INTERNAL MEDICINE

A Descriptive Study on Quality of Life among Adolescents with Beta-Thalassemia Major in the Maldives

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ABSTRACT

Background: **The Maldives has the highest prevalence of thalassemia in the world. However, there is little research done on the psychosocial aspects of this illness.**

Objectives: **This study aimed to examine health related quality of life (HRQOL) among adolescents with beta-thalassemia major attending the National Thalassemia and Other Hemoglobinopathies Centre (NTC), Maldives Blood Services, Maldives. Thus, appropriate recommendation could be proposed.**

Methods: **A total of 81 adolescents (mean age 15.7 years) with beta-thalassemia major were engaged. HRQOL was assessed using the Pediatric Quality of Life Inventory (PedsQL). Other relevant information was gathered through interview or medical record.**

Results: **The HRQOL was reduced. The mean for physical, emotional, social, school and psychosocial HRQOL was 80.50, 72.30, 88.18, 76.44, and 78.96, respectively. The total HRQOL was 79.50 and this was lower in females (75.29) compared to males (83.29). Ferritin levels of 1,001-2,499 µg/l and > 2,500 µg/l were noted in 34.2% and 53.9%, respectively. Good compliance was reported in 55% of participants.**

Conclusions: **Adolescents with beta-thalassemia major in the Maldives have reduced HRQOL. The high ferritin level could reduce the HRQOL and hence an attempt should be made towards lowering ferritin and improving compliance to chelation treatments. The gender difference in HRQOL signifies the need for more attention to the female patients and for areas of improvement to be explored.**

KEY WORDS

thalassemia, quality of life, ferritin, iron overload, psychosocial

INTRODUCTION

The Republic of Maldives is an island nation of 350,000 people located in the lndian Ocean. It consists of 1900 islands, of which 200 are inhabited. It has one of the highest incidences of thalassemia and has the world's highest concentration of carriers at 16-18% of the population[1)] thought to be due to prevalent consanguineous marriages in the past[2)]. A total of 670 cases have been registered in the National Thalassemia and Other Hemoglobinopathies Centre. It is estimated that more than 30% of the population has been screened to date and the high percentage of carriers lead to 1 in every 120 child being born is a thalassemia major child[3)]. Poor uptake of screening for the condition is one of the main reasons for this high number of new cases[4)].

The Maldivian government identified thalassemia as a national problem in the early 1990s, and took initiative involving awareness, education, the prevention and treatment programs.[4)] Though thalassemia has been identified as an issue of national concern, the infrastructure still lacks the psychological support this group of adolescents need. The lack of awareness of this important aspect is highlighted by a number of patients as well as family members who were noted to have psychological and coping issues, among those met at the daycare centre and the NTC institute. Of note was the unintentional omission of this aspect of the disease in any of the support booklets or meetings carried out.

Beta-thalassemia major patients require regular blood transfusions which lead to iron overload and its complications. In addition, chronic hypoxia due to anemia further increases the toxicity of iron deposition on various organs.[5)] Studies have found that high levels of ferritin are associated with diabetes mellitus, thyroid and parathyroid disorders as well as hypogonadism, with diabetes being the most common[6-9)]. Certain complications, especially those related to growth and other metabolic changes like delayed menses, has a negative impact on the thalassemia children. It has been highlighted that children often endured teasing due to their short-stature, and facies as well as "dark" skin colour leading to lower self-esteem, feeling stressed up and anxious[10)].

Most studies have highlighted that adherence to subcutaneous iron chelation therapy was poor and the reasons were side effects, finding it difficult and burdensome as well as not wanting to do it[10)]. Other studies have found older age, age at the start of treatment and emotional distress to be associated with low levels of adherence[11)]. Chronic illness and its treatment are associated with lower health related quality of life (HRQOL)[12)]. Similarly, studies had demonstrated HRQOL is significantly affected in children with beta-thalassemia major on regular transfusion across all age groups, gender and socio-economic classes and also in their caregivers[13-16)]. Thus, improving on patients and maternal education is crucial as these factors are recognized as independent predictor of better HRQOL[17)].

At present the Maldives has a good program in place for the medi-

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Table 1. Socio-demographic characteristics of subjects (N = 81)

Variables	n (%)
Gender	
Male	35 (43.2)
Female	46 (56.8)
Age (years)	
10-11	5 (6.2)
12-13	14 (17.3)
14-16	29 (35.8)
17-19	33 (40.7)
Schooling/occupational status	
Schooling	58 (73.4)
Working	14 (17.7)
Unemployed	7 (8.9)
Number of siblings	
None	9 (11.1)
1-2	44 (54.3)
3-5	23 (28.4)
> 5	5 (6.2)
Siblings with thalassemia	
No	59 (72.8)
Yes	22 (27.2)
Academic performance	
Good	19 (27.5)
Average	39 (56.5)
Low	11 (16.0)
Age of diagnosis	
0-12 month	51 (75.0)
1-2 years	12 (17.6)
> 2 years	5 (7.4)
Chelation	
None	6 (8.7)
Oral	21 (30.4)
Injectable	16 (23.1)
Both	26 (37.7)
Blood transfusion	
Once a week	12 (15.2)
Once every 2 weeks	44 (55.7)
Once every 4 weeks	21 (26.6)
Once in > 4 weeks	2 (2.5)
Hemoglobin level (gm%)	
6-7	13 (16.0)
8-9	60 (74.1)
> 9	8 (9.9)
Ferritin level	
Normal (≤ 1,000 µg/l)	9 (11.8)
High (1,001-2,499 µg/l)	26 (34.2)
Very high (≥ 2,500 µg/l)	41 (53.9)
Bone marrow transplant	
No	75 (92.6)
Yes	6 (7.4)

cal management of thalassemia. However the psychosocial aspects of the condition are not given much weightage. No similar study has been conducted in the country, and hence this study is hoped to provide a framework for further research, as well as push towards integration of psychological support into the program. With this study the authors hope to make a difference towards improving these children's lives, by submitting a recommendation based on the findings of the study to the local authorities. The study was done with the, intention of stressing the importance of the integration of psychosocial support into the current treatment program.

Table 2. Quality of life of in 81 adolescents (age 10-19) with beta-thalassemia major in the Maldives

	Mean (95% CI)
Physical functioning	80.50 (76.42, 84.57)
Emotional functioning	72.30 (67.23, 77.32)
Social functioning	88.18 (84.23,92.14)
School functioning	76.44 (71.66, 81.21)
Psychosocial functioning	78.96 (75.04, 82.88)
Total functioning	79.50 (75.84, 83.15)

METHODS

The research was approved by Human Research Ethic Committee, USM and Research Committee, Ministry of Health Maldives. This cross-sectional study was conducted from March to May 2013 at the National Thalassemia and Other Haemoglobinopathies Center (NTC), Maldives Blood Services, Maldives. This centre functions as the national referral centre for those suspected or diagnosed with thalassemia, and all thalassemia patients need to be registered here. As of August 2014, a cumulative total of 803 thalassemia patients were registered and a total of 563 were living[1].

The inclusion criteria were; 1) subjects who had been diagnosed with beta-thalassemia major, and was on regular follow-up under NTC, 2) undergoing regular blood transfusion at NTC, 3) adolescents age 10 to 19 years, and 4) able to comprehend English. The exclusion criteria were; 1) had been diagnosed with a psychiatric disorder, 2) family history of mental illness, as this could contribute to emotional distress due to genetic loading and stressful surrounding, 3) patients positive for human immune-deficiency virus.

All patients who fulfilled the criteria during the study period were included after obtaining an informed consent which was available in both English and Dhivehi (national Maldivian language). The questionnaires were given in an envelope, which they were required to fill up and put back in the envelope and seal. The questionnaires were filled up while they were getting their blood transfusion in a cubical with adequate privacy. For those who just came for consultation, they were given a private room to sit and fill in the questionnaires. Medical records were referred to gather clinical information such as hemoglobin and ferritin level.

The Pediatric Quality of Life Inventory (PedsQL) is 23-item questionnaire to measure health-related quality of life (HRQOL) in healthy children, adolescents and those with acute and chronic health conditions. It comprises 4 multidimensional scales; physical (8 items), emotional (5 items), social (5 items), and school functioning (5 items). Scores comprise of total (23 items), physical Health Summary Score (HSS) (8 items) and psychosocial HSS (15 items). Higher PedsQL scores reflect higher HRQOL. The scale is valid and reliable with an internal consistency 0.88 in child self-report and 0.90 for the parent proxy-report[18].

Descriptive statistical analyses were performed for socio-demographic and clinical characteristic using Statistical Packages for Social Sciences (SPSS) version 19 software.

RESULTS

Ninety patients were approached during the study period. A total of 81 subjects were analyzed after exclusion of 9 patients due to reasons such as refusal, inability to understand English, and not returning or completing the questionnaires.

The sample consists of 56.8% female, mean age 15.7 years with majority in older age group. Majority of the subjects were schooling (73.4%). Only a few subjects pursued their studies beyond 10th standard, or their London Ordinary levels. In term of academic performance, majority of them (56.5%) obtained an average result, which was classified either a B or C grades, while 27.5% obtained an A grade or good result and 15.9% obtained a poor result which was categorized as D and below. Twelve subjects did not indicate the last result they obtained.

The parental characteristics showed that the majority of parents were married (75.3%). The rest of the subjects had a single parent of

which 16% divorced, 6.2% separated and 2.5% widowed. This is different from the national data, as the Maldives has one of the highest rates of divorce at 49%[19].

The education level of mothers was mostly at secondary level (53.1%), followed by 39.5% primary and 7.4% tertiary level. In contrast, most fathers had an educational level of primary or below (46.8%) and held non-professional jobs (84.9%). The remaining 41.8% and 11.4% had secondary or tertiary level of education, respectively. National statistics show a male to female ratio of 0.9 in primary education in 1999-2011, a 1.2 ratio in secondary education from 1999-2000 and a ratio of 1.9 in 2003 which had fallen to 0.8 in tertiary education[19].

Almost two thirds (65.4%) of the mothers were housewives and among those who held jobs, 27.2% had non-professional jobs and only 7.4% had professional jobs. Amongst the fathers, 11% had a professional jobs, while 4,1% were unemployed. The Maldives has an unemployment rate of more than one in four economically active young being unemployed in general. Unemployment rates among female is 3 times higher than male.

About three quarters (75.6%) of them were diagnosed before 1 year of age, and only 7.4% being diagnosed after 2 years of age. Most of the subjects received blood transfusion once in every 2 weeks (55.7%), followed by 26.6% in every 4 weeks, 15.2% every week, and 2.6% once a month.

More than a third (37.7%) of subjects was on both oral and injectable chelator, whereas 30.4% and 23.2% were on oral or subcutaneous deferoxamine alone, respectively. It should be noted 7.4% were not on any chelator and this might be the 6 patients who had undergone bone marrow transplant.

The mean hemoglobin (Hb) level was 8.35 (SD 0.95). 42% of subjects had a hemoglobin level of 9 gm%, with another 32.1% having an Hb of 8 gm%. Only 1 participant had an Hb of 11, and another 2 had an Hb of 6 gm%.

The mean ferritin level was 3,339.6 µg/l ranging from 400 to 13,000 µg/l. Due to the vast difference in the range, the ferritin levels were categorized into normal (≤ 1,000 µg/l), high (1,001-2499 µg/l), and very high (≥ 2,500 µg/l) level. Majority of patients had a ferritin levels in the high category (53.9%), and only 11.8% patient was in the normal category.

Almost two thirds (63%) of patients claimed they did not have any medical complications. Amongst the one third (37%) with complications, 81.5% and 17.3% had liver-related or hormone-related complications. The less common complications were related to infection (7.4%) and spleen (6.2%).

Subjects had a mean number of 1.2 admissions to hospital for reasons other than blood transfusion since their diagnosis. 35.8% had no admission while 23.5% had 2 admissions. The highest number of admission was 10 in one (1.2%) patient.

Most patients (55.7%) claimed they were always compliant, while the rest claimed to be compliant sometimes, rarely or not at all at 29.1%, 7.6% and 7.6%, respectively.

The mean level of physical, emotional, social and school functioning was 80.50, 72.30, 88.18 and 76.44, respectively. The mean level for subtotal psychosocial HSS and total functioning was 78.96 and 79.50, respectively. The emotional functioning was lowest, while the social functioning was highest in this study sample.

DISCUSSION

The World Health Organization Quality of Life Assessment (WHOQOL) group defines Quality of Life (QOL) as an individual's perception of their position in life, in the context of culture and value systems in which they live and in relation to their goals, expectations, standards and concerns[20]. This definition by the work group shows that quality of life is deeply intertwined with culture and religion, as well as variety of other factors, which can contribute to psychological distress in patients living with beta-thalassemia major.

The HRQOL in this study was comparable to a similar study conducted in Thailand using the same scale, with 2-8 points difference in most domains[21]. Like the current study, the domain with the highest score was social functioning and lowest was that of emotional functioning. Similar impairment in emotional functioning has also been reported in a study conducted in the United States[22].

The current study showed that the HRQOL of this group was comparable to the levels present in healthy controls in Malaysia[23]. However, the findings were consistent with the Thai study[21]. Similar results could possibly mean that the Thai population was more similar to that of the current population in term of the care they receive and the life experiences. Like the Maldives, Thailand also considers thalassemia a public health problem and has been running several preventive programs since the early 1990s.

A possible explanation for the discordance between the Maldivian and Malaysian thalassemia group could be that the study was conducted one centre in the capital. The control population came from an urban area with hectic lifestyle, which involved travelling and long hours at school and tuitions. Life in the Maldives is different in this sense, especially as Malé, which is the capital is only 3 square km. This removes a lot of hassle involved in logistics and allows children to spend more time at home. In a study,[24] longer clinic admission was a significant determinant of reduced physical health quality of life. Another possible explanation for this could be the national thalassemia program which had been in place since 1994, which has increased the awareness among the thalassemia population and their family as well as the general public.

The mean total functioning scores were different between males (83.29) and females (75.29), by nearly 8 points. On further analysis, a difference of 10 points was found in the level of physical and psychosocial functioning between the genders as well. This difference was further analyzed using the t-test, which showed that a significant mean difference existed between males and females in both total and psychosocial functioning.

Previous studies have also consistently shown that there are lower levels of HRQOL amongst girls when compared to boys[25]. The possible explanation for this gender difference might be the presence of emotional distress in more number of female patients, which translate to poorer HRQOL when compared to males. Apart from that, restricted social roles, culture, low self-esteem, failure in heterosexual relationships, could play a major role in how girls perceived their HRQOL[26].

Academic performance was obtained in an attempt to understand how much living with thalassemia affected them. The study showed that 56.5% and 27.5% obtained an average (B or C report) or a good (A report) result, respectively. This achievement was comparable to that of average adolescents in the United States, as shown in a study where 59% obtained an average and 31% received mostly A's. In contrast, several studies have demonstrated that academic performance of thalassemia children was lower than in the normal population[23].

In the Maldives, 70% of the thalassemia children and adolescents were attending school, whereas in an Indian study more than half were not attending school[27]. Other reasons given for poor academic performances in previous studies were being away from school for various thalassemia-related issues[10,28]. The NTC stays open till 9 pm and Saturdays as well, which makes it flexible and missing school can be avoided. In addition, various awareness campaigns have been run in the Maldives, stressing on the fact that thalassemia children are no different from any other child. Great emphasis has been placed on "normalizing" the lives of these children by organization such as Society for Health Education (SHE).

While conducting the study, the first author also noticed that most children and adolescents came with their books to the daycare centre and would complete their homework while getting transfused. On conversing with the participants, most of them had ambitions and wanted to pursue their studies further, showing that they did not view themselves as being any different academically.

Nearly one fourth of the patients were taken care of by a single parent. Parents of thalassemia children experience high psychosocial burden, in term of disease chronicity, treatment modalities, morbidities and mortality due to complications[10,29]. A study in India, similarly reported greater psychosocial burden as well as poor overall QOL and perception of health in parents of thalassemia children[14].

Most of the participants (55.7%), received a transfusion every two weeks and half (53.5%) were on injectable chelators. The analysis showed that the mean level of ferritin for the study group was 3,339 µg/l. A ferritin level of < 1,000 µg/l is recommended by the Iron Health Alliance, US for those children receiving regular blood transfusion. A level above 2,500 µg/l puts the child at risk of cardiac complications. Further analysis of the data showed that only 11.8% had ferritin levels below the recommended level, whereas 53.9% had levels above 2,500 µg/l, putting them at high risk for further complications. Low HRQOL is associated with high ferritin level[30], use of injectable chelator[31], and complications like cardiac condition, short stature and other metabolic conditions[32,33].

The first author worked in NTC for a short duration of time, and on interviewing the children, some of them justified their reason for non-compliance by stating "there was no point', as they were going to die anyway. Non-compliance is associated with the use of injectable

chelators[34], psychosocial issues[35], and older age[11]. In this study, half of the subjects used intravenous deferoxamine and age above 15, which may account for high level of non-compliance. Older patients had poorer social functioning probably because of increased awareness about the impact of the disease on finding gainful employment, marriage, and parenthood[36].

CONCLUSIONS

Adolescents with beta-thalassemia major in the Maldives have reduced HRQOL. The high ferritin level could be associated with lower HRQOL and hence an attempt should be made towards lowering ferritin and improving compliance to chelation treatments. The gender difference in HRQOL signifies the need for more attention to the female patients and for areas of improvement to be explored.

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