



Review

Psychological Burden among Pediatric Thalassemia Major Patients in Indonesia: A Review

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Abstract: Thalassemia a common hereditary blood disorder resulting in anemia. It is an important public health problem, with a high prevalence in Southeast Asia and Mediterranean countries, and preventable through screening programs. However, due to its chronic nature, permanent physical changes, troublesome complications, and lifelong treatment, pediatric patients with thalassemia major are more prone to mental disorders and cognitive impairment. Internalizing and externalizing problems are higher in pediatric patients with thalassemia. Children with β -thalassemia major exhibit lower IQ scores than healthy children. Neurophysiology and neuroimaging examinations have shown abnormal results in children with thalassemia. Co-morbidity with mental disorders increases the mortality, morbidity, and total healthcare costs of patients with thalassemia. Therefore, routine evaluation of mental health problems is recommended to accommodate the early detection and prompt treatment of mental disorders. A multidisciplinary approach for thalassemia patients and families should be delivered by providing appropriate medical care, psychosocial support, and good transition care to improve survival and well-being, assist good social integration and daily functioning, and cope with the stress of chronic disease.

Keywords: thalassemia major; psychosocial burden; early detection; psychosocial support



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1. Thalassemia in Indonesia

Thalassemia is one of the most common monogenic disorders resulting in defective globin chain synthesis which manifests as chronic hemolytic anemia. Thalassemia can be classified phenotypically based on clinical severity (minor, intermedia, major) and transfusion requirement (non-transfusion-dependent thalassemia/NTDT and transfusion-dependent thalassemia/TDT). Beta thalassemia occurs due to reduced or no production of β -globin chains and a relative excess of α -globin chains that accumulate and form inclusion bodies in the erythroid precursors. These inclusion bodies lead to ineffective erythropoiesis by binding with the membrane skeleton and cause oxidative membrane apoptosis, causing the premature destruction of the erythrocyte precursors in the bone marrow. The excess free α -globin chains also cause membrane damage to peripheral erythrocytes and lead to hemolysis. Both ineffective erythropoiesis and hemolysis lead to anemia. In response to this, the body will increase the production of erythropoietin, which may cause erythroid marrow hyperplasia in medullary and extramedullary sites. Extramedullary erythropoiesis leads to characteristic deformities of the face and skull, extramedullary erythropoietic tissue masses, splenomegaly, and cortical thinning of long bones. Patients with thalassemia major who receive no treatment or are undertreated may have delayed growth due to anemia and high metabolic burden from the erythroid expansion. Anemia may result in cardiac enlargement and cardiac failure. In non-transfused patients, increased intestinal iron absorption may

occur due to the downregulation of hepcidin production by the hepatocytes. This ultimately results in iron overload [1].

Beta thalassemia is highly prevalent in the Mediterranean Basin, Middle East, and Southeast Asia, known as the 'Thalassemia Belt' [1,2]. Indonesia is an emerging middle-income country that is situated along the 'Thalassemia Belt', which has shown an increasing trend in the diagnosis of thalassemia cases. In 2021, it was estimated that the number of patients with thalassemia was 10,973, which showed a 3.06% increment rate from the previous year [3]. The frequency of thalassemia carriers in Indonesia is approximately 3–5%. Assuming that the percentage of thalassemia carriers is 5% with a birth rate of 20‰, and Indonesia's population of 200 million, it is estimated that there will be 2500 newborns with thalassemia [4]. In terms of financing, according to Indonesia National Health Insurance (BPJS), the burden of healthcare costs for thalassemia continued to increase from 2014 to 2020. Thalassemia ranks fifth as the most budget-depleting among other non-communicable diseases, with a total of IDR 2.78 trillion (USD 191 million) disbursed for treating thalassemia in 2020 [5].

To date, the provision of definitive treatment for thalassemia in Indonesia has shown significant progress. This is marked by the initiation of the first bone marrow transplantation (BMT) therapy for a pediatric patient with β -thalassemia major in November 2023. However, BMT requires suitable donors and is only accessible to a minority of patients who are financially privileged to pay for it [2]. The available treatment modalities for thalassemia patients covered by Indonesia's national health insurance are supportive approaches such as routine blood transfusion and iron chelation therapy. However, their availability is uncertain in Indonesia, especially in rural areas [1,2,6]. Blood transfusions may alleviate anemia symptoms and, when given effectively, may result in good energy levels, good growth and development, and sufficiently suppressed intra and extramedullary hematopoiesis [1,2]. However, blood transfusion poses the risk of bloodborne infections (hepatitis B, hepatitis C, HIV) and transfusion reactions, which may significantly affect thalassemia major patients who require routine and life-long transfusions [7]. In addition, regular blood transfusions result in iron overload, which causes irreversible organ damage, leading to heart failure, liver fibrosis, and endocrine abnormalities. Complications from iron overload can be prevented by routine monitoring of iron burden in vital organs and adequate iron chelation therapy to remove excess iron. Until now, three types of iron chelators have been approved and accessible for thalassemia patients in Indonesia, primarily including deferoxamine (DFO) as the first-line iron chelator for thalassemia major that is administered through continuous subcutaneous infusion. However, it has been difficult to find in Indonesia over the last year, and its administration is inconvenient, which greatly affects patient adherence. Alternatively, oral preparations of iron chelators are available, namely deferiprone (DFP) and deferasirox (DFX) [2].

The increasing prevalence, high healthcare costs, and financial burden of thalassemia treatment for patients emphasize the importance of thalassemia screening and prevention. In Indonesia, a preventive measure for thalassemia was initiated in 2017 in the capital city of Jakarta, in which couples preparing to marry are obligated to undergo screening programs to identify the presence of microcytic hypochromic anemia through a complete blood count, including the mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH). The presence of microcytic hypochromic anemia without symptoms of anemia/thalassemia raises suspicion of being a thalassemia carrier or having iron deficiency anemia (IDA). Quantification of the Mentzer Index (MCV per erythrocyte count) may aid in the differentiation between iron deficiency anemia and being a thalassemia carrier. Additional tests such as serum iron, ferritin, and transferrin may exclude IDA and anemia of chronic diseases [8]. Once thalassemia carriers are suspected, they are referred to a hematologist to undergo hemoglobin analysis using electrophoresis to establish the diagnosis of thalassemia [8]. Thalassemia is prevented by discouraging marriage between thalassemia carriers, who have a 25% chance of producing offspring with thalassemia major [6,8]. A preventive strategy for thalassemia through pre-marital screening and subsequent genetic counseling

showed promising results in prevalent regions. For example, a mandatory pre-marital screening program in Cyprus successfully decreased the incidence of thalassemia to only five new cases from 1991 to 2001 [2,9]. Additionally, prospective screening for thalassemia has been conducted in school-age children, specifically first-year secondary school students, across Jakarta. The screening is conducted using a complete blood count and peripheral blood smears in students with a family history of thalassemia [5].

2. Mental Health Problems in Indonesia

Mental disorders constitute a substantial contribution to the burden of disease. Mental disorders are medical conditions that interfere with the ability to think, feel, regulate mood, and communicate with others, hindering daily functioning. Mental disorders have gained attention as a significant health concern impacting everyday life in terms of disability [10,11]. Vigo et al. [12] suggested that the global burden of mental disorders accounts for approximately 32.4% of Years Lived with Disability (YLDs).

In Indonesia, the national prevalence of mental health problems was approximately 7% in 2018 [13]. However, only 9% consume medication or seek professional help [13]. The Indonesia—National Adolescent Mental Health Survey revealed that 5.5% of Indonesian adolescents aged 10–17 years old had mental disorders, with anxiety disorder as the most prevalent [14]. However, only 2% of the Indonesian population had access to mental healthcare (psychiatric counseling and psychosocial support) and more than 43.8% of primary caregivers did not seek psychiatric therapy for adolescents who needed it [14]. The low availability and insight to seek psychiatric help may lead to delays in treatment for adolescents who would benefit from it.

3. Chronic Disease and the Burden of Mental Health Disorders

A systematic review/meta-analysis by Dare et al. [10] showed that the prevalence of co-morbidities of mental disorders and chronic physical disease in developing countries within the Asian continent was 26.8%. The meta-analysis concluded that chronic physical disease increased the odds of anxiety and/or depression by 3.1 times. Thus, individuals with chronic diseases are more vulnerable to developing mental disorders, as unhealthy behaviors, compromised immune functioning, and poor medication adherence are associated with mental disorders [10].

Co-morbidities of mental disorders and chronic diseases are a burden for people living in developing countries. The management of individuals with mental disorders in developing countries is complicated due to the lack of access to medical consultations, the limited number of health centers, and the difficulty in reaching such services. Furthermore, religion and social stigma may hinder the diagnosis of mental disorders. Financial constraints can also hinder those seeking appropriate mental health services [11].

4. Mental Health Problems among Thalassemia Major Patients

The medical burden of patients with thalassemia for supportive care is immense as it is a chronic disease requiring lifelong treatment to sustain life, in addition to financial problems to afford the medical treatments. It is a catastrophic disease that negatively affects patients psychosocially [2,10]. Depressive and anxiety disorders are the predominant psychological burden across all age groups of thalassemia patients [15–18], with thalassemia major patients as the predominant clinical severity of thalassemia being explored. Interestingly, Khoury et al. [15] showed variable psychosocial burden between adult patients with thalassemia major and thalassemia intermedia. Clinically, thalassemia major patients manifest with profound anemia needing medical attention during the first year of their life, requiring regular blood transfusion and iron chelation therapy to sustain life [15]. On the other hand, thalassemia intermedia patients seek medical attention in later childhood, with more favorable hemoglobin levels, and are transfusion-independent [15]. The study [15] concluded that adult patients with thalassemia intermedia were more liable to state anxiety than patients with thalassemia major. This might be attributed to the duration of living

with the diagnosis, in which thalassemia intermedia patients had a shorter duration and lower opportunity to adapt to the disease, treatment, and complications. Additionally, the less severe clinical manifestation in thalassemia intermedia patients allows them to experience “normal” life, rendering it harder to accept and adapt upon their diagnosis [15]. Venty et al. [19] conducted a cross-sectional study in Palembang, Indonesia, and showed that the prevalence of depression among pediatric patients with thalassemia major was 34.4%. Low parental education and deferasirox as iron chelation therapy were found as independent risk factors for depression in children with thalassemia major [19]. It is thought that deferasirox may cause adverse neurological effects such as depression, anxiety, and sleep disturbances [20]. A study [17] in Iran explored the prevalence of psychiatric disorders, psychiatric symptoms, and suicidal behavior in children and adolescents with thalassemia major. The study [17] showed that depressive disorder and separation anxiety disorder were the two most common psychiatric disorders, followed by defiant disorder (3.6%), attention deficit disorder (1.8%), and bipolar mood disorder (0.9%). Almost one-half of the participants suffered from depressive moods, while more than 50% of the participants had irritability and anger [17]. More than 43% had recurrent thoughts of death and about one-third of the participants considered suicide [17]. Cakaloz et al. [18] performed a study involving children with thalassemia major aged 7–18 years old from Turkey and showed a high prevalence of psychopathology among them. Internalizing problems (anxiety and depressive disorder) and externalizing problems (delinquency, attention, and social problems) were higher in children with thalassemia major.

Undetected mental health problems in childhood and adolescence may continue into adulthood. A cross-sectional study [21] among 92 adult thalassemia major outpatients in Indonesia revealed that almost half (40.2%) of the respondents had depressive symptoms, with 38% having suicidal thoughts. Depressive symptoms were highly prevalent in females and among those of reproductive age (20–30-year age group) [21]. Similarly, a cross-sectional study in Iran [22] showed that adults with thalassemia major suffered from stress (18.8%), depression (59.4%), and extremely severe anxiety (60.9%). The study [22] found that single and unemployed thalassemia major patients had significantly higher levels of anxiety. A high prevalence of mental disorders was also found in adult thalassemia patients from Italy, which lead to the conclusion that most of the thalassemia major patients had severe psychosocial problems such as low self-image, depression, somatization, and obsessive-compulsive traits [23]. In contrast, a longitudinal cohort study from North America and the United Kingdom [24] suggested that thalassemia patients did not experience significant anxiety (33%) and depressive (11%) symptoms. The discrepancy in results from both studies might be attributed to different sample sizes and measurement tools [24]. The latter study [24] showed a greater sample size and heterogeneity, with a focus on assessing symptoms of anxiety and depression. The cohort study also demonstrated significant differences in anxiety and depressive symptoms by age (adults had more symptoms of anxiety, whereas adolescents endorsed more symptoms of depression) and gender (higher symptoms in females than males) [24]. In addition, symptoms of anxiety and depression were correlated with low adherence [24]. In the inpatient setting, mental disorders were common in hospitalized adults with β -thalassemia. Of the 10,046 hospitalized β -thalassemia patients in the USA, 24.4% had mental disorders [25]. Mood disorder was the most prevalent (10.3% of patients with depression), followed by anxiety disorder (9.4%) [25]. Approximately 6.5% of the patients reported substance abuse disorder, and a minority (1.6%) had schizophrenia and other psychotic disorders [25]. Co-morbid mental disorders in hospitalized patients with β -thalassemia were found to increase the length of stay by 44.6% and total healthcare costs by 23.4% [25].

The high prevalence and poorer functional health and well-being of thalassemia patients with mental health problems, both in inpatient and outpatient care, highlight the importance of determining the contributing factors to their psychosocial problems. Individuals with thalassemia major may experience physical changes, growth delays, splenomegaly, a yellowish-bronze skin color, and characteristic facial appearances [26].

These factors can negatively impact their self-esteem and make them feel different from others [26]. Thus, they may isolate themselves from society, negatively affecting their mental health and quality of life [26]. Individuals with low self-esteem and body image disorder are more prone to depression, affecting their social relationships [26]. Another important factor underlying mental health problems in thalassemia patients is their anxiety about living a long life and having a good quality of life [26]. Studies have found that children with thalassemia major are at a higher risk of developing anxiety and depression. This is often due to social challenges such as being separated from their family, dealing with physical and facial changes, taking medication that affects their behavior and alertness, having limited social activities, facing limitations in school and physical activities, and feeling anxious about death [27,28]. Depression in children with thalassemia might be directly caused by the disease, its complications, and treatments such as recurrent admission for blood transfusion and daily iron chelating agent consumption. Routine blood transfusion also makes them different because they are reckoned as blood consumers [19]. A study [29] in Pakistan involving adolescent thalassemia major patients revealed that more than half of the respondents reported the disease's impact on their education, inability to engage in outdoor games, and inadequate stamina. Most of the respondents from the mentioned study were not satisfied with their body image, and more than 50% of the respondents reported that the disease limited their social life. Most of the respondents felt different from their siblings and said that their disease posed a burden on their family [29]. Thus, thalassemia disease negatively affects daily activity, emotional condition, family experiences and adjustment, occupational and sporting capabilities, stigmatization, and social interactions of the patients and their caregivers, resulting in a high psychological burden and a higher risk of mental disorders [29].

5. Early Detection of Mental Health Problems in Children with Thalassemia Major

Children with thalassemia are at higher risk of psychopathology [18]. They show increased anxiety, depression, aggression, and social withdrawal, and poor school performance [30,31]. Some behavioral disorders such as pervasive developmental disorders and attention deficit hyperactivity disorder (ADHD) are frequently observed among preschool or young school-aged children, while separation anxiety, anxiety disorders, depression, and eating disorders have a later onset, such as in school-aged children or adolescents [32]. Some mental disorders, for instance, schizophrenia, are noticed through changes in behavior and development during childhood or adolescence before developing their most evident symptoms [30].

Pediatricians are encouraged to consider the diagnosis of a mental disorder if (1) there are problems with school performance that are not attributed to intellectual or physical disabilities or sensory factors; (2) there are problems establishing and maintaining social interactions with family members, teachers, and schoolmates/colleagues; (3) children show inappropriate feelings or behavior towards the everyday situation, such as persistent depression or sadness; and (4) there is tendency towards the development of fears or physical symptoms associated with common problems [30].

From the time of diagnosis, it is expected that the patients and families experience adjustment disorders as they are introduced to a lifelong disease associated with new challenges, constraints, and uncertainties. Sadness, withdrawal, dependency, and anxiety are commonly encountered during the initial adjustment to the diagnosis of thalassemia. Within 3 months of subsequent diagnosis of thalassemia, approximately 30% of children develop adjustment disorder. Adjustment disorder usually resolves within the first year; however, poor adaptation in this initial phase increases the risk of subsequent mental disorders [33].

Symptoms of anxiety are common in children and adolescents with thalassemia. They may occur due to poor disease control. Therefore, it is crucial to help the child discriminate internalizing symptoms associated with anxiety such as palpitation or diaphoresis from the symptoms of anemia [34]. Common anxiety disorders in pediatric thalassemia patients

are separation anxiety disorder and generalized anxiety disorder (GAD). Environmental, familial, and biological factors may contribute to the development of anxiety disorders. Behavioral inhibition and early temperament that are associated with aversion to new situations have been linked with the development of anxiety disorders [35]. Separation anxiety disorder may occur early, after 5 years of age. Younger children typically show an exaggerated and unreal preoccupation with mishaps that might occur to their parents or close relatives, while older children or adolescents show fewer symptoms [30]. In contrast with separation anxiety disorder, which has a single cause, GAD is characterized by persistent and excessive anxiety with a wide series of causes occurring on most days for at least 6 months [36,37]. A diagnosis of GAD can be established if these concerns cause problems and an incapacity in the child's everyday life. Somatic symptoms should be present such as fatigue, poor concentration, irritability, restlessness, muscle tension, or sleep disorder. The onset of symptoms is usually encountered in adolescence but may be found as early as 5 years of age, with fewer somatic symptoms in younger children. Early detection and treatment of these disorders are crucial as they may continue into adulthood and may cause disturbance in daily life [30,36].

Studies have shown the association between depression, worse disease control, and higher complications in patients with thalassemia disorders. Depression may present with overlapping symptoms of poor anemic control such as fatigue, impaired memory, and weight loss, rendering depression to be underdiagnosed in children with β -thalassemia major [29,36]. Therefore, re-evaluation of patients with symptoms of depression after anemic control is recommended, with persistent symptoms indicating the diagnosis of depression [30]. Initial symptoms of depression may be milder and asymptomatic in children. Although several instruments have been developed for the detection of individuals at risk of depression in the pediatric population, early diagnosis of depression is difficult as signs of depression in children are typically seen as normal for their age, alongside reluctance in healthcare professionals to label patients as mentally ill and the child's limitation in identifying and portraying emotions. Children may become too aggressive and irritated to describe what is bothering them. Irritability may be the most prominent symptom of depression in younger children [23,30]. The presence of depression in children is linked to heightened mortality and morbidity. This condition serves as a contributing factor to reduced compliance, increased risk of suicide, substance abuse, teenage pregnancy, poor academic performance, and the development of psychosocial problems [38]. Early diagnosis and prompt treatment before complications arise are crucial, as timely and appropriate treatment may improve symptoms in the majority of patients with depression [39]. Several instruments may be used to screen depression in children such as the Children's Depression Inventory (CDI) [23]. Pediatricians may consider the diagnosis of depressive disorders in the presence of sudden behavioral changes, anger, agitation, aggressiveness, changes in sleep pattern or appetite, alienation from surroundings, low self-esteem, or a disheveled appearance [37]. Somatic symptoms such as headaches might be encountered, especially among pre-adolescent or adolescent girls [40].

6. Neurophysiology of Thalassemia Patients and Its Association with Neurocognitive Problems

Iron deposition in thalassemia major patients involves many organs, including the brain [41]. Iron accumulation in the brain may alter its function because ferritin can bind to oligodendrocytes located adjacent to the blood-brain barrier to be engulfed by microglia in the parenchyma [42]. Iron accumulation leads to an inflammation cascade, which contributes to the development of neurodegenerative diseases [43]. Brain iron deposition is also involved in the progression of mental disorders, including depression, anxiety, schizophrenia, and post-traumatic stress disorder [44]. It seems that the location of iron deposition may influence the type of mental disorder; for example, iron deposition in the thalamus notably affects the severity of depression symptoms [45].

A neuroimaging study found that iron content in the brain can be quantified using many MRI techniques, including transverse relaxation rate, susceptibility-weighted imaging, and quantitative susceptibility mapping [46]. Interestingly, serum ferritin levels do not accurately reflect the iron stored in the brain [47]. Neuroimaging evaluation among children with thalassemia major also revealed that a third of the patients had abnormal MRI, consisting of millimeter-sized ischemia lesions in the cerebral white matter and hyperintense lesions in the basal ganglia [48].

Moreover, iron deposition also affects other nervous systems in the body that may alter normal body function [49]. It indirectly contributes to the aggravation of mental health problems in thalassemia patients [49]. A neurophysiology study [49] in thalassemia major children in Indonesia revealed that among 78 children recruited, abnormal brainstem auditory evoked potentials (BAEPs), electroencephalogram (EEG), and electroneurography (ENG) results were found in 4 subjects (4.64%), 28 subjects (43.8%), and 1 subject (1.6%), respectively.

The study [49] demonstrated that subjects with abnormal BAEP results showed increased interpeak latency in waves I–III in one or both ears when stimulated by click stimuli at 80 dB. Among subjects with abnormality in EEG results, 20 subjects (31.3%) had mild brain hypofunction and 8 subjects (12.5%) had moderate brain hypofunction. One subject with abnormal ENG results showed decreased radial nerve and sural nerve amplitude. The subject was a 14-year-old girl with β -thalassemia major who received a routine transfusion from the age of 7 months, with a mean pre-transfusion Hb level of 9.6 g/dL and ferritin serum of 7384 ng/mL [49].

In terms of cognitive ability, a study [50] in children with β -thalassemia major showed that they had lower IQ scores than healthy children, as well as lower verbal comprehension index, processing speed index, perceptual reasoning index, and working memory index [50]. Interestingly, another study [51] revealed that the IQ score was not correlated with the ferritin serum level. Still, it was correlated with the mean pre-transfusion Hb level, education, and nutritional status [51].

7. Interventions for Mental Disorders during Childhood for Thalassemia Major Patients

The combination of appropriate medical care and psychosocial support for thalassemia patients and families may significantly improve survival and accommodate good social integration, acceptance, and good self-esteem [38]. Psychosocial support is crucial for the management of thalassemia major patients. It requires collaborative efforts from doctors, nurses, paramedical staff, clinical psychologists and psychiatrists, social workers, and volunteers [28].

The most important factor that underlies the mental problem in individuals with thalassemia is their fears and worries about their lives [25]. This anxiety can be relieved with the efforts of hematologists in thalassemia centers by providing information to the patients and their families about the causes and consequences of the disease and emphasizing the importance of lifelong treatment [25]. Coping with chronic illness becomes better once the patients and their families are relieved about the treatment and supported by adequate provision of medical care [25]. Ultimately, proper application of medical care for thalassemia patients may reduce their levels of fear and anxiety and improve their life expectancy and quality of life [25]. However, the increase in lifespan brings more complicated psychosocial problems, such as finding a partner in life and acquiring a dream job, which they do not face during childhood [52]. Therefore, the transition to adult care plays an important role in maximizing the lifelong functioning of the patients [53]. Transition itself is a dynamic and individualized process to meet patients' needs as they move from childhood to adulthood [53].

A study [54] found that most thalassemia patients who enter adulthood (greater than or equal to 18 years) still prefer to be treated under pediatric care. Although some advantages may be obtained for adults being treated in pediatric care, it also brings negative

effects; for example, pediatricians and medical staff may have less knowledge about adult problems such as reproductive health [52,55].

As an effort to ease pediatric patients transitioning to adult care, our center utilizes the same room for examination and blood transfusion for pediatric patients with pediatricians and when they enter adulthood with adult hematologists as their healthcare provider. This effort may accommodate an easier process of linking pediatric patients to adult services. We also provide a service for growth development in the social pediatrics division that accommodates screening for psychosocial problems in adolescents with thalassemia. Our patients also created a community, namely the thalassemia movement, which helped them to inspire and motivate each other. The community also plays an active role in disseminating the importance of thalassemia screening and increasing people's awareness about thalassemia to achieve the ultimate goal of "zero thalassemia births".

One important aspect of providing good transition care for teenagers is to determine the goals that need to be achieved before they move into adulthood [52]. This includes helping them understand their diagnosis and treatment, encouraging them to take an active role in their own healthcare, ensuring that all necessary paperwork related to their condition is provided to their school, promoting programs for teens in hospitals, organizing sharing sessions with successful thalassemia patients, and providing sexual education [52]. In addition, self-care and adaptation to the disease are crucial in therapeutic outcomes. Patients with chronic diseases should receive education on coping strategies to manage negative emotions and reduce stress [56]. Providing psychosocial support for patients and their families is crucial in thalassemia care. Pediatric psychiatry clinics can be established to address mental health problems associated with the disease [57].

The Indonesian Pediatric Association has established a guideline to evaluate psychosocial problems in adolescents [58]. Adolescents must have the opportunity to consult without the accompaniment of parents/guardians/friends. After the adolescents separate from their parents, rapport should be built by explaining that the confidentiality of information is guaranteed, unless there are three special situations, namely a risk of the teenager endangering themselves, a threat that other people will harm the teenager, and a possibility of the teenager harming others. One of the recommended screening tools to evaluate psychosocial problems is the home, education/employment, eating, activity, drugs, sexuality, suicide/depression, and safety (HEEADSSS) questionnaire. This questionnaire has a structured format and is specific to adolescents. Another advantage of this questionnaire is that it can detect not only risk factors, but also protective factors that adolescents may have, whether at home or school, as well as positive traits in adolescents [58].

8. Conclusions

Thalassemia is a chronic disease requiring lifelong treatment to sustain life and prevent complications. Children with thalassemia are at higher risk of psychopathology and cognitive problems due to the nature of the disease, lifelong treatment duration, and its high psychosocial burden. Thalassemia patients with mental disorders show higher mortality, morbidity, length of hospital stay, and total healthcare costs. Depression and anxiety disorders are highly prevalent across all age groups of thalassemia patients. However, the symptoms of anxiety and depressive disorders might be similar to those of poor anemic control and difficult to detect at a young age. Therefore, clinicians should assess not only the physical but also the mental health of these children. Performing routine examinations using questionnaires for early detection and treatment of mental health problems is recommended. A multidisciplinary treatment approach is needed for the patients and families. Providing information about the nature of the disease and its treatment plan, educating on appropriate coping strategies to manage stress, and offering adequate transitional care can help prepare children and adolescents with thalassemia for a challenging youth period and the transition into adulthood.

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