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Glucose 6 Phosphate Dehydrogenase (G6PD) Deficiency and Neonatal Hyperbilirubinemia

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Abstract: Glucose 6 phosphate dehydrogenase (G6PD) deficiency and Neonatal Hyperbilirubinemia. The Prospecutive study was conducted between June 2017 to June 2018 among icteric neonates in Maternity and Children Hospital, Nejran, Saudi Arabia. A total of 200 icteric neonates were included in study, who were admitted in nursery during study period. Each baby was tested for Complete blood count, Reticulocyte count, ABO and Rh blood types, Direct antiglobin test and quantitative G6PD estimation. Out of 200 icteric neonates 56(28%) were found to be G6PD deficient and 144 (72%) had normal enzyme activity.38.7% were males and 12.3% were females among G6PD deficient neonates. Fisher exact test is 0.00 which is highly significant as $p<0.001$. None of them had kernicterus. Haemoglobin and Reticulocyte count in G6PD deficient neonates is statistically significant as $p<0.01$as compared to G6PD normal neonates. Since the Prevalence of G6PD deficiency in our neonates was relatively high. Early detection of this enzymopathy regardless of sex and close surveillance of affected newborn may be important in reducing the risk of severe hyperbilirubinemia.
Keywords: G6PD Deficiency, Kernictrus, Neonatal Jaundice.

INTRODUCTION

G6PD deficiency is an X-linked recessive disease that results in clinical manifestations such as neonatal jaundice, chronic nonspherocytic anemia, infection and drug-induced hemolysis[1]. The gene that codes for G6PD is located in the distal long arm of the X chromosome at the Xq28 locus.

G6PD variant can be classified G6PD Group A- (CLASS III),G6PD Meditrranean(class II) and class I mutations.G6PD Group A-is moderate form of the disease. RBC contain unstableG6PD enzyme but normal activity in younger RBCs and reticulocytes. Accordingly only older RBCs are hemolysis in a hemolytic episode.G6PD Mediterranean is more severe.G6PD enzyme shows normal stability but very low activity in all RBCs. Class I is often associated with chronic non spherocytic anaemia. Both G6PD Mediterranean and G6PD A-represent mutant enzymes that differ from normal variants by a single aminoacid. This change is due to DNA changes in the form of point mutations or missense mutations.

The G6PD enzyme is part of the pentose monophosphate shunt. It catalyzes the oxidation of glucose-6-phosphate and the reduction of nicotinamide adenine dinucleotide phosphate (NADP+) to nicotinamide adenine dinucleotide phosphate (NADPH). NADPH maintains glutathione in its reduced form, which acts as a scavenger for dangerous oxidative metabolites.

Neonatal Jaundice is clinical menifestation of G6PD deficiency.It is common deficiency in Middle East. Our aim of study was to find G6PD deficiency among icteric neonates.

MATERIALS AND METHODS

The study was conducted at Maternity and Children Hospital,Nejran,Saudi Arabia for one year from June 2017 to June 2018.We studied 200 Icteric neonates who were admitted in nursery during study period. . Each infant was studied for birth weight, gestational age, age at the time of presentation, presence of cephalhematoma, sepsis and neurological signs, peak bilirubin level, age at peak bilirubin level, whether

phototherapy or exchange blood transfusion 3 given during hospital stay. Inclusion criteria was full term (gestational age > 37 compeleted weeks, Weight >2.5 kg and Bilirubin total>90 µmol/L and exclusion criteria were Preterm and weight <2.5 kg .Each baby was tested for complete blood count, reticulocyte count, ABO and Rh blood type, direct antiglobulin test and quantitative G6PDestimation. Informed consent was taken from mothers of neonates.

G6PD estimation is based on reduction of NADP as measured spectrophotometrically at 340 nm when haemolysate is incubated with G6P .reference range: 146-376 U/10 [12] RBC.Review of blood film during acute haemolytic episode.

RESULTS & ANALYSIS

During this period, 200 neonates who had jaundice were subjected to different investigations of blood as already mentioned.

Table-1: ABO incompatibility and G6PD deficiency are significant cause of jaundice

Total Cases	ABO(Incompatible)	G6PD Deficient	Physiological Jaundice	Rh Incompatible	Other Causes
200	68	56	38	25	13

Table-2: On applying t-test there is significant difference as p<o.ooo

	N	Mean	SD	p-value
G6PD (Deficient)	56	80.03	49.91	0.000
G6PD (Normal)	144	253.11	78.21	0.000

Table-3: Fisher test is highly significant as P<0.001

	Female	Male	Total
G6PD (Normal)	71(87.7%)	73(61.1%)	144(72%)
G6PD (Deficient)	10(12.3%)	46(38.7%)	56(28%)

Table-4: Hb and Reticulocyte count is statistically significant as p<0.1

		N	Mean	SD	T-test	p-value
Haemoglobin	G6PD (Normal)	144	17.334	1.66	10.031	0.000
	G6PD (Deficient)	56	14.91	1.33		
Reticulocyte count	G6PD (Normal)	144	1.093	0.424	9.633	0.000
	G6PD (Deficient)	56	2.060	0.997		
Bilirubin Total (µmol/L)	G6PD (Normal)	144	202.37	59.02	1.278	0.203
	G6PD (Deficient)	56	214.85	69.09		

There were 56 (28%) patients who were G6PD deficient; 144 (72%) had normal activity of the enzyme. 12 neonates were given photo therapy. The sex distribution was 38.7% males and 12.3% were females among G6PD deficient neonates. Fisher exact test is 0.00 which is highly significant as $p \leq 0.001$. None of them developed kernicterus.Hb in G6PD normal neonates Mean 17.33±1.66 and G6PD deficient neonates Mean 14.9±1.13 which is statistically significant(p>0.1).

DISCUSSION

G6PD deficiency is an inherited condition in which the body doesn't have enough of the enzyme glucose-6-phosphate dehydrogenase, orG6PD, which helps red blood cells (RBCs) function normally. People of Mediterranean heritage, including Italians, Greeks, Arabs, and Sephardic Jews, also are commonly affected.

Our study indicated statistically significant differences in hemoglobin and reticulocyte counts in G6PD deficient compared to normal infants, the reported values for both groups largely remained within the normal range for age-matched newborns. This finding is consistent with published literature related to G6PD deficiency and neonatal hyperbilirubinemia, where anemia and reticulocytosis are typically not evident[2] .

However, there was no statistical difference in the peak bilirubin levels and age at peak bilirubin level in the G6PD deficient groups with or without confounders ($p = 0.873$ and 0.590 respectively). This suggests a lack of significant contribution of confounders towards hyperbilirubinemia in G6PD deficient infants.

ABO incompatability and G6PD deficiency were found to be frequent causes of neonatal hyperbilirubinemia in our study as well as an other studies[3] .

The sex distribution was 46 (38.7%) males and10 (12.3%) were females among G6PD deficient neonates.Fisher exact test is 0.00 which is highly significant as $p \leq 0.001$.This male predominance may be attributed to the G6PD deficiency as it frequently occurs in males than females[4-6] . The tendency of G6PD-deficient females to develop neonatal hyperbilirubinemia is known to be related to the degree of G6PD mosaicism. Red cell mosaicism results in G6PDdeficient and G6PD-normal cell types, and the proportion of these two cell types can vary enormously, ranging from normal activity to complete deficiency. For many years, G6PDdeficient heterozygotes were not regarded as being at risk for illness. However, some studies have shown that female heterozygotes are at risk of developing severe neonatal hyperbilirubinemia[7]. This is in agreement with our study, as we found 10 females with G6PD deficiency out of 200 neonates with neonatal hyperbilirubinemia and. Therefore, it is important to identify G6PD-deficient neonates in an effort to manage severe neonatal hyperbilirubinemia. In addition, our findings strengthen the notion that G6PD-deficient infants should be followed up after discharge.

We found that the frequency of G6PD enzyme deficiency in all studied neonates was 28%. In previous national studies, the frequency of this deficiency was found to be 6.6%, 30.3%, 2%, 30.6%, and 14.7% in Makka, Yanbu[8], Riyadh[9], Al-Qatif[10], and Al Hasa[10] respectively. Studies from Iran[11], Brazil[12], and India[13] China[14] , Nigeria[15] found the frequency of G6PD deficiency to be 2.1%, 4.6%, 7.5%,18.42%, 25.5%, respectively. By contrast, studies Thailand found higher frequencies of G6PD deficiency 38%.

Majority of neonates in our study presented with neonatal jaundice between2nd and 4 th day of life.This is supported by other similar studies[15] .

Out of 56 G6PD deficient neonates 26.78 % has bilirubin more than 342 µ mol/L(>20mg/dL) and 73.22% has bilirubin less than 342µmol/L (20 mg/dL).12 Patients were given phototherapy.

CONCLUSION

Since the Prevalence of G6PD deficiency in our neonates was relatively high.Earlydetection of this enzymopathy regardless of sex and close surveillance of affected newborn may be important in reducing the risk of severe hyperbilirubenemia.

REFERENCES

1. Singhi, S. C. (2003). Does nimesulide induce haemolysis in glucose-6-phosphate dehydrogenase deficiency?. *Acta Pædiatrica*, *92*(5), 637-638.
2. Jalloh, S., Van Rostenberghe, H., Yusoff, N. M., Ghazali, S., Nik Ismail, N. Z., Matsuo, M., ... & Nishio, H. (2005). Poor correlation between hemolysis and jaundice in glucose 6-phosphate dehydrogenase-deficient babies. *Pediatrics international*, *47*(3), 258-261.
3. Alkhotani, A., Eldin, E. E. M. N., Zaghloul, A., & Mujahid, S. (2014). Evaluation of neonatal jaundice in the Makkah region. *Scientific reports*, *4*, 4802.
4. Kaplan, M., Beutler, E., Vreman, H. J., Hammerman, C., Levy-Lahad, E., Renbaum, P., & Stevenson, D. K. (1999). Neonatal hyperbilirubinemia in glucose-6-phosphate dehydrogenase-deficient heterozygotes. *Pediatrics*, *104*(1), 68-74.
5. Iranpour, R., Akbar, M. R., & Haghshenas, I. (2003). Glucose-6-phosphate dehydrogenase deficiency in neonates. *The Indian journal of pediatrics*, *70*(11), 855-857.
6. Muzaffer, M. A. (2005). Neonatal screening of glucose-6-phosphate dehydrogenase deficiency in Yanbu, Saudi Arabia. *Journal of medical screening*, *12*(4), 170-171.
7. Reclos, G. J., Hatzidakis, C. J., & Schulpis, K. H. (2000). Glucose-6-phosphate dehydrogenase deficiency neonatal screening: preliminary evidence that a high percentage of partially deficient female neonates are missed during routine screening. *Journal of Medical Screening*, *7*(1), 46-51.
8. Muzaffer, M. A. (2005). Neonatal screening of glucose-6-phosphate dehydrogenase deficiency in Yanbu, Saudi Arabia. *Journal of medical screening*, *12*(4), 170-171.
9. Niazi, G. A., Adeyokunnu, A., Westwood, B., & Beutler, E. (1996). Neonatal jaundice in Saudi newborns with G6PD Aures. *Annals of tropical paediatrics*, *16*(1), 33-37.
10. Nasserullah, Z., Al, A. J., Abu, H. S., Al, G. Q., Al, S. N., Al, A. A., & Mokhtar, M. (1998). Neonatal screening for sickle cell disease, glucose-6-phosphate dehydrogenase deficiency and a-thalassemia in Qatif and Al Hasa. *Annals of Saudi medicine*, *18*(4), 289-292.
11. Abolghasemi, H., Mehrani, H., & Amid, A. (2004). An update on the prevalence of glucose-6-

phosphate dehydrogenase deficiency and neonatal jaundice in Tehran neonates. *Clinical biochemistry*, *37*(3), 241-244.

12. Carvalho, C. G., Castro, S. M., Santin, A. P., Zaleski, C., Carvalho, F. G., & Giugliani, R. (2011). Glucose-6-phosphate-dehydrogenase deficiency and its correlation with other risk factors in jaundiced newborns in Southern Brazil. *Asian Pacific journal of tropical biomedicine*, *1*(2), 110.
13. Iranpour, R., Akbar, M. R., & Haghshenas, I. (2003). Glucose-6-phosphate dehydrogenase deficiency in neonates. *The Indian journal of pediatrics*, *70*(11), 855-857.
14. Weng, Y. H., Chou, Y. H., & Lien, R. I. (2003). Hyperbilirubinemia in healthy neonates with glucose-6-phosphate dehydrogenase deficiency. *Early human development*, *71*(2), 129-136.
15. Uko, E. K., Agwunobi, S. N., & Udoh, J. J. (2003). Glucose-6-phosphate dehydrogenase (G-6-PD) levels in jaundiced neonates in Calabar. *Nigerian journal of medicine: journal of the National Association of Resident Doctors of Nigeria*, *12*(2), 98-102.
16. Thaithumyanon, P., & Visutiratmanee, C. (2002). Double phototherapy in jaundiced term infants with hemolysis. *Journal of the Medical Association of Thailand= Chotmaihet thangphaet*, *85*(11), 1176-1181.