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ORIGINAL ARTICLE

Incidence of G6pd Deficiency in Young Asymptomatic Males in Pakistan

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ABSTRACT

Background: NADPH is crucial for glutathione reduction. Deficiecy of G6PD leads to excessive oxidised glutathione that denatures hemoglobin and forms Heinz bodies. Heinz bodies damages RBC membrane and cause premature removal of cells by spleen. G6PD deficiency is the most common X-linked inherited red cell enzymopathy that leads to hemolytic anemia and neonatal jaundice in enzyme deficient patients under oxidative stress. G6PD is the rate limiting enzyme in pentose phosphate pathway, a dominant form of glycolysis in RBCs. G6PD converts glucose-6 phosphate into 6-phosphonogluconolactone and reduces NADP to NADPH.

Objective: To determine incidence of G6PD deficiency in young healthy males in Pakistan.

Study design: A descriptive cross sectional study

Place and duration: Study was carried out at PAF Hospital Sargodha from Jan 2021 to Feb 2023

Methodology: G6PD levels were checked in young healthy male volunteers of 12 to 18 years of age, after taking informed consent from subjects and their parents.

Results: Out of 1493 volunteers, only 61 were G6PD deficient and rest all had normal levels. This shows an incidence of 4.08% in our population.

Conclusion: Comparing with previous studies suggests 2-4% incidence of G6PD deficiency in Pakistani population. A larger study including females and studying variants of disease is needed. Patients with lab confirmed P.Vivax should get screened for G6PD deficiency, so that they receive Primaquine.

Keywords: Incidence, G6PD deficiency, Malaria, Primaquine.

INTRODUCTION

G6PD is the rate limiting enzyme in pentose phosphate pathway, a dominant form of glycolysis in RBCs. G6PD converts glucose-6 phosphate into 6-phosphonogluconolactone and reduces NADP to NADPH. NADPH is crucial for glutathione reduction[1]. Deficiecy of G6PD leads to excessive oxidised glutathione that denatures hemoglobin and forms Heinz bodies. Heinz bodies damages RBC membrane and cause premature removal of cells by spleen. G6PD deficiency is the most common X-linked inherited red cell enzymopathy that leads to hemolytic anemia and neonatal jaundice in enzyme deficient patients under oxidative stress[2]. It was 1st described in 1956 while investigating Primaquine (an antimalarial drug) sensitivity of erythrocytes[3]. Greater than 150 different mutations and isoenzymes have been described since then, most of which are prevalent in malaria endemic countries and support malaria protection hypothesis but global migrations is now increasing its incidence even in western countries[4] [5] [2] [6].

Pakistan is a malaria endemic country. According to WHO report , from Jan to Aug 22, over 170000 laboratory confirmed cases were reported with suspected cases reaching 3.4 millions. Out of 170,000 lab confirmed cases 77% were due to plasmodium vivax (P.vivax) and 23% were due to plasmodium falciparum (P. falciparum)[7]. P. vivax exists in dormant stage in liver in form of hypnozoites and can reactivate to blood stage infection after weeks, months or even years. Primaquine prophylaxis can eliminate this hypnozoite stage[8]. Primaquine damages RBCs to burst and cause severe hemolytic anemia in G6PD enzyme deficient individuals[9], so enzyme levels must be checked before administering primaquine prophylaxis or treatment. Young healthy individuals tend to participate in outdoor games and strenous physical activities, which can also lead to increased oxidative stress[10].

In pakistan previously conducted studies showed a 2-4% incidence of G6PD enzyme deficiency[1] [11]. We conducted this study in healthy young voulnteers to get an update of data as most of the affected population are male members of society due to its X linked recessive trait.

METHODOLOGY

This study was conducted in PAF Hospital Sargodha from Jan 2021 to Feb 2023. 1493 young healthy male volunteers of 12 to 18 years of age, from all across the country were recruited in this study. Informed consent was taken from them and their parents. Their G6PD levels were performed in labs and data was collected.

RESULTS

Total 1493 young healthy males with no known comorbids participated in this study and 61 of them turned out to be G6PD deficient i.e 4.08% . 431 were recruited in study during year 2021, out of which only 11 were deficient with an incidence of 2.5%. 555 participated in 2022 and 16 of them were enzyme deficient, making an incidence of 2.88%. Total 507 males participated during 2 months duration of 2023 and 34 of them were enzyme deficient, which makes an incidence of 6.7%.

Table 1: G6PD year wise deficient

Year	Number of tests	Enzyme deficient	Percentage
2021	431	11	2.5%
2022	555	16	2.88%
2023	507	34	6.7%
Total	1493	61	4.08%

DISCUSSION

G6PD deficiency affects about 400 million people worldwide; most of them remain asymptomatic until exposed to severe oxidative stress including exposure to certain medications and infections [12]. The most common manifestation of enzyme deficiency is neonatal jaundice and acute haemolytic anaemia, which is usually triggered by an exogenous agent. Some G6PD variants cause chronic haemolysis, leading to congenital non-spherocytic haemolytic anaemia[2].

A study in 2020 recommended universal screening of G6PD deficiency in neonates to prevent, diagnose and manage hyperbilirubinemia induced neurotoxicity or kernicterus in infants. Study mentioned G6PD deficiency as one of three most common causes of pathological hyperbilirubinemia in infants [6].

A literature review of 23 papers and 1 website was published in 2009 which revealed highest prevalence of G6PD deficiency in Africa, southern Europe, the Middle East, Southeast Asia, and the central and southern Pacific islands; however it revealed that disease is emerging now worldwide due to mass migrations. Authors recommended that suspected individuals should be

screened, oxidative stressors should be avoided in deficient and they should be informed about risk and features of hemolytic crisis. They further recommended that clinician must be able to identify hemolytic crisis and should admit such patients in close observation [13].

A 5 year retrospective study of Egypt published in 2018 showed data of 1000 G6PD deficient pediatric patients who presented with hemolytic crisis. Precipitating cause was food in 83.4% cases, infections in 12.4% cases and drugs in 4.2 cases. Study revealed that most of the patients with acute hemolytic crisis were of 1 to 3 years of age [14].

Another Egyptian study conducted in neonates admitted with hyperbilirubinemia revealed that 8.9% of patients admitted with indirect hyperbilrubinemia were G6PD deficient and all were males [15].

A study in Sub Saharan Africa revealed prevalence of 15.3% [16]. A meta-analysis in 2009 reported highest incidence in Sub Saharan African countries out of 88 countries included [17]. A study in Tehran revealed incidence of 2.1% in newborns with 3 fold increased risk of hyperbilirubinemia in G6PD deficient individuals [18]. The prevalence of G6PD in India varies from 5.7 to 27.9 % in different tribes [19].

A review article by a Pakistani Author in 2013 reveals incidence of 2 to 4% in Pakistani males with higher incidence in Pathans i.e 8%. Study also documented from previous literature that out of multiple neonatal jaundice related admissions, 8% had G6PD deficiency [1]. An older study on patients with anemia revealed an overall incidence of 1.36% and 3.4% in anemic individuals [20]. A study in healthy young adults revealed incidence of 1.8% with no ethnic variability except in Pathans[21]. An article on molecular genetics revealed that G6PD Mediterranean was commonest variant in Pakistani population i.e 78% of the sample, followed by G6PD Chattham and Orissa which were 5% and 0.7% respectively [22].

A study was published in 2017 which proposed a model that a step wise increase in daily primaquine dose will be safer in milder G6PD deficiency [9].

CONCLUSION

Data from our study and comparing with previous studies suggests 2-4% incidence of G6PD deficiency in Pakistani population. A larger study including females and studying variants of disease is needed to get actual incidence of disease. At least all patients with lab confirmed P.Vivax should get screened for G6PD deficiency, so that they receive Primaquine prophylaxis to kill hypnozoites and burden of blood stage active disease can be reduced.

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