Demographic and Laboratory Characteristics of β-Thalassemia Major Patients in Zahedan, Southeast of Iran

Ebrahim Miri-Moghaddam Ph.D 1, Maryam Yaghoobi MSc2*, Majid Naderi MD3, Atefeh Nootizaei BSc4

1. Genetics of Non-Communicable Disease Research Centre, Department of Genetics, Zahedan University of Medical Sciences, Zahedan, Iran
2. Pregnancy Health Research Center, Zahedan University of Medical Sciences, Zahedan, Iran
3. Genetics of Non-Communicable Disease Research Centre, Department of Pediatric Hematology & Oncology, Faculty of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
4. Students Scientific Research Center, Zahedan University of Medical Sciences, Zahedan, Iran.

*Corresponding author: Maryam Yaghoobi MSc, Pregnancy Health Research Center, Zahedan University of Medical Sciences, Zahedan, Iran. Tel. +989153413296. E-mail: myaghoobi@yahoo.com

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Abstract
Background: B-thalassemia is known as the most common inherited form of anemia worldwide and Iran. Considering high birth rate in the province, it seem necessary to study demographic factors and to assess common laboratory tests in order to find out whether patients receive adequate care or not.

Materials and Methods: A cross-sectional descriptive analytical study was conducted on 603 patients aged 1-46 years who had been referred to thalassemia clinic at Ali Asghar Hospital in Zahedan in 2014. Overall mean transfusion interval was 23.4 days with 22.8 days for males and 24.1 days for females. Demographic and laboratory data of the patients were gathered through interviews and the patients’ records.

Results: Out of 603 patients, 323 (54.3%) were male and 280 (45.7%) were female. In total, 77.2% were Balouch, 18.3% Sistani, 3.1% Afghani, and the rest belonged to other ethnic groups. Consanguinity was seen in 57.8% (close relatives) and 19.7% (distant relatives) of cases. Mean number of their offspring was 4.7 and mean number of β-thalassemia children was 1.5 for each family. The mean hemoglobin level before the last three blood transfusions was 9.5 g/dl, and mean ferritin level according to the last three examinations was 3801.9ng/ml. The highest frequency of blood group belonged to “O” (38.4%). In the population studied, the mean volume of transfused blood was 468.5 mL per injection. Regarding used blood products, 93% of the patients received packed cells and 7% washed cells.

Conclusions: In spite of different training programs implementation, the quality of the evaluated indices in this province was lower compared to other regions that can be attributed to high rate of thalassemia incidence. Therefore, regular consultation programs in media seem necessary considering the local culture and language especially through influential local people.

Keywords: Demographic, Iran, Laboratory, Population, Thalassemia

Introduction
B-thalassemia is an autosomal recessive disorder in which β-globin chain synthesis is either decreased or absent. This condition leads to varieties of clinical symptoms. The annual incidence of diagnosed β-thalassemia with clinical symptom is 1 per 100,000 throughout the world if no preventive program implemented (1). Frequency of β-thalassemia gene carriers vary in different parts of Iran (2). This disease is more prevalent in the north bordering of the Caspian sea, the south bordering the Persian Gulf and the Oman sea(3). Prior to recent decades, β-thalassemia was accounted as a fatal disease in the first decade of life; however, due to recent medical advances and iron chelating protocol, the life span of thalassemic patients has been expanded. Common treatments used for β-thalassemia are bone marrow transplantation and continuous
transfusion (4). Transfusion causes iron overload and multiple complications such as lowering the quality of life (1). Measuring serum ferritin is a reliable test to assess the accumulation of iron in patients’ body, predicting complications and effectiveness of chelating therapy (8). Today, improving the quality of life of such patients is the most important issue (5). Unpleasant, prolonged and repeated treatment regimens along with increased life expectancy among thalassemic patients have confronted physicians with increasing social and psychological problems that have brought up the need to pay more attention to these patients.

Sistan and Balouchistan province is located in the southeast of Iran neighboring Pakistan and Afghanistan with 2,700,000 population. This province has about 2500 β-thalassemia patients which allocated the highest rate to itself in Iran (6). Lack of premarital screening and any prevention program in the early 1990 can be accounted as the primary reason for such a high number of patients in the province. Though national premarital screening program was started in 1997 and prenatal diagnosis center was established in the province as early as 2002 in Ali Asghar Hospital in Zahedan, Sistan and Balouchistan province in 2014. The research project was approved by the Ethical Committee of Zahedan University of Medical Sciences.

**Materials and Methods**

**General material**

This cross-sectional descriptive and analytical study assessed demographic information and laboratory tests of 603 patients aged 1-46 years who had been referred to thalassemia clinic at Ali Asghar Hospital in Zahedan, Sistan and Balouchistan province in 2014. The research project was approved by the Ethical Committee of Zahedan University of Medical Sciences.

**Data Sample Collection**

Medical records of deceased cases, those whose medical files had been transferred to other centers and also those patients who had received less than eight transfusions per year were excluded from the study. All patients had completed a written consent prior to the study.

**Statistical Methods**

Data were collected using interviews and adoption of medical records. The interviews underwent by three trained persons in a 3 month period of time. The patients generally visited the center every 2-4 weeks. Results of interviews had been recording in a sheet with name of the patient on the top. Thereafter, a separate sheet identified with patient’s names was used for writing down the laboratory records of the patients. Demographical and laboratory data both were collected by the same three trained colleagues. Finally, the two set of the obtained information were incorporated together. The results were entered and analyzed by SPSS (version19) and numerical data presented as mean ± SD. Cross tabulation using Chi Square was done for blood groups, Rh system, and type of blood products transfused. The P
<0.05 was considered as statistically significant.

Results
From a total of 603 patients, 323 (54.3%) were male and 280 (45.7%) were female. Regarding ethnic origin, 77.2% were Balouch, 18.3% were Sistani, 3.1% were Afghan, and 1.5% belonged to other ethnicity. Habitation of 82.7% of families was urban and the rest (17.3%) lived in rural areas. Regarding living status, in 91.2% cases, the patients’ fathers and in 98.4% cases their mothers were still alive. Demographic information of the patients is shown in Table I. Results revealed that the average number of children in the families was 4.7± 2.4 and mean number of thalassemia children was 1.4± 0.6 per family. The study revealed that 57.8% of parents were close relatives, 19.7% were distant relatives, and 22.5% were unrelated. Mean transfusions intervals, in the total, were 23.4 days, but it was 22.8 days for males and 24.1 days for females. The average volume of blood transfusion per injection per person was 468.5 ml. The mean hemoglobin level in patients before the last of the three blood transfusions was 9.5 g/dl, and mean ferritin level according to the last three examinations was 3801.9 ng/ml (Table I). Ninety-three percent of the patients received packed cells while the rest have been transfused with washed red blood cells. The frequency distribution of blood product usage based on sex is presented in Table II. The highest frequency of blood group belonged to “O” (38.4%) (Details are showed in Table II).

Table I: Demographic and laboratory data of Zahedan thalassemia patients in south-east of Iran

<table>
<thead>
<tr>
<th></th>
<th>Sex</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>M</td>
<td>1.5</td>
<td>33</td>
<td>13.82</td>
<td>7.61</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>2</td>
<td>46</td>
<td>12.70</td>
<td>7.85</td>
</tr>
<tr>
<td>Father age (year)</td>
<td>M</td>
<td>21</td>
<td>80</td>
<td>44.28</td>
<td>11.02</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>24</td>
<td>85</td>
<td>42.52</td>
<td>11.60</td>
</tr>
<tr>
<td>Mother age (year)</td>
<td>M</td>
<td>18</td>
<td>68</td>
<td>38.22</td>
<td>9.74</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>17</td>
<td>80</td>
<td>36.69</td>
<td>10.15</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>M</td>
<td>8</td>
<td>76</td>
<td>33.12</td>
<td>15.18</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>8</td>
<td>68</td>
<td>28.66</td>
<td>13.23</td>
</tr>
<tr>
<td>Light (cm)</td>
<td>M</td>
<td>50</td>
<td>179</td>
<td>134</td>
<td>25.3</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>60</td>
<td>170</td>
<td>126</td>
<td>23.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>M</td>
<td>10.19</td>
<td>32</td>
<td>17.32</td>
<td>3.56</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>10.29</td>
<td>39.86</td>
<td>17.06</td>
<td>3.87</td>
</tr>
<tr>
<td>Volume of transfused Blood (ml)</td>
<td>M</td>
<td>120</td>
<td>900</td>
<td>481.62</td>
<td>159.86</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>120</td>
<td>680</td>
<td>452.8</td>
<td>165.24</td>
</tr>
<tr>
<td>Hb mean level at the last three transfusion (g/dl)</td>
<td>M</td>
<td>5.6</td>
<td>12</td>
<td>9.4</td>
<td>0.72</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>7.6</td>
<td>12.9</td>
<td>9.5</td>
<td>0.66</td>
</tr>
<tr>
<td>Ferritin mean level at the last three measurements (ng/ml)</td>
<td>M</td>
<td>165.6</td>
<td>10400</td>
<td>3685</td>
<td>2319</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>170.6</td>
<td>14000</td>
<td>3939</td>
<td>2116</td>
</tr>
</tbody>
</table>
Discussion

Treatment of thalassemia patients is complex and expensive. Today, due to a great deal of advances in protocol for treatment and increase in life span of thalassemic patients, improving their quality of life has become very important. The results showed that the mean age of the patient was 13.3 years, with a four years increase compared to a previous study which had been performed in Zahedan in 2002 (15). In another study which had been carried out in Mazendaran, north of Iran, it was revealed that mean age of patients were 23 years (10). This mean age has been reported to be 26.3 in Tehran (9) and 14.7 in Kerman (east of Iran) (14). In overseas studies, the mean age have been reported to be 20 years in France (13) and 15.5 in Hong-Kong (11). In comparison, the mean age of these patients was lower than other centers. This may be due to the high frequency of new cases in this province (7). Though national screening for thalassemia has been in practice since 1997, its effectiveness in Sistan and Balouchistan province has been under question since families' compliances have been low for various reasons (7, 16). According to the findings of previous study, the most common cause of new thalassemia cases is parental unawareness of being thalassemia minors (7). Therefore, premarital screening tests and its follow up are of utmost significance. Moreover, the result showed that the mean age of fathers and mothers were 43.5±11.3 and 37.5±10 years respectively and 27% of fathers and 49% of mothers were illiterate. Similarly, Ghazanfari has reported that in the east of Iran, these mean ages were 42 and 35 years. Furthermore, 35% of parents were illiterate and 26% had a diploma or a higher education level in mentioned study (17). According to a study carried out in Pakistan, neighboring Sistan and Balouchistan province, 73% of parents had elementary education (18). According to these findings, there appears to be a high consistency between low educational level of the parents and high prevalence of thalassemia. In this regard, special attention and proper educational programs for increasing education level in these populations is needed. Increasing levels of education, allows implementation of various training and enhancing quality of life for the families and their children. The study demonstrated that 57.8% of thalassemia patients’ parents were close relatives, 19.7% of them were distant

Table II: Frequency of transfused blood products, Blood groups and Rh in Zahedan thalassemia patients in south-east of Iran

<table>
<thead>
<tr>
<th>Transfused Blood products</th>
<th>Blood Groups</th>
<th>Blood RH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P. c*</td>
<td>W. C**</td>
</tr>
<tr>
<td>Male</td>
<td>313 (94)</td>
<td>20 (6)</td>
</tr>
<tr>
<td>Female</td>
<td>259 (92.5)</td>
<td>21 (7.5)</td>
</tr>
<tr>
<td>Total</td>
<td>572 (93.3)</td>
<td>41 (6.7)</td>
</tr>
</tbody>
</table>

*; Packed cell, **; Washed cell
relatives, and 22.5 % were unrelated. Among these patients, 77.2% of them were from Balouch ethnicity. A study in the south-west of Iran revealed that 65% of them were first cousin, 8.3% were second cousin, and 26.6% were unrelated(19). A study in Pakistan found that the most racial marriages occurred among Panjabies (60.7%), and followed by Sarakies (25.5%) (18). A previous study in Sistan and Balouchistan maintained that over 77% of parents having children with β-thalassemia had consanguinity(7).

In addition, the results showed that the average number of children per family was 4.5 and average number of thalassemia children in each family was 1.4. In these families, in spite of posing children with thalassemia, frequency of births is high, in a way that there were even up to 4 thalassemia cases in some of the studied families. This could be due to unawareness in knowing the natural disease as well as stiff religious beliefs of “the determined fates coming from God should be embraced willingly” of the families. However, by applying educational programs appropriate to specific people’s culture and advising men and women to undergo premarital tests, one expects reduction of new cases as it has been witnessed in most other provinces in Iran. It has been claimed that more than 90% of new cases are born in populations of three adjacent provinces (i.e. Sistan and Balouchistan, Hormozgan, and Kerman) (16). Various reasons can be attributed to these higher incidences. Some have been summarized here and others can be due to lower income to seek prenatal diagnosis, religious beliefs hardship in going far distances for the prenatal tests and etc. Therefore, it is necessary to take proper actions to tackle each of these problems.

Results revealed that the patients’ mean height, mean weight, and mean BMI were 1.3 M, 31.08 Kg and 17.2 kg/m 2 ; respectively. Azarkayvan, in Adult Thalassemia Care Center in Tehran, found that mean height of patients was 1.59 M, and mean weight was 51.6 kg (9). In a study in Esfahan, Tabesh reported that mean weight, mean height, and mean BMI of the patients were 44.5 kg,1.52m , and 19.2kg/m 2, respectively (12). It is claimed that iron chelators, which thalassemia patients have to receive after several rounds of blood transfusion, also remove micronutrient such as zinc. This can have a significant relationship with the decrease of weight/height and may stunt and create other developmental problems in these patients (12). Since inadequate and imbalanced nutrition have significant on the health and life expectancy of major thalassemia; therefore, nutritional education of these patients is necessity.

The mean ferritin level in the last three assessments was 3801ng/dl. However, according to two other studies conducted in the east of Iran, the ferritin level was 3270 ng/ml (14) and 3248.64 ng/ml (20). This was 1755ng/ml in Tehran, the capital (9), 2000 ng/ml in Mazendaran in the north with better medical care (10). In other studies, the mean serum ferritin level in five-year in the south-west of Iran(21), in France(13), and in Hong-Kong (11) were:3279ng/ml,1240ng/ml,6638 pmol/l; respectively. High ferritin level causes several complications in patients. A study showed that ferritin level greater than 2500ng/ml has a direct relation with higher mortality (5). The effect of high ferritin level can be reduced through proper use of chelators and also patients’ awareness of its complications. In the present study, it was found that some patients had regular blood transfusions to some extent; however, some of them were unwilling to receive desferrioxamine injection. There could be several reasons for lack of compliances: being tired of continuing therapy; having few recreational activities in the family, posing affected child/children in the family; rather high expenses for traversing and providing medicine communication problems due to lack of proper education in the family, financial strains and etc. Therefore,
continuous supporting of patients and their families by the health authorities is needed. Moreover, proper actions are expected to be taken by the local and national authorities to overcome these problems aiming at increasing the living standards for the current patients and reducing the birth of new cases.

Conclusion
The findings of the present study revealed that in spite of implementation of different training programs, the quality of the evaluated indices in this province was lower compared to other regions that can be attributed to high rate of thalassemia incidence in this province. Therefore, it seems necessary to present regular consultation programs in media considering the local culture and language especially through influential local people, and to increase awareness among groups who seem to have more thalassemia cases due to marriage of close relatives. The Society of Support of Thallasemic Patients can also benefit from the cooperation of psychologists in health care centers and can support the programs financially.

Conflict of interest statement
The authors declare that they have no conflicts of interest.

Acknowledgement
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