ORIGINAL ARTICLE

NEONATAL HYPERBILIRUBINEMIA AND ITS CORRELATION WITH G6PD ENZYME DEFICIENCY IN A TERTIARY CARE HOSPITAL IN GUJARAT

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ABSTRACT

Background: Neonatal Hyperbilirubinemia is one of the commonest abnormal physical findings in the new borns. Although, not a major cause of neonatal mortality, its morbidity during neonatal period makes its early recognition and management important. Amongst the various etiological factors, G-6-PD enzyme deficiency is one of the important causes of neonatal hyperbilirubinemia.
Objective: The purpose of this study is to identify incidence of G-6-PD enzyme deficiency among hyperbilirubinemic neonates & to know about particular caste involved in the studied area.
Methods: In the present study neonates were tested and analysed by a micromethod (based on classical methhemoglobin reduction test) which requires only 20 µl of blood in a minimal laboratory set up as a routine investigation. Influence of various other etiological factors i.e. mode of delivery, birth weight, consangious marriages etc. on neonatal serum bilirubin level were also analysed.
Results: Most of neonates (81.2%) having G-6-PD deficiency were male. Bhanushali (17.85%) and Muslim (11.6%) caste showed higher incidence of G-6-PD deficiency. ABO Incompatibility and Prematurely were associated with 32.6% and 30.6% G-6-PD deficiency neonates respectively.
Conclusion: The present study concludes that higher incidence of Neonatal Hyperbilirubinemia in G-6-P.D deficient neonates due to clustering of casts in some geographical areas of Gujarat.

Key worlds: G-6-PD, Hyperbilirubinemia, Prematurity, Methhemoglobin.

INTRODUCTION

Human red cell is remarkable for its shape, structure, biosynthetic apparatus and relative stability inspite of a very traumatic existence in the circulation. The integrity of the erythrocyte depends much on the proper function of numerous enzymes. One of them is Glucose-6-phosphate dehydrogenase. It is a catalyst for the initial step & occupies key position In H.M.P. shunt pathway. The main function of this pathway is to provide NADPH for reduction of oxidized glutathione, which plays an important role in maintaining sulphhydryl enzyme within the red cell in active form and detoxifying small quantity of hydrogen peroxide protecting red cell membrane from oxidative injury[1].

G-6-PD deficiency is probably the most common inborn error of metabolism in humans and was the first erythrocyte enzyme deficiency discovered [2], which in adults can cause chronic hemolytic anemia or drug induced or stress induce acute hemolysis, where as in neonates it is one of the common etiological factor causing Neonatal Hyperbilirubinaemia. And today extensive work on the genetics, biochemistry and molecular pathology of the disorder has made it the best understood and the most thoroughly studied of the enzymopathies.

The Purpose of this study is to detect the incidence of G-6-PD deficiency in Hyperbilirubinemic Neonates, to evaluate relationship of G-6-PD deficiency in neonates with different epidemiological factors (i.e. sex, consanguinity, cast etc.), various perinatal factors & to derive the extent of different etiological factors in Neonatal Hyperbilirubinemia.

MATERIAL METHOD

150 neonates, having hyperbilirubinaemia (serum bilirubin >10 mg%) admitted to NICU of tertiary care hospital attached to medical college in Gujarat., were studied for the detection of G-6-PD deficiency by Micromethod (Micromodification Of Classical

M.R.T.).[3] Detailed clinical history regarding cast, drug history, maternal antenatal condition, mode of delivery, birth weight and maturity, h/o exchange blood transfusion, mother-baby blood groups, and time of appearance of Hyperbilirubinaemia was noted along with Hb level, serum bilirubin, DCT/ICT (in case of incompatibility).

OBSERVATION

Overall incidence of G-6-P.D deficiency in the studied population was 10.66%. In the caste wise distribution, Bhanushali (17.85%), Muslim (11.6%) showed higher incidence followed by Lohanas (9.09%), Sindhi (9.09%), Bania (6.25%) & Patels (5.85%).

Table 1: Caste Wise Distribution of G-6-PD Deficient Neonates (n=150)

Caste	Newborns	Newborns With G6PD Deficiency (%)
Bhanushali	28	5 (17.85)
Muslim	43	5 (11.6)
Brahmin	13	1 (7.69)
Lohana	11	1 (9.09)
Patel	17	1 (5.85)
Bania	16	1 (6.25)
Sindhi	11	1 (9.09)
Kadiya	03	0 (0)
Charan	02	0 (0)
Harijan	02	0 (0)
Prajapati	01	0 (0)
Total	150	16 (100)

Among G-6-P.D deficient neonates, there were 13 (81.2%) males & 2(12.5%) females.

Only 1 female neonate showed intermediate G-6-PD enzyme activity.

Table 2: Sex Wise Distribution of G-6-PD Deficient Hyperbilirubinemic

G6PD Status	Male	Female
Normal G-6-PD activity	95	39
Deficient G-6-PD activity	13	02
Intermediate G-6-PD activity	00	01

Four neonates (25%) out of 16 deficient neonates showed history of consangious marriage of their parents.

Table 3: Relation of Consanguineous Marriage with G-6-PD Deficiency

Hyper-bilirubinemic neonates	Cases	History of consanguineous marriage	
		Yes (%)	No (%)
Normal G-6-PD activity	134	36 (26.8)	98 (73.1)
Deficient G-6-PD activity	16	04 (25.0)	12 (75.0)
Total	150	40 (26.6)	110 (73.0)

Among the etiological factors of Uncongugated Hyperbilirubinemia in present study, ABO Incompatibility is most common, than comes Prematurity, G-6-PD deficiency **,** Rh Incompatibility , Sepsis in that order. Out of them most common combination is Prematurity and G6PD deficiency.

Table 4: Incidence of Different Etiological Factors in Development of Indirect Hyperbilirubinemia

Etiological Factors	Cases (%) (n=150)	Mean Hb gm%	Mean Serum Bilirubin mg% (indirect)	D.C.T		CRP
				+ve	-ve	+ve
Prematurely	47 (30.66)	13.33	12.54	-	-	-
ABO Incompatibility	49 (32.66)	12.50	13.12	31	16	-
Rh Incompatibility	14 (9.33)	13.31	12.66	7	14	-
G-6-PD deficiency	16 (10.66)	12.26	12.60	-	-	-
Infection	09 (05.33)	13.91	12.50	-	-	-
Idiopathic	15 (10.00)	12.61	12.45	-	-	09

Various modes of delivery were having little influence on severity of hyperbilirubinemia showing minor variations in each individual group. It was observed that total 15 neonates required exchange transfusion. Among them 1/3rd neonates were having deficient G6PD activity.

DISCUSSION

The present study was done to detect the incidence of G-6-PD deficiency in Hyperbilirubinemic Neonates & to evaluate relationship of G-6-PD deficiency in neonates with different epidemiological factors. An attempt was made to establish the extent of neonatal hyperbilirubinemia with the common eitologies of same with chief focus on neonatal G-6-PD deficiency.

The incidence of G-6-PD deficiency in Indian population varies from 0 to 27.02%[4]. In Gujarat, the incidence of G-6-PD deficiency follows following chronology in descending order. Warli (19.53%), Kutchhi Bhanushali (13.80%), Gonds (11%), mix

population (11.70%), Konkana (8.43%), Dodia (6.15%), Brahmins (3.54%), Kutchhi Lohana (3.17%)[4]

Table 5: Combination of Different Etiological Factors in Neonatal Hyperbilirubinemia

Etiological Factors	Cases	Serum Bilirubin mg% Mean (Range)
Prematurity + ABO incompatibility	02	14.56 (14.4-14.7)
Prematurity + Rh incompatibility	02	14.53 (12.1-17.0)
Prematurity + G6PD deficiency	03	12.75 (11.8-13.7)
G6PD deficiency + ABO incompatibility	01	- (12.6)

Table 6: Mode of Delivery in Development of Hyperbilirubinemia

Mode of Delivery	Cases (n=150)	Serum Bilirubin (mg%) Mean (Range)
Normal vaginal	68	12.74 (10.1-19.8)
Preterm vaginal	40	12.71 (10.0-23.7)
Caesarean section	23	12.30 (10.0-20.0)
Forceps	15	12.94 (10.01-14.6)
Vacuum	04	12.92 (10.1-14.90)

Table 7: Birth Weight and Maturity in Development of Hyperbilirubinemia

Birth Weight And Maturity	Cases (n=150) (%)	Serum Bilirubin (Mg%) Mean (Range)
> 2.5 kg full term	70 (46.67)	11.9 (10.0 -16.7)
< 2.5 kg full term	33 (25.33)	13.0 (10.2 -19.8)
<2.5kg premature	47 (31.3)	12.54 (10.3 -23.7)

Table 8: Exchange Blood Transfusion in Hybilirubinemic Neonates Having G6PD Deficiency

G6PD Status	Blood Transfusion		Total
	Yes	No	
G6PD Deficient	4	12	16
Normal G6PD	11	123	134
Total	15	135	150

Among hyperbilirubinaemic neonates the higher incidence(10.66%) in present study, can be compared to that of Bhanderi et al[5] (4%) , Handa et al[6] (8.07%) & Baxi et al[7] 1964 can again be explained by the clustering of casts.

In present study, the finding of higher incidence among Kutchhi Bhanushalis, Muslims, Lohanas can be supported by above mentioned studies (Table 1).

In present study as per expectations, the male neonates more commonly showed G-6-PD enzyme defect compared to female patients. This can be explained by location of gene on X chromosome, which occurs in males only in hemizygous form ,where as the female heterozygote can be protected by the other functional X chromosome of the pair.

In present study 1/4th deficient neonates show H/O consanguineous marriage. It can be explained by clustering of deficient gene among them by the virtue of custom of consanguineous marriage.

Among Indian neonates, the common causes of Neonatal Hyperbilirubinaemia includes, ABO incompatibility, Immaturity, G6PD deficiency, Rh incompatibility, Infection, Breast milk jaundice & Physiological jaundice, etc. Similar observation was made by Weisz B. et al[8] in 1996.

In this study G6PD deficiency is ranking third followed by Rh incompatibility. This can be explained by relatively higher incidence of G6PD deficiency in studied population.

No extra adverse effect can be found due to combination of ABO incompatibility and G6PD deficiency. The later finding can be supported by the finding of Kalpan M, et al[9]1998 which had stated that the combination of G-6-PD deficiency and ABO incompatibility had no additional deleterious effects compared to either of them alone.

It has been observed in the present study, that neonates delivered by forceps and vacuum are more prone to develop higher serum bilirubin levels compared to other modes of deliveries. However, some of the patients who had undergone other modalities of delivery showed higher bilirubin values than the neonates delivered by forceps & vacuum. Hence the difference is statistically insignificant.

It has been observed from obtained results, that there is not much difference in mean serum bilirubin value between neonates of different birth weights and maturity. This concludes that as far as the magnitude of Hyperbilirubinaemia is concerned, the birth weight and maturity shows no remarkable difference.

It has been observed from the present study that a higher percentage(25%) of G-6-PD deficient neonates undergoing exchange blood transfusion as a treatment modality than the non G-6-P.D deficient neonates. These findings can be compared with a study made by Doxiadis S.A. and Valacs T. in 1994[10] at Athens, Greece.

CONCLUSION

The present study concludes that higher incidence of Neonatal Hyperbilirubinemia in G-6-P.D deficient neonates due to clustering of casts in some geographical areas of Gujarat. Among these Bhanushalies & Muslims showed higher incidence

followed by Sindhis & Lohanas. G-6-P.D deficient males were more common than females. Consangious marriages have a positive correlation with G-6-P.D deficiency. ABO incompatibility was the most common etiology followed by Prematurity as the second most common cause of neonatal hyperbilirubinemia. G-6-P.D deficiency was the third most common cause of higher s.bilirubin level in neonates. Mode of delivery in Neonatal Hyperbilirubinemia is statistically insignificant factor. There is no remarkable difference in the magnitude of Hyperbilirubinemia with the birth weight & maturity. Rate of exchange transfusion is much higher in G-6-P.D deficient neonates. Over study concludes that, G-6-PD enzyme testing can be introduced as a routine laboratory investigation with minimal laboratory set up and cost in geographical areas & particular caste of Gujarat to prevent future drug induced haemolytic complications in deficient persons.

REFERENCES

1. Bertler E. Drug induced hemolytic anaemia. Pharmacological reviews. 1969; 1(21):73-97.
2. Denis R. Miller. Hereditary Enzyme deficiencies of red cells. The paediatric clinics of North America. 1972. 19:880-87.
3. Millar D. R. and Kotak D. Microscreening test for G6PD deficiency Paediatrics. 1968; 42: 528-30.
4. Soni S. Screening of G6PD deficiency in newborns and it's relation with neonatal hyperbilirubinaemia. dissertation submitted to the Saurashtra University, Rajkot, 1994.
5. Anju Bhandari, Crowell E.B. , Scrowell, Khanna S.D. Incidence of G6PD deficiency in Punjabi jaundiced neonates. Ind. J. Path. and Micro bio. 1982; 25 :272-82.
6. V. Handa, R.A. G. Mukharjee, R. Z. Patel, R.M. Oza. G6PD deficiency in new borne. J. of Ind. Mde. Asso. 1985; 3: 225-26.
7. Baxi A.J. Undeiva J. V. and Bhatia H. M. Role of G6PD deficiency in acute hemolytic crisis and neonatal jaundice. Ind. J. Med. Sci. 1964; 18: 572-82.
8. Weisz B. , Belson A., Mill Bauer B., Reif S. Complication of exchange transfusion in term and preterm newborns. Harefuah. 1996; 130(3): 170-3, 223.
9. Kalpan M., Hammerman C. Severe Neonatal Hyperbilirubinaemia : A potential complication of G-6-PD deficiency : Clini. Perinatal. 1998. 25(3) : 575-90.
10. Doxiaids S.A. , Valacs T. The clinical picture of G6PD deficiency in early infancy. Arch. Dise. Chil. 1964; 39:545-550.