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Abstract

Background: Research focusing on health-related quality of life (HRQoL) in thalassaemia patients remains limited in Saudi Arabia.

Aims: To report on HRQoL outcomes in thalassaemia patients, and study associations with psychosocial and clinical factors.

Methods: Thalassaemia patients attending King Abdulaziz University Hospital were sequentially approached for enrolment. HRQoL outcomes were assessed using a validated Arabic version of the Medical Outcomes Study Short form (SF-36).

Results: This study included 105 individuals with β-thalassaemia major, with a mean age of 22.9 (± 11.7) (range 5–35) years, and 52.4% were male. Participants aged ≥ 14 years had a mean physical HRQoL score of 43.7 (± 10.1) and mental HRQoL score of 46.6 (± 10.5). Participants aged

Conclusions: Controlling for other variables, higher pretransfusion haemoglobin and younger age were associated with better mental HRQoL outcomes in thalassaemia patients. Professionals reported better physical HRQoL outcomes, compared to non-professionals. Preventive and comprehensive care models are needed in Saudi Arabia to improve HRQoL outcomes in thalassaemia patients.

Keywords: age, haemoglobin, quality of life, Saudi Arabia, thalassaemia.

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Introduction

Haemoglobinopathies, including thalassaemia, are considered a serious health care burden worldwide. Although originally more prevalent in the Mediterranean and Sub-Saharan regions, with the high rates of immigration, their prevalence has increased globally (1–4). An estimated 300 000 children are born with haemoglobinopathy every year, and 7% of the world's population are carriers (1,4,5). Countries in the Gulf Region, including Saudi Arabia, have reportedly the highest prevalence rates of haemoglobinopathy worldwide (6). In Saudi Arabia, data derived from the Saudi Premarital Screening Program database, which includes > 480 000 individuals, showed that 3.22% of the screened population were carriers, and around 0.07% had thalassaemia (7).

Thalassaemia is an inherited haemolytic anaemia characterized by a decrease or complete absence of globin chain production (1). Thalassaemia has a wide phenotypic spectrum and β-thalassaemia major is a severe transfusion-dependent form of the disease, associated with numerous complications caused by tissue hypoxygenation and iron overload. The 2 main sources of iron overload are repeated transfusions and increased intestinal iron absorption (8). In high-income countries, provision of safe blood transfusions, oral and parenteral iron chelating agents, noninvasive and regular iron monitoring, plus many other methods of supportive care, are among the numerous measures implemented to prevent disease-related complications and improve outcomes for thalassaemia patients (9,10). However, in countries with limited resources, these measures are difficult to adopt and sustain, especially with other challenges complicating transfusion therapy, such as red cell alloimmunization (11,12), transmission of

chronic infections (11–13), iron overload leading to tissue injury and end-organ damage (14,15), and adverse effects associated with chelating agents (15).

As a chronic disorder, thalassaemia is a clinical and psychosocial burden for patients and their families, and despite progress in clinical management, there has been little improvement in health-related quality of life (HRQoL) (16). Measurement of HRQoL for these patients is essential to assess the true burden of thalassaemia. HRQoL can clearly define the individual needs of patients, and better inform their disease management plans (17). Despite the high rates of thalassaemia in Saudi Arabia, research on HRQoL remains limited. This study aimed to assess HRQoL of children and adults with thalassaemia in Jeddah, Saudi Arabia, and its association with clinical and psychosocial characteristics.

Methods

Study design

This cross-sectional study was conducted at a tertiary care academic hospital: King Abdulaziz University Hospital (KAUH) in Jeddah, Saudi Arabia. The study was approved by KAUH Ethical Committee, and other administrative authorization was obtained before the start of data collection. We approached all patients diagnosed with thalassaemia who attended haematology outpatient clinics at KAUH between March 2015 and July 2016 for enrolment. Patients were only excluded if they were unable or unwilling to participate in the study.

Ethical approval

All procedures were in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. After explaining the study design and objectives, informed consent was obtained from the participants or guardians of children aged **Data collection**

The Medical Outcomes Study Short Form (SF-36) is a 36-item tool for measuring health status and outcomes from the patient’s perspective, and the English version is considered a reliable measure for assessing HRQoL subscales (18). The same questionnaire was translated into Arabic, and tested for internal consistency and reliability in a sample from the Saudi Arabian population (19). Data were collected using the SF-36 questionnaire during an interview with a trained data collector. Questionnaires were distributed to patients, and interviewers explained the purpose and content of the questionnaire, and then reassured participants about the confidentiality of their personal data. Adult patients (≥ 14 years) filled in the questionnaires independently, whereas paediatric patients (

Potential recall bias was addressed by offering patients ample time and complete privacy while filling in the questionnaires. Any missing data were brought to the researcher’s attention and

addressed individually by contacting participants or by review of electronic medical records.

Medical records were reviewed for clinical history, including: complete blood counts; pre-transfusion haemoglobin; serum ferritin as a marker of iron overload; liver function tests; urea and electrolytes; history of splenectomy; and echocardiographic evidence of pulmonary hypertension (defined as tricuspid regurgitation velocity ≥ 2.5 m/s). Each haematological and biochemical parameter was reported as a mean value over the last 3 months.

Statistical analysis

The data were analysed using IBM SPSS version 22 (SPSS, Chicago, IL, USA). Simple descriptive statistics were used to define the study variables; counts and percentages for categorical and nominal variables, and means and standard deviations (SDs) for continuous variables. To establish a relationship between patient characteristics and health outcomes, a $\chi 2$ test was used for categorical variables, and independent t test for continues variables. P **Linea r regression analysis**

In order to identify factors associated with physical and mental health and to control for confounders, we constructed 2 multivariate linear regression models. The dependent variable in the first and second models was physical component summary and mental component summary, respectively. We used backwards elimination to select the variables for each regression model. We estimated the regression coefficients (β) and their 95% confidence intervals. For all statistical tests, P

Results

Patient population

All patients approached consecutively agreed to participate in the study. We enrolled 105 β-thalassaemia major patients [55 male, 50 female, mean (SD) age 22.2 (11.7) years, range 5–35 years] (Table 1). Seventy-six (72.4%) patients reported at least 1 sibling with thalassaemia. All participants completed questionnaires successfully and there were no missing data at the time of the analysis.

Education and employment

Only 12 (11.4%) patients were college graduates, and most (81, 77.2%) either only finished school or were still students (Table 1). Eighty-seven (82.9%) patients were unemployed. Among the 18 (17.1%) who were employed, 11 were professionals and 7 were working in various manual and clerical jobs. For paediatric patients, 6 (27.6%) of their fathers were college graduates, 11 (49.5%) of them finished high school, and 5 (22.9%)were illiterate. Only 3 (12.4%) of their mothers were college graduates, while more than half (12; 52.4%) finished high school, and 3 (35.2%) were illiterate.

Disease complications

Ninety-four (89.5%) patients complained of chronic pain, 64 (60.9%) underwent splenectomy, and only 2 (1.9%) were taking chelating agents (Table 1). For 77 (73.3%) patients, mean pretransfusion haemoglobin levels were ≤ 8.6 g/dL and mean ferritin level for all patients was 3257.4 (2113.3) ng/mL. Seventy-six patients (72%), had recent records of echocardiographic screening, but only 3 (3.9%) showed evidence of pulmonary hypertension (tricuspid regurgitation velocity ≥ 2.5 m/s). Further details of all patients' characteristics, and differences between males and females are shown in
Table 1
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Physical HRQoL outcomes

Patients aged > 14 years reported significantly lower scores for physical functioning (P = 0.015), vitality (P Table 2) and overall physical component summary (P = 0.047), compared to the younger age group (Figure 1A). Patients, aged ≤ 14 years showed more evidence of role limitations due to physical health (P = 0.002), and significantly higher scores for bodily pain (P = 0.040) (Table 2). Patients experiencing chronic pain reported lower scores for physical functioning (P = 0.004), general health (P = 0.004), vitality (P = 0.012) and physical component summary (P 14 years were significantly associated with lower scores for physical component summary (P = 0.038 and 0.047, respectively). Among different educational levels, illiterate patients experienced more role limitations due to physical health (P = 0.022). A history of splenectomy was significantly associated with lower scores for vitality (P = 0.014).

Mental HRQoL outcomes

Only chronic pain had a significant effect on social functioning (P Table 3). The scores representing role limitations due to disturbed emotional wellbeing were significantly higher for patients aged ≤ 14 years (P = 0.003). Patients aged > 14 years and those with a history of splenectomy reported significantly lower scores for the mental component summary subscale (Figure 1B) (P = 0.008 and 0.029, respectively).

Regression analysis

According to multiple linear regression, professionals had significantly better physical health than patients with manual or clerical jobs (Table 4). Adults, female patients and employed patients showed a tendency to have worse physical health. Adults had significantly worse mental health than children had, and patients with higher pretransfusion haemoglobin level had significantly better mental health.

Discussion

The rising rates of thalassaemia globally (20) have encouraged more research to assess disease burden and HRQoL outcomes in this population (21). The present study focused on HRQoL outcomes in thalassaemia patients followed in a tertiary care centre in Jeddah, Saudi Arabia, using the SF-36 questionnaire.

Thalassaemia patients reported low scores on all HRQoL subscales, in agreement with previous reports in other patients with thalassaemia (21–23). We found that age was significantly associated with HRQoL. Patients aged ≤ 14 years experienced more physical and emotional limitations, complained more of bodily pain, had lower vitality scores, and exhibited worse mental health features than those aged > 14 years. However, older patients had significantly lower scores for both the overall physical and mental summary components, which may have been due to the cumulative effects of long-standing disease-related complications. Children demonstrated worse HRQoL features than adults did in a global context (9). Only a few studies have reported on the effect of age on HRQoL. One study among Jordanian children with thalassaemia reported lower physical and emotional scores for those aged 8–12 years when compared to those aged 13–18 years; however, no significant difference was detected between the age groups (22). One explanation to this could be the difference in composition of the study population. In our study we investigated HRQoL outcomes in children and adults with thalassaemia, whereas previous studies in Saudi Arabia or elsewhere in the Middle East either only included paediatric patients (21–25) or adults (26) with thalassaemia.

One clinical factor that was strongly associated with lower HRQoL outcomes, in almost all subscales in our study population, was the presence of chronic pain, which limited daily activity and affected social functioning. These findings agree with 2 other studies in the Middle East: one in Jordan where children complained of limiting pains and low energy when performing their daily activities (22), and another in the Syrian Arab Republic, which reported a significant association with lower physical health scores among children and adolescents with thalassaemia (27). Chronic pain in our study population was associated with lower social functioning, which echoes the findings of the Jordanian study, in which children felt physical inadequacy limited their interactions with their peers (22). While some of these studies were conducted using different HRQoL assessment instruments other than SF-36, all assessment instruments were previously validated in the corresponding population, which renders comparison of results across studies viable.

Although splenectomy is an effective measure to reduce transfusion requirements in thalassaemia, it does not prevent disfiguring skeletal changes, delayed growth and puberty, or chronic pain (28,29). Moreover, splenectomy increases the risk of infection and venous thromboembolism (28,29). In our study, patients who underwent splenectomy had significantly

worse mental health and mental health component summary scores, which were most likely caused by the adverse effects of the operation.

Upon controlling for other variables, the association between older age and worse mental HRQoL outcomes persisted. Higher levels of pretransfusion haemoglobin positively affected mental HRQoL, and participants holding professional jobs had better mental HRQoL scores compared to those working in clerical or manual jobs.

Several studies on HRQoL reported low psychological and mental health scores for thalassaemia patients, and identified different forms of mental health disorders such as depression, anxiety and stress (30–32). A study from Turkey found that thalassaemia patients and their caregivers suffered from depression and anxiety (32), which represented an additional burden for the families. Few studies have focused on the relationship between mental HRQoL outcomes and patients' socioeconomic and clinical characteristics, despite the importance of psychological and mental integrity to improve disease outcomes (30). The psychological burden is often over looked in Middle Eastern populations, and there is a need to devote more resources to understand this important aspect of the disease.

Comprehensive management models should ideally be developed to cater for individual patient needs, empower patients and support family members. Raising awareness and education in the community will facilitate social integration of thalassaemia patients and ultimately improve HRQoL outcomes.

The following limitations to our study should be acknowledged. The study focused only on patients and did not include HRQoL of their caregivers; a factor that significantly increased the disease burden. There was concern for potential bias, including patients' report of pain and other symptoms. Patients were given complete privacy and an adequate time to fill in the forms in order to avoid recall bias. There was also concern for selection bias as we only included thalassaemia patients from a single centre, and most of the participants attended clinics regularly and were thus considered to be more compliant and vigilant about their health management. However, since KAUH has the largest number of thalassaemia patients in Saudi Arabia and all participants were approached consecutively at the time of their outpatient visits, we believe that they were representative of the thalassaemia population.

In conclusion, thalassaemia is a chronic disease with myriad complications, presenting serious challenges to patients and families. There is a need for comprehensive care centres in Saudi

Arabia to improve HRQoL outcomes in thalassaemia through providing early preventive care, as well as social and psychological support to patient and families.

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Competing interests: None declared.

Résultats en matière de qualité de vie des patients thalassémiques en Arabie saoudite : étude transversale

Résumé

Contexte : Les recherches sur la qualité de vie liée à la santé (QVLS) des patients thalassémiques restent limitées en Arabie saoudite.

Objectifs : La présente étude visait à présenter les résultats du questionnaire sur la QVLS des patients thalassémiques ainsi qu'à étudier les associations avec les facteurs psychosociaux et cliniques.

Méthodes : Les patients thalassémiques qui consultaient à l'Hôpital universitaire Roi Abdulaziz ont été contactés lors de leur visite pour participer à l'étude. Les résultats du questionnaire sur la QVLS ont été évalués à l'aide d'une version arabe validée de la forme abrégée du questionnaire généraliste SF-36 du Medical Outcomes Study.

Résultats : L'étude a été menée auprès de 105 personnes atteintes de bêta-thalassémie majeure, dont l'âge moyen était de 22,9 ans (± 11,7) (âge compris entre 5 à 35 ans), et 52,4 % étaient des hommes. Les participants adultes âgés de 14 ans et plus ont obtenu un score moyen de 43,7 (±10,1) dans la sous-échelle physique du questionnaire sur la QVLS et un score

de 46,6 (±10,5) dans la sous-échelle mentale du questionnaire. Les participants de moins de 14 ans ont obtenu des scores correspondants de 48,4 (±10,7) et 52,9 (±8,0) respectivement. Les scores pour le fonctionnement physique étaient significativement moindres chez les patients plus âgés ainsi que pour ceux qui signalaient une douleur chronique. Des scores plus faibles pour la sous-échelle vitalité étaient associés à un âge plus avancé, à la douleur chronique et aux antécédents de splénectomie. Un âge plus avancé et des antécédents de splénectomie étaient associés à des scores plus faibles pour la santé mentale. En tenant compte d'autres variables, un âge plus jeune et une hémoglobine pré-transfusionnelle plus élevée

étaient associés à un meilleur score pour la sous-échelle mentale du questionnaire sur la QVLS. Les cadres ont obtenu de meilleurs scores pour la sous-échelle physique du questionnaire que les non-cadres.

Conclusion : En tenant compte d'autres variables, un taux d'hémoglobine pré-transfusionnelle plus élevé et un plus jeune âge étaient associés à de meilleurs scores pour la sous-échelle mentale du questionnaire sur la QVLS des patients thalassémiques. Les cadres faisaient état de meilleurs résultats physiques dans le questionnaire par rapport aux non cadres. Des modèles de soins préventifs et complets sont nécessaires en Arabie saoudite pour améliorer les scores du questionnaire sur la QVLS des patients thalassémiques.

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