ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF ALLIED HEALTH SCIENCES

DEPARTMENT OF NURSING AND MIDWIFERY

ASSESMENT OF MAGNITUDE AND ASSOCIATED FACTORS OF NEONATAL HYPERBILIRUBINEMIA AT NEONATAL INTENSIVE CARE UNIT OF TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA, 2017.

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A THESIS SUBMITTED TO ADDIS ABEBA UNIVERSITY COLLEGE OF HEALTH SCIENCE SCHOOL OF ALLIED HEALTH SCIENCE DEPARTMENT OF NURSING AND MIDWIFERY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTERS OF SCIENCE IN PEDIATRICS AND CHILD HEALTH NURSING.

JUNE, 2017

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Abbreviations and Acronym

NICU: Neonatal Intensive Care Unit

TASH: Tikur Anbessa Specialized Hospital

G-6PD: Glucose-6-Phosphate Dehydrogenase

MDG: Million Development Goal

Rh: Rhesus

NH: Neonatal hyperbilirubinemia

Abstract

Background: Neonatal hyperbilirbinemia (NH) is a recognized cause of brain damage and bilirubin encephalopathy resulting in long-term sequel like sensory-neuronal hearing loss in the survivors and death.

Objective: To assess magnitude and associated factors of NH among neonates admitted at neonatal NICU from September 11/2014 to September 11/2016 in TASH.

Methodology: Retrospective cross sectional study was conducted on neonates admitted at NICU of TASH and 356 neonates were systematically selected among all admitted neonates. Study was conducted from January 2017 to June 2017. Supervisors and data collectors were BSc health professionals. Pre-test was conducted on 5% of sample before the starting of actual data collection. Checklist was adopted and modified from literatures to collect data. Supervisors were checked the collected data daily for completeness. Data was first entered to Epi Info version 7 and exported to SPSS version 20.0 to clean and analyze data. Relation between dependent and independent variables were assessed and presented using odd ratios and confidence intervals. Statistical association was considered as significant if p-value was less than 0.05. Ethical clearance for the study was received from Addis Ababa University, College of Health Sciences. A formal letter was written to TASH and permission was secured at all levels.

Result: Medical record of 356 neonates were reviewed and 160(44.9%) of them developed NH. 89(25%) of males and 71(19.9%) of females were developed neonatal hyperbilirubinemia. Their serum bilirubin level was from 5.6mg/dl to 77.7mg/dl. Among associated factors of NH: ABO incompatibility 57(35.6%), sepsis 30(18.8%), idiopathic cause 22(13.8%), breast feeding jaundice 16(10%) and Rh isoimmunization 14(8.8%). Age of neonates was significantly associated with neonatal hyperbilirubinemia in logistic regression.

Conclusion and Recommendation: Magnitude of neonatal hyperbilirubinemia in this study was near to half of selected neonates. Among identified associated factors of NH, ABO incompatibility and sepsis were the leading cause. So, early prevention and timely treatment of NH is important since it was a cause of long term complication and death in neonates.

Keyword: Magnitude, Neonatal hyperbilirubinemia

1. INTRODUCTION

1.1. Background

Neonatal hyperbilirbinemia is a serum bilirubin greater than 85μmol/l (5mg/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. Newborn's immature liver often cannot remove bilirubin quickly enough, causing hyperbilirubinemia (2).

Neonatal jaundice is a very common condition worldwide occurring in up to 60% of term and 80% of preterm newborns in the first week of life (2). Study conducted by S. S. Tikmani et al on incidence of neonatal hyperbilirubinemia in Pakistan showed that 27.6% of neonates were diagnosed as neonatal hyperbilirubinemia. In this neonates hyperbilirubinemia was seen between 0-6 days old in 64% (3). According to study done by Oteikwu Ochigbo S et al in Calabar in 2016 magnitude of neonatal hyperbilirubinemia out of 2820 neonates was 553(19.6%). Mean age weight and onset of jaundice of neonates were 13 days, 2880gram and 3.2days respectively. Magnitude of bilirubin encephalopathy was 21(0.74%) of which 19% of them were expired. 81% were male and 19% were females. In this study the established factors associated with kernicterus among jaundiced neonates were infection, i.e., septicemia 71.4%, ABO incompatibility 19.1%, and glucose-6-phosphate dehydrogenase(G6PD) deficiency 9.5% (4).

It is one of the most common conditions requiring medical attention in newborn babies. According to study done in Nigeria, the most common cause of admission to this hospital and Children's Emergency room within neonatal period was hyperbilirbinemia which accounts for 17% (5). Hyperbilirbinemia was among the cause of morbidity and mortality in neonates according to study done by Ekwochi U et al in Enugu State University Teaching Hospital in 2014. Prevalence of neonatal hyperbilirubinemia in this hospital was 17% and sepsis accounted 38.6% of 261 neonates admitted during the study period. Among jaundiced neonates 25% were due to G-6PD deficiency, 19% were due to neonatal sepsis and 13% were due to fetomaternal

ABO incompatibility. Prevalence of neonatal mortality in this hospital was 14.2% of all admissions at the hospital (6).

Hyperbilirubinemia in neonates can causes kernicterus (bilirubin encephalopathy). Kernicterus is caused by unconjugated hyperbilirubinemia that develops either as a result of hemolytic disease such as Rh incompatibility or because of inability of the liver to conjugate bilirubin due to either defect of glucuronyl transferees enzyme or when this enzyme is not fully functional (7). In the neonate unconjugated bilirubin, which is potentially toxic to neural tissue can penetrate the membrane that lies between the brain and the blood (the blood brain barrier) (8).

Bilirubin induced neurologic dysfunction is the clinical signs associated with bilirubin toxicity such as hypotonic followed by hypertonia and is typically divided into acute and chronic phases. Acute features include: hypotonic, poor feeding, high pitched cry, lethargy. Progression of acute symptoms may occur and include: Hyper tonicity with opisthotonus or retro Collis, seizures, impaired conscious state, coma. Features of chronic bilirubin encephalopathy include: Athetoid, cerebral palsy, sensory-neural deafness, seizures, developmental delay, oculomoter dysfunction, and neurocognitive impairment. Study conducted by Ogunlesi TA et al on predictors of acute bilirubin encephalopathy in 2010 showed 49.7% had acute bilirubin encephalopathy out of 152 neonates (8).

There are certain factors that influence the passage of bilirubin into the brain and hence increase the risk of acute bilirubin encephalopathy. Among them preterm birth, sepsis, hypoxia, seizures, acidosis and hypoalbuminemia. The rate of rise of the level of bilirubin is equally important hence the increased risk of kernicterus in babies with hemolytic disease such as G-6PD deficiency, ABO or Rhesus hemolytic disease (8),(9),(10). Study conducted by Shilongo SN et al in Namibia showed that the potential to develop prevalence of bilirubin encephalopathy was estimated to 12.4% and the most affected age group were 3-6 days old after birth which accounted of 9.6% of bilirubin encephalopathy cases (11).

1.2. Statement of the problem

Neonatal hyperbilirbinemia is a recognized cause of brain damage (12) with unconjugated bilirubin causing kernicterus (maximum risk of neonatal hyperbilirubinemia), which results in long-term sequel like sensory-neuronal hearing loss (13). Recent global study estimates that about 1.1 million babies would develop hyperbilirubinemia with or without bilirubin encephalopathy worldwide yearly. Among those neonates 481,000 were term neonates of whom 114,000 were die annually and more than 63,000 survive with moderate or severe disability. The vast majority, 75% of affected neonates reside in sub-Saharan Africa, the region where Ethiopia located, and South Asia (14).

Study conducted by Narayan in India on pattern of admissions and outcome in a neonatal intensive care in 2012 showed that breast milk jaundice accounts 4%,prematurity 13% and neonatal infection accounts 6% of neonatal admission to neonatal intensive care unit. This study suggested that early recognition of neonatal jaundice and immediate intervention led to few complications and sequel due to hyperbilirubinemia (15). According to study done by Goyal M in Maharashtra in India on prevalence among associated factors of neonatal jaundice were ABO incompatibility (11.1%), Rh incompatibility (4.6%), sepsis (12%), breast milk jaundice 2.8%, physiologic jaundice (44.6%), G6PD deficiency (0.9%), and idiopathic 20.4% (16). According to study conducted by S. S. Tikmani et al in 2010 on incidence of neonatal hyperbilirubinemia showed that a significant burden of untreated severe neonatal jaundice, causing potential neurological sequel, exists in developing countries (3). Other study conducted by Muhammad et al in 2011 showed that jaundice is common among infants and thus, hyperbilirubinemia should be identified early and promptly treated, in order to reduce infants' morbidity and mortality as well as the risk of kernicterus and cerebral palsy in the survivors (17).

After several years of neglect and exclusion from the global child health agenda under the million development goal (MDG) initiative, hemolytic disease in newborns and other neonatal hyperbilirubinemia are increasingly acknowledged as important contributors to global neonatal deaths (18)(19). The emerging interest in the early childhood developmental difficulties faced by many survivors of the current maternal and child health interventions in low and middle income countries under the MDG framework has also drawn attention to neonatal hyperbilirbinemia (15) (20, 21).

However, the global burden of neonatal hyperbilirbinemia and the underlying factors in low and middle income countries are still poorly characterized to guide programmatic policy initiatives (22). In Africa, neonatal jaundice is commonly associated with sepsis which is a major contributor to neonatal mortality (23, 24). Neonatal morbidity and mortality remain very high in developing countries of Sub-Saharan Africa and one of the important contributors to this morbidity and mortality is neonatal hyperbilirbinemia. Onset of jaundice in 1st and 2nd day was 27% and 43% respectively (25). A research conducted by Kamara IK in Seiralion on factors associated with neonatal hyperbilirubinemia showed that hyperbilirubinemia was the cause of neonatal death which accounted 24% of death in neonatal intensive care unit (26).

Mortality rate of neonates in Ethiopia was 37 in 1000 live births according to Ethiopian demographic health survey of 2011 (27). Hyperbilirubinemia was among the causes of neonatal admission and death in Gondar Teaching Hospital according to study done by Kokeb M and Desta T in 2016. Among neonates admitted to neonatal unit 31.7% of them were due to hyperbilirubinemia. Among all neonates admitted to the hospital 23.1% were died (28). A study conducted in Calabar in 2016 by Oteikwu Ochigbo S showed that 3.8% of jaundiced infants(19.6%) had bilirubin encephalopathy of which male to female ratio was 5:1 and 38% of neonates with kernicterus were died (4). A survey conducted in 2014 by Omekwe DE on survey and management outcome of neonatal jaundice revealed that neonatal jaundice remains high among cases admitted into the special care baby unit in developing nations. 40.7% preterm and 56.8% of term neonates were developed hyperbilirubinemia. 41.2% of them developed jaundice at 1 to 2 days after birth of life. Some of the risk factors are modifiable and can be changed through maternal education, early and comprehensive antenatal care as well as specialized neonatal care. Therefore antenatal and neonatal care should be improved and supported by all health care stakeholders (29).

Study conducted by Ogunlesi TA and Ogunfowora OB on predictors of acute bilirubin encephalopathy showed that newborn deaths can be reduced by strengthening newborn care within existing child and maternal programs (8). This study showed that mortality among children under five appears to be decreasing and there has been little progress in reducing neonatal deaths. As child health programs succeed in reducing deaths after the first month and

year of life, an increasing proportion of under five deaths are neonatal and action must now be taken to reduce newborn deaths (8).

Magnitude and associated factors of neonatal hyperbilirubinemia in Tikur Anbessa Specialized Hospital is not known yet. Therefore, determining its prevalence (magnitude) and associated factors is important, to reduce the risk for future babies to develop kernicterus, for early intervention and for prophylaxis e.g. anti-D and treatment. It is hoped that the result of this study would be a necessary tool in formulating measures of improving prevention, early detection and management of neonatal hyperbilirubinemia; thereby reducing newborn deaths by strengthening newborn care and maternal health programs.

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.

It also hoped that the result of study will provide insight to health care provider in identification mechanism of common associated factors of neonatal hyperbilirubinemia to overcome the challenges of early diagnosis and its management to 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 associated 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 study to assess magnitude and associated factors of neonatal hyperbilirubinemia.

2. LITERATURE REVIEW

2. 1.Magnitude of Neonatal Hyperbilirbinemia

There were studies done on magnitude of neonatal hyperbilirbinemia and its associated factors in different countries. As in India, the etiology of hyperbilirubinemia in the infant was attributed to ABO incompatibility in 35%, infection in 18%, prematurity in 11%, G-6PD deficiency in 5%, rhesus incompatibility in 3.5% and no identified cause was identified in 9% infants (25). The prevalence of hyperbilirubinemia in male neonates was about two times than female neonates. A study done by Chime HE et al on prevalence of neonatal jaundice showed that 89 of 272 neonates were developed neonatal hyperbilirubinemia. Among them, 21% were males and 12% were females. Majority of the cases such as 72.4% males and 70.8% females) had known predisposing factors (30). Study done by Stevenson DK et al on understanding newborn jaundice showed that neonatal factors of hyperbilirubinemia include infections; infrequent feedings; male gender; G-6PD deficiency; prematurity and previous sibling with hyperbilirubinemia and maternal factors include blood type ABO or Rh incompatibility (31). Hyperbilirubinemia in neonates has different predisposing or associated factors. According to study done in GB Pant hospital of India, breast feeding jaundice was the leading factor of hyperbilirubinemia among the identified causes. It accounted for 84 cases of 124 jaundiced neonates. Those who had breast milk jaundice and jaundice due to prematurity were 5 cases each. Physiologic and pathologic cases of neonatal hyperbilirubinemia were 24 and 6 respectively (32). As a study conducted by Narayan in level II Care NICU at Sikkim Mani pal Institute of Medical Sciences at Gangtok, on the pattern of admissions and outcome in NICU, more than half percent, 54%, of total (212) neonatal admission were due to neonatal jaundice. These jaundiced neonates were due to physiologic jaundice in 48%, breast milk jaundice in 4% and the rest (2%) were due to other cause (15).

Studies done in Warri, Delta State, Nigeria showed that prevalence of neonatal hyperbilirubinemia was 33% and other study in Federal Medical Center of Abakaliki revealed that neonatal hyperbilirbinemia accounted 35% of all NICU admissions (33, 34). Overwhelming majority of the subjects (89.6%) developed jaundice within the 1st week of life. Half of those developed bilirubin encephalopathy were expired (34). A retrospective study in a district hospital in rural Kenya found that neonatal hyperbilirubinemia subjects had significantly more

neurological, motor and developmental difficulties. Among them 43% of the neonatal hyperbilirbinemia cases were unable to sit and/or stand independently and 18% died after discharge (35). A research conducted by Kamara IK sierra leone on factors associated with neonatal hyperbilirubinemia showed that magnitude of neonatal hyperbilirbinemia was the primary diagnosis in 17% of 1000 admissions during the first 7 days of life (26).

A study done by Bahbah MH et al in 2015 revealed that preterm babies develop hyperbilirubinemia early after birth than term babies. The average gestational age in preterm babies was 32.78-34.82 weeks and hyperbilirubinemia started 1.88-5.52 days after birth. But, in term babies the average gestational age was 37.28-39.12 weeks and hyperbilirbinemia started 3.36-6.44 days after birth (36). Other study by Muhammad et al in Usman Danfodiyo University teaching Hospital on 93 neonates of 0-14 days old revealed that prevalence of hyperbilirubinemia was 93.94% in 0-3 days old, 86.67% in 4-7 days old and 83% in 8-14 days old of neonates. Number of jaundiced neonates decreases as their age increases (17).

 A retrospective study by Omekwe DE et al on survey and management outcome of neonatal jaundice from a developing Tertiary Health Centre in 2014 revealed that prevalence of neonatal jaundice was 17.9% out of 664 neonates admitted into the special care baby unit of the pediatrics department. Majority of which were aged between 1-2 days making about 41.2% of the neonates admitted. Prevalence of male gender was 60.8% and in females was 39.2%. This survey showed that prevalence of neonatal jaundice was increasing in consecutive years. 19.1% in 2010, 28.1% in 2011 and 52.8% in 2012 (29).

 Study conducted by Kokeb M and Desta T in 2016 showed that neonatal hyperbilirubinemia and prematurity were among the reason of neonatal morbidity admitted in Gondar University Hospital at neonatal unit. Out of 325 neonates at this hospital 31.7% were admitted due to neonatal hyperbilirubinemia (28). A study done retrospectively by Worku B and Kassie A in 2012 on predictors of early neonatal mortality at a neonatal intensive care unit of a specialized referral teaching hospital in Ethiopia showed that 13.5 % of neonates admitted in TASH with hyperbilirubinemia were died and 86.5% of them were survived (37).

2.2. Serum Bilirubin Level

Serum bilirubin measurement should be performed in all infants at high risk of hemolysis, early or jaundiced. Infants at high risk of early hemolysis (e.g. Rh Isoimmunization, hemolysis requiring in-utero transfusion) should have serum bilirubin performed on cord blood initially and then 4 - 6 hourly to determine the rate of rise (30). A research conducted in Calabar by Oteikwu Ochigbo S in 2016 showed that the mean serum bilirubin level of neonates with hyperbilirubinemia was 321.3 μmol/L (242.5μmol/L–440.3μmol/L) (4). Infants without identified associated factors rarely have total serum bilirubin level above 205μmol/l (16).

A study conducted by S. S. Tikmani et al in 2010 showed that bilirubin level in jaundiced neonates were measured to follow bilirubin level (3). Stevenson DK et al on understanding newborn jaundice showed that as the number of associated factors increases, the potential to develop markedly elevated bilirubin levels also increases (31).

2.3. Associated Factors of Hyperbilirubinemia in Neonates

2.3.1. Physiological Jaundice

Jaundice becomes visible on the 2nd-3rd day usually peaking by the 3rd day at 85-102μmol/l and decreasing to below 34μmol/l between 5th and 7th day of life. Study in India on predictors of neonatal hyperbilirubinemia showed that the 3rd day serum bilirubin of greater than 10.15 mg/dl was used as early predictors of neonatal hyperbilirubinemia. Serum bilirubin in terms is usually less than 12mg/dl and less than 15mg/dl in preterm infants which resolves spontaneously in the first week in terms and 2nd week in preterm infants (10). Study conducted by Narayan in Sikkim Mani pal Institute of Medical Sciences showed that 48% of the total admitted at NICU were physiologic jaundice (15). Study in Iran by Najib KS et al in 2013 on causes and incidence of hyperbilirubinemia among jaundiced neonates (170) showed that 19(11.4%) developed jaundice in the first 24 hours after birth (38) and other study conducted in India by Goyal M et al in 2015 showed that prevalence of physiologic jaundice among the study was 44.4% (16).

2.3.2. Pathological Jaundice

Pathological jaundice appears within 24 hours, increase in serum bilirubin beyond 5mg/dl (85μmol/l)/24hrs, serum bilirubin more than 255μmol/l, direct bilirubin greater than 34μmol/l at any time, presence of clinical jaundice beyond 2 weeks and conjugated bilirubin (dark urine staining the clothes) would be pathological jaundice (39). Study conducted in India revealed that

prevalence of pathologic jaundice of neonatal hyperbilirubinemia was 5% in GB Paint hospital (32). Study conducted in India by Goyal M in 2015 showed that prevalence of pathological jaundice was 55.6% (16).

According to Israel-Aina Y and Omoigberale A on risk factors for neonatal jaundice in babies presenting at the University of Benin Teaching Hospital neonatal sepsis, prematurity, G-6PD deficiency are among risk factors of neonatal hyperbilirubinemia (40). Severe neonatal hyperbilirubinemia can therefore be said to have modifiable associated factors particularly in developing countries. In Australia over a ten-year period, Palmer and Drew found different associated factors of jaundice in infants such as sepsis (3%), bruising (2%) and G-6PD deficiency (0.5%) (41).

2.3.3. Rh Isoimmunization

Erythroblastosis due to Rh incompatibility is still an important cause of hyperbilirubinemia. There are no inborn antibodies in the Rhesus blood group system. The Rh antibody is produced by an Rh negative mother in response to the presence of Rh antigen on the fetal red blood cell membrane. The initial maternal response to this antigenic stimulus produces immunoglobulin (IgG) antibodies, which do not cross the placenta. Later IgG antibodies are formed that cross into the fetus and attaches to antigenic sites on the red blood cells membrane (42). According to study done by Palmer and Drew in Australia Rhesus erythroblastosis was 3% of jaundiced neonates (41). Trot man et al in their study on epidemiology of neonatal jaundice at the university hospital of the West Indies showed that prevalence of neonatal jaundice due to Rh Isoimmunization was 3.5 % (25). Other study done by Goyal M in Maharashtra on prevalence among associated factors of neonatal jaundice showed that Rh incompatibility was 4.6% (16).

2.3.4. ABO incompatibility

ABO incompatibility most commonly occurs when the mother has type O blood and the baby has type A, B or AB blood. The cause of ABO incompatibility is reaction of maternal anti-A or anti-B antibodies to the A or B antigen on the red blood cells of the fetus or newborn. It is seen usually only in type A or B neonates born to type O mothers. Jaundice of ABO incompatibility usually appears within the first 24-72hrs after birth (9, 10). A study done by H. Boskabadi et al revealed that ABO incompatibility, Rh incompatibility and G-6PD deficiency were the most common associated factors of neonatal jaundice (43). According to study done by Goyal M in

Maharashtra in India on prevalence among associated factors of neonatal jaundice were ABO incompatibility which contributed 11.1% of them (16). Other study by Palmer and Drew in Australia prevalence of ABO erythroblastosis was (7%) (41). As Trot man et al in their study showed that the prevalence of neonatal jaundice due to ABO incompatibility was 35% (25). Other study conducted by Oteikwu Ochigbo S on prevalence of bilirubin encephalopathy showed that 19.1% among neonates with kernicterus were due to ABO incompatiblity (4).

2.3.5. G-6PD deficiency

G-6PD deficiency is the commonest inherited red cell enzymopathy worldwide, affecting about 400 million people globally and affecting as many as 4,500,000 newborns worldwide each year (44). The G-6PD gene is located on the X chromosome and homozygous males have the full enzyme deficiency. G-6PD deficiency affects all races, the highest rates (up to 34%) are found in tropical Sub-Saharan Africa, where it has also been associated with a protective effect against plasmodium falciparum malaria (45).

According to study done by Charles AT and Osorio in Port Harcourt Nigeria, male neonates were high prevalent to develop hyperbilirubinemia than female neonates. Among 400 jaundiced neonates more than half of them (52.5%) had G-6PD deficiency. Among the G-6PD deficient neonates, 69% were males while 31% were females which shows male to females ratio was about 2:1(42). Other study by Abosdera MM in Egypt on prevalence of glucose 6 phosphate dehydrogenaseshowed that among 300 jaundiced neonates 50% of them were 4-7 days and 13.83% of them were greater than 7 days after birth of life. 6 % of these neonates were jaundiced due to G-6PD deficiency (46). Other study by Oteikwu Ochigbo S in 2016 indicated that 9.5% of neonates with kernicterus were due to G6-PD deficiency (4).

2.3.6. Infectious causes of jaundice(Sepsis)

Study conducted in hospital of Nigeria in 2011 showed that 35% neonates were admitted due to neonatal jaundice and 5.2% of them were died. Those died neonates were due to sepsis and kernicterus. Half among died were due to sepsis and the rest were due to bilirubin encephalopathy (34). Intrauterine infections may cause giant cell hepatitis and jaundice anytime during neonatal period. Jaundice is a recognized feature of congenital and neonatal malaria (10). According to study done by Onyearugha C et al on prevalence and associated factors of neonatal hyperbilirubinemia in Federal Medical Centre Abakaliki showed that 3.2% of jaundiced neonates

were due cephalohematoma and 32.5% were due to septicemia (34). Infectious causes of bilirubin encephalopathy were 71.4% according to study done by Oteikwu Ochigbo S in 2016 (4).

2.3.7. Breast feeding Jaundice

Breastfeeding jaundice usually occurs early in life (2-3days) after birth due to insufficient milk intake. Decreased frequency of breastfeeding is associated with exaggeration of physiological jaundice. Jaundice associated with breastfeeding in the first few days after birth appears to be related to an increase in enter hepatic circulation of bilirubin. This occurs in the first few days because until the milk has 'come in' breastfed infant nutrient intake is limited, with fewer calories thereby prolonging the intestinal transit time and passage of fewer stools in the first few days of life suggesting that increased amount of bilirubin is absorbed into the enter hepatic circulation (9, 10).

A research conducted on severe neonatal hyperbilirubinemia leading to exchange transfusion in 2014, the prevalence of breastfeeding jaundice of neonates was 35%. In this study onset of jaundice in 40.5% of 93 neonates was on the 2nd day and 10 of them were on the 1st day after birth (47). According to Rennie J et al national institute for health and clinical excellence, at one month of age, approximately 10% of breastfed babies remain jaundiced (48).

2.3.8. Breast milk Jaundice

The etiology of breast milk jaundice is not clearly understood, but the following factors have been suggested to play a role: increased concentration of non-esterified free fatty acids; increased enter hepatic circulation of bilirubin due to increased content of beta glucuronidase activity in breast milk; inflammatory cytokines in human milk; and high epidermal growth factor levels in breast milk which leads to reduced gastrointestinal motility and increased bilirubin absorption and uptake are thought to be responsible for breast milk jaundice in these neonates (10,26).

It is of late onset (after 4-7 days) and has an incidence in term newborns of 2 to 4%. A strong familial predisposition is suggested by the recurrence of breast milk jaundice in siblings (44). Study conducted in Iran in 2014 magnitude of hyperbilirubinemia in neonates with history of neonatal jaundice in siblings was reported in 50% of cases (47) and other study in Iran by Najib KS et al in 2013 showed that 27.9% had history of jaundice in their siblings (38). Prevalence of breast milk jaundice accounts 4% causes of neonatal admission at Sikkim Mani pal Institute of

Medical Sciences in India. According to this study relatively increased incidence of neonatal jaundice was occurred (15).

2.3.9. Prematurity

Although preterm infants develop hyperbilirubinemia by the same mechanisms as term infants, it is more common and more severe in preterm infants and lasts longer. This outcome is related to the relative immaturity of the red blood cells, hepatic cells, and gastrointestinal tract. Sick preterm newborns are more likely to have a delay in initiating enteral nutrition, resulting in an increase in enter hepatic circulation (24). A study conducted by Palmer and Drew in Australia showed that 20% among jaundiced neonates were due to prematurity (41). Prematurity was among the leading associated factors of neonatal jaundice in Federal Medical Centre Abakaliki, Nigeria, which accounts to 17.5% of neonates (35). Study conducted by Kokeb M, Desta T in 2016 in Gondar University Hospital showed that 27.4% of neonates were admitted due to prematurity (28).

2.4. Conceptual framework
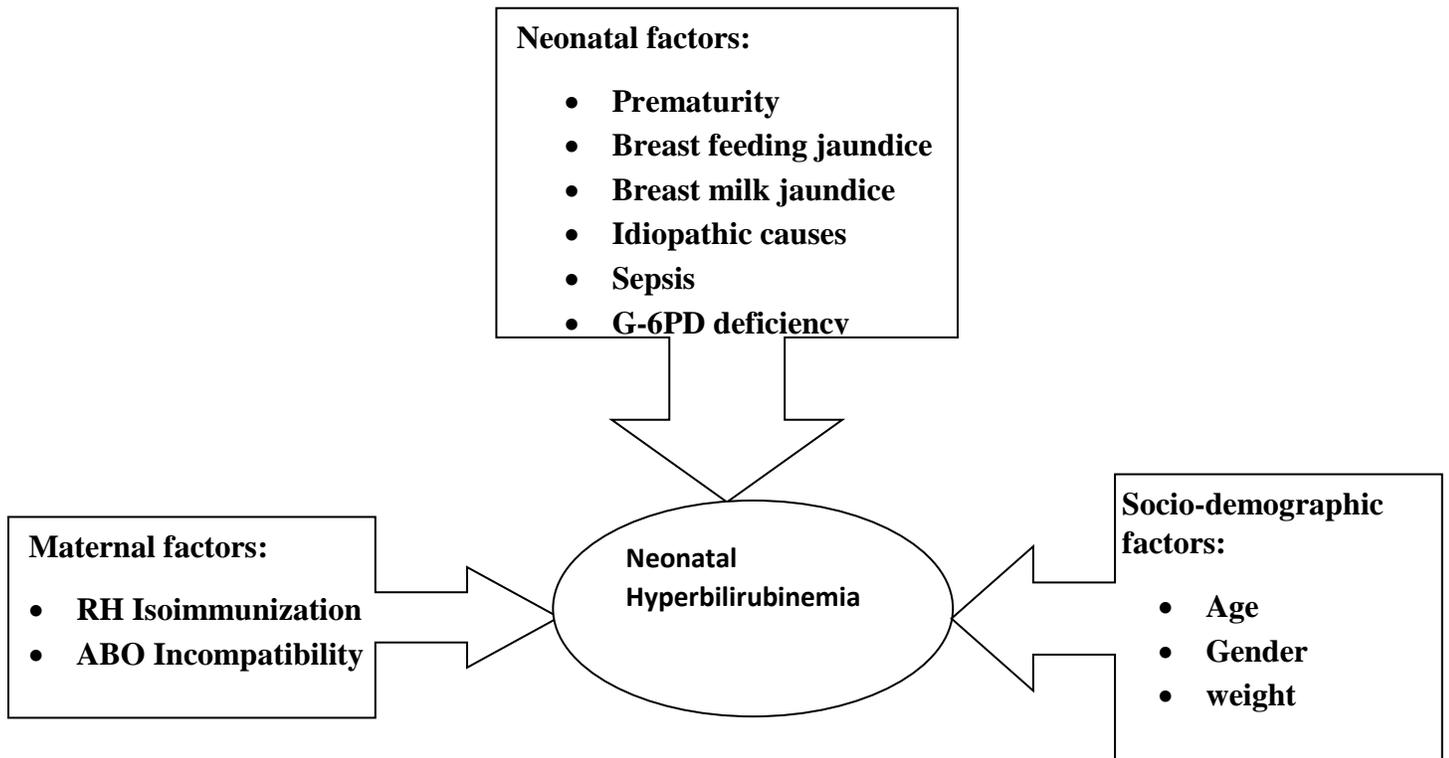
Figure 1. Conceptual framework of neonatal hyperbilirubinemia in TASH, Addis Ababa, 2017 (Source: Literature review).

3. OBJECTIVES

3.1. General objective

To asses magnitude and associated factors of neonatal hyperbilirubinemia in admitted neonates at NICU of TASH from September 11, 2014 to September 11, 2016, Addis Ababa, Ethiopia, 2017.

3.2. Specific objectives

 To assess magnitude of hyperbilirubinemia among neonates admitted at NICU of TASH from September 11, 2014 to September 11, 2016, Addis Ababa, Ethiopia, 2017.

To identify associated factors of hyperbilirubinemia among neonates admitted at NICU of TASH from September 11, 2014 to September 11, 2016, Addis Ababa, Ethiopia, 2017.

4. METHODOLOGY

4.1. Study area

The study was conducted in TASH which is located in Addis Ababa. Total population of Addis Ababa as of 2007 GC was 3,384,569. Area of TASH covers 12300m.sq of land with 8 floors and 1262 rooms with 800 beds. The hospital provides a tertiary level of health care service. It offers diagnoses and treatment for approximately 370,000-400,000 patients per year in all wards. TASH is the largest and oldest teaching hospital in the country which is classified in to different departments. NICU runs under the department of pediatrics which is reported to be able to accommodate as many as 60 patients (49).

4.2. Study design and Period

Institutional based cross-sectional study design was conducted from March 2017 to June 2017 in Tikur Anbessa Specialized Hospital.

4.3. Source populations

All neonates admitted at NICU of TASH from September 11, 2014 to September 11, 2016.

4.4. Study populations

Selected neonates among those admitted at NICU of TASH from September 11, 2014 to September 11, 2016.

4.5. Eligibility criteria

4.5.1. Inclusion criteria
Newborn less than 28 days old after birth and admitted at NICU of TASH from September 11/2014 to September 11/2016.

4.5.2. Exclusion criteria
Neonates whose bilirubin level did not measured.

4.6. Sample size determination
Sample size was calculated using single population formula. As neonate's registration cards total neonates admitted at NICU from September 11, 2014 to September 11, 2016 in TASH were 4800. P=35% (proportion of neonatal hyperbilirubinemia in Nigeria was 35%).

$$ni = \frac{\left(z\alpha_{/2}\right)^2 * p(1-p)}{d^2}$$

Where, =initial sample size

p= proportion of neonatal hyperbilirubinemia; 35%=0.35

a= confidence interval (95%)

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

Total number of neonates admitted from September 11/2014 to September 11/2016 was 4800.

ni=(1.96)^2 (0.35) (1-0.35)/ (0.05)^2

  =3.8416(.35) (.65)/.0025 =.873964/.0025=350

For possible dropout rate 10% (35) was added to sample size.

ni= 385

By correction formula:

  Nf = ni/1+ ni/N, where N=4800

 =385/1+385/4800=385/1+.0802083=356

4.7. Sampling procedures

The sample for this study was selected every k^{th} value of neonates where k=13 among those admitted at NICU of TASH from September 11/2014 to September 11/2016.

K=N/nf=4800/356=13

(Where, N total population at NICU of TASH from September 11/2014 to September 11/2016, nf= final sample size of the study).

4.8. Study variables

4.8.1. Dependent variable

Neonatal hyperbilirubinemia

4.8.2. Independent variables.

Socio-demographic variables:	Neonatal factors:
Age	Prematurity
Gender	Breast feeding jaundice
Weight	Breast milk jaundice
Maternal factors:	Infectious causes
ABO incompatiblity	Idiopathic cause
Rh isoimmunization	G-6PD deficiency

4.9. Data collection procedures

Cards of neonates admitted at ICU of TASH from September 11/2014 to September 11/2017 were isolated and counted. Then card number of those neonates were put in their order of admission. Necessary information of neonate at every 13th (K-value) in the order was collected and reviewed from their registration and medical records. Data was collected by 5 trained data collectors and 2 supervisors. All data collectors and supervisors were first degree holders in health professions. Medical records of the neonates were returned to card room at the end of each data collection day.

4.10. 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.

4.11. Data quality assurance

Supervisors and data collectors were BSc health professionals. Data collectors were trained by principal investigator about the objective of the study and ways of data collection. Pre-test was conducted on 5% of sample before the starting of actual data collection. Supervisors were checked the collected data daily for completeness.

4.12. Data processing and analysis

Data was first entered to Epi Info version 7 and exported to SPSS version 20.0 to clean and analyze data. Frequency was used to describe the parameters investigated. Relation between dependent and independent variables were assessed and presented using odd ratios and confidence intervals. Confidence interval of 95% were used to see the precision of the study and the statistical association was considered as significant if p-value was less than 0.05. Multiple and binary logistic regression were done to control possible confounders related to magnitude of neonatal hyperbilirubinemia and its associated factors.

4.13. Ethical considerations

Ethical clearance for the study was received from Addis Ababa University, College of Health Sciences. A formal letter was written to TASH and permission was secured at all levels. Information related to those neonates was confidential in any ways.

4.14. Dissemination plan

The final result of the study would be submitted to Addis Ababa University School of Allied Health Science Department of Nursing and Midwifery. A copy of the finding would also be given to TASH and sent to international journals for publication.

5. RESULT OF THE STUDY

5.1. Socio-demographic characteristics of neonates in the study, TASH.

A retrospective cross sectional study was done on systematically selected 356 neonates among total neonates admitted at NICU of TASH from September 11, 2014 to September 11, 2016 to assess magnitude and associated factors of neonatal hyperbilirubinemia. Number of male and female in this study were 186(52.2%)and 170(47.8%) respectively.

Among neonates included in this study 160(44.9%) of them were developed neonatal hyperbilirubinemia. Age of 176(49.4%) neonates were 3-6 days old at admission. Weight of 241(67.7%) neonates were 2500gm-4000gram at admission. Hospital duration of the neonates were from 1 to 25 days. 231(64.9%) of them were discharged from hospital within a week after admission and 55(15.4%) of neonates were discharged before 2 days. Premature neonates among selected neonates were 135(37.9%) and mother of 22(6.2%) neonates did not know their gestational age (table 1).

Table 1: Socio-demographic characteristics and frequency of neonates according to their category, TASH, AA, Ethiopia, 2017.

Socio-demographic characteristics	Category	Frequency/percentage among all neonates(356)	Frequency(percentage) among jaundiced neonates(160)
Sex	Male	186(52.2%)	89(55.6%)
	Female	170(47.8%)	71(44.4%)
Age at admission (days)	Less/ equal 2	100(28.1%)	24(15%)
	3-6	176(49.4%)	84(52.5%)
	Greater than 6	80(22.5%)	52(32.5%)
Weight (grams)	Less than 2500	104(29.2%)	25(15.6%)
	2500-4000	241(67.7%)	127(79.4%)
	Greater /equal to 4000	11(3.1%)	8(5%)
Gestational age (weeks)	Less than 37 weeks	135(37.9%)	39(24.4%)
	Greater /equal to 37 weeks	199(55.9%)	99(61.9%)
	Unknown	22(6.2%)	22(13.8%)
Hospital stay(days)	Less than 7	231(64.9%)	116(72.5%)
	Greater/ equal to 7	125(35.1%)	44(27.5%)

5.2. Magnitude of neonatal hyperbilirubinemia in the study, TASH.

Among neonates reviewed in this study 160(44.9%) of them were developed neonatal hyperbilirubinemia of which 11(6.9%) neonates were developed bilirubin encephalopathy. Prevalence of neonatal hyperbilirubinemia among male neonates was 89(47.8%) and 71(41.8%) among female neonates. Mean age of neonates at admission with hyperbilirubinemia was 5.29 days and 84(52.5%) of them were 3-6 days old at admission. Mean weight and range of neonates was 2983.24gram and 1770gram-4375gram, respectively. Weight of 127(79.4%) of jaundiced neonates at admission was from 2500-4000gram and 39(24.4%) of jaundiced neonates were premature. Duration of jaundiced neonates in hospital after admission ranges from 1 day to 25 days and 116(72.5%) of them were discharged with in the 1st week of admission (table 1).

Mean onset of hyperbilirubinemia in neonates with hyperbilirubinemia was 2.13 days. Presence (onset) of jaundice in < 3 days old and from 3 – 6 days old after birth was 66.2% and 31.2%, respectively. The onset of jaundice among 11 neonates with bilirubin encephalopathy 7(4.4%) were from 3-6 days old after birth. Onset of neonatal hyperbilirubinemia mostly occurred in less than 3 days old after birth.

Among neonates with hyperbilirubinemia serum bilirubin level of 56(35%) and 43(26.9%) neonates was ≥20mg/dl and from 15mg/dl-20mg/dl, respectively. Mean and range of neonatal serum bilirubin level was 72.1mg/dl (5.6mg/dl-77.7mg/dl) and 19.1175mg/dl, respectively. Hyperbilirubinemia in neonate with 77.7 mg/dl serum bilirubin level was due to neonatal sepsis. Serum bilirubin level of neonates with bilirubin encephalopathy was >30mg/dl except one neonate whom bilirubin level was 21.5mg/dl and 7 of them had more than one associated factors.

5.3. Associated factors of neonatal hyperbilirubinemia in the study, TASH.

The major causes of neonatal hyperbilirubinemia in this study 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. G-6PD deficiency was not the cause of neonatal hyperbilirubinemia according to this study (table 2).

There were more than one associated factors of neonatal hyperbilirubinemia causing increased level of bilirubin level in a neonate. Among them sepsis +ABO incompatibility and prematurity+ ABO incompatibility accounts 4(2.5%) each. Breast milk+ ABO incompatibility accounts

3(1.875%) and sepsis+ other known causes of neonatal hyperbilirubinemia accounts 2(1.25%). Among other known cause of hyperbilirubinemia cephalohematoma was common. 7(4.4%) neonates with NH who developed bilirubin encephalopathy had more than one associated factors. NH in 14(8.8%) neonates were caused by Rh isoimmunization and 3(1.9%) of them developed bilirubin encephalopathy. A mother of one jaundiced neonate caused by Rh incompatibility had history of 3 previous early neonatal death and one intrauterine death.

Sepsis was among the leading cause of NH in this study. Among 160 neonates with NH blood culture of 39(24.4%) neonates was done and blood culture of 4(2.5%) neonates were negative (no growth) but 35(21.9%) of them had positive result of blood culture.

Table 2: Associated factors of NH among neonates with hyperbilirubinemia in TASH, AA, Ethiopia, 2017.

Associated factors of hyperbilirubinemia	Frequency	Percentage
Prematurity	13	8.1%
Breast milk jaundice	10	6.3%
Breast feeding jaundice	16	10%
Sepsis	30	18.8%
Rh incompatibility	14	8.8%
ABO incompatibility	57	35.6%
G6-PD deficiency	0	0.0%
Idiopathic cause of jaundice	22	13.8%
Other known cause of jaundice	13	8.1%
Hemolytic cause of jaundice	10	6.2%

In binary logistic regression age was significantly associated with the occurrence of neonatal hyperbilirubinemia. For example, neonatal age of ≤ 2 days old at admission were 5.8[COR=5.8, CI=95% (3.07-11.25), P-value=0.000] times more likely to occur than those neonates above 6 days old after birth. Weight of neonates was also significantly associated with neonatal hyperbilirubinemia. Neonates weighed less than 2500gm at admission were 8.4[COR=8.4,

CI=95% (2.07-34.2), P-value=0.003] times more likely to develop hyperbilirubinemia than those weighed ≥4000 gram at admission. In multivariate logistic regression age was significantly associated with neonatal hyperbilirubinemia. For example neonates ≤ 2 days old were 6.89[AOR=6.89, CI=95% (3.46-13.69), P-value=0.000] more likely to develop hyperbilirubinemia and those from 3 to 6 days old at admission were 2.2[AOR=2.2, CI=95% (1.23-3.93), P-value=0.008] times more likely to develop hyperbilirubinemia than those neonates greater than 6 days old (table 3).

Table 3: Socio-demographic variables associated to neonatal hyperbilirubinemia in TASH, AA, Ethiopia, 2017

Variables		Did the neonate has hyperbilirubinemia?		COR(crude odd ratio)	AOR(adjusted odd ratio)	p-value	
		Yes	No			COR	AOR
Age of neonate at admission	≤ 2 days	24(6.7%)	76(21.3%)	5.88(3.07-11.25)	6.89(3.46-13.69)	0.000	0.000
	3-6 days	84(23.6%)	92(25.8%)	2.03(1.17-3.51)	2.20(1.23-3.93)	0.011	0.008
	>6 days	52(14.6%)	28(7.9%)	1	1		
Total		160	196				
Gender	Male	89(25%)	97(27.2%)	.78(.514-1.189)	0.72(.45-1.15)	0.249	0.176
	Female	71(19.9%)	99(27.8%)	1	1		
Total		160	196				
Weight of neonate at admission (gram)	< 2500	25(7%)	79(22.2%)	8.42(2.07-34.20)	9.97(2.34-42.38)	0.003	0.002
	2500-4000	127(35.7%)	114(32%)	2.39(0.62-9.24)	2.48(0.62-9.98)	0.205	0.199
	≥ 4000gm	8(2.2%)	3(0.8%)	1	1		
Total		160	196				

5.4. Condition at discharge and management of neonates with hyperbilirubinemia at NICU of TASH.

All neonates with hyperbilirubinemia were treated either by phototherapy alone or both phototherapy and exchange blood transfusion. Among jaundiced neonates, 139 (86.9%) of them were treated by phototherapy alone and the rest 21(13.1%) were treated with exchange blood transfusion combined with phototherapy. Almost half, 10(47.6%), of neonates managed by combined treatment were developed bilirubin encephalopathy. All neonates with bilirubin encephalopathy were planned to be treated with combination of phototherapy and exchange blood transfusion but one neonate was treated only by phototherapy because of unavailable blood in the hospital at the time of neonatal admission. This neonate was died at last.

Neonatal death among those with neonatal hyperbilirubinemia was 5(3.1%) in this study. Among those died, 3(60%) of them were due to bilirubin encephalopathy. 94.4% of jaundiced neonates were improved and discharged to home of which only one neonate discharged with complication (sequel), hearing loss, whom bilirubin level was 77.7mg/dl and had late onset of neonatal sepsis, meningitis. Family of 3 neonates among jaundiced neonates took their neonate home without completing management (left against medical advice) and one neonate was referred to other health facility for ophthalmologic evaluation.

6. DISCUSSION

Neonatal jaundice is a very common condition worldwide occurring in up to 60% of term and 80% of preterm newborns in the first week of life (2). In contrary recent study conducted in Nigeria by Omekwe DE et al (29) showed that among preterm neonates 40.7% and 56.8% of term neonates were developed hyperbilirubinemia which is similar with present study that showed 49.7% among term neonates and 28.9% among preterm neonates were developed hyperbilirubinemia. In this study prevalence of neonatal hyperbilirubinemia was 160 (44.9%) of which 11(6.9%) neonates were developed bilirubin encephalopathy.

Magnitude of NH in Pakistan studied by S. S. Tikmani et al (3) and in west India University 2012 (25) was 27.6% and 4.6%, respectively. Magnitude of NH in TASH is quite high compared to other studies conducted except the study conducted by Narayan in level II care at neonatal intensive care unit in India (15) that showed magnitude of NH in this hospital was 54%. This may be due to difference in study area or socio demographic characteristics.

Study by Kamara IK in Seiralione (26) showed that 24% of neonatal death in NICU was due to hyperbilirubinemia and according to Ogunlesi TA and Ogunfowora OB 2010 (8) were 152 neonates were developed NH of which 49.7% them developed bilirubin encephalopathy. Study conducted by Onyearugha C et al in Nigeria (34) showed that prevalence of NH was 35% of which 9.7% neonates were developed bilirubin encephalopathy. This indicated that 5.2% of neonates with NH were expired and 50% of death were due to bilirubin encephalopathy. Other study in Benin 2012 showed that magnitude of NH was 26.5% of which 12.7 % of them were died. Other study by Oteikwu Ochigbo S et al in Calabar teaching hospital (4) showed that prevalence of NH was 19.6% of which 3.8% of neonates were developed bilirubin encephalopathy and 4(19%) with bilirubin encephalopathy were expired.

Recent study in Gondar university hospital, Ethiopia (28) on predictors of neonatal morbidity and mortality showed that magnitude of NH among 325 neonates admitted at NICU were 103(31.7%) of which 33(32%) were expired (28). In this study neonatal death due to NH was 5(3.1%) of which 3(60%) of them were due to bilirubin encephalopathy. This indicated that hyperbilirubinemia is a serious problem leading to long term sequel in survivors and death in neonates. This confirms Naghavi M et al 2015 that showed after several years of neglect and exclusion from the global child health agenda under the million development goal initiative,

neonatal hyperbilirubinemia are increasingly acknowledged as important contributors to global neonatal deaths.

Present study showed that mean age and weight of the study was 4.426 days and 2813.87gram, respectively and study conducted in south Nigeria (4) showed that mean age and weight of the study was 13 days and 2880gram (1200-4200gram), respectively. Current study found that most affected age group by NH were 3-6 days old at admission which was 52.5% and those > 6 days old were 32.5%. Other study conducted in Namibia 2017 (11) showed similar age group of neonates were affected to develop potential bilirubin encephalopathy were 3-6 days old after birth which accounted of 9.6% and other study conducted in Egypt by Muhammad A 2011 (17) showed that prevalence of neonatal hyperbilirubinemia in 4-7 days old neonates was 27.9% and ≥8 days old neonates were 26.8%. Other study in Egypt 2014 (46) indicated that 50% of jaundiced neonates were from 4-7 days old and 13.83% were > 7 days old after birth. This showed that as age of neonate increases prevalence of neonatal hyperbilirubinemia decreases; prevalence of neonatal hyperbilirubinemia is inversily proportional to age of the neonate.

Present study showed that mean onset of NH and duration of hospital stay was 2.13 days and 5.81 days, respectively and in the study conducted by Oteikwu Ochigbo S et al was 3.2 days and 3 days, respectively. Onset of hyperbilirubinemia in current study was 38.1%, on 1st day and 19.4% on 2nd day and other study in West Indies University 2012 (25) showed that onset of jaundice was 27% on the 1st day and 43% on 2nd day. Other study done in Iran 2013 (38) indicated that 11.4% neonates were developed NH on the 1st day of life after birth. This may be due to newborn's immature liver that often cannot remove bilirubin quickly enough, causing hyperbilirubinemia in neonates.

Current study showed that 99.4% of neonates were developed NH in the 1st week of life. Similarly study done in Benin 2012 (40) showed all neonates were developed NH in the 1st week of life after birth and in Nigeria 2011 (34), 89.6% of jaundiced neonates developed NH in the 1st week of life. Other study by Omekwe DE et al (29) showed 41.2% neonates were developed NH at 1-2 days old after birth. In Pakistan by S. S. Tikmani et al (3) 64% of neonates were developed hyperbilirubinemia between 0 and 6 days after birth.

Among associated factors of NH in this study ABO incompatiblity (35.6%), sepsis (18.8%), idiopathic causes (13.8%), breast feeding (10%), prematurity (8.1%) and other known causes were 8.1%. Similar study in west India University 2012 (25) indicated that among associated factors were ABO incompatiblity 35%, prematurity 11%, Rh incompatiblity 3.5%, idiopathic cause 9%. Prevalence of ABO incompatiblity was the same in both studies. This similarity may be due to similar study subjects. Study in Benin (40) showed that associated factors of NH were ABO incompatiblity(7.6%) and sepsis(45%). The cause of NH due to G-6PD deficiency was not known in TASH like study done by Israel-Aina Y and Omoigberale A in Benin teaching hospital because deficiency of the enzyme in neonates was not screened.

There was no history of hyperbilirubinemia in sibling in current study but study in Iran 2013 (47) showed that 20% of jaundiced neonates had history of jaundice in sibling. In current study 13.75% mothers of jaundiced neonates had no antenatal follow up and did not know their gestational age. Similarly study done in Benin 2012 (40) showed that 38.6% mothers of jaundiced neonates had no antenatal follow up and did not know their gestational age. This may cause difficulty in early detection of hyperbilirubinemia in neonates and increases its complication.

Logistic regression in prresent study showed that weight was associated with the occurance of NH and study conducted by Chime HE et al 2011 in Nigeria (33) indicated that ABO incompatiblity and low birth weight were the major predesposing factors of NH. The most cause of bilirubin encephalopathy in present study were sepsis+ABO incompatiblity (1.9%) and Rh isoimmunization alone (1.3%). Study done in Iran 2013 (38) showed that cause of bilirubin encephalopathy were ABO incompatiblity + Rh issoimmunization (5.9%), sepsis (12%), other cause (3.5%), idiopathic cause (53.1%) and G-6PD deficiency (25.5%). In this study three neonates among those with complicated hyperbilirubinemia had acute symptoms such as unable to feed, muscle rigidity and one of them had additionally chronic symptom which was seizure. Study conducted in Iran by 2013 (38) showed that two neonates had sign of bilirubin encephalopathy such as convulsion and opisthotonus.

Mean serum bilirubin level of present study and by Oteikwu Ochigbo S et al was almost similar, which was 19.11mg/dl and 18.9mg/dl, respectively. Serum bilirubin level of current study was ranged from 5.6mg/dl-77.7mg/dl but study conducted in Benin teaching hospital (40) indicated serum bilirubin level of jaundiced neonates was ranged from 4mg/dl-25mg/dl. In current study

serum bilirubin level of 10 (6.3%) neonates was >30mg/dl and they were among those with complicated hyperbilirubinemia. Study by Ogunlesi TA and Ogunfowora OB (8) showed that serum bilirubin level of 36 (48%) neonates among those with bilirubin encephalopathy was >30mg/dl. In present study most neonates with more than one associated factors had markedly elevated bilirubin level than those with one associated factors. This supports the study conducted by Stevenson DK et al (31) on understanding of newborn jaundice showed that as the number of associated factors increases, the potential to develop markedly elevated bilirubin levels also increases. This may be the added effect of each associated factors causing elevated bilirubin level.

Sepsis was among associated factors causing NH and blood culture is common investigation for neonatal sepsis. In present study blood culture of 39 (24.4%) jaundiced neonates were done of which 35 (89.7%) had posetive result. Other study in Nigeria 2010 (8) showed that blood culture of 48 neonates among 152 jaundiced neonates were done of which 14 (29.25%) posative result. In present study duration of hospital stay among neonates with NH was 1-2 days in 18.1% and after 2 days in 81.9%. There was no neonate discharged before one day after admission but previous study done in west India (25) showed that 15% of jaundiced neonates were discharged before one day and other 85% were discharged at or after one day of which 47 % from 1-2 days and 38% after two days.

In present study 139 (86.9%) of neonates with NH were treated by phototherapy alone of which one neonate need exchange blood transfussion but not transfused due to unavailable blood in hospital and the rest 21 (13.1%) were treated by combination of exchange blood transfussion and phototherapy. Study in Benin (40) indicated that 45% of jaundiced neonates were treated by phototherapy alone. Study in Iran by Najib KS et al (38) showed that 64.5% of neonates need phototherapy alone and 35.5% of them need combination of exchange blood transfusion and phototherapy.

In present study 3 (1.9%) of neonates were left against medical advice and one neonate was referred to other health facility for opthalmologic evaluation and similarly in study done in Nigeria by Onyearugha C (34) showed that 3 neonates among NH were discharged against medical advice and 2 neonates were referred to other health facility. In Benin teaching hospital 8.7% of jaundeced neonates were discharged against medical advice.

7. STUDY LIMITATION AND STRENGTH

7.1. Strength: Medical records of neonates were properly handled and information related to neonatal hyperbilirubinemia was obtained.

7.2. Limitation: This is a retrospective study; hence it was difficult to establish the contribution of G-6PD deficiency since routine screening of this enzyme deficiency was not done in the center.

Inability to locate and follow up documentation on the discharge subjects to ascertain if they were developed long term sequel.

8. CONCLUSION AND RECOMMENDATION

8.1. Conclusion: Magnitude of neonatal hyperbilirubinemia in this study was quite high compared to other researches done on neonatal hyperbilirubinemia. Major factors causing hyperbilirubinemia in neonates were ABO incompatibility, sepsis, Rh isoimmunization, idiopathic cause, breast feeding jaundice. Neonatal hyperbilirubinemia was a cause of neonatal death in NICU. Among neonates died more than half of them were due to complicated neonatal hyperbilirubinemia. Therefore, early prevention and timely treatment of hyperbilirubinemia in neonates is important to prevent or reduce neonatal death due to hyperbilirubinemia.

8.2. Recommendation

Recommendation for health facility: Antenatal clinic record that covers prenatal screening for blood group should be held by women to ensure that all essential information is readily available to the caregiver.

ABO incompatibility and Rh isoimmunization were among the major cause of neonatal hyperbilirubinemia which can be prevented. Therefore, all women should be tested for ABO and Rh as early as possible during each pregnancy and Rh negative women should be administered prophylactic Rh immunoglobulin both during pregnancy and after delivery.

Checking bilirubin level of neonates in the 1st 3 days of life for all neonates would be important for early detection, treatment of NH and prevent its complication.

Recommendation for health policy makers: Plan and deliver necessary training programs for health professionals to give attention and care for neonates regarding to NH.

Community based training and health education about clinical symptoms, complication of NH and importance of checking bilirubin level of all neonates including those delivered at home would create community awareness to take action timely before complication of hyperbilirubinemia occurred.

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Annex I. Data collection Checklist

Data was collected from each medical card of admitted neonate in TASH from September 11/2014 to September 11/2016 accordingly. This checklist was adopted and modified from literatures I used. This checklist was used for each neonate.

Code of neonate: _____/_____

Code	Question	Response	Remark
01	What was the age of neonate at admission?	_____days	
02	What is the sex of the neonate?	1. Male 2. Female 3. Both genitalia	
03	How long the neonate stayed in hospital?	_____days/weeks	
04	What was the Weight of neonate on admission?	_____gram	
05	What was the gestational age of neonate's mother?	_____weeks	
06	Did the neonate developed hyperbilirubinemia (jaundice)?	1.Yes 2.No	
07	Age of neonate at onset of jaundice	_____days	
08	What was the neonate's bilirubin level on admission?	_____mg/dl and/or _____µmol/L)	
09	Did the neonate developed bilirubin Encephalopathy (Kernicterus)?	1. Yes (write if there is any sequel due to BE)._____ 2. No	
10	What was/were the associated factor/s (cause) of	1. Jaundice due to prematurity 2. Jaundice due to breast milk	

		3. Jaundice due to breast feeding	
	hyperbilirubinemia? (Why the neonate developed Jaundice?) (It is possible to choose more than one)	4. Jaundice due to sepsis(infection)	
		5. Jaundice due to RH Isoimmunization	
		6. Jaundice due to ABO incompatibility	
		7. Jaundice due to G-6PD deficiency	
		8. Jaundice due to Unknown(idiopathic)	
		9. Other reason _____	
11	If Hemolysis, what was the cause of hemolysis?	1. RH Isoimmunization	
		2. G-6PD deficiency	
		3. ABO incompatibility	
		4. Other _____	
12	What was the result of blood culture?	1. negative	
		2. positive	
		3. None(not done)	
13	What type of management was given to neonatal hyperbilirubinemia for the neonate?	1. photo therapy	
		2. blood transfusion	
		3. both phototherapy and exchange blood transfusion	
		4. other ____	
14	Condition at discharge	1. improved	
		2. expired	
		3. referred	
		4. other(specify)	

Annex II: Approval by the board of examiners

This thesis by Hoffola Gudeta is accepted by the board of examiners as satisfying thesis requirement for the Degree of Master of Science in Pediatrics and Child Health.

Research Advisors:

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Chair of Department:

Full name	Rank	Signature	Date
_____	_____	_____	_____