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Magnitude and Associated Risk Factors of Neonatal Hyperbilirubinemia Among Neonates Admitted to Tibebe Gion Specialized Hospital, Bahir Dar, Ethiopia

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MAGNITUDE AND ASSOCIATED RISK FACTORS OF NEONATAL HYPERBILIRUBINEMIA AMONG NEONATES ADMITTED TO TIBEBE GION SPECIALIZED HOSPITAL, BAHIR DAR, ETHIOPIA

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Abstract

Background: Neonatal hyperbilirubinemia is a serum bilirubin greater than 85 μmol/L (5 mg/dL). It is the yellowish discoloration of the skin, sclera and mucous membranes resulting from deposition of bilirubin. Based on previous studies, ABO incompatibility, sepsis, breast feeding and prematurity were etiologic factors.

Objective: To asses magnitude neonatal hyperbilirubinemia and associated risk factors among neonates admitted to neonatal intensive care unit Tibebe Gion Specialize Hospital from July 1/2011 E.C to July 30/2012E.C.

Methodology: An institution based Cross-sectional study was conducted on neonates admitted at NICU of TGSH from July 1/ 2011 to July 30/ 2012E.C E.C. From a total of 678 neonates who fulfilled the inclusion criteria, 380 neonates were taken by a simple random sampling. Data on socio demographic characteristics and risk factors were collected by principal investigators and trained health workers. The data were cleared, entered and analyzed using SPSS version21. By descriptive statistics frequency was done and shown with tables and figures. Binary logistic regression analysis were done to identify neonatal hyperbilirubinemia and its associated factors.

Results: In this study, 52.9% neonates had hyperbiliubnemia. Two hundred thirty three (61.3%) neonates were male. The most common etiologic diagnosis were sepsis 29.7 % and prematurity 24.5% .SGH, inadequate breast feeding, prematurity, sepsis and age at admission had significant association with neonatal hyperbilirubnemia.

Conclusion: The result of this study showed magnitude of neonatal hyperbilirubinemia is high and identified etiologic diagnosis were sepsis, prematurity and ABO incompatablity.SGH and age at admission, sepsis, prematurity and inadequate breast feeding were associated risk factors.

Key words: neonate; hyperbilubinemia; risk factors

Acronyms

ABO: blood group A, B or O.

AOR: adjusted odd ratio

BW: birth weight

CI: confidence interval

COR: crude odd ratio

GA: gestational age

G6PD: glucose 6 phosphate dehydrognase

INH: indirect neonatal hyperbilirubnemia

NH: neonatal hyperbilirubnemia

NICU: neonatal intensive care unit

NNH: neonatal jaundice

RH: Rehesus factor

RR: relative risk

SGH: subgaleal hemorrhage

TGSH: Tibebe Gihon specialized Hospital

TSB: total serum bilirubin

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1. Introduction

1.1 Background

Neonatal Hyperbilirubinemia is a serum bilirubin greater than 85µmol/L (5 mg/dL). It is the yellowish discoloration of the skin, sclera and mucous membranes resulting from deposition of bilirubin [1]. Neonatal hyperbilirubinemia is attributed to increased red blood cells volume per weight, decreased red blood cells life span, increased enter hepatic circulation and defective uptake of bilirubin. It is caused by an increased production of bilirubin from senescent fetal red blood cells and/or limited bilirubin elimination in the newborn infant *[1]*.

Based on a study done at tikuranbesa hospital, the prevalence of neonatal hyperbilirubinemia was 160(44.9%) and 11(6.9%) neonates developed bilirubin encephalopathy. This study found that most affected age group by NH was 3-6 days old at admission which was 52.5% and those >6 days old were 32.5%.In this study, etiologic factors of NH were ABO incompatibility (35.6%), sepsis (18.8%), breast feeding (10%) and prematurity (8.1%) were the most etiologic factors. (1) Breastfed newborns are more likely to develop prolonged hyperbilirubinemia than those fed formula, [2].

Neonatal jaundice is a common condition worldwide occurring in up to 60% of term and 80% of preterm newborns in the first week of life [3]. Newborns show clinical signs which tend to start on the head and face and then spread down the trunk and limbs as a result of high serum levels of bilirubin. Jaundice in newborns is a result of increased release of hemoglobin from breakdown of red cells due to high hemoglobin at birth, as well as due to reduced lifespan of newborn red blood cells (70–80 days) compared to that of adults (90–120 days), and reduced hepatic metabolism of bilirubin due to immature hepatocytes. Most of this newborn hyperbilirubinemia is a natural transition which resolves by the first week of life with maturing of the liver. However, hyperbilirubinemia is also the main reason for hospital admissions and readmission during the neonatal period [3]. Hyperbilirubinemia often results in kernicterus with its attendant medical, economic, and social burden on the patients, [3].

Based on study findings from Ghaem Hospital, 2003 to October 2011 for evaluation of jaundice, Neonatal infection was found in approximately 10% of jaundiced newborns. The most common infection associated with neonatal jaundice was UTI (77.9%), Sepsis (16.8%) and pneumonia (5.3%), in order. The most common pathogen isolated from UTI was Klebsiella pneumonia (48 infant), followed by Escherichia coli 2 (38), proteus (6), Staphylococcus epidermidis (5), Staphylococcus aurous (3) and Acinetobacter (2). The most common pathogen isolated from sepsis was

Staphylococcus aurous, followed by Staphylococcus epidermidis, proteus, entrobacter, Klebsiella pneumoniae and Escherichia coli (4)

A study conducted in Canada revealed that ABO blood group incompatibility (n = 48) was the most common cause of hyperbilirubinemia, followed by G6PD deficiency (n = 20). Of those with ABO incompatibility, 32cases (66.7%) involved infants born to mothers with type O blood. In 165 cases (64.0%) no cause was identified for the hyperbilirubinemia. The demographic characteristics did not differ significantly between cases with and with Hyperbilirubinemia often results in kernicterus with its attendant medical, economic, and social burden on the patients, [3]. out a specific diagnosis, although those with no specific diagnosis presented later than infants with an identified cause for the hyperbilirubinemia (4.9 [SD 3.0] v. 4.2 [SD 2.3] days of age; p = 0.05(5)

In a study done in Iran the prevalence of severe hyperbilirubinemia was 15 percent in all neonates with Icterus .the cause of severe hyperbilirubinemia, similar to other previous studies in the world, was ABO and Rh incompatibility (5.9%), G6PD deficiency(25.5%), sepsis (12%) other causes (3.5%) and unknown (53.1%).Causes of severe hyperbilirubinemia in our study were 53.1% unknown.(6)

1.2statement of the Problem

Neonatal Hyperbilirubnmia becomes a global problem and is an important contributing factor for Neonatal morbidity and mortality, especially in developing countries where the highest burden of Neonatal mortality is prevalent.

Neonatal jaundice is a common condition worldwide occurring in up to 60% of term and 80% of preterm newborns in the first week of life (3).

Based on a study done in Iran, the incidence rate of jaundice due to infection was reported 10 % (UTI 8%, sepsis 1.7% and pneumonia 0.3%). In this prospective study the most common pathogens isolated from UTIs were Enterobacter aerogenes 38%, Enterococcus faecalis 25%, Klebsiella pneumoniae 25% and Escherichia coli 12%. Sepsis screen was negative in all except one case with a high C-reactive protein (CRP) level. None of the patients had a positive blood culture (4) (7).

According to study done in Ghana low neonatal birth weight and prolonged duration of labor are associated with neonatal jaundice. Mothers had inadequate knowledge of neonatal jaundice and its causes. Education on the condition and its causes should be intensified especially by healthcare workers during regular antenatal visits (3)

Based on study done in united states the annual NH prevalence was 29.6 to 31.7%; hemolytic NHB, 1.8 to 2.4%; treated hemolytic NH, 0.46 to 0.55%, between 2011 and 2016. The matched analysis included 1373 pair's ≥35 weeks GA. The treated hemolytic NH cohort had significantly more birth

trauma and hemorrhage (4.5% vs. 2.4%, p = 0.003), vacuum extractor affecting newborn (1.9% vs. 0.8%, p = 0.014), and polycythemia neonatorum (0.8% vs. 0%, p = 0.001) than the matched non-NHB cohort(18).

Based on study doneinThai-Myanmar border Out of 2980 records reviewed, 1580 (53%) had INH within the first 14 days of life. INH was moderate in 87% (1368/1580) and severe in 13% (212/1580). From 2009 to 2011, the proportion of severe INH decreased from 37 to 15% and the mortality dropped from 10% (8/82) to 2% (7/449) coinciding with the implementation of standardized guidelines and light-emitting diode (LED) phototherapy (19)

From study done in India, out of 560 newborns delivered during the study period at ASRAM, 273 (48.8%) newborns developed clinical jaundice. Out of 273 newborns with clinical jaundice, 166 (61%) newborns developed physiological jaundice. The overall incidence of non-physiological jaundice in the study group was 19%, (107 out of 560 newborns) [21].

Based on a study conducted among neonates in TikurAnbesa hospital, 160(44.9%) of the studied neonates had developed neonatal hyperbilirubinemiaand11 (6.9%) neonates developed bilirubin encephalopathy. Similarly, the major causes of neonatal hyperbilirubinemia were ABO incompatibility and sepsis which accounts 57(35.6%) and 30(18.8%) respectively. Hemolytic disease-causing neonatal hyperbilirubinemia was 10(6.3%) of which Rh and ABO incompatibility accounts 20% and 80% respectively. (1).

Based on the study done in Mekele city public hospital, the proportion of neonatal jaundice among neonates admitted to the neonatal intensive care unit of Mekelle city public hospitals was found to be37.3% (78). Among these 46 (22%) cases were pathological jaundice and the rest 32 (15%) were found to be physiological jaundice [17).

1.3 Significance of the Study

The result of this study may help policy makers to plan and deliver necessary training programs for health professionals to give attention and care for neonates regarding to the problem. The result of study will provide insight to health care provider in identification common etiologic and associated risk factors of neonatal hyperbilirubinemia to avoid dalliance in diagnosis and to give appropriate management and prevent from developing kernicterus.

It may also help to create awareness to the community based on the result finding, health professionals will give health education to mothers about different etiologic factors of neonatal hyperbilirubinemia at the time of antenatal clinic follow up which help them to be screened and treated early.

It would also be a baseline for other researcher to do prospective study for the future to assess magnitude and etiologic factors of neonatal hyperbilirubinemia.

In summary, it will be important to show the magnitude of hyperbilirubinemia and identify associated risk factors to prevent the problem by taking appropriate preventive and treatment interventional strategies among the concerned offices and bodies.

2. Literature Review

.Based on a study findings from Ghana, over half (54%) of neonates developed jaundice within 1–3 days after birth with 10% having it at birth. Birth weight and prolonged duration of labor were associated with neonatal jaundice; mothers had inadequate knowledge of neonatal jaundice Duration of labour was associated with neonatal jaundice, with majority of mothers with jaundiced neonates having prolonged duration of labour compared to the controls (2).

In one prospective study, they investigated the epidemiology of hyperbilirubinemia in the 2gestational-age subgroups by daily serum bilirubin measurements longitudinally in the first week of life and evaluated the risk status for jaundice on a gestational and postnatal age basis. Infants of 35 to 37 weeks' gestation had significantly lower birth weights, significantly higher serum total bilirubin levels on days 5and 7, and were 2.4 times more likely to develop significant hyperbilirubinemia than those of 38 to 42weeks' gestation. Near-term newborns, thus, should not be treated as term newborns in the approach to management of hyperbilirubinemia (8).

In a study done in Nigeria the prevalence of neonatal jaundice is (52.6). The associated factors included sepsis (66.7%), anemia (3.8%), prematurity (15.2%), ABO incompatibility (5.3%), and lack of breast feeding (9.0%). Majority of the neonates developed neonatal jaundice in their early life probably due to prematurity and septicemia (9)

A prospective study was conducted in a level II maternity unit to investigate the incidence of hyperbilirubinemia in healthy, term, breast-fed and formula-fed infants. Serum bilirubin levels were determined for 176 breast-fed and 164 formula-fed infants in cord blood and on days 1, 2, 3 and 5 after birth. The mean total bilirubin levels were significantly higher on each postnatal day in the breast-fed infants, as was the proportion of infants with peak levels above 12 mg/dl (205 mumol/l; 28% v. 6%). The breast-fed infants also had significantly higher proportional weight losses on each postnatal day than the formula-fed infants. However, there was no correlation between the cumulative weight loss on day 3 and bilirubin levels on the same day with either feeding regimen. None of the infants required an exchange transfusion or prolonged care in hospital for hyperbilirubinemia. (10)

In a study on the natural history of bilirubinemia in a population of predominantly breastfed, mainly white infants, for the first month after birth. The knowledge that, at 1 month, 1:3 infants has a TcB ≥5 mg/dL and 1:5 appears jaundiced, should be of practical value to practitioners who care for newborns

and reassuring to the parents of infants who are still jaundiced at age 4 weeks. We also show that there is a strong relationship between the cephalocaudal and rising bilirubin levels and that this relationship persists up to age 28 days. Although the range of values within each zone is too large to allow an accurate determination of the actual bilirubin value, a score of 0 is highly predictive of a TcB value of <12.9 mg/dL, and a score of ≥4 will usually predict a TcB of ≥10 mg/dL.(2)

In a study done in china Neonatal hyperbilirubinemia is common in Asian populations, including Taiwanese. For example, the studies indicate that the incidence of neonatal hyperbilirubinemia was 7.8% (18 of 232) and 15.6% (33 of 212) in G6PD-normal and G6PDdeficienct Taiwanese neonates, respectively (16), with 14.6% (18 of 123) of the neonates with hyperbilirubinemia in one study having peak bilirubin levels ≥342 μM (11).

In a study done in Malaysia of the 318 newborn infants recruited in this study, 183 were Malay, 70 Chinese and 65 Indian. Neonatal hyperbilirubinemia [peak total SB (PTSB) level ≥250 μmol/l] developed in 16.4% (*n*= 52) of infants, with a median PTSB level of 291 μmol/l[inter quartile range (IQR): 263, 308].Among the 266 infants without neonatal hyperbilirubinemia, 42.1% (*n* = 112) did not develop jaundice during the first month of life, and 57.9% (*n* = 154) had only mild jaundice, with a median PTSB level of 173 μmol/l (IQR: 100, 216). When compared with neonates without hyperbilirubinemia, neonates with hyperbilirubinemia had significantly higher proportion of Malay ethnicity (p = 0.01), significantly lower mean birth weight (p = 0.045) and mean gestation age (p = 0.006 ;) and significantly higher proportion of G6PD mutation (p =0.001). There was no significant difference in the gender distribution, types of feedings, variant c.211G > A UGT1A1 gene and variants OATP2 between the two groups. Seventy-seven percent of hyperbilirubinemic neonates were Malay, and this was significantly higher than normal Malay neonates without hyperbilirubinemia (54%; p = 0.01). The proportion of hyperbilirubinemic neonates of Chinese and Indian ethnicity was lower than their distributions in this study. (12).

In one large, population-based, cohort study examined the incidence of adverse effects, including kernicterus ,deafness, cerebral palsy, developmental delay, gaze palsy, attention-deficit disorder, and autism spectrum disorders, in infants with TSB levels of ≥230 μmol/L (≥13.5 mg/dL) at any time in the neonatal period, compared with infants with no hyperbilirubinemia, in the population of healthy

term and near-term infants born in Nova Scotia between 1994 and 2000. This allowed No cases of kernicterus were diagnosed during the study period; however, only 7% of the infants in the extreme hyperbilirubinemia group had TSB levels between 400 and 499 μmol/L, and <1% had levels of>500μmol/L. The "softer" neurologic adverse effects previously associated with hyperbilirubinemia were not found in this study, with the exception of increases in the rates of diagnoses of developmental delay and attention-deficit disorder, both of which remained significant even when adjustment was made for confounders (14)

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One study From the descriptive results of the data use for the study, 107 neonates were male with 46.1% and 53.9% were female, 79 (34.1%) neonates did not survive the disease. 85(36.6%) neonates were born through Caesarean Section, 53(22.8) neonates were born outside the hospital, 83 (35.8%) mothers were illiterate. 43(18.5%) mothers are presented with illness during pregnancy, 146 (62.9%) mothers are rhesus negative which leads to rhesus incompatibility with the blood group of the neonate, 161 (69.4%) neonates have G6PDdeficiency, 110 (47.4%) neonates were born prematurely while 122 (52.6%) were born with full term and 120 (51.7) neonates has severe jaundice.(15)

In systematic Meta analysis and review a total of 13 studies with 1,951 subjects and 32,208 controls from India, Nigeria, Pakistan, Nepal and Egypt were identified and analyzed. The pooled data showed that prim parity (OR,1.59; 95% CI:1.26-2.00), delivery outside public hospitals (OR, 6.42; 95% CI:1.76-23.36), ABO incompatibility (OR, 4.01; 95% CI:2.44-6.61), Rhesus hemolytic disease (OR, 20.63; 95% CI:3.95-107.65), G6PD deficiency (OR, 8.01; 95% CI:2.09-30.69), UGT1A1 polymorphisms (OR, 4.92; 95%CI:1.30-18.62), low gestational age (OR, 1.71; 95% CI:1.40-2.11), underweight/weight loss (OR,6.26; 95% CI:1.23-31.86), sepsis (OR, 9.15; 95% CI:2.78-30.10) and high transcutaneous/total serum bilirubin levels (OR, 1.46; 95% CI:1.10-1.92) placed infants at increased risk of severe hyperbilirubinemia or bilirubin induced neurologic dysfunctions [18]

In a study done in United States the annual NH prevalence was 29.6 to 31.7%; hemolytic NHB, 1.8 to 2.4%; treated hemolytic NHB, 0.46 to 0.55%, between 2011 and 2016. The matched analysis included 1373 pair's ≥35 weeks GA. The treated hemolytic NHB cohort had significantly more birth trauma and hemorrhage (4.5% vs. 2.4%, $p = 0.003$), vacuum extractor affecting newborn (1.9% vs. 0.8%, $p = 0.014$), and polycythemia neonatorum (0.8% vs. 0%, $p = 0.001$) than the matched non-NHB cohort. The treated hemolytic NHB cohort also had significantly longer mean birth hospital stays (4.5 vs. 3.0

days, p <0.001), higher level 2–4 neonatal intensive care admissions (15.7% vs. 2.4, 15.9% vs. 2.8 and 10.6%vs. 2.5%, respectively, all p < 0.001) and higher 30-day readmission (8.7% vs. 1.7%, p < 0.001)(19).

In systematic review of 1692 subjects From 237 studies identified, 17 studies encompassing 1692 infants were selected. Idiopathic neonatal hepatitis occurred in 26.0 % of cases; the most common specific etiologies were extra hepatic biliaryatresia (EHBA) (25.89 %), infection (11.47 %), TPN-associated cholestasis(6.44 %), metabolic disease (4.37 %), alpha-1 anti-trypsin deficiency (4.14 %), and perinatal hypoxia/ischemia (3.66 %). CMV was the most common infection identified (31.51 %) and galactosemia (36.49 %) was the most common metabolic disease identified (20).

In a study in south India out of 273 newborns with clinical jaundice, 107 newborns developed pathological jaundice. Out of 107 newborns,52 (48%) newborns had breastfeeding jaundice.17 (16%) newborns had ABO incompatibility. 8 (7.54%) newborns were preterms. 6 (5.7%) newborns had cephalohematoma. 6 (5.7%) newborns had Rh incompatibility. 5 (4.8%) newborns had history of previous sibling deaths. 4 (3.8%) newborns had history of birth asphyxia. 4 (3.8%) newborns were born to mothers with history of GDM.3 (2.8%) newborns had sepsis. 1 (0.93%) newborn was born to mother with history of hypothyroidism. 1(0.93%) newborn was born to mother with TORCH infection. Sex factor had an influence on the incidence of non-physiological jaundice among the neonates showing that males 67% (72 out of 107) had higher incidence compared to females 33% (35 out of 107) with p value <0.05. All 4(100%) newborns with history of birth asphyxia developed pathological jaundice. Out of 107 babies with pathological jaundice, 5 newborns had Rh incompatibility, 17newborns had ABO incompatibility, and 1 newborn had both Rh and ABO incompatibility. Out of 273 newborns with clinical jaundice, 2 (1%) newborns required double volume exchange transfusion as a therapeutic intervention for the treatment of jaundice. Both these cases were associated with Rh incompatibility as a risk factor for pathological jaundice (21).

In a study done in Iran From 1134 neonates with indirect hyperbilirubinemia referred to Namazi hospital from February 2009 to February 2010, 170 neonates were included in this study according to inclusion & exclusion criteria. Ninety nine of them (58.2%) were male and 71 (41.8%) were female, 125neonate (73.5%) were delivered with normal vaginal method (NVD) and45 neonate (26.5%) with

cesarean section method, 66 neonate (32.4%) used oxytocin during labor. Birth weight of neonates was 3068 (526) g (Min: 1550 g, Max: 4300gr). 19 neonate (11.4) developed jaundice in first24 hours after birth. 137 neonate (73.5%) developed jaundice after discharging from hospital, 153 mothers (90.3) had known that they should have referred to doctor if the neonate had been yellowish & 118 of mothers (69.4%) also knew that jaundice may cause brain damage. Cause of severe hyperbilirubinemia was ABO and Rh incompatibility (5.9%), G6PD deficiency (25.5%), sepsis (12%) other causes such as spherocytoses and immune hemolytic anemia (3.5%) and unknown (53.1%) (Figure1). Risk factor of hyperbilirubinemia in our patients were 1) Male sex (P = 0.017), 2) previous siblings with severe hyperbilirubinemia (P = 0.006), 3) early discharge (P = 0.035), 4) NVD (P = 0.027) (it may be due to early discharging of neonates with NVD than cesarean section), 5) Brest feeding(P =0.038) and 6) concept of using herbal medicine instead of referring to Doctor when neonate had icterus (P = 0.024).[22]

In a study done in India among 162 patients, 94 patients (58%) were found to be males and 68 patients (42%) were found to be females. Low birth weight neonates (43.20%) were found to be more prone to neonatal jaundices. In this study, it was found that duration of phototherapy was longer in extremely low birth weight neonates (34 hours) in relation to birth weight and average duration of phototherapy. Based on the conventional cause, physiological cause (56.79%) was observed to be highest among other causes of neonatal jaundice. The short-term adverse reactions due to phototherapy were identified using Naranjo's Causality Assessment Scale. The TSB levels were increased before phototherapy (pre- treatment) and decreased after phototherapies (post-treatment) which were assessed by using American Academy of Pediatrics guidelines (23).

In a study done in India incidence of jaundice of the cases of OA incompatibility, where the mother is of 'O' blood group and the baby is of 'A' blood group, the percentage of babies who develop hyperbilirubinemia is 20%. Of the cases of OB incompatibility, where the mother is of 'O' blood group and the baby is of 'B' blood group, the percentage of babies who develop hyperbilirubinemia is 23%. If we take ABO incompatibility together, the incidence of hyperbilirubinemia is 7.17% Rh incompatibility was 4.16 %(24) in a study done in India, the percentage distribution of incidence of Neonatal jaundice among Newborns in the Postnatal ward. Hence results revealed that 60(75%) babies had serum Bilirubin <4 mg/dl, 8(10%) babies had serum bilirubin in the range of 4-8 mg/dl, 7(8.75) babies were in the range of 5-12 mg/dl and 5(6.25%) babies were in the range of 8-16 mg/dl. Out of 80

Newborns, 20 Newborns had Neonatal Jaundice; total incidence rate was 25%. The subject risk factors associated with Neonatal Jaundice shows that majority 14(17.5%) babies had delayed initiation of Breast feed i.e. after 24 hrs, 1(1.2%) babies had previous history of jaundice (25)

Based on astudy done in south India Incidence of clinical jaundice in the study population is 49%. Prematurity was third most common cause in our study. Preterm new borns are prone to developing jaundice due to immaturity of bilirubin conjugating system higher rate of hemolysis, increased enterohepatic circulation, decreased caloric intake (26).

Based on a study done National District Hospital in Bloemfontein the prevalence of neonatal jaundice was 55.2%; however, only 10% of black babies who were diagnosed with jaundice appeared clinically jaundiced. Normal vaginal delivery was the only risk factor associated with neonatal jaundice.(27)

Based on a study done at chilie the main risk factors for developing severe HBR were male sex, prematurity, excessive weight loss, and classic group incompatibility. The highest risk group is late preterm infants, between 34-36 weeks of gestational age, who have a RR of 2.39 (95% CI 1.96- 2.93) regarding term infants,(28)

3 Conceptual Framework

Figure 1 : conceptual framework

4. Objective

4.1 General objective

The general objective of the study was to assess the magnitude of neonatal hyperbilirubinemia and associated risk factors among neonates admitted to NICU, TGSH

4.2 Specific objectives

- ✓ To determine the magnitude and mode of treatment of neonatal hyperbilirubinemia among neonates admitted at NICU of TGSH
- ✓ To identify associated risk factors of neonatal hyperbilirubinemia among neonates admitted at NICU of TGSH

5. Methods

5.1 Study area

The study was conducted at TGSH which is located in Bahir Dar, North West Ethiopia. BahirDar, a capital city of the Amhara Regional State, is located in north western part of Ethiopia about565 km from Addis Ababa, a capital city of Ethiopia. Its astronomical location is 11º38’ north latitude and 37º15’ east longitude. BahirDar is one of the reform towns in the region and has a city administration, metropolitan administration consisting of municipality and nine urban and four rural kebelles.

According to the National Population and Housing Census projection of 2011 G.C the population of the town was 170,267. Out of this 75,302 (44%) were males and 94,965 (56%) were females.

There are two comprehensive specialized referral hospitals in the town. among this TGSH one of the teaching and referral hospitals which have different departments include:Generalsurgery,internalmedicine,orthopedics,dermatology,pediatricsandchild health ,gynecology and obstetrics and radiology department

Pediatrics and child health has NICU which was functional since January 2011 E.C it has 03 wards with total bed of 45.the department has 12 pediatricians and 32 residents .

5.2 Study design and Period

A hospital based cross-sectional study design was conducted from a total of 1200 neonates admitted to TGSH from July 1/2011 to July 30/2012 E.C. From which 522 neonates were exclude due to lack biliubin determination and incomplete documentation.

5.3Source populations

All neonates admitted at NICU of TGSH from july1/2011E.C to july30 /2012E.C.

5.4 Study populations

Neonates who had bilubin determination among those admitted at NICU from july1/2011E.C to july30 /2012E.C.

5.5 Inclusion/exclusion criteria

5.5.1 Inclusion criteria

Newborn up to 28 days old after birth and admitted at NICU of TGSH from July 1/2011E.C to July 30 /2012.E.C

5.5.2 Exclusion criteria

Neonates whose bilirubin level did not measured

Neonates whose chart incomplete or lost

5.6 Sample size determination

Sample size was calculated using a single population proportion formula.

P=44.9% (proportion of neonatal hyperbilirubinemia in tikureanbesa was 44.9%).

$ni = (z\propto 2/)\ 2*(1-p)\ d2$

Where, =initial sample size

p= proportion of neonatal hyperbilirubinemia; 44.9%=0.449

a= confidence interval (95%)

d= is the margin of sampling error tolerated (5%) = 0.05

ni= (1.96)2 (0.449) (1-0.449)/ (0.05)2

=3.8416(0.449) (.0.551)/.0025 =.873964/.0025=380

5.7 Study variables

5.7.1 Dependent variable

Neonatal hyperbilirubinemia

5.7.2 Independent variables.

Socio-demographic variables:

- ✓ Age
- ✓ Gender
- ✓ Weight

Neonatal factors:

- ✓ Idiopathic cause
- ✓ Infectious causes
- ✓ Prematurity
- ✓ Breast feeding jaundice
- ✓ Breast milk jaundice
- ✓ Cephalhematom
- ✓ Subgaleal hemorrhage

Maternal factors:

- ✓ ABO incompatibility /ABO set up
- ✓ Rh isoimmunization/Rh set up

5.8. Operational Definition

Breast Milk Jaundice: Late onset jaundice beginning after 4-7th day of life which is caused by increased reabsorption of unconjugated bilirubin, perhaps due to unidentified factor in human milk. History of jaundice in sibling may indicate occurrence of breast milk jaundice.

Breast feeding jaundice: Occurs in first few days (2-3 days) of life and related to decreased breast milk intake and decreased frequency of feeding as well as history of formula feeding may indicate occurrence of breast feeding jaundice.

Neonatal hyperbilirubinemia: It is a serum bilirubin level of neonates greater than 85µmol/l (5mg/dl).

Bilirubin encephalopathy: Complicated neonatal hyperbilirubinemia (kernicterus) which causes brain toxicity, death, long term sequel like sensorial hearing loss and cerebral palsy

Neonate: a newborn up to 28 days of life.

ABO incompatibility if there is ABO set up and evidence of hemolysis

RH incompatibility if there is RH set up and evidence of hemolysis

ABO set up mean mother has blood group O and neonate has blood group A or B

Rh set up means mother is Rh negative and the neonate has Rh positive

5.9 Data collection tools and procedures

Cards of neonates admitted at NICU of TGSH from July1/2011E.C to July 30/2012 E.C were isolated and counted and the chart evaluated for completeness. And the samples were taken by simple random sampling technique. Necessary information of neonate were collected and reviewed from their registration and medical records and morning logo books by prepared check list. Data were collected by trained data collectors and supervisors. All data collectors and supervisors were residents. Medical records of the neonates were returned to card room at the end of each data collection day.

5.10 Data quality assurance

Supervisors and data collectors were trained health workers. Data collectors were trained by principal investigator about the objective of the study and ways of data collection. Pre-test were conducted by principal investigators to assess whether the questioner was understandable or not and took some correction before the starting of actual data collection. Supervisors had checked the collected data daily for completeness.

5.11 Data processing and analysis

Data were entered to SPSS version 21.0 to clean and analyze data. Frequency were used to describe the parameters investigated. Relation between dependent and independent variables were assessed and presented using crude and adjusted odd ratios and confidence intervals. Confidence interval of 95% was used to see the precision of the study and the statistical association was considered as significant if p-value was less than 0.05.Binary logistic regression was done to know the association between dependant and independent variables.

5.12 Ethical considerations

. Ethical approval was obtained from human research and ethical review committee of the College of Medicine and health Sciences, BairDar university.

Letter was written to TGSH to do data collection process. Confidentiality of information obtained from the patients documentation was secured and never use for other purpose.

5.13 Dissemination plan

The final result of the study will be submitted to Bahir Dar University School of Medicine Department of Pediatrics and Child Health. A copy of the finding will also be given to TGSH. And the result will be presented in the morning session and evaluated by experts' .if possible it will be presented in conferences and published.

6 Result

6.1 Socio demographic characteristics

There were 380 patients included in the study of whom 233 (61.3%) were male one hundred seven (28.2%) were preterms and over half of the neonates 218(57.4%) were admitted in the first three days of life and around 260(68.4%) had GA of 37-42 weeks. Over half, 203(53.4%) neonates had birth weight of in the range of 2500-4000 grams. Seventy (18.4%) neonates had ABO set up while 48(12.6%) had Rh set up.

The three most etiologic diagnosis were sepsis 113(29.7%).prematurity93 (24.5%) and ABO incomparability 34(8.9%).

Table 1: socio demographic characteristics of neonate admitted to Tibebe Gion Specialized Hospital July 1/ 2011 to July 30/ 2012 EC (N=380)

variables	Number (%)
Age at admission :less than 3 days	218(57.4)
3-7 days	129(33.9)
7-28 days	33(8.7)
Sex : male	233(61.3)
:female	147(38.7)
Gestational age :less than 37 weeks	105(27.6)
37-42 weeks	262(68.9)
:>42 weeks	13(3.4)
Birth weight :<1500	29(7.6)
:1500-2499	139(36.6)
:2500-4000	203(53.4)
:>4000	9(2.4)
Parity :primpara	179(47.1)
:multi Para	201(52.9)
Rh of the mother :positive	311(81.8)
:negative	69(18.2)
Previous history :yes	1(.3)
:no	379(99.7)
Blood group of the mother: A	99(26.1)
:B	104(27.4)
:AB	21(5.5)
:O	156(41.1)
Blood group of the neonate: A	151(39.7)
:B	112(29.5)
: AB	22(5.8)
:O	95(25)
Rh of the neonate :positive	347(91.3)

	:negative	33(8.7)
	Parity 0f mother:para 1	179(47.1)
	Multi para	201(52.9)
ABO set up :yes		70(18.4)
No		310(81.6)
RH set up :yes		48(12.6)
No		332(87.4)

6.2 Etiologic diagnosis

Table 2 etiologic diagnosis of neonates admitted to Tibebe Gion Specialized Hospital from July 1 /2011 to July 30/ 2012 EC.

Diagnosis	Frequency(percent)
Prematurity	93(24.5)
Sepsis	113(29.7)
ABO incommutability	34(8.9)
Breast milk jaundice	10(2.60)
SGH	21(5.5)
Cephalhematoma	9(2.4)
Rhisominzation	8(2.1))
Breast feeding jaundice	19(5)
Idiopathic	21(5.5)

6.3 Magnitude of neonatal hyperbiliubnemia

In this study the magnitude of neonatal hyperbilirubinemia was found to be 52.9 %.

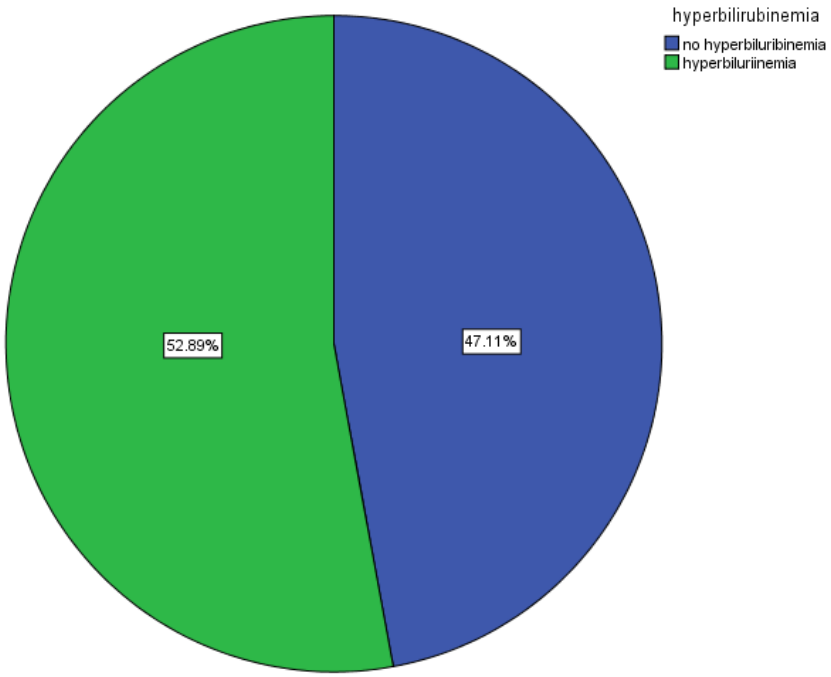

Figure2: magnitude of neonatal hyperbilirobinemia in neonates admitted to Tibebe Gion Specialized hospital from July 1 2011 to July 30 2012 EC

6.4 Mode of treatment

Among neonates with hyperbilirubnemia 184(91.5%) were treated with phothotherapy alone and 17(8.5%) were treated with both double exchange transfussion and phothotherapy. Among 380 neonates admitted to Tibebe Gion Specialized Hospital 357(93.9%), 10(2.6%) and 13(3.5%) improved discharged, left the hospital against medical advice and died respectively.

Binary logistic regression for factors associated with hyperbilirubnemia

Ages at admission, sepsis, prematurity, SGH and in adequate breast feeding were associated with hyperbilirubnemia.

Table 3: Binary logistic regression showing hyperbilirubnemia and associated factors

Variables	Hyperbilirubnmia		COR(95%CI)	AOR(95%CI)
	Yes	No		
BWT :<1500	21	8	1	1
1500-2499	71	68	1.98(1.26-3.1)	1.29(.38-4.33)
2500-4000	102	101	.385(.163-.909)	2.84(.77-10.54)
>4000	7	2	1.33(.222-7.82)	
Age:1-3 days	104	114	1	1
3-7 days	83	46	1.978(1.978-3.095)	2.63(1.50-4.63)*
7-28 days	14	19	.81(.38-1.69)	1.30(.53-3.22)
Rh set up :yes	11	37	0.22(0.11-.45)	0.61(0.27-1.36)
No	190	142	1	1
Sepsis :yes	96	17	8.71(4.92-15.43)	8.24(3.53-14.85)*
No	105	162	1	
Prematurity :yes	76	17	5.79(3.26-10.26)	5.75(2.36-13.98)*
No	125	162	1	1
Cephalhematoma:yes	7	2	3.19(0.66-15.57)	4.33(0.70-26.63)
No	194	177	1	1
SGH:yes	17	4	4.04(1.33-12.25)	6.3(1.94-20.47)*
No	184	175	1	1
Inadequate breast	19	3	6.13(1.78-21.06)	9.98(2.75-36.48)*
feeding :yes	201	179	1	1
No				

7 .Discussion

Among sample size 380 neonates 201 had hyperbilirubnemia and the proportion was 52.9%.this is greater than other studies done in India, ASRAM(48.8%),united state(31.7%),tikuanbessa(44.9%)(.(21,,18,1), this may be due to the risk factors sepsis and prematurity. But comparable to research done in thayi mynamar border(53%)(19) and it is lower than the study done National District Hospital in Bloemfontein The prevalence of neonatal jaundice was 55.2%;(27).

Among associated risk factors prematurity had RR 5.75(95%CI 2.36-13.98) strong association compared to a study done at chili The highest risk group was late preterm infants, between 34-36 weeks of gestational age, who have a RR of 2.39 (95% CI 1.96-2.93) regarding term infants(28).

Inadequate breast feeding was the other risk factors which had association (p value: 0.00) had strong association compared to a study done at Iran (p value: 0.038) (22).

Sepsis had also association (OR8.24, 95% CI3.53-14.85) which is comparable with a systematic Meta analysis and review done in five countries (OR, 9.15; 95% CI: 2.78-30.10) (18)

In this study among etiologic diagnosis identified sepsis and prematurty were predominant. One hundred thirteen (29.7) had sepsis which is comparable to other study(24.7%).asingle patient might have been diagnosed as prematurity plus sepsis.(7) but higher than in a research done tikuanbessa (18.8%)(1). this may be due to difference in infection prevention. But lower than in a research done in Nigeria (66.7%).(9) ninety three neonates(24.5%)were premature which is higher than a research done in tikureanbessa

Among all neonates, 233(61.3%) were male which is higher than a research done at Tikuranbessa (52.2%)(1).and majority of neonates develop hyperbilirubnemia within 3-7 days 120(59.7%) which is higher than research done in tikuranbesa(52.5%)(1).

Among 380 neonates admitted to Tibebe Gion Specialized Hospital 93.9% improved discharged, 2.6% left the hospital against medical advice and the mortality is 3.5% which is much lower than in a study done in Thai-Myanmar border the mortality is 10% this is may be due to early prevention and detection improved discharged, respectively(19)

.

Eleven neonates (5.47%) developed bilubin encephalopathy which comparable with a study done tikuranbessa study (1).

8. Limitation of the study

Since the study was retrospective may not show cause effective relationship.

Was having difficulty to get complete data and incomplete documentation.

9. Conclusion

The magnitude of neonatal hyperbiliubnemia is slightly higher than tikureanbessa but lower than other studies in Nigeria. Sepsis, prematurity, SGH, inadequate breast feeding had statistically significant association for neonatal hyperbilirubnemia.

10. Recommendation

TGSH particularly NICU must have infection prevention strategy and practice to improve Prevention of infection.

TGSH particularly OBY/GYN department professionals will encourage mothers to have regular ANC follow up to avoid preventable cause of prematurity.

Those who are working at TGSH labor ward and NICU jointly working to teach mothers about importance adequate of breast feeding .

Those who are working at TGSH labor ward will know the complication of birth trauma and advised to do as much as they can to avoid birth trauma

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10. Annex:

10.1 Questionnaire

1Age of neonate at admission? (One of the two)

In hours Day☐ ☐

2 Sex: male☐ female ☐

3 Blood group of the neonate

ABABO☐ ☐ ☐ ☐

4 RH of the neonate

Positivenegat☐ ☐

5GA of the neonate

<37 weeks ☐ 37-42 weeks ☐ >42 weeks ☐

6. Weight of the neonate

Birth weight (in grams) ☐

Weight at admission (in grams) ☐

7Does the neonate has jaundice/hyperbiliubnemia

Yes ☐ No ☐

8 Age of the neonate at onset of jaundice

In hours ☐ days ☐

9Bilirubin level (mg/dl)

10Parity of the mother

Para 1 ☐ Multi para ☐

11 Blood group and RH of the mother

A ☐ B ☐ O ☐ AB ☐

12. RH of the mother

Positive neg ☐ ☐

13. Previous similar history

yes ☐

No ☐

14.Did neonate develop encephalopathy: yes ☐ no ☐

15Associated factors or causes of hyperbillirubnemia

ABO incompatablity ☐

RH isoimmunization ☐

Breast feeding ☐

Breast millk ☐

Sepsis ☐

Prematurity ☐

Cephal hematoma ☐

Sabgaleal hemorrhage ☐

Unknown ☐

More than one ☐

16. Evidence of hemolysis

Yes ☐ No ☐

17.If yes ☐

RH isoimmunization

ABO incompatablity ☐

Un known

18. Mode of treatment

Photo therapy ☐

Exchange transfusion ☐

Both ☐

19. Condition at discharge

A. Improved ☐

B.Death ☐

C .Gone against medical advice ☐

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