

Prevalence and risk factors for suicide attempts in first-episode and drug-naïve middle-aged major depressive disorder patients with impaired fasting glucose

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Research Article

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Abstract

Background: Impaired fasting glucose (IFG) is prevalent among the middle-aged population. Recent studies have found an association between suicide attempts and abnormal glucose metabolism in patients with major depressive disorder (MDD). However, there are fewer studies on suicide attempts in middle-aged MDD patients with comorbid IFG. The aim of this study was to investigate the prevalence and risk of suicide attempts in first-episode, untreated middle-aged MDD patients with IFG.

Methods: A total of 830 middle-aged (35-60 years) patients with first-episode and drug-naïve(FEDN) MDD were included in the study. Among them, 119 patients comorbid abnormal glucose metabolism. Sociodemographic and clinical information, as well as depression, anxiety, and psychotic symptoms, were collected and evaluated. Blood glucose levels, lipid levels, and serum thyroid function were also measured. The predictors of suicide attempt risk of middle-aged FEND MDD patients were identified by binary logistic regression.

Results: Prevalence of suicide attempts in middle-aged MDD patients with IFG was 38.66% (46/119). Significant differences in disease duration, anxiety symptoms, depressive symptoms, psychiatric symptoms, blood pressure, anti-thyroglobulin(TGAb),thyroid peroxidases antibody(TPOAb), thyroid stimulating hormone(TSH), and total cholesterol (TC) were found in patients who attempted suicide as compared to those who did not. Furthermore, Hamilton anxiety rating scale(HAMA) score, TGAb and disease duration were predictors of suicide attempts in middle-aged MDD patients with comorbid IFG.

Conclusion: This study showed a high prevalence of suicide attempts in middle-aged MDD patients with comorbid IFG, and we had further identified HAMA, TGAb and disease duration as predictors of suicide attempts in MDD patients with IFG.

Introduction

MDD is a common mental disorder characterized by depressive state, cognitive impairment, insomnia, and fatigue[1]. MDD is associated with suicidal ideation, suicide attempts, and even suicidal behaviors[2]. It is estimated that the lifetime risk of a major depressive episode is currently close to 30%[3]. In the United States, prevalence of suicide among middle-aged and older adults remain higher than other age groups due to mental disorders, especially depression and anxiety[4].

Previous studies have focused on the associated factors of suicide in depressed patients. For instance, some research has shown that sleep disorders, including nightmare disturbances and insomnia, are independent risk factors for suicide in MDD patients[5]. Evidences indicate that individuals with MDD who engage in suicidal behavior are more likely to have comorbid psychiatric disorders such as personality disorders, substance use, and anxiety[6]. Several studies have suggested that metabolic disorders (e.g.glucose metabolism disorders, thyroid dysfunction, and dyslipidemia) are associated with suicide attempts in depressed individuals[7, 8]. Depressed patients who are unmarried, unemployed, and suffer from dysthymia and cyclical depression have a significantly higher rate of suicide risk than the

general population. However, the exact relationship between suicide attempts and depression remains inconsistent [9].

The close correlation between glucose metabolism and mental disorders is well recognized. A growing body of research has been reported that MDD is associated with hyperglycemia and poor metabolic control[10]. Diabetes leads to an increased chance of suicide in MDD patients[11]. On the other hand, research has also found varying degrees of glucose metabolism disorders in patients with MDD, including impaired fasting glucose and changes in hormones such as glucagon, adrenaline, thyroid hormone, and insulin that can affect glucose levels[12, 13]. Furthermore, the incidence of IFG increases with age and similarly, MDD is more prevalent in middle-aged population due to physical illnesses, increased financial burden and social work stress. There is an interactive relationship between impaired fasting glucose, metabolic abnormalities and MDD. Based on the current knowledge, there is limited research on the suicidal risk in middle-aged MDD patients with IFG.

In addition, cultural differences as well as severity and treatment of MDD may be affect suicide rates. For example, in the United States, the suicide attempts rate among MDD patients is 36.3%, while in China, it is 20.1%[14–16]. Therefore, by limiting the study sample to Han Chinese first-episode untreated middle-aged MDD patients, the occurrence rate of suicide attempts can be observed, reducing the impact of confounding factors such as treatment and sociocultural background on the research outcomes and obtaining more reliable results[17]. The purpose of this study was to conduct a systematic analysis of clinical data and laboratory measurement of middle-aged untreated MDD patients of Han ethnicity in China in order to (1) reveal the prevalence of suicide attempts and its association with gender differences, disease duration, fasting blood glucose, blood lipids, thyroid function, and clinical symptoms, and (2) identify risk predictors of suicide attempts in middle-aged FEDN depressed patients comorbid IFG.

Methods

2.1 Participants

The patients enrolled in this study were from the Psychology Clinic of the First Affiliated Hospital of Shanxi Medical University, China. An informed consent (No. 2016-Y27) reviewed by the Ethics Committee of Shanxi Medical University was signed by each enrolled patient. The study period was from 2015 to 2017.

All participants were diagnosed by two trained psychiatrists using the Chinese version of the structured clinical interview, which is based on the DSM-IV criteria. Inclusion criteria were: (1) middle-aged patients (35-60 years old)[18]; (2) Han ethnic; (3) first-episode MDD; (4) no previous treatment of antidepressants, psychotherapy or physical therapy. Exclusion criteria were: (1) other psychiatric disorders on Axis I; (2) pregnant or lactating women; (3) other serious somatic illnesses such as neurological disorders, life-threatening acute infections, organ failure, or malignant tumors; and (4) alcohol or other substance dependence and abuse, except for nicotine.

2.2 Demographic characteristics

A standardized questionnaire was designed to collect basic information and sociological data from the participants, including gender, age, age of onset, education level, marital status, disease duration, and body mass index (BMI).

2.3 Clinical measurements

Depressive symptoms were assessed by the Hamilton Depression (HAMD) Scale. If a subject's total score on this scale is equal to or greater than 24, it indicates a significant level of depressive symptoms[19].

Anxiety symptoms were assessed by the Hamilton Depression (HAMA) Scale. Participants with a total HAMA score of 21 or greater were considered to have higher anxiety symptoms[20].

We used the Positive and Negative Syndrome Scale (PANSS) to assess the severity of the patient's psychiatric symptoms. If the patients had a total PANSS score of 15 or more they were considered to have psychiatric symptoms[21].

Scoring was performed by two qualified psychiatrists who were blind to any other information about each patient. The correlation coefficient between two raters was greater than 0.8.

Suicidal attempts were assessed with Mini-International Neuropsychiatric Interview 5.0 (MINI), a standardized assessment interview based on DSM-IV criteria that is widely used in the diagnosis of mental illness[22].

2.4 Biochemical measurements

Fasting blood of all patients were collected at 6:00-8:00 am and immediately sent to the laboratory for tests including serum glucose,lipid metabolism such as TC, triglyceride(TG), high density lipoprotein cholesterol(HDL-C) and low density lipoprotein cholesterol(LDL-C), thyroid function such as TSH, FT3, FT4, TPOAb, TGAb.

According to the WHO criteria, IFG is diagnosed as the fasting blood glucose≧6.1mmol/L and <7.0mmol/L, while the fasting blood glucose≧7.0mmol/L, or the postprandial blood glucose≧11.1mmol/L, the diagnosis of diabetes is made. Considering that both impaired fasting glucose and diabetes are disorders of glucose metabolism, in our study, we divided all participants into two groups according to the fasting blood glucose, the IFG group was defined as fasting glucose<6.1mmol/L[23-25].

2.5 Statistical analysis

The data analysis of the study was conducted by SPSS version 27.0 (IBM,USA). All tests were two-sided, and statistical significance was set at p<0.05.

All continuous numerical variables involved in this study were evaluated by single sample Kolmogorov-Smirnov test to examine normality distribution. The exact odds ratio(OR) for suicide attempts of the IFG group and NIFG group was calculated using binary logistic regression(backward:Wald). Statistical comparisons were performed between the suicide attempt(SA) subgroup and the non-suicide attempt(NSA) subgroup. The continuous normal distribution variables of two subgroups were analyzed and compared by independent sample T test, the qualitative data were analyzed and compared by chisquare test, and the non-normal distribution or heterogeneous data were analyzed and compared by Mann-Whitney U test. The predictors of suicide attempt risk were identified by binary logistic regression (backward:Wald), and the variables related to suicide attempt were included in this regression for analysis. Variance inflation factor(VIF) >5 was used to determine the multicollinearity between independent variables.

Results

3.1 Suicide attempts rate and details of suicide attempts

We included a total of 830 first-episode untreated MDD patients aged between 35-60 years, of whom 119 comorbid with IFG. The prevalence of suicide attempts was 20.96% (174/830) in all middle-aged MDD patients, and 38.66% (46/119) in patients with comorbid IFG. In addition, MDD patients with IFG had a 2.87-fold (OR:2.87, p<0.001, 95%CI: 1.894-4.349) increased risk of suicide attempts compared to those without IFG.

Furthermore, we found that among these suicide attempters in MDD patients, 67.8% (118/174) had only one suicide attempt, 20.1% (35/174) had two suicide attempts, 11.5% (20/174) had three suicide attempts, and 0.6% (1/174) had four suicide attempts. Of all patients who attempted suicide, 70.11% (122/174) had their suicide attempts occur within two weeks.

3.2 Comparison of clinical and biochemical variables between the suicide attempts(SA) subgroup and nonsuicide attempts(NSA) subgroup

The general information, clinical and biochemical variables of the two subgroups of middle-aged MDD patients are shown in Table 1. There were a total of 119 MDD patients with IFG, including 38 males and 81 females. Among the 119 patients, 46 attempted suicide, including 14 males (58.33%) and 32 females (39.51%). The proportion of male suicide attempters was higher than that of females, but there was no statistical significance (P>0.05).

Compared to non-suicide attempted patients, suicide attempted patients had longer duration of illness(z=-2.236,p=0.025), higher HAMD score (t=-2.989,p=0.003), higher HAMA score (t=-6.468,p<0.001), higher PANSS score (z=-4.071,p<0.001), higher CGI score (z=-4.787,p<0.001), higher TSH level (t=-4.846,p<0.001), TGAb level(z=-3.607,p<0.001), TPOAb level(z=-3.438,p<0.001), TC level (t=-2.406,p=0.018), higher systolic blood pressure (t=-2.283,p=0.025) and higher diastolic blood pressure (t=-2.312,p=0.023).

3.3 Risk predictors of suicide attempts

Suicide risk predictors in middle-aged MDD patients comorbid IFG were identified by binary logistic regression(backward:Wald) analysis (see Table 2), and the suicide attempt risk prediction model is shown in Figure 1 as a nomogram. We found that HAMA total score(OR:1.356, P<0.001, 95%CI:1.174-1.566), disease duration(OR:1.101,P=0.042,95%CI:1.003-1.208), and TGAb(OR:1.005, P=0.035, 95% CI:1.000-1.010) were independent risk factors for suicide attempts in middle-aged MDD patients comorbid IFG.

In addition, all the variables predicting the suicidal risk had VIF <5, indicating weak multicollinearity among the variables.

Discussion

To date, this is the first study to reveal suicide attempts rates and risk factors in middle-aged first-episode untreated patients with IFG. The study found that: (1) suicide attempts rate was 20.98% (174/830) in middle-aged untreated MDD patients, and 38.66% (46/119) in those with IFG, which is significantly higher and 2.87 times higher than the overall middle-aged MDD population. (2) Middle-aged MDD patients with IFG who attempted suicide had longer duration of illness, more depression, anxiety, and psychiatric symptoms, higher blood TSH, TGAb, TPOAb, total cholesterol levels, and higher blood pressure than those without suicide attempts. (3) HAMA, TGAb, and disease duration may act as independent predictors of suicide attempt risk in middle-aged depressed patients comorbid IFG.

Our study indicated that the incidence of suicide attempts in middle-aged untreated depressive patients was 20.9%, which is consistent with previous research on Asian populations. For example, a metaanalysis conducted in Chinese population revealed a lifetime suicide rate of 23.7% and a monthly suicide rate of 20.3%[26]. A study in Thailand reported a suicide rate of 16.9% among MDD patients[27], and In South Korea, Kim reported that 19.8% of MDD patients had attempted suicide once or more[28]. However, in the current study, the suicide rate of depressed patients comorbid IFG increased substantially to 38.66%. This is close to the 35% suicide rate reported by Lalthankimi et al. for patients with severe MDD and the 33.7% suicide rate reported by Azorin JM for patients with unilateral or bilateral disorder[29]. Their findings suggested that the suicide rate related to the severity of the disease. Our study suggested that the suicide rate in middle-aged MDD patients with IFG in China was much higher than that of Asian depressed patients in general, suggesting that the difference in suicide rates may be related to the following reasons. First, IFG or disturbed glucose metabolism directly or indirectly contributes to the increased suicide attempt rate[11]. Second, our study focused on middle-aged adults, who may had a higher rate of somatic diseases compared to the general population. Many somatic diseases, such as chronic pain, thyroid dysfunction, and arthritis, have been associated with increased suicide rates[30, 31]. Third, several other studies had included outpatients and inpatients, a significant proportion of whom were receiving or had received antidepressant treatment, whereas our study focused on untreated patients with MDD. Fourth, differences in the social background, economic status, and medical conditions of the study populations may also contribute to differences in suicide rates[32].

Our findings suggested that among middle-aged patients with MDD, those with longer duration of illness had a higher suicide rate, which is consistent with previous findings on the correlation between the disease duration and patients' risk of suicide. For instance, Fang revealed that the total duration of depression was closely related to suicidal ideation[33]. Kraus et al. found that longer duration of untreated depression were often associated with worse outcomes[34]. Liang et al. reported that recurrent episodes of depression increased the risk of suicide[35]. An analysis of clinical data from 13 psychiatric and general hospitals in China concluded that multiple episodes of depression and a history of suicide attempts were independent risk factors for current suicide attempts[36]. However, there have also been studies that have incorporated disease duration into the selection of suicide risk factors for MDD patients, and the results showed that disease duration did not serve as a predictor for suicide. This inconsistency may be related to age differences and severity of disease among the participants of the studies. We hypothesize that some of the MDD patients who participated in this study did not seek treatment early at the onset of symptoms for social, economic, and cultural reasons. Instead, they sought treatment when their disease progressed to a more severe stage. Thus, the long duration of the disease caused physical or mental harm to untreated MDD patients, increasing the risk of suicide attempts. Our results suggested that early detection and treatment of MDD may reduce the incidence of suicide attempts by shortening the course of the disease. But further research is needed to address this risk factor, and these studies need to quantify the different levels of disease severity.

Our findings revealed a correlation between suicide risk and thyroid autoimmunity in middle-aged MDD patients. We found that blood levels of TGAb, TPOAb, and TSH were significantly elevated in MDD patients with suicide attempts, but without statistically significant differences in FT3 and FT4 levels. Elevated TSH levels with normal FT3 and FT4 levels indicate the presence of subclinical hypothyroidism[37], with a prevalence in the population of 3.8%-4.3%[38, 39]. TGAb and TPOAb play important roles in thyroid autoimmune diseases[40], and TGAb is a marker for autoimmune thyroid disease as is TPOAb[41]. Subclinical hypothyroidism is accompanied by abnormal levels of TGAb and TPOAb, leading to the diagnosis of autoimmune thyroiditis, which is also the main cause of subclinical hypothyroidism[37, 42]. Previous studies have suggested that autoimmune thyroiditis is common in the elderly[43], and TGAb and TPOAb levels are also associated with depressive symptoms[44]. In addition, Our study further suggested that TGAb was also associated with suicide attempts and was a risk predictor of suicide attempts in middle-aged first-episode depressive patients. The mechanism underlying the relevance of abnormal thyroid immune function and suicide attempts in depressed patients may be its effect on neurotransmitters such as serotonin 5-hydroxytryptamine and norepinephrine, which play an

important role in suicide attempts[45]. Second, high levels of TGAb and TPOAb indicate that these patients are in an autoimmune state, and autoimmunity has been linked to suicide attempts through the kynurenine pathway and the hypothalamic-pituitary-adrenal axis[46].

In the present investigation, it was observed that suicide attempts in depressed patients were associated with anxiety symptoms. Moreover, the HAMA was identified as an independent predictors of suicide attempts in these individuals. In fact, there are three aspects that support this discovery we found. First, Anxiety were identified as major risk factors for suicide by various organizations such as the American Association of Suicidology and the American Foundation for Suicide Prevention [47, 48]. Second, many theories regarding suicide also involved anxiety. For instance, Beck's cognitive-behavioral model of suicide suggests that anxiety is focused attention on the external manifestations of suicide, and interacts with despair to increase suicide risk[49, 50]. Joiner's interpersonal theory of suicide states that the state of acute anxiety, such as heightened alertness, panic attacks, or agitation, is consistent with the individual's psychological state prior to suicide[51]. Fawcett's theory aligns with the above viewpoints, suggesting that anxiety/agitation is a determining factor in suicide[52]. Riskind et al. propose that patients with anxiety, if experiencing feelings of hopelessness, may exhibit an impulse to escape the reality of pain, thus increasing the risk of suicide[53]. Suicide attempts are the avoidance response to intense emotions, similarly, the hallmark characteristic of anxiety is behavioral avoidance, which shares common features with suicide attempts[54]. Patients with anxiety also employ other avoidance strategies such as suppression, which further weakens positive self-awareness and increases suicide attempts[55]. Third, many other clinical studies have confirmed the link between anxiety and suicide attempts. A comprehensive retrospective analysis demonstrated a significant association between depression comorbid with an anxiety disorder and suicide[56]. Furthermore, certain studies have indicated that MDD patients with comorbid anxiety exhibit a higher propensity for suicide compared to those without anxiety[7, 57]. Additionally, one retrospective study found that 79% of depressed individuals with anxiety symptoms before suicide[58]. However, some reports show no relationship between anxiety and suicide attempts[59]. Instead, they found lower suicide rates in MDD patients with anxiety symptoms, suggesting that anxiety symptoms may be a protective factor against suicide risk[60]. These conflicting results may be interpreted as follows: the presence of anxiety in MDD patients is often interpreted as a reflection of a more serious illness and emotional instability, leading to increased suicide attempts. Some causal relationship between anxiety and substance abuse may also explain the relationship between anxiety and suicide[60]. On the other hand, an alternative explanation is that anxiety symptoms indicate an individual's worry and fear of illness and death, which were protective against suicide attempts[60]. There may be several reasons for the differing findings on whether anxiety is a risk factor for suicide attempts in MDD patients. First, our study population included MDD patients aged 35-60 years, many of whom were perimenopausal women. The suicide rate among perimenopausal women was relatively higher compared to premenopausal and postmenopausal women[61]. Therefore, our study results may be biased compared to studies with a lower proportion of perimenopausal women in the research population. Second, some of the studies come from different countries and ethnic groups with different social and cultural backgrounds. Suicide attempts may vary according to the religious and moral values

of these societies. Third, our study population was untreated MDD patients, whereas some of other studies involved patients who were hospitalized or had been treated or were being treated, which may affect the results. Therefore, more randomized controlled studies should be conducted on the relationship between anxiety and suicide attempts.

Some limitations need to be mentioned. First, although we identified suicide attempts and associated risk factors (e.g., clinical characteristics and metabolic indicators) in middle-aged MDD patients with IFG, It's difficult to determine a causation because this was a cross-sectional study. Longitudinal studies need to be conducted to determine the causal relationship between them. Second, no healthy control group was set and clinical information and biochemical indicators for statistical analysis were from MDD patients. Third, the study samples we chose were from a single center's psychiatric clinic, and there may be selection bias due to sample source limitations. Fourth, our study excluded patients with substance abuse and personality disorders, many of whom had comorbid depressive disorders and high suicide rates, so the results may be biased. In consequence, our research outcomes should be regarded as preliminary and need to be further confirmed in future large-sample and multicenter longitudinal studies.

Conclusion

In summary, our research showed a higher prevalence of suicide attempts among middle-aged depressed patients comorbid IFG (38.66%) was significantly higher than that in general depressive population. MDD patients comorbid IFG who attempted suicide had longer disease duration, more severe anxiety and psychiatric symptoms, higher blood pressure, and abnormal thyroid function compared to those who did not attempt suicide. For middle-aged MDD patients with IFG, HAMA score, disease duration, and blood TGAb levels were independent risk factors for suicide attempts. However, the findings of this study need to be interpreted with caution because of its small sample size and retrospective study design, and need to be confirmed by future longitudinal studies.

Abbreviations

IFG:impaired fasting glucose; MDD:Major depressive disorder; FEDN:first-episode and drug-naïve; TGAb:Anti-thyroglobulinand;TPOAb: Thyroid peroxidases antibody; TSH:Thyroid stimulating hormone; TC:Total cholesterol; HAMA:Hamilton anxiety rating scale; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; HAMD-17: Hamilton depression rating scale;BMI: Body mass index; CGI-S: Clinical global impression of severity scale;FT3:Free triiodothyronine;FT4:Free thyroxine;LDL:Low-density lipoprotein cholesterol;TG: Triglyceride;HDL: High-density lipoprotein cholesterol; PANSS: Positive and negative syndrome scale;SPSS: Statistical Package for the Social Sciences; NSA:non-suicide attempt; SA: suicide attempt.

Declarations

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Authors' contributions

Study design: Xiangyang Zhang, Guanjun Wang. Investigation: Guanjun Wang, Yunxin Ji. Analysis and interpretation of data: Guanjun Wang, Kuilai Wang. Data curation: Xiaoe Lang.Drafting of the manuscript: Guanjun Wang. Critical revision of the manuscript: Guanjun Wang, Yunxin Ji, Xiangyang Zhang. Approval of the final version for publication: Guanjun Wang, Yunxin Ji, Xiangyang Zhang.

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Availability of data and materials

Data analyzed in this study is subject to the following licenses/restrictions: All data in the current study are stored in affiliates of the PI. And is available from the corresponding author upon reasonable request and completion of the data user agreement. For access to these datasets, please get in touch with Professor Xiangyang Zhang, zhangxy@psych.ac.cn

Ethics approval and consent to participate

This study was conducted at the psychiatric clinic department in a general hospital in Taiyuan, Shanxi province, China. The protocol and informed consent of this study was approved by the Institutional Review Board, the First Clinical Medical College, Shanxi Medical University (No. 2016-Y27). Following a complete description of the study protocol and procedures to each participant by a psychiatrist or research coordinator, then written informed consent was obtained. All methods were carried out in accordance with the Declaration of Helsinki promulgated by the National Institute of Health. Informed consent was obtained from all subjects and/or their legal guardian(s).

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

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References

- Patel V, Saxena S, Lund C, Thornicroft G, Baingana F, Bolton P, Chisholm D, Collins PY, Cooper JL, Eaton J, et al. The Lancet Commission on global mental health and sustainable development. Lancet. 2018;392(10157):1553–98.
- 2. Menard C, Hodes GE, Russo SJ. Pathogenesis of depression: Insights from human and rodent studies. Neuroscience. 2016;321:138–62.
- Kessler RC, Petukhova M, Sampson NA, Zaslavsky AM, Wittchen HU. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. Int J Methods Psychiatr Res. 2012;21(3):169–84.
- 4. Choi NG, DiNitto DM, Marti CN. Middle-aged and older adults who had serious suicidal thoughts: who made suicide plans and nonfatal suicide attempts? Int Psychogeriatr. 2015;27(3):491–500.
- Song TH, Wang TT, Zhuang YY, Zhang H, Feng JH, Luo TR, Zhou SJ, Chen JX. Nightmare Distress as a Risk Factor for Suicide Among Adolescents with Major Depressive Disorder. Nat Sci Sleep. 2022;14:1687–97.
- Lundberg J, Cars T, Lampa E, Ekholm Selling K, Leval A, Gannedahl A, Sjalin M, Bjorkholm C, Hellner C. Determinants and Outcomes of Suicidal Behavior Among Patients With Major Depressive Disorder. JAMA Psychiatry. 2023;80(12):1218–25.
- 7. TP S, TK M, HJ R, US L, PS L-M, ET I. Suicidal ideation and attempts among psychiatric patients with major depressive disorder. J Clin Psychiatry. 2003;64:1094–100.
- 8. Sinclair JM, Harriss L, Baldwin DS, King EA. Suicide in depressive disorders: a retrospective casecontrol study of 127 suicides. J Affect Disord. 2005;87(1):107–13.
- 9. Remes O, Mendes JF, Templeton P. Biological, Psychological, and Social Determinants of Depression: A Review of Recent Literature. Brain Sci 2021, 11(12).
- José María, De la Roca-Chiapas MH-G, Candelario M. María de la Luz Villafaña, Enrique Hernández, Sergio Solorio, Antonio Rivera, Modesto Sosa, José Jasso: Association between depression and higher glucose levels in middle-aged Mexican patients with diabetes. Rev Invest Clin. 2013;65:209– 13.
- 11. Fugger G, Dold M, Bartova L, Kautzky A, Souery D, Mendlewicz J, Serretti A, Zohar J, Montgomery S, Frey R, et al. Major Depression and Comorbid Diabetes - Findings from the European Group for the Study of Resistant Depression. Prog Neuropsychopharmacol Biol Psychiatry. 2019;94:109638.
- 12. Wong H, Singh J, Go RM, Ahluwalia N, Guerrero-Go MA. The Effects of Mental Stress on Non-insulindependent Diabetes: Determining the Relationship Between Catecholamine and Adrenergic Signals from Stress, Anxiety, and Depression on the Physiological Changes in the Pancreatic Hormone Secretion. Cureus. 2019;11(8):e5474.

- 13. Subba R, Sandhir R, Singh SP, Mallick BN, Mondal AC. Pathophysiology linking depression and type 2 diabetes: Psychotherapy, physical exercise, and fecal microbiome transplantation as damage control. Eur J Neurosci. 2021;53(8):2870–900.
- 14. Snowdon J. Differences between patterns of suicide in East Asia and the West. The importance of sociocultural factors. Asian J Psychiatr. 2018;37:106–11.
- 15. Coupland C, Hill T, Morriss R, Arthur A, Moore M, Hippisley-Cox J. Antidepressant use and risk of suicide and attempted suicide or self harm in people aged 20 to 64: cohort study using a primary care database. BMJ. 2015;350(feb18 32):h517–7.
- 16. Dong M, Zeng LN, Lu L, Li XH, Ungvari GS, Ng CH, Chow IHI, Zhang L, Zhou Y, Xiang YT. Prevalence of suicide attempt in individuals with major depressive disorder: a meta-analysis of observational surveys. Psychol Med. 2019;49(10):1691–704.
- 17. Zhou Y, Ren W, Sun Q, Yu KM, Lang X, Li Z, Zhang XY. The association of clinical correlates, metabolic parameters, and thyroid hormones with suicide attempts in first-episode and drug-naïve patients with major depressive disorder comorbid with anxiety: a large-scale cross-sectional study. *Translational Psychiatry* 2021, 11(1).
- Kohnke C, Herrmann M, Berger K. Associations of major depressive disorder and related clinical characteristics with 25-hydroxyvitamin D levels in middle-aged adults. Nutr Neurosci. 2022;25(6):1209–18.
- 19. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960;23:56–62.
- 20. Hamilton M. The assessment of anxiety states by rating. Br J Med Psychol. 1959;32:50-5.
- 21. Kay SRFA, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull. 1987;13:261–76.
- 22. David. SMBA, Y LK, Harnett Sheehan P, Amorim J, Janavs E, Weiller T, Hergueta B. Dunbar: The Mini-International Neuropsychiatric Interview (M.I.N.I.):The Development and Validation of a Structured Diagnostic Psychiatric Interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998;59:uppl60.
- 23. Rosolová H, Prediabetes. Vnitřní lékařství. 2022;68(2):82-4.
- 24. Kim MK, Han K, Koh ES, Hong OK, Baek KH, Song KH, Kwon HS. Cumulative exposure to impaired fasting glucose and future risk of type 2 diabetes mellitus. Diabetes Res Clin Pract. 2021;175:108799.
- Alberti KGMMZP. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. Diabet Med. 1998;15(7):539–53.
- 26. Dong M, Wang SB, Li Y, Xu DD, Ungvari GS, Ng CH, Chow IHI, Xiang YT. Prevalence of suicidal behaviors in patients with major depressive disorder in China: A comprehensive meta-analysis. J Affect Disord. 2018;225:32–9.
- 27. Ruengorn C, Sanichwankul K, Niwatananun W, Mahatnirunkul S, Pumpaisalchai W, Patumanond J. Factors related to suicide attempts among individuals with major depressive disorder. Int J Gen Med. 2012;5:323–30.

- 28. Kim SW, Stewart R, Kim JM, Shin IS, Yoon JS, Jung SW, Lee MS, Yim HW, Jun TY. Relationship between a history of a suicide attempt and treatment outcomes in patients with depression. J Clin Psychopharmacol. 2011;31(4):449–56.
- 29. Azorin JM, Kaladjian A, Besnier N, Adida M, Hantouche E, Lancrenon S, Akiskal H. Suicidal behaviour in a French Cohort of major depressive patients: characteristics of attempters and nonattempters. J Affect Disord. 2010;123(1–3):87–94.
- 30. Smith L, Shin JI, Lee S, Oh JW, López Sánchez GF, Kostev K, Jacob L, Tully MA, Schuch F, Mcdermott DT, et al. The association of physical multimorbidity with suicidal ideation and suicide attempts in England: A mediation analysis of influential factors. Int J Soc Psychiatry. 2023;69(3):523–31.
- 31. Guojun Wang CJ, Zhenyu Ma L. Physical diseases and elderly suicide in rural China: A case–control psychological autopsy study. Aust N Z J Psychiatry. 2022;56:560–8.
- Shioiri T, Someya T, Helmeste D, Wa Tang S. Cultural difference in recognition of facial emotional expression: Contrast between Japanese and American raters. J Neuropsychiatry Clin Neurosci. 1999;53(6):629–33.
- 33. Fang X, Zhang C, Wu Z, Peng D, Xia W, Xu J, Wang C, Cui L, Huang J, Fang Y. Prevalence, risk factors and clinical characteristics of suicidal ideation in Chinese patients with depression. J Affect Disord. 2018;235:135–41.
- 34. Kraus C, Kadriu B, Lanzenberger R, Zarate CA, Kasper S. Prognosis and Improved Outcomes in Major Depression: A Review. FOCUS. 2020;18(2):220–35.
- 35. Liang S, Zhang J, Zhao Q, Wilson A, Huang J, Liu Y, Shi X, Sha S, Wang Y, Zhang L. Incidence Trends and Risk Prediction Nomogram for Suicidal Attempts in Patients With Major Depressive Disorder. Front Psychiatry 2021, 12.
- 36. Xin L-M, Chen L, Su Y-A, Yang F-D, Wang G, Fang Y-R, Lu Z, Yang H-C, Hu J, Chen Z-Y et al. Risk Factors for Recent Suicide Attempts in Major Depressive Disorder Patients in China: Results From a National Study. Front Psychiatry 2018, 9.
- Biondi B, Cappola AR, Cooper DS. Subclinical Hypothyroidism: A Review. JAMA. 2019;322(2):153–60.
- Garmendia Madariaga A, Santos Palacios S, Guillén-Grima F, Galofré JC. The Incidence and Prevalence of Thyroid Dysfunction in Europe: A Meta-Analysis. J Clin Endocrinol Metabolism. 2014;99(3):923–31.
- 39. Hollowell JGSN, Flanders WD, Serum TSH. T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and nutrition examination survey (NHANES III). J Clin Endocrinol Metab. 2002;87(2):489–99.
- 40. The molecular recognition theory applied to bispecific antibodies *Nature Medicine* 1995, 1(12):1222–1222.
- 41. Prentice LMPD, Sarsero D, et al. Geographical distribution of subclinical autoimmune thyroid disease in Britain: a study using highly sensitive direct assays for autoantibodies to thyroglobulin and thyroid peroxidase. Acta Endocrinol. 1990;123(5):493–8.

- 42. Carl'e ALP, Pedersen IB, et al. Epidemiology of subtypes of hypothyroidism in Denmark. Eur J Endocrinol. 2006;154(1):21–8.
- 43. Surks MIOE, Daniels GH, et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. JAMA. 2004;291(2):228–38.
- 44. Leyhe THM, Gallwitz B. Increased occurrence of severe episodes in elderly depressed patients with elevated anti-thyroid antibody level. Int J Geriatr Psychiatry. 2009;24(7):779–81.
- Toloza FJK, Mao Y, Menon L, George G, Borikar M, Thumma S, Motahari H, Erwin P, Owen R, Maraka S. Association of Thyroid Function with Suicidal Behavior: A Systematic Review and Meta-Analysis. Medicina. 2021;57(7):714.
- 46. Brundin L, Bryleva EY, Thirtamara Rajamani K. Role of Inflammation in Suicide: From Mechanisms to Treatment. Neuropsychopharmacology. 2017;42(1):271–83.
- 47. Warning Signs & Risk Factors
- 48. Prevention AFS. Suicide Risk factors. In.; 2015.
- 49. Wenzel ABA. A cognitive model of suicidal behavior: Theory and treatment. Appl Prev Psychol. 2008;12:189–201.
- 50. Wenzel AB, Beck GK. AT: Cognitive therapy for suicidal patients: Scientific and clinical applications. Washington, DC: APA Books; 2008.
- 51. Joiner T. Why people die by suicide. Cambridge. MA, US: Harvard University Press; 2005.
- 52. J F: Treating impulsivity and anxiety in the suicidal patient. Ann N Y Acad Sci 2001, 932:94–102.
- 53. JH R. Looming vulnerability to threat: A cognitive paradigm for anxiety. Behav Res Ther. 1997;35:685–702.
- 54. Briere J, Hodges M, Godbout N. Traumatic stress, affect dysregulation, and dysfunctional avoidance: a structural equation model. J Trauma Stress. 2010;23(6):767–74.
- 55. Kanwar A, Malik S, Prokop LJ, Sim LA, Feldstein D, Wang Z, Murad MH. The association between anxiety disorders and suicidal behaviors: a systematic review and meta-analysis. Depress Anxiety. 2013;30(10):917–29.
- 56. Hawton K, Casanas ICC, Haw C, Saunders K. Risk factors for suicide in individuals with depression: a systematic review. J Affect Disord. 2013;147(1–3):17–28.
- 57. Holma KMMT, Haukka J, Holma IA, Sokero TP, Isometsä ET. Incidence and predictors of suicide attempts in DSM–IV major depressive disorder: a five–year prospective study. Am J Psychiatry. 2010;16(7):801–8.
- 58. Busch KAFJ, Jacobs DG. Clinical correlates of inpatient suicide. J Clin Psychiatry. 2003;64:14–9.
- 59. Hornig CD, McNally RJ. Panic disorder and suicide attempt. A reanalysis of data from the Epidemiologic Catchment Area study. Br J Psychiatry. 1995;167(1):76–9.
- 60. Placidi GPOM, Malone KM, Brodsky B, Ellis SP, Mann JJ. Anxiety in major depression: relationship to suicide attempts. Am J Psychiatry. 2000;157(10):1614–8.

61. An SY, Kim Y, Kwon R, Lim G-Y, Choi HR, Namgoung S, Jeon SW, Chang Y, Ryu S. Depressive symptoms and suicidality by menopausal stages among middle-aged Korean women. Epidemiol Psychiatric Sci 2022, 31.

Tables

Table. 1 Socio-demographics and clinical characteristics of MDD patients comorbid IFG with SA subgroup and NSA subgroup

Variable		MDD comorbid I	<i>t/</i> c ² / <i>Z</i>	<i>P-</i> Value	
		Without suicide attempt	With suicide attempt		
Sample size		N=73	N=46		
Sex	Male <i>n</i> (%)	24(20.17%)	14(11.76%)	0.077	0.842
	Female <i>n</i> (%)	49(41.18)	32(26.89)		
Age [years,mean±SD]		46.89 6.28	46.72±6.93	-0.071	0.943
Education	Primary school <i>n</i> (%)	35(29.41%)	25(21.01%) -0.158		0.875
	High school <i>n</i> (%)	34(28.57%)	15(12.61%)		
	College n(%)	4(3.36%)	3(25.21%)		
	Postgraduate <i>n</i> (%)	0(0%)	4(3.36%)		
Marital status	Single <i>n</i> (%)	0(0%)	1(0.84%)	1.600	0.387
	Married n(%)	73(61.34%)	45(37.82%)		
Age of onset [years,mean±SD]		46.62±6.35	46.35±6.95	-0.180	0.857
Duration of illness [months,mean±SD]		6.97±4.44	8.98±5.09	-2.274	0.025
HAMD[mean±SD]		30.82±2.65	32.37±2.90	-2.989	0.003
HAMA[mean±SD]		20.90±3.21	24.89±3.38	-6.468	<0.001**
PANSS[mean±SD]		8.85±4.00	14.24±7.71	-4.071	<0.001**
CGI[mean±SD]		5.99±0.77	6.67±0.60	-4.787	<0.001**
TSH [uIU/ml,mean±SD)]		6.48±2.54	8.76±2.43	-4.846	<0.001**
TGAb [IU/L,mean±SD]		45.99±60.98	196.77±376.50	-3.607	<0.001**
TPOAb [IU/L,mean±SD]		82.23±261.73	241.42±361.36	-3.438	<0.001**
FT3 [pmol/L,mean±SD]		4.71±0.67	4.91±0.55	-1.710	0.090
FT4 [pmol/L,mean±SD]		16.86±3.18	16.81±2.64	0.101	0.920
FBG [mmol/L,mean±SD]		6.49±0.40	6.56±0.39	-1.507	0.132
TC [mmol/L,mean±SD]		5.55±1.14	6.07±1.14	-2.406	0.018
HDL-		1.17±0.33 Page 16/18	1.09±0.27	1.406	0.162

C [mmol/L,mean±SD)]				
LDL- C [mmoll/L,mean±SD]	3.23±0.93	3.47±0.78	-1.455	0.148
TG [mmol/L,mean±SD]	2.51±1.05	2.47±1.14	0.160	0.873
BMI [kg/cm ² ,mean±SD]	24.77±1.77	24.57±1.92	0.587	0.559
Systolic blood pressure [mmHg,mean±SD]	127.18±7.64	131.13±10.05	-2.283	0.025
Diastolic blood pressure (mmHg, mean±SD]	79.27±6.58	82.37±7.89	-2.312	0.023

Note: HAMD = Hamilton depression scale;HAMA = Hamilton anxiety scale;BMI = body mass index; PANSS= Positive and Negative Syndrome Scale;CGI=Clinical Global Impression of Severity Scale;TSH = thyroid stimulating hormone; TGAb = anti-thyroglobulinand;TPOAb = thyroid peroxidases antibody; FT3 = free triiodothyronine; FT4 = free thyroxine; FBG=fast blood glucose; TC= total cholesterol;HDL-C = high-density lipoprotein cholesterol; LDL-C = lowdensity lipoprotein cholesterol;TG = triglycerides; ** p < 0.001

Table. 2 Binary logistic regression analyses of suicidal risk factors in middle-aged MDD patients withIFG.

Variable	β	Std.error	Wald	Odds ratio	95 % confidence interval		Ρ	VIF
					Lower	upper		
Duration of illness	0.096	0.047	4.136	1.101	1.003	1.208	0.042	1.018
HAMA	0.304	0.073	17.194	1.356	1.174	1.566	<0.001**	1.130
TGAb	0.005	0.002	4.438	1.005	1.000	1.010	0.035	1.124

Note: HAMA = Hamilton anxiety scale;TGAb = anti-thyroglobulinand;

Figures

Points	0 10	20 30	40 50	60	70 80	90 100
Disease_duration	0 4 8 12 18	24				
НАМА	14 16 18 2	0 22 24 26	28 30 32			
TGAb	0 200	400 600	800 1000 12	00 1400	1600 1800	0 2000 2200
Total Points	0 20	40	60 80	100	120	140 160
Risk	0.1	0.3 0.5 0.7	0.9			

Figure 1

Nomographic chart of risk factors suicidal risk factors in middle-aged MDD patients with IFG.

Note:HAMA ,Hamilton anxiety scale;TGAb,anti-thyroglobulinand antibody.