IJBMC
International Journal of Body, Mind and Culture

Volume 11, Issue 6, pp 249-255
DOI: 10.61838/ijbmc.v11i6.1121

Article type:
Original Research

Assessing Emotional and Behavioral Problems in Children and Adolescents with β-Thalassemia Major Using the CBCL: Associations with Serum Ferritin and Transfusion Frequency

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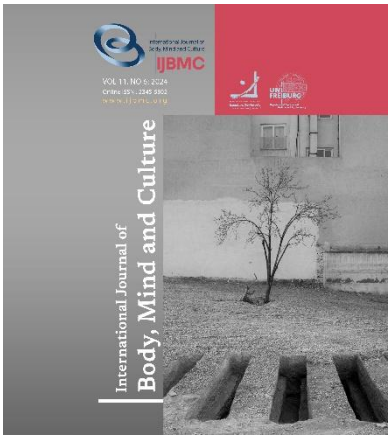

Article history:

Received 21 July 2024
Revised 14 October 2024
Accepted 24 October 2024
Published online 10 December 2024

How to cite this article:
Shakibaei, F., & Vafaei, S. (2024). Assessing Emotional and Behavioral Problems in Children and Adolescents with β-Thalassemia Major Using the CBCL: Associations with Serum Ferritin and Transfusion Frequency. International Journal of Body, Mind and Culture, 11(6), 249-255.

ABSTRACT

Objective: Children and adolescents with β-thalassemia major are at increased risk for emotional and behavioral problems. This study assessed internalizing/externalizing problems using the Child Behavior Checklist (CBCL) and examined associations with serum ferritin level and blood transfusion frequency in two age groups.

Methods and Materials: In this descriptive–analytical cross-sectional study (2022–2023), patients with β-thalassemia major attending Seyyed al-Shohada Hospital, Isfahan, Iran were assessed using the parent-report CBCL. Participants were categorized into children (4–11 years) and adolescents (12–18 years). Data were analyzed with SPSS (significance set at $p<0.05$) using t-test/chi-square and Pearson correlation.

Findings: Total psychological problem scores differed significantly between children and adolescents ($p=0.011$). Several CBCL subscales showed different distributions across age groups, including withdrawal, somatic complaints, anxious/depressed mood, thought problems, attention problems, and behavioral domains. Serum ferritin level was inversely correlated with total CBCL score ($r=-0.24$). Higher problem scores co-occurred with greater blood transfusion frequency.

Conclusion: A considerable proportion of patients with β-thalassemia major exhibited clinically relevant emotional/behavioral problems, highlighting the need for routine psychosocial screening and long-term supportive interventions alongside medical care. Future studies should include representative socio-economic strata and both genders to improve generalizability.

Keywords: β-thalassemia major, Child Behavior Checklist, emotional problems, behavioral problems, serum ferritin, transfusion frequency.

Introduction

Emotional and behavioral problems among children are common across different ages. It is estimated that approximately one in five children each year experiences a significant problem. Many of these children visit a general practitioner; however, about one in ten requires specialized help from a specialist (Fauci et al., 2008). The causes of childhood mental disorders can be grouped into three categories: hereditary factors, physical illness, and environmental factors. Genetic factors in child and adolescent psychiatry are polygenic, and—similar to adult disorders—are influenced by environmental factors. In many cases, genetic influences operate indirectly through the regulation of temperament and intelligence; however, in some conditions they exert more specific effects, such as in autism.

During childhood, any severe physical illness can lead to psychological problems (Beratis, 1993). Acute physical illness is more likely to cause delirium in children than in adults. Chronic physical illness and its treatment affect a child's or adolescent's self-esteem and social development (Gelder et al., 1989). Hospital admission also has important psychological effects on children: a child may become anxious or depressed, or may regress to behaviors typical of earlier developmental stages. These reactions are usually temporary, but repeated hospitalizations—especially in early or middle childhood—can result in behavioral or emotional disorders (Gelder et al., 1989). This is more likely when there are weak family relationships or social difficulties, because all parents experience distress when their child develops a chronic physical illness (Gelder et al., 1989).

Physical and psychological symptoms are often closely intertwined and influence one another. Many mental disorders produce physical symptoms. Conversely, physical symptoms and illnesses can also have psychological consequences, including the development of psychiatric disorders (Aydinok et al., 2005). In the general population, when a physical illness occurs, the likelihood of a mental disorder increases two to three times, and disabling functional symptoms are frequently observed (Gelder et al., 1989).

In primary care, psychological aspects are of particular importance in the treatment of many patients with severe acute or chronic physical illnesses. In hospitals, psychological problems are especially prevalent: approximately one-quarter of patients admitted to medical wards have some form of psychiatric disorder. In outpatient clinics, nearly 15% of patients with a definite medical illness and about 40% of those without a specific medical diagnosis suffer from some type of psychiatric disorder. Another point is that most individuals become more psychologically flexible during illness and can go through the course without major distress (Olivieri & Brittenham, 1997). Nevertheless, all physical illnesses have psychological effects to some extent. In about one-quarter of patients, these psychological effects meet diagnostic criteria for mental disorders and have profound consequences for all aspects of the illness outcome (Shaligram et al., 2007). Some disorders, such as anxiety and depression, may represent psychological reactions to illness. However, severe physical disorders can also directly cause anxiety and depressive symptoms, likely through physiological mechanisms (Tarasiuk et al., 2003). In addition, some medications have psychological side effects, such as corticosteroids, beta-blockers, and anticholinergic drugs (Anie et al., 1996).

Typically, the response to acute illness is anxiety, which is sometimes followed by depression (Ghanizadeh et al., 2006). In approximately 25% of patients, these reactions reach the diagnostic threshold for an anxiety disorder, depressive disorder, or adjustment disorder. Such reactions may lead to poor cooperation with treatment. Among individuals with disabling chronic illnesses, the prevalence of anxiety and depressive disorders is more than twice that of the general population, and psychological and social variables are key determinants of illness outcomes (Pradhan et al., 2003). The more prevalent disorders include adjustment disorder, depressive disorder, anxiety disorder, and delirium. In contemporary psychiatry, factors associated with a high risk of developing psychiatric problems include severe illness, unfavorable treatment, and vulnerability to mental disorders (Louthrenoo et al., 2002). Some illnesses and their treatments threaten the patient's life. Nevertheless, psychological reactions depend more on the patient's perception of the illness than on the illness itself. If the patient has an unfavorable view of the illness or lacks adequate coping capacity, there is a higher likelihood of severe stress and distress (Ahmad, 1992). The reactions of other people can also influence the patient's perception and coping ability.

Thalassemia syndromes are among the conditions that—because of the nature of the disease, treatment methods, and other unique characteristics—predispose affected individuals (most of whom are children and adolescents) to psychological and psychiatric disorders (Shahrivar et al., 2011). Thalassemia comprises inherited disorders of alpha or beta globin production; reduced globin leads to decreased production of hemoglobin tetramers and, consequently, hypochromia and microcytosis. Because other globin chains continue to be produced at a normal rate, an imbalance and accumulation of alpha and beta subunits occurs. The clinical severity of the disease varies and depends on the level of production of the affected chain, changes in the production of other globin chains, and the co-inheritance of other abnormal globin alleles (Shahrivar et al., 2011). Severe thalassemia syndromes are associated with severe hemolytic anemia and are diagnosed in early childhood. In contrast, mild forms such as thalassemia minor often cause mild microcytic anemia or show no evidence of hemolysis; these cases may be mistaken for iron deficiency because of decreased MCV (Dulcan & Wiener, 2004). Therefore, given the relatively high prevalence of thalassemia in our country, the vulnerability of affected patients to psychological and psychiatric disorders, and the fact that no study has yet been conducted on this topic in our country, the present study was carried out to determine the prevalence of psychological and psychiatric disorders among children and adolescents with thalassemia.

Methods and Materials

Study Design

This study was a descriptive–analytical investigation conducted in 2022–23 at the Seyyed al-Shohada (AS) Medical Center in Isfahan, Iran. The target population included children and adolescents aged 5–19 years diagnosed with beta-thalassemia major who attended the aforementioned center. Inclusion criteria were: (1) age range 4–18 years, (2) diagnosis of beta-thalassemia major, (3) having a medical record at the Seyyed al-Shohada Medical Center, and (4) parental and patient consent to participate. It was also stipulated that if participants did not cooperate in completing the questionnaires, they would be excluded from the study.

Data were collected using the Parent version of the Child Behavior Checklist (CBCL), which was completed as a self-administered questionnaire. The CBCL is one of the most widely used instruments in research and clinical practice and is considered a gold standard among behavioral assessment measures. The CBCL is a child behavior checklist developed by Achenbach et al. (1991). It contains 112 items, each with three response options (0, 1, and 2). A response of 0 is selected if the behavior has not been present currently or during the past six months; 1 is selected if the symptom is present to some extent or sometimes; and 2 is selected if the behavior/symptom has been observed frequently or consistently. The cutoff score for diagnosing the presence of emotional–behavioral problems is 41; scores equal to or above 41 indicate the presence of a disorder. Higher scores reflect greater severity of problems (Ahmad, 1992).

In a study conducted in Shiraz by Siamak Samani, the reliability and validity of the CBCL in an Iranian population of elementary school students were evaluated. In that study, reliability coefficients for the total scale and the two broad factors of externalizing and internalizing behaviors were 0.80, 0.65, and 0.68, respectively, all of which were statistically significant at $p < 0.001$. To assess construct validity, factor analysis using maximum likelihood (ML) estimation was performed. Diagnostic validity was examined using an independent t-test to compare mean scores between students with behavioral problems and normal students; the results supported the diagnostic validity of the instrument. Overall, the findings indicated adequate reliability and validity of the CBCL for use by psychiatrists and psychologists in the initial identification of children with behavioral disorders (Shahrivar et al., 2011).

The required sample size was calculated using the formula for prevalence studies. With a 95% confidence level, an estimated prevalence of psychological disorders among thalassemic children set at 0.50 (due to the lack of domestic studies), and an acceptable error margin of 0.05, the sample size was estimated at 196 participants from the population of approximately 400 thalassemic children in Isfahan.

The CBCL questionnaires were completed by one parent of the children or adolescents who attended the thalassemia clinic at Seyyed al-Shohada Medical Center.

Under the direct supervision of the principal investigator, the questionnaires were distributed to parents, who received instructions on how to complete them, and were then completed in a self-administered manner.

Finally, the collected data were entered into a computer and analyzed using SPSS software (version 22). Statistical analyses were performed using the Chi-square test, Fisher's exact test, and the t-test.

Findings and Results

In this study, 195 children and adolescents with thalassemia were evaluated. The mean age of participants was 13.6 ± 4.3 years, with an age range of 5–21 years. Regarding sex distribution, 116 were boys and 79 were girls (59.5% vs. 40.5%). The mean age of boys and girls was 13.5 ± 4.6 and 13.8 ± 4.0 years, respectively, and there was no significant difference between the mean ages of boys and girls (p = 0.71).

The mean score for psychiatric problems in the 4–11-year and 12–18-year age groups was 34.71 ± 17.58 and 41.63 ± 23.39, respectively. Based on the Student's t-test, the difference between these two age groups was statistically significant (p = 0.031). In addition, 13 individuals in the 4–11-year group and 44 individuals in the 12–18-year group had psychiatric problems (18.1% vs. 35.8%). The Chi-square test also indicated a significant difference between the two age groups (p = 0.006).

The status of psychological disorders across the eight CBCL subscales was examined in the two age groups (4–11 years and 12–18 years), as shown in Table 1. According to the t-test, among the eight subscales, social problems, delinquent behavior, and aggressive behavior did not differ significantly between the two groups. However, withdrawal, somatic complaints, anxious/depressed mood, and thought problems were significantly higher in the 12–18-year age group (p < 0.05).

Table 1

Mean ± SD of CBCL subscale scores in two age groups

Subscale	4–11 years (Mean ± SD)	12–18 years (Mean ± SD)	p
Withdrawn	3.8 ± 2.8	5.5 ± 3.7	0.001
Somatic complaints	0.74 ± 1.0	1.2 ± 1.3	0.021
Anxious/Depressed	4.6 ± 3.35	6.5 ± 4.73	0.003
Social problems	4.1 ± 2.1	3.63 ± 2.5	0.17
Thought problems	0.47 ± 0.95	1.65 ± 2.13	<0.001
Attention problems	4.28 ± 3.19	5.22 ± 3.29	0.053
Delinquent behavior	2.44 ± 1.84	2.93 ± 2.31	0.13
Aggressive behavior	7.81 ± 5.65	7.69 ± 5.93	0.90

Based on the findings, students were classified into three categories: normal, borderline, and clinical (abnormal). As shown in Table 2, in the 4–11-year group, 56 participants (77.8%) were normal, and in the 12–18-year group, 66 participants (53.7%) were normal. The Chi-square test showed that the frequency distribution of withdrawal differed significantly between the two age groups (p = 0.003).

For somatic complaints, no abnormal cases were observed in either age group; only one participant in the 4–11-year group and 10 participants in the 12–18-year group were classified as borderline (1.4% vs. 8.1%). Fisher's exact test showed no significant difference in the distribution of somatic complaints between the age groups (p = 0.06).

For anxious/depressed mood, 66 participants in the 4–11-year group and 95 participants in the 12–18-year group were in the normal range (91.7% vs. 77.2%). The Chi-square test indicated a significant difference between the groups (p = 0.037).

The mean internalizing score in the 4–11-year and 12–18-year groups was 8.88 ± 5.6 and 12.8 ± 8.1, respectively, and the Student's t-test showed a significant difference (p < 0.001). Moreover, 17 participants in the 4–11-year group and 49 participants in the 12–18-year group were classified as internalizing (23.6% vs. 39.8%), and the Chi-square test showed a significant difference (p = 0.048).

As presented in Table 2, 7 participants in the 4–11-year group and 12 participants in the 12–18-year group

had social problems (9.7% vs. 9.8%), and the difference was not significant (p = 0.73). In addition, 12 participants in the 12–18-year group had thought problems, whereas no cases were observed in the 4–11-year group. Fisher's exact test indicated a significant difference in the distribution of thought problems (p < 0.001).

Regarding attention problems, 4 participants in the 4–11-year group and 3 participants in the 12–18-year group had attention problems (5.6% vs. 2.4%), and Fisher's exact test showed no significant difference (p = 0.56).

The mean combined internalizing and externalizing problems in the 4–11-year and 12–18-year groups was 8.86 ± 5.2 and 10.5 ± 6.63, respectively; the difference was not statistically significant (p = 0.074). According to Table 2, 4 participants in the 4–11-year group and 6 participants in the 12–18-year group were borderline for delinquent behavior (5.6% vs. 4.9%), and Fisher's exact test showed no significant difference (p = 0.99). Similarly, 1 participant in the 4–11-year group and **2** participants in the 12–18-year group showed aggressive behavior (1.4% vs. 1.6%); Fisher's exact test indicated no significant difference (p = 0.023, as reported).

The mean externalizing score in the 4–11-year and 12–18-year groups was 10.25 ± 6.81 and 10.62 ± 7.43, respectively, and Student's t-test showed no significant difference (p = 0.73). In addition, 9 participants in the 4–11-year group and 12 participants in the 12–18-year group were classified as externalizing (12.5% vs. 9.8%), and the Chi-square test indicated a significant difference (p = 0.016, as reported).

Table 2

Frequency distribution of psychiatric problems by age group

Domain / Subscale	4–11 years: Normal	Borderline	Abnormal	12–18 years: Normal	Borderline	Abnormal	p
Internalizing							
Withdrawn	56 (77.8)	7 (9.7)	9 (12.5)	66 (53.7)	27 (22.0)	30 (24.4)	0.003
Somatic complaints	71 (98.6)	1 (1.4)	0 (0.0)	113 (91.9)	10 (8.1)	0 (0.0)	0.06
Anxious/Depressed	66 (91.7)	3 (4.2)	3 (4.2)	95 (77.2)	15 (12.2)	13 (10.6)	0.037
Internalizing Total	45 (62.5)	10 (13.9)	17 (23.6)	56 (45.5)	18 (14.6)	49 (39.8)	0.048
Borderline/Other							
Social problems	58 (80.6)	7 (9.7)	7 (9.7)	94 (76.4)	17 (13.8)	12 (9.8)	0.73
Thought problems	69 (95.8)	3 (4.2)	0 (0.0)	89 (72.4)	22 (17.9)	12 (9.8)	<0.001
Attention problems	63 (87.5)	5 (6.9)	4 (5.6)	112 (91.1)	8 (6.5)	3 (2.4)	0.56
Externalizing							
Delinquent behavior	68 (94.4)	4 (5.6)	0 (0.0)	117 (95.1)	6 (4.9)	0 (0.0)	0.074
Aggressive behavior	67 (93.1)	4 (5.6)	1 (1.4)	121 (98.4)	0 (0.0)	2 (1.6)	0.99
Total problems	49 (68.1)	10 (13.9)	13 (18.1)	55 (44.7)	24 (19.5)	44 (35.8)	0.023

Note: Percentages are presented as reported in the original text.

Discussion and Conclusion

Beta-thalassemia major is a chronic hematologic disease that is diagnosed in infancy and causes severe hemolytic anemia. From early life, affected patients require blood transfusions (Fauci et al., 2008). Repeated transfusions and frequent hospitalizations for treatment impose physical limitations on patients and create new stressors for children, including loss of independence and autonomy, feelings of reduced abilities and competence, and disruption of daily activities (Dulcan & Wiener, 2004). In this study, a total of 196 patients were examined. The overall aim was to determine the frequency distribution of behavioral and emotional disorders among children and adolescents aged 5–19 years with thalassemia major who attended the Seyyed al-Shohada Treatment Center in Isfahan Province during 2022–23.

The findings showed that 36.9% of participants had behavioral and emotional disorders. Among similar studies, a Turkish study conducted in 2005 assessed 38 children and adolescents aged 6–18 years with thalassemia using the CBCL and reported that 25% had behavioral and emotional disorders (Aydinok et al., 2005); thus, the prevalence reported in that study was lower than that found in the present study. In a study conducted in Shiraz in 2006, 49% of patients were reported to have depression (Ghanizadeh et al., 2006). In another study in India (2007) involving 39 patients aged 8–16 years with beta-thalassemia major, approximately

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E-ISSN: 2345-5802

44% were found to have behavioral and emotional disorders (Shaligram et al., 2007). Another Indian study (2003) examining 30 children with thalassemia reported that 25.56% had some form of psychological disorder (Pradhan et al., 2003). A survey conducted in London in 2001 reported that 80% of individuals with beta-thalassemia major had at least one assessable psychiatric disorder (Anie et al., 1996). In another study in Thailand in 2002, an evaluation of 82 patients with thalassemia major found that 28.05% had a psychological disorder (Louthrenoo et al., 2002).

Given that behavioral and emotional disorders were observed at a relatively high rate among thalassemia patients at the Seyyed al-Shohada Center in Isfahan—and considering that psychiatric disorders can affect physical illness and even influence patients' adherence to follow-up and treatment—it is recommended that appropriate measures be taken to ensure timely diagnosis and adequate treatment of psychiatric problems in these patients.

In caring for these patients, preventive strategies to reduce the emergence and exacerbation of psychological problems include: providing patients with information about the illness; encouraging self-care and treatment adherence; regularly monitoring the patient's clinical progress; providing information to relatives and family members; and explaining how they can support the patient to achieve better adaptation to their condition.

Acknowledgments

The authors express their gratitude and appreciation to all participants.

Declaration of Interest

The authors of this article declared no conflict of interest.

Ethical Considerations

The study protocol adhered to the principles outlined in the Helsinki Declaration, which provides guidelines for ethical research involving human participants. Ethical considerations in this study were that participation was entirely optional.

Transparency of Data

In accordance with the principles of transparency and open research, we declare that all data and materials used in this study are available upon request.

Funding

This research was carried out independently with personal funding and without the financial support of any governmental or private institution or organization.

Authors' Contributions

All authors equally contribute to this study.

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