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Study of immunohematological and biochemical parameters in neonatal jaundice at tertiary care centre

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Abstract
Introduction: Jaundice is most common problem faced by neonates in the first week of life. Although physiological jaundice is more frequent as compared to pathological jaundice, so it is very important to differentiate between the two as pathological jaundice may lead to kernicterus and subsequently brain damage. There are various modalities of investigations for diagnosis of jaundice e.g. complete blood count, Total serum bilirubin, Blood group, Direct and Indirect coomb's test, G-6PD deficiency etc. by which we can reach at diagnosis. Treatment is also dependent upon the amount of total serum bilirubin and various other laboratory investigations. Thus laboratory workup is very important for diagnosis, prevention of neonatal hyperbilirubinemia and its complications. With this background present study was conducted for the analysis of clinicopathological profile among infants with neonatal hyperbilirubinemia.
Aims and Objectives: The current study was planned to assess the hematological profile of neonatal jaundice and to categorize it on the basis of causes and severity.
Materials and Methods: The present study conducted on 140 neonates admitted in NICU, at tertiary care centre, Ahmedabad; during first week of life along with total serum bilirubin level greater than 5 mg/dl. Peripheral blood was drawn from all study subjects under aseptic precautions and study done for Total Serum bilirubin, Direct and indirect coomb's test, Blood group, G-6PD deficiency, complete blood count and CRP.
Results: In our study among 140 cases with neonatal jaundice, Total number of Pre-term babies (< 37 weeks) was 91 (65%). Most of the neonates were present with jaundice at the age of 2-4 days. Physiological jaundice constituted majority in 95 cases (67%). ABO incompatibility was the commonest cause of pathological jaundice followed by septicemia. The rise in total serum bilirubin level was found to be more in pathological jaundice as compare to physiological jaundice.

Keywords: neonatal hyperbilirubinemia, kernicterus, hematological parameters

Introduction
Jaundice is yellowish discoloration of the skin, sclera and mucous membranes resulting from deposition of bilirubin. Neonatal jaundice is defined as total serum bilirubin greater than 5 mg/dl [1]. Jaundice is the most common condition that requires medical attention and hospital readmission in newborns. Neonatal hyperbilirubinemia is a prevalent condition in developing country as well as in developed country.
Jaundice is most common problem faced by neonates in first week of life. The most common cause of neonatal hyperbilirubinemia in India is physiological jaundice. Various other conditions in decreasing order are preterm infant, blood group incompatibility, neonatal septicemia, G6PD deficiency, cephalhematoma, RBC membrane disorders and many others.
Although physiological jaundice is more frequent as compared to pathological jaundice. It is very important to differentiate between the two as pathological jaundice may lead to kernicterus and subsequently brain damage.
Neonatal jaundice is a very common condition worldwide occurring in upto 60% of full term and 80% of preterm newborns in the first week of life [2]. Newborns especially preterm have higher rates of bilirubin production than full term because they have red cells with higher turnover and shorter life span [3].
History, clinical presentation and laboratory profile of the newborn plays a major role, in diagnosing the cause of jaundice.

There are various modalities of investigation e.g. Direct and Indirect Coombs' test, Blood group, G6PD deficiency, complete blood count by which we can reach diagnosis. Thus laboratory workup is very important for diagnosis and prevention of neonatal hyperbilirubinemia in newborn.
It is very important for Pathologist and Pediatricians to differentiate the physiological and pathological causes of hyperbilirubinemia. Treatment is dependent upon the amount of total serum bilirubin and various other laboratory investigations.

Aims and Objectives

- To study the Immunohematological and biochemical parameters related to Neonatal jaundice.
- Analysis of neonatal jaundice according to etiology, age (in days) and gestational age.
- To study the importance of Total Serum Bilirubin parameters for physiological v/s pathological Neonatal jaundice.

Material and Methods

The present study is an analysis of neonates admitted in NICU at tertiary care centre, Ahmedabad; from January 2020 to March 2020.This study includes 140 neonates belonged to 0-7 days with clinical signs and symptoms of jaundice like; fever, lethargy, irritation, feeding problems, hypotonia etc. along with total serum bilirubin level greater than 5 mg/dl. Peripheral blood was drawn from all study subjects under aseptic precautions in sterile vaccute.

Following investigations were done in all cases:

Blood group (abo/rh) of mother, father and baby: The blood grouping was done by using known anti-sera with slide and tube methods and by automated machine.

Total serum bilirubin estimation of baby: Blood collected into plain vaccute for bilirubin determination. The test will be obtained by automated machine.

Complete blood count with peripheral smear examination: It included haemoglobin, total WBC count, different WBC count and peripheral smear examination. It has been done by fully 5 part automated hematology analyzer with standard calibration. For every sample a peripheral smear was prepared and the blood film was stained with giemsa stain and examined under light microscope.

Direct and indirect coomb's test of baby and mother both: The tests are done by gel card and test tube method.

Test for g-6-pd deficiency: It has been carried out by using automated machine.

C-reactive protein of baby: It has been carried out by Latex agglutination slide test method.

Observations and result

The present study included 140 cases of new born admitted in NICU. Laboratory investigation of neonatal jaundice was carried out.

Table 1: Case wise distribution of Neonatal Jaundice

Etiology	No. of cases (%)
Physiological Jaundice	95 (67.8%)
Pathological Jaundice	45 (32.1%)
Total	140 (100%)

Physiological jaundice constituted 67 % cases of neonatal hyperbilirubinemia. In our study, physiological jaundice was more common than pathological jaundice.

Table 2: Etiology wise distribution of Neonatal Jaundice

Etiology	No. of cases (%)
Physiological Jaundice	95 (67.8%)
ABO incompatibility	22 (15.7%)
Rh incompatibility	11 (7.8%)
Septicemia	11 (7.8%)
G6PD deficiency	1 (0.7%)
Total	140 (100%)

ABO incompatibility was the commonest cause of pathological jaundice. Rh incompatibility and septicemia were second commonest causes of pathological jaundice. G6PD deficiency was very rare condition.

Table 3: Age wise distribution of Neonatal Jaundice

Age(in days)	No cases (%)
1	14 (10%)
2	41 (29.2%)
3	39 (27.8%)
4	32 (22.8%)
5	6 (4.2%)
6	5 (3.5%)
7	3 (2.1%)
Total	140 (100%)

Neonatal jaundice was most common in 2nd, 3rd and 4th day of neonatal life.

Table 4: Gestational age wise distribution of Neonatal Jaundice

Gestational age	No of cases (%)
Preterm	91 (65%)
Full Term	49 (35%)
Total	140 (100%)

Preterm neonates were most commonly affected than full term neonates.

Table 5: Hemoglobin level in Neonatal Jaundice

Etiology	Range(gm/dl)	Mean (gm/dl)
Physiological Jaundice	14-18	16
ABO incompatibility	11-16.5	13.8
Rh incompatibility	8-12	10
G6PD deficiency	14.5	14.5
Septicemia	10-14	12

In normal full term baby normal Hb level range is 13.5-21.5 gm/dl. Range of Hemoglobin level in neonatal jaundice of our institute was 8-18 gm/dl. Hb level was low in pathological jaundice as compare to physiological jaundice. In pathological jaundice, hemoglobin level was lowest in Rh incompatibility. In addition; peripheral smear shows hemolytic picture in blood group incompatibility, where as leucocytosis in early phase followed by leucopenia and thrombocytopenia were most commonly seen in septicemia.

Table 6: Total Serum Bilirubin level in Neonatal Jaundice.

Etiology	Mean Billirubin level (mg/dl)
Physiological Jaundice	15
ABO incompatibility	16.5
Rh incompatibility	18
Septicemia	16.3
G6PD deficiency	22.7

The rise in total serum bilirubin level was found to be more in pathological jaundice as compare to physiological jaundice. Highest level of total serum bilirubin was found in Rh incompatibility followed by G6PD deficiency.

Table 7: Result of Coombs' test in Rh and ABO incompatibility

	DCT			ICT		
	+VE	-VE	Total	+VE	-VE	Total
Rh incompatibility	11(100%)	0	11	11(100%)	0	11
ABO incompatibility	14(63%)	8(37%)	22	14(63%)	8(37%)	22

Direct Coombs' test and Indirect Coombs' test were found to be positive in all case of Rh incompatibility; while they were positive in 14 cases of ABO incompatibility out of 22 cases.

Table 8: Diagnostic workup in Neonatal Septicemia

Etiology	No of cases	CRP positive
Physiological Jaundice	95	4
ABO incompatibility	22	2
Rh incompatibility	11	0
Septicemia	11	11
G6PD deficiency	1	0
	140	**17**

CRP was found to be positive in all case of septicemia (100%). It was also positive in a few cases of ABO incompatibility (2 cases) and physiological jaundice (4 cases).

Discussion

The study was carried out at tertiary care centre, Ahmedabad during a period of January 2020 to March 2020; for immunohematological and biochemical profile in neonatal jaundice. Jaundice is a very critical condition in neonates because of consequence of neonatal jaundice is dangerous for neonates.

Gestational age

The present study includes 140 cases of Neonatal jaundice. Among them 91 cases (65%) were preterm (< 37 weeks) and 49 cases (35%) were full term babies. In a study done by Vikram R *et al.*, highest number of preterm infants; 35 cases (n=89) (39.32%) developed jaundice in the first week of life **(10)**. Similarly, Bedowra *et al.* (44 cases) (n=60) (73.3%) and Dr. Ishani *et al.* (363 cases) (n=570) (63.5%) in their studies mentioned that prematurity was a significant risk factor for hyperbilirubinemia.

Preterm newborns are prone to developing jaundice due to immaturity of their bilirubin conjugating system, higher rate of hemolysis, increased enterohepatic circulation and decreased caloric intake [13].

Newborn age between 2 to 4 days shows higher incidence of jaundice in our study; which is comparable to study done by Dr. Amar *et al.* [4].

Physiological v/s pathological jaundice

If jaundice appear in neonates after 24 hours of birth or within 7 days (in full term baby) or upto 14 days (in preterm baby) is considered as Physiological jaundice. If jaundice appear within 24 hour of birth or rate of rise of total serum billirubin level exceed more than 5 mg/dl/day is considered as Pathological jaundice. It can be persists for more than 2 weeks.

Out of 140 cases, 95(67%) cases were physiological and 45(33%) cases were pathological. In the study done by Dr. Amar *et al.* had shown that physiological jaundice contributed to highest 40 cases (62%) incidence. Vikram R *et al.* 44(49%) cases too had reported highest incidence of physiological jaundice in his studies. In the study by Bedowra *et al.*, Bangladesh (n=60), physiological jaundice contributes to 53.3% as the most common cause in their study.

Etiology-wise distribution

In present study, 22 cases of ABO incompatibility, 11 cases of septicemia, 11cases of Rh incompatibility and 1 case of G6PD deficiency were noted. The physiological jaundice was most common than pathological jaundice and ABO incompatibility was most common cause of pathological jaundice followed by septicemia. Similar findings seen in study done by Shailendra P Mosamkar, *et al.* (15% of ABO incompatibility). We correlated our findings with other study.

Table 8: showing percentage distribution of causes of neonatal jaundice in present study in comparison with other study

Etiology	No. of cases in our study (n=140) (%)	No. of cases in study done by Amar shah *et al.* (n=63) (%)	No. of cases in study done by Vikram R *et al.* (n=89) (%)
Physiological Jaundice	95(67%)	40(62%)	44(49%)
ABO incompatibility	22(16%)	9(15%)	18(20%)
Rh incompatibility	11(8%)	4(8%)	7(7%)
Septicemia	11(8%)	8(12%)	20(22%)
G6PD deficiency	1(0.7%)	2(3%)	-

Laboratory parameters

In present study Hb level range of 8-18 gm/dl. Similar findings were noted in the study carried out by Joshi *et al.* [7]. The findings of their study showed Hb level 8-19.4 gm/dl. The result was almost similar to our study. Hb level was low in pathological jaundice and lowest (8 gm/dl) in Rh

incompatibility cases.

Any infant present with hyperbillirubinemia within 24 hours after birth is considered as pathological jaundice and required evolution. This evolution should minimally include a total serum bilirubin and workup for hemolytic disease. Guideline for therapy depends upon the total serum concentration of bilirubin and the patient age. Also total serum bilirubin is most important investigation to judge severity and management of patient. In present study; range of total serum billirubin was 8-26 mg/dl. Highest level of total serum bilirubin was found in Rh incompatibility followed by G6PD deficiency and ABO incompatibility. As compare to direct billirubin; indirect billirubin was found high in most of the cases. Among half of cases range of serum total bilirubin was found between 14-18 mg/dl. Same results were observed in the study of Nepal D *et al.* [8]. They mentioned that maximum number of infants' peak total serum bilirubin fall in the range of 15-19.9 mg/dl.

This study also included peripheral smear study of the neonates. Both physiological and pathological jaundice showed macrocytic hyperchromic picture, but nucleated RBC'S and spherocytes were common among Rh-ABO incompatibility cases; which were less significant among neonates with physiological jaundice. Similar smear findings were seen in study of Vikram R *et al.* In addition, polychromasia, aniso-poikilocytosis, fragmented RBCs, hypochromia, etc. were also seen on smear; in hemolytic causes of jaundice.

Leucopenia, thrombocytopenia and polycythemia, these all findings in present study were correlated with Manroe reference range. Although various tests are used, as a diagnostic tool for neonatal sepsis, the complete blood count with differential is widely used, either singly or in conjunction with other test or clinical findings, The criteria of Manroe *et al.* is the most reliable of the published criteria evaluated which identifies almost all infants with sepsis or with probable sepsis.

DCT and ICT were positive in 100% cases of Rh incompatibility while in ABO incompatibility they were found to be positive in 63% of cases. Study done by Amar *et al.* also shows 77% of positivity of DCT and ICT in ABO incompatibility cases. The reason for this difference may have been that "A" and "B" antigens are weaker antigens and the distance between a/b antigen sites on the fetal red cells as compared to adult red cells is more [4].

In all cases of septicaemia; CRP was positive in present study. It is an acute phase reactant; is synthesized by the liver and it becomes positive after any inflammation. It is a very reliable indicator.

Conclusion

It was concluded from this study that immunohematological and biochemical parameters may serve as an important tool to aid in the differential diagnosis of neonatal jaundice. Total serum bilirubin is most important investigation to judge severity and management of patient.

In our study physiological jaundice was the most common cause of neonatal jaundice. This is followed by ABO incompatibility, sepsis, Rh incompatibility and other causes.

Also, special care must be given to preterm neonates and neonates with higher level of billirubin; in order to avoid future complications of hyperbilirubinemia.

Understanding the etiological and risk factors for neonatal jaundice in our setting helps in prioritizing the group of neonates who require more intensive monitoring for early identification and timely management of this condition.

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