Review Article

Psychosocial Aspects of Thalassemia and Patient's Quality of Life: A Narrative Review

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Abbreviations:
WHO: World Health Organization. QOL: Quality of Life. CBT: Cognitive Behavioral Therapy
CBFT: Cognitive-Behavioral Family Therapy ACT: Acceptance and Commitment Therapy
EFFT: Emotion-Focused Family Therapy

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Abstract

Background & Aims: Mental health and quality of life are commonly affected in patients with thalassemia and their caregivers. This review aims to synthesize the available evidence and to assess the prevalence of depression and anxiety in patients with thalassemia and their caregivers. This review also examines the bidirectional relationship between thalassemia and depression and anxiety and its impact on the quality of life of patients and their caregivers.

Methods: Five electronic databases were searched [PsychInfo, PubMed, Medline, Google Scholar, and EMBASE] and also other sources. This search combined different terms of mental health and quality of life of patients with thalassemia and caregivers. The search went up until January 2019

Results: Forty articles are included in this review. The studies showed a high prevalence of mental illnesses, particularly depression and anxiety, among patients with thalassemia and their caregivers. Many factors have been found that impacts the quality of life of patients with thalassemia and their caregivers, including thalassemia, its related-complications, medical treatment and, psychological distress, and comorbid mental illness. Although all the studies that looked at comorbid mental illness and thalassemia recommended adding a psychological treatment, only three studies did investigate this and had shown some benefits

Conclusion: Thalassemia should be addressed as an illness with biopsychosocial components and should be treated as such. More studies are needed to assess the effectiveness of different psychological interventions for patients with thalassemia and their caregivers. Also, two new psychotherapies are mentioned and discussed as they address the psychological needs of patients and their caregivers.

Keywords:
Thalassemia, Depression, Anxiety, Therapy, Quality of life
Caregivers

الملخص

الخلفية والأهداف: من الشائع أن تتأثر الصحة النفسية وجودة الحياة لدى مرضى الثلاسيميا ومقدمي الرعاية لهم. تهدف هذه المراجعة إلى تجميع الأدلة المتاحة وتقييم مدى انتشار اضطراب الاكتئاب والقلق لدى مرضى الثلاسيميا ومقدمي الرعاية لهم. أيضًا تتناول هذه المراجعة العلاقة ثنائية الاتجاه بين مرض الثلاسيميا والاكتئاب والقلق وتأثيرها على جودة حياة المرضى ومقدمي الرعاية لهم.

طريقة البحث : تم البحث في خمس قواعد بيانات إلكترونية PsychInfo و PubMed و Medline و Google Scholar و EMBASE] وأيضًا مصادر أخرى. جمع هذا البحث بين المصطلحات المختلفة للصحة النفسية و جودة حياة مرضى الثلاسيميا ومقدمي الرعاية. استمر البحث حتى شهر يناير ٢٠١٩.

النتائج: أربعون مقالة مدرجة في هذه المراجعة. أظهرت الدراسات ارتفاع معدل انتشار الأضطرابات النفسية ، وخاصة اضطرابي الاكتئاب والقلق ، بين مرضى الثلاسيميا ومقدمي الرعاية لهم. تم العثور على العديد من العوامل التي تؤثر على جودة حياة مرضى الثلاسيميا ومقدمي الرعاية لهم ، بما في ذلك مرض الثلاسيميا والمضاعفات المرتبطة به ، والعلاج الطبي ، والضغوظات النفسي ، والأضطرابات النفسية المصاحبه لمرض الثلاسيميا. وعلى الرغم من أن جميع الدراسات التي نظرت وبحثت في الأضطرابات النفسية المصاحبه لمرض الثلاسيميا أوصت بإضافة العلاج النفسي لمرضى الثلاسيميا ، إلا أنه فقط ثلاث دراسات حققت في إضافة العلاج النفسي وأظهرت بعض الفوائد له.

الخلاصة : يجب معالجة الثلاسيميا كمرض يحتوي على مكونات نفسية اجتماعية ويجب علاجها على هذا النحو. هناك حاجة إلى مزيد من الدراسات لتقييم فعالية العلاجات النفسية المختلفة لمرضى الثلاسيميا ومقدمي الرعاية لهم. أيضا، تم ذكر ومناقشة اثنين من العلاجات النفسية الجديدة لأنها تلبي الاحتياجات النفسية للمرضى ومقدمي الرعاية لهم.

Introduction

Thalassemia is an Inherited hemoglobin disorder, and it is common in the Middle East, Mediterranean regions, and South and Southeast Asia [1]. According to the WHO, hemoglobin disorders are common in 71% of countries and affecting around 89% of births. 50,000-100,000 children with thalassemia major die each year in low and middle-income countries [2].

Thalassemia is a chronic medical disorder that impacts not only the patient but also the whole family. It impacts their mental health and their quality of life [3,4]

A new study that came out on Nov 2018 again showed that psychosocial issues are common among children with thalassemia [5]. The prevalence of psychological problems in patients with thalassemia is around 43% [6]. Mental illness, particularly depression, is the leading cause of disability worldwide [2]. In low-middle income countries, around 76-85% and around 35-50% in high-income countries of people with mental disorders receive no treatment for their disorder [2].

Different guidelines and reviews have been written on the management and treatment of Thalassemia. However, they tend to cover the biological aspects of this disorder.

Not until 2014 that the Thalassemia International Federation (TIF) did add a chapter on psychological support on the 3rd edition of guidelines for the management of transfusion-dependent thalassemia 2014. Psychological support is important for patients with thalassemia, regardless of it being transfusion-dependent or transfusion independent.

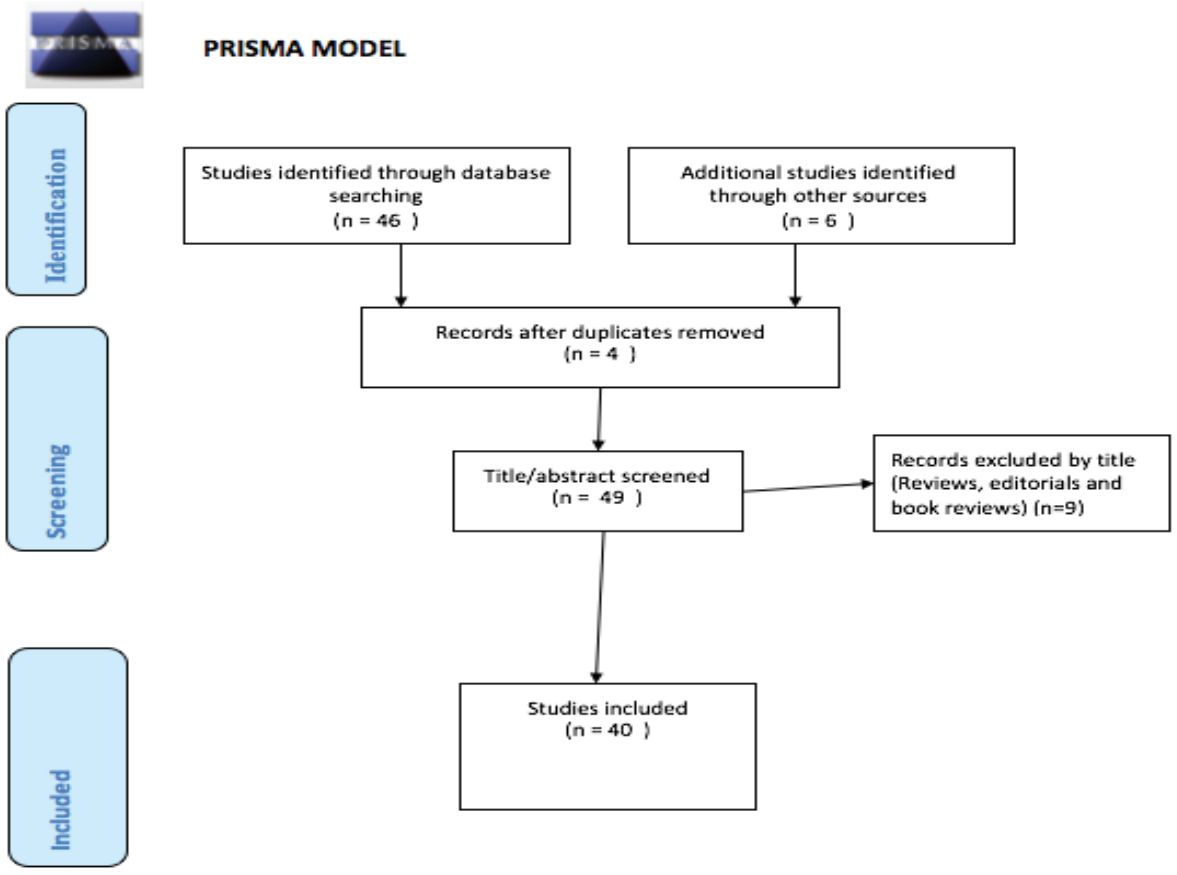
In this article, we will review the prevalence and impact of comorbidity between thalassemia and depression and anxiety and also the quality of life of patients with thalassemia and their caregivers and how to improve the care provided to them. Finally, it will propose methods for addressing areas of uncertainty.

Methods

Five electronic databases were searched [PsychInfo, PubMed, Medline, Google Scholar, and EMBASE] and also other sources. This search combined different terms of mental health and quality of life of patients with thalassemia and caregivers.

The search went up until January 2019 using the following terms “mental illness”, “psychiatric disorder”, psychosocial impact or aspect”, “depression,” “anxiety,” “psychotherapy,” “psychological,” “quality of life”, “caregivers,” or “parents” AND “thalassemia”.

Initially, 52 studies have been identified, and after screening 40 studies have been included in this review. Twelve studies were excluded because of duplications and meeting exclusion criteria. Figure 1



Inclusion criteria:

All thalassemia subtypes are included

Articles included are those written in English only.

Exclusion Criteria:

· Non-English written articles.
· Studies that did not address the search keywords.
· Review articles, editorials, and book chapters.

1-Thalassemia and Depression:

The relationship between thalassemia and depression had been proven in many studies [7-25]. Different scales have been used to assess depression. See Table 1

Depression is the most common psychological health disorder among patient with thalassemia and their caregivers. [11,18,26], Prevalence of depression in children with thalassemia ranges from 19.8% to 62% and around 10.3-35% in adults with thalassemia [16, 17,18, 20,21,26,27]

This wide range in prevalence depends on different factors, for example, the power of the study; the time and place it was conducted. The relationship between depression and thalassemia is bidirectional [26]. Depression did affect the physical and mental health of the children with Beta-thalassemia Major. Depressed children with thalassemia had more fatigue, pain, discomfort, and more sleep disturbance. [26,28]

Table 1

Author	Number	Thalassmia	Scale used	Country
Ahmad Ghanizadeh et al (2006)	110 children	Thalassemia Major	Kiddie-SADS - Life-time Version (K-SADS-PL)	Iran
Burcu Cakaloz, et al (2009)	20 children	Thalassemia major	The child behavior check-list (CBCL) Semi-structured interview with a clinician according to DSMIV	Turkey
Brigitte Khoury et al (2012)	80 Adults	Beta-Thalas-semia Major and Intermedia	The Beck Depression Inventory (BDI)	Lebanon
Akbar Shafiee et al (2014)	56 children	Beta-Thalas-semia Major	Beck's Depression Inventory (BDI)	Iran
Aghbabak Maheri et al (2018)	389 Adults	Beta-Thalas-semia Major	The hospital anxiety and depression scale The Multidimension-al Scale of Perceived Social Support	Iran
Krupa Patel et al (2018)	10,046 Adults	Beta-Thalas-semia Major	USED Clinical Clas-sifications Software (CCS) to utilized the discharge data from the National Inpa-tient Sample (NIS).	United States

Risk factors

Different factors could lead patients with thalassemia to develop depression, either in their childhood and /or adulthood. These factors include: hospitalization and blood transfusion frequency, the separation from the parents and peers, and disease-related complications, such as facial dysmorphisms, skeletal anomalies, gallstones, delayed puberty, hepatosplenomegaly, and heart failure [14,18].

Hypercholesterolemia

Hypercholesterolemia is an independent risk factor for depression [29]. Patients with thalassemia trait have low levels of total cholesterol and LDL-cholesterol [30]. This is one possible mechanism to understand their increased risk of developing depression.

Ferritin level and type of iron chelation therapy

Although the serum ferritin level and type of iron chelation therapy had been thought of as possible factors affecting psychological disorders in patients with beta-thalassemia major. Two studies [17,22] had shown that the type of iron chelation therapy, blood transfusion interval, and ferritin levels had no significant impact on the patient's level of depression or anxiety.

Level of education

Depressed adults with beta-thalassemia major were less likely to have a university degree compared to non-depressed adults with beta-thalassemia [17]. The opposite was also correct, meaning that adults with beta-thalassemia without a high school diploma had higher depressive scores in comparison to those with a high school diploma [17]. This could be because of different factors, for example, people with higher education tend to have a better socioeconomic status, they are more likely to understand their illness, thalassemia, and thus cope better with it. They also might be more resourceful, socially, and financially. All of these factors could be protective against depression.

Age

Three studies [7,32,33] found that adolescents with thalassemia experience fewer depressive symptoms compared to younger children and thus had higher health-related quality of life scores than younger children. This could be a reflection of their ability to adjust and cope with the demands of the disease.

Gender

Six studies [11, 18,19,21,25,34] have looked at the relationship between the gender of the patient with thalassemia and mental illness. Even though there is no difference in the overall prevalence of mental disorders among males and females. Different mental disorders, however, affects females more than males and vice versa. Females are more likely to have depression and anxiety disorders. Males, on the other hand, are more likely to have a comorbid substance use disorder and disruptive behavioral disorders.

Maladaptive cognitive styles

Adults with thalassemia major use verity of maladaptive coping styles. They tend to use escape-avoidance thinking and behavior, and their self-image was found to be low [31]. These coping styles led patients with thalassemia to feel helplessness and hopelessness and eventually depressed.

Factors to help cope with depression

Different factors have been found of help to patients with thalassemia to better cope with mental illnesses.

1. Gender: girls cope better than boys [7]
2. Older Age: adolescents seem to adjust to the demands of thalassemia better as they grow up [33].

3. Level of education also helps patients cope with the disease and to continue treatment [33].

4. Family and social support [33].

5. Negative affect differentiation: Adults who were able to regulate their negative, sad emotions were more able to adapt to their illness (Thalassemia) and were more compliant to treatment [36].

6. Thalassemia and Anxiety

Ten studies reported that the prevalence of anxiety disorder in children with thalassemia is 34%- 64% and 23.7% in adults with thalassemia [6,10,14,17,18,19,20,21,22,27, 37].

Children with thalassemia are more vulnerable to have a specific phobia (blood and injections), separation anxiety disorder, illness anxiety disorder, and generalized anxiety disorder [10,20, 38].

3. Thalassemia and Hospital outcome

Having a comorbid depression or anxiety did not increase the all-cause mortality in adults with beta-thalassemia in comparison to those without a comorbid depression or anxiety [18]. However, the length of stay and total hospital charges are higher in patients with beta-thalassemia and comorbid depression or anxiety. Comorbidity increased the length of stay by 44.6% and total costs by 23.4%. The all-cause mortality rate was reported at 1.9% in overall beta-thalassemia patients [18].

4. Parents of children with Thalassemia

Depression and generalized anxiety are common among parent of children with thalassemia. Out of 100 parents of children with thalassemia, 29% had depression, and 41.3% had generalized anxiety [3,26]. Depression and anxiety are more common among mothers. Mothers also tend to have more severe depressive symptoms compared to fathers [3]. Rates of anxiety were also higher among mothers [26]

Parents' depression and anxiety could be for various reasons. Their uncertainty about their child's future and health, poor support from relatives and society, social isolation, and their low level of education. Also, it had been found that spousal conflicts are more among parents of children with thalassemia. In Greece, for example, [35] fathers tend to blame mothers for the child's illness, thus causing an ongoing conflict.

A study was done in Thailand [39] that involved 15 mothers of children with thalassemia found that the mother's lack of knowledge about thalassemia and its related-complications did impact their mood and quality of life.

One study [40] looked at protective factors that helped parents cope better with their child's illness. They found that higher educational level, high socioeconomic status, social support, and being more informed about their child's illness and its complications did help parents cope better. Also, self-discipline was a positive character relating to the parents' ability to cope with their responsibilities

and the burden of their child's illness.

5. Thalassemia and Quality of life

Different studies used different Quality of life questioners like EQ5D [6], Pediatric Quality of Life (PedsQL™) [19,31,32,41, 42] Health-Related Quality of Life (HRQoL) measurement [31,32,41] and WHOQOL- BREF questionnaire [38,40]. While one study used a subjective measure [21, 43].

The quality of life of children with thalassemia is affected for several reasons, such as complications related to thalassemia and treatment side effects, poor academic achievements, comorbid mental illness, and low family income. Parents tend to assess their children's quality of life significantly lower than the children themselves [6,19,47].

In two studies, higher levels of depression and anxiety caused children with thalassemia to have lower scores on their psychosocial health in comparison to their physical health [32,33].

One study [44] did compare the quality of life of patients with Transfusion independent thalassemia with Transfusion dependent thalassemia patients. They found that both groups had a poor quality of life because of having pain, emotional difficulties, and inadequate social support. Transfused thalassemia patients did, however, have higher scores in term of daily activities and Physical fitness.

Education level and QOL

Seven studies looked at the impact of thalassemia on children's education. Children and adults with thalassemia tend to have a lower educational level compared to those without thalassemia [14,17,21,22 ,31,30,39, 43]. In these articles, many factors have been reported explaining the poor academic achievements in patients with thalassemia. These factors include; frequent school absenteeism, peer relationship disruption, their present mental illness, and their lower for emotional or social functioning, the negative effect of chronic anemia, and disease-related complications. Parent's poverty, parenting style, and level of education are also important factors that impact the patient's academic achievements [32].

Education level does impact the quality of life of patients with thalassemia [21,44].

One study did use a full, standard neuropsychological testing for 23 children and nine young adults [45]. They found that none of the patients with beta-thalassemia demonstrated any abnormal neurophysiological that resulted in any relevant signs or symptoms. They, however, found that patients with beta-thalassemia demonstrated subclinical involvement of the central and peripheral neural pathways and may require a regular IQ testing using (WISC-III) to detect relevant abnormalities and apply appropriate management.

Interestingly, one study showed that when all patients with thalassemia have equal access to a comprehensive treatment program, their educational achievement would be comparable

to those without thalassemia [46].

Blood Transfusion and QOL

Children with thalassemia with a pre-transfusion hemoglobin level higher than 9 g/dL had a significantly higher health-related quality of life than patients whose pre-transfusion hemoglobin level was below 9 g/dL [33].

6. Ferritin level, chelation therapy, and QOL

One study found that the delayed start of iron chelation had a negative impact on the quality of life in children with thalassemia. This is possibly a complications caused by excessive accumulation of iron in body organs, especially heart, liver, or pancreas [41].

Serum ferritin level and disease-related complications significantly affected the quality of life of adults with thalassemia [40, 42].

7. Therapeutic interventions, depression, and QOL

Only three studies have been identified that focused on therapeutic interventions for patients with thalassemia.

Cognitive Behavioral Therapy (CBT)

In 2015 a Cochrane review concluded that Randomized Controlled Trial (RCT) have not been done to assessing the effectiveness of specific psychological interventions for thalassemia [47]. In 2018 an RCT was done to evaluate the effects of CBT on comorbid depression and anxiety among 76 adult patients with thalassemia [48].

This study did show that CBT is an effective intervention to treat depression and anxiety among patients with thalassemia. This RCT was done in one center, and the power of this study is low. It needs to be replicated with adequate-powered, and preferably as a multicenter study.

Cognitive-Behavioral Family Therapy (CBFT)

One study did CBFT for children with beta-thalassemia major and their mothers [49]. They found that children with beta-thalassemia major who underwent CBFT had proper compliance with their medical treatment plan. However, they were still struggling emotionally and physically. Targeting mothers in the therapy did help in improving the relationship with the child and medical staff. This, however, did not improve the mother's quality of life.

Partnership Care Model

One study had been done to investigate a model based on collaboration between patients with thalassemia major, their caregivers, and treating team [13]. The model is called partnership care model (developed first by Wiggins 2006 [50]). After implementing this model, patients with thalassemia had a significant improvement in their mental health, particularly in the level of symptoms of depression, anxiety, social dysfunction, and physical complaints compared to the control group [13].

The partnership care model had been shown to be effective in improving mental health of patients with chronic medical illnesses like patients with cardiovascular disease (e.g hypertension [51] and coronary artery disease [52]), chronic bronchitis [53], and patients undergoing hemodialysis [54]).

Discussion

As it had been shown through this review, patients with thalassemia and their caregivers are at an increased risk of mental illness and also have a decreased quality of life. Also, Patient with thalassemia with undiagnosed comorbid mental illnesses have an increased hospital stay and total treatment cost.

Three studies, however, have been done on the treatment of comorbid mental illness and on improving the quality of life of patients with thalassemia. Only the one that looked at the effectiveness of CBT was an RCT and had a significant outcome in term of alleviating comorbid anxiety and depression.

Cognitive-Behavioral Family Therapy (CBFT) showed some benefits to children with thalassemia and their mothers in term of improving quality of life and thus could be used in combination with additional psychological support. The Third treatment model is the partnership care model, which is useful in improving depressive and anxiety symptoms in patients with thalassemia and their caregivers.

Many thalassemia treatment centers throughout the world, especially in countries where thalassemia is common, unfortunately, did not implement such support. This lack of translation of research and guidelines has an impact on the health and quality of life of patients with thalassemia.

Limitation

This is a narrative review done by one reviewer, and this could lead to unintentional bias in the data collection.

Recommendations

Enhancing Healthcare Team Outcomes

- Quality of life and disease burden of patients with thalassemia is predicted by physical activity, good interpersonal relationships, social/ family support, and good social integration and the accessibility of medical treatment for thalassemia [17,46]. These protective factors could be a target of therapy for patients.
- Patients with thalassemia and their caregivers should be screened for comorbid mental illnesses.
- A team consists of the pediatrician (or family physician), a hematologist, a nurse, a social worker, and a psychologist should be involved in treating patients with thalassemia. If required, psychiatric consultation should be made.
- Medical and psychological education should be provided to caregivers of patients with thalassemia. Caregiver psy-

chological support.

- Mental health support should be considered as part of the individualized treating plan provided by treating team. It is of a significant benefit to having a clinical psychologist and a social worker as part of the treating team

Suggested Psychotherapy Treatments for Future Studies

Different kinds of therapy might be of help, such as Acceptance and Commitment Therapy (ACT) and Emotion-Focused Family Therapy (EFFT) could be of help to patients with thalassemia and their caregivers.

1. Acceptance and Commitment Therapy (ACT)

ACT is considered a third-wave behavior therapy [55]. ACT is a trans-diagnostic approach, a diagnosis-specific intervention aiming for improving the function and quality of life of the individual regardless of the cause of stress or difficulties.

This intervention encourages values-consistent living teaches the willingness to experience difficult and unavoidable internal experiences (like pain, anxiety, fatigue, and depression) as they are without defense.

Acceptance and Commitment Therapy's effectiveness has been proven across many long-term conditions including, Sickle cell disease, epilepsy, multiple sclerosis, cancer, chronic pain, cardiac disease, and diabetes [56-60].

2. Emotion-Focused Family Therapy (EFFT)

Patients with thalassemia and their caregivers struggle with emotional distress. Caregivers also are highly involved in the care of patients with thalassemia. For these two reasons, EFFT could be of help to them as it helps to manage emotions and helps caregivers to be more effective, to be the main coach for the patient.

EFFT is an emotion-processing skills-based approach that helps parents to identify their emotional blocks and how to overcome them [61,62]. Also, through this therapy, parents learn skills on how to support their child in processing his or her emotions and increase his/ her emotional self-efficacy. All of that also improves the parent-child relationship, and this could improve the patient and caregiver's quality of life. In this recent study [61] that involved 124 parents of children with a wide range of mental health issues, EFFT lead to significant improvement in the total clinical symptoms of Children's. Also, parental stress decreased.

The effectiveness of Acceptance and Commitment Therapy and Emotion-Focused Family Therapy for patients with thalassemia and their caregivers with comorbid mental illness need to be studied.

Conclusion

Much research has been done and proved that depression and anxiety are highly comorbid with thalassemia. However, few studies tar-

geting the treatment of comorbid mental illness have been done. Further, many patients with thalassemia and their caregivers do not receive psychosocial support. Treating team should focus on treating patients with thalassemia in a bio-psycho-social approach as this will help improve their physical and mental health and improve their quality of life.

Declaration

No conflict of interest.

References

[1] Weatherall DJ. Thalassemia as a global health problem: recent progress toward its control in the developing countries. Ann N Y Acad Sci 2010;1202:17-23.

[2] Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. Bull World Health Organ. 2008;86(6):480-487.

[3] Aziz K, Sadaf B, Kanwal S. Psychosocial problems of Pakistani parents of Thalassemic children: a cross sectional study done in Bahawalpur, Pakistan. Biopsychosoc Med 2012;6:15.

[4] Anum J, Dasti R. Caregiver Burden, Spirituality, and Psychological Well-Being of Parents Having Children with Thalassemia. J Relig Health 2016;55:941-955.

[5] Raman V, Prakash A, D'Souza F. Psychosocial Issues in Children With Thalassemia: From Identification to a Model for Management in a Developing Country. J Pediatr Hematol Oncol 2018.

[6] Shaligram D, Girimaji SC, Chaturvedi SK. Psychological problems and quality of life in children with thalassemia. Indian J Pediatr 2007;74:727-730.

[7] Mikelli A, Tsiantis J. Brief report: Depressive symptoms and quality of life in adolescents with b-thalassaemia. J Adolesc 2004;27:213-216.

[8] Hajibeigi B, Azarkeyvan A, Alavian SM, Lankarani MM, Assari S. Anxiety and depression affects life and sleep quality in adults with beta-thalassemia. Indian J Hematol Blood Transfus 2009;25:59-65.

[9] Naderi M, Hormozi MR, Ashrafi M, Emamdadi A. Evaluation of Mental Health and Related Factors among Patients with Beta-thalassemia Major in South East of Iran. Iran J Psychiatry 2012;7:47-51.

[10] Moorjani JD, Issac C. Neurotic manifestations in adolescents with thalassemia major. Indian J Pediatr 2006;73:603-607.

[11] Naderi M, Hormozi MR, Ashrafi M, Emamdadi A. Evaluation of Mental Health and Related Factors among Patients with Beta-thalassemia Major in South East of Iran. Iran J Psychiatry 2012;7:47-51.

[12] Yengil E, Acipayam C, Kokacya MH, Kurhan F, Oktay G, Ozer C. Anxiety, depression and quality of life in patients with beta thalassemia major and their caregivers. Int J Clin Exp Med 2014;7:2165-2172.

[13] Shamsi A, Amiri F, Ebadi A, Gha-

deri M. The Effect of Partnership Care Model on Mental Health of Patients with Thalassemia Major. Depress Res Treat 2017;2017:3685402.

[14] Yahia S, El-Hadidy MA, El-Gilany AH, Anwar R, Darwish A, Mansour AK. Predictors of anxiety and depression in Egyptian thalassemic patients: a single center study. Int J Hematol 2013;97:604-609.

[15] Keşkek SO, Kirim S, Turhan A, Turhan FG. Depression in subjects with beta-thalassemia minor. Ann Hematol 2013;92:1611-1615.

[16] Shafiee A, Nazari S, Jorjani S, Bahraminia E, Sadeghi-Koupaei M. Prevalence of depression in patients with β-thalassemia as assessed by the Beck's Depression Inventory. Hemoglobin 2014;38:289-291.

[17] Maheri A, Sadeghi R, Shojaeizadeh D, Tol A, Yaseri M, Rohban A. Depression, Anxiety, and Perceived Social Support among Adults with Beta-Thalassemia Major: Cross-Sectional Study. Korean J Fam Med 2018;39:101-107.

[18] Patel K, Bhivandkar S, Desai R, Antin T. The burden of psychiatric illnesses in adult patients with beta-thalassemia: a 5-year nationwide inpatient evaluation in the United States. Ann Hematol 2018.

[19] Behdani F, Badiee Z, Hebrani P, Moharreri F, Badiee AH, Hajivosugh N, et al. Psychological Aspects in Children and Adolescents With Major Thalassemia: A Case-Control Study. Iran J Pediatr 2015;25:e322.

[20] Ghanizadeh A, Khajavian S, Ashkani H. Prevalence of psychiatric disorders, depression, and suicidal behavior in child and adolescent with thalassemia major. J Pediatr Hematol Oncol 2006;28:781-784.

[21] Gharaibeh H, Amarneh BH, Zamzam SZ. The psychological burden of patients with beta thalassemia major in Syria. Pediatr Int 2009;51:630-636.

[22] Cakaloz B, Cakaloz I, Polat A, Inan M, Oguzhanoglu NK. Psychopathology in thalassemia major. Pediatr Int 2009;51:825-828.

[23] Sharghi A, Karbakhsh M, Nabaei B, Meysamie A, Farrokhi A. Depression in mothers of children with thalassemia or blood malignancies: a study from Iran. Clin Pract Epidemiol Ment Health 2006;2:27.

[24] Saini A, Chandra J, Goswami U, Singh V, Dutta AK. Case control study of psychosocial morbidity in beta thalassemia major. J Pediatr 2007;150:516-520.

[25] Shaligram D, Girimaji SC, Chaturvedi SK. Quality of life issues in caregivers of youngsters with thalassemia. Indian J Pediatr 2007;74:275-278.

[26] Yengil E, Acipayam C, Kokacya MH, Kurhan F, Oktay G, Ozer C. Anxiety, depression and quality of life in patients with

beta thalassemia major and their caregivers. Int J Clin Exp Med 2014;7:2165-2172.

[27] Khoury B, Musallam KM, Abi-Habib R, Bazzi L, Ward ZA, Succar J, et al. Prevalence of depression and anxiety in adult patients with β-thalassemia major and intermedia. Int J Psychiatry Med 2012;44:291-303.

[28] Örengül AC, Ucuz L , Battaloglu NO , Ozek G, Gormez V. Prevalence of psychiatric disorders and suicidality among children and adolescents with thalassemia major—A Turkish sample, Children's Health Care, 48:1, 120-129, DOI: 10.1080/02739615.2018.1500290.

[29] Segoviano-Mendoza M, Cardenas-de la Cruz M, Salas-Pacheco J, Vazquez-Alaniz F, La Llave-Leon O, Castellanos-Juarez F, et al. Hypocholesterolemia is an independent risk factor for depression disorder and suicide attempt in Northern Mexican population. BMC Psychiatry 2018;18:7.

[30] Maioli M, Pettinato S, Cherchi GM, Giraudi D, Pacifico A, Pupita G, et al. Plasma lipids in beta-thalassemia minor. Atherosclerosis 1989;75:245-248.

[31] Messina G, Colombo E, Cassinerio E, Ferri F, Curti R, Altamura C, et al. Psychosocial aspects and psychiatric disorders in young adult with thalassemia major. Intern Emerg Med 2008;3:339-343.

[32] Hakeem GLA, Mousa SO, Moustafa AN, Mahgoob MH, Hassan EE. Health-related quality of life in pediatric and adolescent patients with transfusion-dependent ß-thalassemia in upper Egypt (single center study). Health Qual Life Outcomes 2018;16:59.

[33] Thavorncharoensap M, Torcharus K, Nuchprayoon I, Riewpaiboon A, Indaratna K, Ubol BO. Factors affecting health-related quality of life in Thai children with thalassemia. BMC Blood Disord 2010;10:1.

[34] Gupta V, Singh A, Upadhyay S, Bhatia B. Psychopathology in Children with Thalassemia Major. Psychol Stud 2012) 57(1):55–57

[35] Tsiantis J, Dragonas T, Richardson C, Anastasopoulos D, Masera G, Spinetta J. Psychosocial problems and adjustment of children with beta-thalassemia and their families. Eur Child Adolesc Psychiatry 1996;5:193-203.

[36] Coifman KG, Ross GS, Kleinert D, Giardina P. Negative affect differentiation and adherence during treatment for thalassemia. Int J Behav Med. 2014;21(1):160-168.

[37] Aydin B, Yaprak I, Akarsu D, Okten N, Ulgen M. Psychosocial aspects and psychiatric disorders in children with thalassemia major. Acta Paediatr Jpn. 1997;39(3):354-357.

[38] Aydinok Y, Erermis S, Bukusoglu N, Yilmaz D, Solak U. Psychosocial impli-

cations of Thalassemia Major. Pediatr Int. 2005;47(1):84-89.

[39] Prasomsuk S, Jetsrisuparp A, Ratanasiri T, Ratanasiri A. Lived experiences of mothers caring for children with thalassemia major in Thailand. J Spec Pediatr Nurs 2007;12:13-23.

[40] Jawaria Anum, Rabia Dasti. Caregiver Burden, Spirituality, and Psychological Well-Being of Parents Having Children with Thalassemia. J Relig Health (2016) 55:941–955.

[41] Caocci G, Efficace F, Ciotti F, Roncarolo MG, Vacca A, Piras E, et al. Health related quality of life in Middle Eastern children with beta-thalassemia. BMC Blood Disord 2012;12:6.

[42] Boonchooduang N, Louthrenoo O, Choeyprasert W, Charoenkwan P. Health-Related Quality of Life in Adolescents with Thalassemia. Pediatr Hematol Oncol. 2015;32(5):341-348.

[43] Khurana A, Katyal S, Marwaha RK. Psychosocial burden in thalassemia. Indian J Pediatr. 2006;73(10):877-880.

[44] Ansari S, Baghersalimi A, Azarkeivan A, Nojomi M, Hassanzadeh Rad A. Quality of life in patients with thalassemia major. Iran J Ped Hematol Oncol 2014;4:57-63.

[45] Economou M, Zafeiriou DI, Kontopoulos E, Gompakis N, Koussi A, Perifanis V, et al. Neurophysiologic and intellectual evaluation of beta-thalassemia patients. Brain Dev 2006;28:14-18.

[46] Floris F, Comitini F, Leoni G, Moi P, Morittu M, Orecchia V, et al. Quality of life in Sardinian patients with transfusion-dependent Thalassemia: a cross-sectional study. Qual Life Res 2018.

[47] Anie KA, Massaglia P. Psychological therapies for thalassaemia. Cochrane Database Syst Rev 2014:CD002890.

[48] Mohamadian F, Bagheri M, Hashemi MS, Komeili Sani H. The Effects of Cognitive Behavioral Therapy on Depression and Anxiety among Patients with Thalassemia: a Randomized Controlled Trial. J Caring Sci 2018;7:219-224.

[49] Mazzone L, Battaglia L, Andreozzi F, Romeo MA, Mazzone D. Emotional impact in beta-thalassaemia major children following cognitive-behavioural family therapy and quality of life of caregiving mothers. Clin Pract Epidemiol Ment Health 2009;5:5.

[50] Splaine Wiggins M. The partnership care delivery model: an examination of the core concept and the need for a new model of care. J Nurs Manag 2008;16:629-638.

[51] Mohammadi E, Abedi HA, Jalali F, Gofranipour F, Kazemnejad A. Evaluation of 'partnership care model' in the control of hypertension. Int J Nurs Pract 2006;12:153-159.

[52] Sadeghi S, Razmjooei N, Ebadi A, Najafi M, Asadi Lari , Bozorgzad P. Effect of applying continuous care model on patients' quality of life after Coronary Artery Bypass Graft Iranian Journal of Critical Care Nursing Spring 2009, Volume 2, Issue 1; 1-6

[53] Khoshnevis M, Javadinasab M, Ghanei M, Hoseini S, Karimi Z, Ebadi A, Babatabar D. Effect of using collaborative care model on life quality of chemical injured patients suffering from chronic bronchiolitis. Iranian Journal of Critical Care Nursing Summer 2009, Volume 2, Issue 2; 47-50

[54] Ghavidel F., Mohammadzadeh S., Pirasteh H., Alavi Majd H. Effect assessment of applyin the partnership care model on quality of life in hemodialysis patients referring to Be'sat Hospital of IRI Air Force. Journal of IRIAF Health Administration. 2009;12(2):22–27.

[55] Hayes SC1, Luoma JB, Bond FW, Masuda A, Lillis J. Acceptance and commitment therapy: model, processes and outcomes. Behav Res Ther. 2006 Jan;44(1):1-25.

[56] Masuda A, Cohen LL, Wicksell RK, Kemani MK, Johnson A. A case study: Acceptance and commitment therapy for pediatric sickle cell disease. J Pediatr Psychol 2011;36:398-408.

[57] Lundgren T, Dahl J, Melin L, Kies B. Evaluation of acceptance and commitment therapy for drug refractory epilepsy: a randomized controlled trial in South Africa--a pilot study. Epilepsia 2006;47:2173-2179.

[58] Feros DL, Lane L, Ciarrochi J, Blackledge JT. Acceptance and Commitment Therapy (ACT) for improving the lives of cancer patients: a preliminary study. Psychooncology 2013;22:459-464.

[59] Goodwin CL, Forman EM, Herbert JD, Butryn ML, Ledley GS. A pilot study examining the initial effectiveness of a brief acceptance-based behavior therapy for modifying diet and physical activity among cardiac patients. Behav Modif 2012;36:199-217.

[60] Gregg JA, Callaghan GM, Hayes SC, Glenn-Lawson JL. Improving diabetes self-management through acceptance, mindfulness, and values: a randomized controlled trial. J Consult Clin Psychol 2007;75:336-343.

[61] Foroughe M, Stillar A, Goldstein L, Dolhanty J, Goodcase ET, Lafrance A. Brief Emotion Focused Family Therapy: An Intervention for Parents of Children and Adolescents with Mental Health Issues. J Marital Fam Ther 2018.

[62] Robinson AL, Dolhanty J, Greenberg L. Emotion-focused family therapy for eating disorders in children and adolescents. Clin Psychol Psychother 2015;22:75-82.