Original Article

Examining depression and quality of life in patients with thalassemia in Sri Lanka

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ABSTRACT

Background: With more effective treatments and improved outcomes in thalassemia, there is increasing focus on its psychological sequelae. Most published data on this topic are from high-income countries and much less so from low- and middle-income countries, where thalassemia is more prevalent.

Aim: The aim of this study was to systematically evaluate the psychiatric morbidity and quality of life in relation to demographic- and illness-related variables among Sri Lankan patients with thalassemia.

Methods: This cross-sectional investigation was conducted at the University of Kelaniya Teaching Hospital in Sri Lanka. Patients with all forms of thalassemia, over 12 years of age, and in stable medical condition (n = 120) were recruited. Assessment tools included a general demographic questionnaire, the Beck Depression Inventory-II, and the World Health Organization Quality of Life Measure–Brief. Statistical analysis was conducted using linear regressions, Chi-squares, and analyses of variance.

Results: Lack of family support, longer duration of inpatient admission, and female gender were associated with higher depression scores and reduced quality of life. Environmental and social quality of life were positively correlated with levels of peer support in males, while increased support from religion correlated with lower depression scores and higher satisfaction with environmental and psychological quality of life in women. There was no association between the type of thalassemia and either depression or quality of life measures.

Conclusion: Several factors may influence the psychological state and well-being of patients with thalassemia in Sri Lanka. Specific service innovations (some gender-specific) may help to address these factors to improve treatment outcome and well-being.

Keywords: Depression, quality of life, Sri Lanka, thalassemia

Introduction

Thalassemias are a group of genetic disorders caused by a mutation to the globin chains resulting in decreased hemoglobin (Hb) synthesis. Worldwide, the prevalence of thalassemias ranges from 0 to 19%, with highest rates in Southeast Asia, the Eastern Mediterranean (particularly Cyprus and Sardinia), and Sub-Saharan Africa.[1,2]

Patients with thalassemia often present with a range of clinical presentations depending on the severity of the globin chain mutation.[3] Such variations may also influence their management including specific pharmacotherapy. Within the category of β-subunit affected thalassemias, individuals with β-thalassemia major have the most severe form of the disorder, with a homozygous inheritance of a nonfunctional β-globin subunit. β-thalassemia major

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often results in severe anemia and physical and facial deformities and requires regular blood transfusions and chelation therapy. In comparison, patients with β-thalassemia minor have the least severe form due to a heterozygous inheritance of the abnormal β-globin gene and can often be asymptomatic throughout their entire adult life. Nontransfusion-dependent thalassemia is a term used to identify a group of disorders which are of intermediate severity, and as the name implies, these individuals can survive without regular blood transfusions. The clinical spectrum of this group varies immensely, and in this cluster are the "classic" β-thalassemia intermedia, Hb E β-thalassemia and Hb H disease, as well as sickle cell β-thalassemia traits.

Individuals with thalassemia often experience severe challenges and life stressors that contribute to psychological distress, namely, the impact of symptoms, severity and adverse effects of treatment, physical and facial deformities, as well as the risk of increased mortality.[4,5] Furthermore, they experience social, educational as well as occupational challenges and being often separated from their families to access care. Previous research in countries, including Iran, Turkey, Egypt, Lebanon, and Italy, has found increased levels of depression in patients with thalassemia.[6-10] These patients have also been found to have poor physical- and mental health-related quality of life,[11] increased levels of pain,[12] and impaired sleep, vitality, and social function.[13] Furthermore, a recent study documents the significant psychological problems experienced by transitional youth with thalassemia and the likelihood of adverse long-term impact.[14] These findings strongly support the need for an integrated psychosocial program that includes screening of psychiatric disorders to be part of the overall management of these patients.

Methods

This cross-sectional descriptive study was conducted at the Adolescent and Adult Thalassemia Care Unit of the University of Kelaniya Teaching Hospital in Ragama. This is the only thalassemia unit that treats adults with this illness in the country and is responsible for approximately 300 patients. The study was conducted with ethics approval from the Faculty of Medicine at the University of Kelaniya. Patients with a clinical diagnosis of thalassemia (major and intermedia) confirmed by high-performance liquid chromatography and genetic analysis were included in the study. The differentiation between thalassemia major and intermedia was based on the age of presentation and transfusion history. Patients who needed more than eight transfusions per year were classified as thalassemia major, and those with lesser requirements were considered as thalassemia intermedia.

Participants

Patients on the thalassemia unit were approached to participate in the study. Patients ≥12 years of age, in stable medical condition, and able to communicate effectively in Sinhalese, Tamil, or English, were eligible for inclusion. Patients were excluded from participation if they did not meet these criteria, if they suffered from an altered state of consciousness, or if they refused consent.

Procedures

Patients were presented with a consent letter, information leaflet, and an oral briefing from trained medical personnel to understand the purpose of the study, risk and benefits of participation, and participant responsibilities. Written consent was obtained from all patients who participated in the study, as well as from parents of child or adolescent patients (between 12 and 18 years of age). Enrolled participants then completed a series of self-report questionnaires.

A general questionnaire was devised to gather basic demographic information (age, gender, hometown, highest educational level attained, household income, primary caregiver, and religious affiliation) and illness-related data (diagnosis, length of stay/admission in unit, and details on other affected family members).

The self-administered 4-point Likert scale was used to obtain information about their support network, for example, the strength of support they receive ("Do you feel well supported by __?") from their family, peers, hospital staff, and religion, where 0 = never, 1 = sometimes, 2 = most of the time, and 3 = all the time.

Presence and severity of depression were assessed using the 21-item Beck Depression Inventory (BDI-II).[10] Items on this self-rated questionnaire are rated on a 4-point Likert scale, where higher total scores correspond to greater severity of depression. To make accommodations for those under 18 years and for cultural sensitivity, question 21 (which asks about sexual activity) was eliminated and the total score rating scale was adjusted to accommodate this change.

The World Health Organization Quality of Life–Brief (WHOQOL-BREF)[11] was used to assess the quality of life domains including physical health, psychological health, social relationships, and environment. This 26-item

self-administered questionnaire is a shorter version of the WHOQOL-100 and was used due to time restrictions and to minimize the burden on the patient. Items were rated on a 5-point scale from which a raw item score is transformed into a mean score per domain between 0 and 100, where a higher score indicates to a better quality of life.

Statistical analysis

Statistical analysis was performed using IBM SPSS Version 23, (Armonk, New York, United States). Student's *t*-tests were performed on the survey questions to identify differences in response value within each question. One-way analyses of variance and Chi-squared analyses were performed to identify correlations and group differences. Linear regression was used to predict depressive severity on the BDI-II and satisfaction with physical health, psychological well-being, social relationships, and environment. Demographic factors were used as the independent variables, with the BDI-II and WHOQOL-BREF scores used as the dependent variables. Level of formal education was treated as an ordinal variable, income was analyzed as an interval variable, and type of thalassemia diagnosis was evaluated as a categorical variable. $P \leq 0.05$ was considered statistically significant for all analyses.

Results

Participant demographics can be found in Table 1. The study population consisted of 138 patients, with 59.2% having thalassemia major, 21.7% having Hb E β-thalassemia, 9.2% having thalassemia intermedia, 3.3% having thalassemia minor, 0.8% having Hb S β-thalassemia, and 4.2% having other inherited blood disorders. Across the sample, 53.6% were female and 77.8% were ≥18 years of age (range 12–65 years).

The results of the linear regression analyses are summarized in Tables 2-4. For the patient's sample as a whole [Table 2], increased age significantly predicted reduced satisfaction with social relationships ($P = 0.01$), while female gender was associated with higher depression scores ($P = 0.05$) and lower satisfaction with physical health ($P = 0.02$), psychological health ($P = 0.03$), and social relationships ($P = 0.007$). Longer duration of inpatient stay predicted more severe depression ($P = 0.03$) and lower satisfaction with physical health ($P = 0.03$). More family support predicted lower depression ($P = 0.004$) and more satisfaction with environment ($P < 0.0005$) and physical health ($P = 0.02$). Similarly, increased peer support was also associated with more satisfaction with physical health ($P = 0.04$) and social relationships ($P = 0.04$).

Table 1: Demographic characteristics of participants from the Hemals Thalassemia Clinic

	n (%)
Age (years), mean (range)	25.7 (12-65)
≥18	107 (77.8)
Gender	
Male	64 (46.4)
Female	74 (53.6)
Highest level of education completed	
Grade school	76 (55.1)
High school	28 (20.3)
College degree	21 (15.2)
University degree	5 (3.6)
Religious affiliation	
Buddhist	112 (81.2)
Roman Catholic	16 (11.6)
Hindu	6 (4.3)
Other	3 (2.1)
Household income (LKR per year)	
<20,000	22 (15.9)
20,000-40,000	24 (17.4)
40,000-60,000	27 (19.6)
60,000-80,000	6 (4.3)
80,000-00,000	14 (10.1)
100,000+	30 (21.7)
Diagnosis	
Thalassemia major	79 (57.2)
Thalassemia intermedia	12 (8.7)
Thalassemia minor	4 (2.9)
E/β-thalassemia	35 (25.4)
Other	6 (4.3)
Length of stay (days), mean (range)	3.9 (0-30)

LKR=Sri Lankan rupees

Additional regression analyses were conducted separately for males and females to determine if there were gender differences in predictors of outcomes.

For females [Table 3], higher household income was a significant predictor of more satisfaction with social relationships ($P = 0.02$). Those with thalassemia intermedia diagnosis had lower satisfaction with environment than those with thalassemia major diagnosis ($P = 0.05$). Longer length of stay predicted higher depression scores ($P = 0.04$). Higher family support predicted increased satisfaction with environment ($P = 0.001$), physical health ($P = 0.03$), and psychological health ($P = 0.002$). Increased support from religious beliefs predicted lower depression scores ($P = 0.05$) and higher satisfaction with environment ($P = 0.04$) and psychological health ($P = 0.01$).

For males [Table 4], those with thalassemia intermedia diagnosis had more satisfaction with psychological well-being than those with thalassemia major diagnosis ($P = 0.05$). Greater family support predicted lower

Table 2: Linear regression of predictors of depression and quality of life parameters in the full participant sample (n=138)

	Depression		Satisfaction with environment		Satisfaction with physical health		Satisfaction with psychological health		Satisfaction with social relationships	
	B	*P**	*B*	*P**	*B*	*P**	*B*	*P**	*B*	*P**
Constant	26.11	0.001	44.98	0.001	62.81	0.000	47.87	0.003	62.02	0.000
Age	−0.05	0.65	−0.14	0.41	−0.04	0.81	−0.24	0.25	−0.49	0.01*
Gender (reference female)	3.56	0.05*	−2.50	0.40	−5.98	0.02*	−7.55	0.03*	−8.57	0.007*
Education	0.62	0.56	0.62	0.73	−0.74	0.64	3.02	0.16	−0.65	0.74
Household income	−0.38	0.46	0.69	0.43	0.33	0.66	0.15	0.88	1.74	0.06
Diagnosis - Thalassemia intermedia (reference thalassemia major)	2.76	0.39	−3.06	0.61	3.43	0.51	2.49	0.73	3.61	0.57
Diagnosis - Thalassemia minor (reference thalassemia major)	−2.45	0.63	−1.75	0.85	1.67	0.83	−2.01	0.85	6.67	0.48
Diagnosis - E/β-thalassemia (reference thalassemia major)	0.23	0.92	−3.91	0.33	−2.92	0.39	−0.19	0.97	0.80	0.85
Diagnosis - Other thalassemia (reference thalassemia major)	−2.31	0.57	4.86	0.48	4.34	0.46	3.18	0.70	1.47	0.83
Length of stay	0.24	0.03*	−0.33	0.09	−0.36	0.03*	−0.07	0.77	0.18	0.34
Family support	−3.67	0.004*	8.49	0.000*	4.13	0.02*	4.62	0.06	1.27	0.58
Peer support	−1.11	0. 30	2.83	0.15	3.55	0.04*	2.59	0.26	4.10	0.04*
Hospital staff support	−0.48	0.80	−3.31	0.31	−3.40	0.22	−1.28	0.74	4.85	0.16
Religion support	−1.57	0.16	2.19	0.26	1.77	0.29	3.82	0.10	0.69	0.73

*Statistically significant, $P \leq 0.05$

Table 3: Linear regression of predictors of depression and quality of life parameters among female participants (n=74)

	Depression		Satisfaction with environment		Satisfaction with physical health		Satisfaction with psychological health		Satisfaction with social relationships	
	B	*P**	*B*	*P**	*B**	*P**	*B*	*P**	*B*	*P**
Constant	59.22	0.002	1.74	0.94	34.31	0.08	−31.01	0.26	31.02	0.26
Age	−0.04	0.77	−0.24	0.27	−0.07	0.70	−0.15	0.55	−0.29	0.32
Education	−0.14	0.94	4.82	0.08	1.85	0.40	4.92	0.12	−1.91	0.54
Household income	−0.56	0.49	1.14	0.3352	0.55	0.56	1.15	0.40	3.46	0.02*
Diagnosis - Thalassemia intermedia (reference thalassemia major)	6.14	0.17	−14.69	0.05*	−3.45	0.56	−14.22	0.10	−1.23	0.88
Diagnosis - Thalassemia minor (reference thalassemia major)	1.61	0.80	−16.77	0.10	−5.15	0.53	−17.73	0.13	2.60	0.82
Diagnosis - E/β-thalassemia (reference thalassemia major)	−0.25	0.95	−9.34	0.07	−7.59	0.07	−3.68	0.54	0.81	0.90
Diagnosis - Other thalassemia (reference thalassemia major)	−0.58	0.93	−3.31	0.72	0.43	0.95	−2.77	0.79	2.05	0.84
Length of stay	0.31	0.04*	−0.11	0.62	−0.19	0.30	0.06	0.83	0.30	0.27
Family support	−2.89	0.13	10.54	0.001*	5.38	0.03*	11.17	0.002*	4.62	0.19
Peer support	0.58	0.77	−5.29	0.11	0.53	0.84	−4.06	0.29	2.65	0.49
Hospital staff support	−7.15	0.08	7.16	0.21	0.99	0.83	8.95	0.18	3.69	0.57
Religion support	−3.74	0.05*	5.92	0.04*	2.41	0.31	8.45	0.01*	0.72	0.83

*Statistically significant, $P \leq 0.05$

depression (P = 0.001) and being more satisfied with their environment (P = 0.009). High degree of peer support predicted greater satisfaction with environmental (P = 0.02) and social relationships (P = 0.02).

Patient's level of formal education and degree of hospital staff support were not found to be related to mental health outcomes in any analyses ($P > 0.05$).

Discussion

As with other early-onset chronic diseases, psychological health and day-to-day function are adversely affected by thalassemia itself as well as factors related to its treatment. As newer treatment strategies have improved outcomes of physical symptoms, there is an increased focus on emotional well-being of these patients.

We found that these patients, as a group, had higher depression scores and poorer quality of life scores. This finding is consistent with reports from several other low- and middle-income countries,[1,12,13] which have concluded that thalassemia was associated with increased risk of depression and lower quality of life. We found that the presence of emotional symptoms and reduced quality of life was associated with being female,

Table 4: Linear regression model of predictors of depression and quality of life parameters among male participants (*n*=64)

	Depression		Satisfaction with environment		Satisfaction with physical health		Satisfaction with psychological health		Satisfaction with social relationships	
	B	*P**	*B*	*P**	*B*	*P**	*B*	*P**	*B*	*P**
Constant	26.21	0.007	55.85	0.002	70.55	0.000	68.61	0.001	59.31	0.001
Age	−0.02	0.91	−0.14	0.66	−0.20	0.57	−0.57	0.13	−0.62	0.09
Education	0.08	0.95	−0.74	0.77	−2.13	0.43	4.26	0.14	0.16	0.95
Household income	0.23	0.74	−0.06	0.96	0.47	0.74	−0.60	0.69	−0.25	0.85
Diagnosis - Thalassemia intermedia (reference thalassemia major)	−1.32	0.85	10.94	0.35	16.59	0.20	27.32	0.05*	1.20	0.93
Diagnosis - Thalassemia minor (reference thalassemia major)	-	-	-	-	-	-	-	-	-	-
Diagnosis - E/β-thalassemia (reference thalassemia major)	−0.23	0.95	−0.29	0.97	2.55	0.74	10.09	0.21	−3.06	0.67
Diagnosis - Other thalassemia (reference thalassemia major)	−5.79	0.27	16.47	0.10	8.05	0.46	5.91	0.60	−1.70	0.87
Length of stay	0.16	0.48	−0.85	0.05	−0.69	0.15	−0.50	0.31	−0.09	0.84
Family support	−6.52	0.001*	8.35	0.009*	3.93	0.24	−0.27	0.94	−0.09	0.98
Peer support	−1.84	0.17	6.16	0.02*	3.78	0.16	3.62	0.20	6.18	0.02*
Hospital staff support	3.01	0.22	−4.61	0.29	−3.96	0.41	3.83	0.45	7.45	0.15
Religion support	−0.92	0.57	−1.76	0.57	−0.12	0.97	−3.69	0.30	−1.06	0.74

*Statistically significant, $P \leq 0.05$

a longer clinic exposure, and lack of family support. The finding that females have greater vulnerability to depression compared to males is a well-documented finding worldwide,[15] including Sri Lanka.[14] Several reasons have been proposed for this gender difference, including genetic predisposition,[16] psychological factors, and increased vulnerability to stress. The association of longer duration of treatment with higher depression scores is intuitive and consistent with reports from Western countries that have reported a direct correlation between psychiatric morbidity and length of hospital stay.[17,18] As with our finding, such reports have also noted the association of poor family support with increased likelihood of depression and decreased quality of life.[19] Indeed, based on the expectations in family relationships and cultural practices in Sri Lanka, it can be suggested that the impact of poor family support may be even greater on the psychological state of these patients. It has been previously proposed that including family members in patient care during inpatient admission may aid in the management of depression, improve the quality of life, and thus contribute to recovery.[19]

The thalassemia service had separate inpatient units for men and women, which enabled behavioral observations to be documented in the two groups. The men often socialized more with their peers by coming together during the day and playing games or sharing stories, while the females were quieter and tended to be more solitary. To determine if these differences were also reflected in overall outcome and illness trajectory, the study variables were also analyzed by gender. The results suggested that the degree of peer support was a significant predictor of depression severity among male patients, but not among female patients. Interestingly, higher peer support was also associated with greater satisfaction with environment and social relationships but only in men. This finding is consistent with other studies, which have found social support to be a protective factor against depression in both youth and adults.[20-24]

It is unclear why peer support did not have similar benefits for women in our study, but a possible explanation is that the tendency of the female patients toward solitude and/or less social interaction reduced the potential for benefit from such support. An alternate explanation is that the social support women received by women may be inadequate, inappropriate, or maladaptive. It has been previously reported that although social support is protective against depression for both males and females,[25,26] the degree of benefit may vary depending on the type of support. Positive or helpful social support lowers rates of depression,[27] whereas support, that is, perceived as superficial or is accompanied by support needs of the supporting person has an adverse impact on depression.[27] Further evaluations of the type of social support received by females with thalassemia and the development of appropriate peer support groups that use evidence-based approaches may contribute to the therapeutic benefit of the milieu in the inpatient units.

Furthermore, our study found that support from religious beliefs predicted lower depression and higher satisfaction with environment and psychological health among female

patients, but not in males. This is in line with the literature, which notes that females are more likely to depend on religious beliefs to cope with stressful situations than males.[28] This finding (together with the noted benefit of peer support in men) supports the strategy of unique, gender-based psychosocial interventions. Thus, emphasis on peer inclusion and social events, as well as the availability of sanctioned religious celebrations and prayer time and meditative practices may contribute to psychological well-being.

We noted that scores on certain items of the BDI-II in our study population differed compared to historical reports in the Western, nonthalassemic literature.[8,16] The study patients reported experiencing certain symptoms infrequently, such as feelings of failure and thoughts of suicide. They also reported low frequency of anhedonia, irritability, and poor concentration. However, the levels of self-blame and guilt were high, as were episodes of crying and sleep impairment. Of these, a tendency for crying remained a highly scored response for both genders, which goes against the finding in published literature of major depressive disorder (MDD) which reports females to have an increased frequency of crying when compared to males and weeping in females was seen as a form of coping.[29] Clinicians in Sri Lanka confidentially report seeing these differences and attribute it to be a cultural phenomenon. We also found that females had higher scores of self-criticism and guilt compared to males, in keeping with published literature that women with depression tend to express more self-blame than men.[30] Psychological therapies often focus on guilt and self-criticism as a key symptom to address. In this context, it would be essential to address any gender and cultural bias when developing or adopting psychological interventions for Sri Lankan patients.

While previous studies have reported the significant presence of depression in patients with thalassemia, they did not explore any differences among subtypes (major, minor, and intermedia) of the condition.[1,3,5,31] We found no difference between the three subtypes in the severity of depression or their quality life measures. This was unexpected as the thalassemia major tends to have greater disease burden. This finding may be explained, at least in part, by the variance in diagnosis-related treatment regimens. In general, patients with thalassemia major are treated quite aggressively in accordance with the severity of the disease, while guidelines are less defined for those with thalassemia intermedia or minor.[32] Often, the treatment of patients with thalassemia intermedia or E/β-thalassemia is left to clinical discretion, which can have varying outcomes. That is, it is possible that their medical management may not be as rigorous compared to thalassemia major, contributing to chronicity of symptoms and resulting in impaired quality of life. It is suggested that development of evidence-based algorithms and guidelines for treating the intermedia and minor subtypes of thalassemia may contribute to better understanding of the psychological sequela in this population and lead to better overall outcomes.

Several limitations of this investigation are acknowledged. A key deficiency is the lack of accompanying qualitative data, which likely would have captured the personal, subjective experiences of patients and provided additional measures of psychological distress. It is noted that it is a cross-sectional investigation conducted in a single specialized center, the Adolescent and Adult Thalassemia Care Unit. It serves as the national resource providing comprehensive, specialized care for thalassemia patients. Thus, the findings for this investigation may not be generalizable to Sri Lanka as a whole or to other countries with similar socioeconomic profile in the region. Finally, a methodological deficiency is the lack of syndromal diagnosis of depression (e.g., DSM 5 (Diagnostic and Statistical Manual of Mental Disorders, 5th edition) or International Statistical Classification of Disease II) using a validated interview, the presence of depression with diagnostic cutoffs was not evaluated, and therefore, the prevalence of DSM-5 depression was not documented in our sample.

Conclusion

This study suggests that certain patient factors are associated with higher depressive scores and poorer quality of life in patients with thalassemia. Modification of treatment interventions, such as by capitalizing on the positive benefits of family, peer, and religious support, could help alleviate psychiatric morbidity, improve function, and reduce disability in this population. Adaptation of psychological interventions based on gender may also be useful.

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Conflicts of interest

There are no conflicts of interest.

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