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NEONATAL SCREENING OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY IN MISAN PROVINCE, SOUTH EAST OF IRAQ

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Abstract:

Background: *Newborn screening tests look for developmental, genetic, and metabolic disorders in the newborn baby. This allows steps to be taken before symptoms develop and can be treated if caught early. Neonatal screening for glucose-6-phosphate dehydrogenase (G6PD) deficiency has long been established in many countries with high disease prevalence. The WHO recommends screening all newborn for G6PD Deficiency in population with a prevalence of 3-5% or more in male.*

Aims of study: *to estimate the prevalence of G6PD deficiency in Misan Province, South East of Iraq*

Patients and methods: *A cross-sectional study was done in Al-Sader Teaching Hospital in Misan Province during period from November 2015 to December 2015. 170 neonatal cord blood samples (93 male and 77 female) were screened for G6PD deficiency by using a fully quantitative G6PD screening kit with a cut off of 6.4 U/g Hb. Any newborn with an activity less than this level was diagnosed as G6PD deficient.*

Results: *The total detection rate of G6PD deficiency was 8.82%. A 13.97% for male and 2.59% for female with male to female ratio of 5.4:1.*

Conclusion: *There is high prevalence of G6PD deficiency in neonates delivered in Al-Sader Teaching Hospital in Misan Provence. According to the WHO recommendation of neonatal screening for G6PD Deficiency, this will support the belief of need for establishment of neonatal screening for G6PD deficiency in Iraq.*

Key Words: G6PD enzyme, Screening, neonatal jaundice, kernicterus, hemolytic anemia.

INTRODUCTION

Newborn screening tests look for developmental, genetic, and metabolic disorders in the newborn baby. This allows steps to be taken before symptoms develop and can be treated if caught early. [1, 2]

The types of newborn screening tests that are done vary from state to state based in part to disease prevalence, detection rates, and costs. [1] In United States, The newborn screening tests are decided on a state-by-state basis. [3] By April 2011, all states reported screening for at least 26 disorders on an expanded and standardized uniform panel. The most thorough screening panel checks for about 40 disorders. [2, 3] Neonatal screening for glucose-6-phosphate dehydrogenase (G6PD) deficiency has long been established in many countries with high disease prevalence. [1, 2] The WHO recommends screening all newborn for G6PD Deficiency in population with a prevalence of 3-5% or more in male. [4]

It is an X linked genetically determined enzyme disorder, [5] that primarily affects men. Women may be affected if they are homozygous, which occurs in populations in which the frequency of G6PD deficiency is quite high. Heterozygous women (carriers) can experience clinical disease as a result of X chromosome inactivation, gene mosaicism, or hemizygosity. [6]

It is affecting around 400 million people worldwide, [5, 7, 8] representing an overall 4.9% global prevalence. [5] Mostly African, Mediterranean and far –eastern populations. [7, 9]

Historically the fava bean is thought native to the eastern Mediterranean. The oldest known seeds were found in an archaeological dig near Nazareth and date from 6500 BCE. During the third millennium BCE, the cultivation of fava beans spread over the Middle East, North Africa, and central and southern Europe. The consumption of fava beans causes favism (hemolytic anemia) in certain individuals of Mediterranean or African descent. [10] On the other hand, G6PD deficiency was discovered as an outgrowth of an investigation of hemolytic anemia occurring in some individuals treated for malaria in 1926, but 3 decades passed before the mechanism of hemolysis could be understood. [11] In 1956, Carson and colleagues discovered that the hemolytic anemia was caused by glucose-6-phosphate dehydrogenase (G6PD) deficiency. [12]

In the United States, it is most common among African American males; approximately 11-14% is G6PD deficient. [13] A study by Malay 2015, found that the

overall prevalence was 7.7 per cent in different Tribal groups in India. [14] While in the Philippines 2003, the rate was 3.9%. [15]

G6PD Deficiency is a hereditary abnormality in the activity of an erythrocyte enzyme. This enzyme, glucose-6-phosphate dehydrogenase (G6PD) that involved in the pentose phosphate pathway is essential for assuring a normal life span for red blood cells, [7, 16] and for oxidizing processes. This enzyme deficiency may provoke the sudden destruction of red blood cells and lead to hemolytic anemia with jaundice following the intake of fava beans and various drugs. [16]

G6PD Deficiency is the most common red cell enzyme defect that causes hemolytic anemia. [7, 17]

Most persons with G6PD deficiency are asymptomatic. Symptomatic patients can present with neonatal jaundice and acute hemolytic anemia. [7, 17] A small proportion of G6PD deficient individuals have chronic non-spherocytic hemolytic anemia. [18]

The prevalence of neonatal hyperbilirubinemia is twice that of the general population in males, who carry the defective gene and in homozygous females. [19] Kernicterus is a rare complication of neonatal jaundice. [20] But many of the recently reported cases of kernicterus, even in countries with a low overall incidence of the G-6-PD deficiency such as the United States and Canada, have been found to be enzyme deficient. [21, 22]

The most effective management of G6PD deficiency is to prevent hemolysis by avoiding oxidative stress. Screening programs for the disorder are undertaken, depending on the prevalence of G6PD deficiency in a particular community. [18] In areas in which G-6-PD deficiency is endemic, screening may be performed as a matter of routine, simplifying the physicians' role in identifying the high risk nature of these infants. [21] In 2010, newborn screening program for G6PD deficiency was carried out in the United States. [23]

PATIENTS AND METHODS

A cross-sectional study was done in Al-Sader Teaching Hospital in Misan Province. One hundred seventy neonates enrolled in this study were born in Al-Sader Teaching Hospital during period from November 2015 to December 2015.

The total samples were divided into two groups according to gender (93 male and 77 female samples)

A 2 ml, cord blood sample was collected from each neonate by trained nurses in ethylene diamine tetra acetic acid (EDTA) tubes and delivered immediately to the laboratory where investigations were carried out within 24 hours. The red cell G6PD activity, expressed as units per gram of hemoglobin (U/g Hb), was determined by an enzymatic colorimetric assay for the quantitative determination of G6PD enzyme activity using a commercial kit (BioLabo SA 02160, Maizy, France). The assay was performed according to the instructions included in the kit. On the basis of frequency distribution of activity levels, the critical level for diagnosing G6PD deficiency was considered 6.4 U/g Hb. [(24)] Any newborn with an activity less than this level was diagnosed as G6PD deficient.

All blood samples were tested in the laboratory of medical college, Misan University.

Those neonates (whether male or female) were chosen after getting approval consent from their mothers

Exclusion criteria; neonates in whom consent were not approved.

The study protocol was reviewed; approval and official permission were obtained from the Ministry of Higher Education, Misan directorate of health and Al-Sader Teaching Hospital to conduct the present study. Also an informed written consent was obtained from mothers before delivery.

Data were presented in form of table of number and percentage.

RESULTS

A total of 170 cord blood samples were collected, divided into 2 groups according to G6PD enzyme activity: 15 neonatal samples (8.82%) were G6PD deficient while 155 (91.18%) were G6PD normal as shown in table 1.

Table 1. Cord blood samples screening of G6PD enzyme activity among neonates.

Total number of samples	**G6PD deficient No. (%)**	**G6PD normal No. (%)**
170	15 (8.82%)	155 (91.18%)

According to gender classification; the total male samples were 93, in which 13 males were G6PD deficient (forming 13.97% of total male samples) while the total female samples were 77, in which only 2 females were G6PD deficient (forming 2.59% of total female samples).

On the other hand; 80 males were G6PD normal (forming 86.03% out of total male samples) and 75 females were G6PD normal (forming 97.41% out of total female samples) as shown in table 2.

Table 2. Activity of G6PD enzyme among neonates studied in both groups according to gender

Gender	G6PD deficient No. (%)	G6PD normal No. (%)	Total
Male	13 (13.97%)	80 (86.03%)	93
Female	2 (2.59%)	75 (97.41%)	77

DISCUSSION

G6PD deficiency could be a high risk factor causing delay in the treatment of neonatal jaundice [25] and one of high risk perinatal factors in the early neonatal period. [26] So it is essential to carry out neonatal screening for G6PD deficiency to allow prevention and timely treatment. [27]

The current study revealed that the prevalence of G6PD deficiency was relatively high in neonates delivered in Al-Sader Teaching Hospital of Misan Province, it was 8.82%.

Iraq is a large country of approximately 35 million people with different ethnicity in northern, southern and central provinces. In Northern Iraq among the predominantly Kurdish population, the prevalence of G6PD deficiency was 10.9%. [28] Other studies in Baghdad [29] (central and capital city of Iraq) and Basrah [30] (southern Iraq) were screening adult group for G6PD deficiency, in which the results were 6.0% and 12.5% respectively. So when do comparison between Misan and other provinces in Iraq; Misan's result was higher than Baghdad but less than Basrah and Northern Iraq.

These studies in Iraq showed a remarkable variation in the frequency of G6PD deficiency in each province similar to other studies in Iran. [31, 32] Such variation may be attributed to variable G6PD gene and ethnic variations.

For nearby countries; like Iran, in Isfahan (the central state of Iran), the overall prevalence of G6PD deficiency was 3.2%. [31] While it was 12% in the southern part of Iran (Shiraz). [32] In Turkey, the prevalence of G6PD deficiency was 6.9%. [13] It is obvious that Misan's result is less than Shiraz but more than results of Isfahan and Turkey.

In Gulf countries; like UAE [33], Kuwait [13], and Saudi Arabia (Yanbu) [34], the prevalence of G6PD deficiency were 7.9%, 5.5% and 2% respectively. So those countries are less than Misan's result.

On the other hand; the prevalence of G6PD deficiency in Misan was obviously higher than those of India (2%) [35], Guangzhou, China (3.7%) [27] and Philippines (3.9%). [15]

The present study revealed that there was big gender difference in the prevalence of G6PD enzyme deficiency, in which it was higher in males (13.97%) while in females (2.59%) in a ratio of 5.4:1 which is nearly the same ratio of Isfahan (5.5:1). [31]

G6PD deficiency can be detected reliably in homozygous women and hemizygous males with a number of tests. Diagnosing G6PD deficiency in heterozygous women is difficult, and a large part of this group is missed. [24] For this reason, using a fully quantitative G6PD screening kit with a cut off of 6.4 U/g Hb. (as applied in this present study) will detect partially G6PD deficient female neonates (heterozygotes) as shown in a study by Reclos (2000). [24]

These results of Al-Sader Teaching Hospital in Misan Province would reflect an initial estimate about the prevalence of G6PD deficiency in neonates but further studies with a larger sample is required.

In my country, there is a limited number of similar studies for cord blood sampling to screen neonates for G6PD deficiency, instead there are many studies showed that there is a high correlation between G6PD deficiency and neonatal jaundice causing more morbidity and mortality. [36, 37]

The rates of morbidity and mortality can be effectively reduced by neonatal screening for G6PD deficiency. Cohan showed that after the neonatal screening program, the hospitalization rate of patients with G6PD deficiency significantly decreased in southern Iran. [38]

CONCLUSIONS

There is a high prevalence of G6PD deficiency in neonates delivered in Al-Sader Teaching Hospital in Misan Provence. According to the WHO recommendation of neonatal screening for G6PD Deficiency, this will support the belief of need for establishment of neonatal screening for G6PD deficiency in Iraq

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REFERENCES:

1-Waldemar A. Carlo(2015). The Newborn Infant and Other Measures. Nelson Textbook of Pediatrics. 20th ed. 94: 799.

2-Definition of Newborn screening. Available at http://www.medicinenet.com/script/main/art.asp?articlekey=4564

3-Newborn screening(2015). Centers for Disease Control website. www.cdc.gov/ncbddd/newbornscreening.

4-WHO Working Group(1989). Glucose-6-phosphate dehydrogenase deficiency. Bull World Health Organ 67: 601–611.

5-George B. Segel and Lisa R. Hackney(2015). Glucose-6-Phosphate Dehydrogenase Deficiency and Related Deficiencies. Nelson Textbook of Pediatrics. 20th ed. 463: 3515.

6-Minucci A, Giardina B, Zuppi C, Capoluongo E. (2009).Glucose-6-phosphate dehydrogenase laboratory assay: How, when, and why?. IUBMB Life 61(1):27-34.

7-Frank JE. (2005).Diagnosis and management of G6PD deficiency. Am Fam Physician 72(7):1277–1282

8-Galappaththy GN, Tharyan P, Kirubakaran R.(2013). Primaquine for preventing relapse in people with Plasmodium vivax malaria treated with chloroquine. The Cochrane database of systematic reviews; 10:CD004389

9-Usanga EA, Ameen R.(2000) Glucose-6-phosphate dehydrogenase deficiency inKuwait, Syria, Egypt, Iran, Jordan and Lebanon. Hum Hered 50:158–161.

10-Vandaveer, A. (2003). This metabolic Disorder- G6PD. Retrieved July 10, 2011, from http://www.en.wikipedia.org/wiki/Favism.

11-Beutler E.(2008). Glucose-6-phosphate dehydrogenase deficiency: a historical perspective. Blood 111:16-24.

12- Alving AS, Carson PE, Flanagan CL, Ickes CE (1956) Enzymatic deficiency in primaquine-sensitive erythrocytes. Science 124:484–485.
13-Associazione Italiana Favismo(2008). G6PD Deficiency Favism Association. C1996-2008 (cited date 2008) Available at: http://rialto.com/favism/index.htm
14- Malay B, Roshan B, Martin S, Ghosh K.(2015). Glucose-6-phosphate dehydrogenase (G6PD) deficiency among tribal populations of India. Indian J Med.141(5): 516–520.
15- Gonzales E(2007). Manila Bulletin Health Science 11:52.
16-G6PD Deficiency Favism association. What is G6PD Deficiency?
Available at: http://www.g6pd.org/g6pddeficiency.aspx
17-William W., Myron J., Robin R., et al(2011). Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency. CURRENT Diagnosis & Treatment Pediatrics book. 21st edition, 30: 915.
18-Cappellini MD, Fiorelli G.(2008). Glucose-6-phosphate dehydrogenase deficiency. Lancet 371:64–74.
19-Sukumar S.(2000). Glucose-6-phosphate dehydrogenase deficiency. Immunohaemtol Bull 31:1-12.
20-Kaplan M, Vreman HJ, Stevenson DK, etal(2001). Acute hemolysis and severe neonatal hyperbilirubinemia in glucose-6-phosphate dehydrogenase-deficient heterozygotes. J Pediatr.139(1):137-140.
21-Kaplan, Hammerman (2004). Glucose-6-phosphate dehydrogenase deficiency: A hidden risk for kernicterus. Article (PDF Available), in Seminars in Perinatology 28(5):356-364.
22-Olusanya BO, Osibanjo FB, Slusher TM. (2015).Risk factors for severe neonatal hyperbilirubinemia in low and middle-income countries: a systematic review and meta-analysis. PLoS One 10(2)
23- Nock ML, Johnson EM, Krugman RR, et al(2011). Implementation and analysis of a pilot in-hospital newborn screening program for glucose-6-phosphate dehydrogenase deficiency in the United States. J. Perinatol.31: 112-117.
24-Reclos GJ, Hatzidakis CJ, Schulpis KH. (2000)Glucose-6-phosphate dehydrogenase deficiency neonatal screening: preliminary evidence that a high percentage of partially deficient female neonates are missed during routine screening. J Med Screen 7: 46–51.
25- Gundur NM, Kumar P, Sundaram V, Thapa BR, Narang A.(2010). Natural history and predictive risk factors of prolonged unconjugated jaundice in the newborn. Pediatr. Int. 52: 769-772.

26- Abdel FM, Abdel GE, Adel A, Mosallam D, et al(2010). Glucose-6-phosphate dehydrogenase and red cell pyruvate kinase deficiency in neonatal jaundice cases in Egypt. Pediatr. Hematol. Oncol.27: 262-271.

27-J. Jiang, B. Li, W. Cao, X. Jiang, X. Jia, Q. Chen (2014). Screening and prevention of neonatal glucose 6-phosphate dehydrogenase deficiency in Guangzhou, China. J Genetics and Molecular Research 13 (2): 4272-4279.

28-Allawi N, Eissa A, Jubrael J, Jamal S, Hamamy H.(2010). Prevalence and molecular characterization of Glucose-6-Phosphate dehydrogenase deficient variants among the Kurdish population of Northern Iraq. BMC Blood Disorders 10:6.

29-Al-Musawi B, Al-Allawi N, Abdul-Majeed B, Eissa A, Jubrael J, Hamamy H.(2012). Molecular characterization of glucose-6-phosphate dehydrogenase deficient variants in Baghdad city – Iraq. J BMC Blood Disorders 12:4.

30-Hassan MK, Taha JY, Al-Naama LM, Widad NM, Jasim SN.(2003). Frequency of ß-thalassaemia, haemoglobin S and glucose-6-phosphate dehydrogenase deficiency in Basrah governorate, Iraq. J Eastern Mediterranean Health 9 (2): 45-54.

31-Iranpour R, Hashemipour M, Talaei SM, Soroshnia M, Amini A.(2008). Newborn screening for glucose-6-phosphate dehydrogenase deficiency in Isfahan, Iran: a quantitative assay. J Med Screen 15(2):62-64.

32-Abolghasemi H, Mehrani H, Amid A. (2004).An update on the prevalence of glucose-6 phosphate dehydrogenase deficiency and neonatal jaundice in Tehran neonates. Clin Biochem. 37:241–244.

33- Al-Ani S, Baker A, Al-Athmani A, Al-Jesmi B.(2008). Neonatal screening of glucose-6-phosphate dehydrogenase deficiency in Khorfakkan, United Arab Emirates. J Saudi Med. 29 (12): 1826-1828.

34-Mohammed, A.M.(2005) Neonatal screening glucose-6-phosphate dehydrogenase deficiency in Yanbu, Saudi Arabia. J.of Medical screening. 2:170-171

35-Mritunjay, Kulkarni, Gupta, et al (2005). Neonatal Screening for Glucose 6-Phosphate Dehydrogenase Deficiency. J Indian Pediatr. 72 (10): 835-837

36- Al-Hiali S.(2008). Glucose 6 phosphate dehydrogenase deficiency among neonates with hyperbilirubinaemia in western Iraq. Fac Med Baghdad 50 (4).

37-Al-Mendalawi MD.(2010). Epidemiological, clinical and laboratory profile of glucose-6-phosphate dehydrogenase deficiency in the middle and north of Iraq: a comparative study. Eastern Mediterranean Health Journal 16 (8): 846-850.

38-Cohan N, Karimi M, Khalili AH, Falahzadeh MH, Samadi B, Mahdavi MR(2010). The efficacy of a neonatal screening programme in decreasing the hospitalization rate of patients with G6PD deficiency in southern Iran. J. Med. Screen17(2): 66-67.