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Original article:

Neonatal Jaundice: Prevalence, risk factors and outcome among inborn babies in a neonatal unit in port Harcourt, Nigeria

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Abstract

Introduction: Neonatal jaundice, a frequent occurrence in the neonatal period with high prevalence in sub-Saharan Africa, Asia and Latin America is a common cause of morbidity and mortality.

Methods: It was a prospective cross-sectional study carried out in the neonatal unit of RSUTH over an 18 months period. For every inborn neonate with clinical jaundice, serum bilirubin was estimated as well as full blood count and blood groups of the baby and mother.

Observation and Results: Two hundred and seventy-five inborn neonates had NNJ of 809 babies admitted giving a prevalence of 34.0% and a M: F ratio of 1.5:1. Commonest risk factors for NNJ were breastfeeding 264 (96.0%), prematurity 149 (54.2%) and probable NNS 106 (41.7%). ABO incompatibility was significantly associated with pathologic NNJ (P value < 0.05). Twenty-three (8.4%) neonates had EBT of which 21 (91.3%) had a session. The mean SB of neonates with pathologic NNJ of 131.11 ±58.45µmol/L after treatment was significantly lower than 198.26 ± 61.12µmol/L before onset of treatment (P value=0.000). Mean duration of hospital stay was 12.8 ± 10.6 days. Two hundred and sixty-three (95.6%) neonates were discharged. Six (2.2%) had acute bilirubin encephalopathy with seizures 4(23.5%), hypertonia 3 (23.5%) and stupor 3 (17.6%) being the commonest clinical features.

Conclusion : The prevalence of NNJ among inborn neonates in RSUTH is high with breastfeeding, prematurity and probable NNS being the commonest risk factors. Knowledge of the risk factors of NNJ is thus important for early diagnosis, prompt treatment and prevention of complications.

Key words: Neonatal jaundice; Inborn; Port Harcourt

Introduction

Neonatal jaundice (NNJ) is defined as the yellowish discolouration of the sclera, mucous membranes and skin of new born babies resulting from hyperbilirubinemia within the first 28 days of life[1]. It is a frequent occurrence during the neonatal period, affecting about 60% of all term babies and 80% of preterm babies.[2] Although it is a preventable and easily treatable clinical condition, it is a common cause of neonatal morbidity and mortality with high prevalence in sub-Saharan Africa, Asia and Latin America.[3,4] Jaundice in new borns becomes clinically evident when the serum bilirubin levels exceed 85µmol/L.[5]

Neonatal jaundice may be conjugated or Unconjugated; the unconjugated form being the most commonly encountered.[6] It may also be physiologic or pathologic based on the aetiology. Risk factors for NNJ includes neonatal sepsis, prematurity, maternal diabetes mellitus, race, drugs, cephalheamatoma, breastfeeding, blood group incompatibilities between mother and baby, enzyme deficiencies such as G6PD deficiency etc.[3,4,7] These

factors vary according to geographic locations; prematurity, infection, G6PD deficiency are mostly implicated in the developing countries whereas blood group incompatibilities are observed more in developed countries.[8,9]

Early diagnosis and prompt treatment of NNJ is key in preventing its adverse effects. Specific management of NNJ involves the exposure of the baby to ultraviolet light (phototherapy) in mild to moderate cases and exchange blood transfusion (EBT) in severe cases.

The major complication of NNJ, acute bilirubin encephalopathy (ABE) or Kernicterus is a common presentation which arises if not properly managed. With poor health seeking behaviour, late presentation and paucity of neonatal units, ABE is still a common complication of NNJ in Sub-Saharan Africa and Asia.[10-12] This subsequently leads to long term neurologic sequelae such as cerebral palsy, seizure disorder, hearing impairments etc.[11,12]

The present study was carried out to determine the prevalence, risk factors and outcome of inborn babies with NNJ in the neonatal unit of the Rivers State University Teaching Hospital as similar studies have not been carried out.

Materials and methods

This was a prospective cross-sectional study carried out among babies delivered and cared for in the neonatal unit of the Rivers State University Teaching Hospital (RSUTH) Port Harcourt, Nigeria over an 18 months' period from 1st April 2018 to 31st September, 2019. The Rivers State University Teaching Hospital is one of the two major Public Health facilities in Port Harcourt, Nigeria. It serves as the referral hospital for all of the states' owned general Hospitals and Primary Health care facilities. It is a 375 bedded Hospital which now serves as the training facility for the State owned University.

The neonatal unit is a 30 bedded unit consisting of an inborn and an out born unit. The inborn unit consist of 14 cots, 7 incubators, a resuscitaire and 8 phototherapy machines while the out born unit consist of 6 cots, 3 incubators, a resuscitaire and 4 phototherapy machines. The unit is run by 2 consultant paediatricians, resident doctors and house officers as well as a minimum of 3-4 nurses manning each of the 3 shifts. New born babies are admitted into the Neonatal Unit through the labour ward or through the labour ward theatre, either for observation or when there are clinical indications of illnesses.

Informed consent was obtained from parents or authorized caregivers in the absence of the parents after thorough explanation of the study. All babies term or preterm aged 0-28 days old with clinical and laboratory confirmation of jaundice whose parents/caregivers gave consent were consecutively recruited into the study. Babies whose parents/caregivers did not give consent and those without laboratory confirmation of jaundice were excluded. Ethical approval was obtained from the RSUTH Health Research Ethics Committee.

Detailed clinical history was obtained for each baby recruited. This included; age, sex, birth order, birth weight, gestational age, mode of delivery, age at onset of jaundice, history of jaundice in other siblings, age at commencement of feeds, types of feeds as well as maternal age, mother's level of education, occupation and the use of menthol containing substances in the storage of babies clothings. Gestational age was calculated using the first day of the last menstrual period or ultrasound scan result done early in the pregnancy.

All babies who were noticed to have jaundice were examined by the consultant Paediatrician for the severity of jaundice and evidence of other illnesses like sepsis. Venous blood samples were collected in Lithium Heparin bottles (at least 2ml) and sent to the Chemical pathology laboratory of RSUTH where they were centrifuged to extract serum for the estimation of serum bilirubin (SB) - both the conjugated and unconjugated Bilirubin

fraction. The Diazo- method of Bilirubin estimation was used for estimation which involved adding the diazo reagent to the centrifuged serum resulting in a change in colour. Reaction with the Diazo- reagent without the addition of alcohol measured the direct or conjugated fraction while reaction with the presence of alcohol measured the value of the unconjugated fraction.[13] The blood group of mother and baby as well as the full blood count of baby were carried out for every baby with jaundice recruited. Glucose-6-phosphate dehydrogenase (G6PD) assay was however not assayed in our laboratory during the period of the study.

Babies with SB levels above 85µmol/L within 24hours of life or values ≥220µmoL/L in term babies or weights ≥2.0kg or ≥ 170µmol/L in babies 1.5-2.0kg or ≥119µmol/L in babies 1.0-1.5kg or the rate of rise greater than 85µmol/L per day or persistence of jaundice beyond 8 days for term and 14 days for preterm were said to have pathologic jaundice and were commenced on phototherapy while the contrary were said to have physiologic NNJ and did not require phototherapy.[14] Repeat SB estimation was done daily to monitor the trend in severity of NNJ to enable the decision to either step up treatment or to discontinue phototherapy. Babies were said to have severe NNJ if the SB was ≥340µmol/L for term babies or weights > 2.0kg or ≥ 255 in babies 1.5-2.0kg or ≥204µmol/L in babies 1.0-1.5kg or ≥170µmol/L in babies with weights < 1.0kg.[14] Exchange blood transfusion (EBT) was done for such babies in addition to phototherapy. Babies who had other co-morbid conditions such as probable neonatal sepsis (NNS), birth asphyxia etc were managed appropriately alongside the NNJ. Phototherapy was stopped when there was 2 consecutive downward decline of SB below the phototherapy ranges for gestation age and birth weights. Probable neonatal sepsis was defined as full blood count with white blood cell count of ≥20 x 10^9/L or < 5 x 10^9/L or neutrophil count of > 75% or < 40%.[15] A baby's NNJ is suspected to be due to ABO incompatibility if baby's blood group is 'A' or 'B' while the mother is blood group '0' in the absence of other causes of NNJ. Diagnosis of Acute bilirubin encephalopathy (ABE) was made based on the presence of severe SB with any one or combination of the following clinical features; poor suck, high pitch cry, involuntary movements, seizures, paralysis of upward gaze, drowsiness, hypotonia (early stage) and hypertonia (late stage).

Data was entered into an Excel spread sheet and thereafter analysed using SPSS version 22. The results were presented in frequency tables, percentages, pie and bar charts. P value < 0.05 was considered significant at 95% confidence interval.

RESULTS

Eight hundred and nine inborn neonates were admitted into the SCBU during the period of study of which 275 had NNJ giving a prevalence of 34.0%. One hundred and sixty-five (60.0%) were males and 110 (40.0%) females giving a M: F ratio of 1.5:1. One hundred and ninety-nine (72.4%) were 1st - 2nd born. One hundred and forty-nine neonates (54.2%) were delivered at GA < 37 weeks and 178 (64.7%) were delivered by Caesarean section. Birth weight less than 2.5kg predominated, 140 (50.1%). Two hundred and twenty-eight (82.9%) neonates developed jaundice within the first 3 days of life. Of 264 neonates who had commenced feeds, 214 (81.1%) did so within the first 3 days of life and 258 (97.7%) were on breastmilk. Thirty-two (11.6%) neonates had anaemia at presentation, Table I.

Table I: Characteristics of neonates with neonatal jaundice

Variables	**Frequency, n =275 (%)**
Gender	
Male	165 (60.0)
Female	110 (40.0)
Birth order	
$1^{st} - 2^{nd}$	199 (72.4)
$3^{rd} - 4^{th}$	64 (23.3)
$5^{th} - 6^{th}$	10 (3.6)
$\geq 7^{th}$	2 (0.7)
Mode of delivery	
CS	178 (64.7)
SVD	96 (34.9)
Instrumental	1 (0.4)
Gestational age	
<37	149 (54.2)
≥37	126 (45.8)
Birth weight (kg)	
<2.5	135 (49.1)
≥2.5	140 (50.9)
Age at onset of jaundice (days)	
<1	4 (1.5)
1-3	228 (82.9)
4-6	38 (13.8)
≥7	5 (1.8)
Age at commencement of feeds(days), n = 264	
1 – 3	214 (81.1)
4 – 6	46 (17.4)
≥7	4 (1.5)
Types of feeds (n = 264)	
Breastmilk	258 (97.7)
Breastmilk substitutes	6 (2.3)
Presence of anaemia at presentation	
Yes	32 (11.6)
No	243 (88.4)

CS = Caesarean section, SVD = Spontaneous vaginal delivery

Maternal socio-demographic characteristics

Mean age of mothers was 32.1 ±4.7 years with majority being 30 – 34 years, 108 (39.3%). One hundred and seventy-two (62.5%) mothers had tertiary level of education with majority 117 (42.6%) engaged in unpaid jobs, Table II.

Table II: Maternal socio-demographic characteristics

Variable = 275(%)	**Frequency, n**
Mother's age	
20 – 24	17 (6.2)
25 – 29	62 (22.5)
30 – 34	108 (39.3)
35 – 39	71 (25.8)
≥40	17 (6.2)
Mothers level of education	
Tertiary	172 (62.5)
Secondary	91 (33.1)
Primary	12 (4.4)
Mother's occupation	
Paid jobs	93 (33.8)
Unpaid jobs	117 (42.6)
Unemployed	65 (23.6)

Risk factors for neonatal jaundice

The commonest identified risk factors for NNJ were breastfeeding 264 (96.0%), prematurity 149 (54.2%) and probable neonatal sepsis 106 (41.6%) while the least was use of menthol containing substances 22 (8.0%), Table III.

Table III: Risk factors for neonatal jaundice

Variable (%)	**Frequency, n = 275**
Breast feeding	
Yes	264 (96.0)
No	11 (4.0)
Prematurity	
Yes	149 (54.2)
No	126 (45.8)
Probable neonatal Sepsis, n = 254 (%)	
Yes	106 (41.7)
No	148 (58.3)

History of jaundice in sibling	
Yes	62 (22.5)
No	213 (77.5)
ABO incompatibility	
Yes	45 (16.4)
No	230 (83.6)
Use of menthol containing substances	
Yes	22 (8.0)
No	253 (92.0)

Types of neonatal jaundice

Two hundred and eleven (76.7%) neonates had pathologic jaundice while 64 (23.3%) had physiologic NNJ, Figure 1.

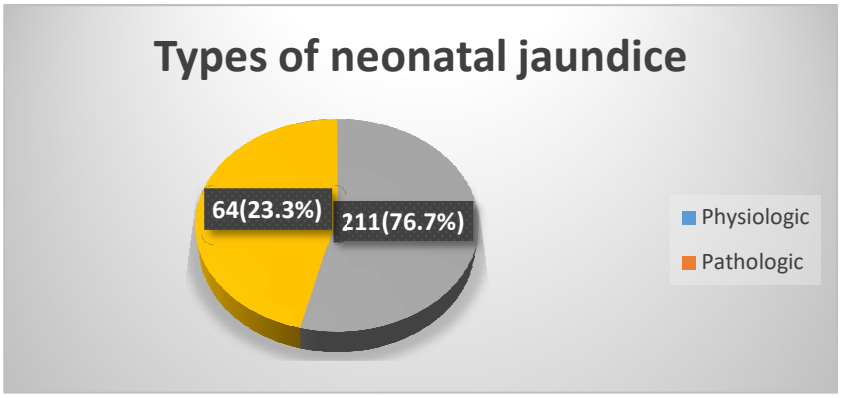

Figure 1: Types of neonatal jaundice

Factors associated with pathologic neonatal jaundice

Neonates with ABO incompatibility were significantly associated with pathologic NNJ and almost 3 times more likely to develop NNJ (P value < 0.05). There was no significant association of history of jaundice in sibling, anaemia at presentation and gestation age with pathologic NNJ (P value > 0.05), Table IV.

Table IV: Factors associated with pathologic neonatal jaundice

Variable	Prevalence, n=211 (%)	p value	OD
ABO incompatibility	Yes 40 (88.9)	0.035*	2.760
	No 171 (74.3)		
History of jaundice in sibling	Yes 52 (83.9)	0.130	1.766
	No 159 (74.6)		
Anaemia at presentation	Yes 27 (84.4)	0.278	1.732
	No 184 (75.7)		
Gestational age (weeks)	< 37 116 (77.9)	0.486	1.233
	≥37 77 (74.0)		

*=Statistically significant

Management of neonates with neonatal jaundice

All neonates with pathologic NNJ received phototherapy with the mean duration being 5.7 ± 3.2 days. Twenty-three (8.4%) neonates had exchange blood transfusion (EBT) of which 21 (91.3%) had one EBT session done while 2 (8.7%) had 2 EBT sessions done. The mean serum bilirubin (SB) of neonates with pathologic NNJ of 131.11 ± 58.45umol/L after treatment was significantly lower than the SB of 198.26 ± 61.12umol/L before onset of treatment (P=0.000). The mean duration of hospital stay was 12.8 ± 10.6 days.

Outcome of neonates with neonatal jaundice

Of 275 neonates with NNJ, 263 (95.6%) were discharged home, 4 (1.5%) discharged against medical advice while 8 (2.9%) died.

Of the 8 deaths, 3 (37.5%) was neonatal jaundice related, Table V.

Table V: Outcome of neonates with neonatal jaundice

Outcome	Frequency, n = 275 (%)
Discharged	263 (95.6)
Discharged against medical advice	4 (1.5)
Died	8 (2.9)

Neonates with acute bilirubin encephalopathy (ABE)

Of 275 neonates with NNJ, 6 (2.2%) neonates had acute bilirubin encephalopathy. Commonest symptoms of acute bilirubin encephalopathy were seizures 4 (23.5%), hypertonia 3 (17.6%), stupor 3 (17.6%), paralysis of upward gaze 2 (11.8%) and poor suck (11.8%), Figure 2.

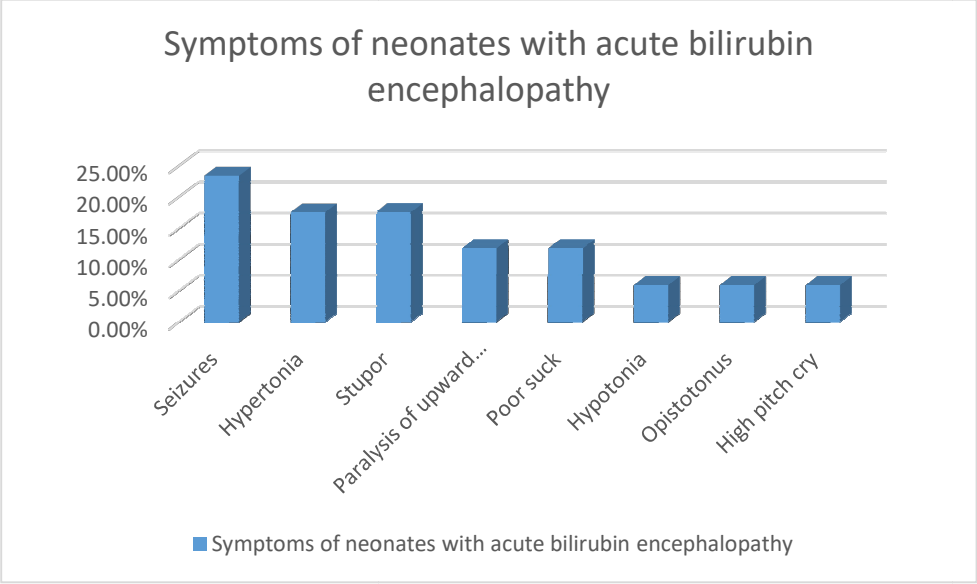

Figure 2: Symptoms in neonates with acute bilirubin encephalopathy

Discussion

Jaundice is one of the commonest conditions in newborns requiring medical attention as shown in the present study where a prevalence of 34.0% was observed among the inborn neonates. This is comparable with the 32.9%, 35.0%, 35.94% and 37.3% reported in Cape coast[16] Ghana, Abakaliki[9] South East Nigeria, Ondo State[17] South West Nigeria and Northern Ethiopia[18] respectively. It was lower than the 44.8%, 52.6%, 55.2% and 64%

prevalence observed in Iran,[19] Nigeria (Delta State),[20] South Africa[21] and India[22] respectively. The lower prevalence observed in the present study could be because only the inborn babies were recruited unlike the latter studies that included both the inborn and out born babies. The prevalence in the present study was however much higher than the 26.5%, 24.8%, 17.9%, 16.6% and 12.6% reported in Benin city[23] Nigeria, Croatia,[24] Bayelsa[25] Nigeria, Egypt[26] and Tehran[27] respectively. These varying prevalence could be attributed to the varying ethnic/geographic differences, risk factors to NNJ as well as varying study designs.

In the present study, more males had NNJ with a M: F ratio of 1.5: 1. Similar male preponderance was also observed in different states in Nigeria[9,28,29] as well as in Ethiopia[18] and Ghana.[30] These findings corroborates the finding by Scrafford et al[12] which showed male gender as one of the predisposing factors of NNJ. Male preponderance in NNJ could be attributed to the fact that male neonates have relatively immature liver and thus unable to process all the bilirubin formed from the red blood cells.[31] In contrast, female preponderance was observed in Ibadan,[32] Nigeria. The reason for this conflicting finding could not be ascertained.

More than two thirds of neonates delivered via Caesarean section had jaundice in the present study as also observed by Gupta et al,[33] Tamook et al[34] and Najib et al.[35] In contrast, Brits et al[21] in South Africa and Oluwafemi et al[28] in Ondo state, Nigeria reported normal vaginal delivery as being associated with a higher chance of NNJ. The lower prevalence of NNJ in neonates delivered via Caesarean section in the study in South Africa could be attributed to the fact that majority of the CS deliveries were elective and as such not exposed to birth trauma and possible bruising that usually predispose to jaundice.

Jaundice was observed more in preterms than full term babies in the present study as observed world-wide.[2] Similar findings were reported in Ethiopia[18] and Cape coast,[16] Ghana. This is not surprising as preterm neonates have immature bilirubin conjugating system, higher rates of haemolysis, increased enterohepatic circulation and decreased caloric intake.[36] Contrary to the present study, jaundice was observed more in term than preterm babies in Ibadan,[32] Nigeria. This difference could be attributed to the fact that the latter was a retrospective study with information retrieved from the neonates' case notes in the children outpatient units and so the possibility of improperly filled data and missing data.

Majority of neonates (82.9%) in the present study presented with jaundice within days 1-3 and the least (1.5%) in the first day of life. Similar finding was observed in Ghana.[30] Early presentation of NNJ within the first week of life was also reported in other parts of Nigeria[20,28,29] and Ethiopia.[18] This early presentation could be attributed to the association of the major risk factors of NNJ being sepsis and prematurity with early neonatal life.[8,20,28,29] Sepsis usually cause haemolysis of the red blood cells as well as hepatic dysfunction that leads to accumulation of serum bilirubin in the body.[37]

Majority of mothers whose babies had jaundice had tertiary education as observed by Mostafa et al[38] in a hospital based case control study carried out in the Gaza Strip. This is not in doubt because of the possibility of earlier presentations to the hospital with their sick babies as compared to the less educated mothers. This better health care-seeking behaviours of more educated women was observed in several studies.[29,39-41] Neonates of mothers with jobs (paid or unpaid) had a higher percentage of jaundice than neonates of mothers that were unemployed. This finding is consistent with a community based study carried out by Olusanya et al[42] in which neonates born to mothers with full employment were more likely to have jaundice.

Commonest risk factors for NNJ in the present study was observed to be breastfeeding followed by prematurity, sepsis and history of jaundice in sibling while the least was use of menthol containing substances. A cross

sectional study in South Africa[21] corroborates the present study which showed that of 95% babies breastfed, 56% developed NNJ. Heydarian and Majdi[43] also reported majority of neonates (57.6%) with severe NNJ were exclusively breastfed when compared with neonates on mixed feeds (26.3%) and breast milk substitutes (11%). Studies have attributed the jaundice in breastfeeding babies with low calorie intake, increased enterohepatic circulation of bilirubin and dehydration.[6,44] Other studies in Ibadan[8] and Abakalilki,[9] Nigeria reported prematurity, G6PD deficiency, sepsis and negative traditional practices as the commonest risk factors of NNJ. Oluwafemi[27] and other researchers in Ondo state, South-Western Nigeria reported sepsis as the commonest risk factor followed by prematurity, birth asphyxia and history of jaundice in sibling. Common risk factors identified in Enugu,[29] Nigeria were sepsis, prematurity, congenital malaria and ABO incompatibility while in Delta state[20] sepsis, prematurity and lack of breastfeeding were the commonest risk factors associated with NNJ. It is important to note that ABO incompatibility was one of the least risk factors of NNJ in the present study as observed in other parts of Nigeria[20,28,29,45] and Africa,[30] it was however reported as the leading risk factor of NNJ in Canada,[46] India[22,47] and Iran.[48] ABO incompatibility however was significantly associated with pathologic NNJ in the present study with 2.7 times increased odds of developing pathologic NNJ. G6PD assay was however not done in the present study and no case of Rhesus isoimmunisation was identified as also observed in Abakaliki,[9] south east Nigeria. These varying risk factors could be attributed to the varying geographic locations and study methods.

The anaemia seen in the present study at presentation could be a complication resulting from haemolysis from any of the risk factors. This was also observed in Enugu,[29] Nigeria.

Diagnosis and prompt treatment of NNJ is critical in preventing its complications. It is important to note that the mean SB after treatment of the neonates was significantly lower than the SB before treatment. This was also observed in Ondo state[17] Nigeria. The percentage of neonates in the present study that had EBT was 8.4% which was much lower than the 20.8% and 23.7% reported in Abakaliki,[9] south east Nigeria and Ondo state,[17] south west Nigeria but lower than the 5% in Gaza strip in the middle East.[38] The lower rate of EBT in the present study when compared to those of Abakaliki and Ondo State could be because only inborn neonates formed the study population unlike the other studies which comprised both inborn and out born neonates. No neonate however needed EBT in the study carried out in South Africa[21] and Ethiopia.[18]

Complications arising from NNJ are rare in developed countries but common in developing countries often resulting in acute bilirubin encephalopathy (ABE), cerebral palsy, seizure disorders, speech impairments and hearing impairment with its attendant medical, economic and social burden on the child, family and community.[10] In the present study, 2.2% had ABE. A higher percentage of 4.0%, 14% and 9.7% were observed in Ondo state[17,28] and Abakalilki,[9] Nigeria. This high prevalence in the earlier studies could be attributed to the fact that both inborn and out born neonates were recruited, presentation may have been delayed as well as ethnic/geographic locations with varying risk factors.

Conclusion

The prevalence of NNJ is high among inborn neonates in RSUTH. Breastfeeding, prematurity and probable NNS are the commonest risk factors for NNJ while ABO incompatibility is almost 3 times likely to cause pathologic NNJ. High index of suspicion with the knowledge of the risk factors of NNJ will facilitate early diagnosis and with prompt treatment will reduce morbidity and mortality of NNJ.

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