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Research Article

The Use and Abuse of Supplements among Thalassemia Major Patients, Cross Sectional Study from Saudi Arabia

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Abstract

Background: Thalassemia is a congenital hemolytic disease. Beta- thalassemia major is a disease that requires regular blood transfusion and diverse supportive measures. we evaluated the effect and types of supplements use among B-Thalassemia major patients.

Methods: This study was conducted among thalassemia major patients in King Abdul Aziz University Hospital in Jeddah between February 2019 - March 2019 after receiving IRB approval and patient consent. Data were collected by using a questionnaire. Sample size 63 both genders. The data were analyzed using SPSS version 25.

Results: 283 individuals were accepted to participate in this study as they were diagnosed with beta thalassemia. Only 63 questionnaires were completed. The median age of the patients was 21 years (range 67 years). The majority of our sample were adults at 47%. The general health status in 58.7% was reported to be excellent. The prevalence of supplement use was (95.2%), folic acid being the most commonly used supplement (88.88%), vitamin D and calcium came in second (74.6%). Physicians held the accountability as the highest rank of information source for the patients (84.1%). The increase in general health was the main reason for supplement use (88.88%).

Conclusion: The majority of patients were found to have used folic acid, vitamin D and calcium, respectively to improve general health and well-being. Based on that we recommend to raise awareness and educate the physicians about the importance of the least used supplements in our study such as zinc, vitamin C and vitamin E.

Keywords: *Thalassemia; Folic Acid; Vitamin D; Calcium*

Introduction

Thalassemia is described as a collective disease where a group of hemolytic diseases are found due to faulty hemoglobin synthesis, proven to be hereditary. Thalassemia is more prevalent in Mediterranean, Asian, and African countries [1]. It ranks among the world's most common monogenic diseases [2]. It's classified based on the severity of clinical features of the patient into transfusion-dependent and non-transfusion-dependent thalassemia [3]. The most common type of thalassemia is Beta- thalassemia major or Cooley anemia in which the synthesis of B-globin chains on chromosome 11 is completely absent, while the synthesis of a-globin chains is normal. This defect is a result of point mutation affecting the production of the functional mRNA. furthermore, the a-globin chains alone are not efficient when it comes to forming stable tetramers, leading to their precipitation and eventually causing premature cell death leading to inadequate erythropoiesis levels, and the normal (Hb A) will be replaced by (Hb F) and (HbA2) [1,4,5]. Thalassemia patients initially present with growth retardation, poor immunity, microcytic anemia resulting in a spleen enlargement, liver enlargement, cardiac toxicity with iron overload, certain skeletal changes, and increased oxidative stress. Moreover, as a compensatory mechanism the body decreases bone marrow mineralization [5,6].

Thalassemia patients depending on the severity of the disease might need to regularly undergo blood transfusions. One of poor outcomes of repeated blood transfusion is iron overload, which causes significant morbidity and mortality in these patients [7,8]. To overcome this, iron chelators such as deferoxamine (DFO), deferasirox (DFX) and deferiprone (DFP) are prescribed for the patients to help excrete the excess iron from their bodies [8].

Patients suffering from thalassemia are prescribed different types of supplements. In a double-blind, randomized, placebo-controlled trial study published in 2013 challenged the effect of zinc supplementation on bone mass in patients with thalassemia with a sample size of 42 patients, the study concluded that zinc supplementations resulted in greater gains in total-body bone mass in the zinc group ($P = 0.02$) compared to the placebo group [9].

Recently in the last three years, patients with thalassemia have been given supplements such as folic acid, vitamin C, vitamin E, vitamin D and zinc.

In a previous before-after controlled clinical trial conducted in North of Iran on thalassemia patients who have been taking folic acid for more than 5 years and the results showed that cessation of folic acid supplements in beta thalassemia major patients can lead to a significant decrease in serum folic acid ($P < 0.0001$) and increased homocysteine (Hcy) levels ($P = 0.008$) in patients [5].

Another study conducted back in 2016, took into consideration the benefits of vitamin C supplementation in patients with beta thalassemia [6]. This study started by going over iron overload complications due to multiple blood transfusions and then further going into it being a major cause in vitamin c deficiency in beta thalassemia patients. The study dealt with the fact that vitamin c can reduce both ferric and ferrous irons, also facilitating the accessibility of iron [6].

Furthermore, there was another study using vitamin c as an adjuvant therapy with iron chelators in beta thalassemia major patients concluded that vitamin C potentiate the efficacy of iron chelators in reducing iron burden in the moderately iron overloaded vitamin c deficient patients with beta thalassemia without side effect. Although the former study showed the benefits of vitamin c in beta thalassemia patients, it also addressed potential areas of concern and the need for more studies investigates the use and effects of vitamin C [10]. It has been noted in recent studies that there are some supplements also used by these patients such as calcium and vitamin D in patients with thalassemia-associated osteoporosis and as a part of general protective measures for fracture prevention [11]. It has been suggested that these supplements to be taken in case of decreased dietary intake but the exact treatment regimen have not yet been defined [12].

Moreover, in Thailand there was a prospective, double blind, randomized placebo-controlled, crossover study published in 2018 investigating vitamin E effect on transfusion requirements in beta thalassemia pediatric patients. In the trial patients were randomized to two groups, either vitamin E supplement group or placebo for six months followed by a three months washout period (crossover), the study concluded that the levels of vitamin E normalized and there was no significant improvement in the oxidative stress of the vitamin E group compared to the placebo group [13]. Another recent study published in 2017 mentioned the use of alternative medicine to aid in improving the overall health status of patients with chronic hemolytic disease, including beta thalassemia patients. This study included mint juice, garlic, vitamin c, and chamomile. It concluded with satisfactory results especially with digestive discomfort and care during crisis [14].

Further data are still needed to determine the most frequently used supplements and factors associated with use of potentially inappropriate supplements related to thalassemia major patents in Saudi Arabia.

Aim of the Study

The aim of this current study is to evaluate the effect of supplements use and determine the inappropriate use among B-Thalassemia major patients at a tertiary care hospital in Jeddah, Saudi Arabia.

Methods

A descriptive cross-sectional study was conducted addressing the use and abuse of supplements among thalassemia major patients admitted to King Abdul Aziz University Hospital in Jeddah, Saudi Arabia. This study was approved by the hospital Scientific Research Review Committee and It was conducted in cooperation with the hematology department. All participants acquired a written consent to join this study.

All ages from both genders were included in this study. Exclusion criteria included pregnant patients, patients with liver/renal problems or hypoparathyroidism. The questionnaire covered demographic data, types of supplement taken, duration of using supplements, frequency, and the reasons for using supplements.

The study's primary objective was to assess the use and abuse of supplements in patients with thalassemia major. Secondary efficacy objectives included the side effects that came with taking or neglecting the supplements. Data entry was performed by using Microsoft Excel 2019 and processed by Statistical Package for the Social Sciences (SPSS) software, version 25.

Results

Two hundred and eighty-three individuals accepted to participate in this study as they were diagnosed with beta thalassemia by hemoglobin electrophoresis. Only 63 questionnaires were completed. All patients suffering sickle cell anemia, hypoparathyroidism, bone tumors and pregnant/lactating females were excluded.

The study population was a majority of male patients (60.3%) and the minority of patients were females (39.7%). They were classified into four groups on the basis of age: children consisted of patients between the ages of 2 and 14 years, adolescents between 15 and 21, group 3 between 22 and 65, and the last group was patients above the age of 65. The majority of respondent were adults at 47% (Table 1).

Characteristic	Total 63
Age	
Mean	23.127 ± 12.9484
Range	
2< Childiren≤14 y	67
14< Adolescents≤21y	Mean 9.75 ± 3.59642
21< Adult <65	Mean 18.5833 ± 1.44338
≥ 65	Mean 32.3333 ± 7.54907
2< Childiren≤14 y	20 (31.7%)
14< Adolescents≤21y	12 (19%)
21< Adult <65	30 (47.6%)
≥ 65	1 (1.6%)
Male	38 (60.3%)
Female	25 (39.7%)
General Health status	
Excellent	37 (58.7%)
Good	24 (38.1%)
Poor	2 (3.2%)

Systematic disease	
Yes	17 (27.0%)
No	46 (73%)
Herbs use	
Mint	8 (12.69%)
Chamomile	3 (4.76%)
Garlic	6 (9.52%)

Table 1: *Sample demographics and health status.*

The data distribution of the sample's age was not within the normal range and so we went on with the median, which was 21 years (range 67 years), the mean was 23.127 ± 12.9484 (Table 1).

Going through the questionnaire, we had inquired about each patient's general health status, where 58.7% of the sample responded with excellent when questioned about their general health, 38.1% responded with good, while the remaining 3.2% responded with poor. Besides that, 27% of the sample was already diagnosed with other systemic diseases (Table 1).

The prevalence of supplement use among b-thalassemia major patients was widespread (95.2%) with 48% of them being adults (Table 1). Folic acid was the most commonly used supplement representing 88.88% of the sample as shown in table 1. Vitamin D and calcium came in second as 47 patients used them (Table 2). Patient liability with their physicians as their information source ranked the highest (84.1%) as shown in table 2.

Characteristic	**Total**	**Children 20 (31.7%)**	**Adolescents 12 (19%)**	**Adult 30 (47.6%)**	**≥ 65 1 (1.6%)**
Supplements use					
Yes	60 (95.2%)	20 (28.84%)	11 (15.86%)	28 (40.38%)	1 (1.44%)
No	3 (4.8%)	0	1 (1.6%)	2 (3.2%)	0
Folic acid	56 (88.88%)	19 (30.155%)	11 (17.45%)	25 (39.678%)	1 (1.587%)
Vitamin D, Calcium	47 (74.6%)	17 (26.98%)	8 (12.697%)	22 (34.0%)	0
Zinc	3 (4.76%)	2 (3.17%)	0	1 (1.586%)	0

Table 2: *The most commonly used supplements.*

The increase in general health and wellbeing is the main reason for supplement use, accounting for nearly all of the sample's population n = 56. While other reasons included: improvement of osteoporosis and decreasing iron. With an unremarkable number of patients not using any supplements (Table 3).

Characteristic	N (%)
Reasons for using supplements	
Increase general health and well being	56 (93.33%)
Improvement of osteoporosis	13 (21.66%)
Decreasing iron	13 (21.66%)
Increasing hemoglobin	9 (15%)
Other reasons	4 (6.66%)
Improvement of gastrointestinal discomfort	2 (3.33%)
Reasons for using supplements	
Don't know about supplements	1 (33.33%)
Other reasons	2 (66.66%)
Information's sources	
Physicians	53 (84.1%)
Family/friends	4 (6.3%)
Other sources	2 (3.2%)

Table 3: *Reasons for using supplements and information resources.*

Discussion

To the authors' knowledge this is the first study in Saudi Arabia to assess supplement and herbs use among B-thalassemia major patients. The median age of our population was 21 years old. Males being the predominant gender (60.3%), compared to a retrospective cross-sectional study done in southern Iran where the mean age was 23 years, and females were the predominant gender (64.8%) [14].

The research samples in other countries North Iran, Tehran, Southern Iran (40, 133, 108, respectively) [5,14,15] compared to Saudi Arabia (63).

95.2% of the participants were using supplements, which represent a higher percentage than other studies done in southern Iran (90%) [14], Tehran (40.7%) [15]. The most prevalent supplement used in our patients was folic acid followed by vitamin D with calcium, and zinc. But in other studies, the most used supplements are vitamin C and vitamin E. Our data showed that the folic acid was the most used at 88.88% by 56 of the patients. While in Rasht, North Iran's clinical trial study, folic acid was used by 72.5% (29 patients) [5]. Similarly, for vitamin D and calcium supplement use, our data shows that 47 patients had used it for relieving the symptoms related to

osteoporosis, moreover other studies related to osteoporosis in thalassemia patient had supported the necessity of vitamin D and other supplement consumptions [16-18]. Where in this study, it was revealed that due to decrease bone density It gave rise to the rate of long-life bone fracture by 71% [16].

Another focus is vitamin D levels and its relation to heart disease. Where its deficiency has been found to be one of the major causes of death in thalassemia patients, through studies demonstrating its association with cardiac dysfunction by various mechanisms such as reducing heart muscle contractility and increasing parathyroid hormone production, which increases heart rate and cardiac hypertrophy, also increases cardiac iron absorption in major patients with thalassemia, leading to iron-induced cardiomyopathy [18].

The smallest percentage of supplements use has been attributed to zinc (1.89%) in our sample population, which has been well recognized for its role in correcting the deficient zinc status due to low dietary intake, chelation therapy, or defective absorption in the duodenum, which needs confirmation by further research [1,19].

Herbal medicine was used in 17.5% our patient, slightly more frequent than Tehran (12%) [15], and lower than southern Iran (88.88%) [14]. the majority of our participant use mint Followed by garlic, chamomile respectively (8,6,3) akin to southern Iran (54,32,31) [14] where they clarified the reason behind mint use is to relive gastrointestinal discomfort, because it is a digestive agent with a worm quality and has tranquilizer effect.

According to a study from southern Iran conducted by Baghersalimi., *et al.* [5] the most common reason for supplement use by thalassemia patients was to increase the general health and well-being, similarly to our patients. Second most common reason is to improve of osteoporosis [16]. Other reasons are decreasing iron, improvement gastrointestinal discomfort, and increasing hemoglobin.

As observed in the information sources for use of supplements in thalassemia patients, the sources varied among different studies. In Baghersalimi., *et al.* [5] study the information sources was mostly physicians and 85% of the patients were influenced by family and friends to use the supplements, which was consistent with our finding.

Conclusion

This study was conducted to assess the effect and determine the use and abuse supplements among B-Thalassemia major patients. The majority of patients were found to have used folic acid, vitamin D and calcium, respectively under their physician's instructions to improve general health and well-being. while there was no observation regrading inappropriate supplement use. Based on that we recommend to raise the awareness and educate the physicians about the important of the least used supplements in our study such as zinc, vitamin C and vitamin E.

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