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BAHIR DAR UNIVERSITY

COLLEGE OF MEDICINE AND HEALTH SCIENCES

SCHOOL OF HEALTH SCIENCES

DEPARTMENT OF Pediatrics and Child Health Nursing

Admitted to Public Hospitals in Bahir Dar City, Ethiopia: Cross-Sectional Magnitude and Associated Factors of Acute Kidney Injury Among Preterm Neonates Study

Principal Investigator: Sayih Mehari (Bsc)

A RESEARCH REPORT SUBMITTED TO DEPARTMENT OF PEDIATRICS AND CHILD HEALTH NURSING, SCHOOL OF HEALTH SCIENCES, COLLEGE OF MEDICINE AND HEALTH SCIENCES, BAHIR DAR UNIVERSITY FOR THE PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTERS OF SCIENCE IN PEDIATRICS AND CHILD HEALTH NURSING.

JULY, 2022

BAHIR DAR, ETHIOPIA

BAHIR DAR UNIVERSITY

COLLEGE OF MEDICINE AND HEALTH SCIENCES

SCHOOL OF HEALTH SCIENCES

DEPARTMENT OF PEDIATRICS AND CHILD HEALTH NURSING

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TITLE	MAGNITUDE AND ASSOCIATED FACTORS OF ACUTE KIDNEY INJURY AMONG PRETERM NEONATES ADMITTED TO PUBLIC HOSPITALS IN BAHIR DAR CITY, ETHIOPIA: CROSS SECTIONAL STUDY
STUDY PERIOD	MAY 20 TO JUNE 20, 2022.
STUDY AREA	PUBLIC HOSPITALS IN BAHIR DAR CITY, ETHIOPIA.

DECLARATION

Through my signature below, I declared and affirmed that this thesis is my original work. I have followed all ethical principles of scholarship in the preparation, data collection, data analysis, and completion of this thesis work. All scholarly matter that was included in the thesis has been given recognition through citation. I affirm that I have cited and referenced all sources used in this document. Every effort has been made to avoid plagiarism in the preparation of this thesis work. The thesis would be deposited in the library of Bahir Dar University and will be made accessible for readers under the rules of the library. I solemnly declared that this thesis has not been submitted to any other institution anywhere for the award of any academic degree, diploma or certificate.

Principal investigator: Sayih Mehari (BSc Nurse)

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APPROVAL BY THE BOARD OF EXAMINATION

This thesis by Sayih Mehari is accepted in its present form by the board of examiners as satisfying thesis requirement for the degree of masters of Science in pediatrics and child health Nursing.

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LIST OF ACRONYMS

ADQI	Acute Disease Quality Initiative
AKI	Acute Kidney Injury
AOR	Adjusted Odds Ratio
APGAR	Appearance Pulse Grimace Activity Respiration
AWAKEN	Acute Kidney Injury Epidemiology in Neonates
CHD	Congenital Heart Disease
CI	Confidence Interval
CKD	Chronic Kidney Disease
COR	Crude Odds Ratio
GFR	Glomerular Filtration Rate
KDIGO	Kidney Disease Improving Global Outcomes
NEC	Necrotizing Enter Colitis
NICU	Neonatal Intensive Care Unit
OR	Odds Ratio
RIFLE	Risk Injury Failure Loss End-stage
RRT	Renal Replacement Therapy
SCr	Serum Creatinine
SDG	Sustainable Development Goal
SPSS	Statistical Product and Service Solutions
USA	United States of America

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ABSTRACT

Background: Acute kidney injury is an independent risk factor for morbidity and mortality in critically ill neonates. Despite the high magnitude of preterm neonates and their being at a high risk for acute kidney injury, there is a paucity of information regarding the magnitude and associated factors of acute kidney injury among preterm neonates in the study area.

Objective: The aim of this study was to assess magnitude and associated factors of acute kidney injury among preterm neonates admitted to public hospitals in Bahir Dar city, Ethiopia, 2022.

Method and materials: An institutional-based cross-sectional study was conducted among 423 preterm neonates admitted to public hospitals in Bahir Dar city from May 20 to June 20, 2022. Epi Data Version 4.6.0.2 was used for data entry and cleaning. Statistical analysis was done by Statistical Product and Service Solutions version 26. Descriptive and inferential statistics were employed. A binary logistic regression analysis was done to identify factors associated with acute kidney injury. Variables with a p-value <0.05 were considered as statistically significant in the multiple binary logistic regression analysis. Model fitness was checked through Hosmer-Lemeshow goodness of fit test. Finally, the result was presented via a table, figures, and text.

Result: Out of 423 eligible, 416 neonatal charts were reviewed with a response rate of 98.3%. The prevalence of acute kidney injury was 18.27 %(95%CI = 15-22). Very low birth weight (AOR = 3.26; 95%CI = 1.18-9.05), perinatal asphyxia (AOR = 2.84; 95%CI = 1.55-5.19), dehydration (AOR = 2.30; 95%CI = 1.29-4.09), chest compression (AOR = 3.79; 95%CI = 1.97-7.13), and pregnancy-induced hypertension (AOR = 2.17; 95%CI = 1.20-3.93) were factors significantly associated with the development acute kidney injury.

Conclusion: Acute kidney injury was high. The odds of acute kidney injury were high among neonates who were very low birth weighted, perinataly asphyxiated, dehydrated, recipients of chest compression, and born from pregnancy-induced hypertensive mothers. Therefore, clinicians have to be extremely cautious and actively monitor renal function in this neonatal population in order to detect and treat acute kidney injury as early as possible.

Key words: Acute kidney injury, Preterm, Magnitude, Bahir Dar, Ethiopia

1. INTRODUCTION

1.1. Background

Acute kidney injury (AKI) is described as a sudden drop in glomerular filtration rate (GFR), resulting in the retention of urea and other nitrogenous waste products as well as a loss of fluid, electrolyte, and acid-base balance(1). It commonly occurs in the neonatal intensive care unit, where it particularly affects preterm neonate. According to several studies, the incidence of AKI among neonates admitted to a neonatal intensive care unit ranges from 11% to 56% (2-5).

Clinical manifestations of AKI can range from mild kidney injury to diseases requiring renal replacement treatment, depending on the severity of the kidney damage(6). Despite the availability of other diagnostic criteria, the neonatal Modified Kidney Disease Improving Global Outcomes (KDIGO) criteria is currently the gold standard definition for neonatal AKI(7). The modified neonatal KDIGO criteria defines neonatal acute kidney injury as (an absolute serum creatinine rise ≥ 0.3 mg/dL or SCr rise ≥ 1.5–1.9 × baseline SCr within 48 hours and urine output <0.5 ml/kg/h × 6–12 h)(8).

Neonates are more likely to develop AKI in the first few days after birth. This is because they are born with high renal vascular resistance, low GFR, high plasma renin activity, decreased intercortical perfusion, and inadequate sodium reabsorption in the proximal tubules(9, 10). Neonatal AKI can occur as a result of prenatal, perinatal, or postnatal attacks. Generally, AKI in neonates is often multifactorial and may result from prenatal, perinatal, or postnatal insults as well as their combinations(11). Prerenal injury is caused by a reduction in efficient systemic blood flow to the kidneys (85%), intrinsic renal injury is caused by damage to the renal parenchyma tubules (12%), and post-renal injury is due to obstruction to urine flow (3%)(12).

Although the search for treatments to neonatal AKI has remained indefinable, medications have been evaluated in high-risk neonatal cohorts to prevent AKI(13). Methylxanthine has been evaluated in multiple neonatal populations and has had promise as a preventive treatment of AKI in high-risk populations(14, 15). Interventions for AKI are limited to the care of complications related to the acute renal insult, such as renal replacement therapy and continuous kidney support therapy(7, 16). Therefore, the focus of field advancement is now on developing better diagnostic

methods, tactics for preventing and mitigating complications, and treatments for sequelae in AKI(7).

There is evidence that AKI negatively affects other organs. Studies have shown what is known as "crosstalk," when AKI appears to cause other organ failure and vice versa, defying earlier assumptions that it was merely association(17). Neonatal AKI has been associated with poor long-term neurocognitive outcomes, cardiovascular disease, and neurological issues(18).

1.2. Statement of the problem

Although there has been a decrease in the morbidity and mortality of premature babies through improved premature care in recent decades, acute kidney injury is still a high global burden(19). A multinational 24-center study called Acute Kidney Injury Epidemiology in Neonates (AWAKEN) has shown that 30% of neonates have developed AKI during their hospitalization in a critical care unit, among which 66% were less than 36 weeks of gestation at birth(3). In another systematic review study, it has been estimated to occur in 8.4 to 63.3% of critically ill preterm neonates admitted to neonatal intensive care units(20).

As nephrogenesis is not completed until 34 weeks of gestation, most preterms have immature kidneys at birth, with more functional insufficiency of the glomeruli and tubules than mature neonates(21). Preterms are exposed to interventions in the NICU that promote survival but are nephrotoxic, which predisposes them to AKI(22). Low birth weight, prematurity, hypoxic ischemic encephalopathy, perinatal asphyxia, therapeutic hypothermia, and congenital heart disease are factors putting newborns at higher risk for developing AKI than the baseline neonatal population(23-26).

As demonstrated in the AWAKEN study, most critically ill neonates survive after AKI, with numerous long-term complications(3). AKI can lead to CKD, and premature babies with AKI are at a higher risk of developing long-term kidney diseases(11). As a result, methods for identifying neonates at risk of AKI and establishing steps to avoid the development of AKI are critical, given the association of AKI with increased hospital stay and mortality(16).

Neonatal AKI has been linked to increased mortality and length of stay in the hospital, raising the cost of care and posing a problem for nations with low resources(3). Most low- and middle-income countries, including Ethiopia, have limited facilities and qualified health-care personnel to care for patients with kidney illnesses, especially those who require renal replacement treatment, making AKI a double burden(27).

Sustainable development goal (SDG) 3.2 of the World Health Organization aims to eliminate preventable newborn deaths by 2030, with all countries aiming to reduce neonatal mortality to at least 12 per 1,000 live births by 2030(28). However, according to the mini Ethiopian

demographic health survey 2019, the neonatal mortality rate was 30 per 1000 live births(29), reminding us that acute kidney injury is an independent risk factor for the contribution of morbidity and mortality(30).

In recognition of the global problems of AKI, the international Society of Nephrology's 0 by 25 program has proclaimed AKI management a human right issue, with the goal of eliminating AKI-related deaths by 2025. To address these issues, this initiative employs a three-pronged approach: collecting current and future data to prove that AKI contributes to the global burden of health loss; increasing global awareness of AKI to lessen regional variations in management; and building a sustainable infrastructure to support need-based approaches to education, training, and healthcare delivery(31).

Despite preterm neonates being at high risk for AKI and its high magnitude in Ethiopia(32, 33), there is a paucity of information on the magnitude and associated factors of Acute Kidney Injury among preterm neonates in the study area. Furthermore, this study is consistent with the global kidney research agenda on neonatal AKI, emphasizing the importance of understanding the magnitude and risk factors of AKI in guiding efforts on diagnosis and management(34). Therefore, this study was aimed to assess the magnitude and associated factors of neonatal AKI among preterm neonates admitted to public hospitals in Bahir Dar city, Ethiopia.

1.3. Significance of the study

This study aimed to assess the magnitude and associated factors of acute kidney injury among preterm neonates. As a result, the findings from this study would sensitize clinicians to identify vulnerable neonates so that they could prevent and manage risk factors for neonatal acute kidney injury. Additionally, it would help researchers to select neonates at risk for enrollment in future prospective interventional studies designed to reduce the prevalence of AKI. It may also be used as an input for guideline development, policy briefing, and formulating standards of care for policy makers.

2. LITERATURE REVIEW

2.1. Magnitude of acute kidney injury

Acute kidney injury is common among preterm neonates treated in NICU. A prospective study done in the United States of America(USA) has shown a 38.0% prevalence of AKI among extremely low gestational age neonates during their hospitalization(33). In a retrospective study done at Mount Sinai in New York City, acute kidney injury was diagnosed in 30.3% of premature infants less than 30 weeks of gestation(35). Similarly, AKI was found to be prevalent in 22.6% of preterm neonates (30 weeks gestational age) in a study conducted at a pediatric hospital in Portugal(36).

In a cross-sectional study conducted in northwest Paraná State, AKI was diagnosed in 7.5% of admitted preterms(37). In another cross-sectional study conducted in Iran, the prevalence of AKI among preterm neonates was 10.68%(38). Another single-center prospective cohort study conducted in Saudi Arabia has reported a 56% prevalence of AKI among neonates receiving care in level II and III NICUs (39). In a study done in Riyadh, Saudi Arabia, the prevalence of AKI among preterm neonates was 18.7%(40).

In another study conducted in the United Arab Emirates among very low birth weight preterm neonates, an 11.6% prevalence of AKI was reported(41). Similarly, retrospective studies done in Serbia have reported a 26% and a 44% prevalence of AKI among NICU admitted preterm neonates(42, 43). In a study conducted in Taiwan among extremely low birth weight preterm neonates, 56% were diagnosed with AKI(4).

A study done in Turkey has revealed a 20.0% prevalence of AKI among preterm neonates(44). In an observational study done in India among premature neonates, the incidence of AKI was 12%(45). In a study conducted at a tertiary hospital in Tanzania , the prevalence of AKI was 31.5%(46). A study done in Egypt has revealed a 10.8% prevalence of AKI among neonates admitted to NICU, 59.3% of which were preterm(5).

In a study done in Kenya, the prevalence of AKI among all gestational age neonates was 19.78%, with 21.1% less than 35 weeks of gestation(47). In another similar study conducted at

Tikur Anbesa Specialized Hospital, the prevalence of neonatal AKI was 12.7% among the total NICU admitted neonatal population(48).

2.2. Factors associated with acute kidney injury

Studies that have been conducted globally have reported different factors associated with neonatal AKI. These factors are divided in their categorical class into neonatal demographic characteristics, neonatal clinical-related factors, and maternal-related factors.

2.2.1. Neonatal demographic factors

Studies conducted in India, Iran, and a systematic review of 17 studies have shown gestational age, birth weight, 1-min Apgar score, and 5-min Apgar score as significant associated factors with the occurrence of AKI in the neonatal period(20, 38, 42). In another study done in India, the male gender was associated with AKI(49). Outborn (outside of hospital admitted) delivery was associated with AKI in neonates. with studies in Pakistan and USA(50, 51).

2.2.2. Neonatal clinical related factors

In studies done in Netherland, Pakistan, and Tikur Anbesa specialized hospital, perinatal asphyxia was found to be independently associated with acute kidney injury (48, 51, 52). Congenital heart disease, hyperbilirubinemia, necrotizing enter colitis (NEC), and sepsis were found to be associated with AKI in preterm neonates with studies done in Tikur Anbesa hospital, Iran and India (20, 35, 38, 49). Studies have revealed dehydration and chest compression as significantly associated with AKI development (20, 48, 53). In other studies, use of nephrotoxic drugs, congenital heart disease, sepsis, and respiratory distress syndrome were found to be strong predictors of AKI occurrence among premature neonates (37, 38, 42). In a study done in Riyadh, Saudi Arabia, the use of loop diuretics and surgical intervention was found to be an independent predictor of AKI among neonates(40).

2.2.3. Maternal related factors

In studies conducted in Turkey and Taiwan, pregnancy-induced hypertension(4, 44, 54) and prolonged rupture of membrane were significantly associated with AKI(54). In another study conducted at Tikur Anbesa hospital, maternal age was significantly associated with AKI occurrence(48).

2.3. Conceptual framework

For a comprehensive assessment of acute kidney injury among preterm neonates, this conceptual framework was adapted from different literatures (4, 20, 37, 38, 48-50, 54, 55). The figure below shows the relationship of neonatal demographic characteristics, clinical factors, and maternal factors to the occurrence of neonatal acute kidney injury among preterm neonates. (Figure 1)

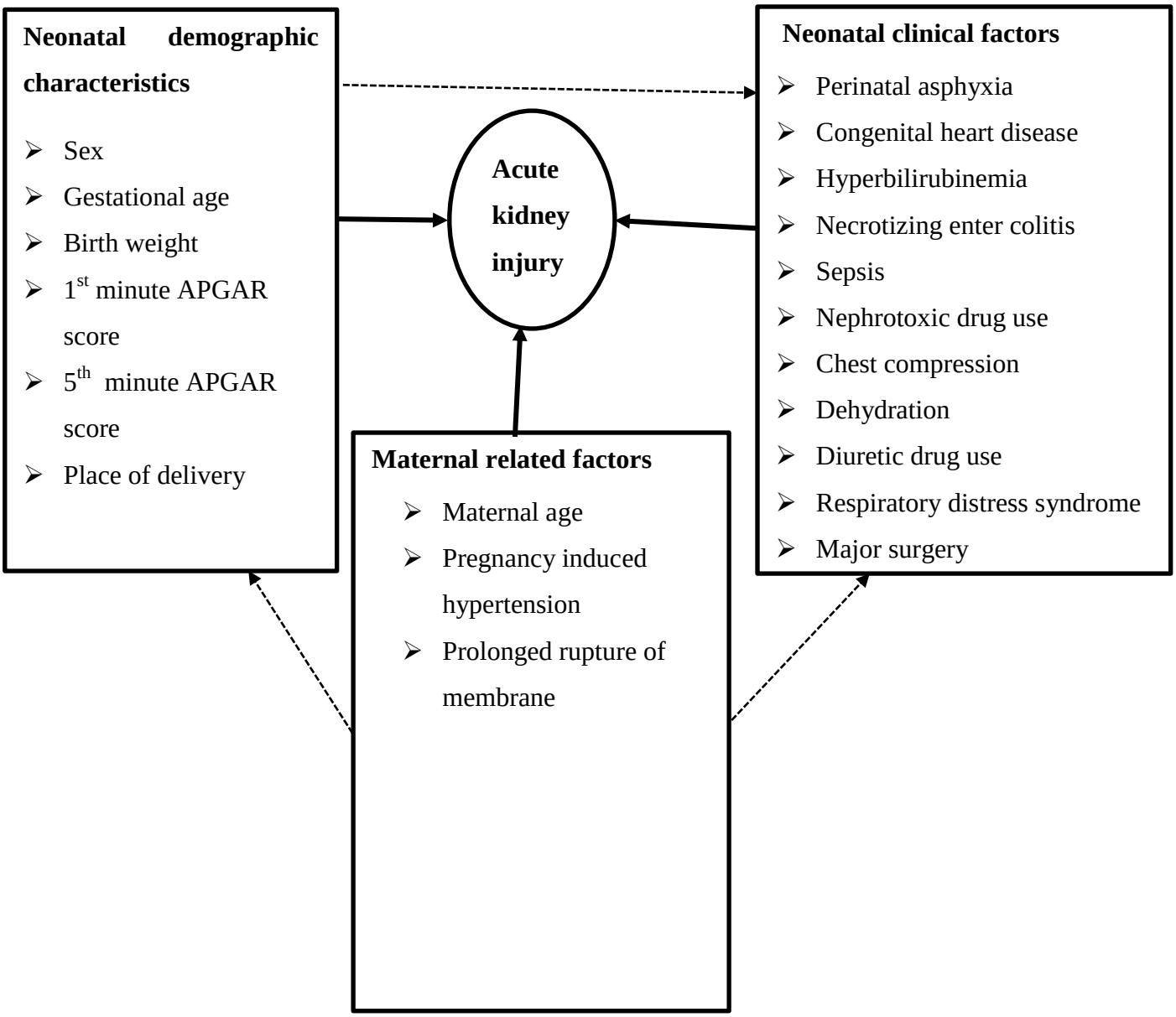


Figure 1: Conceptual framework showing the relationship between neonatal acute kidney injury and its associated factors among preterm neonates.

3. OBJECTIVE

3.1. General objective

- To assess the magnitude and associated factors of acute kidney injury among preterm neonates admitted to public hospitals in Bahir Dar city, Ethiopia, 2022.

3.2. Specific objective

- To determine the magnitude of acute kidney injury among preterm neonates
- To identify factors associated with acute kidney injury among preterm neonates

4. METHOD AND MATERIALS

4.1. Study Area and period

This study was conducted at public hospitals in Bahir Dar city, Ethiopia. Bahir dar city is the capital city of Amhara Region which is found 565km away from Addis Ababa. There are three public hospitals in Bahir Dar city, namely, Tibebe Ghion specialized hospital, Felege Hiwot comprehensive specialized hospital, and Addis Alem primary hospital. All hospitals are currently providing neonatal intensive care for neonates in need.

Felege Hiwot comprehensive specialized hospital- Is a referral hospital found in Bahir City, which officially commenced its function in 1963. In addition to many other clinical services, the hospital now offers a neonatal intensive care service with 71 beds staffed by three pediatricians, six general practitioners, and 35 nurses.

Tibebe Ghion specialized and teaching Hospital- Is Bahir Dar University teaching hospital found in Bahir Dar, which serves more than five million people in the catchment area. It provides intensive care services for seriously ill neonates.

Addis Alem primary hospital- Is a district level hospital found in Bahir Dar city, providing neonatal intensive care service for an estimated 550 neonates per year, of which 90 are preterm.

This study was conducted from May 20 to June 20, 2022.

4.2. Study design

Institutional based cross-sectional study design was employed.

4.3. Population

4.3.1. Source population

All preterm neonates admitted to public hospitals in Bahir Dar city.

4.3.2. Study population

All preterm neonates admitted to public hospitals in Bahir Dar city, from May 30, 2020 to April 30, 2022.

4.3.3. Study unit

Selected preterm neonate admitted to public hospitals in Bahir Dar city from May 30, 2020 to April 30, 2022

4.4. Eligibility criteria

4.4.1. Inclusion criteria

All preterm neonates admitted to public hospital from May 30, 2020 to April 30, 2022.

4.4.2. Exclusion criteria

Neonates who were died/discharged before 24 hours of neonatal age were excluded.

4.5. Sampling method

4.5.1. Sample size determination

Sample size was calculated with the minimum sample size determination by using the single population proportion formula as $ni = \frac{(z_{a/2})^2 p(1-p)}{d^2}$, assuming a 95% confidence level of Z a/2 =1.96, margin of error of 5 %, and taking the proportion of AKI among preterm neonates to be 50% (since no study with the same study population has been conducted in areas nearly similar to the study area).

- Where, ni = initial sample size
- P = Prevalence of AKI among preterm neonate, 50.0%
- Zα/2= critical value 95% confidence level of certainty (1.96)
- d = margin of error 5%
- $ni = \frac{(z_{a/2}{}^2)p((1-p)}{d^2} = \frac{(1.96)^2 0.5(1-0.5)}{(0.05)^2}$ = 384.16≈384

Considering an incomplete chart (non-response) of 10%, the final sample size was gained through adding non-response to the initial sample size as:

- nf= ni+ $(ni * \frac{10}{100})$
- $nf=384 + \left(384 * \frac{10}{100}\right) = 422.4 \approx 423$
- Where, nf= final sample size
- Finally the sample was 423.

4.5.2. Sampling procedure

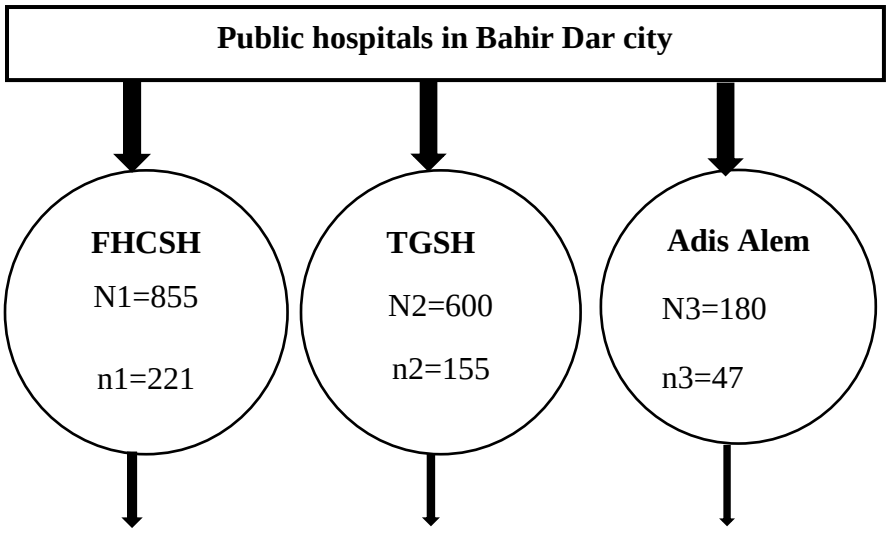
The sample required for the study was recruited from all public hospitals. A sampling frame was prepared from the patient's registration book using their medical record number. Then, the study participants were selected through simple random sampling by a computer-generated number technique. Between May 30, 2020 and April 30, 2022, a total of 1635 preterm neonates were admitted to all hospitals, of which 600 were from Tibebe Ghion specialized hospital, 855 from Felege Hiwot comprehensive specialized hospital, and 180 from Adis Alem hospital(56). Therefore, using the proportional sample allocation formula, the samples required from each hospital were:

- ni= $\frac{nf*Ni}{N}$ Where,
- ni= Sample from each hospital
- Ni=Total population of each hospital
- N= the number total population from three hospital
- nf= is the total sample size

Tibebe Ghion specialized hospital (n1) =$\frac{423*600}{1635}$=155.2≈155

Felege Hiwot hospital (n2) = $\frac{423*855}{1635}$ =221.29 ≈ 221

Addis Alem (n3) =$\frac{423*180}{1635}$ = 46.6 ≈ 47



Total sample (nf) =423)

Figure 2: Schematic presentation of the sampling procedure for the study magnitude and associated factors of acute kidney injury among preterm neonates admitted to public hospitals in Bahir Dar city, Ethiopia, 2022.

4.6. Variables

4.6.1. Dependent variable

- Acute kidney injury- Yes/No

4.6.2. Independent variables

- **Neonatal demographic characteristics** (age, sex, gestational age, birth weight, 1st minute APGAR score, 5th minute APGAR score, mode of delivery, and place of delivery).
- **Neonatal Clinical factors** (perinatal asphyxia, neonatal sepsis, congenital heart disease, hyperbilirubinemia, intestinal obstruction, dehydration, necrotizing enter colitis, sepsis, hyperthermia, chest compression, radiant warmer use, incubation, nephrotoxic drug use, diuretic drug use, major surgery, respiratory distress syndrome, and congenital renal anomaly).
- **Maternal related factors** (Maternal age, pregnancy induced hypertension, prolonged rupture of membranes, antenatal smoking, and number of neonate).

4.7. Operational definition

Preterm neonate: WHO defines preterm birth as all births before 37 completed weeks of gestation, or fewer than 259 days from the first date of a woman's last menstrual period(57).

Acute kidney injury: A serum creatinine-based KDIGO criteria physician diagnosis was used to define AKI in preterm neonates. (An absolute serum creatinine rise ≥ 0.3 mg/dL or SCr rise ≥ 1.5–1.9 × baseline SCr within 48 hours).

4.8. Data collection tools and procedures

Data was collected using a checklist adapted from tools that had previously been used in similar studies (20, 38, 48, 54, 55). It was divided into four sections. The first part consists of nine questions and contains information about the newborn's demographic characteristics; the second part consists of seventeen items dealing with the neonatal clinical conditions; the third section consists of seven questions addressing maternal factors associated with AKI development in neonates; the last section contains an AKI status assessment question. Data was collected from May 20 to June 20, 2022 through medical chart review by four BSc nurses working in the study setting, and supervision of data collection was done by one MSc nursing student.

4.9. Data quality control

Data quality was maintained by using a carefully designed tool for data collection, and pretest was done on 5 %(n=21) of study subjects at Tibebe Ghion specialized hospital. As a result, neonatal mechanical ventilation was removed from the tool due to its unavailability. Face validity was done by supervisors and other clinical experts. A one-day training about the techniques of chart review and data extraction was provided for data collectors. Throughout the data collection time, the supervisor and principal investigator were actively monitoring the data extraction procedure. Every day, the collected data is reviewed and checked for completeness and consistency by the supervisor and principal investigator. The data entry process was evaluated on a daily basis and necessary adjustments were made by the principal investigator.

4.10. Data processing and analysis

The data was checked for accuracy and consistency. It was then coded and entered into Epi data version 4.6.0.2 for cleaning before being exported to SPSS version 26 for analysis. Both descriptive and inferential analysis was done. Then descriptive data for categorical variable was presented through frequency and percent. While for continuous data of normally distributed, mean with standard deviation and for non-normally distributed median with interquartile range was used. Binary logistic regression analysis was used to determine factors associated with acute kidney injury. Enter method regression analysis was done to build the model. First, a bivariable binary logistic regression analysis was performed to find a factor with a 95% confidence interval of P value <0.25. Multicollinearity was checked between predictors using variance inflation factor (VIF) and was found to have no significant correlation at a variance inflation factor (VIF) less than five. Then, variables associated at bivariable binary logistic regression was subjected to a multiple binary logistic regression analysis to eliminate

confounding variables. Finally, those factors with a P value <0.05 at a 95% confidence level was considered as predictors of acute kidney injury among preterm neonates admitted to neonatal intensive care unit. Odds ratio was used to examine the strength of the relationship between outcome and predictor factors. Hosmer-lemeshow goodness of fit test was used to check the model fitness, and was fitted at 0.931. Finally, the findings was presented in the form of text, tables, and figures.

4.11. Ethical consideration

Ethical clearance was obtained from Bahir Dar University, College of Medicine and Health Sciences institutional research board with protocol No-480/2022. Prior to the start of data collection, an official letter of cooperation was obtained from Bahir Dar University, College of Medicine and Health Sciences chief academic research director and given to the hospital chief executive directors. The Chief Executive Directors of each hospital had ensured written permission to communicate with hospital archive workers in their hospital. By not writing known identifiers, information was kept confidential.

4.12. Dissemination plan

The findings of this study will be presented and submitted to Bahir Dar University College of Medicine and Health Sciences, Department of Pediatrics and Child Health Nursing. It will also be distributed to the hospitals under investigation. It may also be presented at academic conferences. It will also be attempted to be published in a peer-reviewed journal for future use.

5. RESULT

5.1. Demographic charactestics of the study participant

Among 423 eligible participants, 416 neonatal charts were reviewed, with a response rate of 98.3%. Regarding the sex of the neonate, 220(52.9%) were male. The median (interquartile range) age at admission was 0.875(0.04-1.00) days. The median (IQR) of the neonate's weight at birth was 2150(1900–2450) grams. The mean (SD) of gestational age was 31.87(±2.68) weeks, in which 254 (61.1%) were 32 weeks and above. Most 392(94.2%) of the participant were born in health facilities, of which 172(43.88%) were inborn. (Table 1)

Table 1: Demographic characteristics of preterm neonates admitted to public hospitals in Bahir Dar city, Ethiopia, 2022, (n=416).

Characteristics	***Category***	***Frequency (%)***
Sex	Male	220(52.9)
	Female	196(47.1)
Age at admission(in days)	≤one	330(79.3)
	>one	86(20.7)
Gestational age (in weeks)	<32	162(38.9)
	≥32	254(61.1)
Place of delivery	Hospital	288(69.2)
	Health center	104(25)
	Home	24(5.8)
Inborn delivery	Yes	172(41.3)

	No	244(58.7)
Mode of delivery	SVD[1]	303(72.8)
	Instrumental	77(18.5)
	Cesarean section	36(8.7)
APGAR[2] score at 1st minute	4-6	270(64.9)
	7-10	146(35.1)
APGAR score at 5th minute	4-6	89(21.4)
	7-10	327(78.6)
Birth weight (in grams)	1000 -1500	44(10.5)
	1500 – 2500	301(72.4)
	≥2500	71(17.1)

5.2. Neonatal clinical factors

Out of 416 participants, 186(44.7%) were septic, 156(37.5%) respiratory distressed, 160(38.5%) hyperbilirubinemic, 108(26%) perinataly asphyxiated, and 154(37%) were dehydrated. More than half (224, or 53.8%) of the participants were provided with nephrotoxic drugs, of which 155(69.1%) were with aminoglycosides. Only 9(2.2%) were diagnosed as having a congenital renal anomaly. Chest compression was done on 79(19%) of the participants. (Table 2)

Table 2: Clinical factors of preterm neonates admitted to public hospitals in Bahir Dar city, Ethiopia, 2022, (n=416).

Variables	***Category***	***Frequency (%)***	***Variables***	***Category***	***Frequency (%)***
Perinatal asphyxia	Yes	108(26)	Congenital renal anomaly	Yes	9(2.2)
	No	308(74)		No	407(97.8)
Neonatal sepsis	Yes	186(44.7)	Diuretic drug use	Yes	65(15.6)
	No	230(55.3)		No	351(84.4)
Dehydration	Yes	154(37)	Chest compression	Yes	79(19)
	No	262(63)		No	337(81)
NEC[3]	Yes	85(20.4)	Radiant warmer use	Yes	123(29.6)
	No	331(79.6)		No	293(70.4)
CHD[4]	Yes	21(5)	Major surgery	Yes	16(3.8)
	No	395(95)		No	400(96.2)

[1] *Spontaneous vaginal delivery*
[2] *Appearance, Grimace ,Activity, Respiration ,and Pulse*

[3] *Necrotizing Enter Colitis*
[4] *Congenital Heart Disease*

Hyperthermia	Yes	29(7)	Incubation	Yes	119(28.6)
	No	387(93)		No	297(71.4)
RDS[5]	Yes	156(37.5)	Nephrotoxic drug use	Yes	224(53.8)
	No	260(62.5)		No	192(46.2)
				Aminogly coside	155(69.2)
Hyperbilirubinemia	Yes	160(38.5)	Nephrotoxic drug type (n=224)	NSAID[6]	50(22.3)
	No	256(61.5)		Others	19(8.5)

5.3. Maternal related charactestics

The mean (SD) of the mother's age was 29.45(±7.75) years. The mean (SD) of the length of time of membrane rupture was 2.54(±7.98) hours. Most mothers (394, or 94.7%) were gave birth to a single neonate from this neonate's pregnancy. Only 11(2.6%) of the mothers had a smoking history while pregnant with their current neonate. (Table 3)

Table 3: Maternal related factors among preterm neonates admitted to public hospitals in Bahir Dar city, 2022, (n=416).

Charactestics	***Category***	***Frequency (%)***
Pregnancy induced hypertension	Yes	113(26.7)
	No	303(73.3)
Number of neonate	Singleton	394(94.7)
	Multiple	22(5.3)
Length of rupture of membrane(in Hours)	<18	384(92.3)
	≥18	32(7.7)
Prolonged rupture of membrane	Yes	32(7.7)
	No	384(92.3)
Chronic kidney disease	Yes	52(12.5)
	No	364(87.5)
Smoking	Yes	11(2.6)
	No	405(97.4)

5.4. Magnitude of Acute kidney injury

[5] *Respiratory Distress syndrome*

[6] *Non-steroidal anti-inflammatory drug*

The prevalence of acute kidney injury among NICU admitted preterm neonates of public hospital in Bahir Dar city was 18.27% (95%CI: 15, 22). (Figure 3)

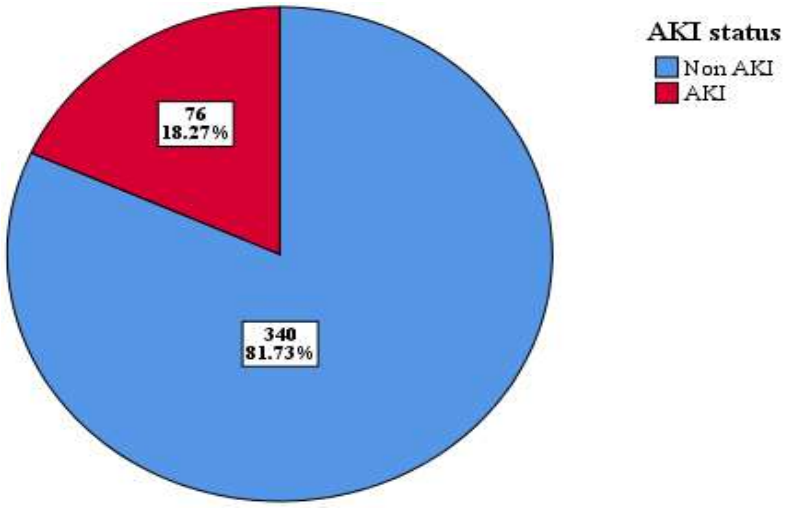


Figure 3: Magnitude of acute kidney injury among preterm neonates admitted to public hospitals in Bahir Dar city, 2022, (n=416).

5.5. Factors associated with acute kidney injury

Among predictors, birth weight, perinatal asphyxia, neonatal sepsis, neonate nephrotoxic drug use, dehydration, respiratory distress syndrome, chest compression, incubation, radiant warmer use, pregnancy induced hypertension, and prolonged rupture of membrane were associated with the development of neonatal AKI in bivariable binary logistic regression analysis at ($p<0.25$).

Those variables that have an association with the outcome variable in bivariable binary logistic regression analysis were included in the multivariable binary logistic regression analysis. Birth weight, perinatal asphyxia, dehydration, chest compression, and pregnancy-induced hypertension during this neonate's pregnancy were variables significantly associated with the development of neonatal acute kidney injury after controlling for the effect of potentially cofounding variables using multiple binary logistic regression at ($p<0.05$).

Neonates with a birth weight of (1001-1500) grams were 3.26 times more likely to develop AKI than neonates with a birth weight of 2500 grams (AOR=3.26; 95%CI [1.18, 9.05]). In perinataly asphyxiated neonates, the odds of developing acute kidney injury were 2.84 times higher (AOR =2.84; 95%CI [1.55, 5.19]) than in non-asphyxiated neonates. Neonates with a clinical diagnosis

of dehydration were 2.30 times (AOR=2.30; 95%CI [1.29, 4.09]) higher in terms of AKI development than non-dehydrated neonates.

Neonates who received chest compression were 3.74 times (AOR=3.74; 95% CI [1.97, 7.13]) more likely to develop AKI than those who did not. Neonates from pregnancy-induced hypertensive mothers were 2.17 times (AOR=2.17; 95%CI [1.29, 3.65]) more likely to develop AKI than neonates from non-hypertensive mothers. (Table 4)

Table 4: Bivariable and multivariable binary logistic regression analysis for factors associated with acute kidney injury among preterm neonates admitted to public hospital in Bahir Dar city, 2022, (n=416).

Variable		***AKI***		***Odds ratio***		***P-value***
		Yes	***No***	***COR(95%CI)***	***AOR (95%CI)***	
Birth weight	1001-1500	15	29	3.16(1.27-7.87)	3.26(1.18-9.05)	0.023*
	1501-2500	51	250	1.24(0.59-2.59)	1.17(0.52-2.65)	0.707
	≥2500	10	61	1	1	
Perinatal asphyxia	Yes	33	75	2.71(1.61-4.57)	2.84(1.55-5.19)	0.001*
	No	43	265	1	1	
Neonatal sepsis	Yes	42	144	1.68(1.02-2.77)	1.54(0.86-2.74)	0.145
	No	34	196	1	1	
Dehydration	Yes	40	114	2.20(1.33-3.64)	2.30(1.29-4.09)	0.005*
	No	36	226	1	1	
RDS	Yes	37	119	1.76(1.07-2.91)	1.56(0.88-2.74)	0.127
	No	39	221	1	1	
Nephrotoxic drug use	Yes	53	171	2.28(1.34-3.88)	1.76(0.97-3.19)	0.065
	No	23	169	1	1	
Chest compression	Yes	29	50	3.58(2.06-6.21)	3.74(1.97-7.13)	0.000*
	No	47	290	1	1	
Radiant warmer use	Yes	31	92	1.86(1.11-3.11)	1.50(0.82-2.76)	0.192
	No	45	248	1	1	
Incubation	Yes	30	89	1.84(1.09-3.09)	1.06(0.57-1.95)	0.86
	No	46	251	1	1	
PROM	Yes	11	21	2.57(1.18-5.59)	2.01(0.79-5.16)	0.145
	No	65	319	1	1	
Preeclampsia	Yes	31	82	2.17(1.29-3.65)	2.17(1.2-3.93)	0.010*
	No	45	258	1	1	

*Note *=statistically significant, RDS= respiratory distress syndrome*

6. DISCUSSION

The aim of this study was to determine the magnitude and associated factors of AKI among preterm neonates admitted to public hospitals in Bahir Dar city. In this study, the prevalence of AKI was 18.27% (95%CI: 15-22). This finding is comparable with studies done in Kenya (19.8%), Saudi Arabia (18.7%), Turkey (20.0%), and the AWAKEN study (18.8%) using the Neonatal KDIGO classification analysis of AKI by serum creatinine only (3, 40, 44, 47).

However, this finding is lower than studies done in the USA with a prevalence of (38.0%) among extremely low gestational age and (30.3%) among preterm neonates of less than 30 weeks of gestation(33, 35). Likewise, it is lower than the finding in a study done in Portugal with a (22.6%) prevalence of AKI among preterm neonates with ≤30 weeks of gestational age(36). This difference may probably be attributed to the study setting and gestational age difference. Due to prenatal fetal distress and exposure to numerous risk factors, including infections, intrauterine growth retardation, placental insufficiency, and maternal medicine, extremely preterm newborns are more likely to develop AKI(58, 59).

This finding is lower than studies done in Taiwan among extremely low birth weight neonates 56%(4), which may probably be attributed to the study population difference. Thus, very low birth weight neonates have underdeveloped kidneys that can be easily affected by nephrotoxic drugs(60). Similarly, this finding is lower than studies done in Serbia (26%) and (44%), Saudi Arabia (56%) among neonates receiving care within NICU of level II and III NICU, and Tanzania (31.5%)(39, 42, 43, 46). This disparity could be attributed to a difference in study design, AKI definition, study setting, or study participant.

This finding is higher than that of Tikur Anbesa Specialized Hospital, which found a prevalence of 12.7%(48), which could be attributed to a difference in neonatal gestational age, as only 11.8% were preterm in that study. Similarly, this finding is higher than a study done in Egypt which showed a prevalence of 10.8%, in which 59.3% of the cases were preterm(5). This difference may probably be due to the diagnosis of AKI in that study was defined only by SCr greater than 1.5mg/dl and the study population difference.

Likewise, this study finding is higher than studies conducted in northwest Parana state (7.5%), Iran (10.68%), India (12 %), and United Arab Emirates (11.6%)(37, 38, 41, 45). This may probably be due to study setting differences (quality healthcare delivery system).

In agreement with studies done in Tikur Anbesa specialized hospital, Pakistan, and Iran (48, 51, 52), this study has showed perinatal asphyxia as independent predictors of AKI occurrence among NICU admitted preterm neonates. Those perinataly asphyxiated preterm neonates were 2.84 times more likely to develop AKI than non-perinataly asphyxiated. This could be because kidneys are extremely sensitive to oxygen deprivation, and as a result, renal insufficiency can occur within 24 hours of a hypoxic ischemic episode, leading to irreversible cortical necrosis, if left untreated(25).

This study revealed that very low birth weight (1001–1500 grams) was significantly associated with an increased risk of AKI in preterm neonates. Thus, the odds of AKI development were 3.26 times higher in very low birth weight neonates than in normal birth weight (≥2500grams) neonates. This is consistent with a study conducted in Iran and a systematic review and meta-analysis done on risk factors for acute kidney injury (20, 38). This might be attributed to the fact that low birth weight has contributed to the lower number and immaturity of nephrons, putting them at risk for AKI(61).

Similarly, this study has shown chest compression as an independent predictor of AKI occurrence, by which chest compression recipient neonates were 3.74 times more likely to develop AKI than their counterparts. This might be due to systemic ischemia/reperfusion injury due to the return of spontaneous circulation, thereby leading to multiple organ dysfunction syndrome (i.e., post-resuscitation syndrome), in which acute kidney injury (AKI) is one of the features of post-resuscitation syndrome (62, 63). This is finding is supported by a study conducted among asphyxiated neonates treated with therapeutic hypothermia(53).

In this study, dehydration has been identified as a significant associated predictor of AKI, by which dehydrated neonates were 2.3 times more likely to develop AKI than non-dehydrated. This may be due to dehydration causing hypo perfusion to the kidneys, causing prerenal damage. Meanwhile, the study conducted in Tikur Anbesa has shown treatment for dehydration has an association with AKI occurrence(48).

In this study, pregnancy-induced hypertension was identified as a significant predictor of AKI. Thus, neonates from preeclamptic mothers were 2.17 times more likely to develop AKI than neonates of non-pregnancy-induced hypertensive mothers. This might be done by increasing the risk of premature birth and low birth weight(64). This is in agreement with a study conducted in Turkey(54), while contradicting a study conducted in Taiwan which showed pregnancy induced hypertension as a protective factor against neonatal AKI(4).

7. LIMITATION OF THE STUDY

Since all hospitals used SCr based criteria of the neonatal modified KDIGO definition to diagnose AKI, a UoP based (oligouric) AKI was missed, which could underestimate the prevalence. And, due to the retrospective nature of the study, it presented limited predictors, although the predisposing factors for AKI are much broader.

8. CONCLUSION

The magnitude of acute kidney injury among preterm neonates was high. Very low birth weight, perinatal asphyxia, dehydration, chest compression, and pregnancy induced hypertension were factors found to be independent predictors of acute kidney injury among NICU admitted preterm neonates.

9. RECOMMENDATION

Early recognition and management of predisposing factors for AKI could reduce the risk of its occurrence. Therefore, responsible bodies have to do their part as:

Clinicians: have to be vigilant and actively monitor renal function in neonates with perinatal asphyxia, dehydration, very low birth weight, chest compression, and from pregnancy-induced hypertensive mothers in order to detect and manage AKI early. Additionally, they have to properly and early manage neonates with perinatal asphyxia and dehydration, reduce the need for chest compression through active management of labor and delivery, teach the community about the prevention mechanisms of low birth weight, and reduce the risk of AKI from pregnancy-induced hypertension through its proper management during focused antenatal care.

Researchers: have to further investigate AKI and its associated factor longitudinally (birth cohort) with large sample size to encompass all possible predictor variables as well as to accurately estimate its magnitude.

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ANNEXES

ANNEX I: Information sheet

Good morning/afternoon

My name is Sayih Mehari, and I am a Masters graduate student in pediatrics and child health nursing at Bahir Dar University, College of Medicine and Health Sciences, Department of pediatrics and child health nursing. As a partial fulfillment of the Master's degree requirement, I am interested in conducting research entitled "magnitude and associated factors of acute kidney among preterm neonates admitted to public hospitals in Bahir Dar city, Ethiopia, 2022" at your institution.

Purpose of the study: To assess the magnitude and associated factors of acute kidney injury among preterm neonates admitted to public hospitals in Bahir Dar city from May 30, 2020, to April 30, 2022.

Time span for data extraction: May 20 to June 20, 2022.

Risk: Since all data will be taken from the medical chart, no potential harm will happen to the patient. The name or any identification will not be recorded in the checklist. The confidentiality of all information taken from the chart will be maintained and secured.

Benefits: There are no direct benefits for those whose documents will be reviewed. However, the findings will be useful to health care professionals, policymakers as an input for guideline development and policy briefing, and researchers as background information for future clinical research. So, in the long run, neonates will benefit from this study.

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Annex II. Checklist

Code…….

Part I: Neonatal demographic characteristics			
S.No	Items	Response	Remark
101.	Neonate's age (in day)	_____	
102.	Sex	1. Male 2. Female	
103.	Gestational age (in weeks)	_____	
104.	Birth weight (in grams)	_____	
105.	APGAR score at 1st minute	_____	
106.	APGAR score at 5th minute	_____	
107.	Place of birth	1. Hospital 2. Health center 3. Home	
108.	Inborn delivery	1. Yes 2. No	
109.	Mode of delivery	1.Spontanous vaginal 2. Instrumental vaginal 3. Cesarean section	
Part II: Items about neonatal clinical factors			
201.	Perinatal asphyxia	1. Yes 2. No	
202.	Neonatal sepsis	1. Yes 2. No	
203.	Hyperbilirubinemia	1. Yes 2. No	
204.	Dehydration	1. Yes 2. No	
205.	Necrotizing enter colitis	1. Yes 2. No	
206.	Congenital heart disease	1. Yes 2. No	
207.	Hyperthermia	1. Yes 2. No	
208.	Respiratory distress syndrome	1. Yes 2. No	
209.	Congenital renal anomaly	1. Yes 2. No	
210.	Did nephrotoxic drug provided for the neonate during his/her stay in NICU?	1. Yes 2. No	
211.	If yes to Q202, which nephrotoxic drug?	1. Yes 2. No	

212.	Did diuretic drug provided for the neonate during his/her stay in NICU?	1. Yes	2. No	
213.	Chest compression	1. Yes	2. No	
214.	Incubation	1. Yes	2. No	
215.	Major surgery (abdominal, cardiac)	1. Yes	2. No	
216.	Radiant warmer use	1. Yes	2. No	
Part III. Maternal factor related items				
301.	Maternal age (in year)	_____		
302.	Pregnancy induced hypertension during this neonate's pregnancy?	1. Yes	2. No	
303.	Length of rupture of membrane	_____		
304.	Prolonged rupture of membrane	1. Yes	2. No	
305.	Chronic kidney disease	1. Yes	2. No	
306.	Smoking during this neonates pregnancy	1. Yes	2. No	
307.	Number of neonates from current neonate's pregnancy	_____		
Part IV. AKI status assessment				
401.	AKI	1. Yes	2. No	