A descriptive study of suspected perinatal asphyxia at Mitchells Plain District Hospital. A case series.

Stofberg, JPJ.
MBChB (SU); Dip HIV Man (SA)
Master of Medicine (MMed) in Family Medicine, University of Cape Town
Contact Details: mail4hanno@gmail.com
0798679327

Supervisors
Spittal, GW
MBChB (Glasgow University); MRCPCH; FC Paed; MMED(UCT); Dip HIV Man (SA)

Hinkel, T
MBChB (UP), FCOG, MMED (SU)

Ras, T
MBChB (UCT), MFamMed (UCT), FCFP (SA)

Index

Declaration:

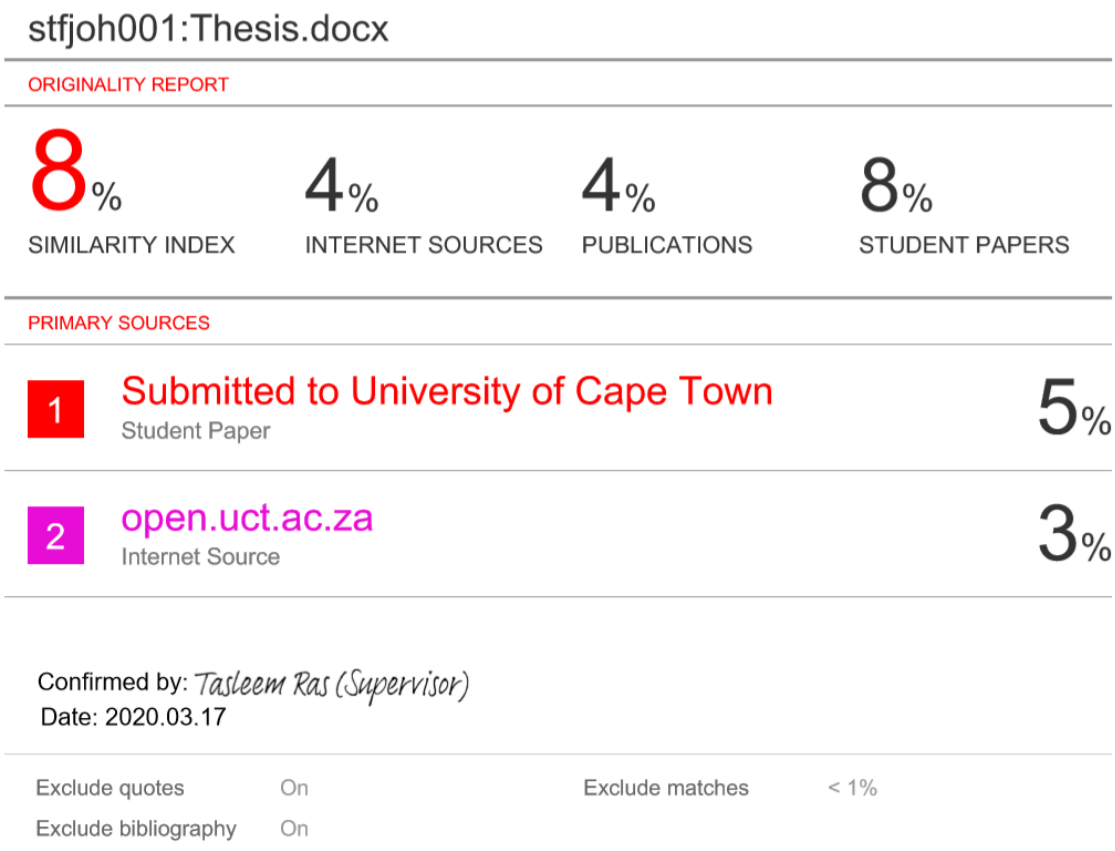
I, Johannes Petrus Jordaan Stofberg, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university. I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signed by candidate

Signature: _____

Date: 17 March 2020

Turnitin Report:



List of Abbreviations:

aEEG - amplitude-Electroencephalogram

CFM - Cerebral Function Monitoring

CTG – Cardiotocogram

C/S - Caesarean Section

DHIS – District Health Information System

ECM - Electronic Content Management System

EMS – Emergency Medical Services

GSH - Groote Schuur Hospital

HIE – Hypoxic Ischaemic Encephalopathy

MDG – Millennium Developmental Goals

MMH – Mowbray Maternity Hospital

MOU – Midwife Obstetric Unit

MPH – Mitchells Plain Hospital

NICE - National Institute for Health and Care Excellence

NVD - Normal Vertex Deliveries

PIPP - Perinatal Problem Identification Programme

ROM – Rupture of Membranes

SDG – Sustainable Developmental Goals

SPSS – Statistical Package for the Social Sciences 25

Chapter One: Literature Review

Introduction

Since 2005 there has been a decline in the global neonatal mortality rate from 36 per 1000 live births to 19 per 1000 in 2015. This marked the end of the Millennium Developmental Goals (MDG) initiative. [1] These figures equate to an approximate decline from 4 million to 2.7 million annual neonatal deaths during these ten years. [1, 2] Despite these successes, neonatal mortality and morbidity prevails as one of the major global health concerns. Furthermore, the reduction of neonatal deaths has been disproportionally slower in comparison to deaths outside of the neonatal period. [3]

South Africa has committed to the Sustainable Development Goals (SDG) as set by the United Nations. Goal 3 of the SDG is "Good Health and Well-Being for people" and aims to end all preventable deaths of new-borns and children under the age of five years. [3] Neonatal deaths form a substantial figure in this particular group and has been estimated to contribute as much as 45% of all deaths under the age of 5 globally. [4] South African figures are even higher and neonatal mortality is estimated to be 50% of all childhood deaths under the age of 5 years. [5]

Historically, South Africa failed in achieving the Millennium Development Goals in terms of neonatal mortality. According to the District Health Information System (DHIS), South Africa is close to the target neonatal mortality rate of 12 deaths per 1000 live births as set by the SDG, reaching 12.6 per 1000 live births. [6] However, the South African Demographic Health Survey reports a much higher neonatal mortality rate of 21 per 1000 live births. [7]

The three most prevalent causes of neonatal mortality in South Africa are complications of prematurity (47.9%), perinatal asphyxia (24.3%) and infections (11.6%). [6] However, when one excludes the extremely low birth weight category (<1000g), perinatal asphyxia is the number one cause of death in neonates. [6] Just over 50% of all birth asphyxia related deaths occur at district level hospitals as opposed to community health centres (2.8%), regional (22.5%) or tertiary hospitals (23.9%). [6] Most of this information is gathered via the Perinatal Problem Identification Programme (PPIP). The programme has many strengths; however, it is estimated to record only 77% of all relevant data. This figure may be attributed to different facilities' commitment to collecting and submitting the information. [6]

For the purpose of reading this document, it is important to distinguish between perinatal asphyxia and Hypoxic Ischaemic Encephalopathy (HIE). Perinatal Asphyxia is the term which describes a condition where there is decreased oxygenation of the fetus during the perinatal period (20 weeks gestation to day 7 of life). When this period of decreased oxygenation is severe and prolonged it may result in cerebral ischaemia severe enough to cause encephalopathy. This pathological process results in a syndrome, which is based on a combination of clinical and biochemical factors, referred to as HIE. [8, 9]

In South Africa it is difficult to estimate the exact prevalence of HIE and it can vary between 2.3-26.5 per 1000 live births. [10, 11] This variability in prevalence is due to a multitude of factors, one of which is dependent on the specific clinical definition used to establish the diagnosis. [11] Various criteria have been suggested and implemented for entry criteria into treatment modalities. In one study performed at Chris Hani Baragwanath Hospital in Johannesburg, the incidence of birth asphyxia was found to range between 8.7-15.2 per 1000 live births. The same study suggested a mortality rate of 8.9-12.3% encompassing all severities of HIE. [12] A study conducted at Groote Schuur, Mowbray Maternity and New Somerset Hospitals showed a similar mortality rate of 13%. [13]

The management of neonates who suffered perinatal asphyxia with suspected HIE is a complex process. This involves time dependent intricate decision making and highly specialised monitoring and treatment modalities which can only be provided at limited facilities. Furthermore, it has significant cost and ethical implications. These factors demand skilled and accurate initial diagnoses, as well as strict entry criteria to allow for appropriate referral and treatment of these cases. [11, 13]

Mitchells Plain Hospital (MPH) is a metro district hospital in Cape Town which provides an obstetric and neonatal service to a large population. It has been noted locally and supported by evidence nationally that PPIP data does not account for all the suspected perinatal asphyxia cases. In addition to the importance of appropriate and rapid referral, the need to review cases of perinatal asphyxia at MPH is highlighted by their underrepresentation. Such an investigation will draw knowledge from previous management performance in the obstetrics and neonatal services and ultimately strengthen current practice.

Literature Review Methodology

This literature search was conducted utilising several databases, including Medline/PubMed, Google Scholar and the Cochrane Library. The search was extended to the references of relevant articles found in the primary literature searches as well as to other literature which cited said articles. The following search strategies were used:

Hypoxic Ischaemic Encephalopathy OR *HIE* OR *Perinatal Asphyxia* AND *Incidence* OR *Prevalence*

Hypoxic Ischaemic Encephalopathy OR *HIE* OR *Perinatal Asphyxia* AND *South Africa*

Hypoxic Ischaemic Encephalopathy OR *HIE* OR *Perinatal Asphyxia* AND *Treatment* OR *Management*

Hypoxic Ischaemic Encephalopathy OR *HIE* OR *Perinatal Asphyxia* AND *Treatment* OR *Management* AND *South Africa*

Hypoxic Ischaemic Encephalopathy OR *HIE* OR *Perinatal Asphyxia* AND *prognosis*

Hypoxic Ischaemic Encephalopathy OR *HIE* OR *Perinatal Asphyxia* AND *Diagnosis* OR *Assessment*

Hypoxic Ischaemic Encephalopathy OR *HIE* OR *Perinatal Asphyxia* AND *Scoring* OR *Classification*

Perinatal Mortality AND *Neonatal Deaths*

Neonatal Mortality OR *Neonatal Deaths* AND *South Africa*

Perinatal Asphyxia OR *Hypoxic Ischaemic Encephalopathy* AND *Antenatal Care*

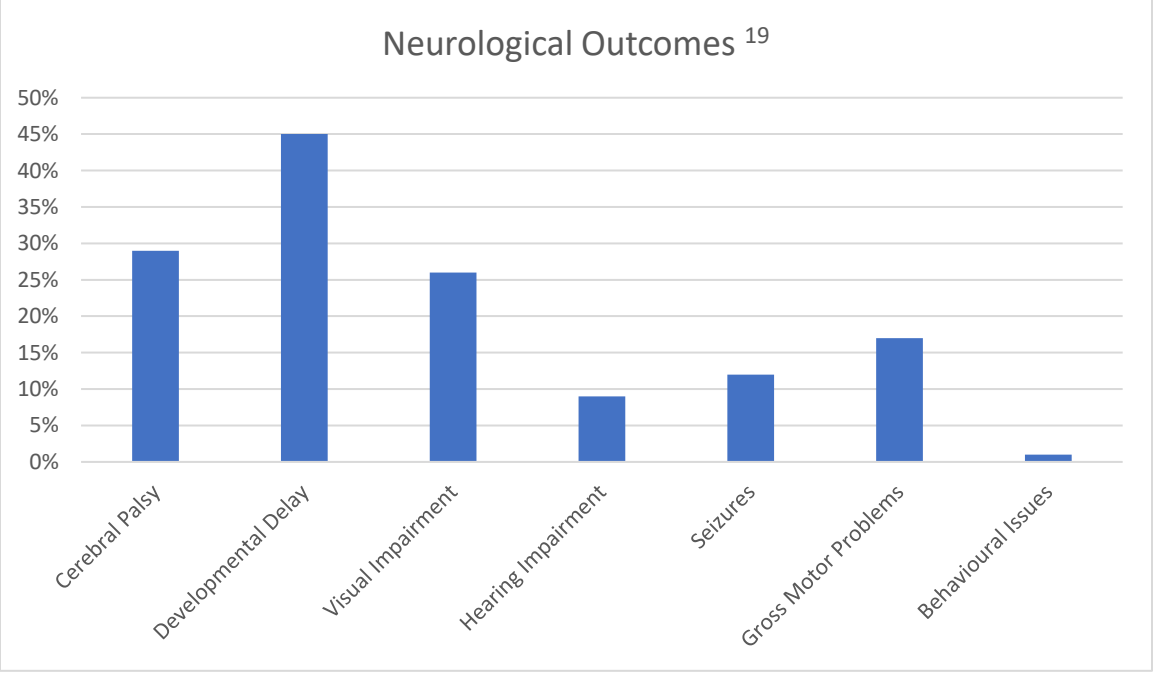
Perinatal Asphyxia OR *Hypoxic Ischaemic Encephalopathy* AND *Intrapartum Care*

Perinatal Asphyxia OR *Hypoxic Ischaemic Encephalopathy* AND *Obstetric Risk Factors*

Epidemiology - Incidence, Morbidity and Mortality

Due to the large variation of criteria which are used by individual facilities, there may be a significant difference in incidence of suspected perinatal asphyxia and HIE depending on which set of criteria is used. As referred to above, detection of such cases is commonly missed and of the true cases identified a considerable percentage are not being captured to contribute to local and national statistics. Furthermore, fresh stillborn babies with asphyxia as cause of death might not be considered in these statistics and further skew the perspective. These are some of the issues owing to the difficulty of establishing the exact incidence rate of perinatal asphyxia and HIE in our setting. In South Africa the incidence rates may vary between provinces and even within the same metropole. [10-12] The international perspective on perinatal asphyxia is slightly more conservative and places the incidence rates at 1-6 per 1000 live births, although this is mostly data from developed countries. [14] Mortality rates may vary between 20% globally and 8.9-13% locally. [12-16]

Clinical sequalae of morbidity are well known and may have profound quality of life and cost implications to the patient and their family. Detrimental neurological outcomes are the most common complication and are present in up to 25% of all cases. [15-16] The mortality and morbidity are dependent on the severity of HIE. [17] A study investigating moderate HIE found up to 36% of their study population to have significant morbidity or have died by the age of 12 months. [18] Of these neurological outcomes, 29% were found to have cerebral palsy, 45% had learning difficulties or developmental delay, 26% had visual impairment (including blindness), 9% hearing impairment, 12% seizures, 17% developed gross motor problems and 1% were behaviourally disturbed. [19]



Clinical assessment and treatment trends

There are a multitude of factors to consider with the early management of possible perinatal asphyxia and HIE. This includes initial resuscitation, clinical assessment and monitoring, fluid administration and management of complications. It also involves specialised monitoring and treatment modalities such as cerebral function monitoring and therapeutic hypothermia.

Therapeutic hypothermia is the mainstay of treatment for neonates with confirmed HIE. It has been established based on the Cochrane Review which considered 11 randomised control trials and found that therapeutic hypothermia is beneficial. It reduces both mortality and morbidity of moderate to severe HIE, with a combined relative risk reduction of 25% and an absolute risk reduction of 15% by 18 to 24 months. [20-21]

Therapeutic hypothermia requires strict gate keeping due to many factors, ranging from cost implications, risk of complications, likelihood of benefit, limited access and ethical contemplations. Due to these constraints, the criteria for therapeutic hypothermia needs due consideration. In 2014, the *Journal of Paediatric and Neonatal Individualized Medicine* published an article considering three consensus statements in an attempt to standardise the criteria for cases of perinatal asphyxia sufficient to result in either moderate or severe encephalopathy. [22] They included the statements of the *American Academy of Pediatrics* and *American College of Obstetrics and Gynecology (1996),* the *International Cerebral Palsy Task Force (1999)* and the *American College of Obstetrics and Gynecology (2002).* All three statements were different, which emphasises the difficulty in establishing these criteria. However, all three of the statements incorporated the following elements: a term or late preterm neonate, a significant peripartum event, metabolic acidosis within the first hour of life (pH <7, Base excess of >12), low Apgar scores, need for prolonged resuscitation and clinical features of encephalopathy. [20]

In current practice, when the elements described above suggest possible encephalopathy, the most valuable special investigation is Cerebral Function Monitoring (CFM) in the form of an amplitude-Electroencephalogram (aEEG). It has shown to be the most sensitive and specific indicator of outcomes when conducted within the first 6 hours of life, with a sensitivity of 89% in predicting a normal outcome if the aEEG is found to be normal. [23-25]

Assessment of the clinical features of encephalopathy are done by using one of two well established clinical scoring systems. These clinical scores are the *Thompson Score* and the *Modified Sarnat Score.* [22, 26] Horn and colleagues investigated the value of these two clinical scores in predicting an abnormal aEEG and an outcome of moderate to severe encephalopathy. They found that the *Thompson Score* (score more than 7) performed similar to the *Modified Sarnat Score* (moderate-severe score) with sensitivities of 100% vs 97% and specificities of 67% vs 71% respectively, in predicting an abnormal aEEG at 6 hours. [13] Foreign studies support the sensitivity and specificity of early neurological and biochemical evaluation in predicting encephalopathy. [27, 28]

Risk factors and antecedents to perinatal asphyxia and HIE

A triennial *Saving Babies* report is published based on the national PPIP data which highlights pitfalls in neonatal morbidity and mortality and emphasises areas needing improvement. However, the last report available from their website is from 2014-2016. [29] Although this report underlines the same contributing factors, the previous report of 2012-2013 specifically highlights factors related to asphyxia related neonatal

deaths. [30] Out of all the identifiable avoidable factors contributing to asphyxia related deaths, it was estimated that close to 50% was associated with healthcare provider behaviour. These factors included failing to identify fetal distress with (8.4%) and without (4.6%) fetal monitoring as well as delays in referral to a secondary or tertiary hospital (4.5%). Furthermore, it included delays in acquiring assistance from experienced help (3.3%), the inappropriate management of the 2nd stage of labour and lastly, the delay in implementing an intervention when it is indicated (3.1%). Patient related factors were identified as delay in seeking medical attention by the patient during labour (6.9%), late antenatal booking (3%) and inappropriate action by the patient in reaction to decreased fetal movements (2.9%). Administrative factors included lack or delay in transport from home to a healthcare facility and between facilities once referred, lack of NICU beds and staff shortages (insufficient nurses and doctors on duty).

A study conducted by the University of Witwatersrand analysed the data from PPIP and similar perinatal mortality audits from other developing countries. [31] The researchers included only data which resulted in neonatal deaths and found that when prematurity is not factored in, asphyxia remains the leading cause of death in these countries. They identified inadequate monitoring of mothers in labour as one of the most significant contributors to probable avoidable factors in asphyxia related deaths. Monitoring included the progress of labour (the use of the partogram) and monitoring fetal well-being (fetal heart rate monitoring and presence of meconium stained liquor). They suggest that poor monitoring in labour has a direct relationship with poor maternal and fetal outcomes, even in pregnancies deemed as low risk. Patient related factors were similar to PPIP and included delayed initiation of antenatal care and seeking medical care late in labour.

This literature search revealed that studies examining factors related to HIE specifically are less common than studies examining solely asphyxia related deaths. The population groups of these studies are also much smaller. Most such studies found were conducted in developed countries (USA, UK, Sweden) as opposed to developing countries (Pakistan, Nigeria, Columbia) and all the studies were performed at tertiary facilities.

Most of the attention is focused on investigating the intrapartum period and few studies considered antenatal elements in depth, if at all. Factors from the antenatal period that were identified to have an association with HIE were mothers with lower parity (nulliparous specifically) and mothers who did not initiate antenatal care ("unbooked" pregnancies). [32-35] In addition, other antenatal factors included gestational age of 41 weeks or more and maternal BMI of more than 40. [33, 36-38] The study comparing booked to unbooked mothers in view of their pregnancy outcomes is from Nigeria and found that unbooked mothers were three times as likely to have an infant affected by perinatal asphyxia as opposed to a mother who booked her pregnancy timeously. [35] A combination of other antenatal factors such as significant maternal comorbidity, intrauterine fetal growth restriction, hypertension and maternal age less than 20 may have a risk relating to HIE when paired with a sentinel intra-partum event or an abnormal fetal heart rate pattern. [36]

Social circumstances during the antenatal period are not well described in the studies investigating risk factors for HIE. Interestingly, two independent studies from Sweden and Columbia describes an association with single mothers and perinatal asphyxia. [34, 39] This would highlight the importance of maternal support by a partner antenatally as well as during labour. The Columbia study further suggests that social difficulties such as poverty, lack of social support and lower level of education in mothers were more common in a group of infants who were diagnosed with HIE.

Intrapartum factors associated with HIE are described more frequently. The strongest associations are with the presence of obstetric emergencies such as abruptio placentae, shoulder dystocia, uterine rupture and umbilical cord prolapse. [9, 32-34, 39] Obstructive labour is also strongly associated with HIE and includes prolonged active phase of labour as well as delayed second stage of labour. [9, 32, 34, 40] The connotation with nulliparous women and the risk of HIE could factor in with prolonged labour often being associated with nulliparous mothers. Furthermore, it has been demonstrated that obstetric emergency training can decrease the presence of HIE dramatically, highlighting the health care providers' avoidable contribution to HIE. [41]

Operative and assisted vaginal deliveries were found to be independent risk factors for perinatal asphyxia. [33, 39] On the contrary, other studies indicated that operative deliveries did not have an association with HIE. [40] This could be explained by elective Caesarean deliveries which had no, or very few associations with HIE in specific studies and that emergency operative deliveries are usually associated with either an obstetric emergency and/or the presence of suspected fetal compromise. This could skew the associations being drawn between operative delivery and HIE. The presence of meconium stained liquor is also identified as an independent factor associated with HIE. [9, 31, 34, 38, 39]

Similar studies and the paucity in literature

The literature review revealed that the only recent and local data available were that of the studies conducted by *Horn et al.* which touches on the topic of interest, [11, 13] and the data from the PPIP *Saving Babies* Report. The latest published report is from 2016. In addition, the *Guidelines for Maternity Care in South Africa* serves as a reference for basic antenatal care to which the study population can be compared. [42]

One study conducted in the United States was found to have similar aims as our study. [33] The study focused on a slightly different population group and was conducted at a tertiary facility in a first world country. Despite the difference in the study population, there are similarities in the methodology and objectives. This study aimed to identify obstetrics antecedents to babies who received therapeutic hypothermia. The study spanned seven years (2005 to 2011) and included 86371 total births and 98 babies who received therapeutic hypothermia. It included all deliveries after 36 weeks gestation and divided the population into two groups: those babies who received total body cooling and those who did not. The researchers screened all the babies for acidaemia to identify the need to undergo further neurological evaluation. A pH of less than 7 or a base deficit of 16 mEq/L or more within the first hour of life were criteria for further evaluation. However, they included slightly higher pH and lower base deficit levels when accompanied by sentinel peripartum events, a 10-minute Apgar score of less than 5 and a need for prolonged resuscitation. When these criteria where met, the babies were evaluated for signs of clinical encephalopathy. The researchers adopted the modified Sarnat score to identify and grade the severity of HIE and based on these scores applied therapeutic hypothermia, or not. Associations were made with maternal age less than 15, maternal Body Mass Index of more than 40, lower parity, gestational diabetes, preeclampsia, induction of labour and obstetric emergencies such as cord prolapse, uterine rupture and abruptio placentae.

This study did not assess the impacts of socio-economic circumstances, earlier antenatal factors, antenatal care nor did it include any participants who delivered at primary or secondary hospitals. This excludes factors relating to interfacility transfers, staff level of training and competencies, amount of staff on duty and facility-bound resources. The study did not include aEEG monitoring as part of the diagnostic process and excluded a subcategory of milder forms of perinatal asphyxia.

A similar study was performed at Tygerberg Hospital and published in 1996. [43] The study was conducted as a retrospective review of babies with perinatal asphyxia born between 1989 and 1991. Over the course of the three years there were a total of 15964 births. The investigators identified 74 babies with perinatal asphyxia, which was based on a five min Apgar score of less than six. Babies had to weigh more than 2000g OR be more than 34 weeks of gestation. No other criteria were used. They investigated maternal and neonatal factors to identify associations with asphyxia. The researchers found the following factors as significant: ten percent of their mothers were grand multiparas, labour was associated with prolonged first (47%) and second (36%) stages, meconium stained liquor was present in 47% of cases. Caesarean sections were performed in 53% of cases of which 44% were performed due to suspected fetal distress. A third of the study population had meconium aspiration. This study is, however, out-dated and the current perspective and management of perinatal asphyxia and HIE has changed significantly since then.

There is thus a deficit in the literature regarding the particulars of this condition at primary and secondary level and a need to describe preceding, contributing and avoidable factors relating to HIE at a district level of care as well as the circumstances and challenges surrounding their management and referral.

References

(1) Lo S, Horton R. Everyone counts-so count everyone. Lancet 2015;386(10001):1313-1314.

(2) Lee BX, Kjaerulf F, Turner S, Cohen L, Donnelly PD, Muggah R, et al. Transforming Our World: Implementing the 2030 Agenda Through Sustainable Development Goal Indicators. J Public Health Policy 2016;37 Suppl 1:S13-31.

(3) United Nations. Sustainable Development Goals: 17 Goals to Transform the World. Available at: https://www.un.org/sustainabledevelopment/sustainable-development-goals/. [Accessed 21 March 2018].

(4) UNICEF. Levels & Trends in Child Mortality. Available at: https://data.unicef.org/resources/levels-trends-child-mortality-report-2014/. [Accessed 21 March 2018].

(5) Bamford L, McKerrow N, Barron P, Aung Y. Child mortality in South Africa: Fewer deaths, but better data are needed. South African Medical Journal. 2018;108(3 Suppl 1):S25-32.

(6) Rhoda N, Velaphi S, Gebhardt G, Kauchali S, Barron P. Reducing neonatal deaths in South Africa: Progress and challenges. South African Medical Journal 2018;3 Suppl 1:S9-16.

(7) National Department of Health, Statistics South Africa, South African Medical Research Council, ICF. South African Demographic and Health Survey 2016: Key Indicators. Available at: http://www.statssa.gov.za/publications/Report%2003-00-09/Report%2003-00-092016.pdf. [Accessed 4 Apr 2018].

(8) Nair J, Kumar VHS. Current and Emerging Therapies in the Management of Hypoxic Ischemic Encephalopathy in Neonates. Children (Basel). 2018 Jul;5(7):99. doi: 10.3390/children5070099.

(9) Torbenson VE, Tolcher MC, Nesbitt KM, Colby CE, El-Nashar SA, Gostout BS, et al. Intrapartum factors associated with neonatal hypoxic ischemic encephalopathy: a case-controlled study. BMC Pregnancy Childbirth. 2017 Dec;17(1): 415. doi: 10.1186/s12884-017-1610-3.

(10) Lawn JE, Lee AC, Kinney M, Sibley L, Carlo WA, Paul VK, et al. Two million intrapartum-related stillbirths and neonatal deaths: where, why, and what can be done? Int J Gynaecol Obstet. 2009;107 Suppl 1:S5-18, S19.

(11) Horn AR, Swingler GH, Myer L, Harrison MC, Linley LL, Nelson C, et al. Defining hypoxic ischemic encephalopathy in newborn infants: benchmarking in a South African population. J Perinat Med. 2013;41(2):211-217.

(12) Bruckmann EK, Velaphi S. Intrapartum asphyxia and hypoxic ischaemic encephalopathy in a public hospital: Incidence and predictors of poor outcome. S Afr Med J. 2015;105(4):298-303.

(13) Horn AR, Swingler GH, Myer L, Linley LL, Raban MS, Joolay Y, et al. Early clinical signs in neonates with hypoxic ischemic encephalopathy predict an abnormal amplitude-integrated electroencephalogram at age 6 hours. BMC Pediatr. 2013 Apr;13:52. doi: 10.1186/1471-2431-13-52.

(14) Antonucci R, Porcella A, Pilloni M. Perinatal asphyxia in the term newborn. Journal of Pediatric and Neonatal Individualized Medicine. 2014;3:1-14.

(15) Finer NN, Robertson CM, Richards RT, Pinnell LE, Peters KL. Hypoxic-ischemic encephalopathy in term neonates: perinatal factors and outcome. J Pediatr. 1981;98(1):112-117.

(16) Vannucci RC, Perlman JM. Interventions for perinatal hypoxic-ischemic encephalopathy. Pediatrics. 1997;100(6):1004-1014.

(17) Robertson C, Finer N. Term infants with hypoxic-ischemic encephalopathy: outcome at 3.5 years. Dev Med Child Neurol. 1985;27(4):473-484.

(18) Carli G, Reiger I, Evans N. One-year neurodevelopmental outcome after moderate newborn hypoxic ischaemic encephalopathy. J Paediatr Child Health. 2004;40(4):217-220.

(19) Mwaniki MK, Atieno M, Lawn JE, Newton CR. Long-term neurodevelopmental outcomes after intrauterine and neonatal insults: a systematic review. Lancet. 2012;379(9814):445-452.

(20) Jacobs SE, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG. Cooling for newborns with hypoxic ischaemic encephalopathy. Cochrane Database Syst Rev 2013 Jan 31;(1):CD003311. doi: 10.1002/14651858.CD003311.pub3.

(21) Edwards AD, Brocklehurst P, Gunn AJ, Halliday H, Juszczak E, Levene M, et al. Neurological outcomes at 18 months of age after moderate hypothermia for perinatal hypoxic ischaemic encephalopathy: synthesis and meta-analysis of trial data. BMJ. 2010;340:c363.

(22) Shalak LF, Laptook AR, Velaphi SC, Perlman JM. Amplitude-integrated electroencephalography coupled with an early neurologic examination enhances prediction of term infants at risk for persistent encephalopathy. Pediatrics. 2003;111(2):351-357.

(23) Hellstrom-Westas L, Rosen I, Svenningsen NW. Predictive value of early continuous amplitude integrated EEG recordings on outcome after severe birth asphyxia in full term infants. Arch Dis Child Fetal Neonatal Ed. 1995;72(1):F34-8.

(24) Spitzmiller RE, Phillips T, Meinzen-Derr J, Hoath SB. Amplitude-integrated EEG is useful in predicting neurodevelopmental outcome in full-term infants with hypoxic-ischemic encephalopathy: a meta-analysis. J Child Neurol. 2007;22(9):1069-1078.

(25) Toet MC, Hellstrom-Westas L, Groenendaal F, Eken P, de Vries LS. Amplitude integrated EEG 3 and 6 hours after birth in full term neonates with hypoxic-ischaemic encephalopathy. Arch Dis Child Fetal Neonatal Ed. 1999 Jul;81(1):F19-23.

(26) Thompson CM, Puterman AS, Linley LL, Hann FM, van der Elst CW, Molteno CD, et al. The value of a scoring system for hypoxic ischaemic encephalopathy in predicting neurodevelopmental outcome. Acta Paediatr. 1997;86(7):757-761

(27) Toh VC. Early predictors of adverse outcome in term infants with post-asphyxial hypoxic ischaemic encephalopathy. Acta Paediatr. 2000;89(3):343-347.

(28) Merchant N, Azzopardi D. Early predictors of outcome in infants treated with hypothermia for hypoxic-ischaemic encephalopathy. Dev Med Child Neurol. 2015;57 Suppl 3:S8-16.

(29) National Perinatal Morbidity and Mortality Comittee. Saving Babies 2014-2016. Triennial report on perinatal mortality in South Africa. Available at: https://www.westerncape.gov.za/assets/departments/health/napemmco_triennial_report_2014-2016_saving_babies.pdf. [Accessed 16 October 2019].

(30) Pattinson R, Rhoda N. Saving Babies 2012-2013: Ninth report on perinatal care in South Africa. Available at: https://www.ppip.co.za/wp-content/uploads/Saving-Babies-2012-2013.pdf. [Accessed 4 Apr 2018]..

(31) Velaphi S, Pattinson R. Avoidable factors and causes of neonatal deaths from perinatal asphyxia-hypoxia in South Africa: national perinatal survey. Ann Trop Paediatr. 2007;27(2):99-106.

(32) Liljestrom L, Wikstrom AK, Jonsson M. Obstetric emergencies as antecedents to neonatal hypoxic ischemic encephalopathy, does parity matter? Acta Obstet Gynecol Scand. 2018 Jul;97(11):1396-1404. doi: 10.1111/aogs.13423.

(33) Nelson DB, Lucke AM, McIntire DD, Sanchez PJ, Leveno KJ, Chalak LF. Obstetric antecedents to body-cooling treatment of the newborn infant. Am J Obstet Gynecol. 2014;211(2):155.e1-155.e6.

(34) Torres-Munoz J, Rojas C, Mendoza-Urbano D, Marin-Cuero D, Orobio S, Echandia C. Risk factors associated with the development of perinatal asphyxia in neonates at the Hospital Universitario del Valle, Cali, Colombia, 2010-2011. Biomedica. 2017;37(0):51-56.

(35) Owolabi AT, Fatusi AO, Kuti O, Adeyemi A, Faturoti SO, Obiajuwa PO. Maternal complications and perinatal outcomes in booked and unbooked Nigerian mothers. Singapore Med J. 2008;49(7):526-531.

(36) Martinez-Biarge M, Diez-Sebastian J, Wusthoff CJ, Mercuri E, Cowan FM. Antepartum and intrapartum factors preceding neonatal hypoxic-ischemic encephalopathy. Pediatrics. 2013;132(4):e952-9.

(37) Liljestrom L, Wikstrom AK, Agren J, Jonsson M. Antepartum risk factors for moderate to severe neonatal hypoxic ischemic encephalopathy: a Swedish national cohort study. Acta Obstet Gynecol Scand. 2018;97(5):615-623.

(38) Herrera CA, Silver RM. Perinatal Asphyxia from the Obstetric Standpoint: Diagnosis and Interventions. Clin Perinatol. 2016;43(3):423-438.

(39) Milsom I, Ladfors L, Thiringer K, Niklasson A, Odeback A, Thornberg E. Influence of maternal, obstetric and fetal risk factors on the prevalence of birth asphyxia at term in a Swedish urban population. Acta Obstet Gynecol Scand. 2002;81(10):909-917.

(40) Nauman Kiyani A, Khushdil A, Ehsan A. Perinatal Factors Leading to Birth Asphyxia among Term Newborns in a Tertiary Care Hospital. Iran J Pediatr. 2014;24(5):637-642.

(41) Draycott T, Sibanda T, Owen L, et al. Does training in obstetric emergencies improve neonatal outcome? BJOG. 2006;113:177–82.

(42) National Department of Health, Republic of South Africa. Guidelines for Maternity Care in South Africa. Available at: https://www.health-e.org.za/wp-content/uploads/2015/11/Maternal-Care-Guidelines-2015_FINAL-21.7.15.pdf. [Accessed 4 Apr 2018].

(43) Hall DR, Smith M, Smith J. Maternal factors contributing to asphyxia neonatorum. J Trop Pediatr. 1996;42(4):192-195.

Chapter 2: Publication-ready Journal Article

Journal: South African Family Practice
Journal guidelines can be viewed at https://safpj.co.za/index.php/safpj/pages/view/submission-guidelines#part_1

Article Title:

A descriptive study of suspected perinatal asphyxia at Mitchells Plain District Hospital.
A case series.

Authors

Stofberg, JPJ. MBChB (SU); Dip HIV Man (SA)
Contact Details: mail4hanno@gmail.com
0798679327
School of Public Health & Family Medicine
Entrance 5, Falmouth Building
Health Sciences Campus
l Anzio Road, Observatory, 7925

Spittal, GW. MBChB (Glasgow University); MRCPCH; FC Paed; MMED(UCT); Dip HIV Man (SA)
Hinkel, T. MBChB (UP), FCOG, MMED (SU)
Ras, T. MBChB (UCT), MFamMed (UCT), FCFP (SA)

Abstract

Background: South Africa aims to end all preventable deaths of children under the age of five as part of their commitment to the Sustainable Development Goals. More than half of these mortalities occur in the neonatal period with perinatal asphyxia as one of the leading causes. This study investigated and identified the characteristics of perinatal asphyxia and its contributing factors at a district hospital in Cape Town.

Methods: A retrospective descriptive case series was performed and included all suspected cases of perinatal asphyxia referred from Mitchells Plain District Hospital (MPH)) to a specialised centre in the years 2016-2018. A data collection tool was used to extract information. Data was processed with SPSS to produce descriptive statistics and to investigate associations between variables using the Chi-square tests.

Results: The study included 29 cases of suspected perinatal asphyxia. Ten (34.5%) had abnormal amplitude Electroencephalograms (aEEG's) indicative of Hypoxic Ischaemic Encephalopathy (HIE) and four (13.8%) demised before day seven of life. Non-operative deliveries (p=0.005), lack of a doctor at the time of delivery (p=0.004) and neonatal chest compressions (p=0.044) were associated with abnormal aEEG's. Babies with Thompson score of equal to or more than 12 (p=0.006), neonatal seizures (p=0.036) and delayed arrival at referral hospital (p=0.005) were associated with abnormal aEEG findings. Mortality was associated with Thompson score ≥12 (p=0.007) and the need for neonatal intubation at delivery (p=0.016).

Conclusions: Significant reversable factors were identified in the peri-and postpartum periods. More capacitated staff would have the greatest impact on outcomes. The profile of HIE is exceedingly complex and challenges the resources and services of district level of care. Therefore, these factors should be targeted for future development and investment to improve outcomes from district hospitals.

Key words: Hypoxic Ischaemic Encephalopathy, Perinatal Asphyxia, Perinatal Care, District Healthcare, Quality of Care

Introduction

Since 2005 there has been a decline in the global neonatal mortality rate from 36 per 1000 live births to 19 per 1000 in 2015. This marked the end of the Millennium Developmental Goals (MDG) initiative. [1] These figures equate to an approximate decline from 4 million to 2.7 million annual neonatal deaths during this period. [1, 2] Despite these successes, neonatal mortality and morbidity prevails as one of the major global health concerns and the reduction of neonatal deaths has been disproportionally slower in comparison to deaths outside of the neonatal period. [3]

Goal 3 of the Sustainable Development Goals (SDG) aims to end all preventable deaths of children under the age of five years. [3] Neonatal deaths constitute 45% in this group globally and in South Africa it is estimated at 50%. [4, 5] According to the District Health Information System (DHIS) SA was close to the target neonatal mortality rate of 12 deaths per 1000 live births as set by the SDG, achieving 12.6 per 1000 live births in 2016. [6] However, the South African Demographic Health Survey reports a higher neonatal mortality rate of 21 per 1000 live births. [7] The difference between these two statistics is acknowledged by the authors. However, the reason for the discrepancy would require an in-depth analysis of their respective methodologies.

The three most prevalent causes of neonatal mortality in SA are complications of prematurity (47.9%), perinatal asphyxia (24.3%) and infections (11.6%). [6] When one excludes the extremely low birth weight category (<1000g), perinatal asphyxia is the number one cause of death in neonates. [6]

Perinatal asphyxia is the term which describes a condition where there is decreased oxygenation of the fetus during the perinatal period (20 weeks gestation to day seven of life). When this period of decreased oxygenation is severe and prolonged it may result in cerebral ischaemia severe enough to cause encephalopathy. This pathological process results in a syndrome, which is based on a combination of clinical and biochemical factors, referred to as Hypoxic Ischemic Encephalopathy (HIE). [8, 9]

In SA it is difficult to estimate the prevalence of perinatal asphyxia and reports vary between 2.3 - 26.5 per 1000 live births. [10, 11] The wide range in prevalence can be explained by the complexity of this condition and numerous diagnostic criteria being utilised. In one study performed in 2011 at Chris Hani Baragwanath Hospital in Johannesburg the incidence of perinatal asphyxia was found to range between 8.7 - 15.2 per 1000 live births. The same study suggested a mortality rate of 8.9 - 12.3% encompassing all severities of HIE. [12] A study conducted in 2009 at Groote Schuur, Mowbray Maternity and New Somerset Hospitals showed a similar mortality rate of 13%. [13]

The diagnosis and management of neonates who suffered perinatal asphyxia with suspected HIE involves time dependent intricate decision making. In addition, specialised monitoring and treatment modalities are required which can only be provided at specialised facilities. Timely referral depends on the attending clinician having a high index of suspicion of HIE prompting the use of validated scoring systems to assist with clinical decision-making. [14, 15] The gold standard diagnostic special investigation is an amplitude-Electroencephalogram (aEEG). When conducted within the first 6 hours of life it has a sensitivity of 89% in predicting a normal outcome (no neurological sequelae) if the aEEG is found to be normal and a sensitivity of 94% in predicting a poor outcome with an abnormal aEEG. [16-18] This modality is not available at district level of care and highlights the importance and urgency to refer patients who might have this condition.

The Saving Babies Report (2012-2013) estimates that nearly 50% of modifiable factors for perinatal asphyxia are associated with healthcare provider behavior. [19] These factors included failing to identify fetal distress (with and without fetal monitoring), delay in perinatal referral to a secondary or tertiary hospital, and inappropriate management of prolonged second stage of labour. Patient related factors were identified

as delay in seeking medical attention by the patient during labour, never initiating antenatal care, late antenatal booking and inappropriate action by the patient in reaction to warning signs. Over 50% of all perinatal asphyxia related deaths occur at district level hospitals as opposed to community health centres (2.8%), regional (22.5%) or tertiary hospitals (23.9%). [6] These figures suggest that there is potential of preventing a substantial number of perinatal asphyxia cases and HIE and therefore a significant amount of morbidity and mortality.

There is a lack of studies investigating the modifiable factors relating to perinatal asphyxia at district level hospitals. The aim of this study was to describe clinical care of the mother-and-baby dyad at Mitchells Plain District Hospital (MPH) to identify possible preventable contributors to perinatal asphyxia. This was achieved by the following objectives: firstly, by describing the antenatal course and peripartum care of the mothers who delivered babies with suspected perinatal asphyxia at MPH. Secondly, by describing the presence and extent of clinical features of perinatal asphyxia in neonates referred from MPH to Groote Schuur Hospital (GSH) or Mowbray Maternity Hospital (MMH) as suspected perinatal asphyxia. Finally, by describing the care of the mother-and-baby dyad in the perinatal period to identify possible modifiable factors which could influence future practice and improve outcomes.

Methodology

Study Design
This study was a retrospective descriptive case series with an analytical component.

Setting
The primary research site was at MPH with extension to Groote Schuur (GSH) and Mowbray Maternity Hospitals (MMH). MPH is a large district level hospital which serves the greater Mitchells Plain community. It provides specialised obstetric services and is the referral centre for several Midwife Obstetric Units (MOU) in this area. GSH and MMH are the tertiary and secondary referral hospitals for MPH respectively.

The Guidelines for Maternity Care in South Africa govern the patient profiles and their appropriate level of care across the referral platforms from primary to tertiary facility.[20] These guidelines are accepted as standard of care and are well established in this setting.

Study Population

The population included all the patients admitted to MPH where neonates were subsequently referred to GSH or MMH with suspected perinatal asphyxia during the period 2016 to 2018 (n=29).

The definitive diagnosis of perinatal asphyxia or HIE requires an investigation (aEEG) and subsequent therapeutic hypothermia which is only available at specialised facilities, and not at district level. Therefore, there exists a low threshold to refer any and all suspected cases which meets the criteria below.

Inclusion Criteria: Babies had one or more of the following factors present

1) A sentinel event in the perinatal course (abruptio placenta, cord prolapse, fetal bradycardia, prolonged second stage of labour)
2) Apgar score of less or equal to seven at five-minutes
3) A need for prolonged resuscitation at birth (more than ten minutes)
4) Proven acidosis within the first hour of life, defined as a pH less than seven or a base deficit more than 10 mmol/l

5) Clinical features of moderate to severe encephalopathy (abnormalities in activity, muscle tone, primitive reflexes, posture, seizures, autonomic system or level of consciousness)

AND had all of the following

1) Be of 36 weeks gestation or more
2) Have a birth weight of 1,8kg or more
3) Be referred from MPH to GSH or MMH

Exclusion Criteria: Babies who met the above criteria and had one of the following criteria was excluded from the study:

1) Have a significant and severe comorbid disease such as an unstable cardiac condition
2) Severe congenital anomaly
3) Required surgery within the first three days of life

Data Collection

A data-collection tool was developed by the authors of this article. It is based on existing literature (content validation) and reviewed by key role players at MPH and subsequently by specialist neonatologist and obstetricians (face validation). A pilot was conducted with the data-collection tool prior to final adjustments. The pilot included ten cases (construct validation). No changes were made after the pilot.

Case finding was performed by reviewing the folders on the electronic content management system (ECM) of all the babies transferred from the MPH-neonatal unit during the 2016-2018 period. Twenty-nine (29) cases met the inclusion criteria and were included in the study. The data-collection tool was used to extract data at MPH and the referral hospitals.

All the Cardiotocograms (CTG's) were reviewed and described by specialist obstetricians. Interpretations by specialists were standardised by implementation of the National Institute for Health and Care Excellence (NICE) guidelines for CTG appraisal.[21] At MPH these guidelines are used in the clinical setting in review of CTG's and are visibly available on each CTG machine.

Data Analysis

Data was initially captured into Excel and subsequently transferred to Statistical Package for the Social Sciences 25 (SPSS) for analysis.[22] Descriptive statistics were performed to obtain frequencies and proportions. Associations between categorical variables with outcome variables where determined by 2x2 tables and Chi-Square tests.

Ethical Considerations

Ethical approval was granted by the University of Cape Town Human Research Ethics Committee (Ref 644/2018). Formal permission was attained from the Western Cape Health Research Sub-directorate (WC_201905_022) as well as from MPH, GSH and MMH respectively. This study adheres to the Declaration of Helsinki. [23]

Results:

A total of 33 cases who were referred from MPH with suspected perinatal asphyxia were identified between the years 2016 and 2018. Four cases were excluded from the study population due to either low birth weight or gestational age.

Maternal Demographics

Table 1 depicts the maternal demographics of the study population and the characteristics of their antenatal care. The median age of the mothers was 24 years, with more than half being primigravid. One mother was HIV positive and two were smokers. The median Body Mass Index (BMI) at the time of booking was 27.5 (20-44). Ninety percent of mothers had a self-reported household income of less than R100 000 ($6720) per annum and all mothers live in urban areas.

Table 1: Maternal Characteristics and Early Antenatal Care

Demographic	**n (%)**	**Median (IQR)**
Mother Age at presentation		**24 (21 – 29.5)**
Mother Parity	**n=29**	
Nulliparous	16 (55.2)	
Multiparous	13 (44.8)	
Past Obstetric Complications	**n=6**	
Miscarriage	2 (6.9)	
Termination of Pregnancy	1 (3.4)	
Preterm Labour	1 (3.4)	
Caesarean Section	2 (6.9)	
Mother BMI	**n=29**	**27.5 (22.5 – 31.8)**
Missing	4 (13.8)	
18-24	7 (24.1)	
25-29	9 (31)	
30-39	7 (24.1)	
>40	2 (6.9)	
Mother HIV status	**n=29**	
Negative	28 (96.6)	
Positive	1 (3.4)	
Smoker	**n=29**	
Smoker	2 (6.9)	
Non-Smoker	27 (93.1)	
Early Antenatal Care	**n (%)**	**Median (IQR)**
Gestational age at Booking	**n=29**	**21 (16 - 25.5)**
<12	5 (17.2)	
13-26	19 (65.1)	
27-40*	5 (17.2)	
No. of Antenatal Visits attended	**n=29**	**5 (3 – 6)**
<5	12 (41.4)	
≥5	17 (58.6)	
Gestational age at Presentation	**n=29**	**39 (37.5- 39.5)**
36-40	24 (82.8)	
>41	5 (17.2)	
First care facility	**n=29**	

	Midwife Obstetric Unit	19 (65.1)	
	Mitchell's Plain Hospital	10 (34.5)	

*Two mothers presented in this category who were unbooked

Early Antenatal Care

The median gestational age at booking was 21 weeks, with 17.2% mothers in this study booking before 12 weeks. Two mothers were unbooked and 58.6% had five visits or more. Nineteen (19) mothers initially presented to the MOU and ten to MPH directly. One baby was born at home and one at the MOU before presenting to MPH. Spontaneous labour occurred in 82.7% of mothers and 6.9% were induced.

Peripartum Care

Table 2 describes the peripartum course and care from the time of admission. Ten (52.63%) of the 19 patients referred from the MOU were referred on the premise of possible fetal compromise. This decision was based on clinical features such as abnormal fetal heart rate on auscultation, meconium stained liquor or decreased fetal movements. Some of these mothers also had complications such as prolonged rupture of membranes or delayed second stage of labour along with fetal compromise. For the purpose of this study the suspicion of fetal compromise was given priority as reason for referral. Failure of progress in labour (15.8%) and delayed second stage (15.8%) were the second most common reasons for referral. The partogram was used in nine of the referred mothers, however it was deemed to be inaccurate in 22.2% of cases when assessed by the receiving clinician. Intrapartum resuscitation was performed in most cases with 89.6% receiving intravenous fluid and 78.9% a urinary catheter. A single patient received tocolysis, as indicated by severe fetal distress. Left lateral position and oxygen administration was poorly documented, despite it being standard practice. Priority-one transfers (highest priority) was booked for 42.2% of the transfers. The median transfer time was 72 min from the MOU to MPH.

Table 2: Course of clinical care at MOU and MPH from admission

Characteristics at MOU	**n = 19 (%)**	**Median (IQR)**
Partogram Used		
Yes	9 (47.4)	
Used incorrectly	2 (22.2)	
No	10 (52.6)	
Primary reason for referral to MPH		
Possible Fetal compromise	10 (52.63)	
Failure to Progress	3 (15.8)	
Delayed second stage of labour	3 (15.8)	
Breech in labour	1 (5.3)	
Other	1 (5.3)	
Prolonged rupture of membranes	1 (5.3)	
Suspicion of Fetal compromise		
Yes	10 (52.36)	
No	9 (47.37)	
Action Taken		
IV Fluid	17 (89.5)	
Position (Left lateral documented)	0 (0)	
Urinary Catheter	15 (78.9)	
Ambulance Priority Level		
Not Documented	5 (26.3)	
Regular ambulance	1 (5.3)	
Urgent ambulance	5 (26.3)	
Flying squad	8 (42.1)	
Time from referral to MPH arrival (minutes)		**72 (45 – 110)**
Characteristics at MPH	**n=29 (%)**	**Median (IQR)**
Time from triage to first assessment by a doctor (minutes)		**60 (22.5-94)**
Doctor attending intrapartum care		
No	6 (20.7)	
Yes	23 (79.3)	
Fetal Presentation		
Cephalic	26 (89.7)	
Breech	3 (10.3)	
Rupture of Membranes (ROM)		
No Rupture (C/S)	5 (17.2)	
Spontaneous	19 (65.1)	
Artificial	5 (17.2)	
Duration of ROM (minutes)		**360 (120 - 765)**
Augmentation of labour with Oxytocin		
Yes	5 (17.2)	
No	24 (82.8)	
Suspicion of Fetal compromise		
Missing	1 (3.4)	
Yes	25 (86.2)	
No	3 (10.3)	

Actions Taken			
	IV Fluid	26 (89.7)	
	Position (Left Lateral Documented)	9 (31)	
	Urinary catheter	21 (72.4)	
	Tocolysis	1 (3.4)	
Doctor present at delivery			
	No	10 (34.5)	
	Yes	19 (65.1)	
Mode of delivery			
	Caesarean	10 (34.5)	
	Vaginal	19 (65.1)	
Complications of delivery			
	None	8 (27.6)	
	Fetal distress	9 (31)	
	Delayed second stage of labour	5 (17.2)	
	Breech	3 (10.3)	
	Shoulder dystocia	3 (10.3)	
	Antepartum haemorrhage	1 (3.4)	
Episiotomy performed		7 (24.1)	
Caesarean Section Details		**n=10**	
	Indication		
	Fetal distress	6 (60)	
	Failure to Progress	1 (10)	
	Failed Assisted Delivery	1 (10)	
	Antepartum Haemorrhage	1 (10)	
	Elective	1 (10)	
	Time from Decision to Delivery (minutes)		45 (34-66)
	Reason for Delay*		
	No Delay	3 (30)	
	None Documented	2 (20)	
	Theatre Not Available	2 (20)	
	Surgeon Not Available	2 (20)	
	Urgency Not Recognised	1 (10)	

**Delay: more than 45min*

At MPH triage and midwife assessments occurred simultaneously in most cases. The longest delay was 50 minutes. Fetal presentation was cephalic in 90% of cases and the median duration of rupture of membranes (ROM) was 360 minutes. Sixty-five percent (65%) had spontaneous ROM, 17% of membranes were ruptured artificially, and the remainder were unruptured prior to C/S. Seventeen percent (17%) received oxytocin augmentation of labour and a total of 65% delivered vaginally. There were three (10%) assisted deliveries performed with vacuum extraction. One was successful, one failed however delivered vaginally after bilateral episiotomy was performed. The last assisted delivery failed and was delivered via Caesarean Section (C/S).

The median time from decision of C/S to delivery was 45 minutes (IQR 23-97) and included one elective C/S. Occupied theatres and unavailability of the surgeon were the two main reasons for delay.

Cardiotocogram characteristics:

Table 3: Cardiotocogram Characteristics

CTG Details		n (%)	Median (IQR)
CTG used		**n=29**	
	Yes	25 (86.2)	
	No	3 (10.3)	
	Missing	1 (3.4)	
Triage to CTG (minutes)			10 (3:40-16)
NICE CTG Descriptions by attending clinicians		**n=25**	
	Normal/Reassuring	7 (28)	
	Suspicious	1 (4)	
	Pathological	2 (8)	
	Description not according to NICE	7 (28)	
	None	8 (32)	
CTG interpretation according to NICE*		**n=25**	
	Correct	8 (32)	
	Incorrect	17 (68)	
CTG NICE description*			
	Normal/Reassuring	4 (16)	
	Suspicious	2 (8)	
	Pathological	17 (68)	
	Inconclusive	2 (8)	
Correct Action Taken on CTG			
	Yes	14 (56)	
	No	11 (44)	

*As interpreted by specialist Obstetrician

CTG – Cardiotocogram

NICE – National Institute for Health and Care Excellence

Table 3 demonstrates the particulars of intrapartum fetal monitoring with CTG. Monitoring with CTG's were performed in 86% of the cases and had a median time of 10 minutes from triage to first CTG.. In 32% of the cases clinicians did not document any interpretation and in 28% they used nomenclature other than that of NICE. Comparing the interpretation of the CTG's by the attending clinician to specialist Obstetrician's interpretation applying NICE, only 32% of the attending clinicians were correct. According to Obstetrician NICE interpretation 68% of the CTG's were pathological.

Seventeen percent (17%) of the deliveries occurred on weekdays between the hours of 07:30 and 16:30. During these times a full complement of staff is on duty. More than 80% of deliveries occurred during after-hours where there is only one medical officer and an intern on duty with one theatre available which is shared with the surgical department.

Figure 1 depicts an overview of the outcomes of the babies. Twenty-seven (27) of the babies were born at MPH, one at home and one at the MOU. Twenty-four (24) babies arrived at the referral hospital (GSH or MMH respectively) before 6 hours of life. Seven had abnormal aEEG's and met criteria for therapeutic hypothermia. One was excluded due to critical ill health.

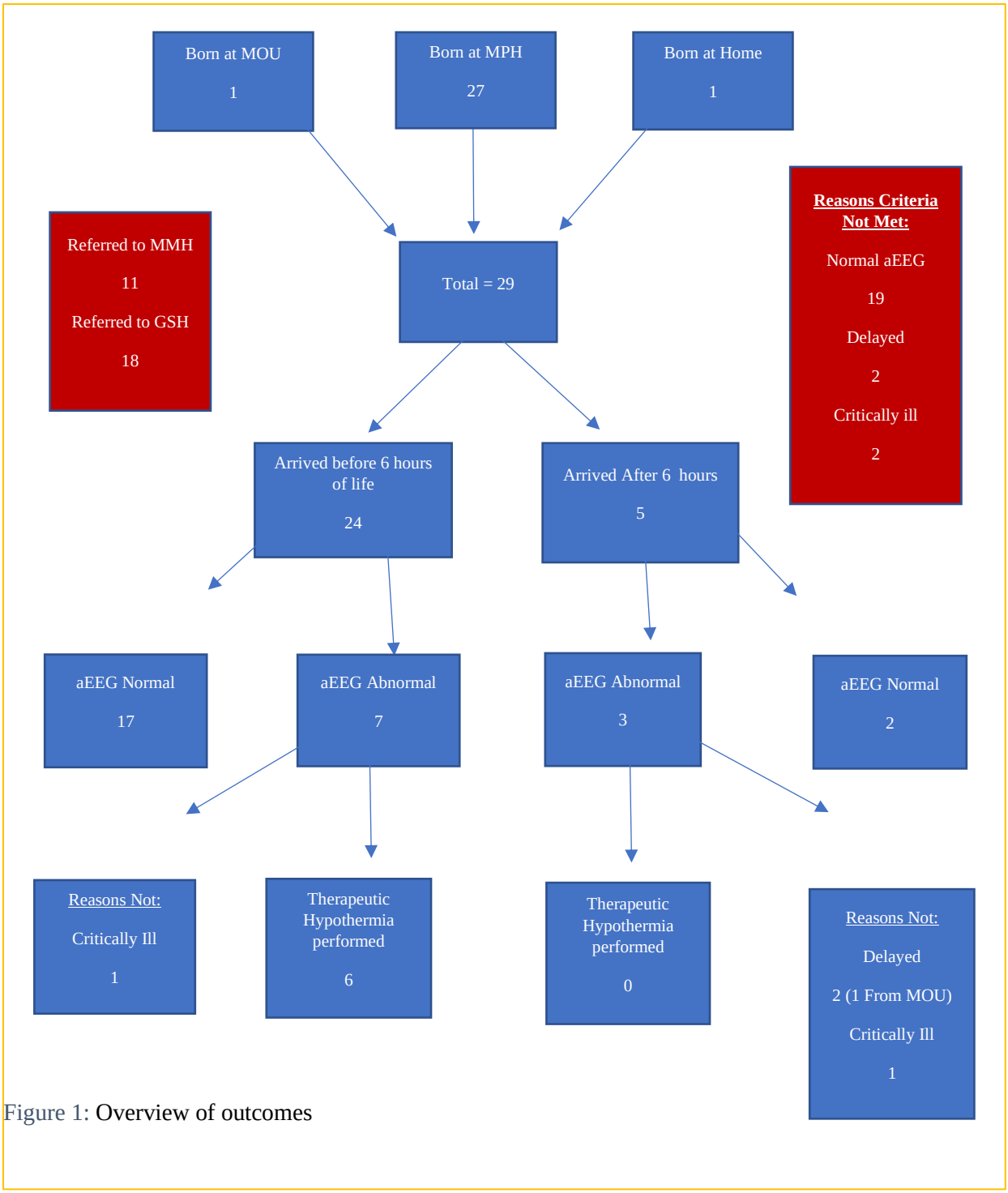


Figure 1: Overview of outcomes

Table 4: Details describing the babies' clinical and therapeutic course from birth to day seven of life

Features	n (%)	Median (IQR)
Female sex	13 (45)	
Gestation (weeks)		39.0 (37.5 – 39.5)
Weight (kilograms)		3.0 (2.7 – 3.6)
Presence of documented fetal compromise	11 (38)	
APGAR scores		
1 min		3.0 (1.0 – 4.0)
5 min		6.0 (5.0 – 7.0)
10 min		8.0 (6.0 – 9.0)
Bloodgas in 1st Hour of Life		
pH#		7.1 (7.0 – 7.2)
Lactate (mmol/L)		11.0 (7.5 – 15.0)
Base Excess		-13.9 (-18.4 – -10.9)
Management		
Intubation performed	11 (37.9)	
Adrenaline administered	1 (3.4)	
CPAP* required	13 (44.8)	
Missing	1 (3.4)	
Total time CPAP required (hours)		4 (2.6 – 6.0)
IPPV& required (minutes)	24 (82.8)	9 (5 – 14)
Chest compressions required (minutes)	10 (34.5)	2.0 (0.9 – 2.8)
Time to spontaneous respiration (mins)		5.0 (2.5 – 8.5)
Missing	8 (27.6)	
Time to heart rate > 100 beats (mins)		45s (0.01 – 5.00)
Missing	1 (3.4)	
Post-resus management		
Intra-Venous fluids (Potassium free)	29 (100)	
Iintra-Venous antibiotics	29 (100)	
Inotropes	4 (13.8)	
Thompson HIE$ score		9.0 (6.5 – 11.5)
Presence of seizures[+]	10 (34.5)	
Time from Birth till Arrival at Referral Centre (hrs)		4.8 (4-5.75)
aEEG+ before 6 hours of life	24 (82.8)	
aEEG after 6 hours of life&	5(17.2)	
Delayed Presentation	1(3.4)	
EMS Delay	2 (6.9)	
Delay in Discussion with Referral site	2 (6.9)	
aEEG Findings	**29 (100)**	
Continuous Normal Voltage	19 (65.1)	
Discontinuous Normal Voltage*	4 (13.8)	
Grossly abnormal	3 (10.3)	
Burst suppression	1 (3.4)	
Status epilepticus	1 (3.4)	
Continuous low voltage	1 (3.4)	
Alive Day 7	25 (86.2)	

[+] All seizures were treated with phenobarbitone, according to standard of care

#pH – Power of Hydrogen
*CPAP – Continueous Positive Airway Pressure
&IPPV – Intermittend Positive Pressure Ventilation
HIE$ – Hypoxic Ischaemic Encephalopathy
aEEG+ – Amplitude Electroencephaologram

Table 4 depicts the clinical details and course of the first 7 days of life of the babies. Fifty-five (55%) of the babies were male and the median gestational age and weight were 39 weeks and 3kg respectively. The median five-minute Apgar scores were six, pH 7.1 and base excess -13.9. One baby received adrenaline during resuscitation, however ten babies required chest compressions and 11 were intubated. Ten babies had documented seizures which were all treated with phenobarbitone. The median HIE score was nine.

Transfer from MPH to the referral hospitals took on average 4.8 hours (median) and directly resulted in two babies arriving after six hours of life. All babies received aEEG monitoring despite five arriving after the therapeutic window. The aEEG's were shown to be normal in 19 babies and abnormal in ten. Four babies with abnormal aEEG's did not meet criteria for therapeutic hypothermia as two were delayed and two were critically ill. On day seven of life 92% of babies had good clinical outcomes. There were four deaths in total (13.8%).

Table 5: Associations between variables and outcomes (aEEG and mortality) represented by crosstabulations and chi-square tests

Variable		**Abnormal aEEG n=10**	**Normal aEEG n=19**	**Total n=29**	**P**
Crosstabs (chi-squared tests) Observed and Expected counts					
BMI category					
	BMI >30	2 (3.2)	7 (5.8)	9	.264
	BMI ≤30	7 (5.8)	9 (10)	16	
MSL Present					
	Yes	4 (5.2)	11 (9.8)	15	.840
	No	6 (4.8)	8 (9.2)	14	
Early Antenatal Booking (1st trimester)					
	Yes	2 (1.7)	3 (3.3)	5	.775
	No	8 (8.3)	16 (15.7)	24	
Antenatal visits 5 or more					
	Yes	4 (5.9)	13 (11.1)	17	.14
	No	6 (4.1)	6 (7.9)	12	
Nulliparous					
	Yes	6 (5.5)	10 (10.5)	16	.144
	No	4 (4.5)	9 (8.5)	13	
Partogram				**19**	
	Yes	5 (3.3)	4 (5.7)	9	.130
	No	2 (3.7)	8 (6.3)	10	
Suspected fetal distress at MOU				**19**	
	Yes	4 (4.1)	7 (6.9)	11	.663
	No	3 (2.9)	5 (5.1)	8	
Suspicious or Pathological CTG					

	Yes	7 (6.7)	13 (13.3)		.699
	No	1 (1.3)	3 (2.7)		
CTG: Correct interpretation				**25**	
	Yes	2 (2.6)	6 (5.4)	8	.265
	No	6 (5.4)	11 (11.6)	17	
Doctor was present at delivery					
	Yes	**3 (6.6)**	**16 (12.4)**	**19**	**.004**
	No	**7 (3.4)**	**3 (6.6)**	**10**	
Mode of delivery					
	Vaginal	**10 (6.6)**	**9 (12.4)**	**19**	**.005**
	Caesarean	**0 (3.4)**	**10 (6.6)**	**10**	
Delayed second stage of labour					
	yes	2 (2.1)	4 (3.9)	6	0.947
	no	8 (7.9)	15 (15.1)	23	
After hours delivery					
	Yes	9 (8.3)	15 (15.7)	24	.424
	No	1 (1.7)	4 (3.3)	5	
Chest compressions					
	Yes	**1 (3.4)**	**9 (6.6)**	**10**	**.044**
	No	**9 (6.6)**	**10 (12.4)**	**19**	
Baby's pH ≤ 7.15 in first hour of life				28	
	Yes	5 (5.1)	11 (10.9)	16	.907
	No	4 (3.9)	8 (8.1)	12	
Baby's Lactate ≥ 11				28	
	Yes	4 (4.5)	10 (9.5)	14	.686
	No	5 (4.5)	9 (9.5)	14	
HIE score ≥ 12				**28**	
	Yes	**5 (2.1)**	**1 (3.9)**	**6**	**.006**
	No	**5 (7.9)**	**17 (14.1)**	**22**	
Clinical Seizures					
	Yes	**6 (3.4)**	**4 (6.6)**	**10**	**.036**
	No	**4 (6.6)**	**15 (12.4)**	**19**	
NICU Arrival before 6 hours of life					
	Yes	**4 (7.2)**	**17 (13.8)**	**21**	**.005**
	No	**6 (2.8)**	**2 (5.2)**	**8**	
Baby Alive on Day 7					
	Yes	7 (8.6)	18 (16.4)	25	.066
	No	3 (1.4)	1 (2.6)	4	
Variable		**Alive day 7 n=24**	**Demised day 7 n=4**	**Total n=28**	**p**
Crosstabs (chi-squared tests) Observed and Expected counts					
Early Antenatal Booking (1st trimester)					
	Yes	4 (4.3)	1 (0.7)	5	.568
	No	20 (19.7)	3 (3.3)	23	

Antenatal visits 5 or more					
	Yes	13 (13.7)	3 (2.3)	16	.417
	No	11 (10.7)	1 (1.7)	12	
Delayed second stage of labour					
	Yes	4 (4.1)	1 (.7)	5	0.687
	No	20 (19.7)	3 (3.3)	23	
Baby's pH ≤ 7.15 in first hour of life				28	
	Yes	13 (13.7)	3 (2.3)	16	.613
	No	11 (10.3)	1 (1.7)	12	
Baby's Lactate ≥ 11				28	
	Yes	10 (12)	4 (2)	14	.098
	No	14 (12)	0 (2)	14	
HIE score ≥ 12*				**27**	
	Yes	**3 (5.3)**	**3 (0.7)**	**6**	**.007**
	No	**21 (18.7)**	**0 (2.3)**	**21**	
Intubation of Baby				**28**	
	Yes	**7 (9.4)**	**4 (1.6)**	**11**	**.016**
	No	**17 (14.6)**	**0 (2.4)**	**17**	
NICU Arrival before 6 hours of life					
	Yes	20(18.1)	1 (2.9)	21	.052
	No	5 (6.9)	3 (1.1)	8	
Suspicious or Pathological CTG$				24	
	Yes	15 (15.8)	3 (2.3)	18	.546
	No	6 (5.3)	0 (0.8)	6	
Chest Compressions					
	Yes	10 (8.6)	0 (1.4)	10	.265
	No	14 (15.4)	4 (2.6)	18	

*One patient's HIE score was not documented
$Only including Pathological or Suspicious CTG's

Table 5 represents the statistical analysis of the data collected. It depicts associations between variables and abnormal aEEG results as well as mortality respectively, Significant associations were shown between normal aEEG and vaginal deliveries (p=0,005), the presence of a doctor at time of delivery (p=0.004) and clinical features, including an HIE score of more than 12(p=0.006) and seizures(p=0.036). Neonatal arrival at the referral hospital within 6 hours was associated with normal aEEG's (p=0.005).

Mortality was shown to have correlation with the need for neonatal intubation (p=0.16) and a HIE score of more than 12 (p=0.007).

Discussion

This study aimed to describe the characteristics of the antenatal and perinatal care of the mother-baby dyad as well as the clinical features of HIE in the babies referred with suspected perinatal asphyxia. The purpose is to identify contributing factors which could be preventable.

Antenatal Care

Current guidelines dictate booking prior to 12 weeks gestation and for uncomplicated antenatal course (low risk cases), a minimum of 5 antenatal visits. [20] Sixty-six (66%) of mothers obtained the recommended five or more antenatal visits. Seventeen percent (17%) of mothers booked in the first trimester and the median gestation at booking was 21 weeks. Two mothers were unbooked. Despite late booking gestation, mothers had frequent visits which accounts for the majority of patient's having adequate antenatal attendance. A study from Nigeria found mothers who had no antenatal care to have three times the risk of HIE compared to mothers with adequate care. [24] Contrarily, antenatal attendance and gestation at booking showed no association with abnormal aEEG or mortality in this study. Nulliparity and raised BMI have been linked with increased risk of HIE. [25-28] Fifty-five percent (55%) of mothers were nulliparous, although did not have significant association with abnormal aEEG (p=0.144) nor mortality (p=0.299), as can be seen in Table 5. The median booking BMI of mothers was 27.5 and included two patients with BMI's above 40. However, BMI had no significant association with outcomes. In addition, smoking, maternal age and previous obstetric complications were not found to be significant.

There was only one mother included in the study who was HIV positive, despite the estimation of up to 20% of babies delivered at MPH being HIV exposed. She was virally suppressed and had good antenatal attendance. It is possible that the lower than expected incidence of mothers with HIV in the study population could be explained by the promotion of antenatal care by specialised HIV clinics. Subsequently, resulting in earlier diagnosis of pregnancy, initiation of antenatal care and improved antenatal care attendance. A study performed in Lesotho supports this correlation with known HIV positive women and antenatal care. [29]

Perinatal Care

The antenatal service provided in South Africa is based on a robust referral system. There are clear guidelines on the appropriate level of care for the spectrum of clinical complexity. Levels of care involves an MOU, district hospital (MPH), secondary (MMH) and tertiary hospitals (GSH). Guidelines suggests all low risk pregnancies to be managed entirely at MOU level of care. [20] This explains why the majority (65.5%) of the study population presented to the MOU initially. Furthermore, current guidelines dictate highest priority emergency transport whenever fetal compromise is suspected. However, this level of transport was booked for only 42.1%. Not all mothers with suspected fetal distress (52.36%) were transferred via the fastest means available. Although the MOU is within 5km of MPH, the median transfer times were 72min. Intra-partum resuscitation was done appropriately in nearly all the patients.

MPH staff related factors were important. A doctor present at delivery was shown to be a protective factor (aEEG p=0.004). Midwife assessments of patients were rapid. However, time to doctor assessments was significantly longer (median 60 minutes). Six of the mothers (20.7%) were not assessed by a doctor at any time during admission. More than 80% of deliveries occurred after-hours, however time of delivery showed no statistical significance (aEEG p=0.424, mortality p=0.55.) as an independent variable. Similarly, a study conducted in Sweden indicated no associated risk with perinatal asphyxia and time of birth. [30] This study was conducted in a developed country and at a tertiary hospital so direct comparisons are unlikely transferrable to our study population.

Caesarian Section was performed in ten cases (34.5%) and had statistically significant (p=0.005) better outcomes than the babies born via Normal Vertex Deliveries (NVD). None of these babies had abnormal aEEG's, suggesting that timeous operative delivery in this population was a protective factor. There were three assisted deliveries, of which one led to an outcome of an abnormal aEEG. Studies have shown strong associations with obstetric emergencies (cord prolapse, ruptured uterus, shoulder dystocia, abruptio placenta) and perinatal asphyxia. [25, 27, 31] Similarly, our patient population included emergencies. However, due to infrequent occurrence statistical associations could not be analysed. In contrast to other studies [27, 31], delayed second stage of labour in our population were not found to be significant (aEEG p=0.947, death p=.687).

CTG monitoring is the mainstay in identifying fetal compromise. Correlation between pathological CTGs and clinical outcomes were not shown to be statistically significant in this study. However, concerns remain that attending clinicians were able to identify the fetal heart rate patterns correctly in only 32% of the cases. Correct identification of pathological patterns (62.1%) could have prompted expediting delivery via C/S and potentially altered outcomes.

Neonatal factors relating to perinatal asphyxia

Chest compressions appeared to be a protective factor (aEEG p=0.044). This speaks to adequate resuscitation of babies who received chest compressions. Therefore, the lack of chest compressions in other babies when indicated, could implicate an association with perinatal asphyxia. The same was not true for the need to intubate during resuscitation. Intubation was associated with higher mortality (p=0.016). This correlation with intubation and mortality could suggest that these babies were saved from a terminal clinical condition and that their prognosis remained unchanged despite being referred. On the contrary, this correlation could infer resuscitation was inadequate and therefore necessitated intubation.

Our study is consistent with the findings from other studies which have shown that the Thompsons HIE scoring system is useful for predicting outcome. [13, 15] An HIE score of more than 12 was associated with abnormal aEEG (0.006) and supports the Thompson score as a relevant tool in our setting. In addition, mortality (13.7%) of this study population was similar to that of other local populations and was associated with a Thompson score of more than 12 (p=0.007). [12, 13] These finding adds to the validity of the study, displaying correlation with a well-established screening tool and comparability to similar studies. [13, 15] Finally, clinical seizures at the referral site were predictive of abnormal aEEG's (p=0.036). This correlation speaks to the consistency of accurately identifying an independent, clinical variable at district level of care which can be used to predict HIE.

Delay in arrival at the referral centre was another predictive factor for abnormal aEEG's (p=0.005), however not for mortality (p=0.052). The reasons for delays were delayed presentation, delayed diagnosis and delay with transfer (EMS). EMS is faced with many challenges, including limited vehicle fleet and personal, dangerous areas classified as red zones and an extremely high workload. This could have played a role. However, it is definitely not the only factor at play. The management of babies with suspected perinatal asphyxia is complex with many steps where care can be altered. It is vital to have a multifaceted approach to management and any change in management needs to be adopted throughout the health system.

Identification of perinatal asphyxia is vital to allow opportune referral and treatment. Identification relies on the attending clinician's interpretation of clinical and biochemical features of the newborn baby. Firstly, Apgar scores are often used as an indicator of concern. [32] Conversely, our study did not find significant associations with five-minute Apgars <5 (aEEG p=0.291, death p= 0.107). Secondly, a blood gas analysis within the first hour of life can be used to guide diagnosis. [32] In particular, the pH and lactate values are used. However, these variables had no relation with outcomes in this study.

Limitations

Although the study was inclusive of all cases over the span of three years, the study population is small and representative of a singular study site. The study did not include mild forms of asphyxia which did not require referral, nor did it include unrecognized cases from the MOU. Furthermore, fresh stillborn babies and neonatal deaths at MPH which might have been as a result of asphyxia were not included in this study. Although diligence was taken to promote scientific validity, the strength of the study relied upon adequate recording of data in clinical notes. These factors may have influenced the results of this study.

Recommendations

The authors of this study would propose the following:

1) The findings highlight the importance of early identification of high-risk labour and the appropriate management thereof. This may be achieved by
    a. Ongoing training of all front-line obstetric staff on CTG interpretation and management.
    b. Heightened fetal surveillance with continueous CTG monitoring, optimised intra-partum resuscitation, removal of precipitating factors and early consideration for operative delivery in high risk cases with suspected fetal distress.
2) Training in neonatal resuscitation – across the care team.
3) Recognition and management of neonatal seizures were managed well. As this is a significant identifier of HIE, ongoing training in the use of the Thompson score and the recognition and management of neonatal seizures, should be emphasised.
4) Use tools to standardise care within the referral pathway and to ensure appropriate booking of priority ambulances and enable the safe and timeous transport of the mother-baby dyad. Tools may include the physical referral form which is completed for every referral at MPH from the MOU. This will identify possible high-risk patients who could either be referred to a higher level of care, indicate the priority of transfer required and allow for preparation in anticipation of a particular patient scenario. Other tools may access to the EMS booking website where the clinician may book transport him or herself.
5) Further research is required:
    a. At other district level facilities to support and further explore the findings of this study. As well as, to broaden the study population.
    b. Throughout the referral pathway (MOU to tertiary hospital) investigating staff experiences and working conditions.
    c. Investigating the impact and need for doctors present at the time of high-risk deliveries.

Conclusion

This study highlights the complex challenges in care pathways in facilitating the timely diagnosis and management of perinatal asphyxia, particularly at district level. It has shown the necessity for having a low threshold for referral demanded by the high morbidity and mortality associated with perinatal asphyxia. Furthermore, the diagnosis and management of perinatal asphyxia are complicated by the deficiency of resources at this level of care. Although antenatal factors are important, significant reversible factors were identified in the peri-and postpartum periods. Adequate number of staff with the competency to identify fetal compromise, manage obstetric emergencies and neonatal resuscitation would have the greatest impact on outcomes. The highest burden of HIE lies at district level of care and future investment should target these factors to improve outcomes.

References

(1) Lo S, Horton R. Everyone counts-so count everyone. Lancet. 2015 Oct 3;386(10001):1313-1314.
(2) Lee BX, Kjaerulf F, Turner S, Cohen L, Donnelly PD, Muggah R, et al. Transforming Our World: Implementing the 2030 Agenda Through Sustainable Development Goal Indicators. J Public Health Policy. 2016;37(1):13-31.
(3) United Nations. Sustainable Development Goals: 17 Goals to Transform the World. Available at: https://www.un.org/sustainabledevelopment/sustainable-development-goals/. [Accessed 21 Mar 2018].
(4) UNICEF. Levels & Trends in Child Mortality. Available at: https://data.unicef.org/resources/levels-trends-child-mortality-report-2014/. [Accessed 21 Mar 2018].
(5) Bamford L, McKerrow N, Barron P, Aung Y. Child mortality in South Africa: Fewer deaths, but better data are needed. South African Medical Journal. 2018;108(3 Suppl 1):S25-32.
(6) Rhoda N, Velaphi S, Gebhardt G, Kauchali S, Barron P. Reducing neonatal deaths in South Africa: Progress and challenges. South African Medical Journal 2018;3 Suppl 1:S9-16.
(7) National Department of Health, Statistics South Africa, South African Medical Research Council, ICF. South African Demographic and Health Survey 2016: Key Indicators. Available at: http://www.statssa.gov.za/publications/Report%2003-00-09/Report%2003-00-092016.pdf. [Accessed 4 Apr 2018].
(8) Nair J, Kumar VHS. Current and Emerging Therapies in the Management of Hypoxic Ischemic Encephalopathy in Neonates. Children (Basel). 2018 Jul;5(7):99. doi: 10.3390/children5070099.
(9) Torbenson VE, Tolcher MC, Nesbitt KM, Colby CE, El-Nashar SA, Gostout BS, et al. Intrapartum factors associated with neonatal hypoxic ischemic encephalopathy: a case-controlled study. BMC Pregnancy Childbirth. 2017 Dec;17(1): 415. doi: 10.1186/s12884-017-1610-3.
(10) Lawn JE, Lee AC, Kinney M, Sibley L, Carlo WA, Paul VK, et al. Two million intrapartum-related stillbirths and neonatal deaths: where, why, and what can be done? Int J Gynaecol Obstet. 2009;107 Suppl 1:S5-18, S19.
(11) Horn AR, Swingler GH, Myer L, Harrison MC, Linley LL, Nelson C, et al. Defining hypoxic ischemic encephalopathy in newborn infants: benchmarking in a South African population. J Perinat Med. 2013;41(2):211-217.
(12) Bruckmann EK, Velaphi S. Intrapartum asphyxia and hypoxic ischaemic encephalopathy in a public hospital: Incidence and predictors of poor outcome. S Afr Med J. 2015;105(4):298-303.
(13) Horn AR, Swingler GH, Myer L, Linley LL, Raban MS, Joolay Y, et al. Early clinical signs in neonates with hypoxic ischemic encephalopathy predict an abnormal amplitude-integrated electroencephalogram at age 6 hours. BMC Pediatr. 2013 ;13:52. doi: 10.1186/1471-2431-13-52.
(14) Shalak LF, Laptook AR, Velaphi SC, Perlman JM. Amplitude-integrated electroencephalography coupled with an early neurologic examination enhances prediction of term infants at risk for persistent encephalopathy. Pediatrics. 2003;111(2):351-357.
(15) Thompson CM, Puterman AS, Linley LL, Hann FM, van der Elst CW, Molteno CD, et al. The value of a scoring system for hypoxic ischaemic encephalopathy in predicting neurodevelopmental outcome. Acta Paediatr. 1997;86(7):757-761.
(16) Hellstrom-Westas L, Rosen I, Svenningsen NW. Predictive value of early continuous amplitude integrated EEG recordings on outcome after severe birth asphyxia in full term infants. Arch Dis Child Fetal Neonatal Ed. 1995;72(1):F34-8.
(17) Spitzmiller RE, Phillips T, Meinzen-Derr J, Hoath SB. Amplitude-integrated EEG is useful in predicting neurodevelopmental outcome in full-term infants with hypoxic-ischemic encephalopathy: a meta-analysis. J Child Neurol. 2007;22(9):1069-1078.
(18) Toet MC, Hellstrom-Westas L, Groenendaal F, Eken P, de Vries LS. Amplitude integrated EEG 3 and 6 hours after birth in full term neonates with hypoxic-ischaemic encephalopathy. Arch Dis Child Fetal Neonatal Ed. 1999 ;81(1):F19-23.

(19) Pattinson R, Rhoda N. Saving Babies 2012-2013: Ninth report on perinatal care in South Africa. Available at: https://www.ppip.co.za/wp-content/uploads/Saving-Babies-2012-2013.pdf. [Accessed 4 Apr 2018].
(20) National Department of Health, Republic of South Africa. Guidelines for Maternity Care in South Africa. Available at: https://www.health-e.org.za/wp-content/uploads/2015/11/Maternal-Care-Guidelines-2015_FINAL-21.7.15.pdf. [Accessed 4 Apr 2018].
(21) National Institute for Health and Care Excellence. Interpretation of cardiotocograph traces. Available at: https://www.nice.org.uk/guidance/cg190/resources/interpretation-of-cardiotocograph-traces-pdf-248732173. [Accessed 25 Aug 2018].
(22) IBM Corp. IBM SPSS Statistics for Windows. 2017;25.0.
(23) World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191-2194.
(24) Owolabi AT, Fatusi AO, Kuti O, Adeyemi A, Faturoti SO, Obiajuwa PO. Maternal complications and perinatal outcomes in booked and unbooked Nigerian mothers. Singapore Med J. 2008;49(7):526-531.
(25) Liljestrom L, Wikstrom AK, Jonsson M. Obstetric emergencies as antecedents to neonatal hypoxic ischemic encephalopathy, does parity matter? Acta Obstet Gynecol Scand. 2018 ;97(11):1396-1404. doi: 10.1111/aogs.13423.
(26) Liljestrom L, Wikstrom AK, Agren J, Jonsson M. Antepartum risk factors for moderate to severe neonatal hypoxic ischemic encephalopathy: a Swedish national cohort study. Acta Obstet Gynecol Scand. 2018;97(5):615-623.
(27) Nelson DB, Lucke AM, McIntire DD, Sanchez PJ, Leveno KJ, Chalak LF. Obstetric antecedents to body-cooling treatment of the newborn infant. Am J Obstet Gynecol. 2014;211(2):155.e1-6. doi: 10.1016/j.ajog.2014.02.013.
(28) Herrera CA, Silver RM. Perinatal Asphyxia from the Obstetric Standpoint: Diagnosis and Interventions. Clin Perinatol. 2016;43(3):423-438.
(29) Gill MM, Machekano R, Isavwa A, Ahimsibwe A, Oyebanji O, Akintade OL, et al. The association between HIV status and antenatal care attendance among pregnant women in rural hospitals in Lesotho. J Acquir Immune Defic Syndr. 2015;68(3):e33-8.
(30) Milsom I, Ladfors L, Thiringer K, Niklasson A, Odeback A, Thornberg E. Influence of maternal, obstetric and fetal risk factors on the prevalence of birth asphyxia at term in a Swedish urban population. Acta Obstet Gynecol Scand. 2002;81(10):909-917.
(31) Torres-Munoz J, Rojas C, Mendoza-Urbano D, Marin-Cuero D, Orobio S, Echandia C. Risk factors associated with the development of perinatal asphyxia in neonates at the Hospital Universitario del Valle, Cali, Colombia, 2010-2011. Biomedica. 2017;37(0):51-56.
(32) Jacobs SE, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG. Cooling for newborns with hypoxic ischaemic encephalopathy. Cochrane Database Syst Rev 2013 Jan 31;(1):CD003311. doi: 10.1002/14651858.CD003311.pub3.

Appendix: Data Extraction Tool

DEMOFRAPHICS
Case Number
Mother's Folder Number
Baby's Folder Number
Maternal age
Residential Area
MEDICAL AND OBSTETRIC HISTORY
1. Booking Details
Gravidity
Parity
Miscarriage/Ectopic/TOP
Gestation at Booking
Gestation determined by
Sure Dates
Booking SF
Early U/S
Late U/S
Length (m)
Weight (kg)
BMI
Antenatal attendance (Number of Visits)
COMMENTS:
2. Past Obstetric History
Previous Complications
Complication
ENND/Stillbirths
Previous Caesarean Section
Indication
COMMENTS:
3. Past Medical History
Known Medical Conditions
Adequately Managed/Controlled
Smoker
Substance User
RPR status
Adequately Treated if reactive
HIV Status
ART duration
Latest VL
COMMENTS:

4. Current Obstetric History
Mother's Date of Admission to first care facility
First care Facility: MOU/MPH
Gestational age at presentation (Weeks)
GPH in this pregnancy
Inappropriate Response to Warning Signs
COMMENTS:
MOU
Reason for referral from MOU
Partogram used
Partogram details (correct use, complications)
Fetal Heart Monitoring Recorded
Abnormal fetal heart rate recorded
MSL Grade: 0/1/2/3
Clinical suspicion of Fetal Distress
Intrapartum Care Initiated (IV fluid, catheter, position, tocolysis)
IV fluid
Catheter
Position
Tocolysis
Referral details documented (time, receiving health care provider, instructions given, etc)
COMMENTS:
TRANSPORT
Emergency transport utilised
Reference Nr
Call to EMS (date)
Call to EMS (time)
Transport requirements documented
Priority
Time of EMS arrival at MOU
Time of EMS arrival at MPH
Time from booking EMS to Arrival at MPH (min)
COMMENTS:
MITCHELLS PLAIN DISTRICT HOSPITAL
1. Triage
Time of Triage
Time of Midwife Assessment
Time of Doctor Assessment
Time from triage to patient being seen by Dr (min)
COMMENTS:
2. Labour Ward
Labour Initiation (Spontaneous/ Induction)
Rupture of Membranes

Spontaneous
Artificial
Prelabour
Duration of Ruptured Membranes (hour)
Management if Prelabour/Prolonged (Misoprostol Induction, Oxytocin Infusion, Ampicillin)
Induction Method (Bulb Catheter/Misoprostol/Oxytocin)
Induction Indication ()
Fetal Presentation (Cephalic/Breech)
Duration of 1st Stage (Hours)
Duration of Latent Labour (hours)
Duration of Active Labour (hours)
Duration of 2nd Stage (min)
Augmentation ever used?
Details of Augmentation
Obstetric Emergency
Prolapse
Dystocia
Abruptio
Delayed Second Stage
Breech in Labour
Management of Complication
COMMENTS:
Meconium Stained Liquor Present
Need for Intrauterine Resuscitation
Method of Resuscitation Used
IV fluid
Catheter
Position
Tocolysis
Maternal Condition (Stable/Pneumonia/Sepsis/Pyrexial)
COMMENTS:
CTG
CTG used
Time of first CTG
Evidence of Intrapartum CTG review
Description of CTG (Reassuring/Suspicious/Pathological)
Features Described
Baseline
Variability
Accelerations
Decelerations
CTG interpreted correctly
Appropriate action on CTG assessment
Details

COMMENTS:
STAFF
Doctor consulted during intrapartum care
Experience level of doctor (intern/MO/registrar/consultant)
Specialist ever consulted during management
Doctor present at delivery
Experience level of doctor (intern/MO/registrar/consultant)
COMMENTS:
DELIVERY
Mode (Vaginal/Caesarean)
Complications at Delivery (specify)
Actions taken with complication (other than assisted delivery)
Episiotomy Y/N
Assisted Delivery
Vacuum
Prerequisite conditions met
Forceps
Prerequisite conditions met
Successful
Vacuum- number of pulls
Paediatric Doctor Present (Intern/MO/Registrar/Consultant)
COMMENTS:
CAESARIAN SECTION
Decision time
Indication for Caesarean Section
Decision time to delivery time
Prolonged time to delivery
Reason for delay (specify)
Paediatric Doctor Present (Intern/MO/Registrar/Consultant)
COMMENTS:
PLACENTA
Description
Histology
MCS
COMMENTS:
NEONATE
1. General
Time of Birth
Place of Birth (Home/MOU/MPH)
Birth Weight (gram)
Gender (male/female)
APGAR scores
1min
5min

10min
COMMENTS:
2. Resuscitation
Required
Airway clearance (suctioning)
Intubation
IPPV (Duration min)
CPAP (Duration min)
Chest compressions (Duration min)
Adrenaline
Nalaxone
Time to first Gasp (min)
Time to spontaneous respiration (min)
Time to HR >100 (min)
COMMENTS:
3. Bloodgas (<1 hour of life)
pH
BE
Lactate
HCO3
Hgt
COMMENTS:
4. Clinical Assessment
HIE Score Thompson Initial
HIE Score repeat (specify time after birth)
Clinical Seizures
Management of Seizures
Co-Morbid Condition
COMMENTS:
5. Initial Clinical Management
IV Fluid - K+ free 40ml/kg TFI
No over heating
IV Antibiotics
Ventilation
Nasal Prongs
CPAP
Intubated
Fi02
Use of Inotropes (specify)
COMMENTS:
6. aEEG
Initial aEEG Time after birth performed (hours)
MPH or GSH/MMH
Findings

Features of Seizures Present
Repeat aEEG
Findings
COMMENTS:
7. Blood Results
FBC
Hb
WCC
Plt
Blood Culture
CRP
COMMENTS:
8. Transport
Flying squad Reference
Time Paediatric Flying Squad booked
Time of arrival at MPH
Time of Arrival at GSH/MMH
Time after Birth (Hours)
Delay
Reason for delay
COMMENTS:
9. NICU
Arrival before 6 hours of life
Therapeutic Hypothermia Criteria met
Reason if criteria not met
Therapeutic Hypothermia performed
Maximum HIE Score
Alive at day 7
HIE score on day 7
Adequate suck on day 7
COMMENTS: