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ORIGINAL PAPER

Prevalence and associated factors of obesity in patients with major depressive disorder at different ages of onset

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Abstract

Major depressive disorder (MDD) and obesity are two serious public health problems. Although there have been some research on both, there have few studies on differences in obesity among MDD patients at different ages of onset. The study aims to evaluate the prevalence and factors associated with obesity in MDD patients at different ages of onset. This study totally recruited 1718 first-episode drug-naive MDD patients aged from 18 to 60 years. All subjects were divided into two subgroups: early adulthood onset (EAO, 18–45 years) and mid-adulthood onset (MAO, 45–60 years). Clinical symptoms of patients were evaluated using the 17-item Hamilton Depression Rating Scale (HAMD-17), Hamilton Anxiety Scale (HAMA), and Positive and Negative Syndrome Scale (PANSS) positive subscale. Baseline parameters including body mass index (BMI), blood pressure, and hematological biochemical parameters were assessed to investigate the association between these parameters and weight gain risk. The percentages of overweight and obesity patients with MDD in EAO group were 54.4% and 4.1%, respectively, and the percentages of overweight and obesity patients with MDD in MAO group were 60.4% and 2.8%, respectively. MDD patients in the MAO group had a longer duration of illness and higher scores in HAMD, HAMA, and PANSS positive subscale. They also had higher levels of thyroid stimulating hormone (TSH), anti-thyroglobulin (TgAb), fasting blood glucose (FBG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), systolic and diastolic blood pressures (SBP and DBP) levels. BMI did not differ significantly between the two groups. In the EAO group, statistically significant differences were found among normal weight, overweight and obese group in duration of illness, age of onset, TSH, TgAb, thyroid peroxidase antibody (TPOAb), free thyroxine (FT4), TC, triglycerides (TG), SBP and DBP. The TSH, TgTb and SBP were identified as risk factors for weight gain. In the MAO group, statistically significant differences were found among normal weight, overweight and obese group in TSH and FBG. The two indicators were identified as risk factors for weight gain. There were no significant differences in the weight of MDD patients at different ages of onset, while the factors that could potentially lead to obesity did show some differences.

Keywords Major depressive disorder · Different ages of onset · Obesity · Overweight

Introduction

Major depressive disorder (MDD) and obesity are two major public health problems that affect large numbers of people worldwide. For now, twelve-month prevalence of MDD is approximately 7% [1–3], and WHO estimates that by 2030, MDD will be the leading global disease and one of the leading causes of disability worldwide [4]. Meanwhile, in 2016, more than 1.9 billion adults worldwide were estimated to be overweight, and more than 650 million of them were obese [5]. It is worth noting that these two major public health problems tend to co-occur within individuals.

Several studies have shown that MDD and obesity have a bidirectional relationship [6]. They are interconnected

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through a vicious, mutually reinforcing cycle of adverse physiological adaptations [6, 7]. Studies have shown that obesity increases the risk of developing MDD, and in turn MDD further increases the likelihood of obesity. A recent US study reported that 43% patients with MDD were overweight or obese [8]. A meta-analysis involved 17,894 Chinese children and adolescents found that depression was more prevalent in subjects who were overweight or obese [9]. Adolescents with obesity reported 1.3 times higher risk of depression, and adolescents with depression had a 70% increased risk of being obese [10]. Different depression subtypes have different risk of being obese. A meta-analysis of observational studies reported that atypical depression is significantly associated with elevated BMI compared with melancholic depression [11].

Metabolic status is a major influencing factor in the interconnection of MDD and obesity. In an analysis of 30,337 obese individuals, the risk of depression was only slightly increased in obese individuals with good metabolic status compared to non-obese individuals, but the risk of depression was greater when obese individuals were associated with adverse metabolic conditions (e.g., hypertension, dyslipidemia, high C-reactive protein, or insulin resistance) [12]. However, the mechanisms underlying the association between depression and obesity remain controversial. A meta-analysis showed that one potential factor contributing to obesity in MDD was the use of antipsychotic drugs, but this still remains controversial [13, 14]. In a study of 1000 depressed patients, we found that only the use of mirtazapine was associated with weight gain through more than two years of follow-up [15]. However, in a meta-analysis of weight changes due to antidepressant use, Serretti and mandelli [14] suggested that although most antidepressants affect patients' weight, this effect is transient and negligible in the short term. In a large study involving 2545 subjects, depressive states, but not antidepressants, were found to be responsible for weight gain at 2-year follow-up [16]. Some common biological pathways exist in depression and obesity, such as genetics, alterations in systems involved in homeostatic adjustments and brain circuitries integrating homeostatic, mood regulatory responses and the gut microbiota [14, 17].

Among patients with MDD, differences in the age of first onset may have a differential impact on depressive symptoms. Adolescents with depression have a higher incidence of physical illness and an elevated risk of suicide during their lifetime [18]. In addition, the earlier age of onset of depression, the more severe their depressive symptoms, the more severe their cognitive impairment, and the less effective their antidepressant treatment [19]. Previous studies have found different brain imaging in patients with depression at different ages of onset. A meta-analysis showed that patients with early-onset depression had larger lateral ventricles and smaller amygdala and hippocampal volumes compared to healthy controls, unlike patients with late-onset depression [20]. Another study found that after the first episode of major depression, gray matter volumes in brain regions associated with mood regulation were reduced in drug-naïve adult patients, while gray matter volume changes differed between patients with early-onset and late-onset depression [21]. In a retrospective review, the early-onset late-lie depression had higher body mass index, greater risk of affective disorders in the family history, and poor treatment response [22]. It has been proposed that early-onset depression and late-onset depression differ phenomenologically. Low spirits and feelings of worthlessness were more frequently found in early-onset depression, they were sufficient discriminators to distinguish elderly subjects with early-onset depression and late-onset depression [23]. There is a large body of research on the differences in the age of depression onset, but no research on differences in body weight of depressed patients by age of onset, and even less research on factors associated with obesity in depressed patients by age of onset.

In light of these findings, the purpose of this study was to assess weight differences in MDD across age of onset and to explore factors associated with obesity in MDD. To avoid the effects of antidepressants on the weight of MDD patients, the subjects recruited for this study were untreated patients with first-episode MDD.

Methods

Subjects

This cross-sectional study was conducted at the psychiatric outpatient clinic of the First Hospital of Shanxi Medical University. A total of 1718 patients who met the diagnostic criteria for MDD were enrolled between 2015 and 2017. All subjects met the following inclusion criteria: (1) experienced an acute episode of MDD, as verified by two research psychiatrists based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV); (2) not receiving any antidepressant or other antipsychotic medication prior to the assessment; (3) the 17-item Hamilton Depression Rating Scale (HAMD, 17-item) score > = 24; (4) age between 18 and 60 years; (5) Han Chinese; and (6) able to understand the instructions of the clinical psychiatrist. Exclusion criteria included: (1) having a serious physical illness prior to study participation (see supplemental material); (2) having a history of drug or alcohol abuse (or dependence), as determined by self-reported substance use and medical records; (3) being pregnant or breastfeeding; and (4) being unwilling to participate.

This study was reviewed and approved by the Institutional Review Board of the First Hospital of Shanxi Medical

University. All participants or their guardians signed a written informed consent form and had the right to decide whether to withdraw at any time if they wished.

Sociodemographic data and clinical measures

All patients were interviewed by two independent psychiatrists via the Structured Clinical Interview for DSM-IV (SCID-I/P). A self-designed questionnaire including age, gender, weight, marital status, age of depression onset, duration of illness, and education level was used to collect demographic information from the patients. In addition, based on previous studies and clinical experience, patients were divided into two groups in this study: early-adulthood onset (EAO, 18–45 years) and mid-adulthood onset (MAO, 45–60 years) [24]. The HAMD-17 was used to assess the severity of depressive symptoms. The Hamilton Anxiety Rating Scale (HAMA) was used to assess the severity of anxiety symptoms. The Positive and Negative Syndrome Scale (PANSS) positive subscale was used to assess psychotic symptoms. Two psychiatrists who were blinded to the clinical status of the participants attended training sessions on how to administer the HAMD-17, HAMA, and PANSS prior to the start of the study. After repeated assessments, the inter-rater correlation coefficients of the HAMD, HAMA, and PANSS scores were all greater than 0.8.

Physical and biochemical parameter measurements

Body mass index (BMI) was calculated from height and weight measurements, and the formula was weight (kg) divided by the square of height (m^2). According to the diagnostic criteria of the Chinese Obesity Working Group, all patients were divided into normal weight group (BMI < 24 kg/m^2), and overweight group (24 kg/m^2 ≤ BMI < 28 kg/m^2), and obese group (BMI ≥ 28 kg/m^2) [25, 26]. After resting for at least 15 min, systolic and diastolic blood pressures (SBP and DBP) were measured on the left arm using an Omron digital sphygmomanometer. The final blood pressure value was the average of the two measurements.

Blood samples were collected from all patients after 12 h of fasting. Then all blood samples were sent to the laboratory center of the hospital within two hours after collection, and were assayed for the following parameter: total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FBG), thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), anti-thyroglobulin (TgAb) and thyroid peroxidase antibody (TPOAb).

Statistical analysis

Data were statistically analyzed using the Statistical Package for Social Sciences (SPSS) version 22.0. The statistical comparison was performed using Mann–Whitney U test for continuous variables and chi-square (χ^2) test for categorical variables. Kruskal–Wallis H test was used for outcome analyses as it is a rank-based non-parametric test that can be used to determine if there are statistically significant differences between two or more groups (normal weight group, overweight group, obese group) of an independent variable on dependent variables that are continuous, but not normally distributed. For those analyses in which the overall test was significant, pairwise comparisons were completed using the Mann–Whitney U test controlling for Type I error across tests with the Bonferroni adjustment. The variables for which p value was less than 0.5 were selected for the ordinal multivariate logistic regression analysis. Sex, marriage, and years of education were used as the most basic characteristics, and these variables may have an effect on clinical symptoms, and body weight. These factors were used as covariates with the aim of controlling for their potential impact on the observed association of Thyroid function, lipids, blood pressure and fasting blood glucose with obesity. *P*-values were two-tailed for all reported results, and the significance level was set at $P < 0.05$.

Results

Basic characteristics of patients grouped by age of MDD onset

As shown in Table 1, compared with the MAO group, the EAO group had higher proportion of males, higher level of education, lower rate of marriage, and shorter duration of depression (all $P < 0.001$).

The MAO group had significantly higher scores on the HAMD-17, HAMA, and PANSS positive subscale scores compared with the EAO group9 (all $P < 0.05$) (see Table 1).

The proportions of overweight and obese patients were 54.4% and 4.1%, respectively, in the EAO group, and 60.4% and 2.8%, respectively, in the MAO group. There was no significant difference in the proportion of normal weight, overweight and obese between the two groups, and no significant difference in BMI between the two groups (see Table 1).

Furthermore, there were significant differences in TSH, TgAb, FT3, FBG, TC, HDL-C, LDL-C, SBP and DBP

Table 1 Basic characteristics of the two groups

Variables	EAO (N = 1258)	MAO (N = 460)	*P*
Age (years)	28.90 ± 8.43	51.19 ± 4.34	< 0.001
Duration of illness (months)	5.69 ± 4.16	8.01 ± 5.70	< 0.001
Age of onset (years)	28.74 ± 8.32	50.85 ± 4.33	< 0.001
Sex			< 0.001
Female (%)	796 (63.3%)	334 (72.6%)	
Male (%)	462 (36.7%)	126 (27.4%)	
Education			< 0.001
Junior high school (%)	165 (13.1%)	248 (53.9%)	
High school (%)	407 (32.4%)	42 (9.1%)	
University degree (%)	601 (47.8%)	159 (34.6%)	
Master's degree (%)	85 (6.8%)	11 (2.4%)	
Marital status			< 0.001
Single (%)	487 (38.7%)	15 (3.3%)	
Married (%)	771 (61.3%)	445 (96.7%)	
HAMD-17	30.19 ± 2.92	30.58 ± 2.99	0.018
HAMA	20.66 ± 3.39	21.18 ± 3.67	0.028
PANSS positive subscale	8.62 ± 4.02	9.49 ± 5.24	0.028
TSH (μIU/L)	4.94 ± 2.53	5.43 ± 2.61	< 0.001
TgAb (IU/L)	85.63 ± 216.67	100.04 ± 289.37	0.040
TPOAb (IU/L)	69.42 ± 158.78	80.05 ± 176.63	0.193
FT3 (pmol/L)	4.93 ± 0.74	4.83 ± 0.69	0.038
FT4 (pmol/L)	16.73 ± 3.08	16.62 ± 3.14	0.405
FBG (mmol/L)	5.37 ± 0.63	5.47 ± 0.68	0.010
TC (mmol/L)	5.20 ± 1.10	5.38 ± 1.10	0.003
TG (mmol/L)	2.18 ± 1.00	2.15 ± 0.94	0.768
HDL-C (mmol/L)	1.23 ± 0.28	1.20 ± 0.30	0.016
LDL-C (mmol/L)	2.94 ± 0.87	3.10 ± 0.83	< 0.001
BMI (kg/m^2)	24.35 ± 1.95	24.42 ± 1.85	0.214
Weight category			0.063
Normal	523 (41.6%)	169 (36.7%)	
Overweight	684 (54.4%)	278 (60.4%)	
Obese	51 (4.1%)	13 (2.8%)	
SBP (mmHg)	116.47 ± 10.35	127.73 ± 7.68	< 0.001
DBP (mmHg)	75.25 ± 6.23	77.87 ± 7.67	< 0.001

Normal: BMI < 24 kg/m^2; overweight: 24 kg/m^2 <= BMI < 28 kg/m^2; obese: BMI ≥ 28 kg/m^2

HAMD-17 17-item Hamilton Depression Rating Scale, *HAMA* Hamilton Anxiety Rating Scale, *PANSS positive subscale* Positive and Negative Syndrome Scale positive subscale, *TSH* thyroid stimulating hormone, *TgAb* anti-thyroglobulin, *TPOAb* thyroid peroxidase antibody, *FT3* free triiodothyronine, *FT4* free thyroxine, *FBG* fasting blood glucose, *TC* total cholesterol, *TG* triglycerides, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *BMI* body mass index, *SBP* systolic blood pressures, *DBP* diastolic blood pressures

between the two groups (all $P < 0.05$). Compared with the MAO group, the EAO group had lower values for TSH, TgAb, FBG, TC, LDL-C, SBP and DBP, but higher values for FT3 and HDL-C (all $P < 0.05$) (see Table 1).

Comparison of basic characteristics of different weigh groups within the EAO group

We compared clinical, physical and biochemical parameters between normal weight, overweight and obese (see Table 2). The Kruskal–Wallis H test found statistically significant difference in duration of illness ($P = 0.040$), age of onset ($P = 0.012$), TSH ($P < 0.001$), TgAb ($P = 0.042$), TPOAb ($P = 0.003$), FT4 ($P = 0.031$), TC ($P = 0.008$), TG ($P = 0.021$), SBP ($P < 0.001$) and DBP ($P < 0.001$) between the group of normal weight and the other two groups.

The Mann–Whitney U test found that the overweight group had a longer duration of illness (Bonferroni corrected $P = 0.045$), older age of onset (Bonferroni corrected $P = 0.009$) than the normal weight group. Besides, the overweight group had higher level of TSH (Bonferroni corrected $P < 0.001$), TgAb (Bonferroni corrected $P = 0.036$), TPOAb (Bonferroni corrected $P = 0.003$), TG (Bonferroni corrected $P = 0.017$), DBP (Bonferroni corrected $P < 0.001$) and SBP (Bonferroni corrected $P < 0.001$) than the normal weight group. The obese group had higher levels of TC (Bonferroni corrected $P = 0.009$) and DBP (Bonferroni corrected $P = 0.023$) than the normal weight group. The levels of TSH, FT4 and SBP in the obese group were higher than the overweight group (Bonferroni corrected $P_{TSH} = 0.012$, $P_{FT4} = 0.046$, $P_{SBP} = 0.014$) and the normal weight group (Bonferroni corrected $P_{TSH} < 0.001$, $P_{FT4} = 0.025$, $P_{SBP} < 0.001$).

Using logistic regression, obesity in EAO group was associated with TSH (95% Cl: 1.083–1.250, P < 0.001, and OR = 1.164), TgAb (95% Cl: 0.999–1.00, P = 0.025, and OR = 0.999) and SBP (95% Cl: 1.008–1.048, P = 0.006, and OR = 1.028).

Comparison of basic characteristics of different weigh groups within the MAO group

A Kruskal–Wallis H test showed that there was a statistically significant difference in TSH and FBG between the different weight groups ($P < 0.001$) (see Table 3). Both TSH and FBG were significantly higher for the overweight group than for the normal weight group (Bonferroni corrected $P < 0.001$).

Using logistic regression, obesity in MAO group was associated with TSH (95% Cl: 1.072–1.347, $P = 0.002$, and OR = 1.202), and FBG (95% Cl: 1.028–1.953, $P = 0.033$, and OR = 1.417).

Table 2 Comparison of basic characteristics of different weigh groups within the EAO group

Variables	Normal weight Mean ± SD	Overweight Mean ± SD	Obese Mean ± SD	P
Duration of illness (months)	5.27 ± 3.70[a]	5.95 ± 4.39[a]	6.37 ± 5.04	0.040
Age of onset (years)	27.96 ± 8.40[a]	29.33 ± 8.25[a]	28.82 ± 7.96	0.012
HAMD-17	30.13 ± 3.11	30.18 ± 2.80	31.00 ± 2.41	0.056
HAMA	20.68 ± 3.34	20.58 ± 3.41	21.41 ± 3.53	0.242
PANSS positive subscale	8.68 ± 4.15	8.52 ± 3.86	9.27 ± 4.75	0.319
TSH (μIU/L)	4.49 ± 2.72[ab]	5.19 ± 2.36[ac]	6.09 ± 1.81[bc]	< 0.001
TgAb (IU/L)	98.46 ± 246.81[a]	77.20 ± 195.41[a]	67.16 ± 140.30	0.042
TPOAb (IU/L)	72.63 ± 152.36[a]	66.24 ± 161.48[a]	79.14 ± 186.97	0.003
FT3 (pmol/L)	4.90 ± 0.72	4.95 ± 0.75	4.99 ± 0.69	0.360
FT4 (pmol/L)	16.63 ± 3.14	16.73 ± 3.00[c]	17.79 ± 3.22[c]	0.031
FBG (mmol/L)	5.33 ± 0.64	5.40 ± 0.63	5.43 ± 0.58	0.117
TC (mmol/L)	5.15 ± 1.14[b]	5.21 ± 1.08	5.58 ± 0.95[b]	0.008
TG (mmol/L)	2.13 ± 1.08[a]	2.21 ± 0.94[a]	2.15 ± 0.91	0.021
HDL-C (mmol/L)	1.25 ± 0.29	1.22 ± 0.28	1.20 ± 0.31	0.203
LDL-C (mmol/L)	2.92 ± 0.85	2.93 ± 0.85	3.32 ± 1.11	0.058
SBP (mmHg)	114.49 ± 10.47[ab]	117.57 ± 10.05[ac]	121.96 ± 9.04 [bc]	< 0.001
DBP (mmHg)	74.39 ± 6.40[ab]	75.77 ± 6.05[a]	76.98 ± 5.87[b]	< 0.001

Normal weight: BMI < 24 kg/m^2; overweight: 24 kg/m^2 < = BMI < 28 kg/m^2; obese: BMI ≥ 28 kg/m^2

HAMD-17 17-item Hamilton Depression Rating Scale, *HAMA* Hamilton Anxiety Rating Scale, *PANSS positive subscale* Positive and Negative Syndrome Scale positive subscale, *TSH* thyroid stimulating hormone, *TgAb* anti-thyroglobulin, *TPOAb* thyroid peroxidase antibody, *FT3* free triiodothyronine, *FT4* free thyroxine, *FBG* fasting blood glucose, *TC* total cholesterol, *TG* triglycerides, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *BMI* body mass index, *SBP* systolic blood pressures, *DBP* diastolic blood pressures

The superscript letter (a, b and c) means that there are significant differences between them (P < 0.05)

Discussion

In our study, both the early-adulthood onset MDD population and the mid-adulthood onset MDD population had higher numbers of overweight than normal weight and obese, respectively 54.4% and 60.4%. Nevertheless, we did not find difference in BMI between patients with depression at different ages of onset. This finding may differ from some previous studies. A previous study on depression and emotional eating found that younger depressed patients had a significant increase in BMI and waist circumference after 7 years of follow-up, while no such changes were found in older depressed patients[27]. This discrepancy may be due to the fact that our study included first-episode patients with depression, most of whom had a disease duration of less than 1 year, and no long-term effects of depression on body weight could be seen. In addition, the course of disease in mid-adulthood onset MDD group was longer than that in early adulthood onset depression group, and the duration of untreated disease could seriously affect the prognosis of patients [28–30], but it did not affect the body weight of patients.

There were differences in blood pressure and hematological biochemical parameters between the EAO and MAO groups. Blood pressure, thyroid stimulating hormone, lipids and fasting blood glucose were high in the MAO group. Blood pressure, lipids and fasting blood glucose are all indicators of metabolic syndrome. In a previous meta-analysis, it was found that the risk of metabolic syndrome in patients with depression decreased with age, with a higher risk of metabolic syndrome below 50 years of age as a cutoff [31]. Another study of elderly depressed patients in Iran found that metabolic syndrome did not increase with age [32]. The results of current studies on depressed patients of different ages with comorbid metabolic syndrome are inconsistent. Our study found high metabolic markers in patients with mid-adulthood onset MDD, which may be related to thyroid stimulating hormone. Studies have shown that thyroid stimulating hormone is a risk factor for various metabolic indicators. High level of thyroid stimulating hormone can directly affect lipid metabolism by binding to TSH receptors, and can also promote cholesterol synthesis and inhibit cholesterol removal [33]. Hepatic endoplasmic reticulum stress mediated by high levels of TSH also plays an important role in dyslipidemia and impaired glucose metabolism [34, 35], and TSH abnormalities can lead to thyroid dysfunction, which in turn can lead to hypertension, hyperglycemia, and dyslipidemia [36, 37]. Kim found that subclinical hypothyroidism

Table 3 Comparison of basic characteristics of different weigh groups within the MAO group

Variables	Normal weight Mean ± SD	Overweight Mean ± SD	Obese Mean ± SD	P
Duration of illness (months)	7.90 ± 6.02	8.11 ± 5.50	7.38 ± 6.05	0.537
Age of onset (years)	51.36 ± 4.55	50.51 ± 4.19	51.69 ± 4.09	0.139
HAMD-17	30.39 ± 2.74	30.68 ± 3.11	31.00 ± 3.37	0.611
HAMA	20.88 ± 3.28	21.37 ± 3.90	20.92 ± 3.38	0.653
PANSS positive subscale	8.69 ± 4.22	9.90 ± 5.67	11.23 ± 6.57	0.069
TSH (μIU/L)	4.73 ± 2.69[a]	5.84 ± 2.52[a]	5.86 ± 1.45	< 0.001
TgAb (IU/L)	60.96 ± 100.35	128.28 ± 360.91	74.80 ± 121.04	0.508
TPOAb (IU/L)	61.91 ± 183.38	91.79 ± 174.58	64.95 ± 104.70	0.484
FT3 (pmol/L)	4.82 ± 0.69	4.86 ± 0.68	4.45 ± 0.71	0.131
FT4 (pmol/L)	16.53 ± 3.29	16.69 ± 3.06	16.26 ± 2.91	0.864
FBG (mmol/L)	5.31 ± 0.67[a]	5.57 ± 0.67[a]	5.50 ± 0.69	< 0.001
TC (mmol/L)	5.28 ± 1.01	5.43 ± 1.15	5.70 ± 1.16	0.214
TG (mmol/L)	2.11 ± 0.89	2.15 ± 0.97	2.57 ± 1.06	0.280
HDL-C (mmol/L)	1.22 ± 0.30	1.18 ± 0.29	1.26 ± 0.43	0.239
LDL-C (mmol/L)	3.08 ± 0.80	3.10 ± 0.83	3.33 ± 1.18	0.742
SBP (mmHg)	127.76 ± 7.92	127.84 ± 7.53	124.92 ± 7.85	0.635
DBP (mmHg)	78.06 ± 7.94	77.94 ± 7.50	73.92 ± 6.92	0.164

Normal weight: BMI < 24 kg/m^2; Overweight:24 kg/m^2 < = BMI < 28 kg/m^2; Obese: BMI ≥ 28 kg/m^2

HAMD-17 17-item Hamilton Depression Rating Scale, *HAMA* Hamilton Anxiety Rating Scale, *PANSS positive subscale* Positive and Negative Syndrome Scale positive subscale, *TSH* thyroid stimulating hormone, *TgAb* anti-thyroglobulin, *TPOAb* thyroid peroxidase antibody, *FT3* free triiodothyronine, *FT4* free thyroxine, *FBG* fasting blood glucose, *TC* total cholesterol, *TG* triglycerides, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *BMI* body mass index, *SBP* systolic blood pressures, *DBP* diastolic blood pressures

The superscript letter (a, b and c) means that there are significant differences between them (P < 0.05)

increased the risk of metabolic syndrome about 7 times in adult depressive patients in Korea [38]. A number of studies have shown that thyroid stimulating hormone increases gradually with age [39–41]. Therefore, we hypothesized that the increase in fasting blood glucose, lipids, and blood pressure in patients with mid-adulthood onset MDD in the present study might be due to abnormalities in thyroid stimulating hormone.

In the present study, mid-adulthood onset depression patients had more severe depressive symptoms, anxiety symptoms, and psychotic symptoms than early adulthood onset depression patients. However, previous studies have shown that patients with early onset depression have more severe depressive symptoms and are more likely to have concomitant anxiety disorders [19, 42, 43]. In another large study by Park et al. [44], the authors did not find significant differences in HAMD and HAMA scores between MDD patients of different ages of onset. Nevertheless, we cannot ignore the role of thyroid stimulating hormone. High levels of thyroid stimulating hormone also play an important role in the clinical symptoms of depressed patients. A previous study has suggested that severe anxiety, depression, and psychotic symptoms, as well as old age and obesity, may be associated with elevated TSH levels [45–47]. A large study found a higher likelihood of depression in patients with subclinical hypothyroidism, and a subanalysis found that the geriatric group had a greater incidence of depression [48]. There are many common biological mechanisms between depression and subclinical hypothyroidism, such as disturbances in the hypothalamic-pituitary-adrenal axis, altered levels of hormones including growth inhibitors and 5-hydroxytryptophan [49]. There is a correlation between thyroid stimulating hormone level and psychotic symptoms. Schizophrenia is independently associated with hypothyroidism [50–52]. Liu found that serum thyroid stimulating hormone levels were independently associated with psychotic symptoms in patients with MDD [53]. In addition, depressed patients with co-morbid anxiety have higher thyroid stimulating hormone levels [54, 55]. Most of the current evidence on the relationship between thyroid stimulating hormone and psychotic and anxiety symptoms comes from observational cross-sectional studies. The underlying mechanisms remain largely unexplored.

A positive correlation between TSH and BMI was found in both the EAO and MAO groups. Many previous studies have found a significant relationship between BMI and thyroid stimulating hormone [37, 44, 56–62]. Previous studies have shown that subclinical hypothyroidism can cause

changes in basal metabolic rate, leading to an increase in BMI, and that obesity can also affect thyroid function through mechanisms such as lipotoxicity and changes in adipokine and inflammatory cytokine secretion [63–69]. Although it has been demonstrated that thyrotropin is associated with basal metabolism and that elevated thyrotropin leads to increased body weight, lipids, blood glucose and blood pressure. However, there are differences in thyrotropin hormones and no differences in body weight in MDD patients of different ages of onset. We hypothesize that the influence of thyrotropin on body weight may decrease with age, and further studies are needed to investigate the exact mechanism.

Interestingly, a positive correlation between TgAb, SBP and weight can be found in the EAO group, while FBG was positively correlated with weight in the MAO group. Blood glucose and blood pressure as indicators of metabolic syndrome have been shown to be strongly associated with obesity [70–74]. In a large-scale study, a significant positive correlation was found between blood pressure and body weight in healthy people under 50 years of age, while this correlation was weaker in people over 50 years of age [75]. The results of this study are similar to our findings. However, there are still few studies on the relationship between body weight and blood glucose and blood pressure in different age groups, and even fewer in depressed patients. In addition, previous studies have found a positive correlation between anti-thyroglobulin and body weight, while the mechanism remains unclear [76].

Both men and women were at risk of obesity and depression bi-directionally. Depression can activate the hypothalamic-pituitary-adrenal axis and lead to accumulation of visceral fat through increasing the secretion of corticotrophin-releasing hormone, adrenocorticotropic hormone, and cortisol [77]. A previous study found a modest overlap of glucocorticoid receptor gene, the corticotrophin releasing hormone receptor gene, the serotonin 2A and 2C receptor genes, and the dopamine receptor D4 gene as the genetic risk factors that increase liability to both depression and obesity [7]. Depression and thyroid stimulating hormone interact with each other through the hypothalamic-pituitary-adrenal axis, growth inhibitors, and 5-hydroxytryptophan. In addition, TSH affects glycolipid metabolism by binding to thyroid stimulating hormone receptors, interfering with cholesterol synthesis and clearance, and mediating hepatic endoplasmic reticulum stress. In turn, changes in lipotoxicity, adipokine secretion, affect thyroid function. Therefore, there is an interaction between obesity, metabolism and TSH in depressed patients, and attention should be paid to all health indicators in depressed patients in order to inhibit the vicious circle. The mechanism of the influence of age of depression onset in this cycle needs to be further explored.

The present study still had some limitations. First, due to the cross-sectional design of this study, it is impossible to establish any causality between body weight and thyroid function, blood pressure and glucose. Second, because this study did not include healthy controls, the effect of depression on body weight cannot be clearly illustrated. Third, since this was a cross-sectional study, we cannot exclude the possibility that some of our patient subjects who verified as having depressive episode could be later diagnosed as with bipolar disorder. Finally, this study included patients with first-episode drug-naïve depression, which has some limitations in terms of clinical generalization. Future studies applying the research method of follow-up studies will further clarify the effects of different ages of onset on the body weight of MDD patients and the risk factors leading to obesity in MDD patients.

In conclusion, the age of onset of MDD does not cause differences in body weight, however, there are differences in the risk factors leading to obesity in patients with MDD at different ages of onset. Thyroid stimulating hormone abnormalities were a risk factor for obesity in all MDD patients. Fasting blood glucose abnormalities were risk factors for obesity in MDD patients with mid-adulthood onset, while anti-thyroglobulin and systolic blood pressures abnormalities were risk factors for obesity in MDD patients with early-adulthood onset.

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Availability of data The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable requests.

Declarations

Conflict of interest The authors have no competing interests to declare that are relevant to the content of this article.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the

Institutional Review Board (IRB) of the First Clinical Medical College, Shanxi Medical University (No. 2016-Y27). The patients/participants provided their written informed consent to participate in this study.

Consent to participate Informed consent was obtained from all individual participants included in the study.

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