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Research Article / Araştırma Makalesi

Investigation of Deficiency of Serum Glucose-6-Phosphate Dehydrogenase Enzyme Level Around and in Mardin Province*

Mardin İli ve Çevresinde Serum Glukoz-6-Fosfat Dehidrogenaz Enzim Düzeyi Eksikliğinin Araştırılması*

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ABSTRACT

Introduction: Glucose-6-phosphate dehydrogenase (G6PD) is a cytosolic enzyme, and the first enzyme to catalyze the pentose phosphate pathway. Our aim is to investigate the G6PD enzyme activity in Mardin province.
Methods: Our study was divided into subgroups according to gender, age, and G6PD levels. A total of 439 individuals, 168 females and 271 males, between the ages of 2 and 80 were included in the study. G6PD enzyme activity was measured by the photometric method using the AU5800 Beckman device.
Results: G6PD enzyme activity in the Mardin region was found to be 13.95±7.29 U/gHb. The mean G6PD enzyme activity in female patients was 14.22±6.98 U/gHb, and the mean in male patients was 13.78±7.48 U/gHb (p>0.05). When evaluated in terms of age, the G6PD enzyme activity was 14.93 (0.03-38.47) in patients aged 2-19, 13.76 (0.01-30.79) between 20-35 years old, 17.05 between 36-50 years old (0.13-27.21), 13.75 (0.05-26.99) U/gHb between 51-80 years old (p=0.301).
Conclusion: In our study, no significant difference was found between G6PD enzyme activity in terms of age and gender. G6PD enzyme deficiency was shown as 6% relative to the reference range. A deficiency of 6.5% in male and 3.5% in female was observed. This study is valuable in that it is the first study conducted in Mardin. There is a need for larger studies to support this study locally.

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ÖZET

Giriş: Glukoz-6-fosfat dehidrogenaz (G6PD) sitosolik bir enzim olup pentoz fosfat yolunu katalizleyen ilk enzimdir. Bu çalışmadaki amacımız Mardin ve çevresinde hastaneye başvuran hastaların G6PD enzim düzeyini ve eksiklik sıklığını araştırmaktır.
Yöntem: Mardin Eğitim ve Araştırma Hastanesine gelen hastaların G6PD enzim aktivitesi retrospektif olarak değerlendirildi. Çalışmamız cinsiyet, yaş ve G6PD seviyelerine göre alt gruplara ayrıldı. Yaş aralığı 2-80 arasında 168 kadın ve 271 erkek olmak üzere 439 birey çalışmaya dahil edildi. G6PD enzim aktivitesi AU5800 Beckman cihazı kullanılarak fotometrik yöntemle ölçüldü.
Bulgular: Çalışmamızda G6PD enzim aktivitesi 13.95±7.29 Ü/gHb olarak tespit edildi. Kadın hastalarda G6PD enzim aktivitesi ortalaması 14.22±6.98 Ü/gHb erkek hastalarda ise 13.78±7.48 Ü/gHb olarak bulundu (p>0.05). Yaş açısından değerlendirildiğinde 2-19 yaş aralığındaki hastalarda G6PD aktivitesi 14.93(0.03- 38.47), 20-35 yaş arası 13.76 (0.01-30.79), 36-50 yaş arası 17.05 (0.13- 27.21), 51-80 yaş arası 13.75(0.05- 26.99) Ü/gHb olarak tespit edildi (p=0.301).
Sonuç: Çalışmamızda yaş ve cinsiyet açısından G6PD enzim aktivitesi arasında anlamlı fark bulunmamıştır. Referans aralığa göre G6PD enzim eksikliği %6 gösterilmiştir. Erkeklerde %6.5 kadınlarda %3.5 eksiklik gözlenmiştir. Bu çalışma Mardinde yapılmış olan ilk çalışma olması açısından değerlidir. Bu çalışmayı yöresel olarak destekleyecek daha geniş çaplı çalışmaların yapılmasına ihtiyaç duyulmaktadır.

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1. Introduction

Glucose-6-phosphate dehydrogenase (G6PD), which has an important cleaning role in all cells, is the first enzyme of the pentose phosphate pathway and is also a cytosolic enzyme that produces NADPH in red blood cells (1). The G6PD enzyme is the rate-limiting enzyme of the pentose phosphate pathway (2). When the activity of this enzyme decreases, oxidative stress develops in red blood cells (3) and therefore hemolytic anemia occurs. The World Health Organization has divided the variants that cause G6PD into five classes. Class I causes the most severe chronic non-spherocytic hemolytic anemia. Class II is also considered severe and is associated with acute hemolytic anemia. Class III is considered a moderate deficiency and is occasionally associated with acute hemolytic anemia, while it has been shown to be asymptomatic in class IV, and V (4).

It has been stated that G6PD enzyme deficiency affects approximately 400 million participants in the world and is the most common human enzymopathy (2). G6PD enzyme deficiency, which is generally asymptomatic, may present with enzyme deficiency due to exposure to various drugs and infections, acute hemolytic anemia after ingestion of certain foods such as broad beans, or severe jaundice in the newborn period (5). It has been demonstrated that G6PD enzyme deficiency is common in regions such as Africa, Asia, the Mediterranean, and the Middle East where malaria is endemic (6). Studies on G6PD enzyme deficiency have been carried out in various regions of Turkey. In a study conducted by Aksu et al. in 1521 individuals in Antalya, 7.4% in male and 1.8% in female, G6PD enzyme deficiency was found (7). Its frequency is 0.5% in Turkey, 8.2% in Çukurova region, 11.4% in Tarsus and Antakya, and 9.2% in Antalya (8). In a study conducted with 306 individuals in Gaziantep, G6PD deficiency was reported to be 2.3% (9).

As far as we know, no study has been found in the literature on the level of G6PD enzyme deficiency in our region. Therefore, we aim to investigate the G6PD enzyme level and deficiency frequency in Mardin.

2. Methods

Our study was performed with the permission Dicle University Clinical Research Ethics Committee (Ethics approval no: 13.10.2021/147). G6PD results of patients who came to Mardin Training and Research Hospital between 03.05.2018-30.07.2021 were evaluated retrospectively. Our study was divided into subgroups according to gender, age, and G6PD levels. A total of 439 participants, 168 (38.3) female and 271 (61.7) male, between the ages of 2 and 80 were included in the study. The study group included 252 participants in the 2-19 age group, 84 participants in the 20-35 age group, 47 participants in the 36-50 age group, and 56 participants in the 51-80 age group (Table 1). G6PD enzyme activity level was analyzed photometrically spread using the AU5800 Beckman device.

2.1. Statistical analysis

Statistical analysis was performed using the SPSS (v. 23) program. The compatibility of the data with the normal distribution was checked with the Kolmogorov-Smirnov test and visual graphics. The 2-group Student-T test was used for parameters that were normally distributed, and the Mann-Whitney-U test was used to compare pairwise groups for parameters that were not normally distributed. The kruskal wallis test was used to compare more than two groups. In all statistical analyzes, those with a p-value below 5% were statistically significant.

3. Results

The demographic distribution of the individuals participating in the study by age and gender is shown in Table 1. The G6PD enzyme activity of the patients participating in the study was found to be 13.95±7.29 U/gHb. According to the reference range, 6% of G6PD enzyme deficiency was detected. A deficiency of 6.5% in male and 3.5% in female was observed.

Table 1. Demographic distribution of individuals by age and gender

Age Group	Female		Male		n	%
	n	%	n	%		
2-19	94	37.3	158	62.7	252	57.4
20-35	36	42.9	48	57.1	84	19.1
36-50	17	36.2	30	63.8	47	10.7
51-80	21	37.5	35	62.5	56	12.8

When G6PD enzyme activity was evaluated according to gender, the mean of G6PD activity in female patients was found to be 14.22±6.98 U/gHb in male patients and 13.78±7.48 U/gHb in male patients, and no statistically significant difference was found (p=0.586) (Table 2).

Table 2. Serum G6PD (U/gHb) enzyme activity of individuals by gender

Gender	n	%	M±SD	Median (Min.-Max.)	p*
Female	168	38.3	14.22±6.98	14.95 (0,01-30,79)	0.586
Male	271	61.7	13.78±7.48	14.49 (0.03-38.47)	

Min.: Mininum Max.: Maksimum. G6PD enzyme activity data are shown as mean±SD (standard deviation): p>0.05 G6PD: Glucose-6-phosphate dehydrogenase.
*Mann Whitney U

When G6PD enzyme activity was evaluated according to age groups, it was found to be 14.93 (0.03-38.47) U/gHb in patients between 2-19 years of age and 13.76 (0.01-30.79) U/gHb in patients between 20-35 years of age. It was determined that it was 17.05 (0.13-27.21) U/gHb in patients between the ages of 36-50 and 13.75 (0.05-26.99) U/gHb in patients between the ages of 51-80. No statistically significant difference was detected (p=0.301) (Table 3).

Table 3. Serum G6PD enzyme activity (U/gHb) minimum and maximum activity by age group

Age group	G6PD	p*
2-19	14.93 (0.03-38.47)	
20-35	13.76 (0.01-30.79)	0.301
36-50	17.05 (0.13-27.21)	
51-80	13.75 (0.05-26.99)	

G6PD enzyme activity by age group data are shown as median (min-max): p>0.05 G6PD: Glucose-6-phosphate dehydrogenase. *Kruskal wallis

When G6PD enzyme activity was evaluated according to age and gender, it was found to be 13.95±7.17 U/gHb in female and 13.77±7.82 U/gHb in male in the 2-19 age group (p=0.861). G6PD enzyme activity was found to be 15.05±6.64 in female aged 20-35 and 12.90±6.81 U/gHb in male (p=0.154). Between the ages of 36 and 50, G6PD enzyme activity was found to be 17.40±3.72 U/gHb in female and 14.52±6.80 U/gHb in male, respectively (p=0.135). Between the ages of 51-80, G6PD enzyme activity was determined to be 11.43±7.86 U/gHb in female and 14.42±7.50 U/gHb in male (p=0.187). When the G6PD enzyme activity of the individuals was compared according to age and gender, there was no significant difference between male and female patients (p>0.05) (Table 4).

Table 4. Serum G6PD enzyme activity (U/gHb) of individuals by age and gender

Age Group	Female	Male	p
2-19	13.95±7.17	13.77±7.82	0.861*
	14.80(0.09-29.15)	15.08 (0.03-38.47)	
20-35	15.05±6.64	12.90±6.81	0.154*
	14.74(0.01-30.79)	13.56 (0.13-26.44)	
36-50	17.40±3.72	14.52±6.80	0.135**
	17.46(9.99-22.23)	15.79 (0.13-27.21)	
51-80	11.43±7.86	14.42±7.50	0.187**
	11.36 (0.83-26.72)	14.32 (0.05-26.99)	

Min.: Mininum Max.: Maksimum. G6PD enzyme activity (U/gHb) of individuals by age and gender data are shown as mean±SD (standard deviation) and median (min-max):p>0.05 G6PD: Glucose-6-phosphate dehydrogenase. Statistical method: *Student-T test,**Mann Whitney U

4. Discussion

According to the results of our study, G6PD enzyme activity was found to be 13.95±7.29 U/gHb in Mardin. According to the reference range, G6PD deficiency was 6%. A deficiency of 6.5% in male and 3.5% in female was observed. There is no study in the literature on G6PD enzyme activity in our region. Therefore, our study is the first clinical study to bring innovation to the literature.

The frequency of G6PD deficiency in the world varies according to geographical region and ethnicity. In the list published by the World Health Organization in 1989, Turkey is among the regions where G6PD enzyme deficiency is most common, along with Italy, Greece, West Africa, and Southeast Asian countries. Regarding the prevalence of G6PD enzyme deficiency, different rates have been demonstrated in the world and our country. It has been shown that 400 million participants are affected by G6PD enzyme activity and approximately 4.9% of the world population has enzyme deficiency (2).

Şekeroğlu et al. found the G6PD enzyme level to be 9.8±1.6 U/gHb for Van and its region (10). Yuregir et al. (11) found the G6PD enzyme level to be 8.6±3.3 U/gHb in their study in Çukurova. In our study, we found the G6PD enzyme activity to be 13.95±7.29 U/gHb, and the findings we obtained were observed to be higher than the 12.1±2.05 U/gHb reported by Beutler (12). This indicates that this situation may be related to the method studied.

In a study involving 306 participants, 166 of whom were female and 140 male, aged between 1-80 years in Gaziantep, it was stated that the frequency of G6PD enzyme deficiency was 2.9% in male, 1.8% in female, and 2.3% in the whole study group (9). In a prevalence study conducted in Denizli on a total of 1950 students aged 14-17, 918 female and 1032 male, the frequency of G6PD deficiency was found to be 1.45% in male, 0.98% in female, and 1.23% when all cases were considered (13).

In the cord blood study, which conducted by the Kılınç in Çukurova region, the frequency of G6PD enzyme deficiency was found 22.1% in male and 18.7% in female (14). In this study, Özlü found the frequency of G6PD deficiency to be 3% in male infants (15). In another study conducted in the Çukurova region by Menziletoglu Yildiz et al., they found the frequency of G6PD deficiency to be 7.11% in 450 healthy individuals (16). In a study conducted with 1421 healthy individuals living in Balıkesir and Çanakkale, the frequency of G6PD deficiency was found to be 7.24% in female, 6.2% in male, and 6.9% in all cases (17).

G6PD enzyme is inherited by the X chromosome (2). Atay et al. showed that G6PD enzyme deficiency was 24% in male and 6% in female in 624 newborns (18). Fotoh et al. reported that the rate of G6PD enzyme deficiency in males was 8.9% in their study conducted on 202 individuals with newborn jaundice in Egypt (19). Kılıç et al. reported that newborn male have G6PD deficiency, but female may also have a deficiency (20). In our study, G6PD enzyme deficiency was detected in 6% of all cases according to the

reference range. A deficiency of 6.5% in male and 3.5% in female was observed. In our study, it was found that the rate of G6PD deficiency was higher in males than in females, which is consistent with the literature. This situation supports our study. The fact that the deficiency rate in our study differs from ethnicity and region to region, and it also suggests that the G6PD enzyme, which is an adaptive enzyme, may be due to this feature. Mardin and its region indicate that there are Arabs, Kurds, and Assyrians in terms of ethnicity and this situation may be due to different ethnicities.

Eren (21) and Yuregir et al. (11) reported in their study that G6PD activity did not change with age. In our study, G6PD activity was evaluated according to four age groups 2-19, 20-35, 36-50, and 51-80. There was no significant difference in our study group according to age group. The results of our study demonstrated that G6PD enzyme activity did not change with age in accordance with the literature, which supports our study.

There are studies in the literature reporting that G6PD enzyme activity does not differ between sexes in studies on gender (9). In our study, it was shown that G6PD enzyme activity did not change in male and female. Yüreğir et al. (11) reported that G6PD enzyme activity did not change according to gender in their study. These results support our study.

There are some limitations in our study. One of these limitations is that genetic variants of the G6PD enzyme have not been investigated. Another important limitation is that a small number of individuals were included in our study.

5. Conclusion

As a result, in our study, G6PD enzyme activity was shown to be 6% compared to the reference range. A deficiency of 6.5% in male and 3.5% in female was observed. No difference was observed between the genders. Our study is valuable because it is the first study to present the deficiency frequency and enzyme level in our region. Therefore, there is a need for large-scale studies to support our study.

Conflict of Interest: There is no conflict of interest in this study.

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Ethics Committee Approval: The study was performed in accordance with the Declaration of Helsinki. Ethical approval was obtained from Dicle University Non-Invasive Clinical Research Ethics Committee (Issue number: 147, dated 13.10.2021).

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