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REVIEW

Gender Disparities in Psychological Disturbances and Quality of Life Among Adolescent and Adult Patients with Thalassemia: A Review

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Abstract: Thalassemia is a chronic disease caused by impaired globin chain synthesis, leading to ineffective erythropoiesis, hemolysis, and chronic anemia. The treatment of patients with thalassemia, including blood transfusion combined with chelation therapy has progressed and improved their survival and prognosis. However, thalassemia-related psychological problems and impaired health-related quality of life (QoL) challenges still exist. Gender is one of the factors that has been suggested, to contribute to the disparities in psychological outcomes. This review article examined the evidence for gender differences in psychological disturbances and QoL in adolescent and adult patients with thalassemia. A non-systematic search of the literature was conducted in PubMed and Google Scholar for English full-text available from 2013 to 2023. We identified 23 studies with a sample size ≥ 100 that examined gender disparities in anxiety, depression, and QoL in adolescent and adult patients with thalassemia (mean prevalence of female = 53.1%; mean age = 28 years). Our review shows that there are gender disparities in psychological distress and QoL in adolescent and adult patients with thalassemia. Statistically significant gender differences were demonstrated in 62% of the psychological and QoL outcomes from 16 studies. Female patients had a higher prevalence of anxiety, depression, and poorer QoL in some studies. However, further studies with sufficient power and design are necessary to confirm the existence of gender disparities in psychological disturbances and QoL outcomes.

Keywords: gender disparities, anxiety, depression, quality of life, thalassemia

Introduction

Thalassemia is a hereditary disorder caused by impaired globin chain synthesis, leading to ineffective erythropoiesis, hemolysis, and chronic anemia.[1–4] This genetic disease is prevalent in the thalassemia belt regions, including the Mediterranean countries (Italy, Greece, and Cyprus), Southeast Asia (especially Thailand, Cambodia, and Indonesia), as well as Turkey, Iran, and India.[3,5–7] The main treatment of thalassemia is repeated blood transfusion to correct the anemia, which can result in iron overload. Therefore, iron-chelating therapy is necessary to prevent complications of iron overload.[1,8–10]

Although the survival of patients with thalassemia has increased through a combination of regular blood transfusion and iron-chelating therapy,[1,9,11–14] serious clinical and psychological challenges still exist.[11,15] Patients with thalassemia face several problems during their lives, including the signs and symptoms of thalassemia, the presence of complications and comorbid chronic conditions, and treatment-related issues including painful injections and regular hospital visits due to blood transfusions.[16–18] It has been known that patients with thalassemia suffer from a wide range of psychological problems and health-related quality of life (QoL).[7,13,19–22] They may develop anxiety and depression because of social problems such as uncertainties about the future and limited social activity.[6,21,23]

Although many studies about psychological disturbances and QoL in patients with thalassemia have been published, only limited studies discussed the impact of gender differences in those aspects. Gender is one of the factors that has been

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suggested to contribute to the disparities of psychological outcomes in chronic conditions.[24–26] Additionally, there is also a rising concern about the impact of gender on psychological and QoL outcomes in patients with thalassemia. Therefore, this review aimed to investigate the association between gender and psychological disturbances, as well as health-related QoL in adolescent and adult patients with thalassemia.

Methods of Review

A comprehensive literature review was conducted using online sources, including PubMed, Scopus, and Google Scholar. The authors used a combination of the following search terms: "mental health" OR "mental illness" OR "psychological distress" OR "psychological disturbances" OR "anxiety" OR "depression" OR "quality of life" AND "thalassemia". The inclusion criteria for the selection of studies for review were as follows: studies related to anxiety, depression, or QoL among adolescent and adult patients with thalassemia. We included original research articles written in English from 2013–2023. Figure 1 shows the article selection process. Articles that did not analyze gender associated with psychological distress or QoL were excluded. The sample size was set at a minimum of 100 to confirm an adequate power for statistical analyses in the studies. Only studies with quantitative methods were selected as the main articles. We identified 16 articles (sample sizes N = 100–10,046; mean prevalence of female 53.1%; mean age = 28 years), which met our inclusion criteria for review. The studies are listed in Table 1. A total of 21 outcomes from the 16 studies were examined in this review.

Anxiety and Depression

Three out of 16 studies analyzed gender differences concerning anxiety.[30,32,33] Two studies demonstrated that female patients with thalassemia reported more anxiety than males.[30] One study showed that females had higher scores on anxiety symptoms, but the difference was not statistically significant.[32]

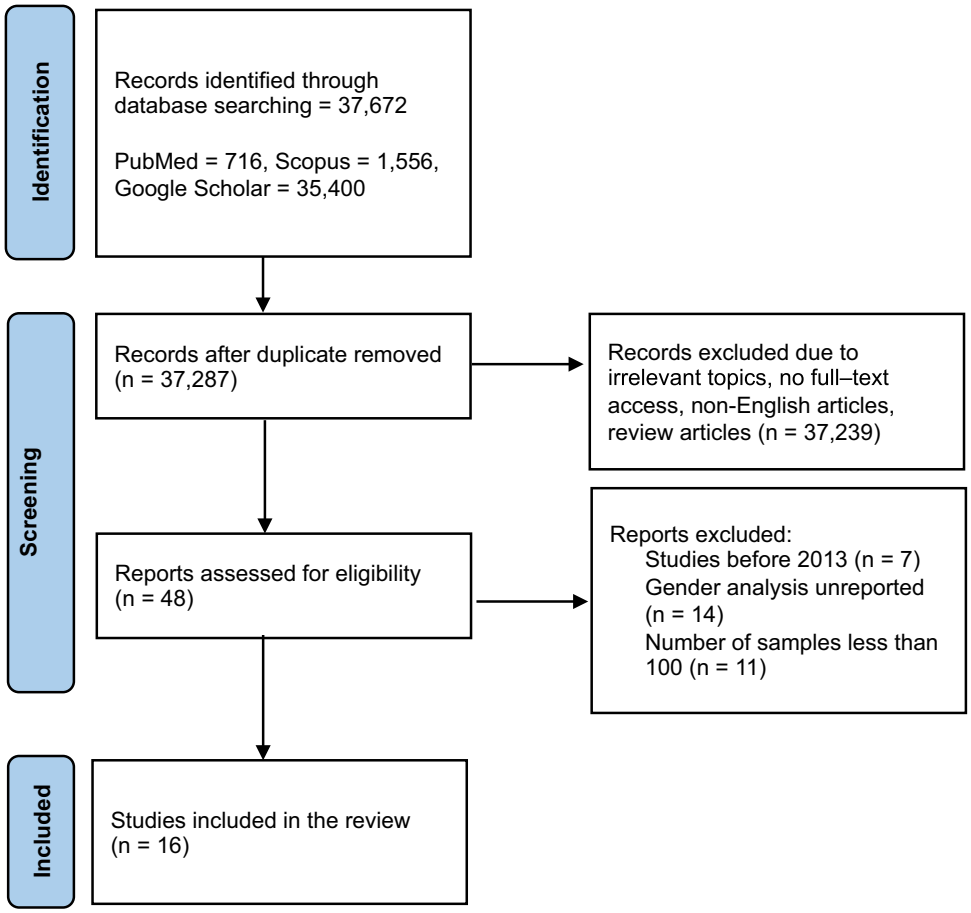

Figure 1 The flow diagram of study selection in this review.

Table 1 Overview of Studies Examining Gender Disparities in Psychological Disturbance and Quality of Life Among Adolescent and Adult Patients with Thalassemia Listed Chronologically According to Year of Publication

Author	Study design	Country	N	% Female (N)	Endpoint	Impact of Gender
Ansari et al* (2014)[27]	Case-control	Iran	250	48.4 (121)	QoL	+
Khairkhah et al* (2015)[28]	Cross-sectional	Iran	150	53.3 (80)	QoL	+
Gan et al (2016)[29]	Cross-sectional	Malaysia	127	62.2 (79)	QoL	-
Seyedifar et al (2016)[30]	Cross-sectional	Iran	512	50.2 (257)	QoL, anxiety, depression	+
Floris et al* (2018)[31]	Cross-sectional	Italy	190	49.5 (94)	QoL	+
Maheri et al (2018)[32]	Cross-sectional	Iran	389	54.0 (210)	Anxiety, depression	-
Patel et al (2018)[33]	Retrospective	United States (US)	10,046	69.6 (6994)	Anxiety, depression	+
Patel et al* (2019)[34]	Cross-sectional	Sri Lanka	120	53.6 (74)	QoL, depression	+
Yousif et al (2019)[35]	Cross-sectional	Iraq	100	53.0 (53)	Depression	+
Goulas et al (2020)[36]	Cross-sectional	Greece	131	56.5 (74)	QoL	-
Rikos et al* (2020)[37]	Cross-sectional	Greece	119	52.9 (63)	QoL	+
Hamdy et al (2021)[38]	Cross-sectional	Egypt	112	43.8 (49)	QoL	+ (VT)
Khodashenas et al* (2021)[39]	Cross-sectional	Iran	100	55.8 (53)	QoL	-
Mardhiyah et al (2022)[40]	Cross-sectional	Indonesia	120	45.8 (55)	QoL	-
Sarhan et al* (2022)[41]	Cross-sectional	Palestine	163	55.2 (90)	Depression	+
Hossain et al (2023)[42]	Cross-sectional	Bangladesh	356	46.0 (163)	QoL	+ (BP, PHS)

Notes: *Gender only used as covariate, VT, vitality (SF-36); BP, bodily pain (SF-36); PHS, physical health summary (SF-36).

Six out of sixteen studies examined gender disparities in depression.[30,32–35,41] Four studies demonstrated that females faced more depression than males.[30,33–35] On the contrary, one study found that males reported more depression symptoms than females.[41] Results from another study showed no relationship between gender and depression.[32]

Quality of Life

Twelve out of sixteen studies investigated gender differences concerning QoL.[27–31,34,36–40,42] Four studies found that women had reduced QoL in terms of lower satisfaction with physical health, psychological health, and social relationships,[34] lower vitality domain,[38] bodily pain, and physical health summaries,[42] and faced more problems on daily activity than males.[30] Contrary to those results, two studies found that females had better QoL[27] and significantly higher scores in the overall perception of the health domain.[31] The other six studies did not show a significant association between QoL and gender, although the scores were lower in females.[28,29,36,37,39,40]

There was a 62% (13 out of 21) statistically significant gender impact associated with the outcomes reported in the 16 studies overall (Table 1). Therefore, there is an indication to suggest the existence of gender differences in psychological and QoL outcomes among adolescent and adult patients with thalassemia.

Discussion

Regular blood transfusion in thalassemia treatment aims to reduce the complications of severe thalassemia by ameliorating anemia and suppressing erythropoiesis. Morbidity and mortality related to thalassemia have been reduced significantly with the administration of iron-chelating therapy.[4,43] Nonetheless, patients with thalassemia suffer from a variety of symptoms, including large spleen and liver, bone disorders, and especially visible changes in head and facial bones with a change in gaze.[6,44] Bone deformities and short stature may contribute to poor self-image. Severe complications such as heart failure, liver disease, and infections are common among patients with thalassemia. Painful and prolonged treatments of thalassemia, physical abnormalities, increased risk of death, and activity limitation expose the patients to mental health and emotional conditions, causing anxiety, depression, and deterioration QoL.[45,46]

Previous studies found that anxiety is prevalent in patients with thalassemia. Thalassemia as a chronic disease can lead to anxiety and worry as other chronic illnesses. Adolescents and adults with thalassemia had several physical problems, which resulted in stress.[47] The stress exposure may be a source of anxiety for patients with thalassemia.[48]

Additionally, the anxiety could be a consequence of repeated blood transfusions, fear of death, concern about family formation, negative thoughts, and different feelings in these patients.[30,32,33,49]

Patients with thalassemia were predisposed to depression. The prevalence of depression in adults with thalassemia ranges from 10.3–35% depending on different factors, including the design and power of the study, different types of questionnaires, as well as the place it was conducted.[50] Depression is a disorder of mental with changes in cognitive function, mood, behavior, and physical health,[51] which may be a result of the long-term treatment and chronicity of the thalassemia.[18,52] Depression and thalassemia have bidirectional relationships. Depressed patients with thalassemia had more fatigue, discomfort, pain, and sleep disturbance, while depression affects the physical and mental health of patients with thalassemia.[48,53] It is related to morbidity and mortality because of its effect on decreased compliance.[54] It has been suggested that all patients with thalassemia should be assessed for depression so that suitable interventions can be implemented.[55]

Genetic components may contribute to the etiology of depression in patients with thalassemia. Genetic studies showed a possible genetic predisposition for depression on chromosome 11, which is close to the gene responsible for thalassemia.[51,56] Additionally, it has been found one of the human tryptophan hydroxylase genes (TPH1) on the short arm of chromosome 11 (11p14-p15.3), which plays the role of a rate-limiting enzyme in serotonin biosynthesis that is associated with depressive symptoms.[22,57] Hypothalamic-pituitary-adrenal (HPA) axis will respond to the depression and cause an increase in basal cortisol levels, which will affect the symptoms of depression and worsen the course of the disease. On the other hand, iron toxicity can alter the HPA axis, which results in lower ACTH levels.[44]

Gender plays a role in the likelihood of the detection process and diagnosis of mental disease. Females may have many psychological disorders. Furthermore, the role of females as caregivers in the family enhances difficulty and stress in their lives. There is a discrepancy between gender role expectations and the needs that may lead to psychological distress.[58] Different psychological disorders affect females more than males. Females tend to have depression and anxiety disorders.[53] However, in this review only one study in Palestine showed that males reported more depression than females.[41] The reasons for this contradiction were high social expectations for marriage, economic success, education, and responsibility for the family in this population of male patients.

Adolescent and adult patients with thalassemia are at higher risk of developing psychological disorders associated with physical, mental, and social problems that result in decreased QoL.[15,47,59,60] QoL measurement is a multidimensional concept that emphasizes the influence of the disease and its treatment on the well-being of an individual.[12,61,62] Thalassemia influences the patients' well-being, which is reported as a difference in QoL regarding psychological, social, and health-related issues. The results varied widely from study to study, which can be attributed to the differences in socioeconomic status, countries where studies took place, and differences in healthcare quality.[63] QoL is an acceptable index to evaluate the overall health of patients with thalassemia.[39] Evaluation of factors associated with the QoL is essential in developing clinical counseling and social support programs that could positively affect the outcome.[55,64]

In this review, impaired QoL due to bodily pain has been observed in patients with thalassemia. Adolescent patients with thalassemia experienced pain similar to the general population, whereas older adults experienced worsened pain. Low vitamin D levels are associated with increased pain and lower bone density. Some possible pain mechanisms in thalassemia include pathologic fractures and impingement on nerve roots by hematopoietic masses. Increased pain was observed with the administration of deferoxamine, which may be due to the route of administration. Pain can reduce QoL in terms of both physical functioning and mental health.[11]

It has been shown that gender differences existed in the observed data of the QoL in patients with thalassemia. Females tend to report lower health-related QoL scores than males.[30,34,38,42] In addition, females may be more willing to discuss symptoms and reporting of health-related QoL than males.[26] Females without social support who are exposed to life events are more vulnerable than males.[25] Female patients may have more emotional distress, which refers to poorer QoL when compared to males. Conversely, two studies found that females had better QoL[27] and significantly higher scores in the overall perception of the health domain.[31] This discrepancy could be due to a burden focused on males in different countries. Additionally, in Western countries, female patients with thalassemia show a better prognosis, which could improve their health perception and QoL.

The findings regarding gender differences in psychological problems and QoL among patients with thalassemia were important for comprehensive thalassemia management. Screening and prevention of the emergence of mental disorders

were recommended for patients with thalassemia.[44] Routine monitoring and treatment of complications were also compulsory. The gender differences in psychological disturbances and QoL suggest the requirement for more attention to female patients and for areas of enhancement to be explored.[56] A gender approach to health means socio-biological factors identification and thoughtful consideration of how gender difference influences health outcomes. A gender approach to mental health assists in the appropriate responses from the mental healthcare system.[25] Adolescent and adult patients with thalassemia require support through personalized psychological and social programs to help them overcome all the problems related to chronic illness and its complications. Such provision may improve the QoL, enhance a productive and hopeful life, and ensure their role and acceptance within their community.[7,13,23,27,35] Additionally, counseling may help to reduce the depression, anxiety, and fear experienced by patients with thalassemia. It also can increase QoL.[46] Studies showed that patients with good psychosocial status demonstrated better treatment adherence, including regular blood transfusion and iron-chelating therapy.[16,53,65]

Although females seem to have higher anxiety or depression symptoms and tend to report poorer QoL, there were some limitations of the studies in this review to be considered. Some of the studies only included gender as a covariate in adjusted analysis rather than focusing on gender differences as the main objective of the study. The methodological differences among the studies, including the study design, timing of the psychological assessment, and the way to assess the outcomes (such as generic questionnaires or medical diagnosis based on diagnostic criteria) should be considered. Additionally, most studies used convenience samples and cross-sectional study design. Therefore, it was difficult to explain and determine the cause and effect of gender on psychological disturbances and QoL.

Conclusion

Based on the reviewed research studies, gender is suggested as an essential contributor to disparities in psychological disturbances and QoL among adolescent and adult patients with thalassemia. Female patients tend to report more anxiety or depression symptoms and tend to have lower QoL than males. Nonetheless, future research with a good study design and including a large-scale population is necessary to elucidate the exact influence of gender on psychological and QoL outcomes. Additionally, patients with thalassemia should be screened for comorbid mental disorders. They are likely to need some assistance with psychological adjustment, especially females. A multidisciplinary team should be involved in treating patients with thalassemia. The provision of psychological-related treatment may result in decreased anxiety and depression, together with improvement of QoL.

Disclosure

The authors declare no conflicts of interest in this work.

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