Evaluation of the Prevalence of Thalassemia and Sickle Hemoglobin in Marriage Applicants Referring to the Genetic Disease Counseling Center in Kazeroun, Iran during 2014-2018

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ABSTRACT

Background: The present study aimed to determine the prevalence of thalassemia minor and sickle hemoglobin in marriage applicants referring to the Genetic Diseases Counseling Center of Kazeroun Health Center over 2014-2018.

Methods: This cross-sectional study was conducted in Kazeroun, Iran. The statistical population included all couples referring to the marriage counseling centers in Kazeroun for pre-marriage tests during 2014-2018. In this study, the registration data associated with the health records of the couples seeking marriage counseling were used.

Results: Over the years under scrutiny, 31114 applicants (15557 couples) referred to the health counseling center for marriage tests during the supervision of the health network. Among the marriage applicants, the highest prevalence of beta-thalassemia, alpha-thalassemia, anemia, sickle cell hemoglobin, and hemoglobinopathy was reported in 2014 (0.07), 2018 (0.15), 2014 (0.66), 2018 (0.9), and 2014 (0.05), respectively.

Conclusion: The results of the present study showed that the prevalence of thalassemia and sickle cell anemia in Kazeroun over the study years was similar to that in other parts of Iran over the same years.

1. Introduction

Thalassemia is a type of chronic hemolytic anemia caused by a defect in the production of one or more of the hemoglobin chains [1]. Thalassemia is inherited from parents to children [2,3]. The distortion of red blood cells into sickle shape is a disorder caused by a mutation in the beta gene; accordingly, amino acid valine substituted for glutamic amino acid [4,5] as blood fails to reach the tissues in position 6 of the beta chain. Sickle cell disease is either an HbSS homozygote or associated with HbS with other hemoglobin variants such as SC and SD or beta-thalassemia [6]. Thalassemia is diagnosed through iron deficiency by measuring hemoglobin A2, serum iron levels, TIBC, and ferritin, since the hemoglobin A2 levels in these patients are higher than the normal subjects [7]. Thalassemia is more common in the Mediterranean and equatorial countries or in the areas near to the equator and in Africa [8]. In other words, the thalassemia belt spreads to the region of the Mediterranean Sea along the Arabian Peninsula, Turkey, Iran, India, and Southeast Asia, especially Thailand, Cambodia, and South China.

The prevalence of the thalassemia gene in these areas is between 2.5 and 15.5% [9]. In Iran, thalassemia is more common in areas around the Caspian Sea, the Persian Gulf, and the Oman Sea, i.e., Mazandaran, Gilan, Khuzestan, Fars, Bushehr, Hormozgan, Sistan-Baluchestan, and Kerman provinces [10].
In Iran, the prevalence of thalassemia genes varies from 3% to 4% by geographical region. It is estimated that approximately two million people carry the beta-thalassemia gene in Iran. Recognizing the carriers of this disease before marriage in areas with high prevalence rate, especially Fars as one of the ten most populated provinces in the country, and precluding marriage between carriers through raising awareness can prevent the birth of people with homozygous thalassemia (major), resulting in significant economic and social damages to the community [11]. Regarding the prevalence of heterozygote type, sickle cell anemia, especially in southern Iran, and the probable association between sickle cell disease and beta-thalassemia, it can lead to sickle cell thalassemia and severe socio-physical problems. Moreover, it should be noted that if the prevalence of sickle cell and β-thalassemia minor is equal in an area, the incidence of sickle cell syndromes is twice that of thalassemia major, and unfortunately, the implementation of thalassemia prevention programs not only fail to diminish the incidence of sickle cell syndromes but also relatively increase it [12,13]. Kazeroun is geographically known as one of the cities with a high prevalence of β-thalassemia and sickle cell (S). Therefore, the authors decided to investigate the prevalence of minor thalassemia and sickle cell hemoglobin in marriage applicants referring to the Genetic Diseases Counseling Center of Kazeroun Health Center, Shiraz University of Medical Sciences during 2014-2018.

2. Materials and Methods

2.1. Study Population

This cross-sectional study was carried out in Kazeroun during 2014-2018. All couples referring to the counseling center of Kazeroun for pre-marriage tests during 2014-2018 were included in this study. The inclusion criterion was applicants with a record in this case, and the exclusion criterion was the records with incomplete information.

2.2. Sampling Method

All the couples referring to the marriage counseling centers in Kazeroun for pre-marriage tests during 2014-2018 were included in the study based on the census.

2.3. Data Collection Instrument

In this study, data in couples’ health records were used for marriage counseling. The marriage applicants were referred to screening laboratories for the detection of thalassemia following referral to the marriage registry office. After thalassemia tests, the results were sent to the counseling health center for interpreting. The counseling physician was responsible for interpreting the tests based on a national algorithm. Further experiments included chains examination, hemoglobin H examination, and DNA study. The results of the above experiments were sent to the academic advisor of the program for final interpretation. According to the diagnosis of the academic advisor, these people were detected to be the carrier couples; hence, the necessary measures were taken based on the plan.

2.4. Data Analysis

Data were analyzed by SPSS V.20, and the normality of the data was assessed by the Kolmogorov-Smirnov test. After confirming the normality of the data, statistical analysis was performed using ANOVA and Chi-square tests.

3. Result and Discussion

During the 5 years of the study, 31114 applicants (15555 couples) referred to the health consulting center under scrutiny for marriage tests. The highest number of marriage applicants was in 2014 with a total of 7748 persons, and the lowest number was in 2018 with a total of 4872 persons. (Table 1).

According to Table 2, ANOVA results showed that there is a significant difference among the study years in terms of the average volume of red blood cells (80-96 normal), the mean of red blood cells, and red blood cells in the study years (P < 0.001). However, there was no significant difference in hemoglobin levels among the study years (P=0.16).

Table 3 shows the prevalence of thalassemia, anemia, sickle cell hemoglobin, and hemoglobinopathy in different study years. In marriage applicants, the highest prevalence of beta-thalassemia, alpha thalassemia, anemia, sickle cell hemoglobin, and hemoglobinopathy was reported in 2014 (0.07), 2018 (0.15), 2014 (0.06), 2018 (0.09), and 2014 (0.05), respectively. In the total population, the highest prevalence of beta- and alpha-thalassemia was in 2014, the highest prevalence of anemia was in 2014, the highest incidence of sickle cell hemoglobin was in 2015, and the highest frequency of hemoglobinopathy was in 2014 (Table 3).

Chi-square test showed a significant difference between the study years in terms of the prevalence of thalassemia, anemia, sickle cell hemoglobin, and hemoglobinopathy (P < 0.001). In 2014, thalassemia, anemia, and hemoglobinopathy had a higher rate than other study years while in 2015, sickle hemoglobin had a higher rate than the other study years (Table 4).

The aim of this study was to determine the prevalence of thalassemia and sickle hemoglobin in marriage applicants referring to the Genetic Disease Counseling Center of the Health Center of Kazeroun over 2014-2018. The results of the study showed that the prevalence of beta-thalassemia in marriage applicants was 35% in all study years (7% in 2014, 6.7% in 2015, 6.6% in 2016, 6.5% in 2017, and 6.5% in 2018).

The prevalence of thalassemia was 5.5% in a study conducted by Forouzan Nejad et al. in Ahwaz in 2018 [14].

Table 1: The number of marriage volunteers in study years

<table>
<thead>
<tr>
<th>Year</th>
<th>Marriage applicants</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>7748 (3874 couples)</td>
</tr>
<tr>
<td>2015</td>
<td>6732 (3366 couples)</td>
</tr>
<tr>
<td>2016</td>
<td>5972 (2986 couples)</td>
</tr>
<tr>
<td>2017</td>
<td>5790 (2895 couples)</td>
</tr>
<tr>
<td>2018</td>
<td>4872 (2436 couples)</td>
</tr>
<tr>
<td>2014-2018</td>
<td>31114 (15557 couples)</td>
</tr>
</tbody>
</table>
In a study conducted in Pakistan in 2015, the prevalence of thalassemia was 6.5% [15]. In the study by Shera et al. in India, the prevalence of beta-thalassemia was reported to be 78.2% [16], and in a study in China in 2017, it was 21.2% [17]. In another study, the prevalence of beta-thalassemia was reported to be 5.6% in Kashmir [18], 3.4% in Hong Kong, and 3.4% in Saudi Arabia [19]. These findings were somewhat consistent with the results yielded in the present study on the prevalence of thalassemia major over the years studied.

The results of the present study showed that the prevalence of alpha thalassemia in marriage applicants was 0.58 (58% in all study years: 1.4% in 2014, 0.05% in 2017, and 0.00% in 2018). In the study by Foruzan Nejad et al. in Ahvaz, the prevalence of sickle cell hemoglobin was 7.05% [14]. In the study by Canton et al. and Foruzan Nejad et al. in Ahvaz, the prevalence of sickle cell hemoglobin was 0.49% [29]. In another study by Genninki et al., the total number of patients with sickle cell anemia was 584, and the highest rate was 13 in 100,000 subjects [30].

The present study indicated that the prevalence of hemoglobinopathy in marriage applicants was 0.99 (9% for the total study years: 5% in 2014, 4% in 2015, 0.02% in 2016, 0.05% in 2017, and 0.00% in 2018).

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Iran is located on the thalassemia belt, and the disease has become widespread due to the history of family marriages. Furthermore, in spite of implementing preventive strategies, preventing and controlling the disease in Iran encounter challenges due to the cultural multiplicity and numerous family marriages. When marriage between two people with thalassemia minor is precluded, these individuals are more likely to marry a person with a sickle cell compared with the previous condition. Accordingly, if the incidence of sickle cell trait is significant in an area where the thalassemia prevention programs are implementing, the problem of major thalassemia prevalence is likely to be replaced by the higher prevalence of hemoglobinopathies, including sickle cell syndrome, particularly sickle-cell-beta thalassemia [13].

### 3.1. Strengths

Large sample size and investigation of marriage applicants' data for several years were the strengths of the study.

<table>
<thead>
<tr>
<th>Type of disease</th>
<th>Blood</th>
<th>Category</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalassemia</td>
<td>In marriage</td>
<td>Beta</td>
<td>0.07</td>
<td>0.067</td>
<td>0.066</td>
<td>0.065</td>
<td>0.065</td>
<td>0.39</td>
</tr>
<tr>
<td></td>
<td>In total population</td>
<td>Beta</td>
<td>0.001</td>
<td>0.0014</td>
<td>0.001</td>
<td>0.0013</td>
<td>0.001</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>In total population</td>
<td>Alpha</td>
<td>0.003</td>
<td>0.003</td>
<td>0.002</td>
<td>0.003</td>
<td>0.002</td>
<td>0.013</td>
</tr>
<tr>
<td>Anemia</td>
<td>In the marriage applicants</td>
<td>Alpha</td>
<td>0.06</td>
<td>0.04</td>
<td>0.05</td>
<td>0.04</td>
<td>0.04</td>
<td>0.24</td>
</tr>
<tr>
<td></td>
<td>In total population</td>
<td>Alpha</td>
<td>0.001</td>
<td>0.001</td>
<td>0.008</td>
<td>0.007</td>
<td>0.009</td>
<td>0.026</td>
</tr>
<tr>
<td>Sickle hemoglobin</td>
<td>In the marriage applicants</td>
<td>Alpha</td>
<td>0.08</td>
<td>0.01</td>
<td>0.05</td>
<td>0.01</td>
<td>0.09</td>
<td>0.024</td>
</tr>
<tr>
<td></td>
<td>In total population</td>
<td>Alpha</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Hemoglobinopathy</td>
<td>In the marriage applicants</td>
<td>Alpha</td>
<td>0.05</td>
<td>0.04</td>
<td>0.002</td>
<td>0.005</td>
<td>0.001</td>
<td>0.09</td>
</tr>
</tbody>
</table>
3.2. Weaknesses

Non-generalizability of the study results and the incompleteness of some of the records were among the weaknesses of the present study.

4. Conclusion

The present study showed that the incidence of thalassemia and sickle cell anemia in the study years was similar to that in other parts of Iran. However, the implementation and continuation of the beta-thalassemia screening programs in this city can effectively prevent the birth of the newborns with major thalassemia and impose unwanted treatment costs.

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