THE UNIVERSITY OF ZAMBIA
SCHOOL OF MEDICINE

SHORT-TERM OUTCOME OF INFANTS BORN WITH LOW APGAR SCORES AT THE UNIVERSITY TEACHING HOSPITAL, LUSAKA, ZAMBIA: A MEDICAL AUDIT.

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Dissertation submitted in Partial Fulfillment of the requirement for the Degree of Master of Medicine in Paediatrics

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DEDICATION

This work is dedicated to my husband, Henry and our two children, Msenya and Luumuno who are the source of my inspiration.

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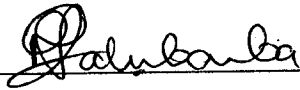
Dr. Susan Tembo for the productive criticism.

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STATEMENT

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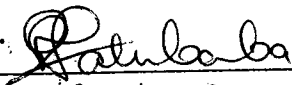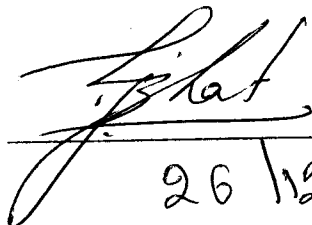
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26 \12 \2003

APPROVAL

THE DISSERTATION OF DR MUTINTA I NALUBAMBA IS APPROVED AS FULFILLING PART OF THE REQUIREMENT FOR THE AWARD OF THE DEGREE OF MASTERS OF MEDICINE IN PAEDIATRICS AND CHILD HEALTH BY THE UNIVERSITY OF ZAMBIA.

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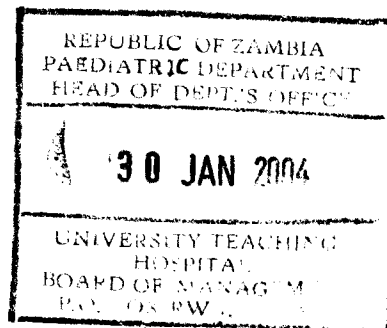
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ABSTRACT

Birth asphyxia contributes significantly to infant morbidity and mortality. Vital centers in the brain are depressed and if the infant survives the initial insult, neurological handicap may arise. Other than the brain, various other organs in the body can be affected by the hypoxia-ischaemia.

This study was carried out at the University Teaching Hospital (UTH) Lusaka, Zambia over a 4 month period. An attempt was made to document immediate complications associated with low Apgar scores as defined by the International Classification of Diseases. Other than complications, predictors of adverse outcome were also looked at.

A total of 1,101 infants were admitted to the neonatal intensive care unit during the period of the study and 161 satisfied the entry criteria of the study and were therefore recruited. Sixty percent of the infants were male and forty percent were female. Eighty of the infants died, eighty were discharged without sequelae i.e generalized hypertonia and one was still on the ward on the 28th day of life. One hundred and forty three infants had hypoxic-ischaemic encephalopathy (HIE). Hypoxic-ischaemic encephalopathy was significantly associated with death. Fifty seven infants had seizure activity recorded but this was not significantly associated with mortality. Seizure activity was either subtle (lip smacking, limb cycling, and high pitched cry) or generalized tonic fits.

Eighty-seven infants developed respiratory distress (tachypnoea and subcostal recession) and 49 required ventilatory support. Ventilation was significantly associated with death; this may be a reflection of the severity of the hypoxic insult rather than ventilation per se. Five infants developed cardiac failure and all of these infants died. Though 40 of the neonates were suspected to have sepsis only 4 had positive blood cultures. However it should be noted that the blood cultures were done after the infants had received antibiotic therapy.

Mortality was significantly associated with Apgar scores less than 4, ventilation, cardiac failure, and hypoxic-ischaemic encephalopathy 3.

Study limitations included lack of an independent observer to assess Apgar scores, missing data rendering analysis of certain variables impossible, and reliance on a number of healthworkers' records as the true and correct analysis of the situation. Further studies are required to assess the long-term impact of the hypoxic insult on these infants who are well at discharge.

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INTRODUCTION

BACKGROUND INFORMATION

Neonatal care is essential not only to reduce mortality and improve the quality of survival by preventing disability but also to promote positive attitudes to family planning [1]. Essential neonatal care includes resuscitation of asphyxiated babies, provision of warmth, promotion of breastfeeding, care of low birth weight babies, and the identification and appropriate referral of sick neonates [1].

Birth Asphyxia represents a serious problem worldwide [2,3,4,5,6]; it can be defined as a clinical syndrome resulting from oxygen deprivation. Birth asphyxia is one of the most common causes of very high neonatal and infant morbidity and mortality in developing countries [3,6,7,8,9]. A study done in Zimbabwe showed that birth asphyxia accounted for 14.8% of hospital admissions to the neonatal unit [10], surpassed only by prematurity and respiratory distress. In contrast, in developed countries there has been a decline in the prevalence of birth asphyxia over the years perhaps as a result of improved obstetric care [7]. In Gothenburg, Sweden the incidence of birth asphyxia was 1.8/1000 live births during the period 1985-1991 [1]. Nigeria has reported incidences of birth asphyxia as high as 26.5/1000 live births and in Tanzania, 229/1000 live births [1]. The most serious impact of asphyxia is on the brain, depressing the vital centers in the brain and leading to neurologic abnormalities known as hypoxic-ischaemic encephalopathy; this

syndrome may result in subsequent neurological handicap [1,8,11,12]. Hypoxic-ischaemic encephalopathy (HIE) has three grades: grade 1(mild), grade 2(moderate), and grade 3(severe). Permanent brain damage resulting from asphyxia around the time of birth is a major tragedy for any child and his or her family and places considerable demands on local medical, social, and economic resources. One of the aims of obstetric and neonatal care is to reduce the number of children damaged in this way [2].

The mortality due to birth asphyxia is fairly easy to estimate [13]. Studies done in various developing countries have given varying figures. In India perinatal mortality due to birth asphyxia was found to be 33.6%, 12.8% in Thailand [14] and 22% in Central Africa [15]. In Zimbabwe neonatal mortality due to birth asphyxia was found to be 23% [16]. In a survey of causes of perinatal mortality in Addis Ababa and in a community of Zulus living near Durban, birth asphyxia accounted for approximately 40% of the perinatal deaths [7].

Morbidity is much more difficult to assess but may, like the hidden base of an iceberg , be a bigger and more significant problem [13] particularly in developing nations where surveillance is rendered difficult due to many factors; frequently neurodevelopment assessment is neither done routinely nor on at risk infants.

STATEMENT OF THE PROBLEM AND STUDY JUSTIFICATION

Birth Asphyxia is a common cause of admission to the Neonatal Intensive Care Unit at the University Teaching Hospital Lusaka. It contributes significantly to the morbidity and mortality of Zambian infants. In the year 2001, 1,120 neonates suffered death and 253 of these deaths were due to asphyxia [17].

At the University Teaching Hospital, birth asphyxia is defined mainly with reference to the Apgar score as well as clinical assessment. Newborns are referred to the neonatal intensive care unit from labour ward with a diagnosis of asphyxia based on the Apgar score alone. It is only in the neonatal intensive care unit where a clinical assessment is added to the Apgar score in the definition of asphyxia i.e an insult to the fetus or newborn due to lack of oxygen and perfusion to organs. Both the American College of Obstetrics and Gynaecology and the American Academy of Paediatrics have challenged the use of the Apgar score alone to define birth asphyxia [18]. In 1996, the American Academy of Paediatrics stated that misuse had led to an erroneous definition of asphyxia [19] and that Apgar scores alone at one and five minutes after delivery correlate poorly with causes or outcome. and as a result, should not be considered evidence for or a consequence of asphyxia [10,19,20]. However, some studies have indicated a strong correlation between neonatal survival and 5 minute Apgar score [5,15,20,21,22,23], but the issue still remains debatable to date. The I minute Apgar is used as an indicator of which

infant requires resuscitation however it is not uncommon to have infants referred

to the neonatal intensive care unit for asphyxia with only the I minute Apgar score

recorded. Other infants with a low 1 minute Apgar score showing an improvement

at 5 minutes with an Apgar score as much as 8 are still referred for severe birth

asphyxia, not indicating any other reason other than the Apgar for labeling the

infant as being severely asphyxiated. Despite the limitation of the Apgar score in

prognosticating the outcome in a baby the method is widely used even in the most

underprivileged of institutions in developing countries [5,10,15,21,24]. However care

should be taken to avoid erroneous definitions.

There is scanty information available in Zambia on infants born asphyxiated and

the complications they suffer. Information available regarding birth asphyxia in

Zambia has concentrated on the prenatal risk factors and perinatal mortality but

little has been documented relating to complications of birth asphyxia and

predictors of neonatal outcome. At the University Teaching Hospital guidelines

exist on the definition of asphyxia and treatment modalities. In the rural settings of

Zambia major shortcomings prevail and asphyxia may be a larger problem than

reflected at the University Teaching Hospital. A study done at the University

Teaching Hospital to look at the incidence of birth asphyxia and risk factors found

the incidence to be 43/1000 live births [25], using the Apgar score to define

asphyxia. A total of 46% of these infants born asphyxiated had prolonged labours;

case fatality rate was 9.2% in the first 24 hours and 45% in the first week of life

for babies whose 5 minute Apgar scores were < 6. However this study did not look at the other complications suffered by the neonates born asphyxiated.

This study therefore attempts to correlate 5 minute Apgar score with short-term clinical outcome and to identify complications associated with low Apgar score and clinical predictors of adverse outcome. It is hoped that this information apart from providing database for the burden of birth asphyxia in Zambia will be useful in the following respects:

1. Reviewing guidelines on admission criteria to the Neonatal Intensive Care Unit in infants born with low Apgar score.

2. Reviewing guidelines on the care and discharge criteria of these infants.

3. To ascertain interventions which can be instituted to alleviate adverse outcome in neonates born with low Apgar scores.

LITERATURE REVIEW

DEFINITION

Asphyxia in the literal sense means stoppage of the pulse [22] and the Oxford English Dictionary defines it as " a condition of suspended animation produced by a deficiency of oxygen in the blood; suffocation." The term birth asphyxia has become widely used to describe a presumed intrapartum hypoxic-ischaemic insult [1] but the clinical definition of birth asphyxia has been a matter of debate and a number of criteria have been proposed to best indicate this situation [1,2,5,18,19,21,22,24,26]. These criteria include acidosis, a low Apgar score, delay in establishing respiration, need for active resuscitation, and evidence of neurological insult. However, as in the definition of other syndromes, no single feature should be used to define birth asphyxia.

In a study done by Larry Gilstrap et al it was found that the combination of low Apgar score and acidemia was a more sensitive predictor of neonatal morbidity than either parameter alone [18]. Taken singly however other authors found that the Apgar score was a better indicator of outcome than umbilical pH [23].

It should also be noted that the timing and severity of the insult may be difficult to ascertain clinically and some of the observed outcomes may not necessarily reflect or be a consequence of the insult. Between the professions concerned with the immediate well being of the newborn the definition of asphyxia may differ but differences have been noted amongst the professions as well. To the obstetrician,

meconium staining, abnormalities of fetal heart rate, and fetal acidosis are indicators of asphyxia [2]. The neonatologist may consider a depressed Apgar score and delay in establishing breathing define asphyxia while the early onset of abnormal neurologic behaviour confirms it.

The traditional way of assessing the newborn is to use the Apgar score [1,19]. The Apgar score system was developed in 1949 by Dr. Virginia Apgar an anesthesiologist from Westfield, New Jersey U.S.A. It was devised as a simple method of assessing the well being of newborn infants. Five signs were used, namely the heart rate, respiratory effort, reflex irritability, muscle tone, and skin colour and each of the parameters was allocated a score of 0, 1, or 2 the maximum score being 10. The newborn was to be assigned the appropriate score by an observer not involved in the mothers care so as to make the assessment more objective. The table below summarizes the Apgar scoring system:

Sign	0	I	2
Heart rate	Absent	<100	>100
Respiratory effort	Absent	Weak cry	Strong cry
Muscle tone	Limp	Some limb flexion	Well flexed
Reflex irritability	No response	Some motion	Cry
Colour	Blue, pale	Body pink	All pink

Apgar did not name her scoring system at inception but a Paediatrician from Colorado, USA was the first to use the letters of Apgar's name as a mnemonic for medical students: A = appearance (color), P = pulse (heart rate), G = grimace (reflex irritability), A = activity (muscle tone), R = respiration (respiratory effort) [19]. Dr. Virginia Apgar however recognized that not all criteria were of equal importance; heart rate and respiratory effort were recognized as carrying more importance than the other parameters. The scoring was originally done at I minute of life [16] but Drage et al in 1964 suggested a second assessment at 5 minutes [10]. The assessment can be continued beyond the second assessment in 5 minute intervals i.e. at 10 minutes, 15 minutes etc.

There are many reasons for a low Apgar score other than hypoxia [27]. The parameters measured are also affected by physiological immaturity, maternal medications, the presence of congenital malformation [19] and infection. In these settings the scores should be interpreted with caution. There has been a tendency to belittle the Apgar score in recent years because it is a poor index of asphyxia (i.e. hypoxaemia plus acidaema) and has little prognostic value. Although these statements may be true, belittling the score fails to understand its purpose: it was never intended as a marker of asphyxia, rather a marker of a baby who has a problem and the sooner the problem is diagnosed the better [1]. However, the Apgar score continues to be the most commonly used method to define asphyxia [5,10,18,21,24]. According to the International Classification of Disease mild asphyxia is defined as Apgar scores 6&7, moderate asphyxia as Apgar scores 4&5, and

severe asphyxia as a 1 minute Apgar score less than 4 [28]. It should be noted that the 5 minute Apgar has a bearing on how effective resuscitative measures have been.

Alternatives to the Apgar score have been suggested to predict outcome and assess the newborn. The Sigtuna score uses only two parameters, breathing and heart rate for assessment [29]. Each parameter, as in the Apgar system, scores 0, 1, or 2 depending on regular, gasping, or absent breathing and fast, slow, or absent heart beat respectively. It was suggested that the scores be given at 1 minute of age, 10 minutes, and a third assessment given after complete resuscitation However, this system requires to be field tested.

The identification of abnormal neurologic signs has been a successful alternative to the Apgar score as a predictor of asphyxia [2]. These abnormal neurologic signs make up a syndrome known as hypoxic-ischaemic-encephalopathy (HIE). Sarnat & Sarnat in 1976 first used HIE as an assessment for asphyxia [1,2] with a specific clinical grading system. This system was later modified by Levene et al [1] and the table below gives an illustration of this clinical grading system for HIE.

Grade 1	Grade 2	Grade3
Hyperalert	Lethargy	Comatose
Mild hypotonia	Marked tone abnormalities	Severe hypotonia
Poor sucking	Weak\absent sucking	Ventilatory support
No seizures	Seizures	Prolonged seizures

In mild encephalopathy, there is a lower threshold for all stimuli including the primitive Moro's reflex. Conversely in moderate encephalopathy there is a higher threshold for primitive reflexes and a differential tone between the upper limbs (more hypotonic) and the lower limbs (more hypertonic) may be seen. In severe HIE primitive reflexes are absent and seizures are prolonged (decerebration) or they may be absent all together (neuronal death).

In terms of outcome mild HIE confers a better outcome than moderate or severe HIE [1,2]. However it should be noted that various conditions other than hypoxia – ischaemia will present as neonatal encephalopathy [22,30]; these include hypoglycemia, meningitis, intracranial hemorrhage, birth trauma cerebral malformations, electrolyte imbalances (hyponatremia, hypocalcaemia), and inborn errors of metabolism (e.g. amino acidemias, pyridoxine dependency, urea cycle disorders) [1,30]. Where possible an effort should be made to exclude these differentials.

The identification of asphyxia during labour and afterwards can be made with a blood gas and acid-base assessment of fetal blood during labour or at delivery [12]. Umbilical arterial pH values less than or equal to 7.2 are taken to indicate the presence of tissue hypoxia and fetal distress. However as with the Apgar score, umbilical arterial acidemias at delivery on it's own is not a good predictor of outcome [1]; a combination of low pH values and low Apgar score is a better predictor of neonatal morbidity [18]. In addition to the above parameters, presence

of abnormal neurologic signs during the neonatal period and evidence of hypoxia to other body systems [27] are of better prognostic value. The fetal heart rate has also been used as a tool to assess asphyxia by the use of the cardiotocograph (CTG). Some studies indicate that marked bradycardia has been associated with increased risk of cerebral palsy [31] whereas others argue that the cardiotocograph has a poor predictive value for cerebral palsy [27]; however the presence of an abnormal CTG requires that action be taken depending on the progress of labour, presence of maternal risk factors, and cervical dilatation among many factors.

PATHOPHYSIOLOGY

Birth is a time of particular risk to the fetus [3] when the placental blood flow is transiently interrupted during labour as the uterus contracts with intrauterine pressures exceeding 30mmHg. The healthy feto-placental unit can adapt so long as the contractions do not last longer than 60 seconds and there is sufficient time in between contractions (at least 2.3 minutes) [1]. In addition to the impairment that results from a contraction several additional stresses may occur giving rise to hypoxic-ischaemic insults that are acute, chronic or acute-on-chronic; these include the following:

1) Interruption of umbilical circulation, e.g. cord compression.

2) Altered or reduced placental gas exchange e.g. placental abruption, maternal hypo/hypertension.

3) Failure to establish adequate cardiopulmonary circulation after birth.

The healthy fetus is able to adapt to the hypoxic ischaemic insults by various mechanisms. The mechanisms include the following:

1. Reduction of body movements to conserve energy.

2. Increased oxygen extraction from the blood with increased erythropoeitin concentrations.

4. Redistribution of blood supply to the heart, brain, and adrenals at the expense of the kidneys, gastro-intestinal tract, liver, and muscles.

5. Increased catecholamine output to increase contractility of the heart and peripheral resistance; this is accompanied by increased anaerobic glycolysis to maintain energy substrate levels in the brain and myocardium.

6. Preferential oxygenation of the brain stem, mid brain, and cerebellum by increasing blood flow within the brain to these areas.

7. Ability of the neonate's brain to utilize lactate, pyruvate and ketones for anaerobic glycolyis.

During the hypoxic insult the brain suffers a primary neuronal insult with depletion of intracellular energy leading to membrane pump failure and entry of water into the cell. Cytotoxic cerebral oedema results with death of neurons. Vasoparalysis may occur which increases cerebral blood flow. There may be activation of neutrophils following damage to the vascular endothelium and also stimulation of platelet activating factor, which further increases vascular permeability. Damage to the blood vessels can also come about due to the formation of free radicals which follows reperfusion and these free radicals can act directly on the vasculature or act indirectly by stimulating neutrophils and platelet activating factor. In the post-hypoxic period, secondary neuronal damage occurs by apoptosis and by necrosis. Approximately 72 hours following the hypoxic-ischaemic insult there occurs a stimulation of neurotrophic factors such as insulin growth factor 1 which may act to rescue neurons.

The animal model for acute neonatal asphyxia has been used to explain the physiological changes in the infant who fails to establish or maintain respiration soon after delivery. It is important to understand the physiology of birth asphyxia in order to resuscitate a newborn baby adequately.

In an animal which does not establish respiration after delivery, the early period where there is no breathing is called primary apnoea and may last up to 10 minutes. After 1 – 2 minutes of primary apnoea the animal may begin to gasp with increasing frequency and vigor, the gasping finally decreasing until the last gasp is taken. The heart rate falls rapidly or may rise in the initial minutes while gasping, then it begins to decelerate; the blood pressure will change according to heart rate in parallel. Cardiac activity can continue up to 10 minutes after the last gasp is taken. Secondary or terminal apnoea lasts from to the time the animal takes the last gasp to the time the heart stops beating. Biochemical changes are those of a mixed acidemia with a pH < 6.5 at the end of terminal apnoea and a P_aO_2 of 0, P_aCO_2 >13.5 kpa (100 mmHg), and serum potassium more than 15mmol/L [1].

Due to the brain's ability to metabolize lactate and ketones, and the large glycogen stores in the liver, brain, and myocardium, a neonatal primate can survive 20 minutes without oxygen but brain damage occurs as more time passes. Survival of these infants can be prolonged, combating the hypoglycemia and acidemia resulting during asphyxia by giving intravenous glucose and bicarbonate.

The above picture is that of acute total asphyxia which can result in death if not relieved. In practice chronic partial asphyxia occurs more commonly. This chronic partial asphyxia can occur several hours or days before birth such that the fetus has time to adjust temporarily prior to birth and can actually be born fairly normal with a fair Apgar score only to develop complications such as hypoxic-ischemic encephalopathy with seizures several hours after birth. Short-lived episodes of partial asphyxia prior to delivery are unlikely to result in serious or long term sequelae where as severe or prolonged episodes are more likely to result in sequelae. During each episode a mixed metabolic and respiratory acidosis results. After a few episodes the heart rate and blood pressure falls and ischemic changes occur in many vital organs.

The brain is the organ most affected by the asphyxial insult [1]. Brain injuries are of two types: hypoxic and vascular [7] and can be explained by the following mechanisms 1) cytotoxic: membrane pump failure leading to an increase in intracellular fluid.

2) vasogenic: capillaries begin to leak because of the impairment in the blood –brain barrier leading to an accumulation of fluid in the interstitial space.

Severe total asphyxia leads to hypoxic damage to oxygen sensitive area such as the brainstem and basal ganglia. Injury to basal ganglia is thought to lead to dyskinetic cerebral palsy [1] seen in some of the survivors of birth asphyxia. Partial hypoxia leads to a rise in cerebral blood flow with resultant brain edema and hemorrhage. Cerebral edema may occur within 24-48 hours, accompanied by

flattening and widening of the gyri with obliteration of the sulci [1]. Injury of the white matter at term produces subcortical leukomalacia. Sometimes a severe hypoxic ischaemic insult results in a mixed pattern of injury known as multicystic leuco-encephalopathy [1]. Occasionally hypoxia-ischemia leads to infarction of the tissues supplied by middle cerebral artery.

The other organs in the body can be affected by hypoxic-ischaemic damage resulting in the following:

1.	**Renal**	:	Acute renal failure
			Hematuria
2.	**Gastrointestinal**	:	Necrotizing enterocolitis
			Feed intolerance
3.	**Cardiovascular**	:	Myocardial ischaemia
			Papillary muscle necrosis
4.	**Haematological**	:	Disseminated intravascular coagulation
5.	**Metabolic**	:	Inappropriate ADH secretion
			Hypoglycemia
			Acidosis
6.	**Pulmonary**	:	Apnoea
			Persistent pulmonary hypertension

BURDEN OF ASPHYXIA

The association of clinical indicators of peripartum asphyxia with childhood neurological handicaps has been known for over a century [32]. Several studies have been undertaken to examine the developmental status of children surviving neonatal depression and neonatal asphyxia. Neonatal asphyxia causing ischaemic encephalopathy may result in the chronic handicapping conditions of cerebral palsy, mental retardation, learning and behaviour disorders, deafness, visual impairment, and epilepsy [5,33]. Although many different clinical indicators of asphyxia have been used and different neurointellectual outcomes have been assessed, a consistent pattern of results emerges; the overwhelming majority of survivors of clinically defined severe neonatal asphyxia are neurologically intact but a small minority have severe handicaps which are frequently multiple [21,32,34]. In a paper from the American National Collaborative Perinatal Project, cerebral palsy occurred in 1 – 6% of the survivors of a low 1 minute score and 5% of those with a low 5 minute score [21]. This project noted that most of the children who survived severe birth asphyxia without very severe handicap did well. Thompson and colleagues concluded that asphyxia has an "all or none effect" [16]. A study done in South Africa however contradicted the above finding that birth asphyxia is an uncommon cause of cerebral palsy [6]. In developed countries this may be associated with the decrease in the incidence of hypoxic ischaemic encephalopathy over the years as documented by Keith Dodd et al in study done in Central England where incidence dropped from 7.7/1000 (1976-80) to 1.9/1000 live births

(1982 – 1986) [35]. However, in developing countries such as South Africa, it appears that birth asphyxia is a more common cause of cerebral palsy than in developed countries [6].

Despite the picture portrayed in most studies that severe birth asphyxia does not have an extremely gloomy prognosis, the impact of asphyxia causing sequelae is felt not only at family level but spanning out to the community as a whole, and also affecting medical resources. It is this socio-economic burden that necessitates interventive strategies to minimize the effects of birth asphyxia.

OBJECTIVES

GENERAL OBJECTIVE

To determine the short term outcome of infants born with low Apgar score at the University Teaching Hospital.

SPECIFIC OBJECTIVES

1. To document the complications associated with low Apgar score at the University Teaching Hospital.

2. To determine the prevalence of known predictors of neonatal mortality in babies born with low Apgar score.

3. To document the clinical outcome in infants with low apgar scores.

4. To determine the association between hypoxic ischaemic encephalopathy and mortality/morbidity.

METHODOLOGY

Study Type and Study Setting

A cross-section descriptive study was conducted in the neonatal intensive care unit at the University Teaching Hospital, Department of Paediatrics and Child Health.

Study Population

Inclusion criteria:

1. Infants born with both the one minute and five minute Apgar score less than 8.

2. Infants with only the 1 minute Apgar score less than 8 and had no recorded 5 minute Apgar score but had any of the signs of HIE such as convulsions and abnormalities in tone.

3. Infants with only the 5 minute Apgar score recorded as less than 8 had no recorded 1 minute Apgar score.

Exclusion criteria:

1. Infants born with a gestational age less than 37 weeks (gestational age taken as the best estimate based on the recorded obstetric parameters or the clinical estimation). In preterm infants, immaturity of the central nervous system makes it difficult to interpret the Apgar score in relation to asphyxia.

2. Infants whose 1 minute Apgar score was less than 8 but 5 minute Apgar score was greater than 7.

3. Infants with only the 1 minute Apgar score recorded as less than 8, had no recorded 5 minute Apgar score and no signs of HIE.

4. Infants with no recorded Apgar score regardless of presence or absence of signs of HIE.

Sample Size

The sample size was calculated at 95% confidence using statistical measures and determined to be 152.

Data Collection

Data was collected on a structured form by the investigator.

Reference was made to the neonatal case records and relevant information extracted from the time of admission until the end of the follow-up period. Follow up was done by reviewing the neonates' case records on a daily basis and relevant information extracted from the notes and entered onto the structured form. Follow up was done within the neonatal period only i.e. the first 28 days of life. The end of the follow up period was described by the following:

a) day of discharge within the neonatal period

b) day of death within the neonatal period

c) a patient who was on the ward after the 28th day of life was not followed up further but the condition on the 28th day was taken as the final outcome. Upon discharge no further information was collected if a patient returned for review or if the patient was re-admitted even if the infant was less than 28 days.

Study variables included the following:

a)   Maternal

- Age

- Parity

- Pregnancy complications and length of labour.

- Mode of delivery and length of labour

b)   Neonatal

- Date/time/place of birth

- Apgar score

- Multiorgan complications:

    - Pulmonary (respiratory distress, apnoea, ventilatory support)

    - Neurological (seizures and abnormalities of tone)

    - Renal (passage of urine)

    - Gastrointestinal /feeding problems (vomiting, abdominal distension, aspiration)

    - Cardiovascular (cardiac failure)

    - Others: included sepsis and other complications noted in the neonatal case record.

Other outcome measures included are mortality and condition of infant at discharge or at the end of the neonatal period.

Data Analysis:

Data was analyzed using EPI-Info Version 6.04 statistical software; where comparisons were performed Chi Square and Odds ratio were utilized with 95% confidence interval.

Ethical Consideration:

Permission to conduct the study was sought from the University of Zambia Research & Ethics Committee, the Managing Director University Teaching Hospital and the Department of Paediatrics and Child Health at the University Teaching Hospital.

Informed consent was not required from the mother or guardians of the infants included on the study, as this was a purely clinical study involving extraction of information from neonatal case records without omitting or adding to the usual management on the ward.

RESULTS

A total of 1,101 infants were admitted to the neonatal intensive care unit over the period in which the study was conducted from December 2001 to March 2002. Two hundred and eighty five of these infants were referred with a diagnosis of asphyxia; 61 were excluded on the basis of prematurity, 2 had no recorded Apgar scores (one of these infants was born at home), and 3 didn't have 5 minute Apgar scores recorded and had no features of asphyxia. . Fifty-eight infants were excluded because their 5 minute Apgar scores were greater than 7. A total of 161 patients were recruited into the study; of these 141(87.6%) were born in UTH and the remainder at the local clinics. The percentage of male infants was 60.2% and females 39.8%. The gestational ages ranged from 37 to 42 weeks. Three of the infants were born with isolated congenital anomalies namely polydactyly, bilateral cleft lip and palate, and talipes equinovarus. The number of patients delivered by spontaneous vaginal delivery was 100, by breech extraction 10, by forceps 10 and 40 by caesarian section. Information regarding mode of delivery was missing for 1 infant. The reasons for performing a caesarian section were numerous as shown in table 2, the commonest being fetal distress (43.6%) though the parameters defining fetal distress were not specified on the neonatal case record. The mode of delivery was not significantly associated with outcome nor was it significantly associated with low Apgar scores . A total of 42 patients had pregnancy or risk factors recorded as shown in table 3-1. The presence of pregnancy risk factors was not significantly associated with outcome. Table 3-2 shows that the length of the

second stage of labour was significantly associated with outcome. The greatest length of second stage of labour was 1 hour 40 minutes.). Seventy two infants did not have a recorded second stage of labour and 40 of these were delivered by caesarian section.

A total of 123(76.4%) infants had birth weights appropriate for the gestational age, whereas 14.9% were large for gestational age and 8.7% were small for gestational age. Appropriate weight for gestation at term was taken to be 2500-3500g; a weight below 2500 was taken to be low for gestation and an infant with a weight more than 3500 was considered large for gestation. The lowest weight recorded was 1960g and the highest was 4940g. Birthweight was not significantly associated with outcome.

Table 1: Delivery modes

Mode of delivery	Frequency	Percentage
Vaginal vertex	100	62.5
Breech extraction	10	6.2
Instrumental	10	6.2
Caesarian section	40	24.5
Not known	1	0.6
Total	161	100
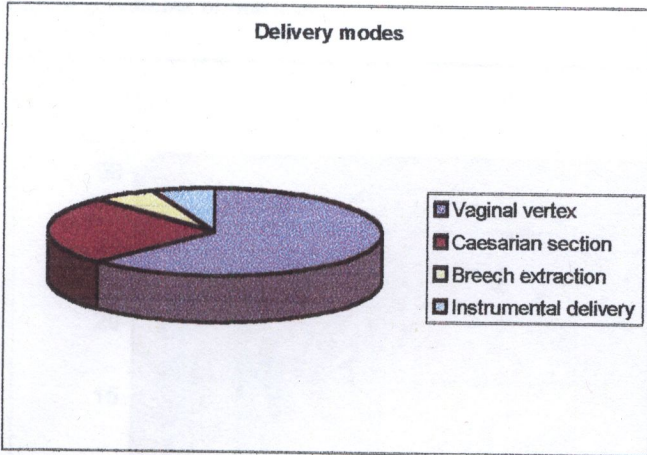
Table 2: Indications for caesarian section

Reason for caesarian section	Frequency	Percentage
Antepartum haemorrhage	2	5.2
Breech presentation	3	7.8
Cord prolapse	1	2.6
Cephalopelvic disproportion	1	2.6
Eclampsia	2	5.2
Fetal distress	17	43.6
Pregnancy induced hypertension	1	2.6
Placentae praevia	1	2.6
Previous caesarian section	4	10.3
Prolonged 1st stage	7	17.1
Transverse lie	1	2.6
Total	40	100

Figure 1: Number of Seizures
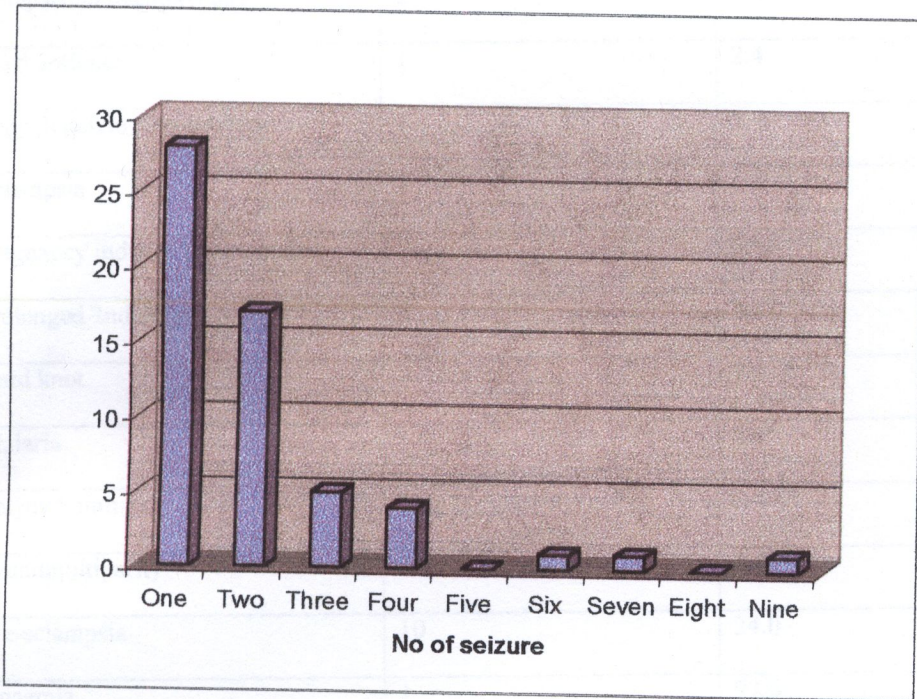
Figure 2: type of HIE
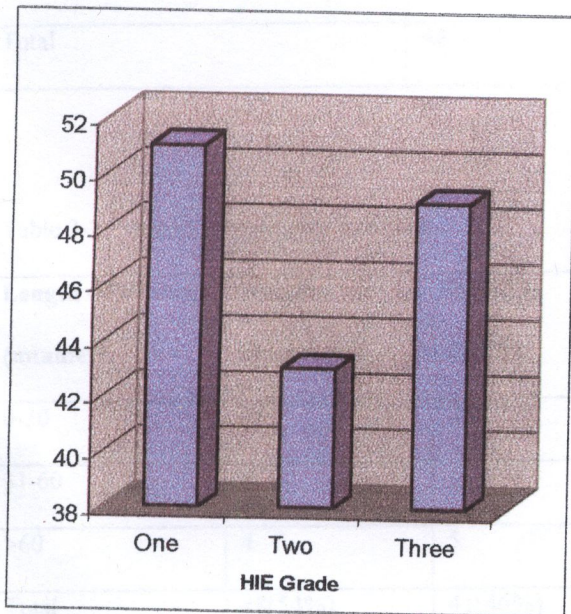
Table 3-1: Pregnancy complications

Pregnancy risk factors	Frequency	Percentage
Antepartum haemorrhage	2	4.8
Cord prolapse	1	2.4
Cephalopelvic disproportion	1	2.4
Eclampsia	2	4.8
Pregnancy induced hypertension	7	16.7
Prolonged 2nd stage	4	9.5
Cord knot	3	7.2
Malaria	1	2.4
Polyhydramnios	1	2.4
Grandmultiparity	3	7.2
Pre-eclampsia	10	24.0
Anaemia	1	97.6
Previous caesarian section	4	9.5
Premature membrane rupture	1	2.4
Syphilis	1	2.4
Total	42	100

Table 3-2: Second stage versus outcome

Length of 2nd stage (minutes)	Number discharged	Number of deaths	Total
0-30	38	21	59(66%)
31-60	6	15	21(24%)
>60	4	5	9(10%)
Total	48(54%)	41(46%)	89

Outcome

A total of 80 infants died (49.7%), 80 were discharged and 1 was still on the ward on the 28th day of life. All the deaths but one occurred in the perinatal period; 35 died within 24 hours of life, 20 on the second day, 7 on the third day, 8 on the fourth day, 2 on the fifth day, 4 on the sixth day and 1 on the seventh day. One infant died on the sixteenth day. The causes of death are tabulated in table 4. These causes of death are taken as they appear in the neonatal case records and death certificate book; where HIE appears as the actual defining reason of cause of death, no other complication was recorded. The discharges were spread out over a wide range of days the earliest being the second day (5 infants) and the latest being the eighteenth day (1 infant). The majority of the infants, a total of 58, were discharged within the first seven days of life; 9 on day 3, 6 on day 4, 14 on day 5, 12 on day 6, and 12 on day 7. The patient who was on the ward on the 28th day of life was being treated for culture negative septicemia.

Table 4: Cause of death

Cause of death	Frequency	Percentage
HIE	63	79.7
Septicemia	6	7.6
Pulmonary haemorrhage	3	3.8
Anaemia	2	2.5
Meconium aspiration	2	2.5
Hypothermia	1	1.3
Cardiac failure	2	2.5
Aspiration pneumonia	1	1.3

The discharged infants were neurologically intact when going home. The most noted adverse outcome therefore was death. Predictors of death therefore were an Apgar score less than 4, presence of tone abnormality, development of cardiac failure and requirement of ventilation.

Neurological complications

Abnormalities in tone:

One hundred and thirty seven (85%) of the infants had abnormalities in tone with 131 being hypotonic and 6 being hypertonic. All but one of the infants had the abnormalities from the time of admission i.e on day 1; the exception's abnormality in tone (hypertonia) was noted on the second day of admission. No record however of intrapartum drug exposure was available.

Having abnormality in tone was significantly associated with mortality with 80 of the infants affected dying (p value < 0.001). However there was no significant association between the different types of tone abnormality and mortality (p=0.09). Out of the 6 infants with hypertonia, 5 were discharged and 1 died. Out of the 131 infants with hypotonia, 79 died and 52 were discharged.

Table 5: Tone abnormality versus outcome

Outcome	Tone abnormality	No abnormality
Discharged	56(40.8%)	24(100%)
Death	80(58.9%)	0
Still on the ward	1(0.3%)	0
Total	137	24

Seizures:

Fifty-seven of the infants had at least one seizure recorded and of these 45.6% had focal or subtle seizure activity and 54.4% had generalized seizures. The maximum number of seizures was 9 in 1.8% of the 57 patients (see figure 1). Eighty-nine percent of the infants exhibited seizure activity within 24 hours of life, 7.0% on the second day, 1.8% percent on the fourth day, and 1.8 percent on the tenth day. The presence of seizures was not significantly associated with mortality (p=0.24) as shown in table 6. Table 7 shows that there is no significant association between seizure type and outcome (p=0.45).

Hypoxic-ischaemic encephalopathy:

One hundred and forty-three of the 161 infants had hypoxic-ischaemic encephalopathy (HIE) as shown in figure 2. HIE was defined using the Sarnat & Sarnat classification shown on page 17. The grade of hypoxic-ischaemic encephalopathy was significantly associated with mortality (p value < 0.001); 80 of the affected infants died and 46 of these had HIE 3 (table 8). The causes of death of the 46 infants with HIE 3 were recorded as HIE (43 infants), pulmonary haemorrhage (2 infants) and cardiac failure (1 infant). Nineteen of the 43 infants with HIE 2 died; HIE was recorded as the cause of death in 13 infants, septicemia in 4, and anaemia in 2. Out of the 51 infants with HIE 1, 15 died; HIE was recorded as the cause of death in 9 infants, hypothermia 1, meconium aspiration 1, pulmonary haemorrhage 1, septicemia 2, and aspiration pneumonia 1.

Table 6: Seizures versus outcome.

Outcome	Seizures present	No seizures
Discharged	25	55
Death	31	49
Still on ward	1	0
Total	57	104

Table 7: Seizure type versus outcome

Seizure type	Discharged	Death	Still on ward	Total
Subtle	10	16	0	26
Generalized	15	15	1	31
Total	25	31	1	57

Table 8: HIE versus outcome

Outcome	HIE 1	HIE 2	HIE 3	Total
Discharged	36	23	3	62
Death	15	19	46	80
On the ward day 28	0	1	0	1
Total	51	43	49	143

Infection

Forty of the infants were suspected to have infection. The basis of suspicion included the following: pyrexia (39 infants), prolonged hypotonia (5 infants), jaundice (6 infants), abdominal induration (1 infant), convulsions (5 infants), increased respiratory distress (1 infant), and sclerema (1 infant). It should be noted that some of these signs are not specific for infection and can occur in HIE e.g convulsions and respiratory distress. Prolonged hypotonia was considered as a basis of suspicion for infection because in an infant with HIE the usual progression for the tone abnormality is hypotonia turning into hypertonia within 48 hours of age. Only 4 of the patients had culture positive sepsis and the organisms isolated were E.coli, Enterobacter cloace, Klebsiella pneumoniae, and Salmonella species. This isolate pattern is consistent with bacterial isolates of 168 blood cultures from the neonatal intensive care unit analyzed from November 2001 to March 2002. Enterococci were the commonest isolate (34%) followed by Staphylococcus aureus (31%), Klebsiella pneumoniae (17%) and Salmonella species (3%). Other isolates included E.coli, Citrobacter species and Acnaebactericae. Of these infants with culture positive sepsis, 1 presented with pyrexia, 1 with jaundice, 1 with neonatal convulsions and 1 with a combination of pyrexia and jaundice. The presence of infection was not significantly associated with mortality (p value=0.1436).

Respiratory complications

Among the 161 study infants 87(54.1%) developed respiratory distress and 81 of these had respiratory distress within 24 hours of admission. The presence of respiratory distress was not significantly associated with mortality with a p value of 0.07826.

Forty-three of the neonates (26.7%) experienced an episode of apnoea; 83.7% of these infants became apnoeic within 24 hours of admission, 9.3% on the second day of life, and 7.0% on the third day. Apnoea was significantly associated with death (p value <0.001). Out of the 43 infants who became apnoeic, 40 died and 3 survived to be discharged later.

Forty-nine infants(40.5%) required ventilatory support; 41 were ventilated on the first day of life, and 4 on the second and third day each. Ventilation was significantly associated with death (p value <0.001). Out of the 49 infants that were ventilated 46 died and 3 were weaned off the ventilator and later discharged. Of the 41 infants ventilated on the first day of life 27 died on the same day of initiation of ventilation, 7 died in the ensuing 24-48 hours and 2 died 72 hours after onset of ventilation. Of the infants ventilated on the second day of life, 2 died on the same day and 2 on the fourth day of life. Of the 4 infants ventilated on day 3 of life, 3 died on the same day and 1 after 48 hours.

Seven of the neonates had other respiratory problems as indicated in table 9.

Table 9: Respiratory complications

Respiratory complication	Frequency
Haemo-pneumothorax	1
Aspiration pneumonia	3
Pulmonary Haemorrhage	5

Renal Complications

None of the infants were noted to have any renal complications clinically. One hundred and thirty-one infants passed urine within 24 hours of birth and one passed urine on the second day of life. The remaining 29 infants died on the first day of life before passage of any urine was noted.

Cardiac Complications

Five of the neonates had clinical signs of heart failure appearing on day 2 (2 infants), day 4 (1 infant), day 5 (1 infant) and day 12 (1 infant). No other cardiac problems were noted. All the infants who developed cardiac failure died; two of these infants died on the same day they developed the cardiac failure and this was recorded as the cause of death. The remaining three died as a consequence of septicemia. The table below illustrates the day of onset of cardiac failure and the day of death.

Table 10: Cardiac failure versus outcome

Day of cardiac failure onset	Number of infants	Day of death
2	2	2,5
4	1	4
5	1	6
12	1	13

Gastrointestinal Complications

Eighty-seven of the 161 infants had oral feeds initiated and the majority were fed

in the first 72 hours of life (see table 11). One of the infants fed on day 1 aspirated

feeds the same day of initiation and died on day 3. Three infants developed

abdominal distension with vomiting and one of these died; none of these infants

had abdominal x-rays done and a diagnosis of NEC was not definitively made. The

infants were initially fed formula milk prior to the initiation of breastfeeding or

cup feeding with expressed breast milk.

Table 11: Onset of feeds

Day breastfed	Frequency
1	23
2	38
3	8
4	9
5	6
6	1
9	1
10	1

Apgar Scores.

The frequency tables for the 1 minute and 5 minute Apgar scores are shown in figures 3 & 4. Eight infants did not have a recorded 1 minute Apgar score and fourteen did not have a 5 minute Apgar score. The 5 minute Apgar score was significantly associated with outcome; 15 of the 16 infants whose Apgar scores were less than 3 died (see figure 5).
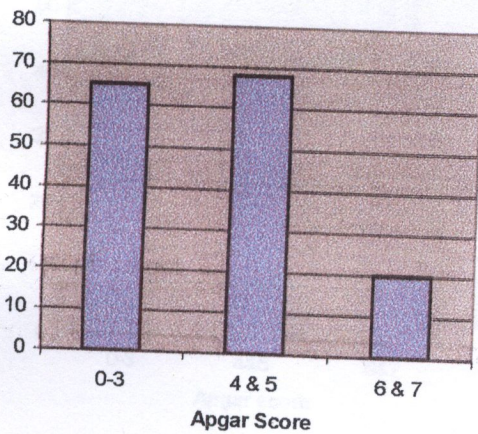
Figure 3: 1 minute Apgar score
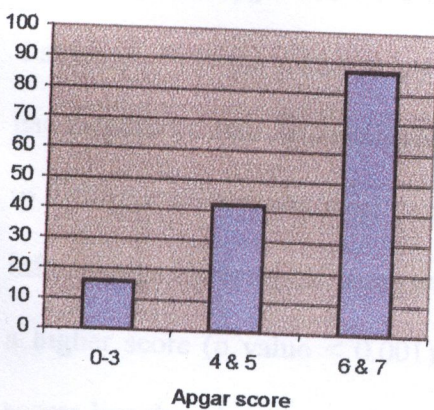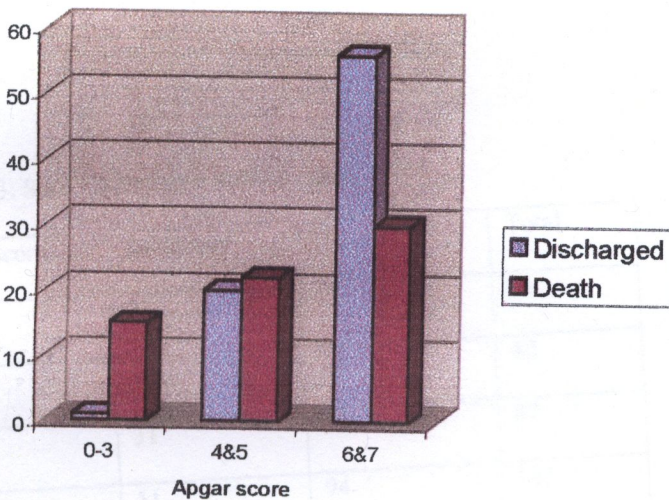

Figure 4: 5 minute Apgar score

Table 12: 5 minute Apgar scores versus HIE

Apgar score	HIE 1	HIE 2	HIE 3	Total
0-3	1	1	14	16
4-5	15	11	15	41
6-7	31	27	12	70
Total	47	39	41	127

Figure 5: 5 minute Apgar score versus outcome

The lower the Apgar score the higher the chances of developing respiratory distress; 91% of the infants whose Apgar scores at 5 minutes were less than 6 had respiratory distress as compared to only 14% of those whose scores was 6 to 7. These differences were statistically significant (p value = 0.0172). An infant with a lower Apgar score was more likely to be ventilated than one with a higher score (p value < 0.001); 87% of the infants with 5 minute Apgar scores less than 4 were ventilated as compared to 36% of those whose scores

were between 4 and 5 and 14% of those whose scores were between 6 and 7.

Table 12 shows that there was a significant association between the 5 minute Apgar score and the grade of HIE (p value = 0.000).

The Apgar scores at 5 minutes were not significantly associated with seizures as demonstrated in table 13 (p value = 0.63). Other parameters not significantly associated with low Apgar score at 5 minutes included the following:

1. Infection (pvalue = 0.26).

2. Pregnancy complication (p value = 0.23).

3. Cardiac failure (p value = 0.26).

Table 13: Seizures versus 5 minute Apgar score

Apgar score	Seizures	No seizures	Total
0-3	3	13	16
4-5	17	25	42
6-7	31	56	87
Total	51	94	145

Regarding resuscitation, 88 infants were recorded to have received oxygen by bag and mask in labour ward; 13 of these were intubated in labour ward prior to transfer to the neonatal intensive care unit (NICU). In the NICU 26 infants were given oxygen by bag and mask and 13 were intubated upon admission to the NICU. Medication given for resuscitation was frequently not recorded therefore not analyzed.

DISCUSSION

There is no single or universal definition for the term birth asphyxia [2,24,36,37]. The Apgar score is still being used to define asphyxia [5,10,15,18,21,24,28]. It has been argued that the Apgar scoring is subjective and that most labour ward staff tend to over score, more so when the actual score is low [26,38]; another disadvantage may be that the score may not reflect the duration of asphxia [10]. In developing countries where health institutions are underprivileged, the Apgar score continues to have a place as a method to assess the well being of the newborn [10,19,23,26,38,39] and also to define asphyxia [5,10,15,18,21,24,28], taking into consideration it's limitations. Some studies have reported that the Apgar score was a more sensitive indicator of outcome than lowered umbilical cord pH [23].

In this study low 5 minute Apgar scores i.e less than 8, were associated with reduced chances of neonatal survival: 49.7% of the newborns suffered neonatal death. This is similar to a study done in Harare by Nathoo et al where 41.7%of the infants with low Apgar scores died [10]. An Apgar score less than 4 was the most ominous in this study with 94% of the affected infants succumbing to death; only one infant survived and was neurologically intact on discharge. Study results from other parts of the world show varied results: in the USA an Apgar score less than 4 was associated with 44% mortality, in Zimbabwe 77% mortality [10], and in Sweden with 21% mortality [40]. A study done in Singapore by VC Toh demonstrated that a 5 minute Apgar score less than 4

had a predictive value of death of 84.2% [41]. Unfortunately the higher survival rate in Sweden was accompanied by high rates of neurological handicap. In this current study all the surviving infants were neurologically intact on discharge in concordance with authors reporting that asphyxia has an all or none effect [21,32]. Follow up beyond the hospital stay would however be necessary to determine the long-term effects of the low Apgar scores on these infants.

Multiple system complications have been documented following clinically defined asphyxia [12,37]. One of the systems most affected in this study was the central nervous system. Seizures were noted in 35.6% of the infants. Seizure activity ranged from subtle lip smacking and limb cycling to generalized tonic fits. Previous publications have reported incidences of seizures as high as 50-70% in acutely asphyxiated newborn infants [8]. Seizures were not significantly associated with mortality in this study. Similarly Aggarwal et al did not find a significant association between seizures and outcome [42]. In contrast Nathoo et al in Zimbabwe noted a high case fatality rate in association with seizures [10] and John C Mulligan in Pittsburgh obtained similar results [9]. But the effect of seizures on long-term morbidity needs to be assessed in the Zambian setting. Perinatal hypoxic ischaemic injury is a major cause of death [43]. In this study an infant with HIE 3 was more likely to die than one with HIE 1 or 2. This was probably related to the fact that these babies were ventilated and ventilation was significantly associated with death; 93.9% of the ventilated babies suffered death. Previous studies have reported similar results [42,44,45].

Ventilation was initiated due to apnoea in 43 infants and due to increased respiratory distress in 6 infants. Respiratory distress was a common occurrence; 93% of the infants experienced respiratory distress within 24 hours of admission. Failure to initiate or maintain adequate respiration led to requirement of ventilatory support in 30.4% of the infants. The high mortality associated with ventilation may be a reflection of the severity of the hypoxic-ischaemic insult. However with the lack of adequate monitoring of ventilated infants in the neonatal intensive care unit, further analysis is required to assess the impact of ventilation on hypoxic-ischaemic associated mortality. The respiratory complications were probably a reflection of central nervous system depression or respiratory distress syndrome.

Twenty five percent of the infants were suspected to have sepsis but only 10% of these had culture proven sepsis. An infection audit done in the neonatal intensive care unit between November 2001 and March 2002 showed positive isolates on blood culture to be 17.26% [17]. Infection is known to mimic the signs of perinatal asphyxia [6] therefore with a background of diagnosing asphyxia using the Apgar score alone or in combination with clinical signs such as hypotonia or convulsions without laboratory evidence of acidosis, a lot of the infants being treated for asphyxia may actually be septicemic.

Passage of urine was used to assess the infants renal system. The study demonstrated that the renal system was not affected at all. All but one of the infants who survived beyond 48 hours of life passed urine within 24 hours of admission. Unfortunately the assessment was qualitative rather than

quantitative in that the actual amount of urine passed was not measured but rather the presence of a wet nappy was taken to indicate that urine was passed. Therefore if the infant had significant oliguria the assessment used would not have been accurate. Laboratory backup for the renal system was not available in the hospital. In a study done by James A. Low et al to assess newborn complications following asphyxia, the renal system was the least affected of all the systems studied, namely the central nervous, cardiac, renal, and respiratory systems; 25% of the newborns had renal complications as compared to 50% with respiratory and 60% with central nervous system complications [37]. In his study Low included haematuria and elevated serum creatinine to assess the function of the kidneys but these test were not being done routinely at the University Teaching Hospital at the time the study was conducted. It is possible therefore that involvement of the kidneys could have been missed.

Three percent of the study infants developed cardiac complications namely cardiac failure. James Low demonstrated a higher percentage of infants with cardiovascular complications (60%). This difference may be a reflection of the fact that infants with isolated tachycardia or bradycardia were not included as having cardiac complications in this study and there was no formal assessment of hypertension or hypotension due to lack of appropriate equipment; all of these parameters were considered by Low.

Infants in this study had oral feeds initiated early. A total of 87 infants were fed orally and 61 of these infants were fed within the first 48 hours. Overall the infants tolerated the feeds well. Only one of the infants fed on day one

aspirated feeds and died 2 days later. None of the infants who died within 24 hours were fed. Of the infants ventilated, only 3 were fed orally after they stabilized off the ventilator. None of the infants were documented as having necrotizing enterocolitis on clinical grounds however abdominal x-rays were not done.

CONCLUSION

Complications associated with low Apgar scores were multiple as noted in this study. Abnormalities in tone and seizure activity occurred frequently. Respiratory distress was common as was apnoea. Cardiac failure though infrequent was noted. There was a high associated mortality. Mortality was significantly associated with Apgar scores less than 4, ventilation, cardiac failure, and HIE 3.

Study Limitations

This study involved the extraction of information from neonatal case records. Various healthcare providers were responsible for the clinical care of the infants therefore the results depended upon the acumen of these healthcare providers as well as their accuracy in writing the clinical notes. Subjectivity therefore could not be ruled out and there was no blinding of the healthworkers assessing the infants in the NICU in relation to the birth history. Certain variables could not be analyzed due to missing data e.g detailed notes on resuscitative procedures.

The study was carried out in a referral hospital therefore the results cannot be generalized.

The shortages (health staff, laboratory facilities, financial) that plague this hospital led to the unavailability of information that could have been helpful; for instance it was not possible to do blood gas analysis or blood chemistry.

Without an independent observer for the Apgar scores, the possibility of over or under scoring cannot be ruled out completely.

Due to lack of financial support and time limitation, follow up could not be done beyond the neonatal period.

Recommendations

A study to follow up these infants beyond the neonatal period is required to fully assess the impact of asphyxia on the Zambian infant and it's contribution to cerebral palsy.

Studies to assess the treatment instituted versus the outcome would also be of value.

Blood-gas analysis is required to avail appropriate intensive care to these neonates. This may assist in assessing the effect of ventilation in asphyxiated infants.

Considering the poor prognosis of infants born with low Apgar scores, appropriate obstetric intervention is required to minimize the number of such infants.

The impact of neonatal sepsis on Apgar scores needs further evaluation using more sensitive methods than blood cultures; screening from the first day of life would be more appropriate than several days after admission when antiobiotics have already been given.

Studies of this nature are required in other settings country wide to compare incidence and outcome in order to avail appropriate interventions.

In-service training is required for staff working in the NICU and labour ward to re-orient them on diagnosis of asphyxia, resuscitative procedures, and the need to clearly document findings at all times.

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ANNEX 1
QUESTIONNAIRE

Study No. ----------------------

1. Maternal Information
1. Mother's initial _____ _____
2. Age (years) _____
3. Parity _____
4. Pregnancy Complication   Y   N
    If yes specify _____
5. Mode of delivery   a) Vaginal Vertex
                b) Vaginal breech
                c) Assisted/instrumental delivery
                d) Caesarean Section
                   Reason for Caesarean section _____
6. Length of labour 1st stage _____ hrs _____ mins   N/R   N/A
                  2nd stage _____ hrs _____ mins   N/R   N/A

2 Neonatal Information
A. General
1. Date of birth _____ / _____ / _____
2. Place of birth _____
3. Time of birth ____ ____ : ____ ____
4. Time of arrival in Neonatal ICU ____ ____ : ____ ____
5. Sex _____
6. Gestational age _____ weeks
7. Birth weight _____ g
8. Apgar Score 1 minute _____
               5 minute _____
9. Heart rate _____ per minute
10. Respiratory rate _____ per minute
11. Hematocrit _____
12. Dextrostix _____
13. Any congenital anomaly   Y   N
    If yes specify _____
14. Resuscitation   a) Labour ward   Y   N   N/R
                 If yes specify _____
                b) NICU   Y   N   N/R
                 If yes specify _____

B. Respiratory
1. Respiratory distress   Y   N   If yes day of appearance _____ duration _____
2. Apnoea   Y   N   If yes day of appearance _____ duration _____
3. Ventilation   Y   N
    If yes day infant ventilated _____
    Duration of ventilation _____
4. Other respiratory problem   Y   N
    If yes specify _____

C. Renal
1. No urine passed
2. Passed urine   a) within 24 hours
                 b) 24-48 hours
                 c) 48 hours (specify age) _____

Cardiovascular
1. Cardiac failure   Y   N   If yes, day of appearance _____ duration _____
2. Other complications   Y   N
   If yes specify _____

Gastrointestinal
1. Any feeding or other gastrointestinal problem   Y   N
   If yes specify _____
2. Breastfed / cup fed   Y   N
   If yes specify day infant fed _____

Neurological
1. Abnormalities in tone   Y   N
   If yes specify _____ Day of appearance _____ Duration _____
2. Seizure   Y   N
   If yes: specify type _____
          Number of seizures _____
          Day of appearance _____
          Day last seizure recorded _____
3. Other neurological problem?   Y   N
   If yes specify _____
4. With above information, specify grading of HIE if applicable _____

G. **Infection**
1. Any infection   Y   N
   If yes a) suspected
          Specify specific reasons for suspicion _____
       b) culture proven with _____ (specify organism)

1. **Other**
1. Other complications noted   Y   N
   If yes specify _____

Final Outcome
1. Discharged and well
2. Discharged with complication
   Specify complication _____
3. Death
   Cause of death _____
4. Still on ward on Day 28
   Complications_____

   Day of final outcome_____

   Note: if the answer is yes to any of the above, day of appearance of the specific
   complication has to be noted as well as the duration.

3. Comments

ANNEX 2
TABLES

1 – Delivery mode

2 – Indication for caesarian section

3-1 – Pregnancy complications

3-2 – Second stage versus outcome

4 – Cause of death

5 – Tone abnormality versus outcome

6 – Seizures versus outcome

7 – Type of seizures versus outcome

8 – HIE versus outcome

9 – Respiratory complications

10 – Cardiac failure versus outcome

11 – Onset of feed

12 – 5 minute Apgar scores versus HIE

13 – 5 minute Apgar scores versus seizures