PREVALENCE, RISK FACTORS AND OUTCOME OF NEONATAL ACUTE BILIRUBIN ENCEPHALOPATHY AMONG NEONATES ADMITTED TO NEONATAL INTENSIVE CARE UNIT IN TASH AND GMH, ADDIS ABABA, CASE CONTROL STUDY, 2024/25G.C.

A RESEARCH PROPOSAL TO BE SUBMITTED TO ADDIS ABABAUNIVERSITY, COLLEGE OF HEALTH SCIENCES, PEDIATRICS ANDCHILD HEALTH DEPARTMENT IN PARTIAL FULFILMENT OFTHE REQUIREMENT FOR THE SPECIALITY CERTIFICATE PROGRAM IN PEDIATRICS AND CHILD HEALTH

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ADDIS ABABA, ETHIOPIA

APPROVAL SHEET

ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES SCHOOL OF MEDICINE DEPARTMENT OF PEDIATRICS AND CHILD HEALTH

I, as the undersigned Pediatrics and Child health resident, declare that I have submitted my original proposal on the title Prevalence, risk factors and outcome of neonatal acute bilirubin encephalopathy among neonates admitted to neonatal intensive care unit of Tikur Anbesa Specialized hospital and Gandhi Memorial hospital, Addis Ababa, Ethiopia.

A Case Control Study on Prevalence, risk factors and outcome of neonatal acute bilirubin encephalopathy among neonates admitted to neonatal intensive care unit of Tikur Anbesa Specialized hospital and Gandhi Memorial hospital, Addis Ababa, Ethiopia in partial fulfillment of the specialty program.

Submitted by:

Name of resident	**Signature**	**Date**
Dr. Yoseph Mente	**…….**	**……..**

This proposed work has been submitted with my approval as an advisor.

Approved by advisor	**Signature**	**Date**
Dr. Tamirat Moges	**……**	**……..**

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Abbreviation and Acronyms

AAP……. According to American academy of pediatrics
ABE……Acute bilirubin encephalopathy
ANC……Antenatal care
APGAR score……. Appearance, pulse, grimace, activity, respiration score
CBE……Chronic bilirubin encephalopathy
CFR……. Case fatality rate
CNS…… Central nervous system
C/S……...Cesarean section
EHB……Extremely severe hyperbilirubinemia
G.C. ….....Gregorian calendar
GMH……Gandhi Memorial hospital
G6PD…. . .Glucose-6-phosphate dehydrogenase
HDN….....Hemolytic disease of newborn
HIC……. High-income countries
KMC……. Kangaroo mother care
KSD……Kernicterus spectrum disorder
LBW……. Low birth weight
LMICs……. Low-middle-income countries
NH……. Neonatal hyperbilirubinemia
NIHCD……. National Institute of Health and Clinical Development
NICU……. Neonatal intensive care unit
NMR……. Neonatal mortality rate
NJ……. Neonatal jaundice
PI ……. Principal investigator
Rh ……..... Rhesus
SDG……. Sustainable Development goal
SNJ……. Severe neonatal jaundice
SVD……. spontaneous vaginal delivery
TASH……Tikur Anbessa Specialized hospital
TSB……...Total serum bilirubin
WHO……. World health organization

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Abstract

Background – Acute bilirubin encephalopathy (ABE) is a clinical syndrome associated with bilirubin toxicity in the CNS, resulting in chronic and permanent sequelae. Despite ABE complications contribute to a substantial burden of neonatal deaths and several neurodevelopmental disorders in the country, there is limited study showing the prevalence and factors associated to ABE. Even the available limited studies were only showing the prevalence of jaundice rather than ABE.

Objective – To determine Prevalence, risk factors and outcome of neonatal acute bilirubin encephalopathy among neonates admitted to neonatal intensive care unit of Tikur Anbesa Specialized Hospital (TASH) and Ghandi memorial hospital (GMH) from September 11, 2020 to September 11, 2023 G.C.

Methods: A Case Control study was conducted on 218 neonates admitted to intensive care unit of TASH and GMH in Addis Ababa. From the total 2492 of neonates who have neonatal jaundice, 109 neonates who develop acute bilirubin encephalopathy and 109 neonates who did not develop acute bilirubin encephalopathy was included in the study. The total neonates who develop acute bilirubin encephalopathy were 109 and we take all. Simple random sampling was used to select neonates without acute bilirubin encephalopathy. Descriptive statistics used to present the prevalence, the socio-demographic and medical profile of the study participants. Binary and multiple logistic regression analyses were done to identify factors associated with ABE. Finding was reported using adjusted odds ratios with 95% confidence interval and statistical difference was declared at P-value <0.05.

Result:

A total of 218 neonates were studied in case control study (ABE vs non ABE among jaundiced neonates) and the prevalence of ABE is 4.4%. Factors associated with ABE in study were incompatibility (ABO and RH), previous history of jaundice, neonatal sepsis, severity of hyperbilirubinemia, preterm birth and low Apgar score. In this study, Outcome even after treating with phototherapy and double exchange transfusion were death (16.5%) and chronic bilirubin encephalopathy or kernicterus (11%)

Conclusion and Recommendation:
The prevalence of ABE in this study was still high as compared other studies
With regard to this high ABE prevalence, there is need for health care providers in TASH and GMH to put more emphasis on RH and ABO incompatibility all women
tested early as possible during ANC follow up and if women blood group O should be always considered ABO setup.

Keywords

Acute Bilirubin Encephalopathy, Neonatal Jaundice, Neonates

1. Introduction

1.1 Background

Poverty, neonatal hyperbilirubinemia almost always results in acute bilirubin encephalopathy, a preventable neonatal death and childhood morbidity. Acute bilirubin encephalopathy is caused by the ionized bilirubin neurotoxicity in the midbrain, pons, basal ganglia, and cerebellum of susceptible infants, leading to irreversible brain injury. When acute, its outcome may be death, whereas when chronic, its outcome may be manifestations of brain injury. (1) Pre-discharge jaundice evaluation, parent teaching, and follow-up determined by the infant's clinical status and potential for causing severe hyperbilirubinemia on an hour-specific nomogram constitute a systematic approach to monitoring neonatal hyperbilirubinemia in industrialized countries. (2)

While the strategy works very well in developed nations, as evidenced by the very low incidence of acute bilirubin encephalopathy and chronic bilirubin encephalopathy, it works less well in developing nations, where bilirubin follow-up does not exist and is patchy.(5) In areas with high home deliveries G6PD (7), ABE is among the causes of infant mortality (6). As most newborns with ABE are already symptomatic at admission to those facilities that can treat severe hyperbilirubinemia, early care seeking is essential. (9), Parents most probably will be the ones to detect jaundice and seek care early to avoid ABE in settings where health staff do not closely monitor. (10)

Hyperbilirubinemia during the neonatal period of early infancy is very frequent. Following an increase during the first few days of life, the bilirubin levels plateau by the seventh day. (11). In certain infants, bilirubin levels may increase to an extent where they cross the blood-brain barrier and result in acute bilirubin encephalopathy. (12) ABE refers to a collection of pathologic and clinical problems resulting from bilirubin intoxication in the nervous system. ABE is defined academically as an acute symptom occurring in the first week of life by the American Academy of Pediatrics (AAP). (13) ABE is the most common disorder in newborns and a leading cause of cerebral palsy, developmental delay, and hearing loss, particularly in developing nations. (14)

A 5-14% risk of augmented mortality and 2 to 3 times higher risk of neurological abnormality have been reported in ABE surviving neonates. (15) ABE has three stages; reversibility occurs in stage one but stage two and three have higher risk of kernicterus (due to chronic bilirubin encephalopathy, or CBE).(16). Socioeconomic factors such as home delivery, lack of antepartum care, uneducated birth

attendants, level of income, and family structure discouraging early medical care were implicated in some studies to be linked with ABE and delayed treatment.(17) Some others were concerned about the state of unawareness and jaundice belief patterns among parents towards ABE risk.(14).

Proper treatment is postponed in either situation only by the resultant failure to diagnose jaundice or by unsuccessful interventions such as trial with routine medications, antibiotics, or unfiltered (early morning) sunlight.18.
Beyond its direct role in neonatal death [19], ABE also tends to underlie many juvenile neurodevelopmental disorders, most prominently hearing loss, cerebral palsy, and seizure disorders [20]. Indeed, in a third-world economy, ABE plays significant role in society, particularly when social security is poor. According to narrative description, ABE is rare in the developed world and in certain technologically advanced high income countries as a result of effective preventive strategies like intensive phototherapy, strict follow up of management protocol, and pre-discharge risk assessment [21].

1.2. Problem's statement

In 2016, 2.6 million newborns died worldwide, with Pakistan, India, the Democratic Republic of the Congo, Nigeria, and Ethiopia being responsible for a large proportion among them. Bilirubin encephalopathy and Rh disease were responsible for more than 22% of the mortality, with South Asia and Sub-Saharan Africa accounting for the largest proportion at 39% and 35%, respectively (14).

Most deaths that occur among newborns in certain nations, including India (30.8%), Kenya (14%), Nigeria (34%), the United Kingdom (2.8%), and Egypt (6.7%), are caused by severe neonatal jaundice (6). With or without ABE, severe hyperbilirubinemia affects about 1.1 million infants annually worldwide. Severe hyperbilirubinemia is the seventh and eighth cause of death among neonates in sub-Saharan Africa and South Asia, respectively (24). Severe neonatal hyperbilirubinemia/jaundice mortality is 1.19 per 1,000 live births in low- and middle-income countries but is significantly lower in high-income countries, at 0.01 (25). In Ethiopia, jaundice is a major cause of neonatal death (25). Jaundice was responsible for 31.7% of admissions and 32% of deaths in a study at Gondar University (27). Hyperbilirubinemia was the main diagnosis in 44.9% of patients and BE in 6.9% of them in a study at Tikur Anbessa Hospital (28). It has been reported in a study done at Mizan Tepi University teaching hospital to establish survival status and predictors of mortality among preterm neonates that jaundice has caused 24.3% newborn mortality among jaundiced neonates (29). Despite the fact that ABE cases are responsible for a large percentage of neonatal deaths and some neurodevelopmental abnormalities in the country, little or no research on the

prevalence and etiology of ABE has been done. The little work done only validated the prevalence of jaundice and not that of ABE.

1.3. Study's significance

The prime targets of the study were to define risk factors and result of ABE in newborn babies who have been admitted into NICU at TASH and GMH and also its frequency.

The research results will act as helpful background for health care professionals, thereby leading their timely recognition of normal ABE risk factors and therefore neonatal ABE mortality rate decrease.

Such awareness will lead towards tackling problems in early diagnosis and treatment.

These findings will also be of use in formulating suitable treatments and strategies.

Furthermore, healthcare program implementers, decision makers, evaluators, and monitors will also gain from these findings since they can apply the findings to improve maternal and newborn care policies. Since no detail study on prevalence, risk factors, and outcome of neonatal ABE was conducted in our environment, it will also act as a scientific reference for future research studies in allied fields

2. Literature Review

2.1- prevalence of ABE

Hyperbilirubinemia is most often found in neonates; more than 80% of cases involve preterm newborns. 30 Acute bilirubin encephalopathy (ABE) in newborns stands as one of the gravest consequences and may cause irreversible damage to the central nervous system. 31 Though its frequency in developed nations has decreased, it still appears with 0.4 to 2.7 occurrences per 100,000 babies, with greater incidence in Africa, Asia, and the Middle East. 14

Theoretically speaking, we could remove this condition completely if we could forecast and react rapidly. Total serum bilirubin levels (TSB) have been linked to ABE rising. Hyperbilirubinemia has been classified by the National Institute of Health and Clinical Development (NIHCD) as very serious EHB if TSB goes over 30 mg/dl. 33

Early signs of ABE include lethargy, failing Moro reflexes, and insufficient feeding; later-stage ABE is shown by extreme weakness, a piercing cry, respiratory distress, convulsions, poor neonatal reflexes, and opus th onus posturing. Most babies showing neurological symptoms either pass away or have major impairments including choreiform movements and either spastic diplegia or monoplegia. 34

2.2 Associated factors for ABE

Typically, in Europe, the ABE site will influence risk variables such male sex, rhesus iso-immunization, and gestational age of 35 to 38 years. In a methodical study conducted in several underdeveloped nations, including Pakistan, low birth weight and short gestational age, rhesus iso-immunization, G6PD deficiency, and sepsis were discovered to be frequent causes of ABE.36

Even with numerous therapy alternatives meant to lower the incidence of severe hyperbilirubinemia and ABE [38], research done in several regions of the world still reveals ABE among newborns with jaundice, which is alarming. Though a Nigerian poll undertaken in 1985 showed 12.4%, a 1996 Turkish study found an ABE prevalence rate of 14.5% [40]. In two other tertiary hospitals, a bi-center Nigerian study from 2000 to 2005 discovered 14.8 and 17.2% among jaundiced newborns (21). ABE appears to have had regular occurrence in this area of the world during the last three decades. Particularly in this area of the world, it is especially important to clearly identify the potential epidemiological factors underlying the ABE problem. Underdeveloped practitioners instructed using these guidelines may be taught to identify severely hyperbilirubinemic newborns at risk of developing ABE and start suitable therapy.

According to the Global Burden of Disease survey, like BE and SNJ, they are among the top 5–10 causes of newborn mortality in countries with most neonatal fatalities [41]. Early estimates of SNJ's global and local effects have come under criticism because of insufficient data. Bhutan et al. forecast 481,000 SNJ cases worldwide among term/near-term newborns, with 114,000 fatalities and 75,000 of survivors living through kernicterus.

Africa and Asia have the most disease load, several studies [6] indicate. High glucose-6-phosphate deficiency (G6PD) prevalence's, late presentation from high incidence of out-of-hospital births, caregivers' inability to promptly identify jaundice, caregivers' inclination to seek alternative therapies, lack of or inadequate phototherapy, and unavailable or unreliable access to bilirubin estimates are among the causes these local burdens include [44]. Because most of the data is hospital-based and there is extremely little population-based data accessible, low-income nations find the real weight of SNJ unknown. By include a more consistent range of resources from several countries, this review of hospital-based data seeks, albeit imperfectly, to evaluate the burden in low and lower-middle income nations (LMICs).

In a Bangladeshi prospective cohort research, fifteen of newborns suffered from neonatal jaundice (NJ). 2.8% of these newborns had kernicterus, a severe form of brain damage induced by bilirubin. Five kernicteric babies died; thus, the case fatality rate (CFR) is 55.6% (45). Only 0.2% died from jaundice-related consequences in a similar study conducted in Bangladesh, therefore suggesting a case fatality rate (CFR) of 3.9% (46).

Among the 3200 infants admitted to the NICU in Turkey between 2017 and 2018, 7% had extreme hyperbiliruburia and 115 of them died (36). Among 1710 newborns surveyed in Thailand, 22% had neonatal hyperbilirubinemia (NH); 83% of cases were found in preterm infants and 19% in full-term infants. Therefore, 249 per 1,000 live deliveries (95% CI: 225, 403) represents the overall incidence rate. The mortality rate from acute bilirubin encephalopathy in those with severe NH was 10%, hence it matched the threshold of 5.3%. Furthermore, about one-fourth (26.3%) of NH occurrences showed 48 symptoms during the first 24 hours was discovered.

Only 42 of the 300 newborns with hyperbilirubinemia—14.0%—had Acute Bilirubin Encephalopathy (ABE) in an examination conducted at a tertiary care facility in Pakistan. Among these cases, 25 (8.3%) had moderate ABE and 17 (5.7%) had mild ABE (49). Another study in Egypt discovered that the CFR for infants with ABE was 22.4% (50). In contrast, a Kenyan hospital study of kids with SNJ revealed a CFR of 14.3% (51).

In Uganda, about 22.7% of newborns experience major hyperbilirubinemia, with a case fatality rate of around 20% (46). Meanwhile, in Nigeria, they found that severe hyperbilirubinemia shows up in roughly 25 out of every 1,000 babies hospitalized, with a variety of symptoms noted (47). Early signs in these babies often include trouble sucking (15.2%) and weakened primitive reflexes (24.5%). Other common symptoms include a high-pitched scream (11.9%), muscle stiffness (6.9%), and vomiting and seizures (6.3%) (50). In India, a study showed that about 28.6% of newborns had jaundice, and 21 of those, around 0.74%, developed bilirubin encephalopathy (51).

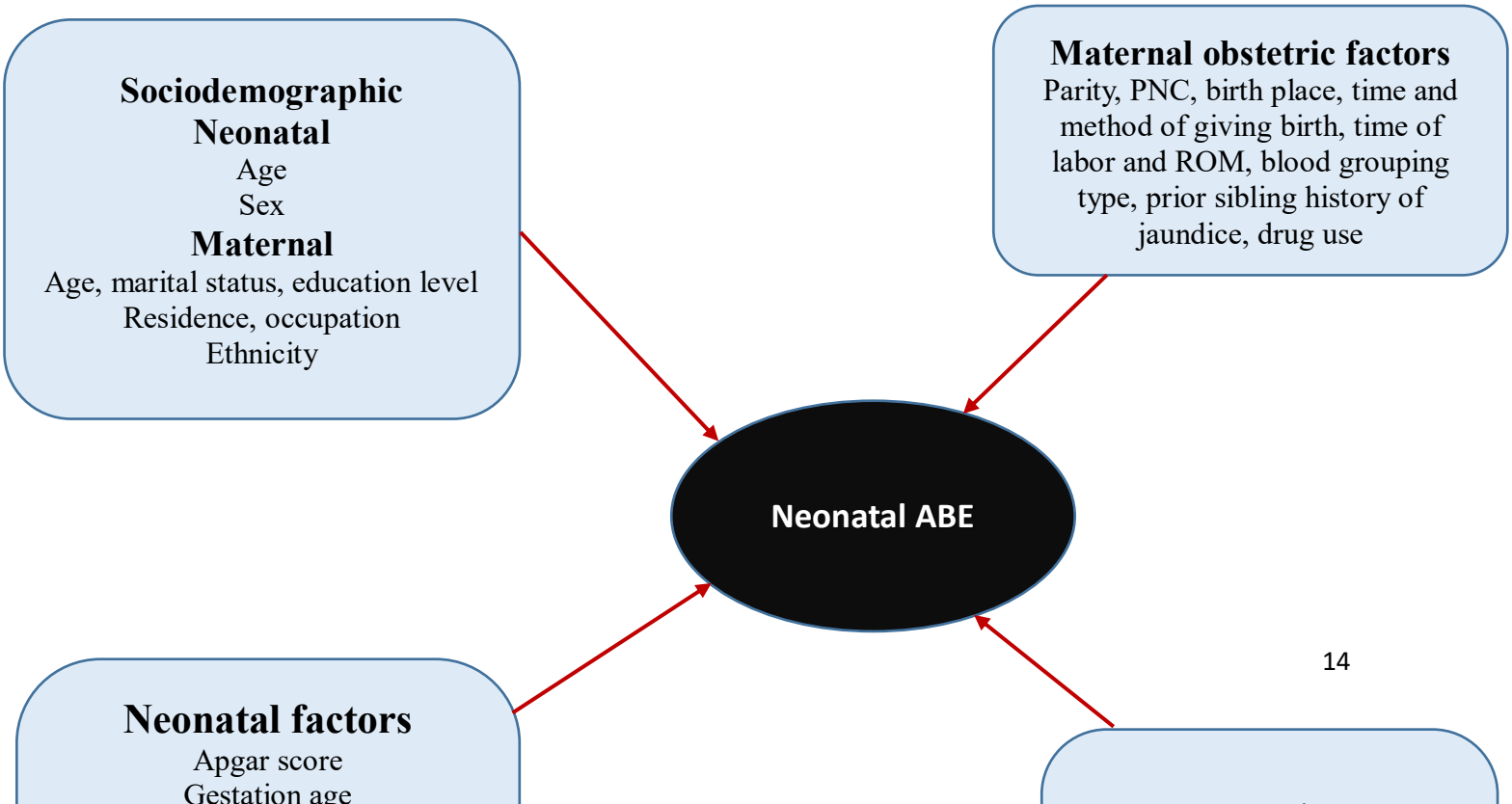
In Ethiopia, research by Kokeb M and Desta T pointed out that prematurity and neonatal jaundice were major reasons for both death and illness among 325 babies admitted to Gondar University Hospital. When they arrived, most had issues like cephalohematoma, subgaleal hemorrhage, sepsis (77.8%), hypothermia (57.5%), low birth weight (32.9%), jaundice (31.7%), prematurity (27.4%), and birth trauma (16%), which were common among the NICU patients (27).

2.3. Outcomes of ABE

Based on the American academy of pediatrics (AAP), ABE manifests acutely during the initial week of life post-birth. 13 ABE represents one of the highly common neonatal diseases and contributes significantly to hearing impairment, developmental delay, and cerebral palsy, predominantly in developing nations. 14 ABE correlates with a 5% to 14% elevated mortality risk and a 2 to 3 times heightened risk of neurological impairments in neonates surviving ABE. 15 ABE progresses through three stages; the illness is reversible in the first stage, whereas the 2nd and 3rd stages are linked to an increased kernicterus risk (resulting from chronic bilirubin encephalopathy (CBE)). 16

In addition to its primary role in newborn mortality [19], ABE frequently triggers various childhood neurodevelopmental disorders, notably hearing loss, cerebral palsy, and seizure disorders [20]. Undeniably, chronic ABE carries substantial social ramifications in developing economies, particularly without robust social security systems. Observational data indicates ABE is infrequently observed in developed nations and certain technologically advanced developing nations, owing to effective prevention strategies, including pre-discharge risk assessment, strict adherence to treatment protocols, and efficient therapies like intensive phototherapy.

3. Conceptual Framework & Study variables



4 - Objective of study

General objective of study

To determine the prevalence, risk factors and outcome of neonatal acute bilirubin encephalopathy among neonates admitted to neonatal intensive care unit of Tikur Anbesa Specialized hospital and Gandhi Memorial hospital, Addis Ababa, Ethiopia from September 11, 2020 to September 11, 2023 G.C.

Specific objectives

- To assess the prevalence of ABE among neonates admitted to NICU according to clinical and sociodemographic characteristics of neonates in TASH and GMH from September 11, 2020 to September 11, 2023 G.C.
- To identify associated determinants for ABE in newborns admitted to NICU from September 11, 2020 to September 11, 2023 G.C.
- To assesses how patients were managed in NICU from September 11, 2020 to September 11, 2023 G.C.
- To determine outcome of ABE among neonates admitted to NICU from September 11, 2020 to September 11, 2023 G.C.

5 - METHODS

5.1. Areas of study

The research was carried out at Tikur Anbessa Specialized Hospital and GMH within Neonatal ICU, Addis Ababa, Ethiopia. TASH featured a NICU with 36 beds, 12 incubators, and 6 KMC beds. The NICU department included 1 neonatologist alongside 2 neonatology fellows from varied levels of residents, MSC students, and nurses (both BSC and MSC) as per the NICU registry. Founded in 1974, TASH is the largest tertiary care hospital in the nation. The facility is managed by Addis Ababa University and stands as the oldest and largest teaching hospital in Ethiopia, catering to approximately more than 400 medical students and 300 residents on an annual basis. TASH offers diagnosis and treatment services to nearly 400,000 patients each year.

GMH is located in Addis Ababa and was built in 1959 G. C. The NICU comprised a 24-beds, 10 infant incubators, and 2 KMC beds, along with 2 senior pediatricians, 8 pediatric residents, 6 General Practitioners (assigned to the NICU), and 24 BSC (Bachelor of Science) nurses as documented in the NICU ward register.

5.2. Design of study

A case control study was conducted on 218 neonates admitted to intensive care unit of TASH and GMH in Addis Ababa.

5.3 – Period of study

The study was conducted from September 2020-January 2023 G.C.

5.4 – population source for study

Every neonate admitted to NICU in TASH and GMH.

5.5 Study population

All neonates diagnosed & managed to have ABE among neonates at NICU for the case group and selected neonates with jaundice but do not have ABE for the control group in TASH and GMH.

5.6 Sample Size

Sample size calculation for Case group

$$ni = Z^{2}_{\alpha/2}\, p(1-p)/d2$$

ni= sample size
$Z_{\alpha/2}$ = 1.960
p = There were neonatal jaundice prevalence study was done in TASH in 2016 G.C. From that study prevalence of ABE is 6.9%
q = 1-p
d = level of uncertainty, which is 5%

Initial sample size, ni = 99 (calculated by above equation)

Since the source population is finite N=2492, we used the correction formula,
n=$\frac{n_0}{(1+\frac{n_0}{N})}$,
n= 96

For possible nonresponse rate = 10% (~ 10), so
nf= (1/ (1-y %)) x n_0

The final sample size will be 109

Sample size for control group
We have a limited number of ABE cases. There are only 109 total ABE cases in the NICU unit of the two hospitals so we included all of them. Then, for the non-ABE group, we match them to the ABE cases using 1:1 ratio, selecting 109 non-ABE neonates.

Finally, 109 ABE/cases + 109 non-ABE/controls = 218

5.7 Sampling methods

Random methods of sampling

5.8 Selection criteria

Inclusion Criteria for cases

- Under 28 days old newborn
- Admitted to neonatal ICU at study period
- Neonates who developed ABE after pathologic jaundice.

Inclusion criteria for controls

- Under 28 days old newborn
- Admitted to neonatal ICU at study period

- Neonates who do not developed ABE after pathologic jaundice.

Exclusion criteria

• Infants whose details in the health record were lacking
• Hospital readmission for the same medical issue throughout the research time frame.

5.9 – variables of study

Independent Variable of study

Duration of newborn after birth and gender of neonate, maternal age, educational and marital status, maternal occupation, asphyxia, prematurity, newborn weight at birth, PNC follow up, maternal and neonate's blood group, place of birth, birth place, neonatal infection, etc.

Dependent variable of study

- Acute Bilirubin encephalopathy (ABE)

6 - operational definition of study

Neonatal ABE prevalence: -The proportion of newborns with bilirubin encephalopathy relative to all hospitalized neonates with neonatal jaundice during the data collecting period.
LBW: A baby weighing smaller than 2,500 grams at delivery
Newborn: a baby born and up to 28 days old.
Premature: smaller than 37weeks of gestation
Extended duration of labor: A labor that lasts longer than 1day
Early rupture of amniotic membrane: - is rupture of the amniotic membranes after the 28 weeks of gestation, but before labor starts.
NBW of newborn: between 2.5 and 4 kg at delivery
NJ: - babies assessed as jaundiced by medical professional.
BE: ABE + KSD
ABE: hyperbilirubinemia associated neurologic manifestation in the early period of life
Maternal ANC follow up investigations: VDRL, PITC, HBsAg
KSD: chronic BE which includes kernicterus, BIND, subtle kernicterus, hearing loss, dystonia, choreoathetosis, paralysis of upward gaze, dental enamel dysplasia
Severe hyperbilirubinemia: means if TSB > 25mg/dl
Non severe hyperbilirubinemia: means if TSB < 25mg/dl
Extremely severe hyperbilirubinemia: means if TSB > 30mg/dl
Outcome – neonates who was died, develops chronic bilirubin encephalopathy like kernicterus or alive without complications

7 - Data collection and Measurement

Medical records (charts, logbooks) will be reviewed in detail for variables. A structured questionnaire format will be developed to collect the data. The questionnaire will be pretested and necessary modifications will be made to it accordingly. The data will be collected by the primary investigator.

The data will be thoroughly cross-checked and entered into the Microsoft Excel spreadsheet for further analysis. Descriptive statistical analysis will be performed with mean, mode, median, percentages and frequencies, and minimum and maximum will be used when appropriate.

8 – data analysis

From the beginning to the end of each data collection period, the obtained data was coded, entered, cleaned, and verified for accuracy, consistency, and completeness. Analyzed with SPSS Statistics 25 and Epi Data Manager 4.2. Using descriptive statistics (mean, frequency, and percentage), the study participants' medical profile, socio-demographics, and prevalence were displayed. Logistic regression and non-conditional analysis were the main methods used. To find factors linked to ABE in the interim, multiple logistic regression, binary, and descriptive analyses were conducted. The factors linked to ABE were evaluated using the bivariate analysis.

To account for the possible impact of confounders, variables that were linked to both the exposure and outcome variables in the bivariate analysis at a P-value of ≤ 0.25 were exported to the multivariate analysis. 95% CIs for adjusted odds ratios were computed. A P-value of less than 0.05 indicates a significant relationship between the independent and dependent variables.

9 – assurance data quality of study

To ensure the quality of the data, a well-designed data collection tool was created prior to the actual data collection process, the principal investigator closely monitored the process, any issues encountered during data collection were discussed, and corrective action was taken right away. The program was designed for data collectors with a nursing bachelor's degree.

The pre-test was completed 14 days prior to the real data collection period, and questions that impact data consistency were modified. The supervisor and investigator went over the questionnaire and verified that it was real, consistent, and comprehensive.

10 - Ethical considerations

The research and publications committees of the School of Medicine, College of Health Sciences, and the Pediatrics and Child Health Department at Addis Ababa University provided ethical approval. The chief executive director of each hospital was informed of the study's purpose, and written consent was obtained before data collection started.

11 - dissemination of findings

Following the conclusion of the research and defense at the university of Addis Ababa at the Pediatrics and Child Health, the findings will be given to the Addis Ababa University School of Graduate Studies, the thesis's the head office and co-advisors, for the medical director's office at each hospital where the study was conducted. Training sessions and conferences will be used to spread the word about the outcome, and significant impact, worldwide journal will publish it.

12 - result of study

12.1. Maternal socio-demographic characteristics

Eighty-nine (40.8%) of mothers were between age range of 25-29 years. Majority (97.2%) of them were married and 50% of them had degree in education. Regarding employment, 38.5% were government workers and majority (96.8%) of them were from urban area. Regarding ethnicity, 46.3% were Amhara.

Table 1.Socio-demographic characteristics of study participants of the study to measure the prevalence, associated factors and outcomes of ABE.

Variables	ABE		Total
	Yes N (%)	No N (%)	N (%)
Mother's age			
18 - 24 years	27 (24.5)	23 (21.1)	50(22.9%)
25 - 29 years	43 (39.4)	46(42.2)	89(40.8%)
30 - 34 years	20 (18.3)	23 (21.1)	43 (19.7)
≥35 years	19 (17.4)	17(15.6)	36(16.5)
Residency or living area			
urban or city	106(97.2)	105 (96.3)	211 (96.8)
rural area/countryside	3 (2.8)	4(3.7)	7(3.2)
Marriage			
married	105 (96.3)	107 (98.2)	212 (97.2)
unmarried	4 (3.7)	2 (1.8)	6 (2.8)
Degree of education			
Elementary	5 (4.6)	9 (8.3)	14(6.4)

High school	31 (28.4)	22 (20.2)	53 (24.3)
Diploma	18 (16.5)	23 (21.1)	41 (18.8)
Degree	55 (50.5)	55(50.5)	110 (50.5)
Occupation status			
Housewife	35 (32.1)	29 (26.6)	64(29.4)
Merchant	31 (28.4)	35 (32.1)	66(30.3)
Gov't worker	41 (37.6)	43 (39.4)	84 (38.5)
NGO worker	2 (1.8)	2 (1.8)	4 (1.8)
Ethnicity			
Amhara	42 (38.5)	59 (54.1)	101 (46.3)
Oromo	32 (29.4)	25(22.9)	57 (26.1)
Others	35(32.1)	25(22.9)	60(27.5)

12.2. Maternal medical and obstetric factors

Sixty-four point seven percent (seventy-three of ABE and sixty-eight of non-ABE) of the mothers were Multipara and 35.3% of mothers were prim parous. 97.2% of them had ANC follow up and 90.8% were negative baseline investigations (VDRL, HBsAg) and all were PITC negative. More than 50% of them were GA below 37 weeks who developed ABE. Normal labor duration and amniotic membrane rupture in 95.9% and 69.3% respectively. Above 63% of mothers were delivered via SVD. 26.6% of them had previous history (sibling) of jaundice.

Table 2.Maternal medical and obstetric variables for the study to measure the prevalence, associated factors and outcome of ABE.

Variables	**ABE**		**Total**
	Yes	**No**	
	N (%)	**N (%)**	**N (%)**
Parity			
Prim parous	36(33.1)	41(37.6)	77(35.3)
Multiparous	73(66.9)	68(62.3)	141(64.7)
ANC maternal Investigations			
Negative (for all\including PITC)	96 (88.1)	102(93.6)	198(90.8)
VRDL	4 (3.7)	2 (1.8)	6 (2.8)
HBsAg	6 (5.5)	2 (1.8)	8 (3.7)
Toxo, Rubella, CMV	3(2.8)	3 (2.8)	6 (2.8)
Blood group			
A	20(18.3)	23(21.1)	46(19.7)

B	4(3.7)	6(5.5)	10(4.6)
AB	5(4.6)	8(7.3)	13(6)
O	80(73.4)	72(66)	152(69.7)
Previous history of sibling jaundice			
Yes	36(33)	22(20.2)	58(26.6)
No	73(67)	87(79.8)	160(73.4)
Prenatal care follow up			
present	106(97.2)	108(99.1)	214(98.2)
absent	3 (2.8)	1(0.9)	4 (1.8)
Gestation Age (weeks)			
< 37 weeks	51 (46.8)	6(5.5)	57(26.1)
37-42 weeks	50 (45.9)	90(82.6)	140 (64.2)
>42 weeks	8 (7.3)	13 (11.9)	21 (9.6)
Mode of delivery			
SVD	69 (63.3)	70 (64.2)	139 (63.8)
CS	40 (36.7)	39 (35.8)	79 (36.2)
Labor duration			
Normal	103 (94.5)	106 (97.2)	209(95.9)
Prolonged	6 (5.5)	3 (2.8)	9 (4.1)
Timing of amniotic membrane rupture			
Normal	80 (73.4)	71 (65.1)	151 (69.3)
Prolonged	29 (26.6)	38 (34.9)	67 (30.7)

12.3. Neonatal factors

Case control study was conducted systematically in 109 newborns with ABE cases & 109 controls among jaundiced neonates admitted at NICU of TASH and GMH from September 11, 2020 to September 11, 2023 G.C. to assess the prevalence, risk factors and outcome of ABE.

Males and females in this study were 78(71.6%)and 31(28.4%) develop ABE respectively. Most (85.3%) of them were AGA and their birth weight were less than 2.5kg in 56.9% who developed ABE.

Table 3. Neonatal factors for the study to measure the prevalence, associated factors and outcomes of ABE.

	ABE		
Variables	**Yes**	**No**	**Total**
	N (%)	**N (%)**	**N (%)**
Newborn gender			
males	78 (71.6)	84 (77.1)	162(74.3)
females	31 (28.4)	25(22.9)	56 (25.7)

newborn weight at delivery			
< 2.5 kg	62 (56.9)	7 (6.4)	69 (31.7)
2.5-4.0 kg	41 (37.6)	87(79.8)	128 (58.7)
> 4.0 kg	6 (5.5)	15(13.8)	21 (9.6)
Weight for Gestation age			
SGA	12(11)	4 (3.7)	16 (7.3)
AGA	93 (85.3)	104 (79.8)	197 (90.4)
LGA	4 (3.7)	1 (0.9)	5 (2.3)
Birth trauma			
Yes	35(32.1)	21(19.3)	56 (25.7)
No	74 (67.9)	88 (80.7)	162 (74.3)
Duration of hospital stay			
< 14 days	30 (27.5)	99 (90.8)	129 (59.2)
≥ 14 days	79 (72.5)	10 (9.2)	89 (40.8)
Apgar score			
Normal	92 (84.4)	103 (94.5)	195 (89.4)
Abnormal	17 (15.6)	6 (5.5)	23 (10.6)
EONS			
Yes	62 (56.9)	37 (33.9)	99 (45.4)
No	47 (43.1)	72 (66.1)	119 (54.6)
RH isoimmunization			
Yes	80(73.4)	44 (40.4)	94 (43.1)
No	29(26.6)	65(59.6)	124 (56.9)

EONS			
Yes	84 (77.1)	16 (14.7)	100 (45.9)
No	25 (22.9)	93(85.3)	118 (54.1)
Blood group			
A	50(45.9)	35(32.1)	85(39)
B	39(35.8)	12(11)	51(23.4)
AB	8(7.3)	10(9.2)	18(16.5)
O	12(11)	52(47.7)	64(29.4)
CBC (Hemoglobin level)			
4-10g/dl	71 (85.1)	15(13.8)	86 (39.4)
≥11g/dl	38 (34.8)	94 (86.2)	132 (60.6)
TSB level			
Non severe hyperbilirubinemia	16 (14.7)	65 (59.6)	81 (37.2)
Severe hyperbilirubinemia	48 (44.0)	39 (35.8)	87 (39.9)
Extremely severe hyperbilirubinemia	45 (41.3)	5 (4.6)	50 (22.9)
Type of management			
Phototherapy	89 (81.7)	108 (99.1)	197 (90.4)
Double exchange transfusion	20 (18.3)	1 (0.9)	21 (9.6)
Outcome of ABE			
Alive	79(72.5)	105 (96.3)	185(84.4)
Died on discharge from NICU	18 (16.5)	3 (2.8)	21 (9.6)
Kernicterus	12 (11.0)	0(0.0)	12 (6.5)

12.4. Prevalence of ABE

In this study, the prevalence of acute bilirubin encephalopathy from 109 neonatal jaundice neonates was 4.4% (95% CI, (4.48, 4.66))

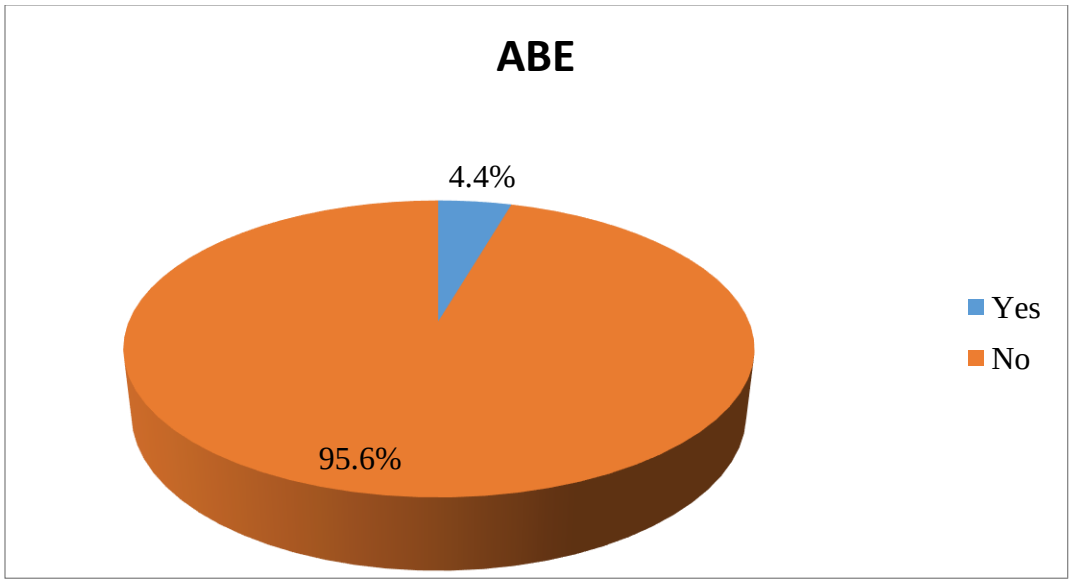


Figure 2.Prevalnce of ABE among NICU ward of TASH and GMH

12.5. Factors associated with ABE

At a p-value less than 0. 25, the results of the binary logistic regression analysis in this study indicated ABE related with mothers' education level, past history of jaundice, gestational age, duration of ROM, neonatal birth weight, birth trauma, bilirubin level, neonatal Apgar score, RH and ABO is immunization, and early-onset neonatal sepsis (EONS).

In the binary logistic regression study, confounders were not controlled, therefore it was difficult to assess the independent impact of the covariate.
To prevent too many variables and unstable estimated values in the final study results, the multivariate logistic regression analysis included only variables with a P-value under 0.05.

Our research revealed that preterm newborns (gestational age of 14 days) have a twofold increased risk of developing ABE (AOR = 2. 01, 95% CI: 1. 14–4. 48). Babies with an irregular Apgar score also show considerably greater chance of developing ABE (AOR = 4. 5, 95% CI: 2. 69–7. 66). Early-onset neonatal sepsis is a major risk factor for ABE, according to the study (AOR = 3. 48, 95% CI: 2. 43–9. 18). The odds of ABE were doubled among babies with severe hyperbilirubinemia (AOR = 2. 02; 95% CI: 1. 92–4. 76). ABO incompatibility triples the likelihood of developing ABE (AOR = 3. 04; 95% CI: 2. 81–4. 58).

Table 4. Factors associated with ABE for the study to measure the prevalence, associated factors and outcomes of ABE.

Variables		**Prevalence of ABE**		
	Crude odds ratio (95% CI)	**P - value**	**Adjusted odds ratio (95% CI)**	**P – value**
Ethnic group				
Amhara	1		1	
Oromo	1.80(0.91,3.44)	0.08	1.67(0.09,2.12)	0.20
Others	1.97(1.03,3.76)	0.04	1.92(0.21,3.25)	0.97
Educational status of mothers				
Elementary	1			
High school	2.54 (0.47, 8.61)	0.13	2.57(0.14,4.69)	0.22
Diploma	1.41 (0.41, 4.94)	0.59	2.27(0.19,2.80)	0.73
Degree	1.81 (0.57, 5.71)	0.31	1.18(0.05,4.14)	0.54
Previous history of jaundice				
Yes	1.95 [1.05,3.61]	0.03	2.01(0.17,34.89)	**0.05**

No	1			
Gestational age < 37 weeks 37 to 42 weeks >42 weeks	 13.81(4.07,46.84) 0.90(0.35,2.32) 1	 <0.01 0.83	 2.73(1.47,12.98) 0.84(0.06,1.12)	 **0.03** 0.94
ANC maternal Investigations All negative (including PITC) VRDL positive HBsAg positive Toxo, Rubella, CMV positive	 1 2.12 3.18 1.06	 0.39 0.16 0.94	 2.55(0.19,7.86) 7.72(0.92,16.72) 7.88(0.96,10.22)	 0.92 0.93 0.89
Duration of rupture of membrane Normal Prolonged	 1 1.476(0.83, 2.63)	 0.19	 1.44(0.04,5.05)	 0.09
Weight for Gestation age SGA AGA LGA	 0.75(0.06,8.83) 0.22(0.02,2.03) 1	 0.82 0.18	 0.02(0.01,2.47) 0.07(0.03,6.45)	 0.71 0.64
Duration of hospital stay < 14 days ≥ 14 days	 1 26.07(12.02,56.55)	 <0.01	 2.01(1.14,4.48)	 **0.02**
Apgar score Normal Abnormal	 1 3.17(1.20,8.39)	 0.02	 4.5(2.69,7.66)	 **0.01**
EONS Yes No	 19.53(9.76,39.07) 1	 <0.01	 3.48(2.43,9.18)	 **0.01**
Birth weight of neonate ≤ 2.5 kg 2.5 - 4.0 kg ≥ 4.0 kg	 22.14(6.49,75.58) 1.18(0.42,3.26) 1	 <0.01 0.75	 5.67(0.92,12.87) 3.47(0.39,5.67)	 0.50 0.94

Birth trauma				
Yes	1.98(1.06, 3.70)	0.03	2.24(0.05,3.78)	0.24
No	1			
Bilirubin level				
Non-severe hyperbilirubinemia	1			
Severe hyperbilirubinemia	5.00(2.50, 9.98)	<0.01	2.02(1.92,4.76)	**0.02**
Extreme hyperbilirubinemia	36.56(12.95, 106.99)	<0.01	1.01(1.88,5.16)	**0.03**
ABO isoimmunisation				
Yes	2.57(1.48,4.44)	<0.01	3.04(2.81,4.58)	**0.03**
No	1			
RH isoimmunisation				
Yes	4.07(2.30,7.22)	<0.01	1.13(1.05,2.34)	**0.02**
No	1			

13 – discussion of study

In our investigation, acute bilirubin encephalopathy had a 4.4% prevalence; the 95% confidence interval was (4.48, 4.6). Related variables included ABO incompatibility, RH incompatibility, neonatal sepsis, preterm delivery, hyperbilirubinemia severity, low APGAR score, and long hospital stay.

Studies at Tikur Anbessa Hospital found that hyperbilirubinemia, which accounted for 44.9% of newborns, was a major contributor to newborn death in Ethiopia—32% of infant deaths and 31.7% of neonatal admissions. Six point nine percent were impacted by ABE. Among the 300 hyperbilirubinemic infants, only 42 (14.0%) were found to have Acute Bilirubin Encephalopathy at a more advanced medical facility in Pakistan. Mild cases totaled 17 (5.7%); moderate cases 25 (8.3%); 49. ABE is one of the most prevalent diseases affecting infants in impoverished nations and a major cause of hearing loss, neurodevelopmental disorders, and cerebral palsy (14). Infants who survive ABE have a 5–14% higher death rate and a 2 to 3-fold raised incidence of neurological and developmental abnormalities.

Early stage ABE is reversible; however, chronic bilirubin encephalopathy is more likely to result from later phases which is irreversible (16). Low economic indicators—such as home deliveries,

lack of prenatal care, etc.—that hinder prompt medical attention are correlated by several studies with ABE and delayed treatment. (17). Others have concentrated on the attitude and ignorance of parents about jaundice and/or its possible effects. Proper care is just delayed in either case—the resulting inability to diagnose jaundice or failed therapies involving trials of alternative therapies, antimicrobials, or morning sunlight exposure.

Especially in connection to hearing loss, brain injury, and seizure syndromes [20], ABE considerably raises neonatal mortality [19] and is a common cause of many child neurodevelopmental abnormalities. Clearly, in developing or underdeveloped countries, chronic ABE has a great socioeconomic effect. In the developed world [21], ABE is rare since effective preventative strategies involve total compliance to management and good management practices like phototherapy prior to discharge assessment. In this study, ABE was associated with 16.5% (18 out of 109 ABE developed infants) and 11% (12 out of 109 ABE developed infants) had kernicterus (chronic bilirubin encephalopathy). In this investigation, most ABE generates newborns under strong phototherapy and double exchange transfusion.

14 - Strength and Limitation of the study

The first of its kind in the field, this study lays the groundwork for future studies.

Information on neonatal ABE was compiled; neonatal medical records were properly handled.

Since this study is retrospective, it was difficult to assess how G-6PD insufficiency contributed to the hemolysis seen in ABE given that the center did not regularly check for this issue.

15 - Conclusion

In this study, prevalence of ABE is 4.4%. Factors associated with ABE in study were incompatibility (ABO and RH), neonatal sepsis, severity of hyperbilirubinemia, preterm birth, prolonged hospital stay and low Apgar score. In this study, Outcome even after treating with phototherapy and double exchange transfusion were death (16.5%) and chronic bilirubin encephalopathy or kernicterus (11%)

16 - Recommendation

Considering this study's results, I would recommend the following**: -**

1. **For caregivers and parents**

   Parents should keep an eye on their infants for signs of excessive bilirubin before ABE and ask for prompt evaluation and treatment. Parents should be aware of their blood type and take early protective steps for expectant mothers.

2. **Medical/healthcare professionals**

   Health professionals should educate parents on the signs and symptoms of hyperbilirubidemia as well as the need of prompt getting and treatment before ABE manifests. This could also help to improve consequence for infants with ABE and avoid serious, irreversible damage

3. **Healthcare locations**

   Improve treatment, care, and research quality by means of comprehensive patient data, full computer record keeping, and database creation.
   All infants should have a TSB test before they are released from the hospital to prevent A BE; this is especially true for those who are at high risk.

4. **Scholars**

   To overcome the restrictions of this investigation, future studies should consider using prospective designs with a larger sample size, more extensive data collecting, and statistical analyses able to consider potential confounding variables. To solve the problem of newborn hyperbilirubinemia and improve outcomes for affected infants, legislators, healthcare providers, and researchers must cooperate.

17 - Reference

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Annex: Data collecting Questionnaire

Addis Ababa University College of Health Science

School of Medicine Department of Pediatrics and Child Health

Study title: Prevalence, risk factors and outcome of neonatal ABE among neonates admitted to neonatal intensive care unit of TASH and GMH, multi-center case control study, Addis Ababa, Ethiopia

Data collection date: _____ Name of Data collector _____ Signature_____ Serial No _____ Card No_____

Part I. Socio Demographic Data

1. Maternal age ……. (in years)

2. Marital status A. single B. married C. divorced D. widowed E. cohabited

3. Maternal residency A. urban B. rural

4. Ethnicity A. Amhara B. Tigre C. Oromo E. others(specify)

5. Occupation A. government employee B. Merchant C. Farmer D. house wife E. others(specify)

6. Maternal education level

A. read and write B. elementary C. high school D. diploma/degree

E. others(specify)

7. Parity

A. Primiparas B. multiparas C. Grandparas

8. Maternal Investigations:

A. PITC: NR /R B: VDRL NR/R C: HBSAG POS/NEG

9. Similar history of neonatal jaundice in previous child

A. yes B. No

10. ANC follow up

A. yes B. No

Part II. Clinical data

1. Neonate age at admission…….. (in days)
2. Sex A. Male B. Female
3. Gestational age at delivery……. (in weeks)
4. Duration of labor ……. (in hours)
5. Duration of ROM……. (in hours)
6. Mode of delivery A. SVD B. C/S C. instrumental
7. Place of delivery A. home B. health center C. hospital
8. Birth order……. (1^{st}, 2^{nd}, etc.)

9. Maternal illness

A. GDM B. Preeclampsia C. PROM D. others(specify)…….

10. Maternal BG & RH

A. A +VE B. A –VE C. B+VE D. B –VE E. AB +VE F. AB –VE
G. O +VE H. O –VE

11. Birth weight

A. ELBW B. VLBW C. LBW B. NBW C. Macrosomia

12. Weight for GA of newborn:

A. SGA B.AGA C. LGA

13. APGAR Score on admission……

14. Neonatal BG & RH

A +VE B. A –VE C. B+VE D. B –VE E. AB +VE F. AB –VE

G. O +VE H. O –VE

15. Associated conditions (birth trauma)

A. No B. Yes, if yes pleases Specify _____

16. Age at diagnosis of neonatal jaundice before developing BE…….... (in days)

17. How long the neonate stayed in hospital……? (in days/weeks)

18. Cause of neonatal jaundice which leads to BE

A. ABO incompatibility B. RH incompatibility C. Neonatal Sepsis (Blood culture result) D. BFJ E. BMJ F. Birth trauma (subgaleal hemorrhage) I. Others(specify)

19. Feeding type

A. EBF B. Formula feeding C. Mixed feeding

20. CBC profile (WBC- RBC- Hg- Hct- MCV- RDW- PLT-

21. After how many days of admission neonates develops Symptoms of ABE?
    .....(n days)
22. What are symptoms and signs of ABE
    A. Irritability/excessive crying B. seizure/ LOC C. fever/poor sucking/vomiting
    D. retrocollis-opthotonus position/hyper-hypotonia E. others(specify)

23. What type of management was given to ABE for the neonate?
    A. Phototherapy B. exchange transfusion C. others(specify)…….
24. Condition at discharge or outcome
    A. Alive B. died C. Referred D. others(specify)…….