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Glucose-6-Phosphate Dehydrogenase Deficiency among Neonates with Neonatal Indirect Hyperbilirubinaemia Attending a Tertiary Care Centre

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Abstract*:*
Background*- The study was carried out to identify the prevalence of G6PD deficiency in newborns with NIH,to compare patients with reduced G6PD activity with those with normal G6PD activity in terms of level of indirect hyperbilirubinemia,need for exchange transfusion(ET) and development of kernicterus.**Method**:-In a hospital based observational study,205 neonates with NIH admitted in neonatology ward,B.S.Medical college& hospital were evaluated for this study from dec 2018 to may 2019.**Results**:-Incidence of G6PD deficiency was 12.68%.Incidence in male was 76.9% & in female was 23.07%.The deficient patients having lower Hb levels(p<0.01),lower hct levels(p<0.01)but higher maximum bilirubin levels(p<0.01).Max.bilirubin level was a significant risk factor for kernicterus(p<0.01)and independently related to ET(p<0.01).*
Conclusion*:-G6PD deficiency is an important risk factor for severe NIH,so early screening programme should be instituted to avoid subsequent irreversible complications.*
Key Words*:-Neonatal Hyperbilirubinemia,G6PD,kernicterus,screening*

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I. Introduction

NIH(Neonatal Indirect Hyperbilirubinemia) is a common problem during the neonatal period occurring in upto 60% of term & 80% of preterm babies in the first week of life[(1,2)].NIH carries a substantial risk for harmful complications which include long-term neurologic impairments and death[3]. Although significant complications of NIH have become rare in the recent years with therapeutic interventions[3],severe NIH secondary to reduced Glucose 6-phosphate dehydrogenase (G6PD) activity is still complicated by kernicterus which is a serious neurological disease[(3,4,5,6,7)].G6PD deficiency is the most common red cell enzyme abnormality associated with hemolysis.It is also known to be associated with neonatal jaundice, kernicterus, and even death. The marked elevation of bilirubin levels that sometimes occurs in the neonatal period raises the risk of kernicterus.Infants with G6PD deficiency are at higher risk of mortality secondary to bilirubin encephalopathy if total serum bilirubin (TSB) is ≥40 mg/dL[3].G6PD is a cytoplasmic enzyme in the pentose monophosphate pathway and catalyzes the conversion of nicotinamide adenine dinucleotide phosphate (NADP) to its reduced form, NADPH,which keeps glutathione in its reduced form. It helps to protect the red blood cells (RBCs) from oxidative damage[8].The mechanism by which G6PD deficiency causes neonatal hyperbilirubinemia may be due to hemolysis, but other mechanisms like secondary impairment of bilirubin conjugation and clearance by the liver may play a role.Though the exact incidence in india is not known,various studies have reported an incidence ranging 2-27% in different communities in India[9]. There is a paucity of data evaluating the G6PD deficiency in neonates in west bengal.The aim of this study is to identify the prevalence of G6PD deficiency in newborns with NIH and to compare patients with reduced G6PD activity with those with normal G6PD activity in terms of level of indirect hyperbilirubinemia, need for exchange transfusion (ET) and development of kernicterus.

II. Material And Method

Study area:-Neonatology ward(sncu),Department of Paediatric Medicine,Bankura Sammilani Medical College and hospital.Bankura,West Bengal.
Study subjects:-Babies upto age 28 days admitted to neonatology ward in B.S.Medical College & Hospital were approached for this study.Accompanying mothers were the respondent during interview.
Study period:-Dec 2018 to May 2019
Study type:-Hospital based observational study

Inclusion & Exclusion criteria:-Both inborn and outborn babies were included in this study.Babies were excluded from the study if they had cholestatic jaundice.In order to eliminate other facors causing NIH such as-polycythemia,sepsis,ABO&Rh incompatibility,infant of diabetic mother,cephalhematoma were excluded from this study.Those who have got blood transfusion before determining g6pd were excluded to avoid false results.
Data collection:-Total of 205 newborns with indirect hyperbilirubinemia were admitted to our clinics during the study period.Physical examination was performed.sex, weight at admission, the time of onset of jaundice,serum bilirubin level at admission, maximum bilirubin level, phototherapy duration, duration of hospital stay and need for exchange transfusion were recorded.Laboratory evaluations included blood grouping & typing of mother&new born,complete blood count,PBS,serum total and direct bilirubin level,direct coombs test,reticulocyte count,reducing substance in urine,erythrocytic G6PD level.Informed consent was obtained from all subjects. Approval from ethics committe of the institution was taken before commencing the study.For determination of erythrocyte G6PD activity, 2 ml blood was collected in a tube containing EDTA as anticoagulant.confirmatory tests were performed according to lab.procedure.All the babies were followed up for at least 1 week.kernicterus was suspected in patients who has early neurological symptoms & signs.
Criteria for variables:-Blood of individual having G6PD activity below 7.24eu/g of Hb(normal 8.83±1.59 eu/g of hb) were considered as deficient[10]total serum Bilirubin >15mg/dl was considered as having significant jaundice[11].
Statistical analysis:-It was performed with SPSS (Statistical Package for Social Sciences) for Windows 10.0. For comparisons of data mean,standard deviation, Student t-test,Chi-square tests were used. P values of less than 0.05 with confidence interval of 95% were considered to be statistically significant

III. Results

Table 1:-

Gender		**total**
Boys	115	205
Girls	90	
Gestational age		
Early neonate	49	205
Late neonate	156	
G-6-P-D deficiencient		
Boys	20	26
Girls	6	
Early neonate	15	26
Late neonate	11	

A total sample of 205 patients with NIH was collected for the study,among them 115(56.09%) were boys & 90(43.91%) were girls**.[Table1].**49(23.9%)were early neonates (age 0-7days after birth) &156(76.1%) were late neonates (8-28days after birth).Among 205 subjects, 26(12.68%) were detected with G-6-P-D deficiency,of which 20(76.9%)were male babies& 6(23.07%)were female babies. The difference between sex in relation to G-6-P-D deficiency was statistically significant (x2=5.433,P value<0.05)

Table 2:-

	G-6-P-D normal neonates(n=179)	G-6-P-D deficient neonates(n=26)	P values
Onset of jaundice(day)	6.7±4.0	6.1±3.3	0.46
Hb%	18±2.2	16±2.7	<0.01
Hct%	46.6±6.4	42.4±3.6	<0.01

G-6-P-D deficient neonates having lower Hb% level than G-6-P-D normal neonates(p value <0.01),lower Hct value(p value <0.01)(table 2). No statistical significance was detected between G-6-P-D deficient newborns & G-6-P-D normal newborn group in relation to onset of jaundice (table 2).

Table 3:-

	G-6-P-D normal neonates(n=179)	G-6-P-D deficient neonates(n=26)	P values
TSB@time of admission(mg/dl)	20.78±3.29	24.0±6.12	<0.01
Maximum bilirubin (mg/dl)	21.02±3.56	25.98±5.89	<0.01
Suspected kernicterus	3	5	<o.o1
Exchange transfusion	24(13%)	10(38%)	<o.o1

Total 34 patients needed exchange transfusion,among them 24 were G-6-P-D normal neonates,rest 10 were G-6-P-D deficient neonates. But G6PD deficient neonates have higher TSB at the of admission(p value <0.01),higher maximum bilirubin value (p value <0.01),higher rate of suspected kernicterus(p value <0.01)& higher requirement of exchange transfusion(p value <0.01).(Table 3)

IV. Discussion

One of the most common of all clinically significant enzyme defects is G-6-P-D deficiency.Its prevalence varies in different parts of the world.NIH is more common in Asian & African than European G6PD deficient newborn.In the study of Pao et al[12,] 2.0% were having G6PD deficiency,in study of Goyal,Garg et al[13,]Prevalance in West Bengal is 14.68%.Our study shows total incidence of G6PD deficiency is 12.68%,which is closely similar to the study findings of Goyal et al. G6PD deficiency is a x-linked recessive condition,so males are more commonly& severely affected than females.here our study shows male& female ratio is 3.33:1.The ratio between affected early neonate&late neonate was 1.36:1.we were unable to collect exact data about birth weight of all babies.The study of chrakroborty et al[14] showed no significant relationship between G6PD deficiency and birth weight &gestational age.The present study shows G6PD deficient newborns having lower Hb and lower Hct levels compared to G6PD normal neonates. In G6PD deficient neonates acute hemolysis may occur after ingestations of certain drugs,foods,exposure to certain chemicals,hypoxia.they could be attributable to early onset hemolysis due to oxidative stress as a result of perinatal events.lower Hb level is associated with higher peak serum TSB levels.in our study,the TSB at presentation and the maximum level were higher in G6PD deficient individuals.Hyperbilirubinemia,though results from hemolysis,may also resuls from reduced hepatic conjugation and excretion of bilinrubin. Although rare,significant NIH poses a possible risk for kernicterus.In our study,5 neonates developed kernicterus.Kernicterus is a preventable condition,the duration of phototherapy can be used as a surrogate marker of severity Of NIH, but it can also be shortened by ETs.In this study,10 G6PD deficient neonates required ET,whereas 24 neonates of normal gr.required ET.

V. Conclusion

G6PD deficiency is quite common in infants with NIH & an important risk factor for severe NIH which may lead to kernicterus.so,management of NIH should be hastened to avoid irreversible neurological complications.Thus early neonatal screening programmes should be instituted,especially in the regions where prevelance of enzyme deficiency is high.A protocol for assessment of NIH should be established in nurseries.systematic assessment for risk of severe NIH,close follow up and prompt intervention are important to prevent complications.early detection of enzyme deficiency is feasible,cost-effective & allows early prevention of complications.More studies are required to evaluate the relationship between G6PD enzyme level and severity of NIH.as early treatment will reduce the incidence of severe NIH.[15]The study was limited by lack of data about birth weight and about exact levels of G6PD enzyme activity for all G6PD deficient newborns.

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