PREVALENCE AND SHORT-TERM OUTCOMES OF ACUTE KIDNEY INJURY IN TERM NEONATES WITH PERINATAL ASPHYXIA AT THE KENYATTA NATIONAL HOSPITAL NEWBORN UNIT

A dissertation submitted in partial fulfillment of a Masters of Medicine Degree in Pediatrics and Child Health, University of Nairobi

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DECLARATION

This dissertation is my original work and has not been presented for the award of a degree in any other university

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LIST OF ABBREVIATIONS

AKI - Acute kidney injury

AKIN - Acute Kidney Injury Network

ANC- Antenatal Clinic

APGAR - Appearance, Pulse, Grimace, Activity, Respiration

APH - Antepartum Haemorrhage

BP - Blood Pressure

CM – Centimeter

CRF- Case Report Form

eCCl - Estimated Creatinine Clearance

GFR – Glomerular Filtration Rate

HIE - Hypoxic Ischemic Encephalopathy

IUGR - Intrauterine Growth Restriction

KDHS - Kenya Demographic Health Survey

KG - Kilogram

KNH - Kenyatta National Hospital

NICU - Neonatal Intensive Care Unit

NBU - Newborn Unit

P RIFLE - Pediatric risk, injury, failure, loss, and end-stage renal disease

PROM - Prolonged Rupture of Membranes

RCT - Randomized Control Study

RIFLE - Risk, injury, failure, loss, and end-stage renal disease

SCr – Serum Creatinine

SIN - Subject Identification Number

SOP - Standards Operating Procedures

WHO - World Health Organisation

DEFINITION OF TERMS

Term newborn: Infants born at or after 37 completed weeks of gestation using Finnström score. [34] The score is shown in appendix I; it only uses seven external characteristics and is not influenced by the neurological state of the infant.

Apgar Score: A simple and repeatable method to quickly and summarily assess the health of newborn children immediately after birth and at 5, 10, 15 and 30 minutes. The Apgar score is determined by evaluating the newborn baby on five simple criteria on a scale from zero to two, then summing up the five values thus obtained. The resulting Apgar score ranges from zero to 10. [32] The five criteria are summarized using words chosen to form an acronym (**A**ppearance, **P**ulse**, G**rimace, **A**ctivity, and **R**espiration). The score is shown in appendix II.

Perinatal asphyxia: "Failure to initiate and sustain breathing at birth." [1] **plus** Apgar Score less than 7 **plus** clinical evidence of hypoxic ischemic encephalopathy Sarnat and Sarnat stage 1, 2 or 3 as shown in appendix III. " [33]

Acute Kidney Injury: AKI is a serum creatinine level above 133 µmol/l at 72 hours. [26]

Short term Outcomes: Death, discharge home or continued treatment on day 7 of life.

ABSTRACT

Background

Perinatal asphyxia contributes significantly to perinatal morbidity and mortality especially in resource poor countries, with a mortality of 31.1% by day 7 of life in Kenyatta National Hospital Newborn Unit. The high incidence of perinatal asphyxia (50-72%) and its severity appear to correlate with increasing incidence of AKI. The kidney is the most damaged organ in asphyxiated full-term infants, with effects seen within the first 5 days of birth with up to 40% of survivors having residual kidney dysfunction.

The study was designed to provide local data on this condition.

Objectives

To determine the prevalence and short term outcomes of perinatal asphyxia-associated acute kidney injury (AKI).

Methods

We conducted a prospective cohort study including 60 full-term neonates admitted at the Kenyatta National Hospital newborn unit in Nairobi and suffering from perinatal asphyxia from 1st June 2012 to 30th November 2012. Renal function was assessed by measuring serum creatinine on day 3 of life. AKI was defined by a level of creatinine above 133 µmol/l. The hypoxic ischaemic encephalopathy (HIE) (degree of neurological impairment) was determined according to Sarnat classification daily until patient discharge, death or day 7 of life.

Results

Of the 968 newborns admitted into the KNH NBU during the study period, 60 infants met the inclusion criteria with 36.2% of the neonates having HIE I, 51.7% HIE II and 12.1% HIE III. The mean weight was 3373 g (SD=427.3) and length 52.3 cm (SD=2.1). The neonates weight ranged from 2620 to 4600 g. There were 37 male neonates and 23 female neonates. Most of the neonates were delivered in KNH (76%), 24 % delivered in other health facilities.

Seven out of the sixty neonates met criteria for AKI on day 3 giving a prevalence of 11.7 %. Out of the neonates with AKI, 11.1 % (4/36) of the males were affected versus 12.5 % (3/24) of the females. There was a 15 fold increase risk of developing AKI in HIE III compared to HIE I, p=0.034 {95% CI (1.2-183.6)}. The mortality rate in perinatal asphyxia associated AKI was 71.4 % with a 24 fold increase risk of death in neonates with AKI, p=0.001{95% CI (3.7-157)}. Median day of death in neonates with AKI was 4.5 days. Of all the neonates admitted 36% without AKI remained admitted beyond day 7 of life compared to 14.3% with AKI. Of the neonates with AKI, 5 died by day 7 of life. Only 14.3% of neonates with AKI were discharged home by day 7 of life.

Conclusions

AKI is common in neonates with asphyxia (1 out of every 8 neonates) and associated with poorer outcomes in the background of perinatal asphyxia (mortality rate of 71 %.). AKI correlates well with the severity of HIE. Larger studies need to be done to correlate maternal factors and perinatal asphyxia-associated AKI, and to assess the long term outcome of babies with perinatal asphyxia-associated AKI discharged from the newborn unit.

1. INTRODUCTION AND LITERATURE REVIEW

Perinatal asphyxia and Acute Kidney Injury

Perinatal asphyxia is defined by the World Health Organisation (WHO) as "Failure to initiate and sustain breathing at birth."[1] In the Kenya Demographic Health Survey (KDHS) 2008, the perinatal mortality rate is 37 deaths per 1000 pregnancies; a marginal decline from the 40 deaths per 1000 pregnancies recorded in the 2003 KDHS.[2] Data from Kenyatta National hospital newborn unit records indicate that birth asphyxia is one of the three leading causes of newborn death; the other two being infections and prematurity. On average twenty percent of weekly admissions to KNH NBU are due to perinatal asphyxia .[3]

It has been estimated that nearly 5% to 8% of newly born infants suffer different degrees of perinatal asphyxia leading to admission to the neonatal intensive care unit (NICU).[4-7] In a study done by Maalim et al at Kenyatta National Hospital Newborn Unit (NBU), perinatal asphyxia had a poor outcome with a mortality of 31.1% by day 7 of life and a further 31.1% continuing treatment beyond day 7 for complications of asphyxia. The rest of the infants (37.8%) were discharged from the hospital with 6.7% being discharged with neurologic sequelae and 31.1% discharged with no sequelae.[8]

There is a high incidence of AKI among the asphyxiated term infants, (50 – 72%). [9, 10] The presence of perinatal asphyxia and its severity appear to correlate with increasing incidence of AKI. [9 , 11] Asphyxia is an important cause of acute kidney injury (AKI) and transient kidney impairment with adverse effects, especially in the first five days of birth.[12, 13] The kidney is the most damaged organ in asphyxiated full-term infants. [13] Hypoxia and ischaemia can cause damage to almost every tissue and organ of the body and various target organs involved have been reported to be kidneys in 50%, central nervous system in 28%, cardiovascular system in 25% and lungs in 23% cases.[14] Gunn et al reported that all the infants with hypoxic-ischemic encephalopathy included in their study developed signs of Acute Kidney Injury.[15]

Circulatory adaptive responses to perinatal asphyxia may lead to renal injury as a consequence of decreased perfusion of the kidney. [16] Acute hypoxemia is associated with an increase in renal vascular resistance and a decrease in GFR and filtration fraction. During oxygen deficit, when adenosine triphosphate hydrolysis prevails over adenosine triphosphate synthesis, adenosine (a direct degradative product of 5′adenosine monophosphate) increases and activates its receptors resulting in an increment of the renal vascular resistance (pre glomerular vasoconstriction and post glomerular vasodilatation) thus decreasing GFR and filtration fraction.[17] Hemodynamic renal changes produced by adenosine were observed during ischemic or hypoxemic experimental studies.[18] Moreover, adenosine administrated into the renal artery led to decreased GFR in humans.[19]

Acute, relatively mild injury to the kidney or impairment of kidney function, manifest by changes in urine output and blood chemistries, have serious clinical consequences. [20] Urinary output is slightly less in neonates with severe birth asphyxia but is statistically insignificant when compared with cases of mild and moderate asphyxia. [9] But oliguria has been reported in higher number of neonates by other authors with figures ranging from 25% to 69.2% babies. [21, 22]

Diagnosis of Acute Kidney Injury in Birth Asphyxia

There lacks an internationally acceptable definition of AKI in neonates. Most previous investigators have defined AKI in neonates as serum creatinine above 133 µmol/l. [23, 24] Some investigators such as Jayashree et al. [25], Nouri et al.[26] and Gupta et al.[9] defined AKI in neonates as serum creatinine above 90 µmol/l. According to the Acute Kidney Injury Network (AKIN), AKI is an absolute increase in serum creatinine of ≥ 26.4µmol/l (or a percentage increase in serum creatinine of at least 50%) or urine output < 0.5ml/kg per hour for more than 6 hours. [23]

Oliguria is not a sensitive marker in AKI diagnosis. A high proportion (60-70%) of post-asphyxial AKI is non-oliguric. However if the definition for AKI relies on the presence of oliguria then there may be a large percentage of neonates misdiagnosed. [9, 10]

A recent clinical practice assessment in the UK concluded that only 50% of neonates with AKI were considered to have received a ‘‘good’’ overall standard of care. This figure fell to just over 30% if AKI developed during a hospital admission rather than being diagnosed before admission. The authors also felt that there was an unacceptable delay in recognizing AKI in 43% of those that developed the condition after admission and that in a fifth of such patients its development was predictable and avoidable. Their recommendations were simple: risk assessment for AKI as part of the initial evaluation of emergency admissions, along with appropriate serum biochemistry on admission and at frequent intervals thereafter. [27]

The retrospective prevalence study by Karlowicz [10] in the US aimed to determine the prevalence and types of acute renal failure in moderate and severe asphyxiated full-term neonates and to evaluate the accuracy of an asphyxia morbidity score in predicting acute renal failure. Acute renal failure was defined as serum creatinine > 1.5 mg/dl (133 µmol/l) with normal maternal renal function within the first week of life. Acute renal failure was present in 20 of 33 (61%) infants with severe asphyxia scores and 0 of 33 with moderate asphyxia scores ($P < 0.0001$).

In Tunisia, in a prospective prevalence study by Nouri [26] involving 87 full-term neonates, the prevalence of AKI was 17.2%. Of these 9 (10.3%) had HIE I, 67 (77%) HIE II and 11 (12.6%) HIE III. Renal failure involved 15 neonates (17.2%) Renal function was assessed by measuring plasma urea and creatinine at age 48 h. Renal failure was defined by a level of creatinine above 90 µmol/l. Neurologic examination was performed on day 7. Eight neonates died, of whom 3 had renal failure. Neurologic examination was abnormal in 36 out of 72 (50%) neonates without

renal failure and in 9 of the 12 (75%) survivors with renal failure. Among the 12 neonates with renal failure, 7 had abnormal neurologic features at discharge. This is the only African study on perinatal asphyxia associated –AKI.

In a prospective study conducted by Kaur [28] in India involving 36 consecutive inborn neonates moderate birth asphyxia was present in 11 (30.6%) and severe birth asphyxia in 25 (69.4%). AKI developed in one of 11 infants (9.1%) with moderate asphyxia and in 12 of 25 (56%) with severe asphyxia, making a total incidence of 41.7%. AKI persisted in 16.6% infants at 96 hours of life. Ten infants (27.7%) had serum creatinine levels above 133 µmol/l. Those whose creatinine was above 133 µmol/l within 6 hours of life took longer to achieve a normal level than those in whom it rose after 6 hours of life. One infant died and one who was critically ill was discharged against medical advice; both had AKI. The incidence of AKI in asphyxiated infants using AKIN staging was 41.7%. Only ten of the infants had serum creatinine greater than 1.5 mg/dl. Liu et al. recently reported similar findings. [29] Of their 30 infants with severe asphyxia, AKI using AKIN criteria was present in 56.7%, while serum creatinine was greater than 1.5 mg in only 20 % of infants. It seems that a significant number of neonates with AKI could be missed if the new classification systems are not used.

A case control study of (70 asphyxiated babies and 28 healthy controls) by Gupta [9] in India reported blood urea and serum creatinine being significantly higher in asphyxiated babies compared to the control group ($P<0.001$). AKI was defined as serum creatinine above 90 µmol/l. Of the 70 asphyxiated babies 33 (47.1%) had renal failure, which was of the non-oliguric type in (26/33) 78% cases and oliguric type in (7/33) 22% cases. The severity of renal function abnormality correlates well with the degree of asphyxia.

Three major studies, namely: Jayashree et al. [25], Nouri et al.[26] and Gupta et al.[9] have assessed the incidence of AKI in resource poor settings (Nouri et al in Africa) successfully drawing valuable conclusions that drive neonatal care management. Our study therefore borrowed heavily from these studies. These results from the resource poor settings are comparable to the resource rich setting as described in the Karlowicz [10] study above.

Table 1: Summary of Studies on Acute Kidney Injury in Perinatal asphyxia

Study design	Sample size	Study Title	Outcome
1. Karlowicz.[10], 1995 Retrospective Survey Country- USA	66	Non oliguric and oliguric acute renal failure in asphyxiated term neonates	Acute renal failure was present in 20 of 33 (61%) infants with severe asphyxia scores and 0 of 33 with moderate asphyxia scores ($P < 0.0001$). An asphyxia morbidity score, which can be determined at 1 h of age, predicted acute renal failure in full-term infants with 100% sensitivity and 72% specificity.
2. Nouri S. [26],2006, Prospective Longitudinal Survey Study Country- Tunisia	87 Term neonates	Acute kidney injury in term neonates with perinatal asphyxia	HIE I- 10.3% II- 77% III- 12.6% AKI was observed in 15 neonates (17.2%) of whom 10 neonates (11.5%) from HIE II Overall mortality- 8 neonates (9.2%) of whom 3 neonates (3.4%) had AKI.

Table 1: Summary of Studies on Acute Kidney Injury in Perinatal asphyxia

3. Kaur S. [28] ,2007, Prospective Cohort Study Country- India	36 ≥ 34 weeks neonates	Evaluation of glomerular and tubular function in neonates with moderate and severe perinatal asphyxia	AKI developed in 9.1% (1/11) in neonates with moderate asphyxia AKI developed in 56% (12/25) Total incidence of AKI = 41.7% Overall mortality- 1 neonate (2.8%) who had AKI
4. Gupta [9] , 2009 Prospective Case Control Study Country- India	98 (Exp vs. control 70/28)	To determine the incidence of acute kidney injury in asphyxiated neonates	Of the asphyxiated babies (N = 70) 38 cases (54.25%) had HIE with HIE I-12.8% II - 28.5% III - 12.8% Blood urea and serum creatinine were significantly higher in asphyxiated and HIE babies compared to the control group (P<0.001) and (P <0.05) respectively. Of the 33(47.1%) neonates with ARF 5 (14.1%) expired four were having HIE grade III and one had HIE grade II.

2. STUDY JUSTIFICATION/ UTILITY

Perinatal asphyxia accounts for 20% of the weekly admissions to the Kenyatta National Hospital Newborn Unit and has a poor outcome with a mortality of 31.1% by day 7 of life and 6.7% are discharged with neurologic sequelae.[8] The kidney is the most damaged organ in asphyxiated full-term infants with up to 40% of survivors having residual kidney dysfunction.[5, 30] Clinical prediction of outcome of neonates with perinatal asphyxia is important in guiding management decisions as well as instituting timely rehabilitative measures especially for those projected to have acute kidney injury.

The study was designed to provide local data on this condition. Creating awareness of perinatal asphyxia associated-AKI among the clinicians makes them more alert in suspecting the condition.

3. OBJECTIVES

3.1 Primary Objective

To determine the prevalence of perinatal asphyxia-associated AKI on the third day of life in term neonates admitted at KNH NBU.

3.2 Secondary objectives

To determine the short-term outcomes of perinatal asphyxia-associated AKI in term neonates admitted at KNH NBU.

4. METHODOLOGY

4.1 Study Design

This was a hospital based prospective cohort study.

4.2 Study Area

The study was conducted at the Newborn Unit at the Kenyatta National Hospital (KNH), the tertiary referral and teaching hospital for the college of health sciences, University of Nairobi. It is also the main inpatient hospital for the low and middle-income society in Nairobi and its environs. The newborn unit admits all sick neonates born in KNH, those born elsewhere in the first twenty-four hours of life, and also handles transfers from other hospitals. The unit admits between 160 and 200 neonates each month, over 20% whom are term babies diagnosed with perinatal asphyxia with.

4.3 Study Population

The study population included term neonates with perinatal asphyxia admitted within 24 hours of delivery into the NBU.

4.4 Sample size

Sample size (n) was calculated using Fischer's formula:

n= Minimum sample size

Z= standard normal deviate for 95% confidence interval (= 1.96)

P= is the estimated proportion of AKI in term neonates with perinatal asphyxia. This has been put at 50% as we do not know the local proportion.

d= level of precision (set at±5%)

$$n = \frac{z_{\propto}{}^2\, p(1-P)}{d^2} \qquad n = \frac{1.96^2\ X\ 0.50\ \ (1-\ 0.50\ )}{0.05^2} = \ 384$$

The KNH NBU has 50 admissions per week of which 10 (20%) have perinatal asphyxia. Of these 10 neonates, 6 (60%) have hypoxic ischaemic encephalopathy (HIE). This gave a total of 96 neonates as having perinatal asphyxia over the study period (4 months). [3, 8] Based on this information and since the total population of newborns with perinatal asphyxia in KNH newborn unit is less than 10,000 in a year, the following formula was employed to adjust the above sample size.

$$n_f = \frac{\mathbf{n}}{\mathbf{1 + n/N}} \qquad n_f = \frac{384}{1 + 384/100} = 56$$

n= the calculated sample size = 384

N= the estimated total population of newborns with perinatal asphyxia within the study period (4 months) = 100.

A minimum sample size of **56 neonates** was recruited into this study.

4.5 Study Period

The study was carried out over a 6 month period (June 2012 to November 2012).

Individual participants were in the study from birth to day 7 of life. One research assistant, who was a clinical officer was trained for 3 days on patient recruitment and data collection. Pretesting questionnaires and recruitment of subjects was completed in 6 months. Data analysis, presentation to the department and manuscript preparation was completed in two months.

4.6 Recruitment of study participants

The investigator screened all term neonates aged 0-24 hours admitted at KNH NBU for perinatal asphyxia using the Apgar scoring [32] and Sarnat and Sarnat clinical staging of hypoxic ischemic encephalopathy [33] outlined in appendix II and III respectively. The most severe sign was used to categorize the severity of the perinatal asphyxia.

The **inclusion criteria** were:

- Term newborn as per *Finnström gestational age assessment* as outlined in appendix I. [34]
- Age 0-24 hours at initial assessment
- "Failure to initiate and sustain breathing at birth." [1] **plus** Apgar Score less than 7 **plus** clinical evidence of hypoxic ischemic encephalopathy Sarnat and Sarnat stage 1, 2 or 3 as shown in appendix III. " [33]
- Consent by the parent or caregiver.

The **exclusion criteria** were:

- Newborns with neurological congenital malformations and other gross congenital malformations.
- Refusal to consent

Sampling technique

All consecutive term newborns that satisfied the above inclusion criteria were enrolled within the first 24 hours of life irrespective of day or night admission.

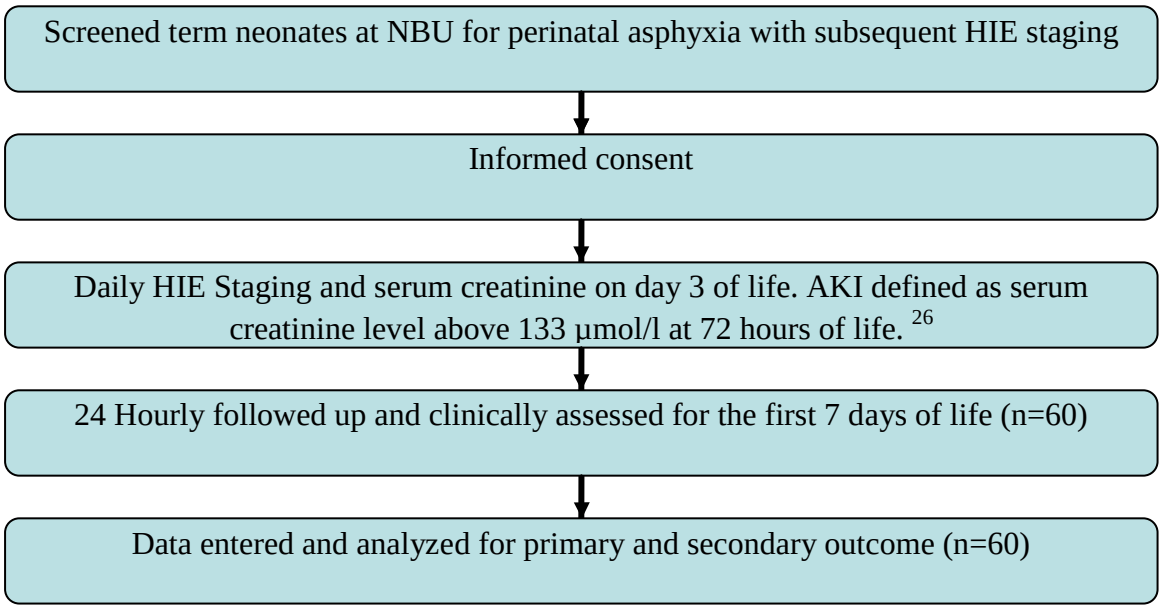
The parents or caregivers of the term neonates with perinatal asphyxia that met the inclusion criteria were requested to participate in the study. Written informed consent was obtained after clear explanation of the purpose of the study, expected benefits and potential harms.

Newborns with a malformation syndrome and those who died within 3 days of admission were excluded from the study.

The blood sample was collected on day 3 of life by quick heel sampling of 0.5ml to 1ml into a microtainer. The sample was then centrifuged within 2 hours and analysed using Cobas Integra machine using the compensated Jaffė method as detailed in appendix V. AKI was defined as a serum creatinine level above 133 µmol/l at 72 hours. [26]

4.7 Study Flow Diagram

The flow diagram below summarizes the pathway from recruitment of study population to the follow up for the outcomes.



4.8 Data Collection

All term neonates aged 0-24 hours admitted at KNH NBU for perinatal asphyxia were assessed by either principal investigator or study assistant and the findings recorded in a standard tool (see appendix IV).The neonate's length, body weight and head circumference were measured as per the standard operating procedures (SOP) outlined in appendix V.

The mothers of newborns diagnosed with perinatal asphyxia were interviewed; their case files and ANC records checked to correlate birth details and to determine their socio-demographic characteristics and obstetric history as outlined in appendix IV.

The NBU team independently carried out the appropriate patient management.

The protocol consisted of initial management points following:

The total fluid/ milk intake on day one of life was 60 ml/kg per day (10% dextrose) and this was increased to 80ml/kg/day on day two of life during which milk was introduced via nasogastric tube at 10mls 3hourly and the feed was increased by the same amount every day and the intravenous fluids reduced to keep within the total daily volume until intravenous fluid was stopped. The introduction of oral feeding on day 2 of life was done based on the ability of the neonate to retain the feed. In the neonates without bowel sounds, oral feeding was not initiated on day two of life. In cases of convulsions, a loading dose of phenobarbital (20 mg / kg) administered intravenously to neonates in HIE grades II and III who had convulsions; correction of metabolic acidosis;

The following procedures were performed, assessment of renal function by measuring serum creatinine at age 72h AKI was defined by a level of creatinine above 133 µmol/l at 72h. Neurologic examination was performed daily up till day 7 of life. Patients were evaluated clinically every day for a week for HIE and this data was recorded in the questionnaire in appendix IV. The discharge from the NBU was authorized after 48 h s life for newborns born in HIE grade I and grades II and III in the absence of breathing or feeding difficulties and for the resolved AKI patients. Phenobarbital was prescribed systematically at the time of hospital discharge for newborns with HIE grades II and III. A maintenance dose of phenobarbital (3 to 5 mg / kg per day) was prescribed if convulsions persisted after the first 48 hours of life.

Patients who developed AKI were subsequently followed up by the renal team and renal replacement therapy was initiated for the severe cases.

The discharged neonates were followed in the neonatology clinic by the same senior paediatric resident and neonatologist, and those who had severe AKI were referred to the renal clinic.

To determine the prevalence, severity and risk factors of perinatal asphyxia-associated AKI and to evaluate the place of renal damage in the short-term neurological outcome we evaluated the following parameters: Apgar score at 5 min, the HIE grade, presence of convulsions, neurological examination to 7^{th} day of life, deaths and neurological examination on discharge.

4.9 Primary and Secondary Outcomes

The primary outcome of this study was the prevalence of acute kidney injury in term neonates with perinatal asphyxia on the third day of life.

The secondary outcomes of this study were:

- Discharge status on day 7 of life
- Correlation between HIE staging and AKI staging
- Length of hospital admission
- Mortality by day 7 of life

5. DATA MANAGEMENT AND ANALYSIS

Data from the questionnaires was coded, entered and cleaned in Microsoft Excel. Data quality was assured by visual scanning before entry and immediate data entry after data capturing.

Several cleaning processes were used such as logical checks to clean variables such as gender and parity. Range checks were used to clean variables such as days of life, and to eliminate babies older than seven days of life. Cross tabulations were used to detect inconsistencies such as male having had three pregnancies.

On each day, neurologic exam was carried out and the infants categorized as normal versus abnormal based on the key below

	Level of consciousness	**Muscle tone**	**Seizures**	**Suck reflex**	**Moro reflex**	**Grasp reflex**
Abnormal- Grade II &III	Coma /Lethargic	Hypertonic /Hypotonic	Present	Absent /Weak	Absent /Depressed	Absent /Depressed
Normal – Grade I	Alert	Normal	Absent	Active	Normal	Normal

The Statistical Products and Services Solutions (SPSS) software version 17.0 software was used to analyze the questionnaires and daily assessment forms and created reports and graphs.

Categorical data such as neurological scores and AKI scores was summarized using proportions, while continuous data such as gestational age, birth weight, length, head circumference, were summarized using means/medians.

Bivariate analysis was used to test associations between the neonates /maternal factors and the adverse outcomes were performed using Chi-square test for categorical variables and comparisons of means and medians was done using Student's t test and Mann Whitney U test respectively.

Multivariate analysis was used to test the discharge status.

A mean score for each AKI stage was computed and compared using ANOVA test.

All tests of associations and comparisons were performed at 5% significance level (95% confidence interval).

6. ETHICAL CONSIDERATIONS

The study was undertaken after approval by the department of Paediatrics, UON and the Ethical Review Committee, KNH. Parents/ caregivers were given full explanation of the study and a written consent was sought from them. Emergency care and resuscitation was a priority to any other procedures. Study details were given to the immediate caregivers. No beneficial treatment was withheld from the study subjects. All information about the patient was treated with the strictest confidence.

7. RESULTS

7.1 General characteristics of all the mothers and neonates

Of the 968 newborns admitted into the KNH NBU during the study period, 60 infants met the inclusion criteria. The mean weight was 3373 g (SD=427.3) and length was 52.3 cm (SD=2.1) The neonates weight ranged from 2620 to 4600 g. Only 9% of the neonates admitted had a very low Apgar score as shown in table 1 below.

Table 2: Characteristics of the 60 neonates on admission

Variable	**Frequency (%)/ Mean (SD)**
Gender	
Male	37 (62)
Female	23 (38)
Mean clinical gestation in weeks	39.4 (0.87)
Mean birth weight in grams	3373 (427.3)
Mean length in cm	52.3 (2.1)
Mean head circumference in cm	34.8 (1.6)
APGAR Moderate Score : 4 – 6	49 (91)
Severe Score: 0- 3	5 (9)

Table 3: Characteristics of the delivery of the 60 neonates admitted

Variable	**Frequency/ (%)**
Place of delivery KNH Other health facility	 44 (76) 14 (24)
Mode of delivery Vertex vaginal Breech vaginal C/S Vacuum Extraction (V/E)	 33 (61) 1 (2) 18 (33) 2 (4)
APGAR Score Moderate (4-6) Severe (0-3)	52 (87) 8 (13)
Resuscitation with Bag Mask Valve (BVM)	24 (40)
Intubation + Mechanical ventilation	11 (18)

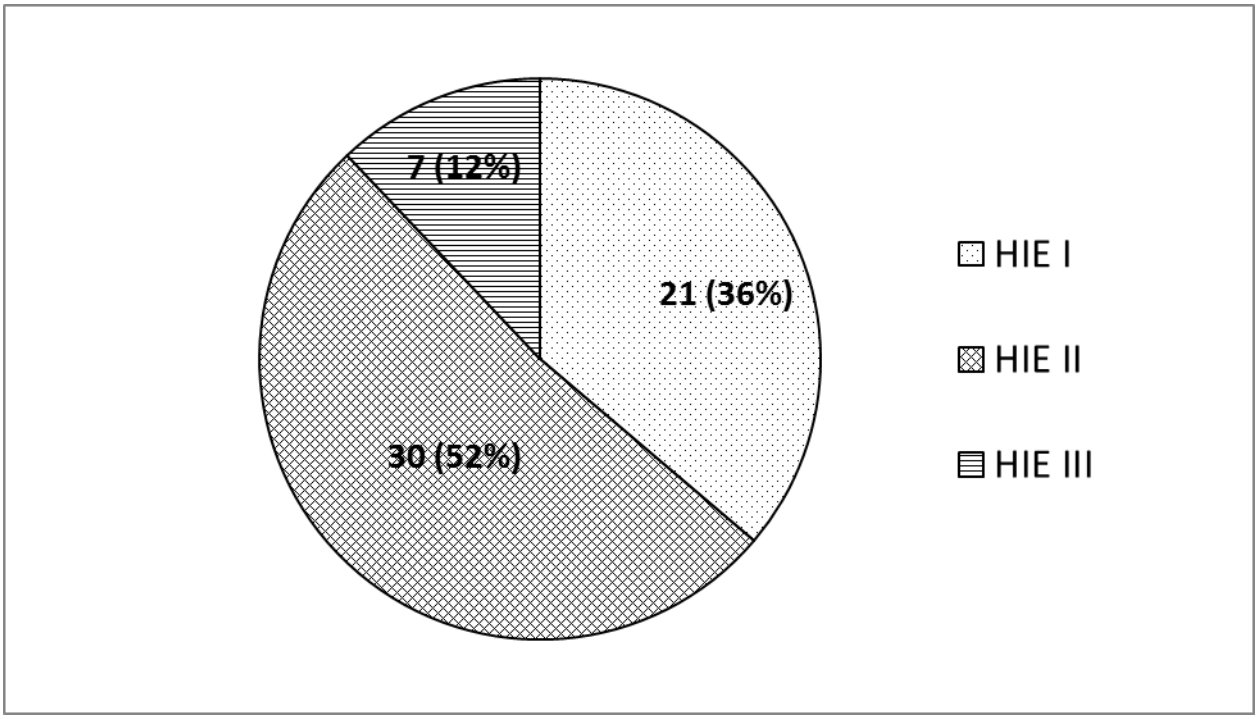
Most of the neonates were delivered in KNH- 76% but none was delivered at home. Most of the neonates were delivered by the vaginal route (63%)

Table 4: Characteristics of the mothers of the 60 neonates admitted

Variable	**Frequency (%) / N=60**
Marital status Married	 48 (80%)
Parity 0 (Primi) 1 2 ≥ 3	 32 (53%) 11 (18%) 6 (10%) 4 (7%)
Occupation Employed Unemployed	 41 (68%) 8 (13%)
Education level Primary and below Secondary and above	 9 (15%) 45 (75%)
ANC visits	54 (90%)
Number of Antenatal clinic visits Twice More than twice	 9 (15%) 45 (75%)
Maternal fever	4 (7%)
Antepartum haemorrhage	6 (10%)
High blood pressure	1 (2%)

The average age of the all the mothers was 26 years; 80% of them were married and 53% were primigravidae. The majority of the mothers were employed (68%) and had attained secondary level of education and above (75%). Almost all the mothers (90 %) reported having attended ANC with 75% having attended ANC more than twice as shown in table 4 above.

Figure 1: HIE stage of the 60 neonates on admission

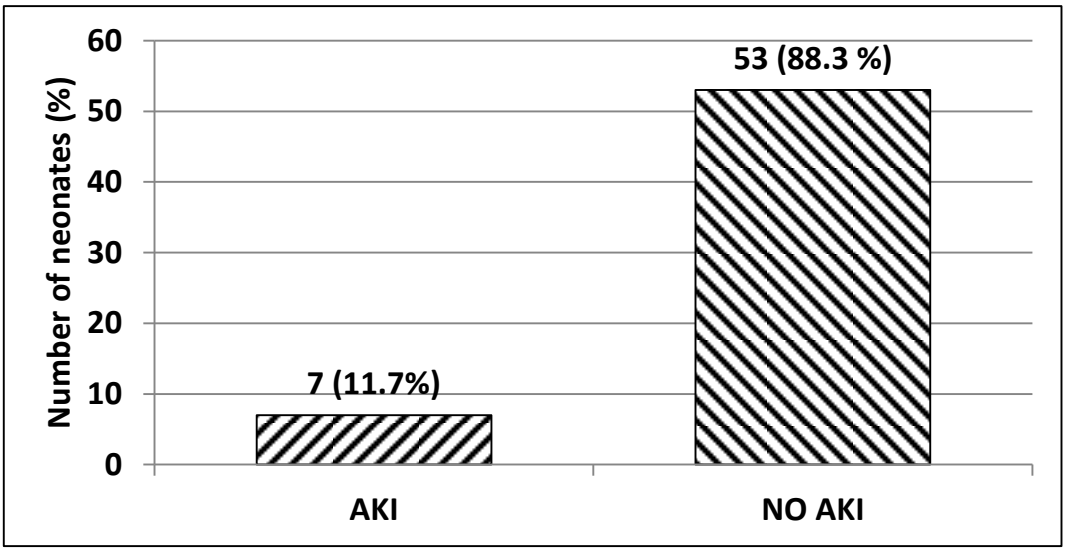


The degree of perinatal asphyxia was staged using Sarnat and Sarnat staging of Hypoxic Ischaemic Encephalopathy (HIE) on admission. Majority (52%) had stage 2 as shown in figure 1.

7.2 Characteristics of the neonates with AKI

Out of the neonates with AKI, **11.1 % (4/36)** were males and **12.5 % (3/24)** females.

Figure 2: Prevalence of AKI on day 3 of life



7 out of 60 neonates met criteria for AKI on day 3 which translates to a prevalence of **11.7%**

Figure 3: Correlation between HIE and AKI

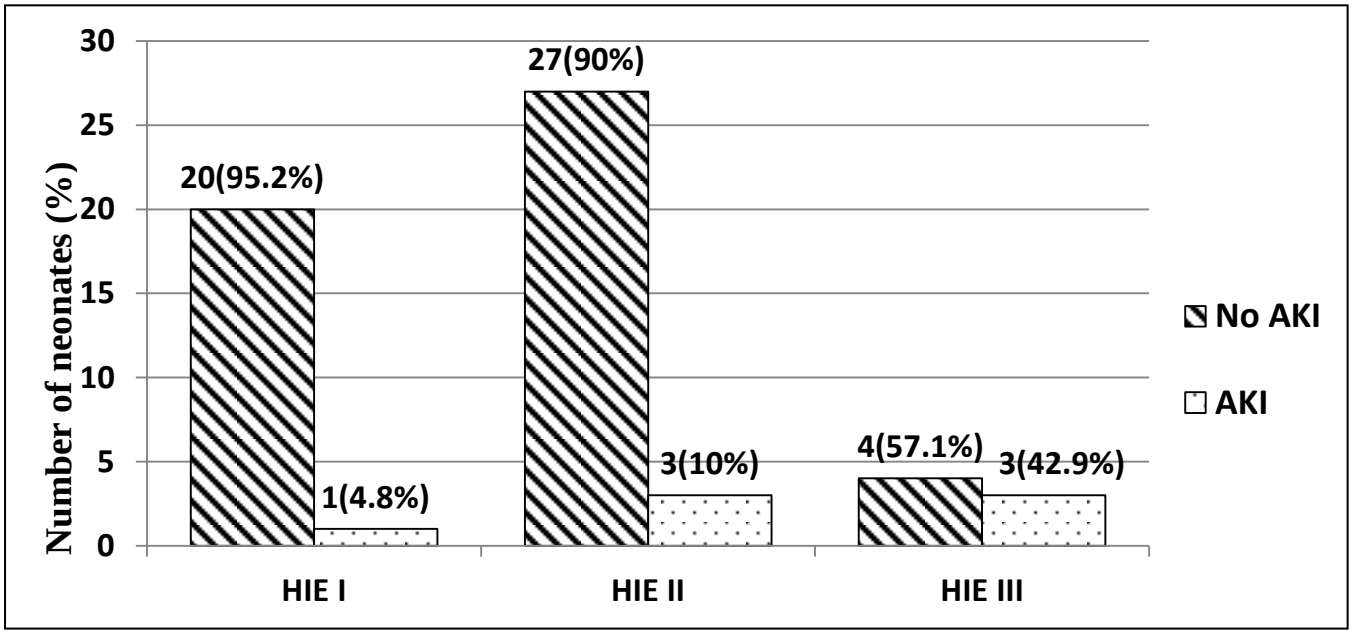


Figure 3 shows AKI was highest in the neonates with HIE 3 (42.9%) on day 3 of life and lowest in the neonates with HIE 1 (4.8%).

Table 5: Tests of Association between Neonatal characteristics and AKI

		AKI (n= 7)	No AKI (n= 53)	P value
Sex	Male	4 (57%)	32 (60%)	1.000
	Female	3 (43%)	21 (40%)	
Apgar	Moderate	6 (86%)	46 (87%)	1.000
	Severe	1 (14%)	7 (13%)	
Resuscitation		5 (83%)	19 (45%)	0.188
Place of delivery	KNH	5 (71%)	40 (75%)	1.000
	Other health facilities	2 (29%)	13 (25%)	
Intubation		1 (14%)	6 (12%)	1.000

*significant difference (P <0.05)

Table 5 above, shows there was no significant association between the mentioned neonatal characteristics and AKI.

Table 6: Tests of Association between Maternal characteristics and AKI

		AKI (n= 7)	No AKI (n= 53)	P value
Maternal Age {Median (IQR)}		29 (19-33)	27 (24-29)	0.630
Marital status	Single	1 (14%)	4 (9%)	0.522
	Married	6 (86%)	42 (91%)	
Occupation	Employed	4 (57%)	37 (88%)	0.075
	Unemployment	3 (43%)	5 (12%)	
Maternal Fever		1 (14%)	3 (6%)	0.220
APH		1 (14%)	5 (11%)	1.000
Level of education	Primary and below	2 (29%)	7 (15%)	0.330
	Secondary and above	5 (71%)	40 (85%)	
Mode of delivery	Vertex Vaginal	3 (43%)	30 (64%)	0.494
	Breech Vaginal	0 (0%)	1 (2%)	
	Caesarean	4 (57%)	14 (30%)	
	Vacuum extraction	0 (0%)	2 (4%)	

*significant difference (P <0.05)

According to the results summarized in the table 6 above, there is no significant association between maternal characteristics and AKI.

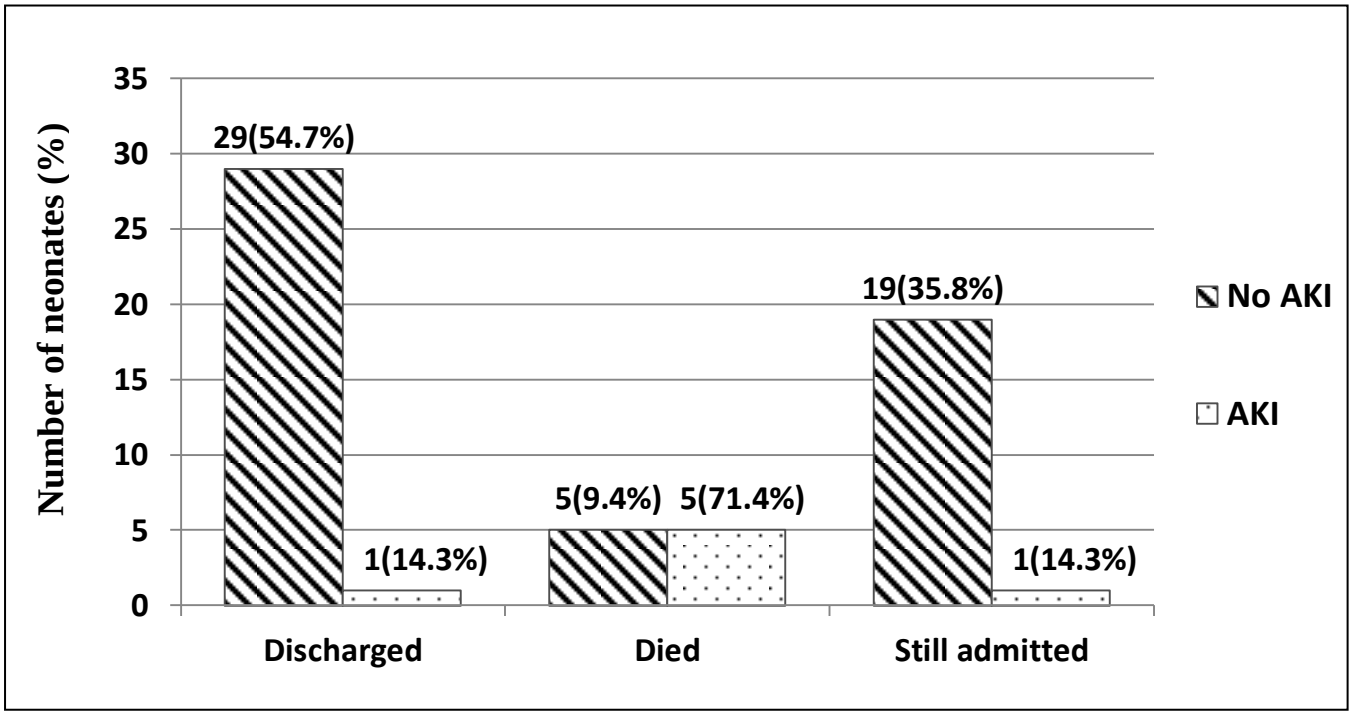
Table 7: Short-term outcomes of perinatal asphyxia associated AKI

	AKI (N=7)	No AKI (n=53)	OD (95% CI)	P Value
HIE I	1 (14%)	20 (38%)	1.00	
II	3 (43%)	27 (51%)	2.22 (0.2-23.0)	0.5
III	3 (43%)	4 (8%)	15 (1.2-183.6)	0.034*
Discharge in days {Median (IQR)}	5 (4-7)	5 (4-7)		0.56
Mortality	5 (71%)	5 (9%)	24 (3.7- 157)	0.001*
Time of death { Median (IQR)}	4.5 (3.5 -5)	4 (2-4)		0.45

* significant difference ($P < 0.05$)

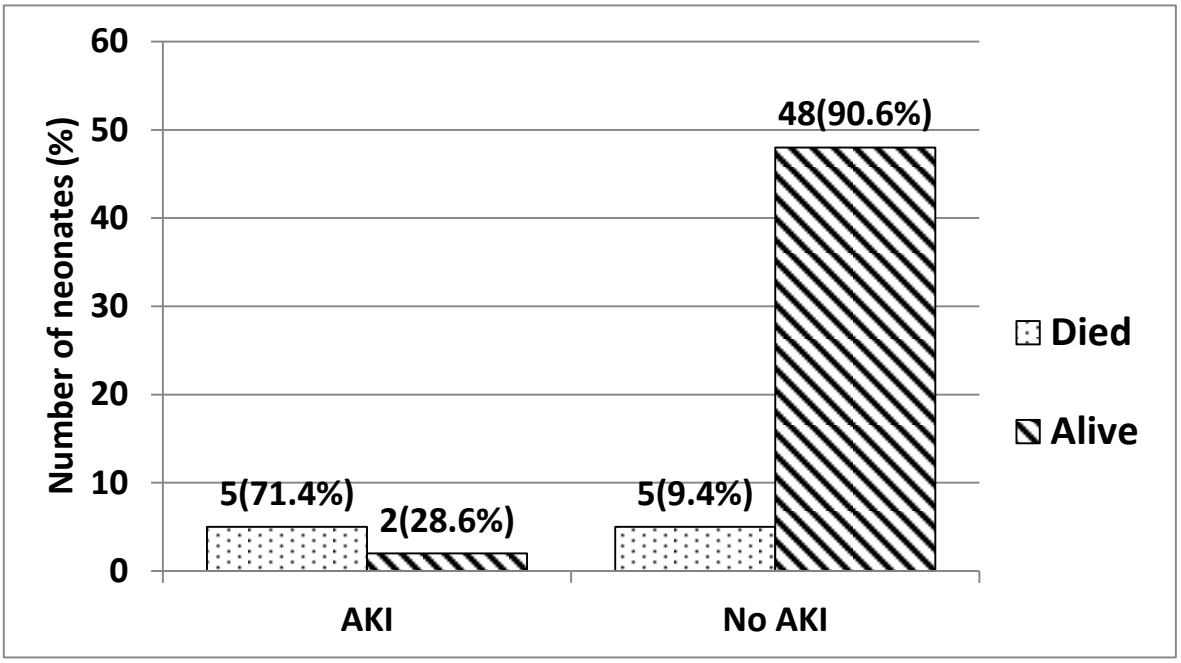
The mortality rate in perinatal asphyxia associated AKI was 71.4 %. There was a 15 fold increased risk of developing AKI in HIE III compared to HIE I, p=0.034 with {95% CI (1.2-183.6)}. There was 24 fold increase risk of death in AKI in HIE III compared to HIE I, p=0.001 with {95% CI (3.7-157)}. Median day of death in neonates with AKI was 4.5 days

Figure 4: Outcome of the neonates with AKI on day 7 of life



The figure 4 explains the outcome of all the neonates recruited by the 7th day of life. Out of all neonates recruited 54.7% of the neonates without AKI were discharged compared to only 14.3% of those with AKI by the 7th day of life. The higher percentage of the neonates who died with AKI (71.4%) compared to only 9.4% without AKI can be attributed to the small sample size. The small sample size can also explain the smaller percentage (14.3%) of those with AKI still admitted by day 7 of life compared to 35.8% without AKI.

Figure 5: Mortality by AKI diagnosis



The figure 5 shows a greater mortality rate (71.4 %) in the neonates with AKI. This value may be very high due to the small sample size number. The survival rate in the neonates without AKI is much better (90.6%) than those with AKI.

8. DISCUSSION

According to the Acute Kidney Injury Network (AKIN), AKI is an absolute increase in serum creatinine of $\geq$ 26.4µmol/l (or a percentage increase in serum creatinine of at least 50%) over two consecutive days. [23] Creatinine in the normal newborn at term by Schwartz is 79 µmol / l at day 1 and drops to 44 µmol / l) at day 5. [35] Before 48h of life, the serum creatinine reflects that of the mother. [24]

Studies by Jayshree et al. [25], Nouri et al. [26] and Gupta et al. [9] chose the threshold of 90 µmol / l for serum creatinine at 48 hours of life. Studies by Karlowicz [10] Kaur [28] chose the serum creatinine threshold of 133 µmol/l at 48 hours to make a diagnosis of AKI. In our study, the threshold of 133 µmol / l for creatinine at 72 hours of life was chosen in order to increase our possibility of diagnosis as there would be a marked reduction in the maternal creatinine level by then.

There is a high incidence of AKI among the asphyxiated term infants (7 – 72%). [9, 10] AKI after perinatal asphyxia was noted in 42% of cases by Martin-Ancel et al. [11] , 47% by Gupta et al. [9] , 68% for Aggrawal et al. [24] ,70% by Gluckman et al. [36], 17.2 % Nouri et al.[26] and 33% in our study. Our study noted a 11.7% prevalence rate hence lying within the range of most of the studies done. The prevalence rate would have been much higher than the Tunisia study if serum creatinine was sampled at 48 hours and a threshold of 90 µmol / l used.

The available studies show that the prevalence rates were similar in both resource poor and resource rich areas proving that AKI in perinatal asphyxia is a global problem.

The presence of perinatal asphyxia and its severity appear to correlate with increasing incidence of AKI. [9, 11] A study by Nouri et al. [26] showed that two thirds of newborns with AKI had HIE of grade II and 1/3 with AKI had HIE of grade III. However in his study no renal impairment was observed in newborns with grade I. The difference was not statistically significant (p = 0.13). Gupta et al.[9] however showed that blood urea and serum creatinine were significantly higher in asphyxiated and HIE babies compared to the control group ($P<0.001$) and ($P<0.05$) respectively hence showing the correlation between AKI and HIE. Kaur et al.[28] showed that AKI developed in one of 11 infants (9.1%) with moderate asphyxia and in 12 of 25 (56%) with severe asphyxia. Our study noted a 15 fold increase risk of developing AKI in HIE III compared to HIE I, p=0.034 with {95% CI (1.2-183.6)}. However there was no correlation between HIE II and I (p=0.50), and this could be explained by the small sample size. AKI was highest in the neonates with HIE 3 (42.9%) on day 3 of life and lowest in the neonates with HIE 1 (4.8%).

The small sample sizes in most studies have been a major hindrance in realizing associations between neonatal or maternal characteristics and AKI. Some authors have shown a correlation significant association between a low Apgar score at the 5th min and AKI, with a level of significance as low as p = 0.0013 by Nouri. [11,26] In our study 14% of the patients with severe Apgar score had AKI while the majority (86%) of the patients with moderate asphyxia had AKI. This could be explained by the fact that many of the patients who have severe asphyxia die before day 3 of life and hence are not included in the study. However, we found no significant correlation between the Apgar score and AKI (p=0.473). The outcome of AKI in critically ill neonates is poor; however, independent risk factors have not been definitively established. [37]

There are considerable rates of morbidity and mortality in asphyxiated newborns with acute renal failure, but the exact rates are difficult to estimate given the heterogeneity of the available studies. The presence of multiorgan dysfunction certainly seems to predict a worse outcome in infants with acute renal failure from any cause, including those with perinatal asphyxia. [4, 10, 21] The severity of initial asphyxia, as measured by either Apgar score at 5 minutes or hypoxic ischemic encephalopathy score, predicted renal failure better than serum creatinine or urinary B2M. [24] The severity of asphyxia best correlates with both the overall neurologic and renal outcomes. [10]

The mortality rates of perinatal asphyxia-associated AKI ranges between 2% and 20 % (p=0.11) [9, 26, 28] Our study revealed a 71.4 % mortality rate by day 7 of life in neonates with AKI compared to only 9.4% in the neonates without AKI. The median day of death in the neonates with AKI was 4.5 days. There was 24 fold increase risk of death in AKI, p=0.001 {95% CI (3.7-157)}. The high mortality rate and wide confidence interval could have been contributed to by the small sample size. AKI is not normally a direct cause of death. [38] The cause of death for patients diagnosed with AKI may not be the same as the cause of AKI. The mortality rate depends on other associated conditions like other organ failure, particularly cardiac failure, HIE and serious infection hence the difficulty in attributing the exact mortality secondary to AKI in our study and the previous ones.

9. STUDY STRENGTHS

- The study site has clinical guidelines on management of the common neonatal conditions. The residents working in the NBU have been trained in these guidelines; this reduced variations in supportive care for the study population.

- The principal investigator and assistant recruited all the neonates and were able to follow them up every day in the NBU. The daily observations of the study were similar to the standards used in the NBU hence data collection was without difficulty.

10. STUDY LIMITATIONS

- KNH is a tertiary hospital and one third of the patients in this study had been referred due to the severity of their illness. We were therefore unable to get a good representation of less severely asphyxiated babies.

- Duration of the study. The moderate and severely asphyxiated newborns are not common and the study would have needed to be conducted over a longer period to get a larger sample size.

- The study was unable to generate correlates and risk factors due to the small sample size.

11. CONCLUSION

1 out of every 8 neonates with perinatal asphyxia is likely to develop AKI with 5 out of 7 of these neonates likely to die by day 4 of life. AKI correlates with HIE, and the risk of developing AKI is higher with a more severe form of HIE. The neonates who have HIE III have a 15 times increased risk of developing AKI as compared to HIE I. The neonates who develop AKI have a 24 times increased risk of death as compared to HIE I. 1 out of 7 of the neonates who develop AKI will be discharged by day 7 of life.

12. RECOMMENDATIONS

- Clinicians should therefore endeavor to diagnose AKI and institute relevant measures from day 3 of life as late diagnosis of AKI leads to a severer form of AKI with poor prognosis.
- Larger studies need to be done to correlate maternal factors and perinatal asphyxia-associated AKI.

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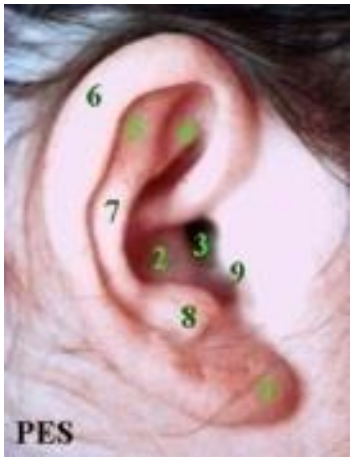
14. APPENDICES

APPENDIX I: FINNSTRÖM SCORE [31] (Add the total score and get the gestational age from the table below)

Score	**1**	**2**	**3**	**4**
Breast size	< 5 mm	5 – 10 mm	> 10 mm	
Nipple formation	No areola or nipple visible	Areola present, nipple well formed	Areola raised, nipple well formed	
Skin opacity	Numerous veins and venules present	Veins and tributaries seen	Large blood vessels seen	Few blood vessels seen or none at all
Scalp hair	Fine hair	Coarse and silky individual strands	Each hair appears as a single strand	
Ear cartilage	No cartilage in antitragus	Cartilage in antitragus	Cartilage present in antihelix	Cartilage in helix
Fingernails	Do not reach finger tips	Reach finger tips	Nails pass finger tips	
Plantar skin creases	No skin creases	Anterior transverse crease only	Two-thirds anterior sole creases	Whole sole covered

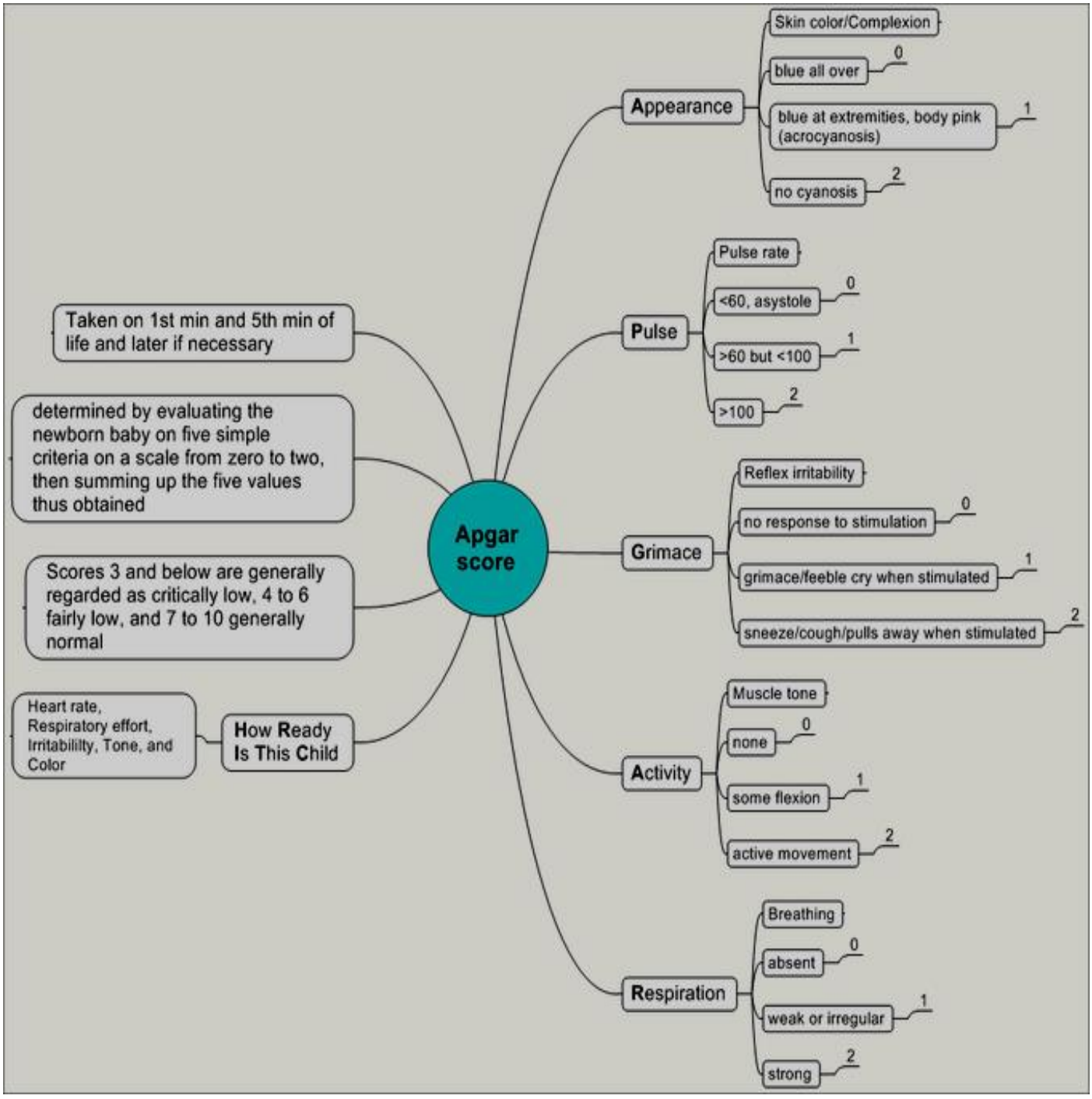
Maturity Score (Total)	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
Gestational age (weeks)	27	28	29	30	31	32	33	34	35	36	36.5	37.5	38.5	39.5	40	41	42



1 Lobe or lobule
2 Concha Bowl
3 External Acoustic meatus
4 Triangular fossa
5 Scapha
6 Helix
7 Antihelix
8 Antitragus
9 Tragus

Notes:
1. Test fingernails by scratching them along your hand.
2. Skin creases are the deep creases not the fine lines.
3. Palpate both ears and base your assessment on the most mature one

APPENDIX II: APGAR SCORE [29]



APPENDIX III: DEFINITION AND STAGING OF PERINATAL ASPHYXIA.

"Failure to initiate and sustain breathing at birth."[1] PLUS clinical evidence of hypoxic ischemic encephalopathy Sarnat and Sarnat stage 1, 2 or 3.

Sarnat and Sarnat Clinical Staging of Hypoxic Ischemic Encephalopathy. [30]

Variable	**Stage 1**	**Stage 2**	**Stage 3**
Level of consciousness	Alert/Hyperalert	Lethargy	Coma
Muscle tone	Normal	Hypotonia	Flaccidity
Seizures	Absent	Focal or Multifocal	Generalised
Reflexes			
Suck	Active	Weak	Absent
Moro	Exaggerated	incomplete	Absent
Grasp	Normal/ Exaggerated	Weak	Absent

APPENDIX IV:

INCIDENCE OF ACUTE KIDNEY INJURY IN MODERATE AND SEVERE PERINATAL ASPHYXIA STUDY QUESTIONNAIRE:

Questionnaire Serial Number:

1.0 Registration					
1.1 Questionnaire Serial No.		**1.2 Patient's Hospital No.**		**1.3 Date (dd/mm/yy)**	
2. 0 Personal details					
2.1 Gender	[_0_] Male		[_1_] Female		
2.2 Date of birth (dd/mm/yy)					
2.3 Time of admission into NBU (24 hr clock)					
2.4 Clinical gestation in weeks					
2.4 Birth weight in grams					
2.5 Length in centimeters					
2.6 Head circumference in centimeters					
2.8 Apgar score at 5 minutes	❑ Don't know				
2.9. Resuscitation with BVM	❑ Don't know		[_0_] No [_1_] Yes		
	2.9.1 *If yes for 2.9, what was the duration* in minutes?				
3.0 Intubation+ mechanical ventilation	[_0_] No [_1_] Yes				
4.0 Sarnat and Sarnat clinical staging of HIE					
4.1 Level of consciousness 2(alert/hyper alert), 1(lethargic),0(coma)					
4.2 Muscle Tone 2(normal),1(hypotonic),0(flaccid					
4.3 Suck reflex 2(active),1(weak),0(absent)					
4.4 Moro reflex 2(exaggerated),1(incomplete), 0(absent)					
4.5 Grasp reflex 2 (normal/exaggerated), 1(weak) 0(absent)					
4.6 HIE stage I(Normal), II(Abnormal) or III(Abnormal)					

5.0 Mother's Data		
5.1 Date of birth (dd/mm/yy) Enter at least year	❑ Don't know	[__|__]-[__|__]-[__|__]
5.2 Relationship to the newborn. If not mother	❑ Non-relative	[_1_] Mother [_2_] Father [_3_] Sibling [_4_] Grandparent [_5_] Other relative
5.3 Parity	❑ Don't know	
5.4 Marital status	❑ Don't know	[_1_] single [_2_] Married [_3_] Separated [_4_] Widowed
5.5 Occupation	❑ Don't know	[_1_] Salaried formal employment [_2_]Informal employment [_3_] Self employment [_4_] Casual worker [_5_] Unemployed
5.6 Level of education	❑ Don't know	[_1_] None [_2_] Primary not completed [_3_] primary completed [_4_] Secondary not Completed [_5_] Secondary completed [_6_] Tertiary and Beyond
5.7 Antenatal clinic visits	❑ Don't know	[_0_] No [_1_] Yes
5.7.1	*If yes for 5.7 how many times?*	[_1_] Once [_2_] Twice [_3_] more than twice
5.9 Place of delivery		[_1_] Home [_2_] KNH [_3_]Other health facility [_4_] On way to health facility
6.0 Mode of delivery		[_1_] Vertex vaginal [_2_] Breech vaginal [_3_] C/S [_4_] V/E
6.1 Maternal fever(within one week before delivery)	❑ Don't know	[_0_] No fever [_1_] Fever
6.2 Ante partum haemorrhage	❑ Don't know	[_0_] No bleeding [_1_] Bleeding
6.3 High blood pressure(Mother's case record)	❑ No info	[_0_] NO [_1_] YES
6.4 Convulsion during pregnancy	❑ Don't know	[_0_] NO [_1_] YES
6.5 Other chronic diseases	❑ Don't know	[_0_] NO [_1_] YES
6.5.1	*If yes for 6.5 what disease*	
6.6 Duration of labour	❑ Not known	
6.7 Duration of rupture of membranes	❑ Not known	
6.8 Amniotic fluid colour	❑ Not known	[_0_] Green [_1_] Clear

6.0 DAILY CLINICAL ASSESSMENT							
Time after initial assessment **Sign**	Day 1 Date: Time:	Day 2 Date: Time:	Day 3 Date: Time:	Day 4 Date: Time:	Day 5 Date: Time:	Day 6 Date: Time:	Day 7 Date: Time:
6.10 Level of consciousness 1(alert),2(lethargic),3(coma)							
6.11 Muscle tone 1(normal), 2(hypotonic), 3(flaccid)							
6.12 Seizures 1(absent), 2(focal/multifocal) 3(generalized)							
6.13 Suck reflex 1(active), 2(weak), 3(absent),							
6.14 Moro reflex 1(normal/exaggerated) 2(weak), 3(absent),							
6.15 Grasp reflex: 1(normal), 2(weak), 3(absent)							
6.16 HIE Stage: I(Normal), II(Abnormal) or III(Abnormal)							
6.20 Intubation+ mechanical ventilation [_0_] No [_1_] Yes							
6.30 Mode of feeding in 24 hours 1 (IVFluids) 2 (Breastmilk) 3(Formula) 4(Mixed feeding)							
6.31 Amount of feed in 24 hours 1(Less) 2(Adequate) 3(More)							
6.40 Serum creatinine in µmol/l on day 2 and 3							
6.50 Medications administered							
6.60 Status 1(Alive) 2(Dead)							
6.70 Discharge status 1(Yes) 2(No)							
6.71 If yes 1(with AKI) 2(without AKI)							

APPENDIX V:

STANDARD OPERATING PROCEDURES FOR THE MEASUREMENT OF WEIGHT, LENGTH, HEAD CIRCUMFERENCE AND URINE COLLECTION AND ASSESSMENT

Weight: Babies were weighed in the NBU nude in a warm environment using a basin scale with high sides to ensure baby's safety. Three weight readings were taken and an average taken to the nearest 0.1grams (gm). The scale was checked against a standard weight of two kilograms (kgs) at the beginning of each day and calibrated to zero.

Length: Length was measured with the help of an assistant using a stadiometer. Three supine measurements were taken and the average recorded to the nearest 0.1 centimeter (cm).

Head circumference: Head circumference was measured using a tape measure. Three occipitofrontal circumference measurements were taken and the average recorded to the nearest 0.1cm.

All fluid volume infusions, transfusions, and medications administered will be recorded.

Serum Creatinine collection and assessment

Serum creatinine values on first two days reflect maternal values. Normally creatinine level falls quickly from 70 µmol/l) at birth to 44 µmol/l at 5 - 7 days and reach a stable level of 26 µmol/l to 35umol/l by 9 days. [25]

The blood sample was collected on day 3 of life by quick heel sampling of 0.5ml to 1ml into a microtainer. The sample was then centrifuged within 2 hours and analysed using Cobas Integra machine using the compensated Jaffė method. The Cobas Integra automatically calculated the

analyte concentration of each sample. The Cobas Integra used the Precinorm U or Precinorm U plus for reference range control, while the Precipath U or Precipath U plus for pathological range control. The control interval was 24 hours. The machine was calibrated every seven days using deionised water as zero calibrater according to the standard reference material guidelines.

The test principle involved creatinine reacting with picric acid to form a yellow-red complex. The rate of the dye formation (color intensity) was directly proportional to the creatinine in the specimen. It was determined by measuring the increase in absorbance at 512nm. Serum and plasma samples contain proteins which react non-specifically in the Jaffé method. For compensation of serum and plasma results, values were automatically corrected by -18µmol/l.

APPENDIX VI: CONSENT FORM FOR PARENTS/ GUARDIANS OF PARTICIPANTS

TITLE	**PREVALENCE AND SHORT-TERM OUTCOMES OF ACUTE KIDNEY INJURY IN TERM NEONATES WITH MODERATE TO SEVERE PERINATAL ASPHYXIA AT THE KENYATTA NATIONAL HOSPITAL NEWBORN UNIT**				
SCOPE	This informed consent form is for enrolled participants in the study, and will be read to them by a qualified research assistant before answering the questionnaire.				
SERIAL NO.		DATE		SITE	KNH NBU

Investigator: Dr. Dan Alaro,

Tel 0721-298722 Email: danalaro@gmail.com

Address- 25750-00100 Nairobi, Kenya

Sponsor: KNH- Department of Programs and Research

This Informed Consent Form has two parts:

- Information Sheet (to share information about the study with you)
- Certificate of Consent (for signatures if you choose to participate)

You will be given a copy of the full Informed Consent Form.

Part 1: Information Sheet

Introduction We are inviting you to participate in this study to determine the prevalence and short-term outcomes of acute kidney injury in term neonates with moderate to severe perinatal asphyxia at the Kenyatta National Hospital Newborn Unit.

Perinatal asphyxia is a condition resulting from your new born baby failing to breathe immediately after birth. This problem may be associated with kidney disease and its early detection will help early initiation of appropriate care.

You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

This consent form may contain words that you do not understand. Please stop the research assistant to stop as you go through the information and they will take time to explain. If you have questions later, you can call the investigator at any time.

Purpose of the study: The study primarily aims to determine the prevalence and short-term outcomes of acute kidney injury in term neonates with moderate to severe perinatal asphyxia at the Kenyatta National Hospital Newborn Unit. This information will help us in making certain recommendations regarding service provision so as to improve health care.

Procedures: You will be provided with a questionnaire. You may answer the questionnaire yourself, or it can be read to you and you can say out loud the answer for the investigator or assistant to write it down. If you do not wish to answer any of the questions included in the survey, you may skip them and move on to the next question. This interview is expected to last about 20 minutes The information recorded is confidential, your name is not being included on the forms, only a number will identify you, and no one else except the research investigators have access to your details.

Sampling: The kidney function of your baby will be assessed by taking a blood sample on the second and third days of life. The amount of urine passed by your baby will be collected on the third day of life by way of a urethral catheter and a urine bag.

Risks: We are asking you to share with us some very personal and confidential information, and you may feel uncomfortable answering some of the questions. You do not have to answer any question if you don't wish to do so. You do not have to give us any reason for not responding to any question.

Benefits: You will benefit from improved quality of services provided at the newborn unit as a result of this study.

Confidentiality: We will not be sharing information about you to anyone outside of the research team. The information that we collect from this research project will be kept private. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up under lock and key. It will not be shared with or given to anyone except the research team who will have access to the information.

Sharing Results: Nothing that you tell us today will be shared with anybody outside the research team, and nothing will be attributed to you by name. The knowledge that we get from

this research will be shared with you and other parents of babies in the newborn unit before it is made widely available to the public. Each participant will receive a summary of the results. There will also be small meetings and these will be announced. Following the meetings, we will publish the results so that other interested people may learn from the research.

Who to contact: If you have any questions, you can ask them now or later. If you wish to ask questions later, you may contact the principal investigator on the contacts given in this consent form.

This proposal has been reviewed by the Kenyatta National Hospital/University of Nairobi Ethics and Review Committee (KNH/UON ERC) which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find about more about the IRB, contact

The Chairman,

Kenyatta National Hospital/University of Nairobi Ethics and Review Committee

P.O.BOX 20723

Nairobi, Kenya.

Part II: Certificate of consent.

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions I have been asked have been answered to my satisfaction. I consent voluntarily to be a participant in this study

Print Name of Participant_____

Signature of Participant _____

Date _____ Day/month/year

If illiterate1: I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

1 A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

Print name of witness_____ Thumbprint of participant 

Signature of witness _____

Date _____

Day/month/year

Statement by the researcher/person taking consent

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that a questionnaire will be administered to the participant. I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Date _____ (Day/month/year)

FOMU YA KUPATA KIBALI CHA WAZAZI / WALEZI WA WASHIRIKI

Kifunguo: Hii fomu ya kupata idhini ni kwa ajili ya watoto waliolazwa katika Hospitali ya Taifa ya Kenyatta, ambao tunuwakaribisha kushiriki katika utafiti. Jina la mradi wa utafiti wetu ni "Ufanisi wa kiwango cha ugonjwa wa kupumua na figo kwa watoto wachanga. "

Mimi ni Dk. Dan Alaro, mwanafunzi katika Chuo Kikuu cha Nairobi kutafuta masomo ya utaalamu katika afya ya watoto. Mimi ninafanya utafiti juu ya ugonjwa wa kupumua kwa watoto ambao wamekishazaliwa kwa muda usiozidi siku moja ambayo ni kawaida sana katika nchi hii. Nitakupa taarifa na kukukaribisha kwa utafiti huu.

Kunaweza kuwa na baadhi ya maneno ambayo huelewi. Tafadhali uliza na mimi nitachukua muda kueleza. Kama una maswali baadaye, unaweza bado kuniuliza

Sababu ya utafiti: Ugonjwa wa kupumua unaweza kusababisha magojwa mengine kwa kila kiungo kwa watoto ambao wamekishazaliwa. Utafiti huu utazingatia ugonjwa wa figo kwa hawa watoto ambao wamekishazaliwa na shida ya kupumua. Ugonjwa huu husababaisha maafa mengi kwa watoto wachanga ndiposa umuhimu wa kuuangaza mapema na kuutibu mapema.

Maandalizi ya utafiti: Utafiti huu utahusu kupima damu na makojoo kwa motto wako ili kuweza kupata ugonjwa wa figo mapema na kuitibu mapema. Utafiti utafanyiwa kwa njia ya kupitia mahojiano ya moja kwa moja.

Kushiriki katika utafiti huu ni wa hiari kabisa. Ni uchaguzi wako kama kushiriki au la. Usipochagua kushiriki bado utapokea huduma zote katika hospitali hii. Unaweza kubadilisha mawazo yako baadaye na kuacha kushiriki hata kama walikubaliana awali. Unaweza kujiondoa katika utafiti huu wakati wowote.

Utafiti utafanyika katika kipindi cha siku saba za kwanza za maisha ya motto wako. Wakati huo, tutathmini afya ya mtoto wako kila siku.

Maadhara: Utafiti wetu haitamthuru mtoto wako.

Habari kukuhusu ambayo tutakusanya kutoka mradi wa utafiti huu utakuwa siri.

Mawasiliano: Kama una maswali yoyote unaweza kuuliza hivi sasa au baadaye, hata pia baada ya utafiti imeanza. Kama unataka kuuliza maswali baadaye, unaweza kuwasiliana nami kupitia nambari hizi: 0721298722.

Nimesoma/ Nimesomewa maelezo haya na nimepewa nafasi ya kuuliza maswali kuhusu hayo maelezo. Nimeidhini kwa hiari kushiriki katika utafiti huu.

Jina la lako_____

Sahihi ya Mshiriki _____

Tarehe_____

Nina uhakika kuwa nimemsomea mwakilishi fomu hii, na kwa kadri ya uwezo wangu nilihakikisha kwamba mshiriki ameelewa.

Niluthibitisha kuwa mshiriki alipewa nafasi ya kuuliza maswali kuhusu utafiti nakuyajibu vema kwa kadri ya uwezo wangu. Mimi nathibitisha kwamba mwakilishi hakulazimishwa kutoa kibali

Jina la Mtafiti / Mtu kuchukua kibali_____

Sahihi ya Mtafiti / mtu kuchukua kibali_____

Tarehe _____