

ORIGINAL ARTICLE

Medicine Science 2021;10(3):873-6

Premarital screening test results for beta thalassemia in Malatya Province **Mehmet Erten***Public Health Laboratory, Department of Medical Biochemistry, Malatya, Turkey*

Received 17 March 2021; Accepted 19 April 2021

Available online 01.08.2021 with doi: 10.5455/medscience.2021.03.090

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**Abstract**

Hemoglobinopathies are the most common monogenic hereditary diseases worldwide. After sickle-cell disease, beta thalassemia has the highest incidence. Premarital screening is performed to detect beta thalassemia carriers and prevent pathological births. We aimed to reveal the frequency of beta thalassemia carriers in Malatya. The study was retrospectively conducted with 4840 participants who applied for premarital screening to our laboratory. Samples were analyzed with Primus ultra² Resolution Variants Analyzer (USA) by conducting High Performance Liquid Chromatography (HPLC) method. HbA2 values over 3.5% were considered as beta thalassemia carrier. As a result of the premarital screening; 42 of 4840 individuals were evaluated as beta thalassemia carrier. This corresponds to a rate of 0.8%. Our results show that the rate of thalassemia carriers in our region is lower than our country and world. We suggest that it may be more cost-effective to perform examinations such as medical history and complete blood count in premarital screening where the prevalence is low, and then performing an HPLC scan when necessary.

Keywords: Premarital screening, beta thalassemia, HPLC, thalassemia trait, HbA2**Introduction**

Beta thalassemia is an hematological pathology characterized by hypochromic microcytic anemia, which can also be called Mediterranean anemia or Cooley anemia. The genetic defect is responsible for the pathogenesis, leading to a decrease in hemoglobin beta chain synthesis, which shows an autosomal recessive transition [1,2].

Major and intermedia forms of beta thalassemia can reveal various clinical findings such as hepatosplenomegaly, regular blood transfusions, and disorders due to iron accumulation. [2]. Apart from these forms, there are thalassemia carriers that have a normal appearance and can only be detected by screening to prevent genetic transmission [3]. Because of the autosomal recessive transition, there is a 25% probability of being thalassemia at each birth in the marriage of two carrier individuals. However, if one of the parents is a carrier, children could have a 50% risk. In terms of premarital screening and genetic counseling may be beneficial in order to prevent thalassemia.

In our country, the incidence of beta thalassemia was determined as 2.1% [4,5]. However, there are higher prevalences in Mediterranean regions [6]. As a result of the previously performed hemoglobinopathy control programs, it was determined as 19430 patients (34% thalassemia) and 409654 carriers (64% thalassemia) since 2003 [4]. According to the official data, thanks to the premarital screenings, the number of patients decreased from 300 to 100 births [4]. Because of these positive outcomes, premarital beta thalassemia screening program was expanded to the entire country since 2019. Therefore, it started in Malatya at the same time. There was not any sufficient data on beta thalassemia in our region. Thus, we aimed to reveal the frequency of beta thalassemia carriers in Malatya.

Materials and Methods

Our study was retrospectively conducted between January 2019 and March 2020, thalassemia test requests 4840 participants who applied for premarital beta thalassemia screening to our laboratory. In this screening program, it was sufficient for including one spouse of the couples. If the screened individual was positive, the other spouse was expected to participate in the screening. In addition, those who requested retest were excluded from the study. It had to be limited to fifteen months due to the COVID-19 pandemic. The study protocol was approved by the local clinical research ethics

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committee (October 2020 and 156 session number). Samples were analyzed with Primus ultra² Resolution Variants Analyzer (USA) device by conducting High Performance Liquid Chromatography (HPLC) method. HbA2 values over 3.5% of the patient results were considered as beta thalassemia carriers. Besides, abnormal Hb variant types were determined based on the catalog of the device. The present HPLC device has two different operating programs: Quick scan and high-resolution mode. After all samples were run in quick scan mode, samples with HbA2 values which were outside reference values were rerun in high resolution mode to confirm the results. The beta-thalassemia carriers' gender-specific complete blood count parameters were statistically evaluated. Differences between groups were investigated with Student's t-test or Mann-Whitney U test. Complete blood count test was analyzed with Sysmex XN-1000 Hematology Analyzer system (Sysmex Corporation, USA). The results were expressed as mean $\pm$ standard deviation. SPSS 22.0 (IBM Corporation, USA) package program was used for statistical analysis. Two-tailed P values <

0.05 were considered statistically significant.

Results

During the screening period, 42 out of 4840 individuals were identified as carriers. This rate corresponds to about 0.8% and this is lower than the mean of Turkey. The mean age of the carriers was 27.9 ± 5.4 years. Of the carriers, 69% were male, 31% were female. Except for the erythrocyte distribution width, complete blood count tests were determined to be higher in men than women ($p < 0.05$) (Table 1). Also shown, a hypochromic microcytic pattern is observed in both genders complete blood count results (Mean Erythrocyte Hb < 27, Mean Erythrocyte volume < 80). Additionally, Hb variants were found in our study. Hb D-Los Angeles (0.08%), Hb S (0.04%), and Hb Q-Iran (0.02%) were determined during screening period. Moreover, we found that pure alone HbF increased in 0.26% of the patients (HbF > 2%).

Table 1. Gender-specific complete blood count parameters

	Female (n: 13)	Male (n: 29)
Hemoglobin (g/dL)	11.44 ± 1.65	$13.89 \pm 1.41^*$
Hematocrit (%)	36.79 ± 4.88	$43.31 \pm 4.65^*$
Erythrocyte ($10^6/\mu\text{L}$)	5.79 ± 0.84	$6.37 \pm 0.64^*$
Mean Erythrocyte Hb (g/dL)	19.82 ± 2.06	$21.99 \pm 2.97^*$
Mean Erythrocyte Volume (fL)	63.77 ± 4.07	$68.38 \pm 7.53^*$
Mean Erythrocyte Hb concentration (g/dL)	31.04 ± 1.52	$32.10 \pm 1.38^*$
Erythrocyte Distribution Width (%)	18.1 ± 4.1	$16.0 \pm 2.0^*$

* $p < 0.05$ was determined as statistically significant. Hb: Hemoglobin, n: number

Discussion

Beta thalassemia is the second most common hereditary hemoglobin disease, after sickle cell anemias, with an annual rate of 22000 births and 4.9% worldwide [7]. The places where thalassemia is frequently seen in the world are Middle East, Central Asia, South Asia, and South America, especially the countries that have shores in the Mediterranean Sea. Among these, the places where thalassemia trait is most common are Cyprus (14%) , Sardinia (10,3%), and Southeast Asia. However, the rates of thalassemia carriers' in most regions have not yet been fully elucidated [2].

The prevalence of beta thalassemia trait in Turkey is 2.1% according to previous data [4]. However, the frequency varies between 0.6% and 13% when considered regionally. In a recent meta-analysis study was conducted on the results of thalassemia screening programs after 2000 in Turkey and some Middle East Islamic countries [1]. They evaluated and made comparisons with these results. It is emphasized that Iran has successfully reduced the number of carriers with both training programs and screenings. Additionally, it has been revealed that the differences between countries related to consanguineous marriage, termination of pregnancy, and similar sociocultural factors create significant differences in the control of this disease.

In our country, thalassemia screening programs have been widespread since the 2000s and then premarital screenings

have become mandatory throughout the whole country in 2019. Therefore, we started in 2019 as a premarital screening. There was not any prevalence study in our province. Our results show that the rate of thalassemia carriers in our region is lower than our country and world. We noticed that the prevalence of our location (0.8%) was similar to the inner and eastern regions according to other studies (Table 2). Hb S, one of the abnormal hemoglobins, was found with a frequency of 0.3% throughout the country and 10% in the southern coastal regions [5]. We also observed a lower prevalence of HbS (0.04%) in our study.

HPLC was the most widely accepted and used method in the beta thalassemia screenings [7]. In a study made in Erzurum, which has similar demographic and geographical features such as our working area, the prevalence was found 0.7%. In the relevant study, it has been questioned the necessity of scanning with a relatively more expensive method such as HPLC in non-endemic areas in terms of cost-effectiveness. Therefore, it is suggested that less costly scans such as ELISA can be used in regions with lower prevalence [8]. However, studies that compares ELISA and HPLC methods, it was recommended to use ELISA in the regions where thalassemia has a high prevalence [9,10].

As a result, taking into account the medical history and red blood cell indices can be used more efficiently for screening. Our results will contribute to elucidate regional and world prevalences.

Table 2. Prevalence of beta thalassemia carriers in provinces

Author / Year	Province	Prevalence (%)	Participants (n)	Study Type	References
Bircan et al. 1993	Antalya	10.2	1616	FS	[11]
Keskin et al. 2000	Denizli	2.6	19804	PMS	[12]
Tosun et al. 2006	Mersin	2.1	79000	PMS	[13]
Guler and Karacan 2007	Konya	1.7	72918	PMS	[14]
Acemoglu et al. 2008	Erzurum	0.7	1610	PMS	[8]
Sarper et al. 2009	Kocaeli	0.9	88888	PMS	[15]
Guler et al. 2010	Kahramanmaras	2.1	11040	PMS	[16]
Genc et al. 2012	Adiyaman	1.9	1616	PMS	[17]
Karakukcu et al. 2012	Kayseri	1.7	10261	PMS	[18]
Uysal et al. 2013	Izmir	5	38554	PMS	[19]
Incebiyik et al. 2014	Sanliurfa	2.4	75924	PMS	[20]
Ulutas et al. 2014	Adana (Kadirli)	4.9	1994	PMS	[21]
Uludag et al. 2016	Canakkale	1.4	8904	PMS	[22]
Oktay 2016	Hatay	6	70226	PMS	[23]
Altikat et al. 2016	Kutahya	5	14815	PMS	[24]
Akagac et al. 2019	Uzak	3	3324	PMS	[25]
Our Study	Malatya	0.8	4840	PMS	

n: number, FS: Family screening, PMS: Premarital screening

Conflict of interests

The authors declare that they have no competing interests.

Financial Disclosure

All authors declare no financial support.

Ethical approval

We carried out the study under local good clinical practice guidelines and current laws and obtained approval from the ethics committee of our hospital for the use of patient data (approval no: 156/2020).

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