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Neonatal Hyper Bilirubinemia in Level II NICU And Its Outcome - A Tertiary Care Centre Experience

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Abstract:
Aims and Objectives: *To know the Aetiology of Neonatal Hyperbilirubinemia and to study the morbidity and mortality pattern in Neonatal Jaundice.*
Methods: *A prospective study done in Niloufer Hospital for babies admitted in NICU II during a year 2015 – 16. The study group consists of 100 neonates presenting with jaundice.*
Results: *The incidence of Clinical Jaundice was 42.03% out of which 64% were males and 36% were females. 66% had low birth weight, 43% had Sepsis, 12% ABO Incompatibility, 10% Rh Incompatibility, 9% with Cephalohematoma, 4% with Biliaryatresia, 6% with Neonatal Hepatitis. 36% had abnormal OAE test.*
Conclusion: *The incidence of Neonatal Jaundice in our study was 42.03% with male to female ratio of 1.7:1. The major cause of Neonatal Jaundice in our study is Neonatal Sepsis (43%).*
Keywords: *OAE (Oto Acuostic Emission), PT-Phototherapy, ET-Exchange Transfusion.*

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I. Introduction

Jaundice is derived from Latin word Galbinus meaning greenish yellow.Jaundice from French (jaune, yellow) and icterus is derived from Greek word icteros meaning yellow discolouration of tissues (skin, sclera) caused by deposition of bilirubin 3. Neonatal jaundice is one of the most common problem affecting 65% normal newborns. Neonatal jaundice may be defined as the presence of visible jaundice and thus usually occurs in neonates if bilirubin levels are greater than 15 mg/dl. Jaundice is observed during the first week of life in approximately 60% of term infants and 80% of pre term infants (1). Since bilirubin is potentially toxic to the CNS early detection and appropriate management of neonatal jaundice is of paramount importance especially because when bilirubin even in physiological ranges may cause permanent neuronal injury (2).

II. Aims And Objectives

1. To know the aetiology of neonatal hyperbilirubinemia.
2. To know the causes of significant hyperbilirubinemia.
3. To study the morbidity and mortality pattern in neonatal jaundice.
4. To study the clinical profile of babies with different aetiological factors.
5. To evaluate the interventions undertaken for the babies with neonatal jaundice
6. To determine relation level of serum bilirubin and the initial abnormal otoaccoustic emission (OAE) and brainstem audiometric evoked responses (BAER) abnormalities with hyperbilirubinemia and the possible reversibility following treatment.

III. Materials And Methods

A prospective study done in Niloufer Hospital admitted in NICU II. The study group consists of 100 neonates of age group 0 – 14 days presenting with Jaundice who required phototherapy / exchange transfusion for treating the hyperbilirubinemia. Cases were followed up to the age of six months.

Inclusion Criteria:

All term and late pre term babies with significant hyperbilirubinemia requiring phototherapy or exchange transfusion (>15mg/dl).

Exclusion Criteria:

- Pre term <34 weeks of gestation
- Babies with meningitis
- All new born babies with major congenital anomalies

All cases of hyperbilirubinemia were analysed. Neonatal and maternal blood groups, ABO, Rh typing direct coombs test, CBP, Reticulocyte count, Serum bilirubin and septic screen were done. LFT, urine for bile salts, bile pigments, ultra sound abdomen, bullida scan and liver biopsy was performed in cases of conjugated hyperbilirubinemia. Torch profile, VDRL, Thyroid profile, urine for reducing substances, G6 PD levels were done when ever required. Serum bilirubin was measured by Jendrassik and Grof method. OAE recordings were obtained by using OAE probe. Quick screen OAE stimulus was used for recording the emissions. BAER was performed in a dark quite room by computerized electric response audio meter Nicolette 1170.

Diagnostic Criteria:

1. Rh hemolytic disease of new born

a) Mother Rh negative
b) Baby Rh positive
c) Direct coombs test positive
d) Jaundice appearing within 24 hours of life

2. ABO incompatibility

a) Mother blood group 'O'
b) Baby blood group 'A' or 'B'
c) Direct coombs test positive

3. Septicemia

a) CRP positive
b) Raised micro ESR
c) Positive blood culture
d) Band count greater than 20%
e) Leucopenia less than 5000 mm^3 or leucocytosis greater than 20000 per mm^3
f) Direct bilirubin greater than 20% of total serum bilirubin.

Positives septic screen defined as positivity of two of the five above mentioned criteria. Second definition is culture positive sepsis.

4. Physiological Jaundice
   The diagnosis of the physiological jaundice in term and pre term infants is based on the following criteria. Jaundice appearing after 48 hours in term babies and disappearing by the 10^{th} day with a peak on 4^{th} day and serum bilirubin does not exceed 13mg per dl. In pre terms jaundice appearing after 30 hours of life peaking on 5^{th} and 6^{th} day with peak serum bilirubin value less than 15mg per dl and subsiding for 14 days of life.
5. Cephalhematoma
   a) History of difficult labour
   b) Sub periosteal well defined swelling of the scalp
   c) Unconjugated hyperbilirubinemia crossing physiological limits.
6. Breast Milk Jaundice
   a) Jaundice appears usually at the end of the second week of life and peaking of serum bilirubin levels up to 20mg per dl to 25 in exclusively breast fed babies.
   b) Decrease in serum bilirubin levels rapidly after temporarily stopping breast feeds.
7. Biliary atresia
   a) Persistent conjugated hyperbilirubinemia
   b) Persistent acholic stools
   c) Liver biopsy – showing bile duct proliferation, cholestasis with bile duct lakes and fibrosis.
   d) Bullida scan - suggestive of biliary atresia
8. Neonatal Hepatitis
   a) Persistent conjugated hyperbilirubinemia
   b) Liver biopsy – giant cell transformation, cholestasis in hepatocytes, hepatocellular necrosis
   c) Bullida scan – suggestive of neonatal hepatitis

IV. Results

In the presence study 1080 babies of various ages were admitted during the study period of one year at NICU II Niloufer Hospital.

Table 1: Incidence of Neonatal Jaundice

Total Nursery Admissions	No. of newborns with Jaundice	Incidence Percentage
1080	452	42.03%

Table 1 shows 452 (42.03%) newborns have clinical jaundice of these 100 were included in the study and thoroughly worked up Babies with unconjugated hyperbilirubinemia less than 15md/dl did not require therapeutic intervention except close clinical observation and those babies with yellow tinge but clinically not requiring any work up were not included in this study (352)

No. of Newborns with TSB<15mg/dl	No. of Newborns with TSB>15mg/dl
352 (77.87%)	100 (22.12%)

Table 2: Sex distribution in Neonatal Jaundice

Sex	No. of newborns	Percentage
Male	64	64
Female	36	36
Total	100	100

Table 2 shows in the present study 64(64%) were male and 36 (36%) were female. Male: Female ratio is 1.7: 1

T able 3: Age of onset of Jaundice

Age of onset of Jaundice	No. of newborns	Percentage
0 – 24 hours	10	10
24 – 72 hours	54	54
>72 hours	36	36

Table 3 shows in 10 (10%) new born jaundice appeared within 24 hours, in 54 (54%) jaundice appeared between 24 to 72 hours, in 36 (36%) jaundice appeared between72 hours and 14 days of life.

Table 4: Gestational Age and Neonatal Jaundice

Gestational Age	No. of newborns	Percentage
Preterm	31	31
Term	69	69

Table 4 shows 31 (31%) preterm with gestational age between 34 to 37 weeks with neonatal jaundice and 69 (69%) were term babies.

Table 5: Birth Weight and Neonatal Jaundice

Birth weight	No. of newborns	Percentage
<2.5 kgs	66	66
>2.5 kgs	34	34

Table 5 shows 66 (66%) newborns had birth weight less than 2.5 kgs and 34 (34%) newborns had birth weight greater than 2.5 kgs.

Table 6: Place of Birth and Neonatal Jaundice

Place of Birth	No. of newborns	Percentage
Hospital	62	62
Home	38	38

Table 6 shows 62 (62%) newborns were born in hospital, 38 (38%) newborns were born at home.

Table 7: Mode of Delivery and Neonatal Jaundice

Mode of Delivery	No. of newborns	Percentage
Spontaneous Vaginal Delivery	65	65
Caesarean Section	18	18
Forceps	17	17

Table 7 shows in 65 (65%) newborns were born by spontaneous vaginal delivery, 18 (18%) newborns were born by caesarean section and 17 (17%) were by forceps delivery.

Consanguinity and Jaundice:
In this study 27 (27%) newborns were product of consanguineous marriage and 73 (73%) babies were born to non consanguineous parents.

Sibling History and Neonatal Jaundice:
In this study only 5 (5%) cases there was history of jaundice in their siblings.

Antenatal Maternal illness and Jaundice:
In the present study 12 (12%) babies were born to mothers with pregnancy induced hyper tension. 21 (21%) babies were born to mothers with history of premature rupture of membrane (PROM). These babies were tested positive for septic screen.

Timings of Breast Feeds in babies with Neonatal Jaundice:
In the present study only 39 (39%) babies were breast fed within six hours of life, 29 (29%) newborns were breast fed after 24 hours of life. Remaining 32 (32%) of babies were top fed for various reasons.

Table 8: Symptomatology on Admission

Symptoms	Newborn	Percentage
Yellowish discolouration with good activity	52	52
Jaundice with refusal of feeds	21	21
History of delayed cry	11	11
Fever	7	7
Breathlessness	5	5
History of acholic stools	2	2
Vomiting	2	2

Table 9: Aetiological diagnosis of Jaundice

Aetiology	No. of Newborns	Percentage
ABO Incompatibility	12	12
Sepsis	43	43
Rh Incompatibility	10	10
Cephalhematoma	9	9
Neonatal Hepatitis	6	6
EHBA	4	4
Birth Asphyxia	11	11
IDM with PIH	1	1
Hypothyroidism	4	4
Total	100	100

Sepsis:
In this study 43 (43%) babies with septicemia developed jaundice. Of these, 28 were low birth rate ranging from 1.2 kgs to 2.5 kgs, and 15 babies had weight more than 2.5kgs. Poor feeding was predominant presenting manifestation in 19 cases. . Serum bilirubin levels range from 15 to 28 mg/dl.

ABO Incompatibility:
In this study ABO incompatibility was diagnosed in 12% cases born to 'O' group mothers. Birth weights ranged from 1.5 kgs to 3.2 kgs. Jaundice was the main presenting complaints. Serum bilirubin levels range from 19.2 to 32.6 mg/dl. Two cases developed kernicterus and permanent hearing loss.

RH Incompatibility:
Total number of cases in this group was 10 (10%) with birth weights ranging from 1.4 kgs to 3.2 kgs. Six cases were of 2nd Para, three cases were 3rd para and one caesarean of 4th Para. Only one case developed kernicterus and hearing abnormalities were persistent up to the age of six months.

Management:
74 (74%) cases were managed with phototherapy while, 26 (26%) cases were treated with exchanged transfusion. All new born babies with sepsis received antibiotics depending on the culture and sensitivity.

Table 10: Treatment of Neonatal Jaundice:

	Treatment	N	Mean	Sig-value	p-value
Age of onset of Jaundice in hours	PT ET	74 26	79.0676 47.5385	0.000	P<0.05*
Peak Serum Bilirubin (mg %)	PT ET	74 26	20.4959 28.2692	0.000	P<0.05*

Table 11: OAE and Neonatal Jaundice

	OAE		P-value
	Normal (n, 69)	Abnormal (n, 31)	
Age of onset jaundice (hours)	79.15	52.41	0.000
Peak serum bilirubin (mg/dl)	20.13	24.81	0.000

Hearing Assessment:

Of the 100 babies 31 (31%) were found to have abnormal OAE (Otoacoustic emission). The mean age of onset of jaundice for babies with normal OAE was 79.15 hours and in those with abnormal OAE was 52.41 hours with the P value of <0.05 which is statically significant. The peak serum bilirubin in babies with normal OAE was 20.13 in contrast to babies with abnormal OAE which was 24.81 mg/dl. Out of 31 babies with abnormal OAE test, 27 babies received exchange transfusion and the rest of four had phototherapy.

Table 12: BAER and Neonatal Jaundice

	BAER		P-value
	Normal (n, 9)	Abnormal (n, 22)	
Age of onset jaundice (hours)	71.88	44.45	0.041
Peak serum bilirubin (mg/dl)	26.10	28.50	0.005

All babies with OAE abnormality were subjected to BAER test and 22 babies were found to have BAER abnormality. The BAER abnormality was increased in the latency and wave III and V. the mean bilirubin for abnormal BAER was found to be 28.5 mg/dl. The age of onset of jaundice in babies with BAER abnormality was 44 hours in contrast to 71.8 hours in babies with normal BAER test. All babies with abnormal BAER received exchange transfusion.

Table 13: Follow up of BAER Test

	Follow up of BAER Test		P-value
	Normal (n, 28)	Abnormal (n, 3)	
Age of onset jaundice (hours)	54.60	32.00	0.285
Peak serum bilirubin (mg/dl)	27.36	32.00	0.000

The BAER abnormalities are transient under reverted back to normal on follow up BAER test following treatment. Only three babies which were brought to Niloufer Hospital in kernicterus had consistent BAER abnormality. The serum bilirubin was more than 32 mg/dl.

In our study OAE test was found to be abnormal beyond serum bilirubin level of 24.81 mg/dl and abnormal BAER beyond 28.5 mg/dl.

tAble 14: Outcome

Outcome	No. of Newborns	Percentage
Discharged	96	96
Hearing Abnormality	03	03
Death	01	01

Of the hundred newborns in our study 96 (96%) cases were discharged and 3 (3%) babies had sensory neural hearing loss and 1 (1%) baby expired due to sepsis with pneumonia.

IV. Discussion

The results of our study show that the incidence of clinical jaundice was 42.03% in level II NICU. Which is lower to compare studies done by the various workers i.e., Singh M. et al (7) (77%), Anand V R et al (6) (74%), Baj Pai et al (3) (54.56%) and Merchant et al (5) (50%), The aetiology of jaundice in the present study was different in comparison with other studies from our country, sepsis (43%), being major cause of jaundice, reason being extra mural origin of our neonates.

Sex:

Of hundred newborns with neonatal jaundice in this study 64% were males and 36% were females. Male to female ratio was 1.7. Sex incidence was similar to other studies (Meharban Singh et al (7) (56.8%) were male and Anil Naranag et al (2) study 64.2% were male).

Birth Weight and Neonatal Jaundice:

The study group had 66% with low birth weight, which is much higher compared to studies done by M. Singh et al (29.5%) and Anil Narang et al (34.5%). Low birth weight is one of the contributing factors for hyper bilirubinemia.

Breast Feeding and Neonatal Jaundice:

67% babies with hyper bilirubinemia were breast fed and were comparable to Meharban Singh et al (7).

Time of onset of Jaundice:

The present study 64% newborns developed jaundice between 48 hours and 7 days of life. V.R.Anand and M.L.Magotra et al (6) reported 45.74% of newborn developed jaundice on 3rd post natal day and 35.53% on 4th post natal day. Our study results were correlated with V.R.Anandand Magotra et al (6).

Sibling History and Neonatal Jaundice:

In our study 5% newborns had sibling history of neonatal jaundice. Khoury et al (8) have reported an increased risk in siblings if previous sibling is jaundiced.

Causes of Neonatal Hyperbilirubinemia:

Septicemia with neonatal Jaundice:

In the presence study**,** Septicemia with Hyperbilirubinemia was seen in 43% of the cases. Septicemia was a leading cause of jaundice in our study may be due to more number of home deliveries, branding, poor socio economic conditions prevailing in rural places.

ABO Incompatibility:

In our study 12% newborns with ABO incompatibility were admitted. It is lower as compared to Baj Pai et al (4) reported 16% Merchant et al (5) reported 22.66%.

Rh Incompatibility:

Our study had 10% newborns with Rh incompatibility i.e. higher than Baj Pai et al (4) (2%) and M.Singh et al (7) (8.1%).

Cephalhematoma:

In present study 9 (9%) newborns were admitted with Hyperbilirubinemia due to cephalhmatoma. V.R.Anandand Magotra et al, Baj Pai et al (4)(4%) of cases of cephalhmatoma. M.Singh et al (7) reported 2.9%.

Biliary Atresia:

In present study 4 (4%) newborns were reported. Merchant RH et al (5) reported 4.1%. Our study correlates with Merchant RH et al (5).

Neonatal Hepatitis:

In this neonatal hepatitis were reported 6 (6%). Merchant RH et al (5) has reported 8%.

Hearing Assessment:

In present study 31 babies had abnormal OAE test. These babies were later screened with BAER, and 22 babies had abnormality. The follow up of BAER was persistently abnormal in only 3 of 19 babies whose initial assessment was abnormal. All three were having kernicterus.

Outcome:

In our study 96 (96%) babies with neonatal hyperbilirubinemia discharged. It is comparable with Manorama et al reported 79.80% discharged. 3% developed kernicterus. One baby died due to sepsis with pneumonia.

V. Conclusions

Incidence of neonatal jaundice in our study was 42.03% with male to female ratio of 1.7: 1. The major cause of neonatal jaundice in the present study is neonatal sepsis 43%, followed by 12% ABO incompatibility, 11% birth asphyxia, 10% Rh incompatibility and neonatal hepatitis contributing 6%. The management of unconjugated hyperbilirubinemia is phototherapy, 74% were given phototherapy alone. Exchange transfusion was required in 26% cases. In our study group 31 babies showed abnormality to OAE test who were subsequently screened with BAER test. Out of 31 cases 22 had initial BAER abnormality, which reverted back to normal in 19 cases, with persistent hearing impairment in three newborns that developed kernicterus. OAE can be a useful screening tool for hearing assessment. If OAE is abnormal the babies can be sent for BAER at higher centers for further evaluation.

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