# Frequency of G6PD Deficiency in Anemic Patients Visiting to Rehman Medical Institute Peshawar

**Rahim Ahmad[1] , Ijaz Ahmad[2], Naheed[3] ,Tanveer tara [4],Tajala[5],Abdul Hannan yousafi [6] Umair rasool[7], Sadia khalil[8],Bilal Ahmad[9], Zeeshan Ahmad[10*]**

[1]Baqai institute of Hematology, Medical University Karachi.

[2] Department of pathology MTI, HMC Peshawar.

[3] Department of Dermatology MTI HMC / KGMC Peshawar

[4] Department of Medical lab Technology National Skill University Islamabad, Pakistan.

[5] Department of Allied health sciences, Sarhad University of Science and Information Technology Peshawar, Pakistan.

[6] Department of Medical laboratory Technology, Riphah international University Lahore

[7] Department of physiology ,Riphah college of veterinary sciences.

[8] Institute of pharma.phys. and Pharmacology Faculty of Veterinary sciences

[9]Department of Medical Lab Technology, Abbottabad Univeristy of Science and Technology

[10]Department of Microbiology, Hazara University Manshera kpk,Pakistan

***Corresponding author:** zeeshanmicro100@gmail.com

## Abstract

**Objectives:** To identify the frequency of glucose-6-phosphate dehydrogenase (G6PD) Deficiency in Anemic patients in tertiary care hospital Peshawar among male and female patients.

**Method:** A Cross-sectional study was conducted among G6PD deficient patients of KPK in tertiary care hospital of Peshawar. Participants were selected through convenient sampling technique. The area of interest was Rehman Medical Institute (RMI) laboratory Peshawar.

**Result:** Total number of 104 patients was enrolled in this study, conducted in tertiary care hospital. Among them 86 (82.76%) patients were males and 18(17.3%) were females. In out of 104 patients, 7 patients were G6PD deficient. Only one female patient was found G6PD deficient while rest of G6PD deficient patients was males. Result showed that G6PD deficiency anemia were more frequent in males comparatively than females. All variables including gender of the patients, hemoglobin level, G6PD status and indirect bilirubin were compared to each other. Study result show that no significant co relation was exists between G6PD assay and hemoglobin level. Significant co-relation over exists among G6PD level and indirect bilirubin with P value 0.006 as shown in table 03. Result revealed that lower the G6PD level will be high the bilirubin level.

**Conclusion:** In out of 104 patients, 7 patients were G6PD deficient. Only one female patient was found G6PD deficient, while rests of G6PD deficient patients were males. Thus,

this study shows that G6PD deficiency anemia was more frequent in male comparatively than females.
**Key Words:** G6PD, anemic patients, hemoglobin, bilirubin

**Tob Regul Sci.™ 2022;8(1): 2278-2289**
**DOI: doi.org/10.18001/TRS.8.1.172**

## INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) is an important enzymes which is present in many amounts in different cells of the human body, including red blood cells (1). G6PD is required for production of reduced glutathione in red blood cell (RBC). G6PD is an important enzyme for the regulation of many biochemical reactions in the body and it also keeps blood cells healthy for appropriate function and to maintain normal life span (2). It catalyses the initial reaction of the pentose phosphate cycle (PPC) through glucose 6 phosphate (G6P) is oxidized to 6-phosphogluconolactone which then produces Nicotinamide adenine dinucleotide phosphate (NADPH). PPC changes glucose into pentose phosphates and their products, reducing power in the form of NADPH. Then in RBCs, the NADPH is vital for to defence against oxidative stress. In the absence of glutathione oxidant which form haemolysis and where it can leads to anaemia (3). G6PD deficiency affects RBCs because, most of known mutations in gene cause decreasing in the stability of enzyme, and hence these cells do not keep the ability to synthesis normal proteins level, so the enzyme level decreases as well as the cells' age, during their 120 days lifespan in circulation, it does not remain at the normal level. Secondly, RBCs are quite vulnerable to their oxidative stress which forms exogenous oxidizing agents in the blood; the haemoglobin cycles between its deoxygenated and oxygenated are forms ,so the oxygen radicals continuously generating. G6PD have weakened the ability to tolerate stress when they are deficit; therefore, haemolysis occurs (4). G6PD deficiency is present in more than 400 million people worldwide (5). About 7.5% of population worldwide are the carriers for G6PD deficiency; it ranges from 0.1% in Japan, also in some European areas. 35% people are from different countries in the world are; Africa, Southern Europe, the Middle East, and Southeast Asia (6). Deficiency states is common in tropical and subtropical regions and a report was submitted to World Health Organization (WHO) by Saleem (1993) that Glucose6-phosphate dehydrogenase deficiency was reported as 3.8% in Pakistan (2). A recent meta-analysis where they have showed 4.5% G6PD deficiency globally prevalence, and also indicated an incidence of 1.8% in Pakistan; However, our locally published non indexed papers had been ignored and their reported incidences are of 2% to 4% in Pakistani males while a high incidence of 8% in Pathan's tribes (7). The majority of G6PD deficient individual shows no manifestation while publically health importance of this condition come from the effected patient and their potential risk of developing clinical symptoms. When their cells are exposed to exogenous oxidative stresses, so they cannot defend themselves and their symptoms appears. Enzymes deficiency plays in important role that how a

symptom is severe and their required subsequent treatment. It also depends on the nature dose of oxidative agents, course of exposure, and additional oxidative stress and pre-existing factor i.e. age, haemoglobin concentration and concurrent infection (4). The most effective management strategy for G6PD deficiency is to prevent haemolysis by avoiding oxidative stressors which are caused by taking of certain drugs and fava beans. Previous haemolysis episodes or a screening programmed also played important roles. In rare cases usually with children, the transfusion of red blood cells is required due to acute haemolysis leading to severe anaemia. A statement has been made that vitamin E, due to its quality of anti-oxidant effect, it might help in the protection against chronic haemolysis (8). G6PD variants are classified on the basis of the severity of G6PD deficiency which is based on the level of enzyme activity which are then compared with the normal activity in included population (9). G6PD deficiency was discovered when the outgrowth of haemolytic anaemia was occurred in some individuals, while they were treated for malaria with 6-methoxy-8-aminoquinoline drugs. Cordes5, in 1962 also reported the occurrence of acute haemolysis in such patients. Later at 1956, it was discovered by Alving and his colleague, as they were investigating haemolytic anemia that was occurring in the same individual who were treated for malaria with Primaquin in blacks (African). It was also recognized that G6PD deficiency was not only confined to African (Black) but also for other ethnic groups to prevent G6PD deficiency worldwide (10)(7). Haemolysis is usually associated with taking of fava beans as well as certain drugs such as, sulphonamides and anti-malarial etc. Hemolytic anaemia in diabetics has predictably been associated with bacterial infections and hemolytic drugs (11). The genes that are coded for G6PD are situated on locus q2 (12), where it contains 13 exons and 12 introns and is 18.5 kb in length. The active enzymes are variably composed of two or four identical 515 amino acid subunits in which each monomer has a molecular weight of 59 kda (13). G6PD enzymes are exist in its dimer or tetramer active form (14). The first exon is noncoding and the other 12 are ranges from 120 to 236 bp. G6PD genes are the highly polymorphic locus in human being which contains over 400 allelic variants in their genes (15). Homozygous male and females have high risk of haemolytic crisis with mutations than in heterozygous females although, due to X-chromosome inactivation heterozygotes are also at some risk (16). Males have only one G6PD gene that must be either normal or deficient while, females who have two genes, these can be either normal, deficient or intermediate (17). In 1950s, a study about family history showed that G6PD deficiency was transmitted from mother to son rather than from father to son, and its evidenced are made by the classical pattern of X- linked inheritance (18). Throughout the world more than 180 mutations have been described. Currently different methods such as, Polymerase Chain Reaction (PCR) or Restriction Fragment Length Polymorphism (RFLP) and Denaturing High Performance Liquid Chromatography (DHPLC) are used to detect G6PD mutations while, on the basis of technical simplicity and convenience, the Reverse Dot Blot (RDB) method have been used to detect genetic disorders (19).In addition to haemolysis, some patients often require exchange transfusion which has neonatal jaundice. Sign and symptoms of G6PD deficiency include abdominal and back pain,

gallstones, splenomegaly, dizziness, headache, dyspnea and palpitation etc. (20). While investigating G6PD deficiency, CBC will show normochromicnormocytic anaemia. White cell count and platelets are typically normal but might be elevated after haemolysis. Reticulocytosis can also be seen and peripheral investigation typically shows sphercoytes, polychromasia, bite and blister cells. At any acute haemolysis, indirect bilirubin and LDH are also elevating. Several tests are used for the diagnoses of G6PD deficiency for examples; Fluorescent Spot Test is used when erythrocytes contain enough functional G6PD in which NADP1 is converted into NADPH. After the addition of G6PD and NADP1, the spot of bloods are fluoresces, when they are motivated at 340 nm (Tan and Whitehead 1969; Beutler 1971). The fluorescent spot test is mostly appropriated for the finding of homozygous males and females. Spectrophotometric assay and Cytochemical assay are also used for the devotion of G6PD deficiency (21).

## MATERIAL AND METHODS

### Study Design

Descriptive Cross-Sectional stud was conducted at Rehman Medical Institute (RMI) Peshawar,Department of haematology pathology laboratory which is tertiary care setup. The study of duration from August 2016 to November 2016.

### Sample Size

Individual of KPK patients who were visited to Rehman Medical Institute Laboratory and submitted the sample for CBC, Indirect Bilirubin and G6PD. A total of 104 samples were collected in the Rehman Medical Institute Laboratory, sample received from the patient visiting to Rehman Medical Institute Peshawar (RMI) both male and female adult and child were enrolled in this study.

### Sample Collection Technique

For the purpose of blood sample collection; the collection site was cleaned with antiseptic solution to kill germs and harmful microbial agents. With the help of export phlebotomist, blood was drained from antecubital vein by means of sterilized syringe and that needle was carefully inserted into the individual vein and finally, the blood was collected. The drawn site was usually situated inside the elbow or back of the hand. About 3 ml bloods were collected from all individual in EDTA tube for complete blood count (CBC) and G6PD assay while 02 ml blood were collected in red top tube (without anticoagulant) for determination of bilirubin assay.

### Complete blood count

All the samples were determined using automated cell analyzer (CELL- DYNE RUBY abbot system) and then the blood samples were immediately transported to the Rehman Medical Institute laboratory. In complete blood counts following parameters were analyzed which includes hemoglobin (HB), Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC), and red blood cell (RBCS)

count. An individual, whose HB level was less than the standard level then their smear were prepared and observed under microscope for further investigation.

## Cell dyne ruby hematology analyzers

EDTA-anticoagulated blood samples were normally process in the instance the cell dyne ruby CBC operational mode. The cell dyne ruby CBC comprises 22 different parameter with many of the primary measurement being made by laser light flow cytometry. While using a single reagent, an analysis was accomplished on up to 10,000 cells from a single dilution and was also captured up to 40,000 data points. The working of hematology analyzer was on technology "MAPSS". MAPSS Laser Technology proved high level of interrogation. MAPSS results were displayed on elegant, multiple, and Color-coded scatterplots. At has discriminated well between neutrophils, eosinophil, basophils, monocytes and lymphocytes. The immature cells and interfering substances was Identified and classified. "MAPSS" technology was providing laser-accurate optical readings for WBCs with differential. Accurate identification using 4-anglescatter measurements. Multiple scatterplot analysis was used for identification of abnormal cells and interfering substances.

## First passed optical platelets and Rights the first time:

The CELL-DYN Ruby™ 2-angle optical Platelet which was count accurately enumerates and their sizes were helping to make ensure first pass reportable results. Sometime, these reduces the reflex testing due to interference from microcytic RBCs and the RBC fragments as well as WBC and non-platelet particles.

## G6PD Enzyme Assay

Nicotinamide adenine dinucleotide phosphate (NADP) will reduce by G-6-PDH in the presence of G-6-P. The rate of formation of NADPH is proportional to the G-6-PDH activity and is measured spectrophotometrically as it increases in absorbance at 340 nm.

## Quality Control

Reliability of test results should be monitored by the use of normal and abnormal control materials with in each run. Trinity Biotech Glucose -6-Phosphatase Dehydrogenase Controls such as the following are suitable for this purpose: Deficient, Catalogue No. G6888; Intermediate, Catalogue No. G5029; and normal, Catalogue No. G6888. A control range should be established by the laboratory to determine the allowable variation in day to day performance for each level of control. Trinity Biotech Reliant C program may also be used to monitor the assay performance.

## Calculation:

$$\text{A per min: } = \frac{FINAL\ A - INITIAL\ A}{5}$$

G-6-PDH activity is expressed as U/$10^{12}$ erythrocytes (RBC) or as U/g hemoglobin (Hb).

$$\text{G-6-PDH (U/}10^{12}\text{ RBC)} = \frac{\Delta A \text{ per min} \times 3.01 \times 10^{12} \times TCF}{0.01 \times 6.22 \times (N \times 1016) \times 1000}$$

Where;

3.01= Total reaction volume (ml)

$10^{12}$= Factor for expressing activity in $10^{12}$ cells

0.01= Sample volume (ml)

6.22=Millimloar absorptivity of NADPH at 340 nm

N$x10^6$= Red cell count (red cells/$mm^3$) determined for each specimen

1000= Conversion of red cell count from $mm^3$ to ml

TCF= Temperature correction factor (1 at 30 C0)

This equation reduces to:

$$\text{G-6-PDH (U/}10^{12}\text{ RBC)} = \Delta A \text{ per min} \times \frac{48.390}{N} \times TCF$$

Where =

N = Red cell count divided by $10^6$

TCF=Temperature correction factor (1 at 30Co)

$$\text{G-6-PDH (Ulg Hb)} = \Delta A \text{ per min} \times \frac{100 \times 3.01}{0.01 \times 6.22 \times Hb\ (g/dl)} \times TCF$$

$$= \Delta A \text{ per min} \times \frac{4839}{Hb\ (g/dl)} \times TCF$$

Where

100 = Factor to convert activity to 100 ml

3.01 = Total reaction volume (ml)

0.01 = Sample volume (ml)

6.22 = Millimolar absorptivity of NADPH at 340 nm

Hb (g/dl/) = Hemoglobin concentration determined for each specimen

TCF = Temperature correction Factor (1 at 30 $^0$C )

## RESULT

Total number of 104 patients was enrolled in this study, conducted in tertiary care hospital. Among them 86 (82.76%) patients were males and 18(17.3%) were females show in table 01. In out of 104 patients, 7 patients were G6PD deficient as shown in table 02. Only one female patient was found G6PD deficient while rest of G6PD deficient patients were males figure 03. Result showed that G6PD deficiency anemia were more frequent in male comparatively than females.

**Table 01:** Gender wise distribution of the study population in Table.

| | | Frequencies | Percentages | Valid Percentages | Cumulative Percentages |
|---|---|---|---|---|---|
| Valid | Male | 86 | 82.7% | 82.7% | 82.7% |
| | Female | 18 | 17.3% | 17.3% | 100.0% |
| | Total | 104 | 100.0% | 100.0% | |

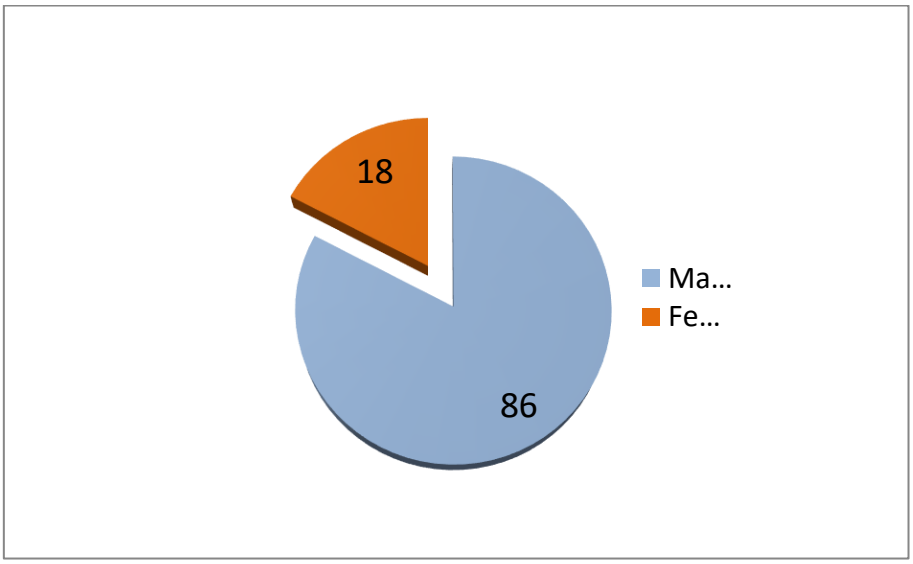


**Figure 01:** Gender Wise Distribution of the Study Population in Pie Chart.

**Table 02:** Prevalence of G6PD deficiency anemia in Table form.

| | Mean | Std. Deviation | N |
|---|---|---|---|
| G6PD Deficient | 1.1586 | .69374 | 7 |
| G6PD Normal | 15.8246 | 4.94962 | 97 |
| | | | |

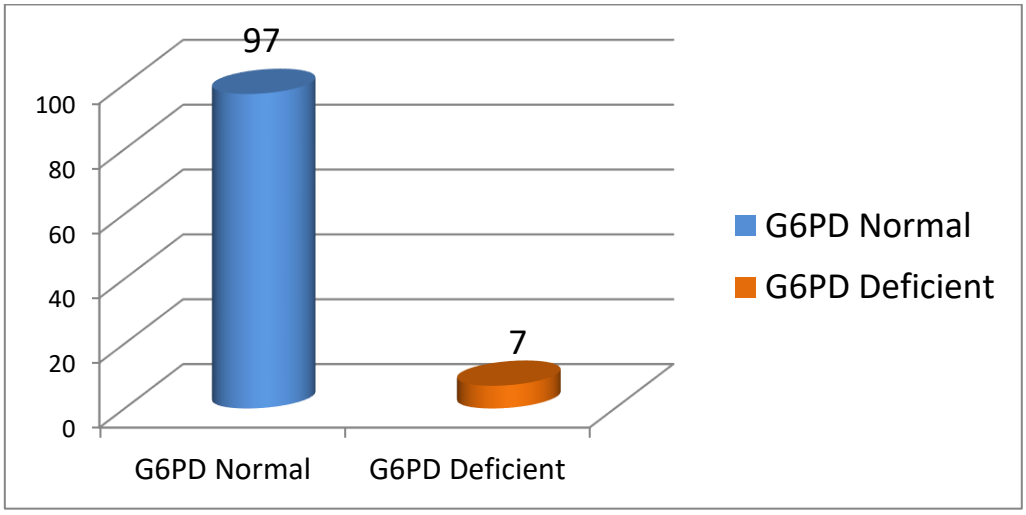


**Figure 02:** Prevalence of G6PD deficiency anemia in Graph form.

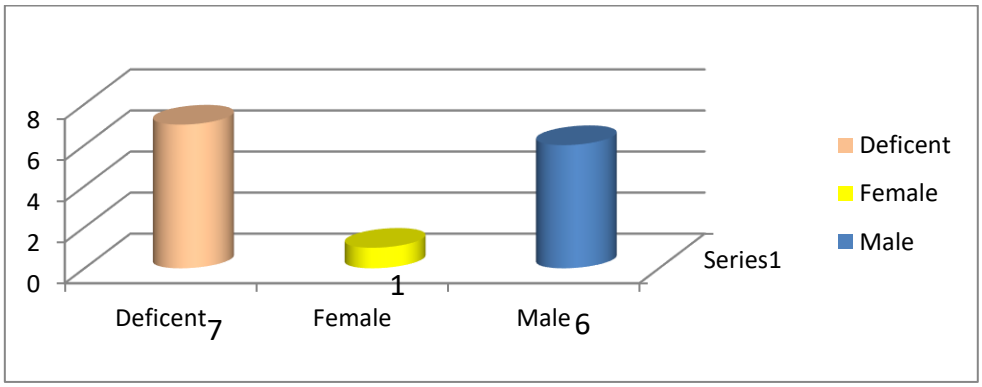


**Figure 03:** Gender Wise Distribution of G6PD Deficiency.

**Table 03:** Co-relation between different variables with P values.

**Paired Samples Test**

| | | Paired Differences | | | | | t | df | Sig. (2-tailed) |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | Std. Deviation | Std. Error Mean | 95% Confidence Interval of the Difference | | | | |
| | | | | | Lower | Upper | | | |
| Pair 1 | G6PD - Indirect B | 2.255933 | 8.233199 | .807332 | .654781 | 3.857084 | 2.794 | 103 | .006 |
| Pair 2 | Hb - G6PD | .379163 | 6.557549 | .643021 | -.896116 | 1.654443 | .590 | 103 | .557 |
| Pair 3 | Gender - G6PD | -13.474394 | 5.853110 | .573945 | -14.612678 | -12.336110 | -23.477 | 103 | .000 |

All variables including gender of the patients, hemoglobin level, G6PD status and indirect bilirubin were compared to each other. Study result show that no significant co relation was exists between G6PD assay and hemoglobin level. Significant co-relation over exists among G6PD level and indirect bilirubin with P value 0.006 as shown in table 03. Result revealed that lower the G6PD level will be high the bilirubin level.

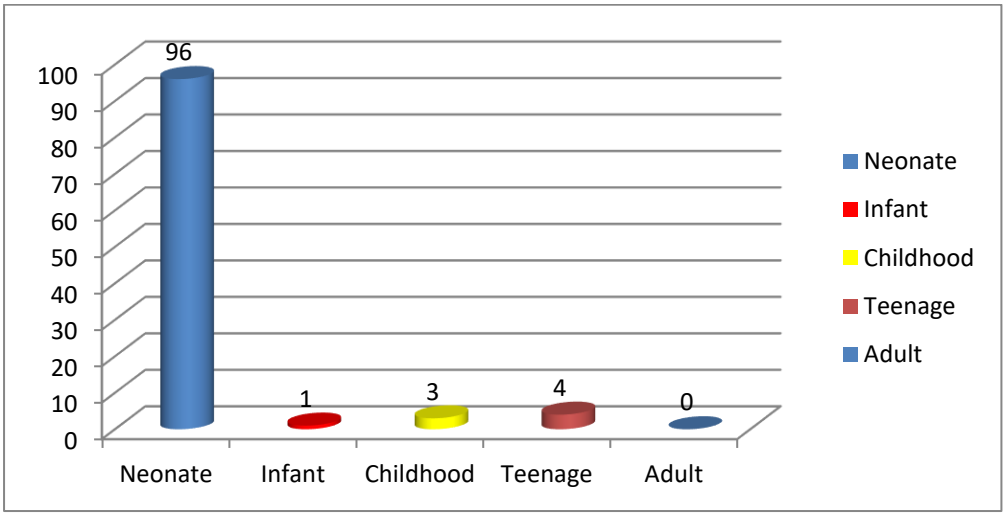


**Figure 04:** Age wise distribution of the studied population in Graph form.

## DISCUSSION

The enzyme glucose-6-phosphate dehydrogenase (G6PD) is an important enzyme in the human body which is present in many amounts in different cells of the body, including red blood cells(1)[1]. G6PD is required for production of reduced glutathione in red blood cell (RBC). It is an important enzyme that regulates various biochemical reactions in the body. It is also responsible for keeping blood cells healthy, so that the blood cells could function properly and live a normal life span (2). G6PD deficiency affects RBCs for two reasons; the main reason is this that most known mutations in gene causes decreasing in the stability of enzyme, hence the cells does not keep the ability to synthesis normal protein level, thus the enzymes level decreases. Secondly, RBCs are very vulnerable to oxidative stress which forms exogenous oxidizing agents in the blood as well as the oxygen radicals continuously generated as haemoglobin cycles between its deoxygenated and oxygenated forms, whenever G6PD activity is deficient, so they weakened their abilities to tolerate stress and thus, the risk destruction such as haemolysis occurs[4]. G6PD deficiency is a supreme common human enzyme defect that is present in more than 400 million people throughout the world(5).Total number of 104 patients was enrolled in this study, conducted in tertiary care hospital. Among them 86 (82.76%) patients were males and 18(17.3%) were females. Out of 104 patients, 7 patients were G6PD deficient. Out of 7 G6PD deficient the number of female patient was 1, while 6 patients were males. A study conducted by Nabeel Al Momen et'al, 2004, by testing the enzyme activity, 83 G6PD-deficient subjects, where 64 participants were males and 19 were females. They showed severely reduced enzyme activity in their red blood cell lysates. While 80 of the normal participants where, 43 participants were males and 37 were females discovered normal activity of the enzyme (14). A study was conducted by Fariba Eghbal, et'al, 2012 and their results showed that males were affected more than females; whereas, Among 196 participants, 125 participants were boys and 71 were girls. While the male to female ratio were equal to 1.76/1.0 with regard to period of year. Haemolytic crisis due to G6PD deficiency occurred largely in spring (173) cases equal to 88.3%) followed by autumn (10 patients equal to 5.1%), winter (7 cases equal to 3.6%) and finally in summer (6 cases equal to 3.1%) with p-value=0.001 were also identified. Peak prevalence of haemolysis was also seen during April and March (20). A study done by Arjumand S. Warsy et'al, 2001 appeared to show that a wide-range of G6PD activities were encountered in the male and female participants' samples. The normal reference range of G6PD was used as 60-130 mU/109 of erythrocytes, with a mean of 95 for Saudi males, and 60-140 mU/109 of erythrocytes with a mean of 100 mU/109 erythrocytes for Saudi females. 23 Individuals with severe G6PD deficiency were considered as those with G6PD activity <20% of the lower normal. Of the total 13,796 males, 1249 were deficient and among the 13,613 females screened, 558 were deficient, giving a frequency of G6PD deficiency of 0.0905 and 0.041 respectively, in the males and females. The samples from different provinces were separated and the frequency of G6PD deficiency were also calculated in each province (12). This study revealed that G6PD deficiency in anaemia was more frequent in neonates. The patients were divided into different ages like

neonates, infants, childhood, teenage and adults. The numbers patients according to different ages neonates were (96), infants (1), childhood (3), teenage (4) and adults (0). Out of the total 96 neonates, 7 (7.29%) neonates were G6PD deficient while rest of the neonates were G6PD normal. It is also observed that no G6PD deficient individual was found in other age of groups.3000 male adults of age between 17 to 23 years were screened for G6PD. 53 (1.8%) participants were G6PD deficient. Past history of fever for more than 7 days was present in 17/53(32%) subjects, and recurrent jaundice in 3/53(5.7%). Liver was palpable in 2/53(3.8%) and spleen in 3/53(5.7%) subjects. Mild anaemia was detected in 2/53(3.8%) and TLC >10 x109/liter in 15/53(28%). There was no statistical difference of frequency of G6PD deficiency among Kashmiris, Punjabis and Sindhis. In Pathans a higher frequency was detected (3.17%, p-value <0.05). Frequency of G6PD deficiency in different ethnic groups was Kashmiris 1.07% (05/460), in Punjabis 1.47% (27/1832), in Sindhis 2.77% (11/397) and in Pathans 3.17% (10/305), thus the Frequencies of G6PD deficiency were 1.8% in young healthy adults with insignificant differences among various ethnic groups except in Pathans group (2). Among 428 children with G6PD deficient, 79 participants were severely ill and 349 participants were with mild disease. Severely ill cases were significantly younger than mild cases. Abrupt onset of Pallor and the passage of cola colour urine were universal presenting symptoms for all the cases. Incriminating factors responsible for haemolysis included ingestion of fava beans (n=399), drug intake (n=30) and infection (n=75). An elevation in serum bilirubin, matching with intravascular haemolysis, a feature in all the 428 children with G6PD deficiency were also identified (6).

## CONCLUSION

For descriptive statistic, frequencies and percentages were calculated for nominal and ordinal data of the participants. The present study was able to determine the standard of result of the Frequency of glucose-6-phosphate dehydrogenase (G6PD) Deficiency in Anaemic patients in tertiary care hospital Peshawar. In out of 104 patients, 7 patients were G6PD deficient. Only one female patient was found G6PD deficient, while rest of G6PD deficient patients were males. Thus, this study shows that G6PD deficiency anaemia was more frequent in female comparatively than males.

## References:

1. Pahlavanzadeh M, Hekmatimoghaddam S, Teremahi Ardestani M, Ghafoorzadeh M, Aminorraaya M. G6PD Enzyme Deficiency in Neonatal Pathologic Hyperbilirubinemia in Yazd. Iran J Pediatr Hematol Oncol [Internet]. 2013;3(2):69–72.Availablefrom:http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3915450&tool=pmcentrez&rendertype=abstract
2. Frequency of glucose-6-phosphate dehydrogenase deficiency in some ethnic groups of Pakistan ORIGINAL ARTICLE FREQUENCY OF GLUCOSE-6-PHOSPHATE

DEHYDROGENASE DEFICIENCY IN SOME ETHNIC GROUPS OF PAKISTAN. 2005;(April).
3. Javadi O, Onsori H. Investigation of Cosenza Mutation in Patients with Deficiency of Glucose-6-Phosphate Dehydrogenase ( G6PD ) in North West of Iran. 2015;5:67–72.
4. Howes RE, Battle KE, Satyagraha AW, Baird JK, Hay SI. G6PD Deficiency. Global Distribution, Genetic Variants and Primaquine Therapy [Internet]. Vol. 81, Advances in Parasitology. Elsevier; 2013. 135-201 p. Available from: http://dx.doi.org/10.1016/B978-0-12-407826-0.00004-7
5. Cappellini MD, Fiorelli G. Glucose-6-phosphate dehydrogenase deficiency. Lancet. 2008;371(9606):64–74.
6. Al-Sweedan SA, Jdaitawi H, Khriesat WM, Khader YY, Al-Rimawi HS. Predictors of severe hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency following exposure to oxidant stresses. Hematol Oncol Stem Cell Ther [Internet]. 2009;2(2):354–7. Available from: http://dx.doi.org/10.1016/S1658-3876(09)50025-8
7. Moiz B. A review of G6PD deficiency in Pakistani perspective. J Pak Med Assoc. 2013;63(4):501–3.
8. Beutler E. G6PD deficiency. Blood. 1994;84(11):3613–36.
9. LaRue N, Kahn M, Murray M, Leader BT, Bansil P, McGray S, et al. Comparison of quantitative and qualitative tests for glucose-6-phosphate dehydrogenase deficiency. Am J Trop Med Hyg. 2014;91(4):854–61.
10. Beutler E. Glucose-6-phosphate dehydrogenase deficiency : a historical perspective Early history. Blood. 2008;111(1):16–24.
11. Agarwal A, Deepak Nayak M, Patil A, Manohar C. Glucose 6 phosphate dehydrogenase deficiency unmasked by diabetic ketoacidosis: An underrated phenomenon. J Clin Diagnostic Res. 2013;7(12):3012–3.
12. Warsy AS, El-Hazmi MAF. G6PD deficiency, distribution and variants in Saudi Arabia: An overview. Ann Saudi Med. 2001;21(3–4):174–7.
13. Soltanian S, Gangi SHM, Yousefi A, Hejazi S, Hitratfar S, Sanati M. Molecular Identification of the Most Prevalent Mutations of Glucose-6-Posphate Dehydrogenase ( G6PD ) Gene in Deficient Patients in Khorasan Province of Iran. 2006;17(2):103–6.
14. Al Momen N, Al Arrayed SS, Al Alawi A. A. Molecular homogeneity of G6PD deficiency. Bahrain Med Bull. 2004;26(4):139–42.
15. Minucci A, Giardina B, Zuppi C, Capoluongo E. Glucose-6-phosphate dehydrogenase laboratory assay: How, when, and why? IUBMB Life. 2009;61(1):27–34.
16. Jamornthanyawat N, Awab GR, Tanomsing N, Pukrittayakamee S, Yamin F, Dondorp AM, et al. A population survey of the glucose-6-phosphate dehydrogenase (G6PD) 563C>T (Mediterranean) mutation in Afghanistan. PLoS One. 2014;9(2).
17. Luzzatto L. Glucose 6-phosphate dehydrogenase deficiency : from genotype to phenotype. Hematol J. 2006;91(10):1303–6.

18. Beutler E. G6PD: Population genetics and clinical manifestations. Blood Rev [Internet].1996;10(1):45–52.Availablefrom: http://www.sciencedirect.com/science/article/pii/S0268960X96900193
19. Peng Q, Li S, Ma K, Li W, Ma Q, He X, et al. Large cohort screening of G6PD deficiency and the mutational spectrum in the Dongguan District in southern China. PLoS One. 2015;10(3):1–10.
20. Eghbal F, Fakoorziba MR, Eghbal MH, Latifnia S. Survey on causes of hemolysis in glucose-6-phosphate dehydrogenase (G6PD) deficient pediatric patients. Pakistan J Med Sci. 2012;28(4):666–9.
21. Peters AL, Van Noorden CJF. Glucose-6-phosphate dehydrogenase deficiency and malaria: cytochemical detection of heterozygous G6PD deficiency in women. J HistochemCytochem[Internet].2009;57(11):1003–11.Availablefrom: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2762880&tool=pmcentrez&rendertype=abstract