

Psychosocial and Biological Factors Associated with Non-Suicidal Self-Injury in Chinese Child and Adolescent Inpatients with Major Depressive Disorder

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Object: This study assessed the prevalence and associated psychosocial and biological factors of non-suicidal self-injury (NSSI) in Chinese child and adolescent inpatients diagnosed with major depressive disorder (MDD) by DSM-5 criteria.

Methods: This cross-sectional study included 177 inpatients aged 10–16 years. Participants were assessed using the Childhood Trauma Questionnaire (CTQ), Hamilton Depression Scale (HAMD-24), Hamilton Anxiety Scale (HAMA), Shame Scale for Middle School Students (SS), and Mobile Phone Addiction Index (MPAI). Fasting blood levels of cortisol, thyroid hormones, and inflammatory markers were measured. Group comparisons (NSSI vs non-NSSI) used t-tests and chi-square tests, followed by binary logistic regression to identify independent associated factors of NSSI.

Results: NSSI prevalence was 69.49%, with a higher proportion of females in the NSSI group. Compared to the non-NSSI patients, the NSSI group exhibited significantly higher scores on the HAMD-24, HAMA, shame, and MPAI scales, as well as higher cortisol and lower free triiodothyronine (FT3) levels. No significant differences were found in other biomarkers (Hypersensitive C-reactive protein, FT4, T3, T4, TSH, Adrenocorticotrophic hormone). Regression analysis identified emotional neglect (OR = 1.223), depression severity (OR = 1.197), anxiety (OR = 1.186), shame (OR = 1.046), and cortisol (OR = 1.081) as significant factors associated with NSSI. Smartphone addiction and thyroid function-related indicators showed no significant association in the regression model.

Conclusion: NSSI is highly prevalent among child and adolescent inpatients with MDD and is associated with emotional neglect, depressive and anxiety symptoms, shame-proneness, and dysregulated cortisol levels. Smartphone addiction and other biological markers (Hypersensitive C-reactive protein, FT4, T3, T4, TSH, and Adrenocorticotrophic hormone) showed no independent association with NSSI in the final model. These findings highlight the importance of integrated management of psychological and biological indicators in high-risk children and adolescents.

Keywords: non-suicidal self-injury, major depressive disorder, child and adolescent inpatients, cortisol, emotional neglect

Background

Depressive disorder is a common mental disorder that places a serious burden on society, families and individuals. In 2019, *The Lancet Psychiatry* published an article on the prevalence of mental disorders in China, reporting a lifetime prevalence of depressive disorders at 3.4%.¹ Subsequently, in 2020, *The Lancet Psychiatry* released further findings on the global prevalence and burden of mental disorders, revealing that depressive disorders accounted for the largest proportion of disability-adjusted life years (DALYs) (37.3%) among all mental health conditions.²

A proportion of depression cases begin in childhood and increase dramatically during adolescence.³ Studies have found that an estimated 25% of teenagers have experienced depressive episodes before the age of 19.⁴ Experiencing Depressive episodes before adulthood predicts a higher risk of self-harm and suicide.⁵ Within this population, Non-Suicidal Self-Injury (NSSI) is particularly prevalent, characterized by deliberate self-harm (eg, cutting, burning, or hitting oneself) without suicidal intent.^{6,7} A study on non-suicidal self-injurious behavior in Chinese adolescents with mood disorders found that the frequency of NSSI was 64.3%.⁸ Another report on NSSI in adolescent psychiatric hospitalization in China showed that the incidence of NSSI was 77.8% and was closely associated with more severe emotional dysregulation, higher suicide risk, and poorer social functioning.⁹ A survey in China showed that 62% of psychiatric inpatients with depression or bipolar disorder in two psychiatric hospitals reported having engaged in NSSI in the past year.¹⁰

The occurrence of NSSI is influenced by multiple factors, including psychosocial and biological determinants.¹¹ At the psychosocial level, childhood trauma has been identified as a significant predictor of NSSI, potentially exacerbating emotional sensitivity and self-loathing, thereby leading individuals to resort to self-harm as a maladaptive coping mechanism.^{12,13} Additionally, the severity of depressive and anxiety symptoms, shame proneness, and behavioral issues such as smartphone addiction may further increase the risk of NSSI.^{8,14–16} From a biological perspective, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, reflected in cortisol levels, adrenaline-stimulating levels, and abnormal thyroid hormone metabolism, may contribute to the pathophysiology of NSSI, while changes in inflammatory factor levels may also be one of the biological indicators of NSSI.^{17–19} However, findings regarding cortisol levels remain controversial. Most studies suggest that patients with NSSI and childhood trauma exhibit reduced cortisol levels,^{20,21} while some reports indicate that factors such as shame, and depressive or anxiety symptoms may lead to elevated cortisol levels.²² This underscores the complexity of HPA axis regulation and highlights the need for further research in clinical samples.

However, most of the current studies have focused on non-clinical samples of children and adolescents, and few studies have focused on the incidence and related influencing factors of NSSI in patients with depressive disorders, and limited research has integrated psychosocial and biological factors to explore risk factors for NSSI. Although the DSM-5 has established clear diagnostic criteria for non-suicidal self-injury (NSSI),²³ a portion of current studies still rely solely on self-injury questionnaires for assessment without strictly adhering to the DSM-5 diagnostic framework.^{8,10} This discrepancy in assessment methods may compromise the accuracy and comparability of prevalence rates and related factors across different studies. Therefore, further research is needed to explore the multifactorial etiology of NSSI—particularly within the framework of the new DSM-5 criteria—by simultaneously examining a wide range of psychosocial (eg, childhood trauma, shame, smartphone addiction) and biological factors (eg, cortisol, thyroid hormones, inflammatory markers).

Therefore, this study aims to apply the DSM-5 criteria to examine the prevalence of NSSI among young patients with major depressive disorder (MDD) and explore its associated risk factors, including childhood trauma, psychopathological symptoms (depression, anxiety), psychological traits (shame, smartphone addiction), and biological markers (cortisol, thyroid hormones, hypersensitive C-reactive protein, etc). We hypothesized that, compared to child and adolescent depression inpatients without NSSI, those in the NSSI group experienced more childhood trauma, higher levels of shame, greater smartphone addiction, more severe anxiety and depression symptoms, and that certain biological indicators such as thyroxine and cortisol levels may influence NSSI. The findings will contribute to the early identification of high-risk individuals in clinical settings and provide a theoretical foundation for developing targeted psychological and biological interventions. Ultimately, this research may help reduce the occurrence of NSSI and improve long-term outcomes for affected individuals.

Methods

Subject

This was a cross-sectional naturalistic study conducted at the Nantong Fourth People's hospital, Nantong City, Jiangsu province, China. 177 inpatients were recruited from July 1, 2024 to June 1, 2025. A schematic of the participant flow was shown in [Figure 1](#).

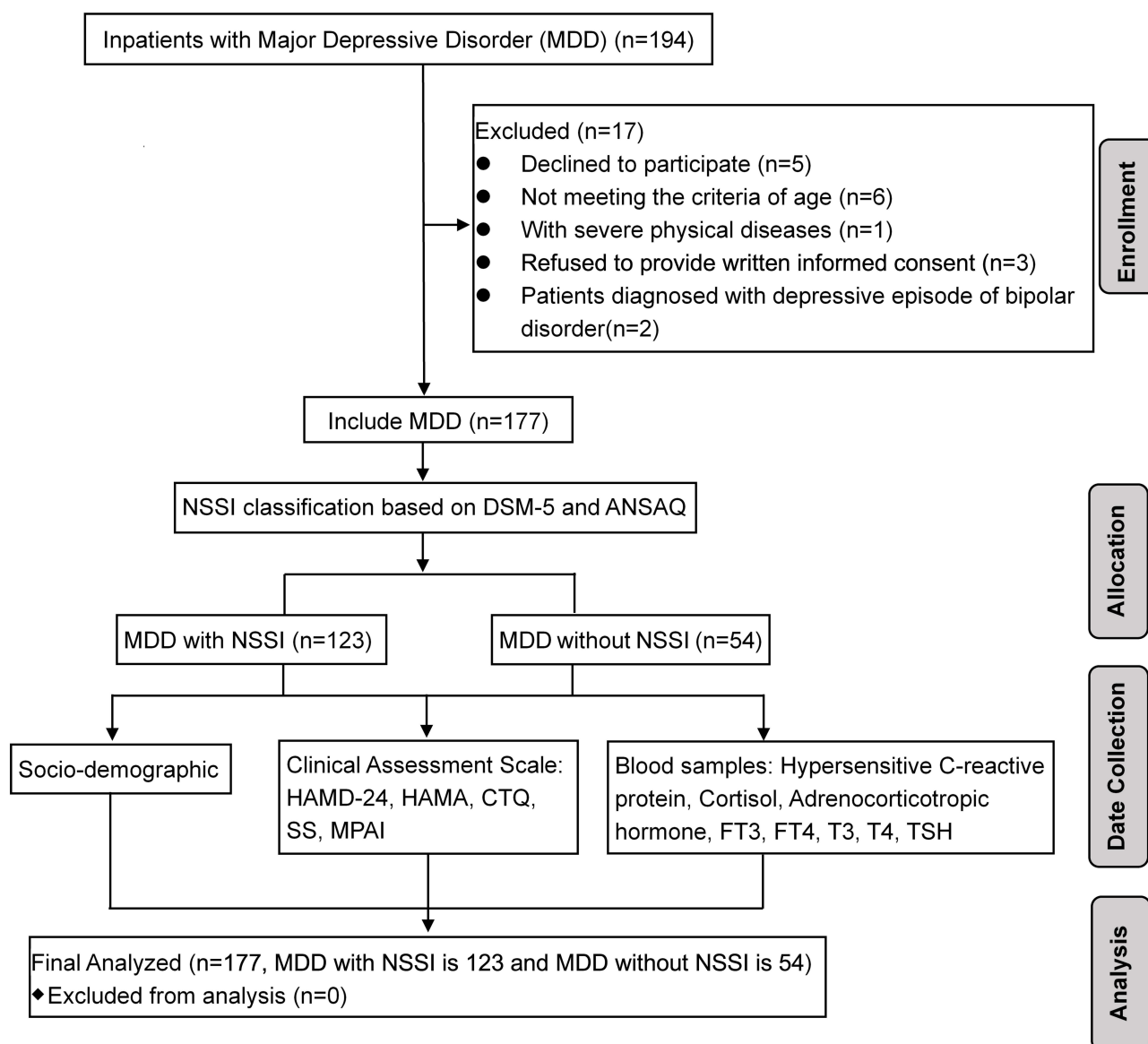


Figure 1 Enrollment and follow-up analysis processes.

Abbreviations: MDD, Major Depression Disorder; NSSI, non-suicidal self-injury; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; ANSAQ, Adolescent Non-suicidal Self-injury Assessment Questionnaire; CTQ, Childhood Trauma Questionnaire; HAMD-24, Hamilton Depression Scale-24 items; HAMA, Hamilton Anxiety Scale; SS, Shame Scale for Middle School Students; MPAI, Mobile Phone Addiction Index; FT3, free triiodothyronine; FT4, free thyroxine; TSH, Thyroid Stimulating Hormone; T3, Triiodothyronine; T4, Thyroxine.

All patients met the following inclusion criteria, 1) 7 to 16 years old; 2) Han Chinese; 3) a primary diagnosis of Major Depressive Disorder (MDD) was independently established for each patient by two psychiatrists, each with over ten years of clinical experience, according to the DSM-5 criteria; 4) the ability to understand the meaning of each scale entry. The exclusion criteria included, 1) with major medical abnormalities, including central nervous system diseases, and acute, unstable or life-threatening medical illnesses (eg cancer, infections); 2) with alcohol or drug dependence/abuse (except tobacco smoking); 3) pregnancy or breastfeeding; 4) refused to provide written informed consent; 5) patients diagnosed with depressive episode of bipolar disorder or post-schizophrenia depression, and co-morbidity with other psychotic disorders.

This study has been registered on the National Health Security Information Platform in China (No., MR-32-24-014696). The study protocol was approved by the Nantong Fourth People's Hospital (2023-k027). Written informed

consent was obtained from the legal guardians of all participants under the age of 18, and assent was obtained from the participants themselves.

Socio-Demographic Characteristics and Clinical Measures

Socio-Demographic

Socio-demographic data were collected using a self-designed questionnaire. Information obtained included gender, age, years of education, marital status, only-child status, single-parent family status, etc.

Non-Suicidal Self-Injury

Non-suicidal self-injury (NSSI) was first identified according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria. According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), non-suicidal self-injury (NSSI) is characterized by intentional, self-inflicted damage to the body surface on five or more days within the past 12 months, resulting in bleeding, bruising, or pain (eg, cutting, burning, hitting), without suicidal intent. The behavior is performed to relieve negative feelings, resolve interpersonal difficulties, or induce positive feelings, and is typically preceded by interpersonal problems, negative emotions, or difficult-to-control urges and thoughts about self-injury. It is not socially sanctioned, not attributable to another mental or medical disorder, and causes clinically significant distress or functional impairment, while excluding occurrences during psychosis, delirium, substance use, or neurodevelopmental repetitive stereotypies.²³

Following diagnostic classification, all participants completed the Adolescent Non-suicidal Self-injury Assessment Questionnaire (ANSAQ), a validated Chinese instrument consisting of a 12-item Behavior subscale and a 19-item Function subscale, each rated on a five-point Likert scale (0–4). The Behavior subscale demonstrated a Cronbach's α of 0.921 and test–retest reliability of 0.843, while the Function subscale had a Cronbach's α of 0.905 and test–retest reliability of 0.805.²⁴ This tool has been shown to possess good psychometric properties and is suitable for assessing NSSI behaviors and their functions among Chinese adolescents. Based on this initial screening, participants were categorized into the NSSI group or the non-NSSI group.

Clinical Symptoms

Two standardized scales were selected for their clinical relevance. The Hamilton Depression Rating Scale (HAMD-24) and the Hamilton Anxiety Rating Scale (HAMA) were used to evaluate depressive and anxiety symptoms, respectively. The 24-item Hamilton Depression Rating Scale, which uses a 5-point Likert scale ranging from 0 (not present) to 4 (severe), was employed to assess the degree of depression in patients.²⁵ The Hamilton Anxiety Scale was administered clinically to assess anxiety severity, with its 14 items rated on a 0–4 point scale.²⁶ Both are clinician-administered instruments widely used in psychiatric assessment, with higher total scores indicating greater symptom severity.

Childhood Trauma

Childhood Trauma Questionnaire (CTQ) was used to assess the childhood traumatic experiences.²⁷ The CTQ is a 28-item self-report instrument, including five subscales, emotional abuse (EA), physical abuse (PA), sexual abuse (SA), emotional neglect (EN), physical neglect (PN). Subscale scores are obtained by summing items within each domain, and the total score is calculated from all clinical items, with higher scores indicating greater trauma severity. Previous research has demonstrated that the Chinese version of the CTQ-SF shows good reliability and validity in undergraduate and depressive samples, supporting its use as an effective tool for assessing childhood trauma.²⁸ All questionnaires were completed anonymously under the supervision of trained research staff to ensure comprehension.

Shame

The Shame Scale for Middle School Students (SS) was used to measure levels of shame among children and adolescents.²⁹ The scale comprises 22 items, each rated on a 4-point scale ranging from 0 (“never”) to 3 (“often”), with higher total scores reflecting greater proneness to shame. The Chinese version of the scale has been validated in

prior studies, demonstrating good to excellent internal consistency, satisfactory test-retest reliability, and robust content, construct, and criterion-related validity.^{15,30} Its subsequent widespread use in adolescent research has provided valuable insights for both clinical practice and educational interventions across China.

Mobile Phone Addiction

The Mobile Phone Addiction Index (MPAI) was employed to measure mobile phone addiction.³¹ This scale contains 17 items and 4 subscales, Inability to Control Craving, Anxiety and Feeling Lost, Withdrawal and Escape, and Productivity Loss. Higher scores on this scale indicate a greater severity of mobile phone dependency. The Chinese version has been validated in a university student sample, demonstrating good internal consistency (Cronbach's $\alpha=0.91, 0.84, 0.83, 0.87$, and 0.81 for the total score and inability to control craving, anxiety and feeling lost, withdrawal and escape, and productivity loss, respectively) and acceptable test-retest reliability over a five-week interval ($r=0.69, 0.61, 0.70, 0.69$, and 0.60 , respectively). This instrument has been validated and demonstrates good reliability and validity in Chinese populations.

Blood Samples

Fasting venous blood samples were collected from all participants between 6,00 and 8,00 am on the day following admission. All blood samples were sent to the laboratory center of hospital immediately after collection, and measured before 10 am on the same day.

Hypersensitive C-reactive, Measured using latex-enhanced immunoturbidimetry on the CRP-M100 specific protein immune analyzer from Shenzhen Mindray Bio-Medical Electronics Co., Ltd. with its corresponding reagents. The reference range is 0–10 mg/l, the internal quality control CV is 1.65%, and quality control materials were provided by Shenzhen Mindray Bio-Medical Electronics Co., Ltd.

Cortisol, Determined by magnetic particle chemiluminescence immunoassay using the Autobio A2000 PLUS fully automated chemiluminescence analyzer and matched reagents from Zhengzhou Autobio Biotechnology Co., Ltd. The reference interval is 4.26–24.85 $\mu\text{g/mL}$, the internal quality control CV is 2.10%, and quality control materials were sourced from Bio-Rad Laboratories, Inc.

Adrenocorticotrophic hormone, Analyzed by magnetic particle chemiluminescence immunoassay on the Autobio A2000 PLUS fully automated chemiluminescence analyzer with reagents from Zhengzhou Autobio Biotechnology Co., Ltd. Reference ranges were defined according to blood collection time, 7.2–63.4 pg/mL for morning samples (6,00–10,00) and 3–3.2 pg/mL for afternoon samples (15,00–17,00). The internal quality control CV was 3.5%, and quality control materials were supplied by Bio-Rad Laboratories, Inc.

Thyroid function parameters, Including FT3, FT4, TT3, TT4, and TSH, all were measured by magnetic particle chemiluminescence immunoassay using the Autobio A2000 PLUS fully automated chemiluminescence analyzer and corresponding reagents from Zhengzhou Autobio Biotechnology Co., Ltd. The respective reference ranges were, FT3 3.5–7 pmol/l, FT4 10–22 pmol/l, TT3 0.8–1.9 ng/mL, TT4 5–13 $\mu\text{g/dl}$, and TSH 0.35–4.75 $\mu\text{IU/mL}$. The internal quality control CVs were 5.21%, 5.57%, 4.40%, 7.0%, and 5.184%, respectively. All quality control materials were provided by Jiangsu Kuole Biotechnology Co., Ltd.

Statistical Analysis

Group differences in socio-demographic, clinical characteristics and peripheral blood biological indicators between patients with and without NSSI were compared by using the *t*-test for continuous variables and the chi-square test for categorical variables. Binary logistic regression analysis was used to analyze the influencing factors of non-suicidal self-injury patients. Coefficient values, odds ratios (OR), and 95% confidence intervals (CI) were calculated to quantify the strength of these associations. Additionally, correlations between NSSI and clinical variables were examined using Spearman correlation coefficients. This nonparametric measure was chosen because NSSI is a dichotomous variable (presence vs absence) while the clinical scales yield continuous scores, and Spearman's rho is appropriate for assessing associations involving such mixed variable types without assuming linearity or normal distribution. Variables included in the binary logistic regression model were selected based on univariate statistical significance. Specifically, all variables

that showed significant differences between the NSSI and non-NSSI groups in univariate analyses (t-tests or chi-square tests, $p < 0.05$) were entered into the regression model. All statistical analysis was conducted using SPSS 22.0, with two-tailed p -values of 0.05 considered statistically significant.

Results

The final dataset comprised 177 participants aged 10–16 years, who were categorized into two groups based on their scores: the NSSI group and the non-NSSI group.

Table 1 compares the socio-demographic, clinical characteristics and peripheral blood biological indicators between MDD with NSSI (non-suicidal self-injury) and MDD without NSSI (non-suicidal self-injury) groups. Among the 177 patients, 123 (69.49%) met the criteria for NSSI—with a significantly higher proportion of females (111/145) than males (12/32)—while the remaining 54 (31.03%) did not meet the criteria for NSSI. Compared with patients without NSSI, NSSI patients had greater scores on HAMD, HAMA, Shame Scale for Middle School Student and MPAAI as well as subscales (inability to control craving, feeling anxious and lost, productivity loss, withdrawal/escape) (all $p < 0.01$). The patients with NSSI also had higher serum cortisol levels and lower serum FT3 levels (all $p < 0.05$).

Table 1 Socio-Demographics, Clinical Characteristics and Peripheral Blood Biological Indicators Between Patients with and without NSSI

Variables	MDD with NSSI	MDD without NSSI	P
Gender, n (%)			<0.001 ^a
Male	12(37.5%)	20(62.5%)	
Female	111(76.5%)	34(23.4%)	
Age (years)	14.34±1.59	14.81±1.90	0.088
Marriage (single/married)	123/0	54/0	1.000 ^a
Education (years)	9.26±1.78	9.76±1.96	0.098
Duration of illness (years)	1.46±0.75	1.33±0.55	0.135
Singleton (yes/no)	36/87	14/40	0.649 ^a
Single-parent family (yes/no)	93/30	39/15	0.634 ^a
Total Score of CTQ	56.10±12.19	50.48±13.90	0.008
Emotional abuse	14.07±4.34	11.50±4.55	<0.001
Physical abuse	7.26±2.91	6.91±2.85	0.456
Sexual abuse	6.71±2.66	6.06±2.92	0.148
Emotional neglect	17.71±3.51	15.81±4.67	0.003
Physical neglect	10.41±2.80	10.20±3.39	0.667
HAMD-24 Total	36.29±4.07	31.28±7.92	<0.001
HAMA Total	26.71±3.67	24.43±4.41	<0.001
MPAAI Total	36.74±14.45	27.54±17.43	<0.001
Inability to control craving	8.19±4.56	5.31±4.76	<0.001
Feeling anxious and lost	13.89±5.94	11.02±7.51	0.007
Productivity loss	6.80±2.76	4.89±3.57	<0.001
Withdrawal/escape	7.85±3.49	6.31±3.47	0.008
Hypersensitive C-reactive protein	2.19±2.22	1.76±2.00	0.225
Cortisol	14.25±6.54	10.77±6.20	0.001
Adrenocorticotrophic hormone	38.22±23.60	38.96±27.79	0.855
FT3	5.40±0.65	5.65±0.78	0.029
FT4	16.47±2.41	16.43±2.65	0.919
T3	1.15±0.17	1.20±0.19	0.058
T4	7.71±1.38	7.42±1.31	0.203
TSH	2.23±1.46	2.51±2.10	0.303

Notes: Values are presented as mean ± SD. ^aChi-square analysis.

Abbreviations: NSSI, non-suicidal self-injury; CTQ, Childhood Trauma Questionnaire; HAMD-24, Hamilton Depression Scale-24 items; HAMA, Hamilton Anxiety Scale; MPAAI, Mobile Phone Addiction Index; FT3, free triiodothyronine; FT4, free thyroxine; TSH, Thyroid Stimulating Hormone; T3, Triiodothyronine; T4, Thyroxine.

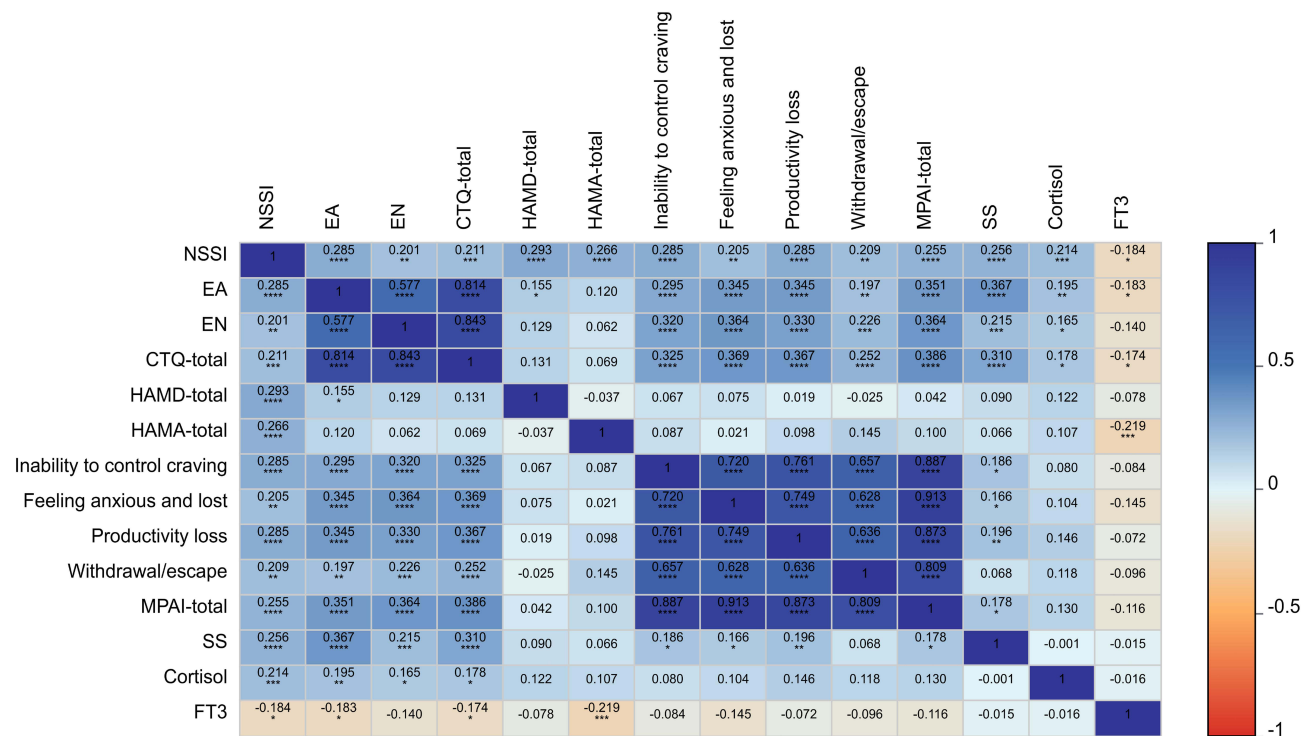


Figure 2 Analysis of the correlation between NSSI and clinical scales and biological indicators.

Notes: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$, **** $p < 0.001$.

Abbreviations: CTQ, Childhood Trauma Questionnaire; EA, Emotional abuse; EN, Emotional neglect; HAMD, Hamilton Depression Scale; HAMA, Hamilton Anxiety Scale; SS, Shame Scale for Middle School Students; FT3, free triiodothyronine.

In Spearman correlation analysis, total score of the CTQ ($r = 0.211$, $p = 0.005$), emotional abuse ($r = 0.285$, $p < 0.001$), emotional neglect ($r = 0.201$, $p = 0.007$), total score of HAMD-24 ($r = 0.293$, $p < 0.001$), total score of HAMA ($r = 0.266$, $p < 0.001$), total score of Shame Scale for Middle School Student scale ($r = 0.256$, $p < 0.001$), total score of MAPI scale ($r = 0.255$, $p < 0.001$) as well as subscales inability to control craving ($r = 0.285$, $p < 0.001$), feeling anxious and lost ($r = 0.205$, $p = 0.006$), productivity loss ($r = 0.285$, $p < 0.001$), withdrawal/escape ($r = 0.209$, $p = 0.005$), cortisol ($r = 0.214$, $p = 0.004$) and FT3 ($r = -0.185$, $p = 0.014$) were significantly related to patients with NSSI (see Figure 2).

Further binary logistic regression analysis showed that emotional neglect (standardized $\beta = 0.201$, $p = 0.049$), total score of HAMD-24 (standardized $\beta = 0.179$, $p = 0.000$), total score of HAMA (standardized $\beta = 0.171$, $p = 0.013$), total score of Shame Scale for Middle School Student (standardized $\beta = 0.045$, $p = 0.039$) and cortisol (standardized $\beta = 0.078$, $p = 0.048$) were significantly associated with patients having NSSI (see Table 2).

Table 2 Binary Logic Regression Associated with MDD Patients with NSSI and without NSSI

Variable	B	S.E.	Wald	Sig.	Exp(B)	95% CI	
Gender (male/female)	1.070	0.565	3.586	0.058	2.915	0.963	8.822
Total Score of CTQ	-0.092	0.048	3.782	0.052	0.912	0.831	1.001
Emotional abuse	0.150	0.098	2.355	0.125	1.162	0.959	1.408
Emotional neglect	0.201	0.102	3.868	0.049	1.223	1.001	1.494
HAMD-24 Total	0.179	0.044	16.720	<0.001	1.197	1.098	1.304
HAMA Total	0.171	0.068	6.234	0.013	1.186	1.037	1.357
Inability to control craving	0.115	0.087	1.755	0.185	1.122	0.946	1.331
Feeling anxious and lost	-0.100	0.060	2.818	0.093	0.905	0.805	1.017
Productivity loss	0.182	0.127	2.060	0.151	1.199	0.936	1.537

(Continued)

Table 2 (Continued).

Variable	B	S.E.	Wald	Sig.	Exp(B)	95% CI	
Withdrawal/escape	0.021	0.103	0.042	0.838	1.021	0.834	1.250
Shame Scale for Middle School Student	0.045	0.022	4.266	0.039	1.046	1.002	1.092
Cortisol	0.078	0.039	3.910	0.048	1.081	1.001	1.167
FT3	−0.532	0.315	2.855	0.091	0.587	0.317	1.089

Abbreviations: NSSI, non-suicidal self-injury; CTQ, Childhood Trauma Questionnaire; HAMD-24, Hamilton Depression Scale-24 items; HAMA, Hamilton Anxiety Scale; FT3, free triiodothyronine.

Discussion

This exploratory study investigated the prevalence and associated psychosocial and biological factors of non-suicidal self-injury (NSSI) among Chinese child and adolescent inpatients with major depressive disorder (MDD), using the DSM-5 diagnostic criteria. While much of the existing research on child and adolescent NSSI has focused on general populations, relatively little is known about its prevalence and determinants among child and adolescent depressive disorder inpatients. Our findings revealed a high prevalence of NSSI (69.49%) in this clinical population, which is basically consistent with the 50%-60% reported in previous studies[7]. In a study on the incidence of NSSI in Chinese patients with depressive or bipolar disorder, 62.2% of patients were also found to have NSSI, including 55.1% diagnosed with depression.¹⁰ This underscores that NSSI is a highly prevalent and serious clinical concern among adolescent inpatients with MDD, a group characterized by high acuity. Notably, female child and adolescents were significantly overrepresented in the NSSI group, which is consistent with previous findings and suggests a higher susceptibility to NSSI among women.³² Female adolescents who suffer depression or anxiety may be more likely to engage in NSSI to relieve negative emotions.³³ But an important nuance emerged from our multivariate analysis regarding gender differences. Although a strong association between female gender and NSSI was found in the univariate analysis (Table 1, $p < 0.001$), its effect was attenuated and became non-significant in the final logistic regression model after adjusting for key covariates (Table 2, $p = 0.058$). This strongly suggests that the relationship between gender and NSSI may be mediated by the other covariates in the model (eg, higher levels of depression, anxiety, and shame). Specifically, being female maybe more closely associated with greater severity of depression and anxiety symptoms, higher shame-proneness, and more severe smartphone addiction, all of which were associate with of NSSI.^{34–36} Women often experience stronger negative emotions, their negative emotions enhance faster than men's, and they have a greater frequency of NSSI actions.³⁷ The study found that adolescent girls experience a faster decline in positive emotions when their level of self-consistency congruence is lower than that of boys. When facing internal and external self-conflict and low self-concordance, girls undergo more intense negative emotional experiences compared to boys.³⁸ Thus, female adolescents with MDD may be more prone to experiencing such internalizing symptoms and negative self-conscious emotions, which in turn drive the need for NSSI. Future research employing formal mediation analysis is crucial to confirm these pathways.

Our study highlights emotional neglect—a frequently emphasized form of childhood trauma—as a significant independent correlate of NSSI, underscoring the importance of emotional support in preventive strategies. Consistent with our hypothesis, patients with NSSI exhibited significantly higher levels of childhood trauma, particularly emotional abuse and emotional neglect, compared to those without NSSI. This is largely in line with the results of other studies. In a study of NSSI risk factors in 153 children and adolescents with depressive disorder in China, the CTQ-SF score for emotional abuse and neglect in NSSI patients was significantly higher than that of non-NSSI patients.³⁹ Another study of Chinese adolescents also found that childhood emotional abuse was linked to greater risk of depressive symptoms and NSSI.⁴⁰ Similarly, You et al also found that NSSI and depression were considerably positively connected with childhood emotional maltreatment, and the NSSI were strongly positively correlated with depression.⁴¹ Emotional abuse and neglect may impair an individual's ability to regulate negative emotions. Individuals who have experienced emotional abuse tend to adopt dysfunctional coping mechanisms, such as NSSI, to relieve painful emotions, especially when faced with further adversity in the absence of resilience-building resources.^{42,43} Further regression analysis found that emotional neglect, in particular, was independently associated with NSSI in the regression model, suggesting that the absence of emotional support may be as detrimental as active maltreatment in fostering self-injurious behaviors. This is

similar to the results of other studies, which found that a positive correlation between depressive symptom scores and CTQ total scores, emotional abuse, and emotional neglect were only observed in the MDD/NSSI group and not in the MDD-only group. Additional regression analyses also identified emotional neglect as a risk factor for NSSI.²⁰ This suggests that inadequate emotional care for children during parenting may make them more prone to self-injurious behaviors in young people.

Furthermore, the NSSI group demonstrated more severe depressive and anxiety symptoms, consistent with prior studies. There is evidence that NSSI is associated with a range of psychological difficulties, including depression, anxiety, and post-traumatic stress disorder.⁴⁴ A systematic evaluation of 39 studies pointed out that, based on adolescents' depressive symptoms, one can predict their chances of committing NSSI in the future.⁴⁵ A longitudinal study with 813 Chinese adolescents also showed that higher levels of depressive symptoms were associated with an increase in NSSI one year later.⁴⁶ Hu et al also confirmed "an increase in the prevalence of depressive symptoms and prevalence of NSSI with depressive symptoms".⁴⁷ Anxiety and depression symptoms often coexist, and the impact of anxiety symptoms on NSSI is also evident. Steine et al found that besides depression, anxiety also positively predicted persistent NSSI during the four-year follow-up period.⁴⁸ Another study also showed that anxiety symptoms are one of the risk factors for NSSI.⁴⁹ Various theories interpreted the relations between NSSI and depression and anxiety. Some scholars argue that children and adolescents are emotionally vulnerable and easily stimulated by negative life events to experience emotional outbursts, which, in turn, produce several negative emotions. When there is an inability to regulate negative emotions, they may resort to NSSI to transfer them. According to the experiential avoidance model proposed by Chapman et al, NSSI can provide temporary relief from children and adolescents' negative emotions. Nevertheless, when adolescents are again exposed to negative emotional stimuli, they tend to use NSSI for relief, which continuously facilitates the occurrence of NSSI.⁵⁰ In addition to this, it has been identified as a key function of NSSI to regulate distressed emotions, as individuals who engage in it do so to escape or avoid negative emotional experiences, thereby experiencing temporary psychological relief and relaxation.⁴⁹

Notably, our results also showed that children and adolescents with NSSI reported significantly higher levels of shame-proneness and more severe smartphone addiction compared to those without NSSI. Shame-proneness was independently associated with NSSI in the regression model. This suggests that children and adolescents who are more prone to shame may internalize negative self-evaluations and emotional distress, leading to self-directed aggression as a form of emotional regulation. Shame is significantly positively correlated with NSSI, which causes individuals to have more negative emotions, but NSSI has a moderating effect on negative emotional states, and adolescent depressive disorder patients use NSSI to alleviate emotional problems caused by shame.⁵¹ This is consistent with previous studies indicating that shame mediates the relationship between mindfulness deficits and NSSI.¹⁵ Similarly, smartphone addiction was significantly more prevalent in the NSSI group, particularly on subscales such as inability to control craving, feeling anxious and lost, withdrawal/escape, and productivity loss. Smartphone addiction may serve both as a precursor and as a consequence of emotional dysregulation. Excessive smartphone use can lead to social isolation, disrupted sleep, and increased anxiety, which may heighten the risk of maladaptive coping mechanisms such as NSSI.¹⁶ Conversely, individuals already engaging in NSSI may turn to digital environments to escape real-life pain, creating a vicious cycle of avoidance and worsening psychological distress. However, although smartphone addiction was strongly correlated with NSSI in univariate analyses, it did not retain an independent association in the multivariate model after adjusting for depression, anxiety, and shame. This implies that smartphone addiction may function as a mediator or comorbid behavior rather than a direct causal factor, potentially facilitating NSSI through exacerbating emotional dysregulation or social impairment.

One of the main functions of NSSI is to regulate unpleasant emotions and interpersonal experiences, and the biological stress response system may play a central role.⁵² It mainly includes changes in the function of the hypothalamic-pituitary-adrenal (HPA) axis and hypothalamic-pituitary-thyroid (HPT) axis.^{53,54} In a study of female adolescents with NSSI, the NSSI group had significantly lower FT3 levels compared to healthy control group.⁵⁵ Similar findings were reported in another study of male adolescents with depressive disorder.¹⁷ Consistent with these results, we observed that reduced free triiodothyronine (FT3) was associated with NSSI. After incorporating FT3 into the regression analysis, it was found that the association with NSSI was not obvious. This suggests that FT3 may have a weak effect on NSSI and cannot be considered as a reliable correlate of NSSI.

Our observation of elevated peripheral blood cortisol levels in children and adolescents with MDD and NSSI contrasts with several previous studies reporting hypocortisolism in similar clinical populations.^{20,56} This divergence highlights the potential complexity and heterogeneity of HPA axis regulation in this population. Several factors may contribute to this discrepancy, including differences in sample characteristics, cultural context, disease stage, comorbid symptoms, and the timing or type of cortisol measurement (eg, acute versus chronic stress exposure). Specifically, the hypocortisolism reported in prior research may represent an adaptive downregulation or a “burnout” state of the HPA axis following long-term, chronic stress, a condition particularly noted in individuals with specific trauma histories like emotional neglect.²⁰ Conversely, our finding of elevated cortisol likely captures a more acute or persistently activated stress state. This interpretation is consistent with our findings that NSSI group exhibited higher levels of anxiety and shame. These intense emotional states are potent psychological stressors in themselves, capable of driving sustained HPA axis activation and leading to glucocorticoid excess. Furthermore, NSSI is often conceptualized as a strategy for temporary relief from negative affect. Individuals who engage in NSSI typically exhibit heightened anger, which is in turn associated with an increased cortisol awakening response.⁵⁷ Childhood trauma likely plays a central role in shaping this heterogeneity in HPA axis responsivity. Trauma does not uniformly suppress or activate the HPA axis; rather, it disrupts its homeostatic regulation, potentially manifesting as both hypocortisolism at rest and hyper-reactivity under challenge.⁵⁸ Indeed, prior research has linked emotional neglect to lower baseline cortisol in patients with MDD and NSSI,²⁰ while other studies have associated early adversity with blunted cortisol reactivity to acute stress.⁵⁹ Consistent with this framework, adverse social environments are known to impair glucocorticoid receptor sensitivity and diminish the anti-inflammatory functions of cortisol.⁶⁰ Therefore, the elevated cortisol in our sample could represent a hyper-reactive response to the ongoing emotional turmoil of high anxiety and shame. This aligns with the conclusion from a meta-analysis that elevated cortisol may function more as a risk state than a stable trait marker.⁶¹ While previous studies have primarily emphasized chronic stress adaptation, our findings may reflect a physiological response to acute or intense psychosocial stressors. Future research must move beyond seeking a unitary biomarker and instead adopt longitudinal designs that track how HPA axis activity evolves alongside changing clinical symptomatology and environmental contexts.

In conclusion, there are differences in many aspects between child and adolescent depressive disorder patients with NSSI and those without NSSI. Multivariate binary logistic regression further confirmed that emotional neglect, depressive and anxiety symptoms, shame, and cortisol levels were significant associated with NSSI. These results suggest that NSSI is not just a simple psychological problem, but the outcome of a complex interplay of psychological, social, physiological and other factors.

Limitations and Future Directions

Several limitations should be considered. First, the broad age range of our sample (10–16 years) encompasses diverse developmental stages, potentially introducing heterogeneity. Moreover, the limited number of participants in the youngest age bracket (eg, only 4 patients under 12 years old) precluded meaningful age-stratified analyses within this range. Second, the cross-sectional design precludes causal inferences. Longitudinal studies are needed to trace the developmental trajectory of NSSI and its predictors. Third, all participants were recruited from a single inpatient setting. In this context, NSSI is a common clinical problem, which may limit the generalizability of our findings to outpatient or community populations. Fourth, although we included several biological markers, other potential biomarkers (eg, inflammatory cytokines, genetic factors) were not assessed. Finally, we did not account for the potential influences of menstrual cycle phases and psychotropic medications on the HPA axis, which could affect neuroendocrine responses and confound the results.

Based on these limitations, future research should, (1) employ developmentally-stratified longitudinal designs with larger and more balanced samples across specific age groups to clarify the developmental trajectory and causal mechanisms of NSSI; (2) validate findings in outpatient and community populations to enhance generalizability; (3) incorporate multi-omics approaches to elucidate the underlying biological mechanisms; and (4) specifically account for key physiological and pharmacological confounders, such as menstrual cycle phase and psychotropic medication use, to obtain a more precise understanding of HPA axis function in relation to NSSI.

Conclusion

In summary, this study provides robust evidence that NSSI is highly prevalent among child and adolescent inpatients with MDD and is influenced by a complex interplay of psychosocial and biological factors. Early identification of high-risk individuals through comprehensive assessment of childhood trauma, emotional regulation, shame, and biological markers may facilitate timely intervention. Integrated treatment strategies addressing both psychological distress and neuroendocrine dysfunction warrant further development and evaluation.

Abbreviations

CI, Confidence Interval; CTQ, Childhood Trauma Questionnaire; EA, Emotional Abuse; EN, Emotional Neglect; PA, Physical Abuse; PN, Physical Neglect; SA, Sexual Abuse; DALYs, Disability-Adjusted Life Years; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; FT3, Free Triiodothyronine; FT4, Free Thyroxine; HAMA, Hamilton Anxiety Scale; HAMD-24, 24-item Hamilton Depression Scale; HPA, Hypothalamic-Pituitary-Adrenal axis; HPT, Hypothalamic-Pituitary-Thyroid axis; MDD, Major Depressive Disorder; MPAA, Mobile Phone Addiction Index; NSSI, Non-Suicidal Self-Injury; OR, Odds Ratio; SS, Shame Scale for Middle School Students; T3, Triiodothyronine; T4, Thyroxine; TSH, Thyroid-Stimulating Hormone.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author Ya-qin Ding upon reasonable request. The data are not publicly available due to ethical restrictions and patient privacy concerns, as they contain information that could compromise the privacy of research participants.

Human Ethics and Consent to Participate Declarations

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Nantong Fourth People's Hospital (2023-k027). Written informed consent was obtained from the legal guardians of all participants under the age of 18, and assent was obtained from the participants themselves.

Acknowledgments

We are grateful to all the physicians and nurses who participated in our study as well as the research staff who contributed to the diagnosis of the subjects and clinical assessments.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by grants from the Nantong Municipal Health Commission Scientific Research Project (QN2023041 to Chao Liu; MS2024074 to Pei-Juan Wang; MS2023085 to Ya-qin Ding; MSZ2023061 to Qi Yan;) and Research and Development Fund Project of Kangda College, Nanjing Medical University (KD2023KYJJ205 to Jian-Cheng Qiu).

Disclosure

The authors declare no conflicts of interest.

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