02 ± 7.76	159.49 ± 8.26	2.17	0.117
Weight	56.84 ± 12.89	60.24 ± 11.72	63.08 ± 8.93	2.95	0.055
BMI (kg/m^2)[bc]	21.48 ± 4.01	22.62 ± 3.80	24.79 ± 3.03	7.27	0.001*
Obesity (%)	8.77	9.18	14.28	-	-
Over weight (%)	12.28	27.55	46.43	-	-
Non obesity (%)	78.95	63.27	39.29	-	-
TC (mmol/L)[abc]	4.60 ± 1.08	5.10 ± 1.09	5.55 ± 1.30	15.56	< 0.001*
TG (mmol/L)[bc]	1.17 ± 0.80	1.31 ± 0.77	1.95 ± 1.00	19.61	< 0.001*
HDL (mmol/L)	1.48 ± 0.33	1.51 ± 0.38	1.45 ± 0.47	0.26	0.772
LDL (mmol/L)[ac]	2.46 ± 0.87	2.78 ± 0.84	3.05 ± 0.77	5.13	0.007*
AST (U/L)	18.79 ± 6.99	20.56 ± 10.27	22.14 ± 7.19	1.46	0.236
ALT (U/L)	19.56 ± 15.71	25.31 ± 23.12	25.64 ± 13.49	1.72	0.182
LDH (U/L)	167.02 ± 38.63	167.16 ± 33.73	178.32 ± 31.43	1.02	0.363
CK-MB (U/L)	13.00 ± 4.59	12.21 ± 3.55	13.98 ± 5.74	2.16	0.118
Urea (mmol/L)[bc]	4.23 ± 1.15	4.42 ± 1.17	5.30 ± 1.92	7.06	0.001*
SCr (μmol/L)[abc]	56.82 ± 11.20	63.85 ± 12.64	72.71 ± 25.02	11.55	< 0.001*
UA (μmol/L)[b]	346.07 ± 85.75	326.22 ± 97.62	391.46 ± 122.82	4.50	0.012*
HbA1c (%)[bc]	5.14 ± 0.33	5.30 ± 0.65	5.87 ± 1.09	10.89	< 0.001*
HsCRP (mg/L)[bc]	1.89 ± 2.35	2.53 ± 5.17	3.89 ± 3.54	8.87	< 0.001*
Hcy (μmol/L)	12.09 ± 9.48	11.32 ± 5.87	11.41 ± 5.22	0.21	0.807

Note: ADD, DD, LDD ,TC total cholesterol, TG triglyceride, HDL high density lipoprotein, LDL low density lipoprotein, AST aspartate aminotransferase, ALT alanine aminotransferase, LDH lactate dehydrogenase, CK-MB creatine kinase isoenzyme, urea, SCr serum creatinine, UA uric acid, HbA1c glycosylated hemoglobin, HsCRP hypersensitive C-reactive protein, Hcy homocysteine; a: ADD vs DD, b: DD vs LLD, c: ADD vs LLD, $p < 0.05$; * indicates the comparison among groups ($p < 0.05$); Values are expressed as mean ± standard deviation.

3.2 Pearson correlation between BMI and various indexes in MDD

The results showed that BMI was positively correlated with age, TC, TG, LDL, AST, LDH, UA, ALT, HbA1c and hsCRP, and negatively correlated with HDL. But CK-MB, urea, SCR and Hcy were not correlated with BMI. (Table 2)

Table 2
Pearson correlation between BMI and various indexes

BMI								
Age*	r	0.389	AST*	r	0.172	SCr	r	0.114
	p	< 0.001		p	0.020		p	0.123
TC*	r	0.281	ALT*	r	0.328	UA*	r	0.335
	p	< 0.001		p	< 0.001		p	< 0.001
TG*	r	0.360	LDH*	r	0.251	HbA1c*	r	0.349
	p	< 0.001		p	0.001		p	< 0.001
HDL*	r	-0.262	CK-MB	r	0.037	HsCRP*	r	0.244
	p	< 0.001		p	0.620		p	0.001
LDL*	r	0.369	Urea	r	0.086	Hcy	r	0.013
	p	< 0.001		p	0.245		p	0.862

Note: TC total cholesterol, TG triglyceride, HDL high density lipoprotein, LDL low density lipoprotein, AST aspartate aminotransferase, ALT alanine aminotransferase, LDH lactate dehydrogenase, CK-MB creatine kinase isozyme, urea, SCr serum creatinine, UA uric acid, HbA1c glycosylated hemoglobin, HsCRP hypersensitive C reactive protein, Hcy homocysteine, * indicates $p < 0.05$.

3.3 Multiple linear regression analysis of the infuencing factors of BMI in MDD

Taking BMI as dependent variable (Y) and age, TC, TG, HDL, LDL, AST, ALT, LDH, UA, HbA1c and HsCRP as independent variables (X), gender as covariate, a stepwise multiple linear regression model ($F = 9.897$, $p < 0.001$) was established. Finally, the elements entering the model were age, AST, ALT and UA. (Table 3)

Table 3
Multiple linear regression analysis of influencing factors of BMI

Model	B	Standard error	Standard coefficient	t	p
(constant)	13.468	2.603	-	5.175	< 0.001*
Age	0.050	0.016	0.223	3.138	0.002*
TC	-0.991	1.246	-0.295	-0.795	0.428
TG	0.493	0.385	0.108	1.281	0.202
HDL	-0.151	1.497	-0.015	-0.101	0.920
LDL	1.981	1.537	0.438	1.288	0.199
AST	-0.094	0.049	-0.217	-1.945	0.049*
ALT	0.055	0.023	0.283	2.441	0.016*
LDH	0.009	0.008	0.085	1.243	0.216
UA	0.006	0.003	0.161	2.325	0.021*
HbA1c	0.646	0.391	0.116	1.651	0.101
HsCRP	0.037	0.060	0.040	0.613	0.541

Note: TC total cholesterol, TG triglyceride, HDL high density lipoprotein, LDL low density lipoprotein, AST aspartate aminotransferase, ALT alanine aminotransferase, LDH lactate dehydrogenase, UA uric acid, HbA1c glycosylated hemoglobin, HsCRP hypersensitive C reactive protein.

4. Discussion

Our study included adolescent depressive depression, adult depressive depression and late-life depression who had treated with fxed doses of drugs for 2 years or more, and excluded smoking and drinking habits. The indicators we measured contained blood lipid, liver function, renal function, cardiac function, blood inflammation and so on, which could comprehensively understand the related factors between MDD and obesity.

First of all, compared with MDD in different age groups, we found that there was little difference in the incidence of obesity between adolescents and adults, while the incidence of obesity was higher in patients with depression in late life. According to a national epidemiological survey, the results indicated that the prevalence of obesity in urban areas in southern China was 2.8–7.2% from 2010 to 2018[17], where the subjects in our study came from. This means that the incidence of obesity in patients with depressive disorder treated regularly would increased at different ages.

In addition, the values of TC TG LDL urea SCr UA HbA1c and HsCRP showed an upward trend in the LLD group. In order to further explore the relationship between these serum metabolic indexes and the

occurrence of obesity in MDD, we made a correlation analysis between BMI and them, witch showed that: BMI was positively correlated with age, TC, TG, LDL, AST, ALT, LDH, UA, HbA1c and hsCRP, and negatively correlated with HDL. Previous research results suggested that the incidence of obesity increases with age, and MDD is no exception[18]. TC, TG and LDL are the most frequently detected blood lipid indicators in clinic. They were recognized as risk factors in lipid metabolism[19] [20] [9]. Therefore, it is easy to understand that their increase increases the risk of obesity. In contrast, HDL has the opposite function and its rose was a protective factor for obesity[21] [22]. These were consistent with our experimental results. Clinically, AST and ALT are commonly used to reflect human liver function, and the liver function plays an important role in lipid metabolism[23]. LDH mainly exists in animal tissues such as myocardium and liver. Clinically, it is often used as an auxiliary index for the diagnosis of myocardial infarction and liver disease. Its rise, like AST and ALT, participated in the process of obesity and overweight[24]. SCr is the product of human muscle metabolism. In muscle, creatine forms creatinine slowly mainly through irreversible non enzymatic dehydration reaction, which is then released into the blood, filtered through the glomerulus and discharged with the urine. The detection of SCr is an important index of renal function. Elevated SCr means impairment of renal function. In the longitudinal study of diabetes, the researchers found that obesity was associated with decreased renal function[25]. The results of this study indicated that there were significant differences in the comparison of SCr in different age groups, and SCr in the older group is higher. However, when we did correlation analysis between SCR and BMI, we get negative results, which was inconsistent with our previous results[9], which might be the impact of the selection of MDD in this study. However, the effect of UA was well recognized, and some people believed that its increase was related to the increase of weight and blood pressure[26]. What's more, its increase was significantly associated with increased risk of diabetes, especially for overweight people[27]. HbA1c is considered to be a reflection of the average blood glucose level in the body for three months. It was considered to be a risk factor for obesity and diabetes[28] [29] [30]. HsCRP is an acute phase protein synthesized in the process of inflammatory stimulation such as tissue injury and infection. As a member of inflammatory factors, it participated in the disease process of MDD[31] and was considered to be related to obesity[32]. Therefore, our study verified the previous research and achieved good consistency.

Finally, the results of regression analysis showed that age, AST, ALT and UA were the risk factors for the increase of BMI. To our surprise, conventional blood lipid indexes such as TC, TG, LDL and HDL did not pass the test. As we know that antidepressants are metabolized by liver and kidney, and taking such drugs will often affect liver and kidney function clinically, especially for ALT, AST, UA, etc[33] [34] [35]. Our results were the same, suggesting that the increase of these indicators is of great significance in the occurrence of obesity in MDD in different age groups.

Unfortunately, in order to obtain a stable blood index of the internal environment of patients with MDD in this study, we selected patients taking drugs regularly for two years or more, and they were also required to rule out serious physical diseases, which caused great difficulties for us to collect elderly samples. At the same time, in order to exclude the influence of smoking and drinking habits, not a few patients were excluded before enrollment, which would cause deviation in our study, but we had to do so.

All in all, we should pay more attention to the monitoring of blood metabolism indicators with the increase of age in MDD, and timely adjust the use of drugs refer to their liver and kidney function, so as to reduce the risk of obesity and improve their quality of life.

Declarations

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Authors' contributions

Liang Jiaquan and Yang Yu have made great contributions to the conception, design and writing of the works; Other authors have provided assistance in the acquisition, analysis or interpretation of data. All authors approve the publication of the manuscript.

Ethics approval and consent to participate

We obtained written informed consent from all patients or their legal guardian(s). This study was approved by the ethics committee of the Third People's Hospital of Foshan, China and the experiments were conducted following the declaration of Helsinki.

Consent for publication

Not applicable.

Competing Interest

The authors have no potential or actual conflicts of interest.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to confidentiality but are available from the corresponding author on reasonable request.

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References

1. Huang Y, Wang Y, Wang H, Liu Z, Yu X, Yan J, et al. Prevalence of mental disorders in China: a cross-sectional epidemiological study[J]. The lancet Psychiatry. 2019,6(3):211-24.

2. Goldstein B, Carnethon M, Matthews K, McIntyre R, Miller G, Raghuveer G, et al. Major Depressive Disorder and Bipolar Disorder Predispose Youth to Accelerated Atherosclerosis and Early Cardiovascular Disease: A Scientific Statement From the American Heart Association[J]. Circulation. 2015,132(10):965-86.
3. Lasserre A, Glaus J, Vandeleur C, Marques-Vidal P, Vaucher J, Bastardot F, et al. Depression with atypical features and increase in obesity, body mass index, waist circumference, and fat mass: a prospective, population-based study[J]. JAMA psychiatry. 2014,71(8):880-8.
4. Marijnissen R, Vogelzangs N, Mulder M, van den Brink R, Comijs H, Oude Voshaar R. Metabolic dysregulation and late-life depression: a prospective study[J]. Psychological medicine. 2017,47(6):1041-52.
5. Fourrier C, Sampson E, Hori H, Schubert K, Clark S, Mills N, et al. Exploratory study of association between blood immune markers and cognitive symptom severity in major depressive disorder: Stratification by body mass index status[J]. Brain, behavior, and immunity. 2020,88:242-51.
6. Gomes A, Gonçalves H, Dos Santos Vaz J, Kieling C, Rohde L, Oliveira I, et al. Do inflammation and adiposity mediate the association of diet quality with depression and anxiety in young adults?[J]. Clinical nutrition (Edinburgh, Scotland). 2021,40(5):2800-8.
7. Lee S, Paz-Filho G, Mastronardi C, Licinio J, Wong M. Is increased antidepressant exposure a contributory factor to the obesity pandemic?[J]. Translational psychiatry. 2016,6:e759.
8. Jokela M, Hamer M, Singh-Manoux A, Batty G, Kivimäki M. Association of metabolically healthy obesity with depressive symptoms: pooled analysis of eight studies[J]. Molecular psychiatry. 2014,19(8):910-4.
9. Li X, Shi X, Tan Y, Yu Y, Tang C, Xu G, et al. Metabolic indexes of obesity in patients with common mental disorders in stable stage[J]. BMC psychiatry. 2022,22(1):91.
10. Schmitz N, Deschênes S, Burns R, Smith K, Lesage A, Strychar I, et al. Depression and risk of type 2 diabetes: the potential role of metabolic factors[J]. Molecular psychiatry. 2016,21(12):1726-32.
11. Zhang L, Wang Z, Wang X, Chen Z, Shao L, Tian Y, et al. Prevalence of overweight and obesity in China: Results from a cross-sectional study of 441 thousand adults, 2012-2015[J]. Obesity research & clinical practice. 2020,14(2):119-26.
12. Yki-Järvinen H, Luukkonen P, Hodson L, Moore J. Dietary carbohydrates and fats in nonalcoholic fatty liver disease[J]. Nature reviews Gastroenterology & hepatology. 2021.
13. Zheng R, Chen C, Yang T, Chen Q, Lu R, Mao Y. Serum Uric Acid Levels and the Risk of Obesity: a Longitudinal Population-Based Epidemiological Study[J]. Clinical laboratory. 2017,63(10):1581-7.
14. McDiarmid S, Harvie M, Johnson R, Vyas A, Aglan A, Moran J, et al. Manchester Intermittent versus Daily Diet App Study (MIDDAS): A pilot randomized controlled trial in patients with type 2 diabetes[J]. Diabetes, obesity & metabolism. 2021.
15. Tonouchi R, Okada T, Abe Y, Kazama M, Kuromori Y, Yoshino Y, et al. Subclass distribution of low-density lipoprotein triglyceride and the clustering of metabolic syndrome components in Japanese

children[J]. Pediatrics international : official journal of the Japan Pediatric Society. 2021,63(6):664-70.

16. Zeng Q, Li N, Pan X, Chen L, Pan A. Clinical management and treatment of obesity in China[J]. The lancet Diabetes & endocrinology. 2021,9(6):393-405.
17. Wang L, Zhou B, Zhao Z, Yang L, Zhang M, Jiang Y, et al. Body-mass index and obesity in urban and rural China: findings from consecutive nationally representative surveys during 2004-18[J]. Lancet (London, England). 2021,398(10294):53-63.
18. Lee J, Busler J, Millett C, Principe J, Levin L, Corrigan A, et al. Association between visceral adipose tissue and major depressive disorder across the lifespan: A scoping review[J]. Bipolar disorders. 2021.
19. Zhang Y, Yang J, Ye J, Guo Q, Wang W, Sun Y, et al. Separate and combined associations of physical activity and obesity with lipid-related indices in non-diabetic and diabetic patients[J]. Lipids in health and disease. 2019,18(1):49.
20. Yin R, Wu D, Miao L, Aung L, Cao X, Yan T, et al. Several genetic polymorphisms interact with overweight/obesity to influence serum lipid levels[J]. Cardiovascular diabetology. 2012,11:123.
21. Stadler J, Lackner S, Mörkl S, Trakaki A, Scharnagl H, Borenich A, et al. Obesity Affects HDL Metabolism, Composition and Subclass Distribution[J]. Biomedicines. 2021,9(3).
22. Woudberg N, Goedecke J, Blackhurst D, Frias M, James R, Opie L, et al. Association between ethnicity and obesity with high-density lipoprotein (HDL) function and subclass distribution[J]. Lipids in health and disease. 2016,15:92.
23. Moreno-Vedia J, Rosales R, Ozcariz E, Llop D, Lahuerta M, Benavent M, et al. Triglyceride-Rich Lipoproteins and Glycoprotein A and B Assessed by 1H-NMR in Metabolic-Associated Fatty Liver Disease[J]. Frontiers in endocrinology. 2021,12:775677.
24. Johansen M, Gade J, Stender S, Frithioff-Bøjsøe C, Lund M, Chabanova E, et al. The Effect of Overweight and Obesity on Liver Biochemical Markers in Children and Adolescents[J]. The Journal of clinical endocrinology and metabolism. 2020,105(2).
25. Kim B, Choi D, Jung C, Mok J, Kim C. Associations between obesity, weight change and decreased renal function in Korean type 2 diabetic patients: a longitudinal follow-up study[J]. BMC endocrine disorders. 2021,21(1):188.
26. Li Q, Li R, Zhang S, Zhang Y, Liu M, Song Y, et al. Relation of BMI and waist circumference with the risk of new-onset hyperuricemia in hypertensive patients[J]. QJM : monthly journal of the Association of Physicians. 2021.
27. Li F, Duan J, Yang Y, Yan G, Chen Z, Wang J, et al. Distinct uric acid trajectories are associated with incident diabetes in an overweight Chinese population[J]. Diabetes & metabolism. 2021,47(2):101175.
28. Chatzianagnostou K, Vigna L, Di Piazza S, Tirelli A, Napolitano F, Tomaino L, et al. Low concordance between HbA1c and OGTT to diagnose prediabetes and diabetes in overweight or obesity[J]. Clinical endocrinology. 2019,91(3):411-6.

29. Hansel B, Giral P, Gambotti L, Lafourcade A, Peres G, Filipecki C, et al. A Fully Automated Web-Based Program Improves Lifestyle Habits and HbA1c in Patients With Type 2 Diabetes and Abdominal Obesity: Randomized Trial of Patient E-Coaching Nutritional Support (The ANODE Study)[J]. Journal of medical Internet research. 2017,19(11):e360.
30. Yoo S, Jung J, Kim H, Kim K, Kim S, Jung J, et al. Predictive Performance of Glycated Hemoglobin for Incident Diabetes Compared with Glucose Tolerance Test According to Central Obesity[J]. Endocrinology and metabolism (Seoul, Korea). 2020,35(4):873-81.
31. Goldsmith D, Rapaport M, Miller B. A meta-analysis of blood cytokine network alterations in psychiatric patients: comparisons between schizophrenia, bipolar disorder and depression[J]. Molecular psychiatry. 2016,21(12):1696-709.
32. Cho S, Lim J, Lee J, Lee J, Jeong H, Lee M, et al. Association between high-sensitivity C-reactive protein levels and depression: Moderation by age, sex, obesity, and aerobic physical activity[J]. Journal of affective disorders. 2021,291:375-83.
33. Solmi M, Fornaro M, Ostinelli E, Zangani C, Croatto G, Monaco F, et al. Safety of 80 antidepressants, antipsychotics, anti-attention-deficit/hyperactivity medications and mood stabilizers in children and adolescents with psychiatric disorders: a large scale systematic meta-review of 78 adverse effects[J]. World psychiatry : official journal of the World Psychiatric Association (WPA). 2020,19(2):214-32.
34. Watt J, Goodarzi Z, Veroniki A, Nincic V, Khan P, Ghassemi M, et al. Comparative efficacy of interventions for reducing symptoms of depression in people with dementia: systematic review and network meta-analysis[J]. BMJ (Clinical research ed). 2021,372:n532.
35. Cipriani A, Furukawa T, Salanti G, Chaimani A, Atkinson L, Ogawa Y, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis[J]. Lancet (London, England). 2018,391(10128):1357-66.