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Research Article

Glucose-6-phosphate Dehydrogenase Deficiency in Patients Attending Tertiary Care Health Setting in Peshawar

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ABSTRACT

Glucose-6-phosphate Dehydrogenase (G6PD) deficiency is an X-linked disorder that mainly affects red blood cells resulting in its lysis manifesting as hemolytic anemia. The purpose of this study is to measure the burden of this genetic disorder in patients presenting to a tertiary care health setting of Peshawar, Pakistan, in order to validate previous findings. The retrospective records of 1440 patients were retrieved from the Hospital Management and Information System for the period spanning from January 2017 to December 2018. The data of 1402 patients were included in the final analysis. The mean (standard deviation) age of the patients was 15.02 ± 15.50 (range, 0.50–91.50) years. Of the total, 78.1% were males and 21.9% were females. The frequency of G6PD deficiency recorded was 12.50%. The highest proportion was noted in age groups of <5 years (76; 43.4%) and 20–40 years (37; 21.1%). The frequency of the disorder in males and females was 13.79% and 7.82%, respectively. This study records the high burden of G6PD deficiency in Pathans which is comparable to those reported in the literature. G6PD deficiency is relatively more prevalent in this area. Screening and educational programs for G6PD deficiency are recommended in these high-risk areas irrespective of sex to prevent G6PD deficiency-related morbidity.

1. INTRODUCTION

Glucose-6-phosphate Dehydrogenase (G6PD) is an enzyme that protects Red Blood Cells (RBCs) from the harmful effects of reactive oxygen species, which are the by-products of cellular metabolism. Loss of function caused by mutations in the gene for G6PD results in accumulation of these species inside RBCs, causing hemolytic anemia, increased susceptibility of hemoglobin to oxidative stress, and its precipitation as Heinz bodies on peripheral smear [1].

Glucose-6-phosphate dehydrogenase deficiency is an X-linked recessive disorder that mainly affects males owing to their single X chromosome, which is sufficient to cause the disease. In females, however, alteration in both genes is necessary for the disease to manifest. G6PD deficiency is also an important cause of jaundice in neonates, kernicterus, and even death. Many people with this disorder, however, are unaware that they have this condition.

An estimate showed that 400 million people are affected worldwide [2], with the highest prevalence in the tropics and subtropics. Traditionally, the geographical distribution of G6PD deficiency parallels the endemicity of malaria. Population transmigration has led to its worldwide emergence. A study from the United States showed a prevalence of approximately 10%, mainly affecting African-American [3]. In Africa, its prevalence is reported to range from 3.6% to 28.0% [4]. In Asia, the prevalence ranges from 6.0% to 15.8% [5]. In India, it is 10.5% [6], and in the Middle East the prevalence varies from 3% to 29% [7]. According to World Health Organization (WHO), the prevalence of G6PD is 10% and 14% in Iran and Bengal, respectively [8]. The global burden of G6PD has been reviewed by the WHO, and records show that about 7.5% of the world population carries a gene for G6PD deficiency [2].

Studies from Pakistan showed that G6PD deficiency prevalence ranges from 2% to 3.8% [9,10], with the highest rate of 8.6% observed in Pathans [11]. Considering the reported prevalence, the current study was proposed to determine the burden of G6PD deficiency in Pathan patients attending a tertiary care health facility in Peshawar, in order to validate the previous findings.

2. MATERIALS AND METHODS

A retrospective study was conducted at Hayatabad Medical Complex, Peshawar, Pakistan. The 1280-bed capacity hospital is a well-equipped tertiary care health facility that provides medical services across the province at a very low cost and also caters for patients from the neighboring country of Afghanistan. Peshawar is the capital city of Khyber Pakhtunkhwa, and the residents are mostly Pashtun, constituting more than 90% of its population.

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Data were retrieved from the Hospital Management and Information System (HMIS; from January 2017 to December 2018). The patients included in this study were of both sexes that came from all districts of Khyber Pakhtunkhwa, excluding Afghani patients.

Among the different methodologies used for estimation of G6PD, dye decolorization qualitative method is used in our setting, which uses the diagnostic reagent kit (BinaxNOW, Alere, USA) for determination of the G6PD activity from the red cell hemolysate. Its principle is based on the reduction of Nicotinamide Adenine Dinucleotide Phosphate (NADP) to NADPH with the help of phenazine methosulfate, which reduces blue-colored 2,6-dichlorophenol indophenol into its colorless form. The rate of decolorization is proportional to the enzyme activity (G6PDH) present in the red cells. The advantage of color decolorization qualitative method is that it is a simple, more specific visual method, requires no colorimeter, and is highly economical. The result interpreted on the basis of decolorization time in between 10 and 60 min was considered normal, whereas that requiring greater than 60 min was considered abnormal (G6PD deficient). Statistical analyses were performed using SPSS (version 21; IBM, Armonk, NY, USA) software. Descriptive statistics was used for data analysis. Ethical approval was granted by the ethical review board of the hospital.

3. RESULTS

A total of 1440 patients were screened for G6PD deficiency; eventually, data from 1402 patients were included in the final analysis. Thirty-eight patients were excluded owing to inappropriate blood sampling taking/phlebotomy error, error in result entry, or error in the sampling process. The mean (standard deviation) age of patients was 15.02 ± 15.50 (range, 0.50–91.50) years. Of the total, 1095 (78.1%) were male and 307 (21.9%) were female. Age groups and sex-based distribution of the study population is shown in Table 1.

The frequency of G6PD deficiency was 12.50%. On comparison by age, it was found that the highest proportion was in the age groups of <5 years (76; 43.4%) and 20–40 years (37; 21.1%). Meanwhile, the lowest deficiency was observed in those who were >60 years (2; 1.1%) and 40–60 years (10; 5.7%). Furthermore, the frequency of deficiency differed by sex, with 151 (13.79%) of male patients versus 24 (7.82%) of female patients (Table 2).

As shown in Table 3, the majority of patients were male (151; 86.29%). The highest proportion of deficiency in males was found in the age group of <5 years (73; 48.3%), whereas in females the highest frequency was noted in age group 20–40 years (14; 58.3%).

Table 1 | Age groups and sex-based distribution of study population

Age groups (years)	Sex, *N*(%)		
	Male	Female	Total
<5	473 (43.2)	89 (29.0)	562 (40.1)
5–10	112 (10.2)	22 (7.2)	134 (09.6)
10–20	206 (18.8)	46 (15.0)	252 (18.0)
20–40	227 (20.7)	117 (38.1)	344 (24.5)
40–60	63 (5.8)	26 (8.5)	89 (06.3)
>60	14 (01.3)	7 (02.3)	21 (01.5)
Total	1095 (100)	307 (100)	1402 (100)

Table 2 | Frequency of G6PD deficiency by age groups and sex in total patients

Age groups (years)	G6PD status, *N* (%)		Total, *N*(%)
	Nondeficient	Deficient	
<5	486 (39.6)	76 (43.4)	562 (40.1)
5–10	111 (9.0)	23 (13.1)	134 (9.6)
10–20	225 (18.3)	27 (15.4)	252 (18.0)
20–40	307 (25.0)	37 (21.1)	344 (24.5)
40–60	79 (6.4)	10 (5.7)	89 (6.3)
>60	19 (1.5)	2 (1.1)	21 (1.5)
Total	1227 (100.0)	175 (100.0)	1402 (100.0)
Sex			
Male	944 (76.9)	151 (86.3)	1095 (78.1)
Female	283 (23.1)	24 (13.7)	307 (21.9)
Total	1227 (100)	175 (100)	1402 (100)

Table 3 | Age groups and sex distribution of G6PD-deficient patients

Age groups (years)	Male, *N*(%)	Female, *N*(%)	Total, *N*(%)
<5	73 (48.3)	3 (12.5)	76 (43.4)
5–10	23 (15.2)	0 (0.0)	23 (13.1)
10–20	23 (15.2)	4 (16.7)	27 (15.4)
20–40	23 (15.2)	14 (58.3)	37 (21.1)
40–60	7 (4.6)	3 (12.5)	10 (5.7)
>60	2 (1.3)	0 (0.0)	2 (1.1)
Total	151 (100)	24 (100)	175 (100)

4. DISCUSSION

Glucose-6-phosphate dehydrogenase is the most common human enzyme deficiency worldwide [12]. It was first reported in a study on Pathans by Stern et al. [13]. In this study, the frequency of G6PD enzyme deficiency is 12.50%. Males were found to have a higher incidence (13.79%) compared with females (7.82%). The highest proportion of overall G6PD enzyme deficiency was noted in the age groups of <5 years (76; 43.4%) and 20–40 years (37; 21.1%). The highest proportion of deficiency in males was found in the age group of <5 years (73; 48.3%), whereas in females the highest frequency was noted in the age group 20–40 years (14; 58.3%).

A meta-analysis by Nkhoma et al. [14] showed that G6PD deficiency had a global prevalence of 4.5%, with an incidence of 1.8% in Pakistan [14]. Similarly, a study by Kumar et al. [15] showed an overall burden of 8.5% in the Indian population. A study conducted in China showed a 7.28% G6PD deficiency [16]. Moreover, prevalence in Iran was 6.7% [17]. A study performed among US military personnel showed that African-American males (12.2%) and females (4.1%) along with Asian males (4.3%) had the highest prevalence of G6PD deficiency [18].

Our finding is consistent with earlier studies conducted locally. There is substantial evidence to believe that the prevalence of G6PD deficiency in Pakistan ranges from 1.8% [9,19], with the highest level (8.6%) recorded among Pathans [11]. Ali et al. [19] reported a rate of 8% in Pathans, whereas Bouma et al. [10] reported that G6PD deficiency in adult male Pathans was 11.4%. Similarly, Khattak et al. [11] reported 12% G6PD deficiency in adults with

hemolytic anemia in Khyber Pakhtunkhwa. Moreover, the earlier study also showed high prevalence in Northern Pakistan, which varied from 2% to 8% in various ethnic groups [20]. Another hospital-based study by Khan et al. [9] showed an 8.3% prevalence in Pathans compared with 3.5% in Punjabis.

In our study, a significant number (76; 43.4%) of participants were younger than 5 years. This finding is consistent with earlier studies conducted in Pakistan. A study on school children (5–10 years old) in Mardan District showed an overall 10% G6PD deficiency [21]. Similarly, a hospital-based study in Peshawar reported that 9% of neonates were G6PD deficient presenting with jaundice [22]. In contrast to our results, Hussain et al. [23] reported 16% of neonates were admitted with jaundice [23]. Another study reported the incidence of G6PD deficiency to be 26% in a district-level hospital Timargara Dir [24]. In addition, an institution-based study in Peshawar reported 11% G6PD-deficient infants with jaundice [25]. In this study, 13.4% of the female patients were also G6PD deficient. Almost similar findings were observed by Hayat et al. [26], whose study focused on neonates, whereas a study from Sargodha reported a much lower percentage of G6PD deficiency in females 0.7% [27]. A recent hospital-based study reported 8% G6PD deficiency in female infants with jaundice [25]. The disease primarily affects males because it is an X-linked disorder. However, females can also be clinically affected because of the skewed lyonization of the X chromosome. Our finding emphasizes the need to set up neonatal and child screening programs to facilitate the identification and effective management of neonates and G6PD-deficient children.

Because a significant proportion of G6PD-deficient people were reported in our study and because G6PD-deficient individuals are highly vulnerable to life-threatening hemolysis, screening tests implementation and educational programs are warranted in these high-risk areas irrespective of sex. Females inherit two copies of the X chromosome; early in embryogenesis one of them is inactivated in a random process of lyonization [28]. G6PD deficiency-related severe hemolysis had been observed in adult heterozygous females who were not biochemically deficient at birth [29]. This phenomenon is explained by the lyonization of the X chromosome.

Glucose-6-phosphate dehydrogenase deficiency management should include avoidance of drugs and foods that predispose to hemolysis, provision of safe red cell transfusion to manage acute hemolysis in acutely affected children, and facility of dialysis services to treat acute renal failure. Genetic studies should also be conducted in the future to look for skewed X chromosome inactivation especially in middle-aged and elderly women.

It is worth mentioning that one limitation of this single-center study is its retrospective design. Other limitations include lack of information on risk factors such as comorbidities, presenting complaints of patients (purpose of visiting the hospital), drug(s) used, and family history. Hospital doctors usually order G6PD tests in pediatric patients to look for the cause of jaundice and anemia, and in adult patients prior to giving antimalarial drugs (primaquin) to destroy hypnozoites of *Plasmodium ovale* and *Plasmodium vivax* in the liver cells; however, the exact reason for the G6PD test was unknown in this study. Other factors were the program used to retrieve data and the limited generalizability of the results. Female participants were outnumbered by males as age might be due to a selection bias. Expression of G6PD deficiency may increase in women older than 65 years; it should be noted that females in our sample were much younger than 65 years and were of childbearing age.

5. CONCLUSION

The frequency of G6PD deficiency was higher among patients in the age group of <5 years with male preponderance. Moreover, female patients were also found to be G6PD deficient. This study's results portray the high burden of G6PD deficiency in Pathans, which is consistent with the available literature on the subject, and results show that G6PD deficiency is relatively more prevalent in this area. We conclude that screening and educational programs for G6PD deficiency are necessary in these high-risk areas irrespective of sex to prevent G6PD deficiency-related morbidity. It is also recommended that a detailed genetics analysis study be conducted to determine the spectrum of mutations in the local female population. Further analysis of risk factors of comorbidity, drugs, family history, etc., should be done.

CONFLICTS OF INTEREST

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

AUTHORS' CONTRIBUTION

ZH and IA contributed in study conceptualization and writing (review and editing) the manuscript. ZH, IA and MK contributed in data curation and writing (original draft). ZH and IA contributed in project administration. IA and FK contributed in formal analysis and writing (review and language editing) of the manuscript. All authors read and approved the final version.

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