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Retrospective Study

Analysis of risk factors of suicidal ideation in adolescent patients with depression and construction of prediction model

11
INTRODUCTION

Major depressive disorder (MDD) is a common mental illness characterized by low mood, loss of interest, and lack of pleasure[1]. Studies have shown that more than half of the population between the ages of 9 and 21 meets at least one of the diagnostic criteria; if unclear diagnoses are included, the proportion exceeds 80%[2,3]. This indicates that the prevalence of mental disorders, particularly depression, is gradually increasing in younger individuals. Currently, the prevalence of depression in adolescents is approximately 8%–23.9%[4]. Under the influence of depression, this group experiences a series of psychosocial problems such as weariness, interpersonal difficulties, mobile phone addiction, violence, self-mutilation, and suicide in severe cases[5]. Recently, adolescent suicides have ranked second among the causes of death in this age group[6].

Suicidal ideation (SI) refers to the idea or behavior of losing life expectations without necessarily causing physical harm[7]. Its manifestations range from brief and vague to very specific ideas. Specific ideas include the choice of program, planning, and completion of the entire suicide process. Although SI is not an actual suicide action, it has a particular predictive effect on suicidal behavior[8]. Studies have shown the emergence of SI in many elements, such as emotional regulation disorders, early trauma experience, family upbringing, adverse life events, and peer relationships, among which early trauma experience plays a role[9]. In addition, studies have shown that depression

may be a susceptibility factor for SI[10]. The World Health Organization has reported that 62% of adolescents with depression have strong SI and suicidal behavior[6]. Therefore, reducing SI in patients with depression is an important goal in the treatment of depression and is also an important sign of depression alleviation.

Logistic regression is often used to identify the factors influencing SI in patients with depression; however, it cannot directly reflect the influence of individual factors on the results. A prediction model can be developed using a nomogram, which has been widely used as a reliable tool for predicting risk[11] and has good prognostic value in disease prediction. However, nomograms are rarely used in the field of mental illness.

Based on previous studies, this study combined biological factors to determine the risk of SI in adolescent patients with depression and developed a nomogram model to predict SI in such patients. We hope this study will help quickly diagnose depression in adolescent patients with a high risk of SI and prevent possible suicide events.

MATERIALS AND METHODS

Research object

The retrospective study method was adopted. The research process is illustrated in Figure 1. Adolescent patients with depression who received treatment at the First People's Hospital of Lianyungang from June 2020 to December 2022 were selected as research participants. A total of 150 patients were included and divided into the SI (n = 91) and non-SI (n = 59) groups according to whether they had SI. The inclusion criteria were: (1) patients diagnosed by two psychiatrists who met the criteria for depressive episodes according to the International Classification and Diagnostic Criteria of Mental Disorders 10th Edition[12]. Among the included patients, the SI grouping was performed according to the fifth edition of the American Diagnostic and Statistical Manual of Mental Disorders[13]; (2) Either item 4 or 5 of the Beck Suicidal Ideation Scale-Chinese Version was found to be "weak" or above; (3) Age 12–18 years; and (4) No drugs affecting blood lipid, blood sugar, or ferritin levels were taken during the first three months of enrollment. Exclusion criteria were patients with (1) a history of severe

organic disease; (2) recent infection and history of trauma; (3) depression caused by psychoactive substances; (4) anemia, endocrine system diseases, hyperlipidemia, and recent use of lipid-lowering and diuretic drugs; (5) severe cognitive dysfunction; and (6) poor communication and understanding skills that make it difficult to complete the assessments.

Clinical data collection

The patients' medical data, including basic patient information, medical records, and test results, were obtained from the hospital records. The collection steps included (1) collecting the basic information of patients, including age, sex, and education level; (2) reviewing the patient's electronic medical record. The attending psychiatrist, with more than two years of working experience, summarized the patient's case data, including the disease course and the child's position in the family, according to the medical record. The presence of a single parent, triggers (frustration in learning, family history of mental illness, poor interpersonal relationships, broken relationships, parent-child tension, *etc.*)[14], history of trauma, and SI were also recorded; (3) The Beck Scale for Suicide Ideation[15] consists of 19 items with three possible ratings. The corresponding scores from lowest to highest are 0, 1, and 2. The higher the score, the greater the suicide risk. If item 4 or 5 of the scale shows "weak" or above, the patient can be judged to have SI. The strength of SI is obtained according to the total score of items 1–5 on the scale, which varies between 5 and 15 points. The higher the score, the stronger the SI; and (4) Test results of patients who fasted 12 h after admission were retrieved from the hospital records and included blood lipids, serum high-sensitivity C-reactive protein (hs-CRP), glutamic oxaloacetic transaminase, and serotonin levels.

Statistical analysis

All collected medical records were sorted into Excel format, and SPSS software (v.26.0) was used for statistical analysis. The chi-square test was used for count data, the *t*-test for measurement data, and the independent sample *t*-test for continuous variables.

Categorical variables are expressed as percentages of positive cases. The measurement data with a normal distribution were expressed as mean ± SD, and the χ^2 test was used. All tests were two-sided. $P < 0.05$ was set as a statistically significant difference.

Based on the results of the multivariate analysis, a nomogram prediction model was constructed using *R* software. To verify its predictive accuracy, bootstrap sampling was used to conduct internal validation 1000 times, and the receiver operating characteristic (ROC) curve, decision curve analysis (DCA), and calibration curve were used to evaluate the predictive efficacy and clinical utility of the nomogram.

RESULTS

Comparison of general factors between the two groups of patients

The statistical analysis showed that compared with the non-SI group, patients in the SI group had more trauma history and predisposing factors, and the difference was significant ($P < 0.05$) (Table 1).

Comparison of laboratory indices between the two groups of patients

According to the comparison of laboratory indicators between the two groups of patients, the study found that the levels of serum ferritin (SF) and hs-CRP in the SI group were higher than those in the non-SI group ($P < 0.05$). In addition, high-density lipoprotein (HDL-C) in patients with SI was lower than that in patients without SI ($P < 0.05$), while there were no statistically significant differences between the other indicators (Table 2).

Multivariate analysis of SI in adolescent patients with depression

Indicators with significant differences were included in the logistic regression analysis. Among them, the presence or absence of SI (yes = 1, no = 0) was used as the dependent variable, and history of trauma (yes = 1, no = 0), presence or absence of triggers (yes = 1, no = 0), and SF, hs-CRP, and HDL-C levels were used as independent variables. The results showed that a history of trauma, triggers, SF > 49.76, and hs-CRP > 3.829 were

risk factors for SI in adolescents with depression [odds ratio (OR) > 1, $P < 0.05$]. An HDL-C level > 0.683 was a protective factor against SI in adolescents with depression (OR < 1, $P < 0.05$) (Table 3). The ROC curve was used to evaluate the diagnostic value of each index. The highest area under the ROC curve (AUC) for SF was 0.695; the others are shown in Table 4 and Figure 2.

Construction of the nomogram model

A nomogram model was constructed based on the results of the multivariate analysis (Figure 3). Internal validation used bootstrap sampling 1000 times, and the AUC, DCA, and calibration curve were used to evaluate the efficacy of the nomogram. The AUC was 0.831, the sensitivity was 0.912, and the specificity was 0.678, with a 95%CI of 0.763–0.899, indicating that the model had predictive capability, as shown in Figure 4A. According to the DCA, the net benefit of the model was greater within a larger threshold range, indicating better clinical efficacy of the model (Figure 4B). In addition, the calibration curve further showed that the predicted value was in good agreement with the measured value, and the average absolute error (0.043) was small, indicating that the nomogram model had good predictive efficacy (Figure 4C).

DISCUSSION

In this study, we analyzed the occurrence of SI in adolescent patients with depression and developed a nomogram model with good predictive efficacy to predict SI risk.

In this study, 60.67% (91/150) of adolescent patients with depression had SI, which is consistent with a previous study[16]. In our study, female patients showed higher SI than male patients, consistent with the results of domestic and foreign studies[17,18]. This may be related to the hormone levels of female patients. The proportion of patients with SI with a history of trauma was significantly higher than that in the control group, suggesting that childhood trauma is a risk factor[19]. In addition, the study also found that a higher proportion of patients with various triggers had SI than those without

triggers, indicating that triggers play a role in SI in adolescent patients with depression[20].

Ferritin is an important marker of inflammation and oxidative stress. It is also a unique protein that stores iron and is often used to assess the level of iron stored in the body. Studies have shown that the mechanism underlying increased SF levels in patients with depression is mainly an oxidative stress reaction caused by increased ferritin[21]. Oxidative stress is directly related to the pathogenesis of depression, indicating that ferritin can indirectly affect the occurrence and development of depressive symptoms by triggering an oxidative stress response. In this study, the SI group had significantly higher SF levels than the non-SI group, suggesting that SF levels are associated with depression.

Furthermore, according to previous studies, elevated serum hs-CRP levels can oversecrete inflammatory cytokines, causing dysfunction of the 5-hydroxytryptamine and noradrenaline systems, thereby inducing depressive symptoms[22]. According to the study of Tabaeizadeh *et al*[23], there is a correlation between hs-CRP levels and depression in adolescent girls. Our study found that adolescents with depression and SI had higher hs-CRP levels. These results indicate that hs-CRP levels are associated with depression. In recent years, an increasing number of studies on the relationship between HDL-C and depression accompanied by suicidal thoughts have shown that patients with depression have a unique lipid metabolism profile compared to those without depression[24]. Our study showed that the HDL-C level in adolescent patients with depression and SI was lower than that in the non-SI group, which is consistent with previous studies. For example, Maes *et al*[25] showed that serum HDL-C levels in patients with depression and SI were low. This suggests that HDL-C may be a biological marker of MDD accompanied by SI. Simultaneously, it provides a new therapeutic target for treating depression and depressive symptoms, especially in patients with depression and SI, by regulating lipid levels through various mechanisms[26,27].

Based on the related risk factors for SI in adolescent patients with depression, we developed a risk prediction model and conducted internal validation. The calibration curve suggests good consistency between the values predicted by the model and measured values, and the DCA suggests that the net benefit of the model is better when the threshold is above 20%, indicating that the model has high clinical practicability. These results indicate that the model has good predictive efficacy. To the best of our knowledge, this is the first nomogram model that includes sociological factors and laboratory indicators to predict SI in patients with depression. This can help implement early clinical measures to reduce suicide mortality in adolescent patients with depression.

This study has some limitations. First, the participants were adolescents with depression. This is a relatively special group, as they are in a period of growth and development; therefore, fluctuations in hormone levels can significantly affect the results. Second, the dietary habits and nutritional status of patients were not considered. This may affect the levels of iron, hs-CRP, and HDL-C in the body, which may have caused bias in the study results. Further external validation is required in future studies. Finally, the insufficient sample size may have affected the validity of the nomogram model.

CONCLUSION

In conclusion, this study found that trauma history, predisposing factors, ferritin level, hs-CRP level, and HDL-C level may be early factors influencing SI in adolescent patients with depression. The nomogram model can effectively predict the occurrence of SI in adolescent patients with depression, which can help to quickly diagnose adolescent patients with depression at high risk of SI to prevent suicidal events.

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Figure Legends

Figure 1 The implementation process of this study. SF: Serum ferritin; hs-CRP: High-sensitivity C-reactive protein; HDL-C: High-density lipoprotein; SI: Suicidal ideation.

Figure 2 The diagnostic value of the receiver operating characteristic curve evaluation index. AUC: Area under the ROC curve; SF: Serum ferritin; hs-CRP: High-sensitivity C-reactive protein; HDL-C: High-density lipoprotein.

Figure 3 Nomogram for predicting suicidal ideation in adolescents with depression. For an individual patient, each variable corresponds to a single point at the top of the nomogram (Points). The total points were the sum of all single points and are indicated in the second line from the bottom (Total Points), and each total point corresponds to a probability of suicidal ideation. SF: Serum ferritin; hs-CRP: High-sensitivity C-reactive protein; HDL-C: High-density lipoprotein.

Figure 4 The nomogram of suicidal ideation in internal validation. A: Receiver operating characteristic of the nomogram for predicting the probability of suicidal ideation (SI); B: Density curve analysis of the nomogram for predicting the probability of SI; C: Calibration curve of the nomogram for predicting the probability of SI. AUC: Area under the receiver operating characteristic curve; SF: Serum ferritin; hs-CRP: High-sensitivity C-reactive protein; HDL-C: High-density lipoprotein; DCA: Density curve analysis; SI: Suicidal ideation.

Table 1 Comparison of general information between the two groups, *n* (%)

Characteristic	SI group (n = 91)	Non-SI group (n = 59)	t/χ^2 value	P value
Sex				
Male	25 (27.47)	20 (33.90)	0.704	0.402
Women	66 (72.53)	39 (66.10)		
Age	14.165 ± 0.793	14.220 ± 0.789	0.186	0.157
Trauma history				
Yes	39 (42.86)	8 (13.56)	14.28	0.001
No	52 (57.14)	51 (86.44)		
Only child				
Yes	60 (65.93)	40 (67.80)	0.056	0.813
No	31 (34.07)	19 (32.20)		
Single parent				
Yes	19 (20.88)	11 (18.64)	0.112	0.738
No	72 (79.12)	48 (81.36)		
First-episode				
Yes	66 (72.53)	46 (77.97)	0.560	0.454
No	25 (27.47)	13 (22.03)		
Are there triggers				
Yes	42 (46.15)	23 (38.98)	13.328	0.039
No	49 (53.85)	36 (61.02)		
Ethnic groups				
Han nationality	82 (90.11)	53 (89.83)	0.003	0.956
Ethnic minorities	9 (9.89)	6 (10.17)		
Educational level				
High school and above	39 (42.86)	21 (35.59)	0.787	0.375
Junior high school and below	52 (57.14)	38 (64.41)		

Religious belief				
Yes	3 (3.30)	4 (6.78)	0.976	0.323
No	88 (96.70)	55 (93.22)		
Residential area				
City	61 (67.03)	36 (61.02)	0.567	0.451
Rural	30 (32.97)	23 (38.98)		
Economic situation				
Poor	15 (16.48)	8 (13.56)		
Medium	55 (60.44)	36 (61.02)	0.284	0.868
Better	21 (23.08)	15 (25.42)		
Father's education level				
Junior high school and below	65 (71.43)	42 (71.19)	0.001	0.974
High school and above	26 (28.57)	17 (28.81)		
Mother's educational level				
Junior high school and below	63 (69.23)	43 (72.88)	0.230	0.631
High school and above	28 (30.77)	16 (27.12)		

SI: Suicidal ideation.

Table 2 Comparison of biochemical indices between the two groups

Index	SI group	Non-SI group	*t* value	*P* value
SF (μg/L)	71.010 ± 13.278	58.422 ± 17.842	-4.945	0.015
Folic acid (mmol/L)	4.350 ± 0.139	4.436 ± 0.172	11.864	0.053
Vitamin D_3 (mg/L)	12.773 ± 0.836	13.200 ± 0.846	4.366	0.054
hs-CRP (mg/L)	4.115 ± 1.497	3.423 ± 1.012	-3.115	0.020
UA (mmol/L)	335.989 ± 16.667	330.924 ± 16.875	-1.809	0.861
TG (mmol/L)	1.073 ± 0.103	1.061 ± 0.105	-0.656	0.794
TC (mmol/L)	3.737 ± 0.048	3.737 ± 0.047	-0.023	0.949
HDL-C (mmol/L)	1.039± 0.210	1.174 ± 0.282	3.351	0.009

LDL-C (mmol/L)	2.079 ± 0.055	2.076 ± 0.061	-0.313	0.411
TP (g/L)	76.312 ± 1.088	75.951 ± 1.230	-1.881	0.062
ALB (g/L)	47.230 ± 0.916	46.716 ± 1.088	-3.549	0.081
TBIL (μmol/L)	14.964 ± 0.218	14.820 ± 0.203	-4.045	0.121
AST (U/L)	42.325 ± 0.543	41.897 ± 0.501	-4.852	0.089
TSH (mmol/L)	150.080 ± 1.180	149.890 ± 1.109	0.986	0.326
T_3 (pmol/L)	1.519 ± 0.292	1.514 ± 0.246	-0.124	0.902
T_4 [M(Q)pmol/L]	86.850 ± 18.366	87.285 ± 19.229	0.139	0.889
FT_3 (pmol/L)	4.317 ± 0.501	4.250 ± 0.437	1.913	0.050
FT_4 (pmol/L)	11.339 ± 1.965	11.244 ± 2.040	-0.284	0.777

SI: Suicidal ideation; SF: Serum ferritin; hs-CRP: High-sensitivity C-reactive protein; UA: Uric acid; TG: Triglyceride; TC: Total cholesterol; HDL-C: high-density lipoprotein; LDL-C: Low-density lipoprotein; TP: Total protein; ALB: Albumin; TBIL: Total bilirubin; AST: Aspartate transaminase; TSH: Thyroid-stimulating hormone; T_3: Triiodothyronine; T_4: Thyroxine; FT_3: Free T_3; FT_4: Free T_4.

Table 3 Multivariate analysis of suicidal ideation in adolescents with depression

Independent variable	B	SE	Wald	*P* value	OR	95%CI
Trauma history	1.106	0.519	4.552	0.033	3.023	1.094–8.354
Triggers	1.311	0.461	8.107	0.004	3.711	1.505–9.153
SF (μg/L)	0.051	0.014	12.598	0.000	1.052	1.023–1.082
hs-CRP (mg/L)	0.453	0.172	6.927	0.008	1.573	1.123–2.205
HDL-C (mmol/L)	-2.104	0.852	6.095	0.014	0.122	0.023–0.648
FT_3 (pmol/L)	-1.217	0.502	5.886	0.078	0.296	0.111–0.791
Constant	-2.293	1.609	2.031	0.154	0.101	-

OR: Odds ratio; SF: Serum ferritin; hs-CRP: High-sensitivity C-reactive protein; HDL-C: High-density lipoprotein; FT_3: Free triiodothyronine.

Table 4 Diagnostic value of receiver operating characteristic curve evaluation index

Independent variable	Cutoff	AUC	Sensitivity	Specificity	Youden index	*P* value	95%CI
Trauma history	-	0.647	0.429	0.864	0.293	0.002	0.558–0.734
Triggers	-	0.651	0.538	0.763	0.301	0.002	0.562–0.740
SF (μg/L)	49.76	0.695	0.989	0.322	0.311	0.000	0.607–0.783
hs-CRP (mg/L)	3.829	0.643	0.593	0.712	0.305	0.003	0.556–0.731
HDL-C (mmol/L)	0.683	0.656	0.967	0.068	0.035	0.001	0.250–0.439

AUC: Area under the receiver operating characteristic curve; SF: Serum ferritin; hs-CRP: High-sensitivity C-reactive protein; HDL-C: High-density lipoprotein.

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