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ORIGINAL ARTICLE

Marital Status and Fertility in Adult Iranian Patients with β-Thalassemia Major

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Abstract Expecting a family is an important component and a great goal for better quality of life for most of adults with β-thalassemia major. The aim of the present study was to examine the marital status of adults with β-thalassemia major. This cross-sectional study examined the marital status of patients with transfusion-dependent β-thalassemia aged over 15 years. Patients' demographic characteristics including age, gender, marital status, duration of marriage, divorce, having or not having children and spouse's health status were recorded. Information about the disease including cardiac and endocrine complications, ferritin level, splenectomy and viral hepatitis were also recorded. Of 228 patients with transfusion-dependent β-thalassemia major aged over 15 years who were treated at this medical center, 32 (14 %) were married. The mean age of married patients was 25.18 ± 4.74 years. Among the married patients, 8 (25 %) were females and 24 (75 %) patients were males. The mean age of marriage was 22.76 ± 4.16 years. The minimum and maximum marriage age was 15 and 33 years, respectively. The median duration of marriage was one year with the range from 3 months to 11 years. Only 8 (25 %) patients (one female and seven males) had children. Therapeutic advances have led to significantly increased survival and improved quality of life and fertility of patients with β-thalassemia major. According to the results, 14 % of patients over 15 years were married which was slightly higher as compared with other similar studies.

Keywords Thalassemia major · Iron chelation · Marital status

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Introduction

β-thalassemia major is a hereditary disorder of hemoglobin caused by impaired synthesis of β-globin chain leading to chronic hemolytic anemia [1]. The patients with β-thalassemia major suffer from partial or complete absence of β-globin gene production [2]. This is a common disease in Mediterranean countries, India, South East Asia and the Middle East including Iran [3, 4]. Regular blood transfusion is essential for long-term survival of these patients. But after a while, patients will suffer from iron overload in various tissues of the body [5, 6]. Since there is no mechanism for active excretion of excess iron in the body, the iron overload can lead to iron deposition in major organs including the liver, spleen, heart myocardium and endocrine system. This results in complications such as growth retardation, liver disease, diabetes mellitus, cardiomyopathy, delayed puberty and etc [6, 7].

The therapeutic advances in the past decades, regular transfusion and iron chelating drugs have dramatically increased the life expectancy and survival of patients with thalassemia major [8, 9]. Therefore, expecting to raise a family and parenthood is an important factor to improve the quality of life in these patients. Although spontaneous fertility can occur in well-transfused patients with iron chelation, most of these patients remain infertile due to hypogonadotropic hypogonadism caused by iron overload. Such patients are in need of assisted reproductive techniques [10]. Recently, a study has been published on the

marital status and child bearing of patients with transfusion-dependent thalassemia major [11]. Other studies on the quality of life only reported the number of single or married patients without any information on clinical, demographic characteristics, marital status and children. The aim of the present study was to examine the marital status of patients with β-thalassemia major.

Methods

This cross-sectional study was carried out on transfusion-dependent β-thalassemia major patients aged over 15 years in Ali-Asghar Hospital. The thalassemia was diagnosed by complete blood count (CBC) and hemoglobin electrophoresis and in some cases by β-globin gene mutation analysis. Patients' demographic characteristics including age, gender, marital status, duration of marriage, divorce, having or not having a child, the spouse's health status (healthy, carrier or β-thalassemia major) were recorded. Information about the disease including heart and endocrine complications, ferritin level, splenectomy, cholecystectomy and viral hepatitis were also recorded. In our hospital, all patients with transfusion-dependent β-thalassemia major are monitored routinely for iron overload complications as follows: Yearly echocardiogram, electrocardiogram (ECG), free T4, TSH, calcium, phosphorus, alkaline phosphatase, parathyroid hormone (PTH), LH, FSH, testosterone(for boys), estradiol (for girls), bone densitometry beginning at 10 years of age. A written consent was obtained from all patients participating in the study and the patient information remained confidential. Statistical analysis was performed using SPSS software version 16 for Windows (SPSS Inc., Chicago). Quantitative variables were shown as mean ± SD. The Chi square test was used to compare qualitative variables. P value less than 0.05 was considered statistically significant.

Results

Table 1 shows the demographic characteristics of the patients. Of 820 patients with transfusion-dependent β-thalassemia major, 228 (28 %) patients aged over 15 years. The mean age of patients over 15 years was 22.36 ± 5.31 years (range 15–48 years). Among them, 110 (48.2 %) were females and 118 (52.8 %) were males. Of 228 transfusion-dependent β-thalassemia major patients aged over 15 years treated at this medical center, 32 (14 %) patients were married. The minimum and maximum age of marriage was 15 and 33 years, respectively. The mean age of married and single patients are shown in Table 1. The mean age of marriage was 22.76 ± 4.16. Among the married patients with thalassemia major, 8 (25 %) were females and 24 (75 %) were males (P = 0.005).

Table 1 Demographic characteristics of married and unmarried patients with beta-thalassemia major

Variable	Married	Unmarried	P value
Age (years) (Mean ± SD)	25.18 ± 4.74	21.90 ± 5.27	0.001*
Male	24 (75 %)	101 (51.5)	0.01**
Female	8 (25 %)	95 (48.4)	

* Independent *t* test ** χ^2 test

The median duration of marriage was one year. The majority of married participants in the study were fresh in marriage when the range of marriage had 10.75 years length. The minimum and maximum years of marriage duration were 0.25 and 11 years, respectively.

Only a divorce case occurred in a female patient. In 19 (59.4 %) cases, the spouse was healthy with no β-thalassemia major or minor. In 8 (25 %), 4 (12.5 %), and 1 (3.1 %) cases, the spouse was suffering from β-thalassemia major, β-thalassemia minor and α-thalassemia minor, respectively. Only 8 (25 %) patients (one female and seven males) had children. The average number of children was 1.62 ± 0.74. In total, the marriage produced 13 children, two with β-thalassemia major and 11 with β-thalassemia minor. The children's birth weight was less than 2,500 g and more than 2,500 g in four and nine cases, respectively.

In one case, a female patient had a spontaneous abortion and a selective abortion of a fetus with β-thalassemia major. The patient had two successful pregnancies (a child with β-thalassemia minor and a child with β-thalassemia major) and a cesarean delivery. In two male cases, the wife was pregnant. There were no cases of intrauterine fetal death (IUFD) and preterm labor in females. Table 2 shows co-morbidity, splenectomy and cholecystectomy in married both and unmarried patients with β-thalassemia major. The average ferritin level in married and unmarried patients was 4,419 ± 2,727 ng/ml and 4,440 ± 2,912 ng/ml, respectively (P = 0.97). The range of ferritin level in married and unmarried patients was 360–13,830 ng/ml and 240–13,200 ng/ml, respectively. All patients were using iron chelating drugs. Accordingly, 12 (37.5 %) married patients used deferoxamine, 8 (25 %) deferasirox, 10 (31.2 %) deferoxamine and deferiprone combination and 2 (6.2 %) patients only used deferiprone. Among the unmarried patients with β-thalassemia major, 12 (37.5 %) used deferoxamine, 8 (25 %) deferasirox, 10 (31.2 %) deferoxamine and deferiprone combination.

Discussion

Expecting a family in patients with β-thalassemia major is an important component to improve the quality of life [10].

Table 2 Comorbidity and previous surgical procedures

Comorbidity	Married no (%)	Unmarried no (%)	P value
Splenectomy	9 (28.1)	23 (11.7)	0.01
Cholecystectomy	1 (3.1)	7 (3.5)	0.89
Cardiomyopathy	19 (59.4)	92 (46.9)	0.19
Diabetes mellitus	3 (9.4)	14 (7)	0.56
Hypothyroidism	1 (3.1)	25 (12.7)	0.11
Hypoparathyroidism	3 (9.4)	39 (19.8)	0.15
Hypogonadotropic hypogonadism	9 (28)	35 (17.8)	0.17
Hepatitis B	1 (3.1)	4 (2)	0.69
Hepatitis C	6 (18.7)	25 (12.7)	0.19

Although spontaneous puberty and fertilization occur in transfusion-dependent patients who use iron chelating drugs, most patients are suffering from hypogonadotropic hypogonadism due to iron overload and thus remain infertile. Such patients are in need of assisted reproductive techniques [12]. Although advances in iron chelation treatments reduce the complications, approximately 50 % of patients with thalassemia major are suffering from hypogonadotropic hypogonadism [6, 13].

Treatment with hormones such as human chorionic gonadotropin in men stimulates spermatogenesis and fertility. Fertilization usually occurs in women with normal menstrual cycles. Otherwise, hormonal treatments can be utilized [14]. The least age of marriage in Iran is 15 and 18 years for males and females, respectively. However, in special cases and with presenting judiciary certification, it decreases to 13 and 15 years, respectively.

In our study, 28 % of patients were suffering from hypogonadotropic hypogonadism which was lower than in other studies. In a study on the quality of life of patients with thalassemia major in Shiraz, of 101 patients aged 12–38 years, only 6 (5.9 %) patients were married. There were no differences in mental and physical health between single and married patients. The marital status had no significant correlation with the SF-36 score [15]. In our study, 14 % of patients aged over 15 years were married which was higher than in the previous study. In a similar study, of 678 thalassemia major patients aged 15–45 years, 85 (12.4 %) patients were married. But this study did not compare the quality of life of married and single patients [16]. The percentage and ratio of married patients in our study was similar to the previous study. In a recent study by Zafari M., 25 % of female (≥15 years) and 32 % of male (≥18 years) patients with transfusion dependent thalassemia major were married which were higher than that of our study [11]. In general, hundreds of pregnancy has been reported in women with thalassemia major. But factors such as cardiomyopathy, increased plasma volume, increased cardiac output and decreased glucose tolerance impact on maternal health [17]. In a study, only two of five pregnancies were uncomplicated and complications such as cardiac arrhythmias, gestational diabetes, hypertension and stillbirth occurred in three other cases [18].

In a study in Italy, 91 % of pregnancies in patients with thalassemia major and intermedia led to successful delivery. The proportion of infants born with intrauterine growth retardation (IUGR) did not differ from the general population [19]. In our study, although only eight females were married, only one of them had a history of four pregnancies including two cases of successful pregnancy, a spontaneous abortion and a selective abortion. Two other females were pregnant and five females had not yet decided the pregnancy. The mode of delivery in patients with β-thalassemia major is a controversy, but a high rate of cesarean section has been reported [20]. There were four couples in our study where both partners were β-thalassemia major. Four (50 %) out of eight female patients who were married, were married to men with β-thalassemia major. While only 4 (16.7 %) out of 24 men with β-thalassemia major had a β-thalassemia major spouse. Therefore suffering from β-thalassemia major may limit partner choices, and more so for women than men. Prenatal diagnosis (PND) is available in our hospital since 2001 and we recommended PND for all minor and major thalassemia couples. If the patients with β-thalassemia major try to reduce the incidence of iron overload complications, most of them will be able to marry and form a family. This will have a significant impact on improving quality the patients' lives with β-thalassemia major.

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