SHORT TERM OUTCOMES OF TERM NEONATES ADMITTED WITH PERINATAL ASPHYXIA IN KENYATTA NATIONAL HOSPITAL NEWBORN UNIT

A dissertation submitted in part fulfillment of the requirements for the Masters of Medicine degree in Paediatrics and Child health in the University of Nairobi.

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DECLARATION

This dissertation is my original work and has not, to my knowledge been submitted in any other university or forum.

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We certify that this dissertation has been submitted for examination with our approval as University supervisors.

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DEDICATION

This dissertation is dedicated to my parents whose love and encouragement in life made me what I am.

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LIST OF ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
ANC	Antenatal Clinic
APH	Antepartum Haemorrhage
BP	Blood Pressure
CM	Centimeter
DALYS	Disability Adjusted Life Years
HIE	Hypoxic Ischemic Encephalopathy
IUGR	Intrauterine Growth Restriction
KG	Kilogram
KNH	Kenyatta National Hospital
NICU	Neonatal Intensive Care Unit
MDG	Millennium Development Goal
NBU	Newborn Unit
PROM	Prolonged Rupture of Membranes

SIN	Subject Identification Number
SOP	Standards Operating Procedures
UK	United Kingdom
WHO	World Health Organisation

DEFINITION OF TERMS:

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 as shown in appendix I

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

Outcome: Clinical improvement, persistence of neurological signs or death by day 7 of life.

Adverse Outcome:

- Persistence of abnormal neurological signs by day 7 of life, including hypotonia, hypertonia, seizures, abnormal suck/Moro/grasp reflexes and impaired level of consciousness. These parameters are outlined in appendix II
- Death

ABSTRACT

Background: Perinatal asphyxia contributes significantly to perinatal morbidity and mortality especially in resource poor countries. In Kenyatta National Hospital (KNH) perinatal asphyxia on an average accounts for 20% of the weekly admissions to the Newborn Unit (NBU). The short term outcomes and factors associated with adverse outcome have not been established.

Study objectives

To determine the short term outcomes and the factors associated with adverse outcomes in term babies with perinatal asphyxia in KNH NBU.

Methods

A hospital based short longitudinal survey study, was carried out at the Newborn Unit, Kenyatta National Hospital during the period of 6 months from June 2010 to November 2010. All term neonates with the diagnosis of perinatal asphyxia based on failure to initiate and sustain breathing at birth PLUS clinical evidence of hypoxic ischemic encephalopathy were eligible for inclusion. Neonates were evaluated clinically every 24 hours for the first 7 days of the neonate's life for the primary outcomes of clinical improvement, persistence of abnormal neurological signs or death by day 7 of life.

Results

119 neonates were enrolled into the study. By day 7 of life, 31.1% of infants with perinatal asphyxia had died and another 31.1% continued treatment. The rest of the infants (37.8%) had been discharged from the hospital with 6.7% being infants discharged with neurologic sequelae and 31.1% discharged with no neurologic sequelae. Babies had increased risk of adverse outcome if their mothers' were unemployed, $P< 0.001$, education level below secondary, $P<0.001$ or had less than two Antenatal Clinic visits (ANC), $P< 0.001$. Delivery outside KNH, prolonged labour, lack of resuscitation with Bag Valve Mask (BVM) and presence of seizures were also associated with adverse outcome ($P<0.001$)

Conclusions

- At KNH NBU, perinatal asphyxia has 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.
- Babies had increased risk of death if they were delivered outside KNH, had an Apgar score of less than 3 at five minutes, had seizures and if their mothers' were unemployed, had education level below secondary or attended ANC≤ 2 times. Other factors include prolonged labour and lack of resuscitation with BVM

Recommendations

- In a resource constrained country like Kenya, efforts should be put on preventing birth asphyxia through sensitizing mothers/communities on the need for regular ANC visits and delivery in good health institutions.
- Follow up study should be done on the long term outcome of babies with moderate and severe asphyxia discharged from the newborn unit.

1. INTRODUCTION AND LITEARATURE REVIEW

Perinatal asphyxia is defined by the World Health Organisation (WHO) as "Failure to initiate and sustain breathing at birth."[1] Accurate estimates of the proportion of neonatal deaths and disability due to perinatal asphyxia are limited by lack of consistent definition for use and by the fact that large proportion of births and deaths occur in non hospital settings. Because of the limited availability of data, the real proportion of mortality and morbidity due to asphyxia is generally underestimated.

Improvements in primary healthcare in most industrialized countries has led to a significant reduction in the incidence of perinatal asphyxia and less than 0.1% newborn infants die from it.[2] Studies in the UK and other developed countries have shown that the incidence of HIE is approximately 6 per 1000 live births and accounts for up to 25% of perinatal mortality in full term infants.[3]

In the developing world perinatal asphyxia remains a major cause of death and disability in the neonatal period. Each year nearly 4 million newborns suffer moderate to severe birth asphyxia with at least 900,000 dying and at least an equal number developing sequelae such as epilepsy, mental retardation, cerebral palsy and learning disabilities.[4]The numbers of disability adjusted life years(DALYS) for birth asphyxia exceeds those due to all childhood conditions preventable by immunization.[5]

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 2003 KDHS.[6] there are very few epidemiological data on birth asphyxia in Kenya. Data from Kenyatta National hospital newborn records indicate that birth asphyxia is one of the three leading causes of newborn death. The other two being infections and prematurity.[7] In KNH on an average twenty percent of weekly admissions to NBU are due to perinatal asphyxia.[7]

Perinatal asphyxia can be caused by events that have their roots in either the antepartum, the intrapartum, or the postpartum period or combinations thereof. In developed countries where intrapartum complications are rare events, cases of perinatal asphyxia are more commonly related to antepartum causes.[8] In developing countries, given the higher incidence of serious

complications in labour and reduced availability of skilled care during delivery, [9, 10] it is likely that intrapartum causes account for a larger proportion of cases of perinatal asphyxia.

The major manifestation of asphyxia results from a combination of hypoxia and ischaemia of the brain and other vital organs. The features of hypoxic-ischaemic encephalopathy are decreased level of consciousness, poor tone, decreased spontaneous movement, periodic breathing or apnea, and seizures. Brainstem signs (oculomotor and papillary disturbances, absent gag reflex) may also be present. The severity and duration of clinical signs correlate with the severity of the insult. These clinical signs related to HIE are useful diagnostic and prognostic tool in birth asphyxia.[39]

Several other techniques are available for use in the first few hours of life to recognize neurological damage and to assess the extent of HIE. These include electroencephalogram (EEG), computer tomography (CT) scan, cerebral function monitoring, cranial ultrasound and Doppler flow ultrasound of middle cerebral artery. Magnetic resonance imaging (MRI), particularly diffusion-weighted imaging is useful in the early evaluation of patients with perinatal asphyxia, [39] these modalities are however not available in many neonatal units in developing countries.

Management is directed at supportive care and treatment of specific abnormalities. Fluids should be restricted initially to 60-80mls/kg; oxygenation should be maintained with mechanical ventilation if necessary. Blood pressure and glucose should be maintained within normal ranges. Hypocalcaemia, coagulation abnormalities and metabolic acidemia should be corrected and seizures treated with intravenous Phenobarbital.[39] In our set up management of neonates with hypoxic ischemic damage is largely limited to supportive medical care.

Early assessment of the degree of resulting hypoxic ischemic damage and the risk for adverse outcome can provide useful information for both clinical management and the potential use of neuro-protective strategies. These strategies can prevent secondary neuronal injury when given within the therapeutic window of 5 to 6 hours from the insult.[21] Several randomized controlled studies have looked at therapeutic hypothermia and outcome in infants with moderate-to-severe hypoxic ischaemic encephalopathy and found that therapeutic hypothermia safely improves

survival without severe neurologic disability[22, 25] however, in resource constrained country like Kenya prevention is more important than treatment.

The most widely used classification of HIE is that of Sarnat and Sarnat which is an objective method of classifying the degree of encephalopathy and predicting outcome.[12] HIE is characterized by variable alterations in consciousness, reflex patterns, muscle tone and possible brainstem and autonomic dysfunction. It has been described as the single most useful indicator that a significant hypoxic ischemic insult has occurred and the best indicator of infants at risk for neurosequelae,[13, 14] its usefulness as an indicator has been demonstrated in several prospective studies with extended follow-up of children to school age.[15-19]

Table 1. Sarnat and Sarnat Staging of Hypoxic Ischemic Encephalopathy.[12]

Variable	Stage 1	Stage 2	Stage 3
Level of consciousness	Alert/hyperalert	Lethargy	Coma
Muscle tone	Normal	Hypotonia	Flaccidity
Seizures	Absent	Focal or Multifocal	Decerebration/ generalised
Reflexes			
Suck	Active	Weak	Absent
Moro	Exaggerated	Incomplete	Absent
Grasp	Normal/ exaggerated	Weak	Absent

The key factor with regard to the predictive power of HIE grade relates both to its severity [15-19] and the actual duration of observed signs.[16-18] Newborns with mild grade tend to have a normal outcome; those with a severe grade of HIE will either die, have significant neuromotor or cognitive disability, or both.[16-18] Those infants with a moderate grade of HIE have a 20% chance of subsequent death or significant neurologic sequale.[16-18] Demonstration of recovery from a more severe grade of neonatal encephalopathy by one week of age is thought to be a good prognostic indicator.[20] In effect, waiting until the infant is one week old allows the individual

child to demonstrate its intrinsic potential for recovery from asphyxia. This potential for recovery can be substantial and has marked inter-individual variability.

Most of the studies on the outcome of newborns with perinatal asphyxia have been carried out outside Africa and have come up with different results. Garbutt et al in a retrospective descriptive study on the outcome of neonates with HIE admitted to the neonatal unit of the University Hospital of the West Indies (UHWI), Jamaica recruited 95 neonates, eighty six of the neonates were born in UHWI. Twenty nine (31%) of infants having stage-I, 41(43%) had stage-II and 25(26%) had stage-III HIE. Discharge neurologic exam was found to be normal in 60 (71%) of the neonates and an abnormality was detected in 17(20%) patients, 26% of stage 2 survivors and 50 % of stage 3 survivors. Stage 3 HIE survivors had increased neurological deficits compared with those with stages 1 and 2 survivors ($p<0.001$). These neurological deficits included hypertonia, hypotonia and persistent seizures. All those who died had stage 3 HIE.[26]

In Papua New Guinea a study by Oswyn G et al on the immediate outcome of newborns with perinatal asphyxia, recruited 125 babies, 36% had stage I, 41.8% stage II and the remaining 22.2% had stage III HIE. They reported 88.2% Mortality in stage III infants. All surviving stage III infants and 52% of stage II had a neurologic deficit. There was no mortality in stage I infants.[27] Factors associated with adverse outcome were prolonged duration of labour ($p< 0.001$) and severity of HIE ($p<0.001$).

In a retrospective study on clinical course and outcome of perinatal asphyxia carried out in a Paediatric unit in Goteborg, Sweden by Thonberg et al involving 65 newborns with HIE found 36 had mild, 17 moderate and 12 severe HIE. All the neonates with severe HIE and one with moderate HIE died. Discharge neurologic exam was normal in all neonates with mild (stage -I) HIE and 50% of those with moderate (stage-II) HIE. Factors that were associated with the outcome (death or neurologic disability) were the stage of HIE, type of resuscitation (BVM versus intubation and mechanical ventilation) and presence of seizures in the infant. There was no association between the outcome and socio-demographic characteristics of the mother and antenatal events.[28]

Finner et al in a prospective study done in Canada on perinatal factors and outcome of HIE in term neonates recruited 95 neonates. 35% had stage-I, 50% were stage-II, and 15% were stage-

III. None of the neonates who had stage-I died or had any significant neurologic handicap, in contrast all those with stage 3 had died or suffered severe neurologic disability. There was only one mortality in stage-II neonates with 20(51%) having neurologic deficit. Factors which significantly correlated with outcome included the Sarnat stage of HIE (p= 0.001), five-minute Apgar score (p<0.001), delayed onset of spontaneous respiration to 30 minutes and need for mechanical ventilation(x2 14.16, p=0.007). There was no association between the presence of seizures(x2= 4.34, p=0.362), inborn versus those transferred infants, socio-demographic, antepartum and intrapartum variables and subsequent outcome.[16]

In a retrospective study by Toh et al in Singapore to evaluate the aetiology, severity, outcome and factors predicting neurological outcome in term babies who sustained perinatal asphyxia, recruited 23 newborns. Two infants (8.7%) had stage- I HIE, 12(52.2%) had stage-II and the remaining 9 (39.1 %) stage-III HIE. Eight infants with stage III and one in stage II died. One infant with stage III and five with stage II survived with neurological sequelae. There were no death or neurologic sequelae in infants with stage I. Factors that were associated with favourable outcome were Apgar score>5 at five minutes (p< 0.05), stage-I HIE (p<0.05). Antepartum and intrapartum factors were not associated with the outcome.[30]

In an observational study conducted in Lahore, Pakistan to determine antenatal and perinatal risk factors for adverse outcome in babies with birth asphyxia, recruited 144 asphyxiated term infants. 36.8% had stage-I, 32% had stage-II and 20.8% had stage III HIE. Mortality was 100% in stage III, 56.52% in stage II and 3.78% in stage I HIE patients respectively. Variables (risk factors) found significantly associated with adverse outcome were late arrival of the newborns to the tertiary unit (p<0.001), stage of HIE (P< 0.001) and prolonged duration of labour (p<0.001). Factors such as parity, mother's age, place of delivery and mode of delivery had no association with the outcome.[31]

Closer to home in Uganda, a study done in Mulago hospital on the immediate outcome of babies with low apgar scores(within the first 48 hours) found HIE was present in 27(24.8%) of the babies with low Apgar scores, 13 of whom had moderate HIE and 1 with severe HIE. Overall Mortality was 12.1%. Poor obstetric history (previous perinatal morbidity and mortality) in the mother was associated with a baby dying in the first 43 hours after birth. In the baby the risk factor for poor outcome included the severity asphyxia and sustaining birth injury (p<0.001).[32]

***Table 2:* Summary of Studies on the outcome of perinatal asphyxia**

Study design	Country	Sample size	Study title	Outcome
Seyal, 2009, Observational study	Pakistan	144	Factors related to adverse outcome in asphyxiated babies	HIE I- 36.8% II- 32% III- 20.8% Overall mortality- 40.3% with 100% mortality in stage III infants. Factors associated with adverse outcome were late arrival, prolonged duration of labour and severe HIE. Parity and mode and place of delivery did not influence outcome
Garbutt,2009, Retrospective descriptive	Jamaica	95	Outcome of neonates with hypoxic ischemic encephalopathy admitted to the neonatal unit in UHWI	HIE I- 31% II- 43% III- 26% Death only happened in stage III infants. Abnormal neurologic exam was found in 26% of stage II and 50% of stage III survivors.
Ondoa, 2003, Prospective case control	Uganda	124	Immediate outcome(48 hours) of babies with low Apgar score in Mulago hospital Uganda	Adverse outcome in 57.3% of cases. Mortality 12.1%. Poor outcome was associated with birth injury and severe asphyxia

***Table 2:* Summary of Studies on the outcome of perinatal asphyxia**

Study design	Country	Sample size	Study title	Outcome
Oswyn, 2000, prospective descriptive	Papua New Guinea	125	Perinatal asphyxia at Port Moresby General Hospital: a study on outcome and factors associated with adverse outcome.	HIE I- 36% II- 41.8% III- 27.2% 88.2% of stage III infants died. Neurological abnormality was found in 52% of stage II and all surviving stage III infants. No mortality in stage I infants. Factors associated with adverse outcome was duration of labour and severity of HIE.
Toh,1999, retrospective descriptive	Singapore	23		HIE I- 8.7%; no death or neurologic disability II- 52.2%; 8.3% died, 41.6 had neurologic sequelae III- 39.1%; 88.8% died, all survivors had neurologic disability. Factors associated with favourable outcome were Apgar score> 5, stage I HIE.
Thonberg, 1995, Retrospective descriptive	Sweden	65	Birth asphyxia: incidence, clinical course and outcomes in Swedish population	HIE I- 55% II- 26.5% III- 18.5% All stage III infants died. Discharge neurological exam was abnormal in 50% of stage II infants. Factors associated with adverse outcome were severity of asphyxia, intubation, presence of seizures

***Table 2:* Summary of Studies on the outcome of perinatal asphyxia**

Study design	Country	Sample size	Study title	Outcome
Finer, 1981, Prospective descriptive	Canada	95	Hypoxic-ischemic encephalopathy in term neonates: Perinatal factors and outcome	HIE I- 35%; no death or neurologic disability II- 50%; 1% death,51% neurologic deficit III- 15%- 70% died and all the survivors had neurologic deficit. Factors significantly correlated with outcome were HIE stage, 5 minute Apgar score, time of onset of spontaneous respiration and mechanical ventilation

2. STUDY JUSTIFICATION/UTILITY

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 neurological disability.

Identifying factors associated with adverse outcome in our set up will facilitate appropriate decision making regarding aggressive interventional treatment in KNH NBU and at the same time suggest preventive measures which can be formulated at KNH and peripheral health facility settings from where these babies are referred from. There is little data on perinatal asphyxia and its outcomes in newborns in KNH and indeed in Kenya; the study results will shed some light on this and help with planning care for such babies in addition to, acting as a guide for other studies on perinatal asphyxia in KNH NBU.

3. STUDY OBJECTIVES

3.1 Primary objective:

- To determine the day 7 outcome of term neonates admitted at KNH NBU with perinatal asphyxia

3.2 Secondary objective:

- To describe infant and maternal factors associated with adverse outcomes in neonates with perinatal asphyxia admitted at KNH NBU.

4. METHODOLOGY

4.1 Study Design:

This was a hospital based short longitudinal survey.

4.2 Study Area:

This study was carried out in the Newborn unit of Kenyatta National Hospital, 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 between160 and 200 neonates each month, over 20% whom are term babies diagnosed with perinatal asphyxia.

4.3 Study Population:

All term newborns admitted within 24hrs of delivery to KNH NBU with diagnosis of perinatal asphyxia during the study period.

4.4 Sample Size

Sample size (N) will be calculated using Fischer's formula

$$n = \frac{z_{\alpha}{}^{2}\, p(1-P)}{d^2}$$

n= Minimum sample size

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

P= is the estimated proportion of death in newborns with perinatal asphyxia. 12.1%[22]

d= level of precision (set at±5%)

$$n = \frac{1.96^2 \, X \, 0.121(1 - 0.121)}{0.05^2} = 163$$

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.

$$n_f = \frac{n}{1 + n/N}$$

n= the calculated sample size = 163

N= the estimated total population of newborns with perinatal asphyxia in a year = 300.

$$n_f = \frac{163}{1 + 163/300} = 106$$

A minimum sample size of 106 babies will be recruited into this study.

4.5 Study Period

This study was carried out from June 2010 to November 2010.

4.6 Recruitment of Study Participants:

Patients were recruited from the KNH NBU. All term neonates admitted at KNH NBU were screened for perinatal asphyxia using the Sarnat and Sarnat clinical staging of hypoxic ischemic encephalopathy outlined in appendix I. The most severe sign was used to categorise the severity of the perinatal asphyxia.

The inclusion criteria were:

- Term newborn as per Finnstrom gestational age assessment as outlined in appendix III
- Admitted into KNH newborn unit within 24 hours of delivery
- Consent by the parent or caregiver.

The exclusion criteria were:

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

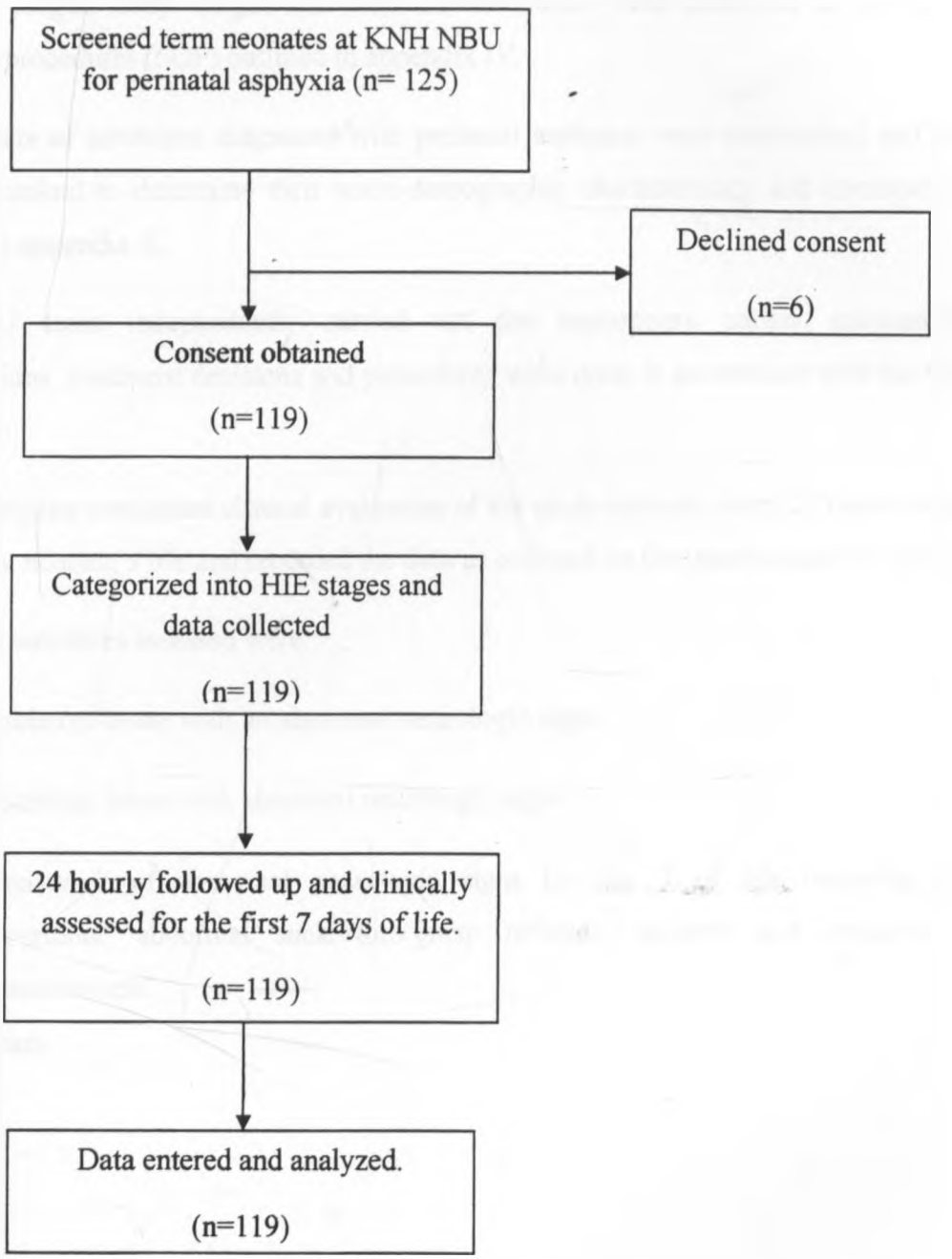
The parents or caregivers of the term neonates with perinatal asphyxia who meet the inclusion criteria were requested to participate in the study. Written informed consent was obtained after clear explanation of the purpose of the study, expected benefits and potential harms. The potential participants were also explained to how the information would be used.

Sampling technique

All consecutive term newborns who satisfied the above inclusion criteria were enrolled between 08.00am to 08.00pm every day. Those who came after 08.00pm and met the inclusion criteria were enrolled the following morning until the described sample size was achieved.

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 admitted at KNH NBU for perinatal asphyxia were assessed and eligible infants enrolled after obtaining an informed consent from the guardian. The infants were examined by the investigator, and the findings recorded on a standard tool (see appendix II).The neonate's length, body weight and head circumference were measured as per the standard operating procedures (SOP) outlined in appendix IV.

The mothers of newborns diagnosed with perinatal asphyxia were interviewed and their ANC records checked to determine their socio-demographic characteristics and obstetric history as outlined in appendix II.

The NBU team independently carried out the appropriate patient management. The investigations, treatment decisions and procedures were done in accordance with the GOK/KNH protocols.

The investigator conducted clinical evaluation of the study subjects every 24 hours for the first 7 days of the neonate's life and recorded the data as outlined on the questionnaire in appendix II.

The study outcomes assessed were:

- Discharge home with no abnormal neurologic signs
- Discharge home with abnormal neurologic signs
- Persistence of abnormal neurologic signs by day 7 of life including hypotonia, hypertonia, abnormal suck/Moro/grasp reflexes, seizures and impaired level of consciousness.
- Death

5. DATA MANAGEMENT AND ANALYSIS

Data from the questionnaires was coded, entered and cleaned in Microsoft Excel. On each day, neurologic exam was carried out and the infants were categorized as normal versus abnormal based on the key below

	Level of consciousness	Muscle tone	Seizures	Suck reflex	Moro reflex	Grasp reflex
Abnormal	Coma /Lethargic	Hypertonic /Hypotonic	Present	Absent /Weak	Absent /Depressed	Absent /Depressed
Normal	Alert	Normal	Absent	Active	Normal	Normal

Data analysis was performed using SPSS version 17.0 software. Categorical and continuous data such as gestational age, birth weight, length, head circumference, neurological scores was summarized using proportions and means/medians respectively.

Tests of associations between the neonates /maternal factors and the adverse outcomes was 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. In analyzing the relationship between HIE stage and outcome, a mean composite outcome score was computed using each of the outcomes as shown in the key below. Death was assigned a value of 1, continued treatment 2, discharge with sequelae 3 and discharge with no sequelae 4. A maximum score of 4 was associated with good outcome and 1 was the worst outcome of death.

Score	Outcome
1	Died
2	Continued treatment
3	Discharged with sequelae
4	Discharged with no sequelae

A mean score for each HIE class 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

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.

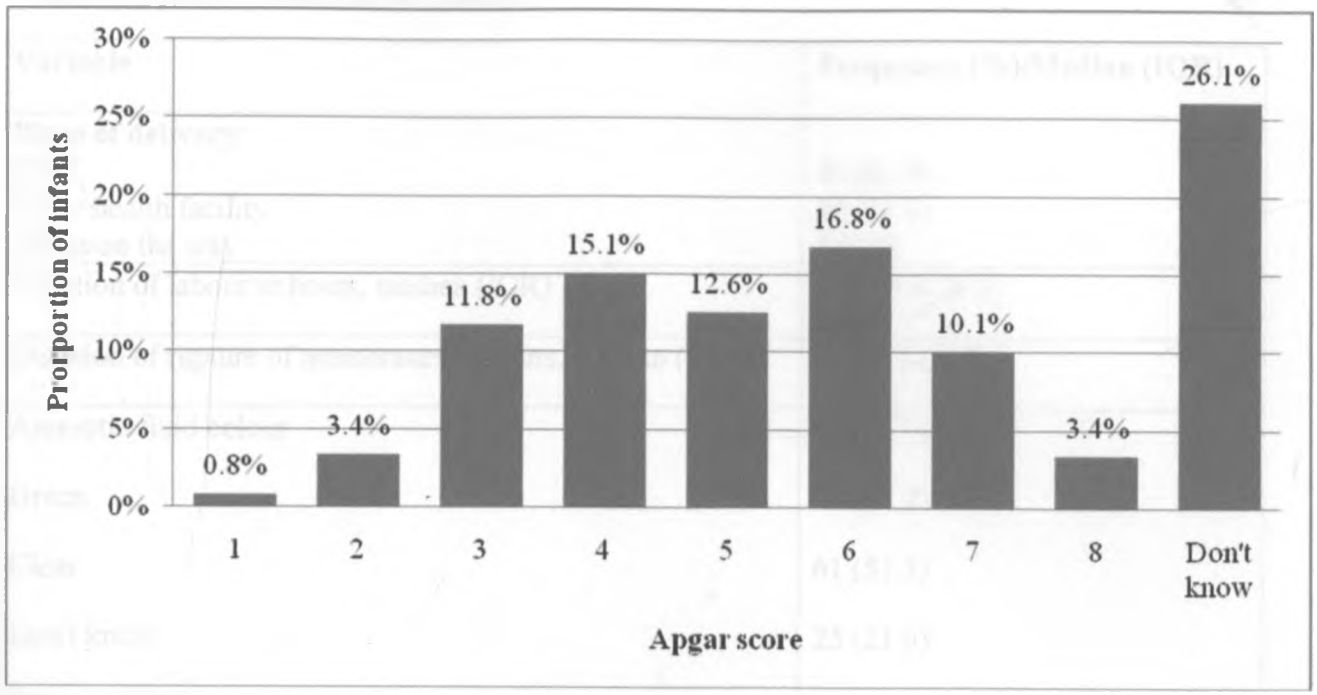
7. RESULTS

One hundred and nineteen (119) infants with perinatal asphyxia were enrolled into the study. The infants were 63% male and were born at an average clinical gestation of 39.7 weeks. The average birth weight of the infants was 3,169.3 grams, mean length of 50.4 centimeters and head circumference of 35.3 centimeters. The infants had a median Apgar score of 6 at 5 minutes after birth as shown in table 1 below.

Table 1: Patient characteristics

Variable	**Frequency (%)/ Mean (SD)/ Median (IQR)**
Gender	
Male	75 (63.0)
Female	44 (37.0)
Mean clinical gestation in weeks	39.7 (1.1)
Mean birth weight in grams	3169.3 (523.4)
Mean length in cm	50.4 (1.4)
Mean head circumference in cm	35.3 (1.0)
Apgar score at 5 minutes, median (IQR)	6 (4 - 9)

Figure 1: **Distribution of Apgar scores at 5 minutes**



119 patients were enrolled, out of which 16% had Apgar score of 1-3; while 26.1% had no documented Apgar scores as shown in figure 1 above.

Table 2: Characteristics of the delivery

Variable	Frequency (%)/Median (IQR)
Place of delivery	
KNH	76 (63.9)
Other health facility	38 (31.9)
Home/on the way	5 (4.2)
Duration of labour in hours, median (IQR)	17.0 (8.0-26.0)
Duration of rupture of membranes in hours, median (IQR)	4.0 (2.5-24.0)
Amniotic fluid colour	
Green	33 (27.7)
Clear	61 (51.3)
Don't know	25 (21.0)
Mode of delivery	
Vertex vaginal	77 (64.7)
Breech vaginal	7 (5.9)
C/S	35 (29.4)
Resuscitation with Bag Mask Valve(BVM) (n=114)	76(63.8)
In KNH	69 (90.7)
Outside KNH	7 (9.3)
Median duration of resuscitation in minutes (IQR)	5.0 (3.0-15.0)
Intubation + Mechanical ventilation	25 (21.0)

Majority (63.9%) of the infants were born in KNH. The median duration of labour was 17 hours whilst the median duration of rupture of membranes was 4 hours. Amniotic fluid was clear among 51.3% of the women while 27.7% had meconium stained liquor.

Overall, 66.7% of the infants received resuscitation with BVM. Out of all the newborns resuscitated, 90.7% were born in KNH and 9.3% were born outside KNH. The median duration of resuscitation was 5.0 minutes. In addition, intubation and mechanical ventilation was performed in 21% of the infants (table 2)

Table 3: Mother's characteristics

Variable	Frequency (%)
Age in years, mean (SD)	24.1 (5.4)
Marital status	
Married	77 (64.7)
Parity	
0 (Primi)	64 (53.8)
1	22 (18.5)
2	20 (16.8)
≥ 3	13 (10.9)
Occupation	
Salaried formal employment	27 (22.7)
Informal employment	26 (21.8)
Casual worker	17 (14.3)
Unemployed	49 (41.2)
Education level	
None	17 (14.3)
Primary completed	34 (28.6)
Secondary not completed	14 (11.8)
Secondary completed	29 (24.4)
Tertiary and beyond	25 (21.0)
ANC visits	118 (99.2)
Number of Antenatal clinic visits	
Once	16 (15.3)
Twice	36 (30.5)
More than twice	64 (54.2)
Maternal fever	23 (19.3)
Antepartum haemorrhage	3 (2.5)
High blood pressure	27 (22.7)
Convulsion during pregnancy	1 (0.8)
Other chronic disease	22 (18.5)
Other chronic disease specified	
Recurrent UTI	7 (31.8)
HIV	15 (68.2)

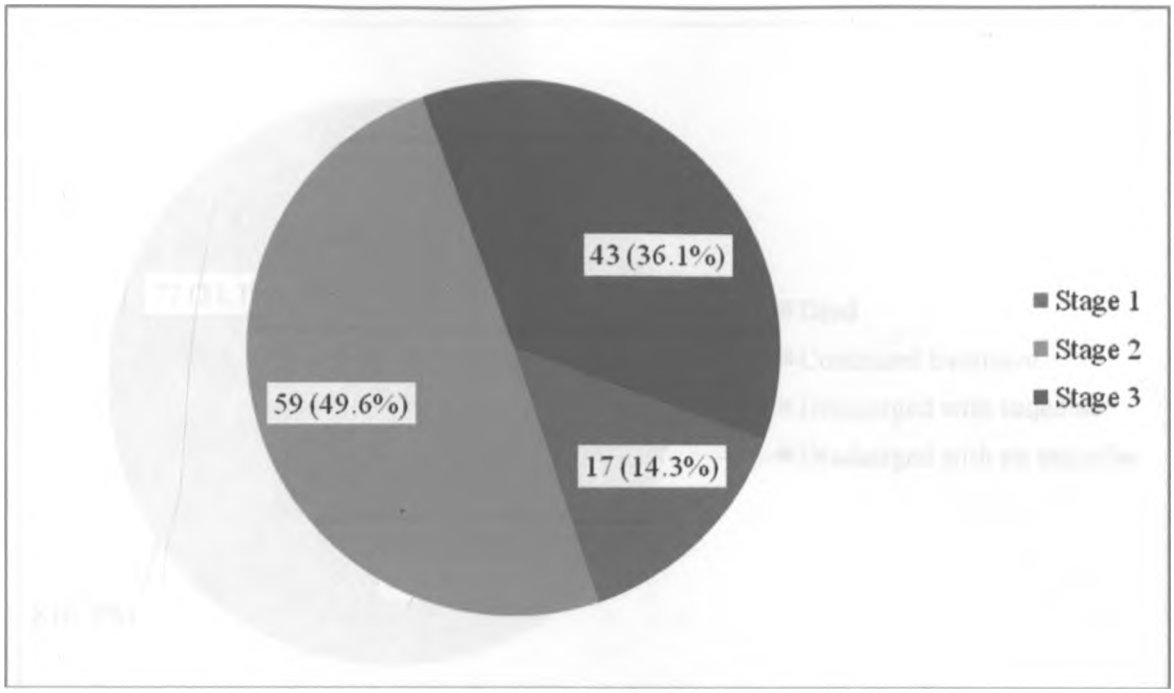
All (100%) the caregivers interviewed were biological mothers with a mean age of 24.1 (5.4) years; 64.7% of them were married and 53.8% were primigravidae. There was a high unemployment rate with 41.2% mothers reporting that they were unemployed while 22.7% were in salaried formal employment, 21.8% in informal employment and 14.3% were casual workers. There was a high level of literacy with 28.6% mothers having completed primary level of

education while 24.4% and 21% had completed secondary and tertiary levels of education respectively. Only 14.3% were illiterate or did not complete primary education.

Almost all the mothers (99.2%) reported having attended at least 1 ANC visit with 54.2% having attended ANC more than twice. The place of delivery for 63.9% of the mothers was KNH while 31.9% delivered in other health facilities and 4.2% at home or on the way. Spontaneous vertex vaginal was the most common mode of delivery at 64.7%. Other modes of delivery included caesarian section (29.4%) and breech vaginal (5.9%).

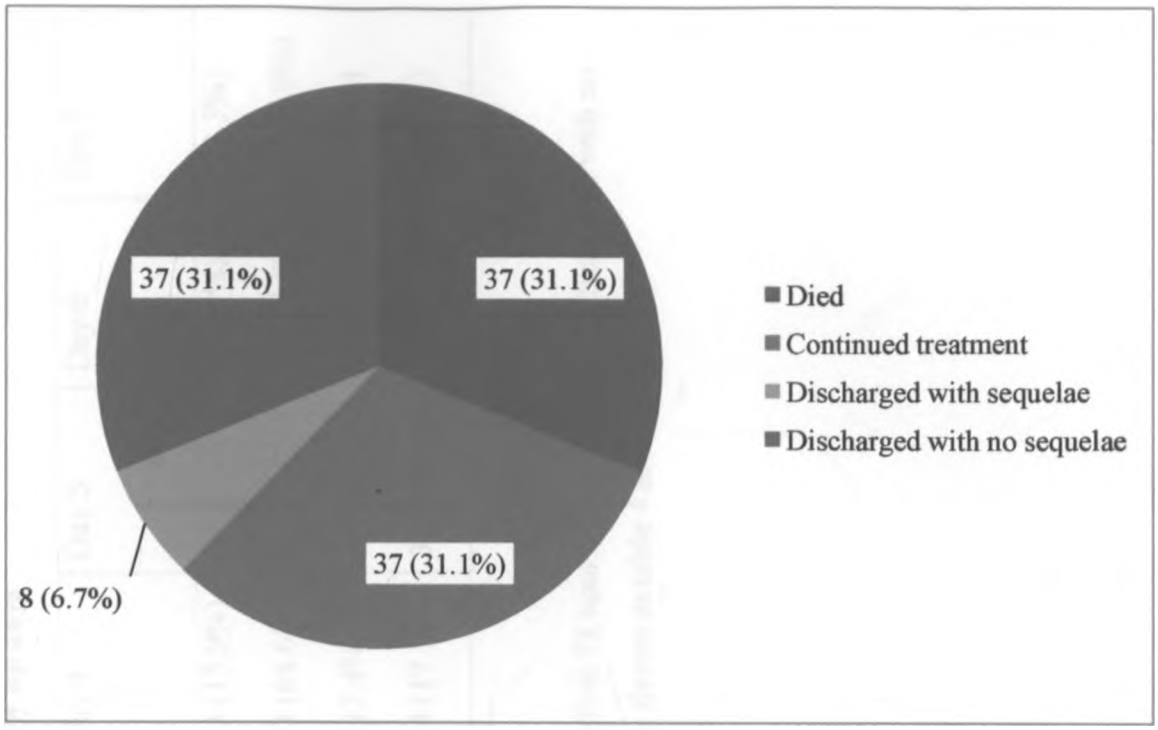
Maternal fever was reported among 19.3% of the mothers, 2.5% had antepartum haemorrhage, 22.7% reported high blood pressure, 0.8% had convulsions during pregnancy and 18.5% reported other chronic diseases among them recurrent UTI and HIV as shown in table 3 above.

Figure 2: HIE stage on Admission



Newborns degree of asphyxia was staged using Sarnart and Sarnart staging of Hypoxic Ischaemic Encephalopathy (HIE) on admission. Majority (49.6%) had stage 2 and a substantial proportion (36.1%) had stage 3 as shown in figure 2 above.

Figure 3: Outcome by day 7 of life



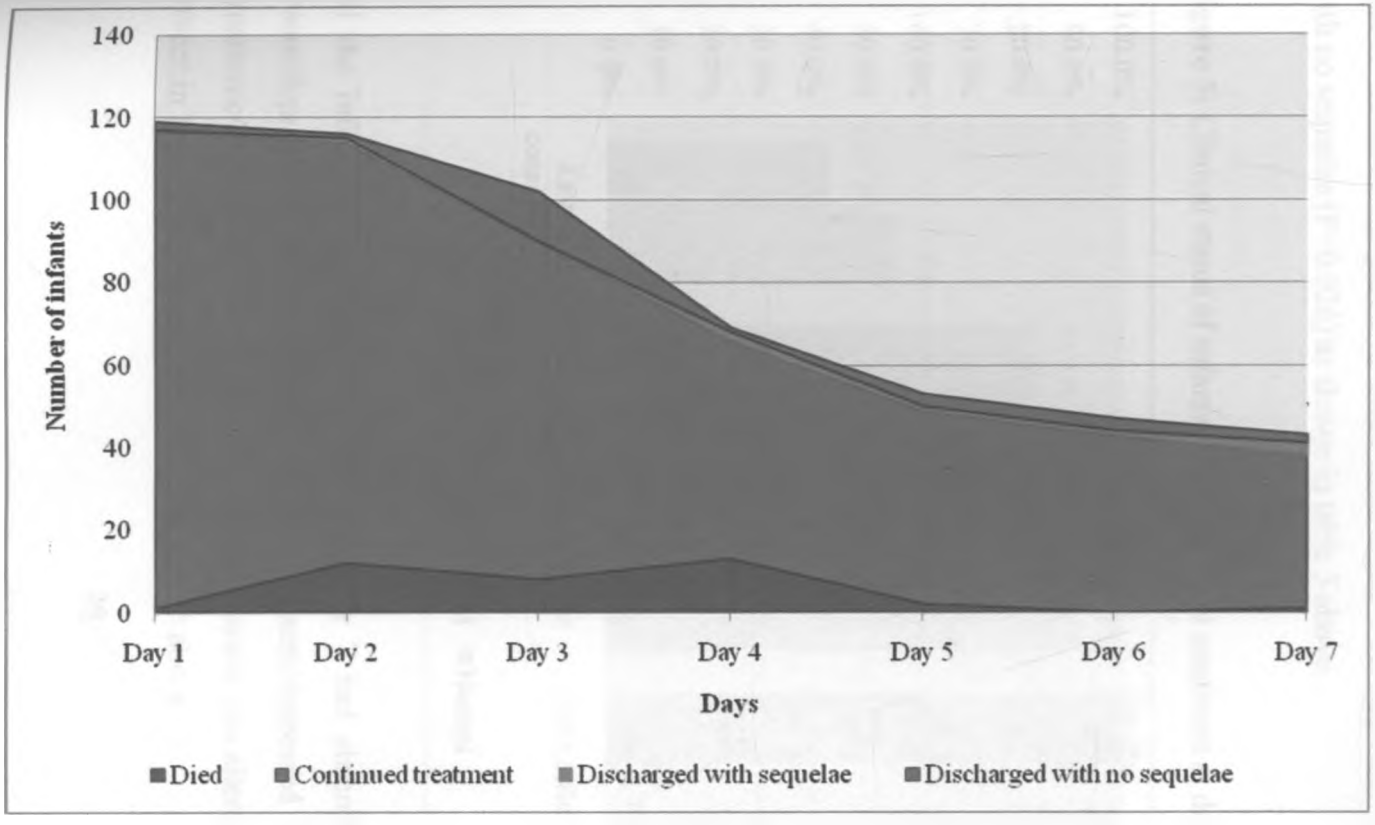
By day 7 of life, 31.1% of infants with perinatal asphyxia had died and another 31.1% continued treatment, while the rest (37.8%) had been discharged from the hospital. Eight infants (6.7%) were discharged with neurologic sequelae whereas 37(31.1%) were discharged with no neurologic sequelae as shown in figure 3 above.

Table 4: Daily outcome in 7 days follow up:

Outcome	Follow up days						
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Died	1 (0.8%)	12 (10.3%)	8 (7.8%)	13 (15.9%)	2 (3.8%)	0 (0.0%)	1 (2.3%)
Continued treatment	116 (97.5%)	102 (87.9%)	82 (80.4%)	53 (64.6%)	47 (88.7%)	43 (91.5%)	37 (86.0%)
Discharged with sequelae	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (2.4%)	1 (1.9%)	1 (2.1%)	3 (7.0%)
Discharged with no sequelae	2 (1.7%)	1 (0.9%)	12 (11.8%)	14 (17.1%)	3 (5.7%)	3 (6.4%)	2 (4.7%)

By 7th day of life31.1% of infants had died, majority of them (56.7%) died in the first 72 hours. 31.1% had been discharged with no neurologic sequelae while 6.7% had been discharged with neurologic sequelae as shown in table 4 above.

Figure 4: Cumulative Outcome of the children during the 7 Days Follow-up:



Case fatality

Follow up time = 443 person days

Deaths = 37

Incidence Density:

Total deaths/Follow up time

= 37/443 x 100

Mortality- 8.4 per 100 child- days

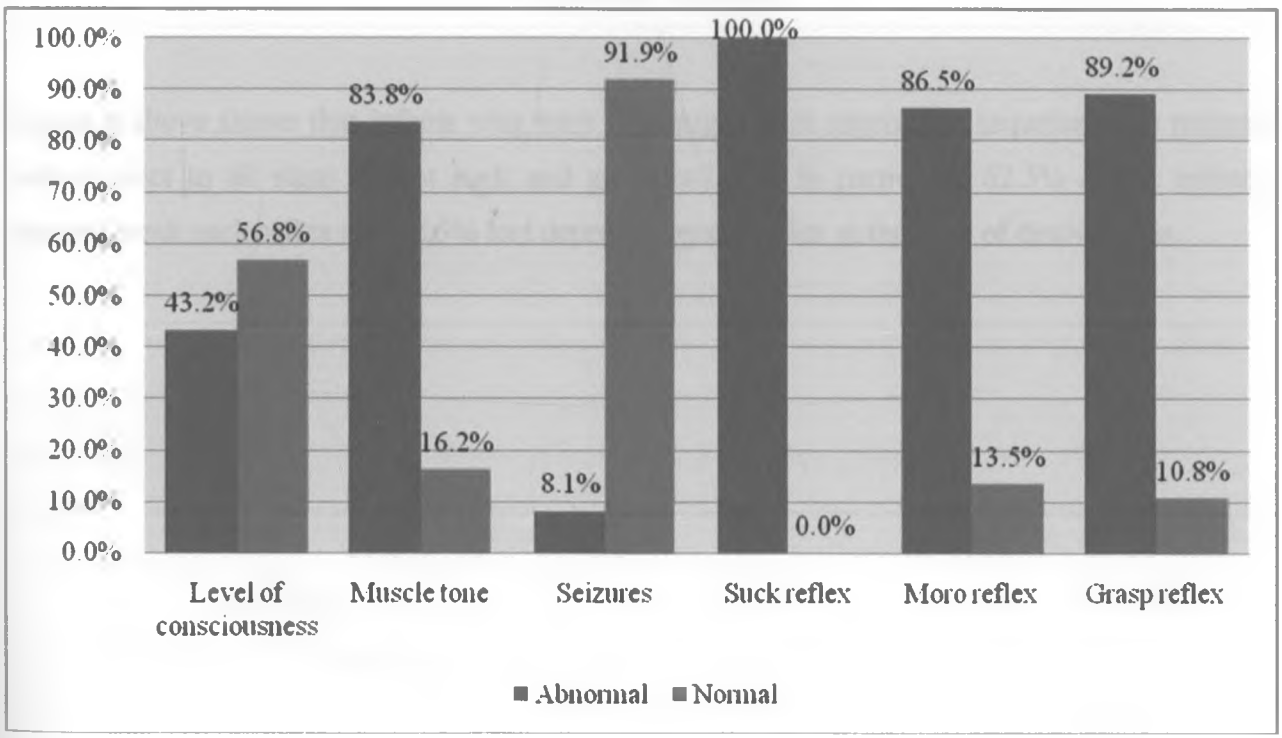
Figure 5 above shows cumulative outcome of study babies. Mortalities occurred between days 1 and 4 with increases on day 2 and 4. Case fatality was found to be 8.4 deaths per 100 person days. On the other hand, the infants discharged with no neurologic sequalae were likely to be those discharged by day 3 and 4. Infants who were discharged with neurologic sequelae were likely to have stayed longer in the hospital with the highest proportion being those infants discharged at day 7. The majority of babies were still admitted on treatment by day 7.

Table 5: Duration of days in the hospital before death or discharge

	Died	Discharged with neurologic sequelae	P value	Discharged with no neurologic sequelae	P value
Days admitted, median (IQR)	2.0 (1.0-3.0)	4.5 (3.0-6.0)	0.004	3.0 (2.0-3.0)	0.026

The mean duration of admission for the children who died was 2.0 days (IQR 1.0-3.0 days), 4.5 days (IQR 3.0-6.0 days) for those discharged with sequelae and 3.0 days (IQR 2.0-3.0 days) for those discharged with no sequelae. The children who died were admitted for a significantly shorter duration compared to those discharged with sequelae (P=0.004) and those discharged with no sequelae (P=0.026) as shown in table 5 above.

Figure 5: Clinical status of infants who continued treatment at day 7 of life (n=37)



All the infants who were on treatment on day 7 had absent/weak suck reflex, 89.2% had absent/depressed grasp reflex, 86.5% absent/depressed Moro reflex and 83.8% hypertonic/hypotonic muscles. Level of consciousness was altered in 43.2% while seizures were present in 8.1% of the infants as shown in figure 5 above.

Figure 6: Clinical status of infants discharged with neurologic sequelae (n=8)

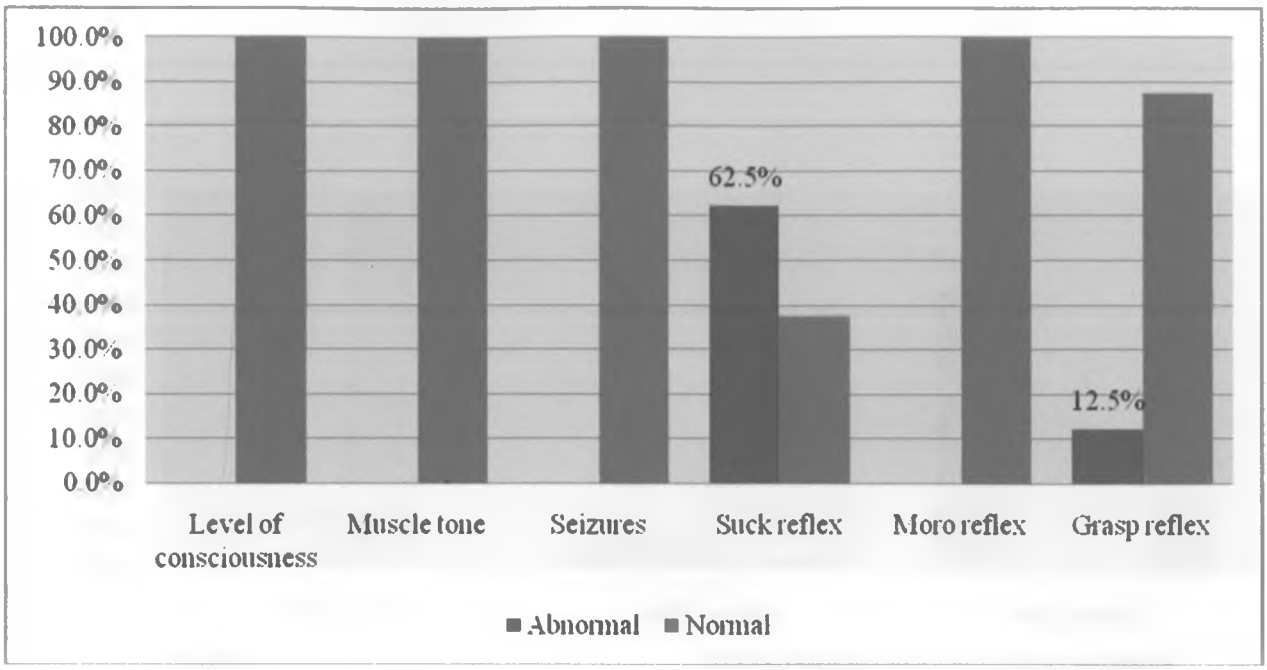


Figure 6 above shows that infants who were discharged with neurologic sequelae were normal with respect to all signs except suck and grasp reflexes. In particular, 62.5% of the infants showed weak suck reflex and 12.5% had depressed grasp reflex at the time of discharge as.

Figure 7: Distribution of HIE stage on admission by outcome

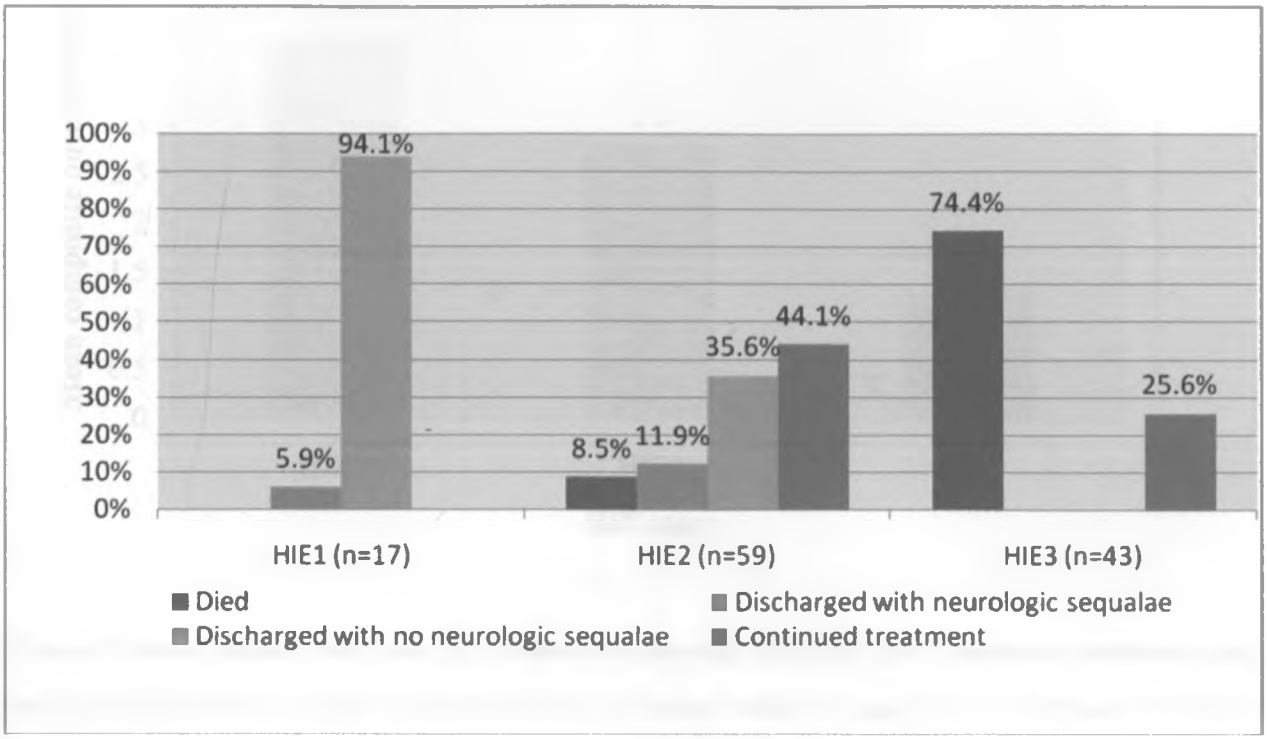


Figure 7 above shows HIE stage on admission was found to be significantly associated with outcome of perinatal asphyxia ($P<0.001$). Infants who were admitted with HIE stage 3 either died (74.4%) or continued with treatment beyond day 7 (25.6%). Also, infants admitted with HIE stage 2 were more likely to continue treatment (44.1%) with a substantial proportion (35.6%) being discharged with no neurologic sequelae. A high proportion of those discharged with sequelae were admitted with HIE stage 2. Infants with HIE stage 1 had a favourable outcome with majority (94.1%) discharged with no sequelae and 5.9% with sequelae.

Figure 8: Relationship between HIE stage and outcome

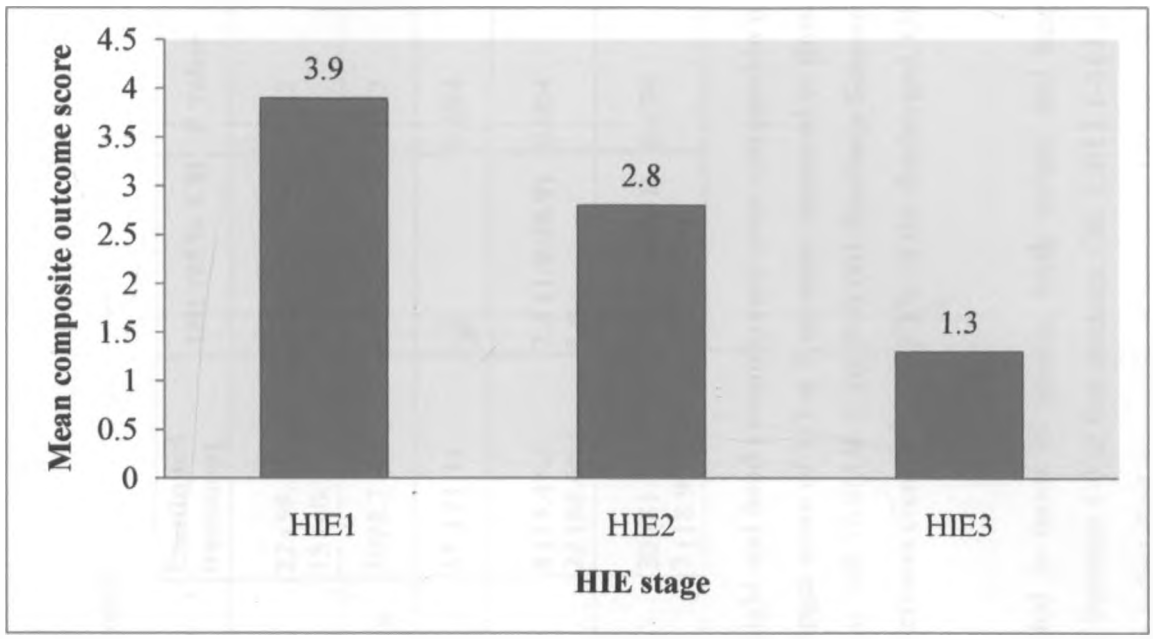


Figure 8 above shows there was an inverse relationship between the composite outcome score and the stage of HIE. Mean composite score of those in HIE 1 was 3.9, 2.9 for those in HIE 2 and 1.3 in HIE 3. The decline in composite score was significant ($P<0.001$)

Table 9: Association between outcome at the 7th day of life and infant characteristics

	Died	Discharged	OR (95% CI)	P value	Continued treatment	OR (95% CI)	P value
Gender							
Male	24 (64.9%)	29 (64.4%)	1.0 (0.4-2.5)	0.968	22 (59.5%)	1.3 (0.5-3.2)	0.632
Female	13 (35.1%)	16 (35.6%)			15 (40.5%)		
Birth weight in grams, mean (sd)	3210.8 (470.4)	3196.7 (433.2)	-	0.888	3094.7 (662.4)	-	0.387
Head circumference in cm, mean (sd)	35.3 (1.0)	35.3 (1.0)	-	0.703	35.1 (1.1)	-	0.594
Apgar score at 5 minutes							
0-3	12 (57.1%)	3 (7.3%)	16.9 (3.9-72.6)	<0.001	4 (15.4%)	7.3 (1.9-28.9)	0.004
4-10	9 (42.9%)	38 (92.7%	1.0		22 (84.6%)	1.0	
Seizures							
Present	34 (91.9%)	6 (13.3%)	73.7 (17.1-317.2)	<0.001	30 (81.1%)	2.6 (0.6-11.1)	0.174
Absent	3 (8.1%)	39 (86.7%)			7 (18.9%)		

Children who died were compared to those who were discharged. Gender, birth weight and head circumference were comparable in these two categories of children. A larger proportion of children who died had an Apgar score of 1-3 at 5 minutes compared to those who were discharged 57.1% versus 7.3% respectively. This difference was significant, OR 16.9(3.9-72.6), P<0.001.Similarly Seizures were significantly associated with mortality with 91.9% of infants who died having seizures compared to 13.3% of the discharged, OR 73.7(17.1-317.2), p<0.001.

Infants who continued treatment after day 7 were comparable to those who died in terms of gender, birth weight and head circumference however, a larger proportion of those who died had an Apgar score of between 1-3 at five minutes, OR 7.3(17.1-317.2), P<0.004. There was no association between the presence of seizures and whether an infant died or continued treatment beyond day 7 of life, OR 2.6(0.6-11.1), P=0.174.

Table 10: Association between outcome and delivery characteristics

	Died	Discharged	OR (95% CI)	P value	Continued treatment	OR (95% CI)	P value
Place of delivery							
KNH	12 (32.4%)	41 (91.1%)	1.0		23 (62.2%)	1.0	
Other facility	22 (59.5%)	3 (6.7%)	25.1 (6.4-98.3)	<0.001	13 (35.1%)	3.2 (1.2-8.6)	0.018
Home	3 (8.1%)	1 (2.2%)	10.3 (1.0-107.8)	0.053	1 (2.7%)	5.8 (0.5-61.4)	0.148
Duration of labour in hours	28.0 (18.0-36.0)	11.0 (7.0-17.0)	-	<0.001	18.0 (15.0-26.0)	-	0.011
Duration of rupture of membranes in hours	10.0 (4.0-26.0)	4.0 (2.0-6.0)	-	0.312	7.0 (4.0-28.0)	-	0.623
Mode of delivery							
Vertex vaginal	27 (73.0%)	27 (60.0%)	1.0		23 (62.2%)	1.0	
Breech vaginal	3 (8.1%)	2 (4.4%)	1.5 (0.2-9.7)	0.670	2 (5.4%)	1.3 (0.2-8.3)	0.798
C/S	7 (18.9%)	16 (35.6%)	0.4 (0.2-1.2)	0.118	12 (32.4%)	0.5 (0.2-1.5)	0.207
Resuscitation with BVM	13 (38.2%)	39 (88.6%)	0.1 (0.0-0.3)	<0.001	24 (66.7%)	0.3 (0.1-0.8)	0.017
Duration of resuscitation in minutes, median (IQR)	20.0 (15.0-25.0)	4.0 (3.0-5.0)	-	<0.001	10.0 (5.0-15.0)	-	<0.001

Table 10 above shows the association between delivery characteristics and outcome. Infants who died were comparable to those who were discharged in terms of mode of delivery and duration of rupture of membranes. A larger proportion of infants who died were born in other health facilities compared to those who were discharged 59.5% versus 6.7% respectively, OR 25.1 (6.4-98.3), P<0.001. Duration of labour was significantly longer in infants who died (28hours) compared to those discharged, P<0.001. Infants who died when compared to those discharged were less likely to have been resuscitated with Bag Valve Mask (BVM) 38.2% versus 88.6%.

This difference was significant, OR 0.1(0.0-0.3), P< 0.001. Among those infants resuscitated with BVM, the duration of resuscitation was longer (20 minutes) in those who died compared to those discharged (4 minutes), P<0.001.

There was no difference in terms of mode of delivery and duration of rupture of membranes between those infants who died and those who continued treatment beyond day 7 of life. However, infants who died were more likely to have been delivered in other health facilities compared to those discharged 59.5% versus 6.7% respectively, OR 25.1(6.4-98.3), P< 0.001. Infants who continued treatment had a shorter median duration of labour (18 hours) in comparison to those who died (28 hours), P= 0.011. A larger proportion of infants resuscitated with BVM continued treatment after day 7 compared to those who died 66.7% versus 38.2% respectively, OR 0.3 (0.1-0.8) P= 0.017. The median duration of resuscitation was shorter (10 minutes) in those who continued treatment compared to 20 minutes in those who died.

Table 11: Association between outcome and mother's characteristics

Variable	Died N= 37	Discharged N= 45	OR (95% CI)	P value[1]	Continued treatment N= 38	OR (95% CI)	P value[2]
Age, mean (SD)	22.6 (5.3)	24.7 (4.6)	-	0.068	24.9 (6.1)	-	0.094
Parity							
0	24 (64.9%)	21 (46.7%)	1.7 (0.4-6.9)	0.449	19 (51.4%)	0.9 (0.2-4.8)	0.948
1	4 (10.8%)	9 (20.0%)	0.7 (0.1-3.8)	0.646	9 (24.3%)	0.3 (0.1-2.2)	0.258
2	5 (13.5%)	9 (20.0%)	0.8 (0.2-4.4)	0.831	6 (16.2%)	0.6 (0.1-4.2)	0.630
≥	4 (10.8%)	6 (13.3%)	1.0		3 (8.1%)	1.0	
Marital status							
Married	20 (54.1%)	35 (77.7%)	1.0		22 (61.1%)	1.0	
Unmarried	17 (45.9%)	10 (22.3%)	4.7 (0.8-9.6)	0.076	14 (38.9%)	2.3 (0.9-5.9)	0.081
Occupation							
Salaried	3 (8.1%)	20 (44.4%)	1.0		4 (10.8%)	1.0	
Informal employment	5 (13.5%)	13 (28.9%)	2.6 (0.5-12.6)	0.247	8 (21.6%)	0.8 (0.1-5.4)	0.848
Casual worker	4 (10.8%)	5 (11.1%)	5.3 (0.9-31.9)	0.067	8 (21.6%)	0.7 (0.1-4.5)	0.679
Unemployed	25 (67.6%)	7 (15.6%)	23.8 (5.4-104.1)	<0.001	17 (45.9%)	2.0 (0.4-9.9)	0.415
Education level							
None	10 (27.0%)	1 (2.2%)	95 (7.6-1180.3)	<0.001	6 (16.2%)	3.3 (0.5-24.1)	0.232
Primary completed	15 (40.5%)	6 (13.3%)	23.8 (4.2-135.0)	<0.001	13 (35.1%)	2.3 (0.4-14.7)	0.376
Secondary not completed	2 (5.4%)	6 (13.3%)	3.2 (0.4-27.6)	0.297	6 (16.2%)	0.7 (0.1-6.9)	0.733
Secondary completed	8 (21.6%)	13 (28.9%)	5.8 (1.1-32.1)	0.042	8 (21.6%)	2.0 (0.3-14.2)	0.488
Tertiary and beyond	2 (5.4%)	19 (42.2%)	1.0		4 (10.8%)	1.0	
ANC visits	36 (97.3%)	45 (100.0%)	-	0.451	37 (100.0%)	-	1.000
Number of visits							
Once	13 (36.1%)	0 (0.0%)	48.0 (5.6-413.9)	<0.001	5 (13.5%)	3.6 (1.0-13.5)	0.054
Twice	13 (36.1%)	5 (11.1%)	10.4 (3.0-36.0)	<0.001	18 (48.6%)	1.0 (0.3-3.0)	0.984
More than twice	10 (27.8%)	40 (88.9%)	1.0		14 (37.8%)	1.0	

Table 11: Association between outcome and mother's characteristics (continued)

Variable	Died N= 37	Discharged N= 45	OR (95% CI)	P value[1]	Continued treatment N= 38	OR (95% CI)	P value[2]
Maternal fever	8 (28.6%)	7 (15.9%)	2.1 (0.7-6.7)	0.197	8 (23.5%)	1.3 (0.4-4.1)	0.652
Antepartum hemorrhage	2 (6.3%	1 (2.2%)	2.9 (0.3-33.8)	0.567	0 (0.0%)	-	0.224
High blood pressure	7 (53.8%)	13 (30.2%)	2.7 (0.8-9.6)	0.186	7 (26.9%)	3.2 (0.8-12.8)	0.157
Convulsion during pregnancy	0 (0.0%)	1 (2.2%)	-	1.000	0 (0.0%)	-	-

Table 11 above shows the association between mother's characteristics and outcome. Mothers of children who died were compared to those who were discharged. Age, parity, marital status, presence of peripartum fever, high blood pressure, antepartum hemorrhage and convulsions during pregnancy were comparable in the two categories of mothers. When compared with children whose mothers had tertiary education or higher, there was a higher risk of death among children whose mothers were illiterate; OR 95.0 (7.6-1180.3), P<0.001 or had primary level of education; OR 23.8 (4.2-135.0), P<0.001. Infants whose mothers were unemployed had a higher likelihood of dying (67.6%) than discharged (15.6%), OR 23.8 (5.4-104.1), P<0.001. In contrast infants whose mothers were casual workers or were in informal employment were not different from those of salaried employment in terms of death. Attending antenatal clinic less than three times increased the risk of death in children, with the highest risk in those whose mothers attended antenatal clinic once; OR 48.0 (5.6-413.9), P<0.001 compared to those who attended twice; OR 10.4 (3.0-36.0), P<0.001.

Mothers of neonates who died compared to those mothers whose infants continued treatment after day seven of life were similar in terms of age, marital status, parity and occupation, level of education, presence / absence of maternal fever, antepartum hemorrhage, high blood pressure and convulsion during pregnancy. However, infants whose mothers attended ANC clinic only once had increased had increased risk of death, OR 3.6 (1.0-13.5), P= 0.054.

Table 12: Predictors of infant mortality in perinatal asphyxia

Variable	Odds Ratio	95% CI	P value
Education level			
Primary and below	7.6	0.6 – 91.3	0.108
Secondary not completed	0.5	0.2 - 12.9	0.680
Secondary completed	4.0	0.4 - 39.1	0.232
Tertiary and beyond	1.0		
Duration of labour	1.1	1.01-1.22	0.024
Place of delivery			
KNH	1.0		
Other health facility	11.2	1.1-114.7	0.042
Resuscitation with BVM			
No	3.0	0.2 –41.9	0.411
Yes	1.0		

Logistic regression analysis was performed to determine the factors independently associated with mortality in children with perinatal asphyxia. The variables used in the model included tertiary and beyond level of education of the mother, duration of labour, place of delivery and resuscitation with BVM. Occupation and number of ANC visits attended were eliminated from the equation because their strong correlation(r=0.70 and 0.67 respectively) with education while Apgar score was eliminated because of its significant correlation (r= - 0.4) with duration of labour. The model showed that duration of labour and place of delivery were the only factors independently associated with death among infants. Infants that experienced longer duration of labour had increased risk of death, OR 1.1 (1.0-1.3), P=0.013. Similarly, those who were born in other health facilities were more likely to die, 11.2 (1.1-114.7), P=0.042.

8. DISCUSSION

This study was done to determine outcomes and the factors associated with adverse outcomes in term newborns with asphyxia. It was carried out at the KNH Newborn unit, between 1st June and 30th November 2010.

More males were enrolled (63%) which is comparable to other studies.[26, 29] By day 7 of life, 31.1% of infants with perinatal asphyxia had died, 31.1% continued treatment, The 6.7% discharged with sequelae and 31.1% discharged with no sequelae. The mean age at death was 2 days. Garbutt[26] and Finner[16] documented a mortality rate of 12% and 7% respectively .The difference in mortality could be attributed to the fact that in this study severe asphyxia (HIE -III) accounted for 36.1% of the total study subjects compared to Garbutt's[26] and finner's[16] of 26% and 15% respectively. KNH is the only tertiary referral health institution in the city of Nairobi and receives newborns referred from other health facilities leading to a selection bias towards recruitment of neonates with severe asphyxia. The fact that 40% of labour ward deliveries are from women who did not attend ANC in KNH further increases the likelihood of high risk infants.

The Sarnat and Sarnat staging[12] performed well in this population with 9 out of 10 infants in HIE-I discharged with no neurologic sequelae and 3 out of 4 infants with HIE-III dying and a more in between picture for infants in HIE-II.

Majority of stage-III HIE cases died < 72 hours of admission into the unit. A prospective study done by Ondoa et al[32] in Uganda and Sayal et al[31] in Pakistan had similar trend in infants with severe asphyxia. It points to the fact that once severe asphyxia occurs, treatment in the newborn unit cannot be very effective, and therefore, more attention needs to be paid to prevention which is possible through increasing awareness level and early recognition of high risk pregnancies at the community level, facilitating referral systems to tertiary care hospitals.

There was no mortality in neonates with mild perinatal asphyxia (HIE stage -I) and discharge neurologic exam was normal in all but one neonate. This is in keeping with many other studies done in Singapore[11], Jamaica[26] and Canada[16] which reported no death or neurologic neonates with HIE stage-I. Stage-I HIE is thought to be self limiting.

The majority of neonates with stage-II (56%) HIE had abnormal neurological examination(abnormal tone, weak suck, grasp and moro reflexes) which is similar to that reported by Thonberg[19] et al of 50% abnormal neurologic exam in neonate with stage 2 HIE. The mortality rate among those with stage-II was 8.5% which is lower that reported by Sayal et al[31] of 56.52% in Pakistan but higher than that reported from similar tertiary hospital settings by Toh et al[11] in Singapore and Finner et al[29] in Canada who reported rates of 0.08% and 0.7% respectively . The reason for this is not clear, but it may be due to lack of facilities for close monitoring in sick neonates who are not in the neonatal intensive care unit (NICU).

There was a significant association between the five minute Apgar score and outcome, especially for the group with the Apgar score of 0 to 3 at five minutes which is in keeping with the initial observations of Drage and Berendes[33] and more recently Nelson and Ellenberg[34] have shown that et an Apgar score of less than 3 at five minutes was an ominous finding with 44% of infants dying and the survivors having 21- fold increased risk of neurologic disability. In our study compared to children with apgar score between 4-10, infants with Apgar 0-3 at 5 minutes had an increased risk of death than discharged, OR 16.9 (3.9-72.6), P<0.001. Similarly, children with Apgar score of 3 or less were more likely to die than continue treatment, OR 7.3 (1.9-28.9), P=0.004.

Studies have demonstrated a poor outcome for newborns with seizures, [35, 36, 37] .In this study, there was a demonstrable relation between the presence of seizures and outcome. Presence of seizures was found to be highly associated with the death of the infant as compared to those who were discharged, OR 73.7 (17.1-317.2), P<0.001. However, there was no significant difference between the infants who continued treatment and those who died, OR 2.6, p=0.174. This relationship between seizures and mortality is not surprising considering that seizures are mainly seen in infants with moderate or severe HIE and that severity of seizures in newborns with perinatal asphyxia is independently associated with brain injury increasing their morbidity and mortality.[36, 37, 42]

Delivery factors associated with adverse outcome were place of delivery, duration of labour and whether the infant was resuscitated with bag and mask device (BVM) .While studies done in Canada[16] and Jamaica[26] have not demonstrated significant difference in the outcome for inborn babies versus those transferred from other health facilities, in this study the outcome was

significantly different for inborn babies versus those transferred from other health facilities. Infants delivered in other health facilities were more likely to die (57.5%) than discharged (6.7%), OR 25.1, p< 0.001. Similarly transferred infants were also more likely to die than continue treatment beyond day 7 if they were born in other health facilities OR 3.2, P< 0.018. This could be explained by the fact that most asphyxia referrals to KNH Newborn unit are from clinics located in peri-urban areas where there are no elaborate plans for the transfer of sick neonates and lack of skilled and trained personnel as well as paediatric supervision leading to lack of proper interventions and late referrals.

Duration of labour was significantly associated with outcome. While studies from developed countries have not reported any association between duration of labour and outcome, [11,16,19,29] some of the studies from developing countries[27, 31] have reported poor outcomes for infants with prolonged duration of labour. In our study there was significant association with the median duration of labour longer among the infants who died (28 hours) than those who were discharged (11 hours), P<0.001. Similarly, infants who continued treatment at day 7 had a shorter median duration of labour (18 hours) than the infants who died (P=0.011). The concept of "active management of labour" advanced by O' Driscoll[40, 41] has received wide acceptance. This concept depends on vigilant observation of the progress of labour and timely intervention when delay is detected. Most primi-gravidae should be delivered within 12 hours of admission and multiparae within 6 hours. In developed countries intrapartum complications like prolonged labour are rare compared to developing countries like Kenya which has higher incidence of serious complications and reduced availability of skilled care in labour leading to increased morbidity in the unborn babies.

This study demonstrates the importance of BVM resuscitation. There was a 90% reduced risk of death in children who were resuscitated. Similarly infants who were resuscitated had a 70% increased chance of being on treatment by day 7. The importance of BVM resuscitation was also demonstrated by a study done in Cirebon district of Indonesia[38] where community midwives were trained to resuscitate newborns using a locally produced bag and mask device and the impact was a 47% decrease in neonatal mortality and morbidity due to birth asphyxia.

Among the maternal factors, education, occupation, antenatal clinic visits were found to be significantly associated with adverse outcome. This study's findings on mother's education level

is similar to the KDHS 2008 findings that: neonates of more educated mothers in general have more chance of survival because the mother's level of education determines her access to health information and increases her income .Women with higher education are more likely to receive antenatal care from a medical doctor than those with no education.[6] However studies done in Europe and North America have not shown any association between maternal education level and outcome. In this study Lower level of education of the mother increased the risk of the infant's death.

Antenatal visit is vital in preventing adverse pregnancy outcomes. Early detection of problems in pregnancy leads to more timely referrals in the case of women in high risk categories or with complications. Most of the studies on outcome have been done in the western world and have not reported an association between the number of ANC visits and adverse outcomes but, in our study not attending ANC more than twice increased the risk of infant death. Infants of women who attended ANC once had increased risk of death OR 48.0 [(95% CI 5.6-413.9), P<0.001]. This difference in newborn outcomes in terms maternal ANC clinic attendance is not surprising given that antenatal care is more beneficial when sought early and continued regularly through to delivery.

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.

10. Study Limitations

- Data on mother's antenatal history and perinatal events was extracted retrospectively from the ANC cards, files and referral notes and the accuracy could not be ascertained.
- KNH is a tertiary hospital and one third of the patients in this study had been referred due to severity of their illness. This introduces a selection bias. These results may not be applicable to non-tertiary centers.

11. Conclusions

- Perinatal asphyxia has 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.
- Babies had increased risk of death if they were not resuscitation with BVM, were born after a prolonged labour, delivered outside KNH, had seizures or an Apgar score of less than 3 at five minutes. Other factors include if their mothers' were unemployed, had education level below secondary or attended ANC$\leq$ 2 times.

12. Recommendations

- In a resource constrained country like Kenya efforts should be put on preventing birth asphyxia through sensitizing mothers/communities on the need for regular ANC visits and delivery in good health institutions.
- Follow up study should be done on the long term outcome of babies with moderate and severe asphyxia discharged from the newborn unit.

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14. APPENDICES

APPENDIX I: 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.

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 II
OUTCOMES OF 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					

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:
5.1 Level of consciousness 2(alert),1(lethargic),0(coma)							
5.2 Muscle tone 2(normal), 1(hypotonic), 0(hypertonic)							
5.3 Seizures 1(absent), 0(present)							
5.4 Suck reflex 2(active), 1(weak), 0(absent),							
5.5 Moro reflex 2(normal/exaggerated) 1 (depressed), 0(absent),							
5.6 Grasp reflex 2(normal),1(depressed), 0(absent),							

APPENDIX III

FINNSTRÖM SCORE

Examine the baby and tick the most appropriate for each of the categories of assessment. The scores will be a = 1 b = 2 c = 3 d = 4.

1. ***Breast size.***
Measure the transverse diameter of each breast with a sliding calliper and record.

Right breast _____ mm Left breast _____ mm

Categorize the largest value registered into either a, b or c and assign a score.

(a) below 5 mm;
(b) 5 to 10 mm;
(c) more than 10 mm

2. ***Nipple formation.***
Inspect the nipple and assess whether it is visible, whether there is an areolar and characteristics of the areolar in relationship to the nipple. Tick the category that best describes the nipple and then assign a score.

(a) nipple barely visible, no areola;
(b) Nipple well defined, areola present but not raised;
(c) Nipple well defined; edge of the areola raised above the skin.

3. ***Skin opacity.***
Inspect the skin and assess the visibility of the blood vessels. Tick the category that best describes visibility of the blood vessels and then assign a score.

(a) numerous veins, tributaries and venules are clearly seen, particularly over the abdomen;
(b) veins and tributaries are seen;
(c) a few large blood vessels are clearly seen over the abdomen;
(d) a few large blood vessels are seen indistinctly over the abdomen, or no blood vessels are seen.

4. Scalp hair.

Inspect the scalp hair and describe the texture and tick the category that best describes it then assign a score.

(a) fine hair, woolly or fuzzy, individual strains difficult to distinguish;

(b) hair coarse and silky.

(c) Each hair appears as a single strand.

5.Ear cartilage.

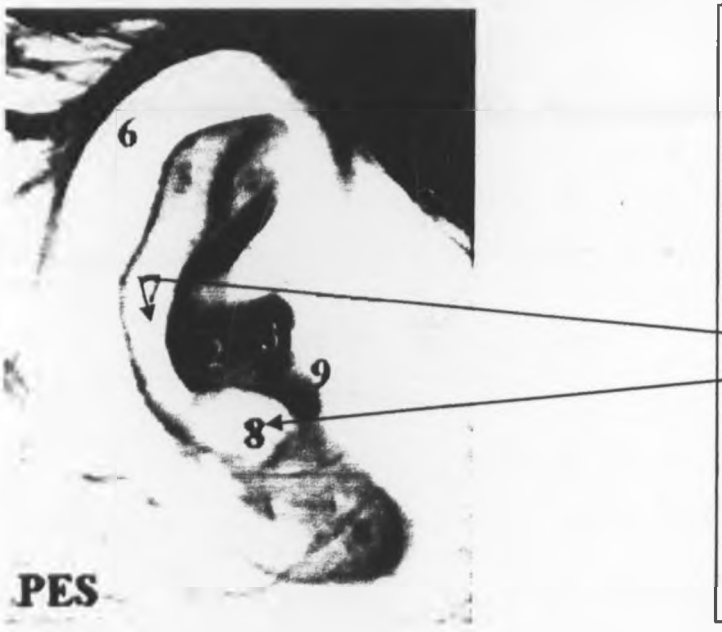
Palpate both ears to estimate the distribution of ear cartilage. In case there is a difference between the two ears, base your the judgment is based on the most "mature" ear:

(a) no cartilage is felt in antitragus;

(b) cartilage is felt in antitragus;

(c) cartilage is present in anthelix;

(d) cartilage formation is completed in helix (i.e. cartilage can be palpated in the dorsal-cranial part).



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

6 .Finger nails.

Inspect the finger nails and palpate the finger tip letting the nail scratch the hand of the examiner. Tick the category that best describes the nails and then assign a score.

(a) the nails do not reach the fingertips;

(b) the nails reach the fingertips;

(c) the nails reach or pass the finger tips, distal edge of the nail is distinct and relatively firm (i.e. the edge of the nail can easily be felt if the nail scratches the hand of the examiner)

7. Plantar skin creases.

Inspect the sole of the foot and only assess the relatively broad creases. Fine superficial lines may be present especially if the skin is dry but usually disappear if the sole is stretched from toes to heel. Categorize the skin creases and then assign a score:

(a) no skin creases are present;

(b) anterior transverse creases only are present;

(c) occasional creases are seen on the anterior two-thirds of the sole;

(d) the whole sole is covered with creases, i.e. also the heel.

Calculation of the Gestational age

Add the scores and then consult the table below for a determination of the gestational age.

Total score _____

GESTATIONAL AGE BASED ON 7-ITEM CHART.

TABLE FOR GESTATIONAL AGE ESTIMATION BASED ON THE FINSTRÖM SCORE

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

Appendix IV

Standard Operating Procedures for the measurement of weight, length and head circumference

Weight:

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

Length:

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

Head circumference:

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

Appendix V- consent form

Questionnaire serial Number:

Outcome of perinatal asphyxia study
Information and consent form

I, being a guardian of _____ (name of Newborn) have had the research information explained to me. I understand that I can withdraw my child from the study at any point and this will not affect my baby's care in any way.

☐ I agree to allow my baby to take part in this research and for the collection of clinical data.

Parents/guardian's signature: _____ Date: _____

Parent/guardian's name: _____ Time:_____

I certify that I have explained to the parent/caregiver the research information. Investigator's signature: _____ Date: _____

Investigator's name: _____ Time: _____

Only necessary if the parent guardian cannot read:

I* attest that the information concerning this research was accurately explained to and apparently understood by the parent/guardian and that informed consent was freely given by the parent/guardian.

Witness' signature: _____ Date: _____

Witness' name: _____ Time:_____

*A witness is a person who is independent from the trial or a member of staff who was not involved in gaining the consent.

Thumbprint of the parent as named above if they cannot write:

KENYATTA NATIONAL HOSPITAL

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Email: KNHplan@Ken.Healthnet.org

17th May 2010

Ref: KNH-ERC/ A/487

Dr. Abdisalan M. Maalim
Dept.of Paediatrics & Child Health
School of Medicine
University of Nairobi

Dear Dr. Maalim

RESEARCH PROPOSAL: OUTCOME OF TERM NEWBORNS ADMITTED WITH PERINATAL ASPHYXIA IN KENYATTA NATIONAL HOSPITAL NEWBORN UNIT" (P94/3/2010)

This is to inform you that the KNH/UON-Ethics & Research Committee has reviewed and **approved** your above revised research proposal for the period 17th May, 2010 to 16th May, 2011.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimens must also be obtained from KNH/UON-Ethics & Research Committee for each batch.

On behalf of the Committee, I wish you a fruitful research and look forward to receiving a summary of the research findings upon completion of the study

This information will form part of the data base that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF A N GUANTAI
SECRETARY, KNH/UON-ERC

c.c. Prof. K. M. Bhatt, Chairperson, KNH/UON-ERC
The Deputy Director CS, KNH
The Dean, School of Medicine, UON
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