ONLINE ISSN :3007-309X
PRINT ISSN :3007-3081

Journal of Medical & Health Sciences Review

Risk Factors Associated with Neonatal Hyperbilirubinemia in Preterm Infants: A Prospective Observational Study at Nishtar Hospital, Multan

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Article Info

Keywords: Neonatal Hyperbilirubinemia, Preterm Hyperbilirubinemia, Neonatal Jaundice, Incidence of Neonatal Hyperbilirubinemia, Causes of Hyperbilirubinemia.

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ABSTRACT

Hyperbilirubinemia is the major perennial situation have an effect on newborns, and preterm neonates account for the bulk of cases over 80%. The Neonatal jaundice was mostly caused by the mother's condition and the babies' incompatibility with ABO and Rh in the Pakistani population, all these factors increase the risk of early severe hyperbilirubinemia and its associated problems among newborns. Still, an extensive number of newborns in underdeveloped nations like Pakistan have low birth weights, and preterm births which is a key risk factor for neonatal jaundice. This research study highlighted that how many new cases of hyperbilirubinemia reported and their possible causes during the study duration in context of pediatric department of Nishtar medical university, Hospital, Multan. This prospective study conducted in neonatal unit of pediatric department Nishtar medical university, hospital multan. Through consecutive sampling, 247 preterm infants included in this study and examined till their discharge, death or shift to NICU. The data was collected through a self-developed Performa consists of a demographic sheet and a routine examination sheet of infant, from 15th Feb 2024 to 15th Aug 2024. The obtained data were analyzed through SPSS version-27. Among 247 preterm infants 58.3%developedHyperbilirubinemia. The significant risk factors are Sepsis ($p<0.001$), Rh incompatibility ($p<0.001$), Hemolytic diseases (p0.004), Birth weight ($p<0.001$), Gestational age ($p<0.001$), Mode of birth (p0.025). Hyperbilirubinemia is a significant concern, affecting 58.3% of the study population. Key predictors include sepsis, Rh incompatibility, gestational age, and family history of jaundice. The findings highlight the targeted interventions and close monitoring of high-risk neonates to prevent complications and improve outcomes.

1. Introduction

1.1 Background and Significance

Hyperbilirubinemia is the major perennial situation have an effect on newborns, and preterm neonates account for the bulk of cases (over 80%) (Sampurna et al., 2023). Sixty percent (60%) of term babies and eighty percent (80%) of preterm infants have increased bilirubin at birth, that usually become apparent up to three days later and goes away ten to fourteen days, often requiring medical attention (Muhammad Waseem Ashraf, 2024). Because of the immaturity of their liver and gastrointestinal systems, as well as the short lifespan of their red blood cells, preterm newborns have hyperbilirubinemia. Different forms of hyperbilirubinemia in infants have been observed, such as hemolytic jaundice including three subtypes caused by ABO blood group incompatibility, , pathological hyperbilirubinemia, physiological jaundice, hyperbilirubinemia resulting from mother's feed, and hyperbilirubinemia linked to insufficiency of G6PD (Ullah S, 2016).

In majority of conditions the rate of disease and death rates and be reduced with timely detection and the interventions for the hyperbilirubinemia. Exchange blood transfusion in extreme cases and blue-light phototherapy are effective type of treatment. Neonates delivered before 37 weeks of pregnancy (preterm infant), neonates' weight at birth less than 2.5 kg (low birth weight) or weight is too low in accordance to weeks of pregnancy (small for gestational age), fetus and mother blood group ABO or Rh incompatibility, and some infant and maternal risk factors such as neonatal inherited disorders like Gilbert's disease and insufficiency of G6PDare linked with elevation of hyperbilirubinemia. Infant suffering from injuries during birth, infants got infected, insufficient mother feed, during the first few days of life loss of fluid and electrolytes, and late development of hyperbilirubinemia (exclusively breast-feed) are examples of postnatal factors. The risk of neonatal hyperbilirubinemia (NH) can be raised by pregnancy-related problems and coexisting illnesses that raise the possibilities growth retardation in womb (intrauterine growth retardation),birth of infant before term pregnancy, or small for gestational age and low birth weight (caterina Fanello, 2023). Further, enteral feeding is frequently delayed, which may slower the intestinal motility and bacterial growth colonization and lower bilirubin clearance. The high extent and duration of newborn hyperbilirubinemia are caused by these developmental and clinical features (caterina Fanello, 2023).

Neonatal jaundice was mostly caused by the mother's condition and the babies' incompatibility with ABO and Rh in the Pakistani population, all these factors increase the risk of early severe hyperbilirubinemia and its associated problems among newborns (Hafsa Naeem, 2023). Still, an extensive number of newborns in underdeveloped nations like Pakistan have low birth weights, and preterm births which is a key risk factor for neonatal jaundice. Most women in rural Pakistan choose home births by midwives. Furthermore, the diagnosis of severe new-born jaundice is sometimes overlooked (Qumer M Fatima T Albert A, 2022). This research study highlighted that how many new cases of hyperbilirubinemia reported and their possible causes during the study duration in context of pediatric department of Nishtar medical university, Hospital, Multan.

2. Literature Review

2.1 Hyperbilirubinemia in preterm infants

Yellowness of body (jaundice) typically present in fifty percent term newborn babies, because the liver of infants become proper function in some days after birth and perform its function to maintain the bilirubin level in blood. Typically, the yellowness of body is not fetal and become settle with or without treatment. Approximately the bilirubin level raised in eighty percent premature newborns after birth. The infants born before 37 weeks of pregnancy prone to develop hyperbilirubinemia than the term babies because of the partially functioned liver. A preterm baby's liver may take a week or

longer to properly function. Most babies respond well to treatment. The intervention for increased bilirubin level is mandatory because In rare situations, severe increase in bilirubin can results brain impairment (Kudhair, 2021). The neurological complications of severe increase in bilirubin includes acute bilirubin encephalopathy and kernicterus 1 in every 2480 births (live) as reported in a study conducted in Canada (Sgro M, 2012).

2.2. Biological Factors

I. Bilirubin

One typical byproduct of hemoglobin degradation is bilirubin. Two molecules are produced as hemoglobin breaks down: heme and globin. Two enzymes in the degradation of heme produce bilirubin as a byproduct(Volpe, 2024). Heme is converted by heme oxygenase to biliverdin and subsequently to nicotinamide adenine.

II. Bilirubin Formation

Reticuloendothelial system has a key function for the formation of bilirubin. The old RBC's (red blood cells) get rid from the circulation with the help of, liver, spleen, and bone marrow, these organs have performed the major function of blood cell release from the protein (heme) and also than convert this to bilirubin(Chung Eun Ha, 2023). Fig. 2.1 summarizes the mechanism for the breakdown and elimination of bile in certain circumstances, hepatocytes, macrophages, and the epithelial cells of the tubules of kidney aid in the production of bilirubin. A microsomal enzyme (Heme oxygenase), differs from an another microsomal enzyme, the oxygenase, that bound to heme in the first instance following its release(Chung Eun Ha, 2023). The phase in the degradation of heme that seems to be rate-limiting is catalyzed by heme oxygenase. Heme induces it, and for it to function, NADPH (Volpe, 2024)and O2 are needed. Senescent erythrocyte sequestration involves the spleen, an organ which has the highest activity of heme oxygenase's inducible isoenzyme form. Heme's breakdown oxygenase's constitutive form is primarily found in two major organs, brain and the liver. The heme's α-methene carbon is hydroxylated (oxidized) then, bind to the α-hydroxy hemin, then autoxidizes to a blue-green pigment called biliverdin, by consuming oxygen and releasing the gases carbon monoxide and iron (which are produced when the α-methene bridge oxidizes)(Chung Eun Ha, 2023). Since this system accounts for the majority of carbon dioxide generated by creatures, the carbon dioxide has to play a pivot role in degradation of heme in the body. A strong competitive agent is Tin (Sn) protoporphyrin which inhibit to synthesize the enzyme heme oxygenase and block its activity effectively, that may be used therapeutically to cure newborn jaundice(Chung Eun Ha, 2023).

Biliverdin is converted to bilirubin by biliverdin reductase, which is dependent on dinucleotide phosphate (NADPH). In liver the enzyme UDP glucuronyl converts it to conjugated bilirubin, after binding to albumin,(Volpe, 2024). The biliary system then excretes the conjugated bilirubin(Volpe, 2024).

2.2. Clinical Factors

I. Hemolytic diseases and ABO incompatibility in preterm infants

The immune-driven red blood cell (RBC) illness known as HDFN (hemolytic disorder of the fetus and newborn) occurs when red blood cells of fetus or neonate attacked by antibodies of mother (Ree IMC, 2017). ABO antibodies are naturally occurring antibodies. ABO antibodies seen in Group "O" people include anti A and anti B. The group "O" individuals, immunoglobulins G (IgG) are predominating, but immunoglobulins M and IgA components are also present. Infants born to Group "O" moms are more likely to have fetal and newborn hemolytic illness than those born to Group "A" or "B" mothers because IgG crosses the placenta easily. Proper and early diagnosis, along with therapy with intravenous immunoglobulins or transfusion with suitable platelets, maybe from the mother, can rescue the newborn from bleeding episodes (Ripal J. Shah, 2023). ABO incompatibility, usually a problem of neonate rather than fetus, is one of the most common maternal-fetal blood group

incompatibility, resulting most commonly in Jaundice in 1st 24 hours of life (Sonawane, 2025).

II. Septicemia in neonates

In low-income and middle-class states particularly suffering from the problem of spreading infection in blood stream of premature infants that results a high rate of mortality and morbidity (Singh et al., 2022). In infants, the elevated level of bilirubin is so prevalent that it is referred to as physiologic. The bacteria most frequently implicated in neonatal sepsis with an early onset is Streptococcus agalactiae, also referred to as Group B Streptococcus (GBS). Although prior research indicates that bilirubin possesses antioxidant qualities and is advantageous in endotoxic shock, there has been no consideration of bilirubin's potential antimicrobial characteristics (Hansen, 2018).Sepsis, also in infant, pediatric, and adult populations is known to be associated with hyperbilirubinemia; in fact, there can be proof that increases in hemoglobin breakdown in critically ill patients lead to an elevation of blood bilirubin levels(Morimatsu H, 2006).

III. **Other risk factors related to Premature hyperbilirubinemia**

Babies that delivered before thirty-seven weeks of gestation, weight less than 2.5 kilogram or intrauterine growth retardation, ABO blood group system incompatibility, and some generation to generation transmitted neonatal disordersG6PD deficiency increase chance of neonatal hemoglobinopathy. Injuries during birth, infections, insufficient mother feed, loss of electrolytes and fluid after early days of birth, and exclusive breastfeeding are examples of postnatal factors.

3. Methodology

This Study was a prospective observational study conducted in Nishtar Medical University, Hospital, Multan, Punjab, Pakistan. The preterm were the study population of this research. Sample size was 247 preterm infants.

3.1.Ethical Consideration

The Data was collected after the Ethical Approval from Institutional Review Board of Nishtar Medical University, Multan, according to Helsinki Standards, letter reference no. 2184/02/02/2024. After the thorough explanation of study, the consent form was signed from the guardians of the preterm infants enrolled in Neonatal Unit of pediatric department at Nishar university, Hospital, Multan.

3.2.Data Collection Tool

Data collection tool consists of Demographic data, Physical Examination of Newborn, Lab Investigations and Treatment.

3.3.Measuring the internal Consistency and Validity of the Instrument

After the step of through proper channel, ethical consideration a short analysis performed for measuring the consistency of the Data collection check list to minimise the Data collection Biases through pilot study.

3.4.Inclusion Criteria

- Gender Male and female
- Age <37weekes
- Birth weight >500 grams
- Preterm neonates of mothers age <45 years age, admitted in Neonatal Unit of Pediatric department NMU Hospital, Multan

3.5. Exclusion criteria

- The preterm infants who got Sick within 24 hours of admission and shifted to NICU
- Preterm infants who will be on Ventilator
- Parents who willingly withdraw the study
- Preterm’s with complications such as congenital heart diseases, and respiratory distress syndrome.

3.6. Data Collection Procedures

After the evaluating reliability through pilot study and validity evaluation of the instrument by the research experts, the researcher started data collection in the pediatric department as follows:

3.7. Enrolment of preterm Neonates

All the preterm babies had been enrolled in Neonatal Unit of pediatric department at Nishar university, Hospital that fulfil the inclusion criteria were included in study after obtaining consent from their parents.

3.8. Assessment of Newborn

I. History

The routine full history taken by the on-duty Doctor with focusing on date of birth, gender, birth asphyxia, birth trauma, mode of birth, gestational age, previous sibling with neonatal jaundice, perinatal and past history for maternal illness, parity, maternal age, history of drug intake during pregnancy such as antihypertensive, antidiabetic, anticoagulants.

II. Physical Examination

As routine examination by the on-duty Doctor, the on-admission included birth weight in kilogram, body temperature, appearance of the infant, level of alertness, blueness of body (cyanosis) and neonatal reflexes. During observation of child till admitted status, assess skin color to see the level of yellowness of skin, onset of jaundice at day of life, and observed the change in infant condition such as septicemia, hemolysis. Some neural observations included tone of muscle and other signs of kernicterus and acute bilirubin encephalopathy (ABE).

III. Investigations

Laboratory investigations as prescribed by pediatrician that included total serum bilirubin, reticulocyte count, hematocrit level, CRP, blood groups of mothers and infants, Combs' test and G6PD assay.

IV. Treatment

In therapy as per hospital protocols suggested by pediatrician, which included phototherapy, intensive phototherapy, and exchange blood transfusion.

3.9.Data Recording

All the relevant data required had been recorded on a self-developed Performa by the researcher. History and on admission assessment were recorded on admission then the routine examination findings were recorded on daily basis follow-up after the morning round by pediatrician.

3.10. Process of statistical analysis

I. Process of entering data

After recoding the data, the data were entered into a secure database, labeled different variables and coding of data to anonymized the study participants to ensure the confidentiality. A review of data performed after the entry of data in tubulation form to confirm the accuracy of data. Concurrent audits perform to monitor the data accuracy.

II. Analyzing the data

The analysis process of data processed through SPSS (software) Version-27.

III. Normality of the Data

Normality of Data were Presented through, Bar-Chart and pi-Charts.

IV. Descriptive Statistics

In Descriptive Statistics Calculate mean and standard deviation for bilirubin levels in preterm infants. Generate frequency distributions to show the incidence of hyperbilirubinemia at different levels.

V. Association between variables

For measuring association between different risk factors and risk of developing hyperbilirubinemia was measured through mean using tests like chi square and fissure.

VI. Significance Level

Significance Computed by P value and seeing the estimated risk odd ratio at 95% confidence interval.

a. Inclusion Criteria

In the final review, a study could be included if it meets the criteria:

i. Any form of graph neural network (e.g., GCN, GAT, MPNN) applied on cardiovascular or CAD- specific datasets.

ii. Disease mapping or progression modeling and clinical diagnosis in a coronary setting.

iii. Cloud-based deployment in training, inference, data management, or federated learning.
iv. Published by peer journals or conferences and bear a valid DOI or institutional indexing.
v. Human subjects or real-world clinical data.

Results

Demographic description of preterm infants

Total 247 preterm infants that enrolled in this study had presented with following demographic characteristics shown in table 4.1.

Table 4-1: Demographic characteristics of Infants (N=247)

Demographic Variables	
Gender of infants	
Male	
Female	
Gestational Age	
<28 weeks	
28-less than 32	
32-less than 37 weeks	
History of Birth Asphyxia	
Yes	
No	
History of Birth Trauma	
Yes	
No	
History of Jaundice in Sibling	
Yes	
No	
Mode of Birth	
C/section	
SVD	
Preterm Infant Weight	
500g-1kg	
1.1-1.5kg	
1.6-2.0kg	
2.1-2.5kg	
>2.5kg	

Demographic description of Mothers

The Maternal Characteristics of 247 preterm infants admitted in neonatal unit that had met the inclusion criteria were presented in the table 4.2.

Table 4-2: Maternal characteristics of Preterm Mothers (N=247)

Variable	N	%
Parity		
Nullipara	61	24.7
Multipara	186	75.3
History of Maternal Diseases		
No disease	175	70.9
HTN	47	19.0
Preeclampsia	13	5.3
Eclampsia	1	0.4
Liver Diseases	1	0.4
Diabetes Mellitus	6	2.4
DM+HTN	4	1.6
History of medicine Taken during Antenatal		
No medicine taken	178	72.1
Insulin +Aldomet	1	0.4
Diazepam	7	2.8
Aldomet	51	20.6
Metformin	3	1.2
Insulin	4	1.6
Aldomet+ Loprin	3	1.2
Socioeconomic status		
Poor	130	52.6
middle class	112	45.3
Upper class	5	2.0
Religion		
Islam	244	98.8
Others	3	1.2
Maternal Age		
18-26	119	48.1
27-35	99	40.1
36 -45	29	11.8

Out of total sample 247(100%) preterm infants 144 (58.3%) developed HB and 103 (41.3%) did not develop HB.

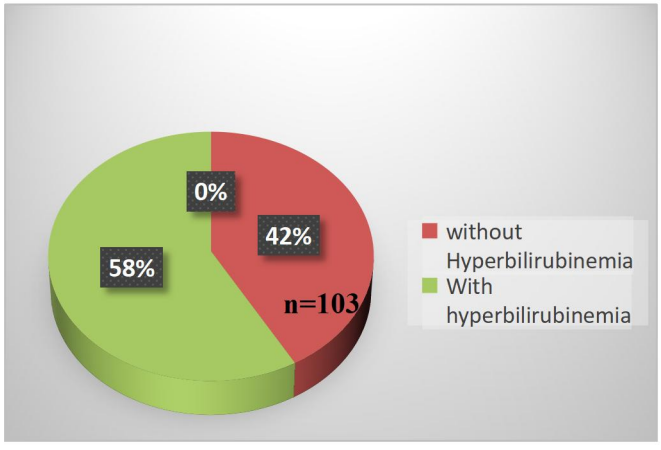

Figure 4-1: Distribution of Hyperbilirubinemia among preterm infants

The out of 144 preterm that had developed hyperbilirubinemia, presented with type of jaundice, as 34 (23.6%) developed physiological jaundice and 110 (76.4%) preterm infants developed pathological jaundice.

Table 4-3: Distribution of physiological and Pathological Jaundice in preterm infants (N=247)

Types of Jaundice	N	%
Physiological	34	23.6
Pathological	110	76.4
Total	144	100.0

The below table 4.4 presents the distribution of hyperbilirubinemia among preterm infants and Pearson Chi-square test applied for determination of relationship between new cases (incidence) of hyperbilirubinemia as well as the different infant characteristics.

Table 4-4: Distribution of Hyperbilirubinemia among preterm infants and Chi-square test for Neonatal risk factors (N=247)

Infants Characteristics	Hyperbilirubinemia			
	Yes n(%)	No n(%)	OR at 95% CI	P-value
Gender of preterm			1.39 (0.83;2.31)	0.200
Male	79 (32.0)	48 (19.4)		
Female	65 (26.3)	55 (22.2)		
Gestational Age			2.57 (1.76;3.52)	<0.001
<28 weeks	35 (14.1)	06 (2.4)		
28- less than 32	30 (12.1)	18 (7.2)		
32- less than 37 weeks	79 (32.0)	79 (32.0)		
History of Birth Asphyxia			1.33 (0.77;2.31)	0.628
Yes	104 (42.1)	68(27.5)		
No	40 (16.1)	35 (14.1)		
History of Birth Trauma			1.07 (0.29;3.91)	0.911
Yes	06 (2.42)	04 (1.6)		
No	138 (55.9)	99 (40.1)		
History of Jaundice in Sibling			7.51 (3.91;14.41)	<0.000
Yes	78 (31.5)	14 (5.6)		
No	66 (26.8)	89 (36.0)		
Mode of Birth			1.79 (1.07;2.99)	0.025
C/section	81 (32.8)	43 (17.4)		
SVD	63 (25.5)	60 (24.2)		
Preterm Infant Weight			2.52 (2.24;2.91)	<0.001
500g-1kg	34 (13.7)	07 (2.9)		
1.1-1.5kg	45 (18.2)	22 (9.0)		
1.6-2.0kg	39 (15.7)	47 (19.0)		
2.1-2.5kg	19 (7.6)	23 (9.3)		
>2.5kg	07 (2.9)	04 (1.6)		

The below table 4.5 presents the distribution of hyperbilirubinemia among preterm infants and maternal risk factors association with hyperbilirubinemia.

Table 4-5: Distribution of Hyperbilirubinemia among preterm infants and Chi-square test for Maternal

risk factors (N=247)

Maternal Characteristics	Hyperbilirubinemia		OR (95% CI)	P value
	Yes n (%)	No n (%)		
Parity				
Nullipara	30(12.1)	31(12.5)	0.61 (0.34;1.09)	0.050
Multipara	114(46.1)	72(29.1		
History of Maternal Diseases				
No disease	98(39.6)	77(31.1)	0.76 (0.39;1.12)	0.224
HTN	27(10.9)	20(8.0)		
Preeclampsia	11(4.4)	2(0.8)		
Eclampsia	0(0)	1(0.4)		
Liver Diseases	1(0.4)	0(0)		
Diabetes Mellitus	4(1.6)	2(0.8)		
DM+HTN	3(1.2)	1(0.4)		
History of medicine Taken during Antenatal				
No medicine taken	101(40.8)	77(31.1)	2.69 (0.26;10.62)	0.533
Insulin +Aldomet	1(0.4)	0(0)		
Diazepam	5(2.0)	2(0.8)		
Aldomet	29(11.7)	22(8.9)		
Metformin	2(0.8)	1(0.4)		
Insulin	3(1.2)	1(0.4)		
Aldomet+ Loprin	3(1.2)	0(0)		
Socioeconomic status			0.61(0.28;1.32)	0.597
Poor	76(30.7)	54(21.8)		
Middle class	64(26.0)	48(19.4)		
Upper class	4(1.6)	1(0.4)		
Religion			0.63 (0.48;1.42)	0.762
Islam	142(57.4)	102(41.2)		
Others	3(1.2)	0(0)		
Maternal Age				
18-26	59(23.8)	60(24.2)	7.14(0.61;84.06)	0.014
27-35	70(28.3)	29(11.8)		
36 – 45	15(6.0)	14(5.6)		

Table 4.6 presents the distribution of Hyperbilirubinemia among 247 preterm infants in relation to clinical risk factors such as Sepsis, Rh incompatibility, ABO incompatibility, Hemolytic Disorders, and Polycythemia.

Table 4-6: Distribution of Hyperbilirubinemia among preterm infants and chi-square test for Clinical Risk factors (N=247)

Risk factor	Incidence of Hyperbilirubinemia			
	Yes n(%)	No n(%)	OR (95% CI)	P value
Sepsis			3.90 (8.13-;13.01)	<0.001
Yes	71(28.7)	14(5.6)		
No	73(29.5)	89(36.0)		
ABO incompatibility			6.00 (0.73;48.73)	0.058
Yes	8(3.2)	1(0.4)		
No	136(55.0)	102(41.2)		

Rh incompatibility			3.030 (8.33;11.02)	<0.001
Yes	15(6.0)	0(0)		
No	129(52.2)	103(41.7)		
Hemolyic disorders			4.17 (0.90;19.26)	0.004
Yes	13(5.2)	0(0)		
No	131(53.0)	103(41.7)		
Polycythemia			1.72 (1.55;1.92)	0.230
Yes	2(0.8)	0(0)		
No	142(57.4)	103(41.7)		

Discussion

The results of this prospective cross-sectional study in neonatal unit of Nishtar hospital Multan, showed that the incidence of neonatal hyperbilirubinemia in preterm infants was 58.3% (144 out of 247 preterm infants). On the other hand, a retrospective study conducted in neonates admitted in neonatal intensive care unit (pediatric department) of Abshway revealed that the prevalence of neonatal hyperbilirubinemia was 59.8% (Al Gameel, 2023).Another, study (analytical cross-sectional) conducted in Zimbabwe in which secondary data retrieved retrospectively found that a neonatal jaundice prevalence was 45.99% (Kahiya, 2023).

In this study, results indicate that the relation of variables sepsis and hyperbilirubinemia (HB) in preterm infants, with a p-value of <0.001. These results are consistence with p value 0.0001 suggests a significant association between sepsis and development of Neonatal HB (Aynalem, 2020).However, the results of other studies have shown conflicting evidence. For instance, a study in Ethiopia found no statistically significant association between neonatal sepsis and HB, with a p-value of 0.217 (Sisay, 2023). Another study conducted at JMC also found no significant association, with a p-value of 0.118 (Asaye et al., 2022).

The differences in results may be due to variations in study design, population characteristics, or sampling techniques. For example, the Ethiopian study included all neonates, whereas our study focused on preterm infants. The JMC study used convenient sampling, which may have introduced bias. More researches needed to explore the association in sepsis and HB among different populations and settings. Our study highlights the importance of close monitoring of preterm infants with sepsis for the development of HB.

The results of this indicate a highly significant association between Rh incompatibility and hyperbilirubinemia (HB) in preterm infants, with a p-value of 0.001. These finding are same as another study (p-value .010) that found a significant association between neonatal HB and Rh incompatibility (Asaye et al., 2022).However, a third study found insignificant results, with a p-value of 0.3100 (Nyangabyaki-Twesigye et al., 2020). The discrepancy between these findings may be due study design, population characteristics, and sample size.

The clinical implications of our findings are significant, highlighting the need for close monitoring of preterm infants with Rh incompatibility for the development of HB. The researcher in the study suggests Rh incompatibility is a significant risk factor for HB in premature babies. Further exploration is needed to explore the association of Rh incompatibility and HB in different populations and settings. Our study highlights the importance of considering Rh incompatibility is a significant cause for HB in premature babies, and the need for further investigation into the underlying mechanisms of this association.

The results suggest a marginally significance link in ABO incompatibility and hyperbilirubinemia (HB), p-value of 0.058 and an Exact Sig. (2-sided) p-value of 0.084. In contrast, other studies have shown stronger evidence of an association between ABO incompatibility and HB. For instance, Sisay (2023) found a significant association with a p-value of 0.005, with 16 out of 26 infants with ABO incompatibility developing HB. Similarly, Asaye et al. (2022) found a significant (p-value .002), with 33 out of 54 ABO incompatibility positive babies developing HB(Asaye et al., 2022).

Another study by Nyangabyaki-Twesigye et al. (2020) presents a significant result (p-value .0317) (Nyangabyaki-Twesigye et al., 2020).The discrepancy in findings may be due to differences in sample, characteristics of targeted population, and study design.

Overall, while This study suggests a possible

association between ABO incompatibility and HB, the evidence is not strong. However, the cumulative evidence from multiple studies suggests that ABO incompatibility may be a risk factor for HB.

The results are significant, consistent with other studies. The Pearson Chi-Square test yields a p-value of 0.004, indicating a significant association. Similar results study by Routray et al. (2021), who found that pathological jaundice was more common than physiological jaundice, with Hemolytic disorders of neonates being the most prevalent cause. In our study, the hemolytic disorder was significantly associated with the neonatal HB in preterm infants, suggesting that it may be a significant predictor of the outcome variable.

The findings of Routray et al. (2021) also highlight the importance of identifying the underlying causes of jaundice, as different causes may require different management approaches. In our study, the hemolytic disorder with an increase chance of jaundice, evidenced it as an important factor to consider in the management of jaundice.

The findings suggest insignificant relation in hyperbilirubinemia and polycythemia, with a p-value of 0.230. However, this result is conflicting with the fact that 2 out of 2 infants with polycythemia developed hyperbilirubinemia. In contrast, a study in Ethiopia found a significant association between polycythemia and hyperbilirubinemia, with 14 out of 23 infants with polycythemia developing hyperbilirubinemia (Sisay, 2023). Polycythemia may be a cause for hyperbilirubinemia, and in future studies should be conducted to confirm these findings with strong evidences.

Interestingly, this prospective study found no cases of G6PD deficiency among the participants. This may be due to the limitations of concerned study. However, existing literature suggests that G6PD deficiency is an important risk-factor that results elevated serum bilirubin level in newborn babies.

In fact, a recent retrospective cross-sectional study in Zimbabwe found a significant (p-value <0.001)result in relation to G6PD deficiency and the risk of developing jaundice(Kahiya, 2023).The absence of G6PDdeficiency cases in our study should not be interpreted as evidence that it is not a significant risk factor. Further investigation conducts to explore G6PDdeficiency and neonatal hyperbilirubinemia.

Conclusion

This prospective study provides robust evidence that neonatal hyperbilirubinemia is a prevalent and significant concern among preterm infants, affecting 58.3% of the study population.

The identified Causes, including ABO and Rh incompatibility, gestational age, and family history of jaundice, underscore the need for targeted surveillance and early intervention. The study highlighting the imperative for

- Enhanced monitoring and early detection of hyperbilirubinemia in preterm infants
- Individualized care and management strategies based on gestational age and underlying causes
- Family education and support to facilitate early recognition and treatment.

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