Prevalence and factors associated with metabolic syndrome in patients with first hospitalization for major depression disorder：a large sample cross-sectional study

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Article

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Abstract

Metabolic syndrome (MetS) is a common comorbidity of major depressive disorder (MDD) that has serious adverse effects on physical health. The purpose of this study is to investigate the prevalence and factors influencing MetS in patients hospitalized for their first episode of MDD. The study included 981 patients who were admitted for MDD. Data on demographic and clinical characteristics were gathered, along with measurements of metabolism-related parameters and assessments of psychological and psychopathological symptoms. The prevalence of MetS in the study population was 9.68%. Patients with both MDD and MetS were found to have more extensive and significant demographic and clinical characteristics, higher levels of metabolism-related parameters, and more severe psychological and psychopathological symptoms. Risk factors for the diagnosis of MetS included the onset age of MDD, higher HAMD scores, and higher TSH levels. The risk factors for higher MetS scores included older age, being married, higher PSS scores, and higher levels of TSH and TC, while higher levels of LDL-C were protective. Our results suggest that MetS is not highly prevalent in patients with MDD, but certain risk factors may increase its likelihood and severity.

1. Introduction

Major depressive disorder (MDD) is one of the most debilitating chronic psychiatric disorders[1], with a 12-month prevalence of approximately 6% in the population[2], and in terms of disease burden is the psychiatric disorder with the highest proportion of disability-adjusted life years of all psychiatric disorders, accounting for 37.3%[3]. One study reported that the life expectancy of patients diagnosed with the disease is reduced by an estimated 10–14 years compared to the general population[4]. Even for those who manage their depressive symptoms, the cognitive deficits resulting from MDD significantly impair family activities, interpersonal relationships, and social engagement[5,6]. Though precision medicine has made strides in psychiatry, the underlying mechanisms of MDD remain largely enigmatic, and the disorder has a high rate of recurrence[7]. Moreover, only about one-third of individuals with MDD experience remission following treatment[8]. Alarmingly, people with MDD also ranked first in population-attributable risk for all-cause mortality and suicide rates that are similarly higher than those for other psychiatric disorders[9].

MDD and even depressive symptoms are also considered risk factors for cardiovascular disease (CVD) incidence, severity, and outcome[10–12]. Meanwhile, one in five CVD patients has MDD[13]. This means that there is a complex interaction between MDD and CVD that is mutually causal and mutually reinforcing. However, indications have shown that the metabolic syndrome (MetS) or metabolic disorders are the mediators or bridges between the two diseases mentioned above. The so-called MetS is a combination of central obesity, hypertension, low high-density lipoprotein cholesterol (HDL-C) levels, elevated triglyceride (TG), and hyperglycemia[14,15]. On the one hand, MetS is considered to be an aggregator of CVD risk factors[16,17], while on the other hand MetS and MDD share common shared genetics and possibly the same risk gene pathways[18,19], resulting in MDD patients being at high risk for MetS-related CVD

morbidity and mortality[20]. Summarizing the findings of previous studies, it is not difficult to conclude that to reduce the detrimental effects of CVD on MDD patients, reasonable and effective management of MetS accompanying MDD patients is necessary, given that most MDD patients do not achieve satisfactory outcomes.

In fact, in-depth research on MetS-related studies in MDD populations has been one of the major areas of interest for researchers and psychiatrists. In addition to reporting that MDD and MetS or its components share a common genetic pathway[18,19,21], researchers have identified important implications of MetS or its components for the MDD population. For example, MDD is a key feature of type 2 diabetes[22], fasting blood glucose (FBG) levels and HDL-C levels are potential markers used to predict suicide in young MDD patients[23], low plasma total cholesterol (TC) levels are associated with recent suicide attempts in MDD patients[24], and TC levels play an important role in the pathophysiology of MDD[25]. All of these strongly signal the need for further clarification and understanding of the role of metabolic disorders in all aspects of the development of MDD disease.

Although the prevalence of MetS in populations diagnosed with MDD is currently being addressed by researchers who have reported a high degree of heterogeneity ranging from 20.2–45.2%[26–31], none of these studies have concentrated on the severity of MetS. The objective of this study was to investigate the prevalence of MetS and its associated factors in a larger sample of first-time hospitalized MDD patients in China. Specifically, we aimed to examine the factors related to the severity of MetS.

2. Materials and Methods

2.1 Subjects

A total of 981 patients with MDD who were first hospitalized at Wuhan Mental Health Center from July 2017 to August 2022 were included.

Patients were eligible to meet the following inclusion criteria:

1. Meet the diagnostic criteria for MDD in the 10th revision of the International Classification of Diseases (ICD-10).
2. There was no history of hospitalization before the inpatient interview that day.
3. Aged 18–60 years old, Chinese Han nationality.
4. Their 17-item Hamilton Depression Scale (HAMD-17) total score needed to be ≥ 24.

Patients who meet one condition will be excluded:

1. Breast-feeding patients are pregnant women.
2. They have a history of material dependence.
3. Patients with serious physical diseases or personality disorders.
4. Patients with a clear history of diabetes mellitus in the past.

5. Those who cannot cooperate with psycho-psychological related scales due to serious behavior disorders and other reasons.

The study was reviewed and approved by the Ethics Committee of Wuhan Mental Health Center, and all participants signed a written informed consent form. All participants have written informed consent signed by the patient himself or his family. Patients have the right to withdraw this study at any time.

2.2 Research design

This study was designed as a cross-sectional study. For the included MDD patients with initial hospitalization, we first calculated their prevalence of MetS, compared the differences in demographics and general clinical treatment between the two clinical subgroups with and without MetS, analyzed the factors associated with MetS, and the factors associated with MetS scores.

For MDD patients who met the inclusion criteria, we completed the collection of general clinical data on the day of the patient's visit, including age, gender, age of onset, course of disease, marital status, whether accompanied by suicidal behavior, and whether there is a history of outpatient treatment. At the same time, the patient's venous blood was collected to detect the patient's blood lipid profile (specifically: total cholesterol, TC; triglycerides, TG; low density lipoprotein cholesterol, LDL-C; high density lipoprotein cholesterol, HDL-C) level, fasting blood glucose (FBG) level, body mass index (BMI), blood pressure level (specifically: systolic blood pressure, SBP; diastolic blood pressure, DBP), and thyroid function (specifically: thyroid stimulating hormone, TSH; free triiodothyronine, FT_3: Free triiodothyronine; FT_4: free tetraiodothyronine) level. The severity of depressive symptoms was assessed using the Hamilton Depression Scale (HAMD-17), the severity of anxiety symptoms was assessed using the Hamilton Anxiety Scale (HAMA-14), the severity of psychotic symptoms was assessed using positive symptom subscale (PSS, a subscale of the Positive and Negative Symptom Scale, containing 7 items, items P1-P7, respectively), and the severity of pre-treatment illness was assessed using the Clinical Global Impression Scale (CGI).

Diagnostic criteria of metabolic syndrome: the diagnostic criteria for metabolic syndrome in China require that at least three of the following five indicators be met[32]: 1. abdominal obesity: waist circumference (WC) ≥ 90 cm in men and ≥ 85 cm in women. 2. hyperglycemia: FBG ≥ 6.1 mmol/L and/or those who have been diagnosed and treated for diabetes mellitus. 3. hypertension: SBP ≥ 130/85 mmHg or DBP ≥ 85 mmHg or confirmed and treated hypertension. 4. TG ≥ 1.70 mmol/L. 5. HDL-C < 1.04 mmol/L.

Scoring rules for MetS: based on previous studies, we have scored the severity of the MetS in including patients of the MetS[33,34]. According to the scoring rules, we first calculated the reciprocal of HDL-C and the mean arterial pressure (MAP) using the formula MAP $=1/3 \times SBP + 2/3 \times DBP$. Following this, we normalized the five MetS parameters: waist circumference (WC), triglycerides (TG), the reciprocal of HDL-C, fasting blood glucose (FBG), and MAP. Next, we performed a principal component analysis with varimax rotation on the five normalized components to derive principal components (PCs) with an eigenvalue of 1.0 or higher, which accounted for a substantial portion of the observed variation. In this

study, PC1 and PC2 explained 25.23% and 20.85% of the variance, respectively [loadings PC1 (PC2): WC 0.26 (-0.63), TG 0.28 (0.50), HDL-C 0.17 (0.61), MAP 0.73 (0.04), and FBG 0.75 (-0.15)]. Finally, the weighted PC scores were determined by the relative weights of PC1 and PC2 in the explained variance. To obtain the MetS score, we added up the individual weighted PC scores.

The assessment of the relevant psychological scales was done by 2 uniformly trained psychiatrists with the title of attending or higher, belonging to the medical institution of the sample source.

2.3 Data analysis

The categorical variables are stated in terms of counts, while the data acquired for the normally distributed continuous measures are reported in terms of mean and standard deviation. T-tests on independent samples were employed to compare continuous variable from various groups. Chi-squared tests was used to compare rates. Then, the variables that differed in the univariate analysis were included in a binary logistic regression model as independent variables, with MetS as the dependent variable, to analyze the factors influencing MetS. The area under the receiver operating characteristics (AUCROC) was used to determine the discriminatory capacity of significant parameters to distinguish between patients with and without MetS. Finally, a multiple linear regression model was constructed with the MetS score as the outcome variable and the factors influencing MetS in binary logistic regression as the independent variables to determine the factors influencing the severity of MetS. All *p* values were 2- tailed, and the significance level was < 0.05. Statistical analyses were performed using SPSS 27 (SPSS, Inc., Chicago, IL).

3. Results

3.1 The differences between clinical subgroups with and without MetS

Out of all the MDD patients included in the study, 94 met the diagnostic criteria for MetS, representing 9.68% (95/981) of the total. There were significant differences in demographic and general clinical data between the subgroups with and without MetS. Specifically, as illustrated in Table 1, the MetS subgroup exhibited higher values in various indicators, including age, onset age, percentage of unmarried individuals, prevalence of suicidal behavior, MetS scores, scores on the four scales (PSS, HAMD, HAMA, and CGI-SI), and TSH, TC, and LDL-C levels, compared to the non-MetS subgroup.

Table 1
The demographic and general clinical data in different clinical subgroups

Index	Total patients (n = 981)	MetS (n = 95)	Non-MetS (n = 886)	t/χ^2	*p* - value
Age - years	35.62 ± 12.44	44.84 ± 11.25	34.64 ± 12.17	-8.29	< .001*
Onset age - years	34.09 ± 12.36	43.63 ± 11.07	33.08 ± 12.06	-8.71	< .001*
Course of disease - months	10.83 ± 4.41	10.36 ± 5.24	10.88 ± 4.32	0.92	0.360
Gender				1.26	0.261
Male	333, 33.94%	27, 28.72%	306, 34.50%		
Female	648, 66.06%	67, 71.28%	581, 66.18%		
Marital status - (n, %)				27.50	< .001*
Unmarried	307, 31.29%	7, 7.44%	300, 33.82%		
Married	674,68.71%	87, 92.55%	587, 73.52%		
Treatment history				2.49	0.115
Yes	636, 64.83%	54, 57.45%	582, 65.61%		
NO	345, 35.17%	40, 42.55%	305, 34.39%		
Suicidal behavior				70.16	< .001*
Yes	132, 13.46%	39, 41.49%	93, 10.48%		
NO	849, 86.54%	55, 58.51%	794, 89.52%		
Educational background				3.10	0.078
High school and below	683, 69.62%	77, 65.95%	606, 68.32%		
Bachelor and above	298, 30.38%	17, 34.05%	218, 31.68%		
PSS	8.67 ± 4.39	12.86 ± 7.12	8.23 ± 3.73	-6.22	< .001*
HAMD	29.43 ± 2.97	31.57 ± 3.53	29.21 ± 2.81	-6.29	< .001*
HAMA	20.28 ± 3.49	22.84 ± 4.15	20 ± 3.3	-6.42	< .001*
CGI-SI	5.83 ± 0.71	6.17 ± 0.81	5.79 ± 0.69	-4.36	< .001*

PSS: Positive symptom subscale; HAMD: Hamilton Depression Scale score; HAMA: Hamilton Anxiety Scale Score; CGI-SI: Clinical Global Impression Scale - Severity of Illness; TSH: Thyroid stimulating hormone; FT_3: Free triiodothyronine; FT_4: Free tetraiodothyronine; MetS: Metabolic syndrome; WC: waist circumference; FBG: fasting blood glucose; TG: triglycerides; HDL-C: high density lipoprotein cholesterol; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: total cholesterol; LDL-C: low density lipoprotein cholesterol; BMI: Body mass index. *p<0.05

Index	Total patients (n = 981)	MetS (n = 95)	Non-MetS (n = 886)	t/χ^2	*p* - value
TSH - uIU/mL	3.98 ± 2.47	7.1 ± 3.72	3.65 ± 2.04	-8.84	< .001*
FT_3 - pmol/L	4.9 ± 0.69	4.83 ± 0.63	4.91 ± 0.7	1.07	0.285
FT_4 - pmol/L	16.78 ± 3.04	16.56 ± 2.95	16.8 ± 3.05	0.75	0.249
MetS scores	0.00 ± 0.35	0.53 ± 0.3	-0.06 ± 0.31	-17.53	< .001*
MetS components					
WC - cm	79.98 ± 8.4	84.13 ± 8.47	79.55 ± 8.28	-5.09	< .001*
FBG - mmol/L	5.26 ± 0.63	5.84 ± 0.89	5.2 ± 0.56	-6.83	< .001*
TG - mmol/L	2.11 ± 1	2.68 ± 1.08	2.05 ± 0.97	-5.91	< .001*
HDL-C - mmol/L	1.32 ± 0.23	1.21 ± 0.24	1.33 ± 0.22	5.00	< .001*
SBP - mmHg	116.39 ± 11.15	132.22 ± 9.74	114.71 ± 9.9	-16.33	< .001*
DBP - mmHg	74.62 ± 6.83	84.44 ± 8.57	73.58 ± 5.71	-12.00	< .001*
TC - mmol/L	4.79 ± 0.92	5.25 ± 0.97	4.74 ± 0.9	-5.17	< .001*
LDL-C - mmol/L	2.67 ± 0.74	2.84 ± 0.8	2.65 ± 0.73	-2.43	0.015*
BMI - kg/m^2	24.18 ± 1.76	24.36 ± 1.8	24.16 ± 1.76	-1.03	0.302

PSS: Positive symptom subscale; HAMD: Hamilton Depression Scale score; HAMA: Hamilton Anxiety Scale Score; CGI-SI: Clinical Global Impression Scale - Severity of Illness; TSH: Thyroid stimulating hormone; FT_3: Free triiodothyronine; FT_4: Free tetraiodothyronine; MetS: Metabolic syndrome; WC: waist circumference; FBG: fasting blood glucose; TG: triglycerides; HDL-C: high density lipoprotein cholesterol; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: total cholesterol; LDL-C: low density lipoprotein cholesterol; BMI: Body mass index. *p<0.05

3.2 Influencing factors of MetS in MDD patients: based on binary logistic model.

Next, we focused on the factors influencing MetS in MDD patients. A binary logistic regression model (Backward: Wald) was constructed with the variables that differed in the univariate analysis as independent variables and MetS as the outcome variable. The results showed that onset age (B = 0.06, p < .001, OR = 1.06), HAMD scores (B = 0.12, p = 0.011, OR = 1.12), and TSH (B = 0.36, p < .001, OR = 1.44) were risk factors for MetS (Table 2). Moreover, AUCROC revealed the following values for each risk factor: onset age was 0.74, HAMD was 0.69, and TSH was 0.78. To identify MetS from non-MetS, the combination of onset age, HAMD score, and TSH produced a higher AUC value of 0.87 (p < .001, 95%CI = 0.83–0.90) (Fig. 1).

Table 2
Binary logistic regression analyses of determinants of MetS in MDD patients

	Coefficients	Std. error	Wald	*p*-value	95% CI for EXP (B)		
	B				Exp(B)	Lower	Upper
Constant	-9.72	1.39	48.78				
Onset age - years	0.06	0.01	21.03	< .001*	1.06	1.04	1.09
Marital status (unmarried *vs.* married)	0.83	0.49	2.90	0.089	2.29	0.88	5.93
HAMD	0.12	0.05	6.41	0.011*	1.12	1.03	1.23
TSH - uIU/mL	0.36	0.04	66.95	< .001*	1.44	1.32	1.57
LDL-C - mmol/L	-0.33	0.18	3.35	0.067	0.72	0.51	1.02
HAMD: Hamilton Depression Scale score; TSH: Thyroid stimulating hormone; LDL-C: low density lipoprotein cholesterol. *p<0.05							

3.3 Influencing factors of MetS scores in MDD patients: a multiple linear regression model.

Finally, we construct a multiple linear regression model (Input) with MetS as the outcome variable and the relevant factors affecting MetS in the previous step as the dependent variables. The results showed that TSH (B = 0.03, t = 3.23, p = 0 .002, 95%CI: 0.01–0.02) was risk factors for higher MetS scores (Table 3).

Table 3
Correlates affecting MetS scores in MDD patients: a multiple linear regression model.

	Coefficients	Std. error	*t*	*p*-value	95% CI	
	B				Lower	Upper
Constant	0.21	0.29	0.73	0.470	-0.36	0.78
Onset age	0.00	0.00	-0.34	0.735	-0.01	0.00
HAMD	0.01	0.01	0.58	0.563	-0.01	0.02
TSH	0.03	0.01	3.23	0.002*	0.01	0.05
HAMD: Hamilton Depression Scale score; TSH: Thyroid stimulating hormone. *p<0.05						

4. Discussion

To the best of our knowledge, this is the only study that reports factors related to the severity of MetS in MDD patients in Chian. The main findings of our study are as follows: 1. The prevalence of MetS in the included group was 9.68%. 2. Compared to the non-MetS subgroup, the MetS subgroup had not only higher levels of a wide range of metabolic parameters, but also more severe psychopathological and psychological symptoms, such as scores on the four scales of PSS, HAMD, HAMA, and CGI-SI, and higher age and onset age of the patients. 3. Onset age, HAMD scores, and TSH levels were risk factors for the diagnosis of MetS. 4. The levels of TSH was risk factor for higher MetS scores.

4.1 Prevalence of MetS in MDD patients.

Several factors contribute to the substantial heterogeneity in the prevalence of MetS among individuals diagnosed with MDD, including variations in ethnicity[35], geography[36], and distinct diagnostic criteria for MetS[14,37]. In our study, we reported a MetS prevalence of 9.68% among MDD patients, which is significantly lower than the figures observed in similar research. Focusing solely on the East Asian population, a small sample from Taiwan, China, showed a 34.3% prevalence of MetS[26], while a large sample from Japan indicated a 14.0% prevalence[38]. Although the MetS prevalence reported in these two studies differs greatly, both percentages were notably higher than those documented in our research. Upon comparison, we discovered that both studies used the same diagnostic criteria for MetS, but their criteria were more stringent than ours, which may account for the marked difference in reported prevalence. In contrast, a recently published national epidemiological survey from China reported a standardized prevalence of MetS of 31.1% among the general adult population in China[39]. This prevalence is roughly comparable to that reported in Taiwan, China, which has the highest prevalence of MetS in MDD patients[26]. In conclusion, we determined that the prevalence of MetS was relatively low among first-time hospitalized MDD patients in China.

4.2 Factors associated with MetS in MDD patients.

MDD is often regarded as an independent risk factor for MetS[40], primarily due to the shared genetic risk pathway between the two conditions[18]. However, does this imply that increased severity of depressive symptoms correlates to a higher risk of MetS diagnosis? Several studies have provided affirmative answers to this question[27,41,42], consistent with our findings. Another study reported a positive correlation in females, but an inverse relationship in males[43]. Further research indicated that the severity of depressive symptoms is associated with specific components of MetS, such as elevated blood glucose levels, higher TG levels, lower HDL-C levels, and increased WC[44,45]. Generally, both MDD and depressive symptom severity are important independent risk factors for MetS comorbidity in MDD patients. Higher TSH levels have previously been identified as significant risk factors for MetS in non-MDD populations[46,47], and our study expands the range of populations for which these findings apply. Additionally, we report that increased onset age of MDD is the third risk factor for MetS diagnosis in MDD patients. While we have not found similar reports to date, age is a crucial contributor to MetS diagnosis in the general population[39], and MDD itself is a risk factor for MetS[40]. Consequently, we consider the age of

MDD onset as a specific result of the dual influence of age and MDD on MetS. In further ROC analysis, we determined that the triad of onset age of MDD, HAMD scores and TSH levels had good combination diagnostic capability for MetS.

4.3 Factors associated with the severity of MetS in MDD patients.

Finally, we report higher TSH levels as a factor influencing the severity of MetS. Up to now, there are relatively few studies on factors related to the severity of MetS in the MDD population. The limited number of studies have reported a large heterogeneity of study objectives or outcomes. For example, one study prospective study reported a significant prospective association between initial depressive symptoms and subsequent MetS scores among clergy[48]. Another study found that in the African American female population, higher depressive symptom scores were associated with higher MetS severity in women[49]. Unfortunately, in the present study our findings differ from the two aforementioned studies in that we report no significant effect of the severity of depressive symptoms on the severity of MetS. Whether the reason for this is due to ethnicity, geography or sampling error needs to be further investigated and verified in the future. As mentioned earlier, TSH is an important risk factor for MetS even in the MDD population. Studies have shown that the development of MetS[50,51], and related parameters of MetS, such as weight gain[52], are positively correlated with TSH levels. It has also been reported that the prevalence of MetS, abdominal obesity and hypertriglyceridemia is higher in subjects with clinical hypothyroidism[53]. Although none of these studies are direct evidence that higher TSH levels are a risk factor for MetS severity, they are certainly the strongest supporting evidence.

The present study also has several limitations. First, as a cross-sectional study, our results cannot clarify the causal relationship between MetS, its severity and influencing factors. This requires further prospective studies. Second, our sample consisted of patients in the acute phase requiring hospitalization, so our findings may not be generalizable to MDD patients in the symptom-stable phase. Third, our sample included both drug-naive samples and samples with a history of outpatient treatment, which increased the confounding factors of this study. Fourth, due to the relatively small number of MetS subgroup cases we actually obtained, this may lead to limitations in the further generalization of the results obtained from our regression analysis. In the future, we will try to properly control for the above shortcomings.

In conclusion, the prevalence of MetS in MDD patients is not high. The risk factors for MetS included onset age of MDD, higher HAMD scores and higher TSH levels. And higher TSH levels were also a risk factor for MetS severity.

Declarations

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Authors' contributions

Jun Ma made substantial contributions to conception and design of the study. Zhongyu Tang drafted the manuscript. Lin Zhang had polished and re-edited the language and logic of the article. Xuebing Liu was responsible for setting up and complement and modify the contents of the manuscript. Jun Ma gave final approval of the version to be published. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Ethics approval and consent to participate.

The ethics committees of the Wuhan mental health center reviewed and approved this study. All subject guardians knew about this study and signed informed consent. All procedures carried out in studies conformed to the 1964 Helsinki Declaration and its subsequent amendments or similar ethical standards.

Consent for publication

Not applicable.

Competing interests

None.

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Figures

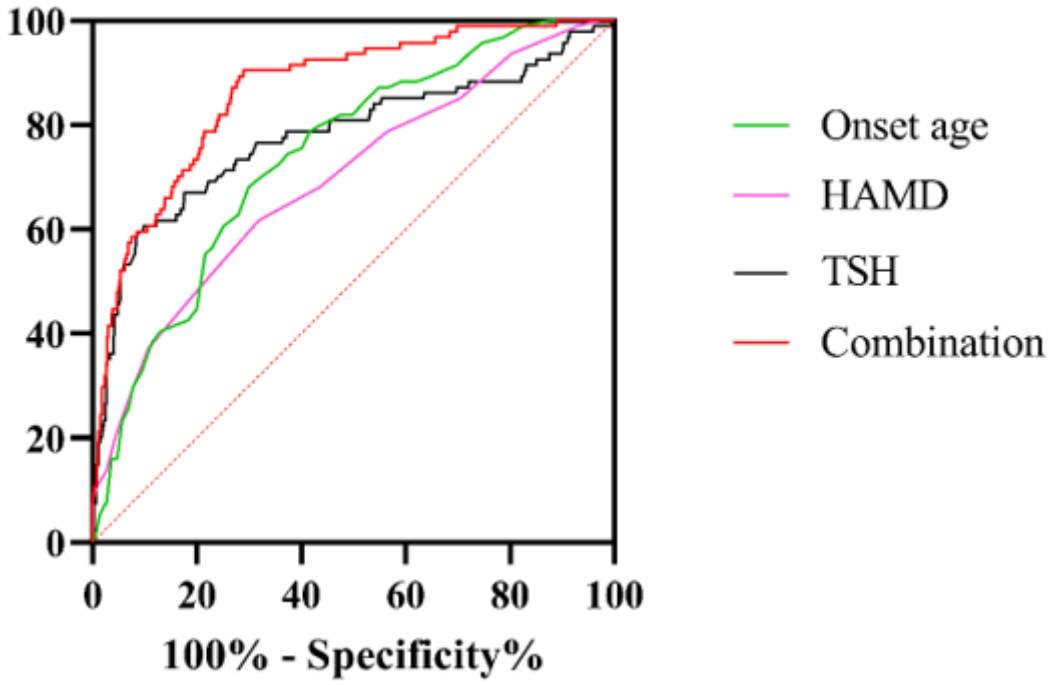

Figure 1

The discriminatory capacity of related factors for distinguishing between patients with and without MetS in MDD patients. The area under the curve of onset age, HAMD score, TSH, and the combination of these three factors were 0.74, 0.69, 0.78, and 0.87, respectively.