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THE PREGNANCY VARIABLE IN WOMEN WITH HETEROZYGOUS BETA THALASSAEMIA

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ABSTRACT

Objectives: This study was designed to determine the RBC indices and HbF and HbA_2 levels of before and during pregnancy periods of heterozygous β-thalassemia individual. **Methods:** The study was designed retrospectively among the 60 heterozygous individuals with heterozygous β-thalassemia. In this study before and during pregnancy periods hematological outcomes of individual have been systematically documented. **Results:** The RBC indices were in non-pregnant group; Mean (min-max): RBC 4.98 mil/mm^3 (3.81-5.80), Hb 11.76 g/dL (9-14.20), Hct 35.39% (30,20- 41) and HbF % 0.7, (0.3-1.4) and HbA_2 % 4.28 (2.7- 4.7) pregnant group; RBC 3.93 mil/mm^3 (2,34-5.23), Hb 10.31 g/dL (7,70-12.30), Hct 31.83 % (22,90- 37,60) and HbF % 2.37 (0.4-4.9), HbA_2 % 4.87 (2.8-4.9) . The 30 heterozygous individuals with β-thalassemia of the non-pregnant group consisting of RBC, Hb and Hct levels were higher than the values in pregnant group. The difference between the two groups was statistically significant ($P < 0.05$). The pregnancy related changes in HbF and HbA_2 levels values have been observed in 30 pregnancies in 60 women with heterozygous β-thalassemia individual. Statistically significant increases in pregnancy period were observed. HbA_2 level is elevated in pregnant women. **Conclusion:** According to the results obtained in this study; pregnancy is a preanalytical variable on individuals with heterozygous β-thalassemia individual for RBC, Hb, Hct, HbF and HbA_2 levels. For this reason; the decreasing values of RBC, Hb and Hct depends to pregnancy may cause to interpret of heterozygous individuals as homozygous.

KEYWORDS: β-Thalassemia, RBC indices, pregnancy, preanalytical variable, HbA_2.

INTRODUCTION

Hemoglobinopathies are among the most common inherited diseases around the world.[1] They are characterized by mutations or deletions in the genes encoding the alpha (α) and beta (β) globin chains of the human hemoglobin molecule (Hb) and are broadly classified as sickle cell disorders and thalassemia.[2] Sickle cell disease (SCD) is caused by sickle hemoglobin (Hb S), a structurally abnormal Hb variant due to a point mutation in the β-globin gene.[3] The HbS is a mutation in the β globin gene, which is the substitution of glutamic acid (GAG) for valine (GTG) and it causes the hemoglobin physicochemical changes This structural change in HbS when in deoxygenation situations is organized in long polymers and change the morphology of the red blood cell, becoming elongated and sickle-shaped.[4] SCD is one of the most common hereditary diseases, and affects approximately 30 million patients worldwide with varying clinical severity and potentially serious complications.[5,6] SCD is caused by a homozygous mutation in hemoglobin S and presents as chronic anemia accompanied by severely painful episodes. The principal defect triggering disease signs and symptoms is impaired microcirculation caused by sickling of rigid erythrocytes.[7] Heterozygous combinations of hemoglobin S with other abnormal hemoglobins (HbSC, HbSE, HbS-beta o-thalassemia, and HbSD) are other clinical conditions causing painful episodes and tissue injury.[8] Beta-thalassemia is due to a defect in the synthesis of the beta-globin chains, leading to alpha/beta imbalance, ineffective erythropoiesis, and chronic anemia. Heterozygous β-thalassemia, the mildest form of β-thalassemic syndromes, by similarity to the hypochromic, hyposideremic anaemia is even today accidentally diagnosed in childhood or in other periods of life, including adults, when a haematological routine examination of peripheral blood reveals microcytic hypochromic anaemia with changes that attract attention, such as moderately low haemoglobin, with decreased MCV erythrocyte indices and significant changes in the erythrocyte series on the blood smear (hypochromia, microcytosis, anisocytosis, etc.) suggesting the suspicion of β-thalassemia.[9,10,11,12] During pregnancy, women with heterozygous β-thalassemia will often show more significant anemia, which is often most prominent during the latter half of the second trimester and early third trimester. There is no specific therapy for thalassemia minor during pregnancy, but if the anemia becomes more

severe, transfusions are sometimes necessary. Thalassemia syndromes constitute a group of inherited hemoglobinopathies that require close maternal and fetal surveillance during pregnancy, including appropriate consultation with maternal fetal medicine and hematology specialists. Even for the women who are asymptomatic before pregnancy, the added stresses of pregnancy on the hematopoietic system can cause deterioration of maternal status. Little is reported regarding perinatal outcome of individual with heterozygous β-Thalassemia. A few studies including small numbers of individual suggested a favourable outcome.[13,14,15,16]

There are rare studies published to date investigating the RBC indices and HbF, HbA_2 values of hematological profile of before and during pregnancy periods. The purpose of this study was investigate the effect of pregnancy variables on hematological data in before and during pregnancy periods on heterozygous β-thalassemia who comes to the University of Cukurova for Medical Sciences for mutation screening test in both periods.

METHODS

The study was designed retrospectively among the 60 heterozygous individuals with hemoglobinopathies. A retrospective chart review was conducted for subjects between 2008 and 2016.

Study participants

This was a retrospective study design, based on review of records of individual seen Medical Sciences. A total of 60 pregnant and nonpregnant individual hematological data were obtained through a review of medical records with the confidentiality of information being preserved.

Design

Clinical data was obtained through a review of medical records. The results of hematological values were obtained through the patient registration system. RBC indices such as RBC, Hb, Hct, MCV, MCH, MCHC, HbF, and HbA_2 were compared between the nonpregnant and pregnant individuals. The Hematological parameter data were recorded on a data collection form and later compiled for statistical analysis.

Statistical analysis

Data are presented as descriptive statistics including means. The Wilcoxon test non-parametric statistical test was used to compare pregnant and nonpregnant groups.

RESULTS

The haematological profiles are shown in table.1. The 30 heterozygous individuals with hemoglobinopathies of the non-pregnant group consisting of RBC, Hb, Hct, HbF and HbA_2 values were higher than the values in pregnant group. The difference between the two groups was statistically significant ($P < 0.05$). The between two groups MCV, MCH, MCHC value wasn't statistically significant ($p > 0.05$).

Table 1: Hematological profile were in heterozygous β-Thalassemia in pregnant and nonpregnant individual.

Variable	Heterozygous hemoglobinopathies Pregnant individual Mean(min-max)	Heterozygous hemoglobinopathies Non-pregnant individual Mean(min-max)	P
Hemoglobin (g/dL)	10.28 (7.77-12.26)	11.42 (9-13.20)	< 0.05
Red Blood Cells (mil/mm^3)	3.93(2.83-5.28)	4.98(3.81-5.80)	< 0.05
Hematocrit (%)	31.80 (22.94- 37.66)	35.28 (30.23- 42)	< 0.05
Mean corpus volume (fL)	81.02 (66.7-91.1)	80.98 (66.5-90.5)	> 0.05
Mean cell hemoglobin (pg)	28.89 (20.1-35.1)	28.33 (19.2-36.2)	> 0.05
Mean corpuscular hemoglobin concentration (g/dL)	32,03 (27.1-35.4)	31.78 (28.9-34.9)	> 0.05
Hemoglobin F (%)	2.37(0.4-4.9)	0.7 (0.3-1.4)	< 0.05
Hemoglobin A_2 (%)	4.87 (2.8-4.9)	4.28 (2.7- 4.7)	< 0.05

DISCUSSION

β- Thalassemia is extremely heterogeneous in terms both of genotype and phenotype, depending on the nature of β-gene mutation and the extent of impairment in β-globin chain production. As a rule, heterozygous carriers of β-thalassemia (one affected allele), are asymptomatic, and only altered laboratory values (low, normal, or slightly subnormal hemoglobin levels, slightly low mean cellular hemoglobin, low mean cell volume, low β:α-globin chain ratio on biosynthesis.[17] This study was performed on individual with heterozygous β-Thalassemia to determine the hematologic outcomes on before and during pregnancy periods. Heterozygous β-Thalassemia individual presented only with mild anemia during pregnancy. The 60 heterozygous individuals with β-Thalassemia of the non-pregnant group consisting of RBC, Hb, and Hct values were higher than the values in pregnant group. As shown in Table 1, Hb values were significantly higher in the non- pregnant group than in the groups of pregnant group ($P<0.05$). In our study, heterozygous β-Thalassemia individual usually maintained Hb >10 g/ dL for both groups. In another study found that these individual usually maintain Hb around 10 g/dL.[18,19] RBC and Hct values increased significantly in pregnant group ($P<0.05$). RBC count of 30 individual with pregnant ranged between 3.81

mil/mm^3 to 5.80 (mil/mm^3) with an average of 4.98 (mil/mm^3). Hct values of pregnant and non-pregnant individual were found to be statistically significant. In our study, Hct of pregnant individual was 35.28 % which is lower than in the normal range. The pregnant individual was found to be significantly lower than non-pregnant groups. Another study Hct values between patients and control subject were not statistically significant.[20] This study showed that HbF was higher in pregnant than non-pregnant groups. The pregnancy appears to have effects on HbF level. In our study, heterozygous β-Thalassemia pregnant individual maintained HbF level between 0.4-4.9 % and that corresponds to published data.[21] In this study, we also noted that HbA_2 levels were statistically different between pregnant and non-pregnant women with heterozygous β-Thalassemia. Interestingly, HbA_2 level is elevated in pregnant women. The between two groups MCV, MCH, MCHC value wasn't statistically significant ($p > 0.05$). The pregnancy related changes in HbF have been observed in 30 pregnancies in 60 women with heterozygous β-Thalassemia in the same individual. The pregnancy appear to have effects on HbF level. Statistically significant increases in pregnancy period were observed. According to the results obtained in this study; pregnancy is a preanalytical variable on individuals with hemoglobinopathies for RBC, Hb, Hct, HbF and HbA_2 levels. For this reason; the decreasing values of RBC, Hb and Hct depends to pregnancy may cause to interpreate of heterozygous individuals as homozygous. In addition, Pregnancy isn't a preanalytical variable on individuals with heterozygous β-thalassemia for MCV, MCH, MCHC values. Also, before and during pregnancy RBC indices and HbF, HbA_2 values outcomes of heterozygous β-Thalassemia have been systematically evaluated in this study.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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