UNIVERSITY OF THE WITWATERSRAND

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Umbilical cord blood gas analysis in a tertiary public hospital in Johannesburg.

MSc (Medicine) Dissertation

Obstetrics and Gynaecology

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DECLARATION

I Roberts Barasa Nyakoe, student number 0010485E declare that the dissertation I am submitting for assessment is my own work, and contains no section copied in whole or in part from any other source unless explicitly identified in quotation marks and with detailed, complete and accurate referencing. I declare this work has not been submitted to any other university or institution for the purpose of a post-graduate degree. It is being submitted for the degree of Master of Science (in the branch of Obstetrics and Gynaecology) at the University of the Witwatersrand, Johannesburg.

Signature of Student: 

Date: 17 September 2021

DEDICATION

This research dissertation is dedicated to:

My late mother Mrs Teresia Nyang'ara Nyakoe who passed on while I was preparing to start this research project.

In loving memory

Teresia Nyang'ara Nyakoe

1953 – 2016.

PRESENTATIONS

Utility of umbilical cord blood gas analysis at birth. At the 39th National Congress of the South African Society of Obstetricians & Gynaecologists. Champagne Conference centre, Central Drakensberg. Parallel session 11: General obstetrics, 10/03/2020.

ABSTRACT

Key words; Umbilical cord blood gas, Birth asphyxia, Hypoxic ischaemic encephalopathy, Cerebral palsy, Obstetric litigation.

Introduction: Obstetric litigation has increased substantially in South Africa, a large proportion of litigation is due to alleged birth asphyxia in brain damaged children. Umbilical cord blood gas (CBG) at birth is an accurate and objective assessment of the fetal acid-base status immediately before birth and may assist in the defence of these cases. The South African Society of Obstetricians and Gynaecologists (SASOG) recommends routine CBG at birth. We investigated the feasibility of routine CBG at birth in a busy tertiary academic hospital.

Methods: Doctors and midwifes were trained on sampling, analysis and interpretation of CBG and were encouraged to do routine CBG on all deliveries. A point of care blood gas machine was used to analyse the cord blood. Participants were prospectively followed until discharge for short term maternal and neonatal outcomes.

Results: There were 1665 live births that were eligible for CBG, 218 (13%) had CBG and 207 were included in the study. There were 191 (96%) singletons, seven pairs of twins (3.5%) and one set of triplets. Of these, 53 (25.6%) had elective Caesarean sections (CS), 90 (43.5%) had emergency CS, 63 (30.4%) had vaginal deliveries and one had an assisted vaginal delivery. Most, 161 (77.8%) were at term gestation. No neonatal resuscitation was required in 134 (64.7%), while 59 (28.5%) neonates were admitted to the Transitional Unit and 14 (6.8%) to NICU. Abnormal arterial or venous CBG were significantly associated with neonatal resuscitation. Problems were encountered with sampling 5.8%, machine calibration 2.9% and lack of supplies 1.5%. Assessment of the quality of the CBG reports revealed minor issues like incorrect labelling and time recording in 66% of instances. There were no issues in 31 (15%) of the CBG, but there was only a venous sample or similar arterial and venous CBG results in 47(23%) of the cases.

Conclusion: Routine CBG is not feasible in our setting. Departmental guidelines and training on CBG are required. Selective sampling and analysis might be the most appropriate policy to adapt in a busy tertiary unit. Larger studies on the cost effectiveness and feasibility of selective CBG analysis in our setting and in the regional hospitals and clinics are needed to guide policy.

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ABBREVIATIONS AND DEFINITIONS

- ACOG – American College of Obstetricians and Gynecologists
- ADHD – Attention Deficit Hyperactivity disorder
- BD – Base Deficit
- BE – Base Excess
- BE_{ECF} – Base Excess in Extracellular Fluid
- BE_b - Base Excess in Blood
- BMI – Body Mass Index
- Ca - Calcium
- CBG – Cord Blood Gas
- CEO – Chief Executive Officer
- CHBAH – Chris Hani Baragwanath Hospital
- CMJAH – Charlotte Maxeke Johannesburg Academic Hospital
- Cl - Chloride
- CO_2 – Carbon Dioxide
- CP – Cerebral Palsy
- CPAP – Continuous Positive Airway Pressure
- CS – Caesarean Section
- CTG – Cardiotocograph
- dL - Decilitre
- ECF – Extracellular Fluid
- FIGO – The International Federation of Gynecology and Obstetrics
- FHR – Fetal heart rate
- FSB – Fresh Stillbirth
- H - Hydrogen
- Hb – Haemoglobin
- Hct - Haematocrit
- HCO_3^- - Bicarbonate
- HIE – Hypoxic Ischaemic Encephalopathy
- HIV – Human Immunodeficiency Virus
- ICU – Intensive Care Unit

- IUFD – Intrauterine Fetal Death
- IUGR – Intrauterine Growth Restriction
- IVH – Intraventricular Haemorrhage
- K - Potassium
- L - Litre
- LBW – Low Birth Weight
- LLC – Limited Liability Company
- LMIC – Lower and Middle Income Countries
- LTD – Lower Than Detectable
- MA - Massachusetts
- mL – millilitres
- M&M – Morbidity and Mortality
- mmHg – Millimetres of Mercury
- MOU – Midwife Obstetric Unit
- MSB – Macerated Stillbirth
- Na – Sodium
- NE – Neonatal Encephalopathy
- NEC – Necrotising Enterocolitis
- NICU – Neonatal Intensive Care Unit
- NNJ – Neonatal Jaundice
- PCO_2 – Partial pressure of Carbon dioxide
- PO_2 – Partial pressure of oxygen
- PPH – Postpartum Haemorrhage
- RBC – Red Blood Cells
- RMMCH – Rahima Moosa Mother and Child Hospital
- RPR – Rapid Plasma Reagin
- SASOG – South African Society of Obstetricians and Gynaecologists
- SD – Standard Deviation
- TU – Transitional Unit
- USA – United States of America
- VL – Viral Load
- WHO – World Health Organisation

Definitions

- **Live birth;** delivery of neonate who is ≥ 26 weeks of gestation and/or ≥ 800 grams birth weight who shows any signs of live at birth.
- **Interpretation of Electronic Fetal Heart Rate patterns-** Should analysis of actual CTG be required these will be as defined by the FIGO guidelines of 2015. Appendix 6, otherwise the CTG will be recorded as they were interpreted by the attending doctor.
- **Maternal pyrexia –**Body temperature of >38°C
- **Major congenital abnormalities –** congenital abnormalities that cause significant functional impairment or are life threatening, excludes clinically less significant condition such as tongue-tie, pre- auricular tags, single umbilical artery etc.

1 INTRODUCTION AND LITERATURE REVIEW

Dr William John Little (1810 – 1894) an orthopaedic surgeon dealing with children who had spastic joint contractures was the first to link intrapartum asphyxia to spastic cerebral palsy then known as “Little’s Disease”.[1] Sir William Osler (1849 – 1928) later coined the term cerebral palsy, [2] which was later defined as “a permanent disorder of development of movement and posture that cause activity limitation and are attributed to a non-progressive disturbance that occurred in developing fetal or infant brain”.[3]

Studies in developed countries show that birth asphyxia (impaired gaseous exchange) is responsible for less than 10% of the Cerebral palsy cases. [4, 5] This may not be the case in lower and middle income countries (LMICs) like South Africa where intrapartum asphyxia is the second leading cause of neonatal deaths [6] and is therefore expected to contribute to a large proportion of neurological disability. [7] A study by Cowan et al in the Netherlands and United Kingdom (London) using brain imaging or post-mortem also supports the view that cases of brain injury in term neonates are due to immediate intrapartum events. [8] Birth asphyxia that is severe enough to cause cerebral palsy must produce evidence of moderate or severe neonatal encephalopathy (NE). [9] Neonatal encephalopathy is a syndrome with multiple causes and is classified as mild, moderate, or severe as described by Sarnat. [10] Intrapartum asphyxia is one of the many pathological pathways that can lead to neonatal encephalopathy. A neonate with NE might recover completely, develop cerebral palsy or non-cerebral palsy neurological sequelae like ADHD, autism and epilepsy, or even result in mortality. [9]

The introduction of electronic fetal heart rate monitoring led to the expectation that medical practitioners would be able to detect signs and symptoms of intrapartum asphyxia and that timeous intervention could prevent poor neurological outcome. [11] Serial antenatal examinations, fetal kick charts, ultrasound and Doppler studies, detection of meconium stained liquor, electronic fetal heart rate (FHR) monitoring coupled with fetal scalp blood pH and Apgar scores have poor predictive values, this has led to an increase in the caesarean section rates with little or no reduction in neonatal neurological morbidity and mortality. [12, 13, 14, 15, 16]

The neonatal umbilical cord blood gas is the best representation of the fetal acid-base status immediately before birth that can be accurately and objectively measured. [17] The acid-base

status of the fetus at birth is important in establishing the link between an intrapartum event that causes asphyxia, and the neonatal condition. [18]

In obstetric litigation, umbilical cord blood gas can be used to differentiate between an acute and chronic acidosis and in some cases to time the onset of the insult. Umbilical blood gas analysis can also provide feedback on FHR tracing pattern interpretation and help to determine if the interventions carried out were appropriate. [19]

Umbilical blood gas analysis can complement other assessment modalities to assist in the management of the compromised neonate, for example, the decision to offer therapeutic hypothermia or ventilation. [19]

Birth asphyxia and hypoxic ischaemic encephalopathy (HIE) leading to cerebral palsy is one of the main causes of litigation in obstetrics. Medico-legal cases in obstetrics have been on the increase in South Africa and other parts of the world. [11 - 13, 20] The pay outs for malpractice has increased substantially in the last few years (by 123% increase from 2010 to 2012) [20] and the trend continues. Employees of the Gauteng Department of Health are indemnified for medical malpractice by the Gauteng province. The reasons for increased litigation maybe due to increased patient awareness of their rights, or the litigation lawyers focussing on medical malpractice since the Road Accident Fund is no longer paying for personal injury claims. [21] As of March 2016, medico legal claims amounted to 37 billion Rand nationally and 13.8 billion Rand in Gauteng Province alone. Seventy percent of these claims are due to maternal and neonatal health problems; a substantial number of claims are on behalf of children with cerebral palsy. [22] The incidence of hypoxic ischaemic encephalopathy (HIE) is much higher in our setting than in developed countries, 8.7-13.3/1000 live births at Chris Hani Baragwanath Hospital (CHBAH) [23] and 3.6/1000 live births at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). [24] The Department of Health does not budget for malpractice claim pay-outs and this money comes out of the normal operational budget thus negatively impacting on the department's ability to provide for other essential services.

Various strategies have been suggested to reduce medico-legal litigation, including practising evidence based medicine (EBM), good record keeping, and umbilical cord blood gas in high risk deliveries. [25, 26]

It is recommended to sample and analyse both the umbilical cord artery and vein. Errors can be introduced at sampling, if the volume of heparin used exceeds 0.1ml, heparin is acidic and might give a falsely low pH. Another common source of error is an air bubble in the syringe

leading to a high PO_2 reading thus one should ensure that all the air is expelled from the syringes. There is very little metabolism in the blood after sampling and it is not necessary to store the sample on ice if the analysis is done within 60 minutes. [27] Normal umbilical cord blood gas parameters are shown in Table 1.1.

Table 1.1: Normal values for fetal umbilical cord gases at birth [19,28]

	Umbilical Artery	Umbilical Vein
pH	7.18 – 7.38	7.25 – 7.45
PO_2	5.6 – 30.4 mm Hg	17.4 – 41.0 mm Hg
PCO_2	32.4 – 66.0 mm Hg	27.0 – 49.4 mm Hg
Base Deficit $_{ECF}$ mean (SD)	4.79 (3.46) mmol/L	≈4.0 (3.5) mmol/L

Ranges based on mean ± 2 SD.

Several factors that could affect the results of cord blood include; gestation at birth, elective caesarean section deliveries have higher pH compared to vaginal or emergency caesarean section, regional anaesthesia, cord length, umbilical cord abnormalities e.g. true knotting, breech vaginal delivery and neonates with meconium stained liquor tend to have lower pH. [27]

The blood gas analysers usually measure the pH, PO_2, and PCO_2 directly and use an algorithm to calculate HCO_3^- and the base deficit. Depending on the analyser other parameters such as haematocrit, electrolytes and lactate can be analysed. [19]

Cord blood gas is pathological (associated with adverse neonatal outcome) if pH ≤7.0 [27,29] and/or Base excess > 12 mmol/L. [19, 30, 31] The arterial cord blood gas represents the acid base status of the fetus while the venous cord blood gas represents the acid base status of the maternal and placental circulation. However, both arterial and venous samples are needed to ensure that the correct specimen was taken. The umbilical arterial cord blood pH and pO_2 are lower than venous blood pH and pO_2. The arterial cord blood pCO_2 and BE are higher than the venous blood pCO_2 and BE. [19]

The pH is the inverse log of the hydrogen ion (H^+) concentration. The pH does not correlate in a linear manner with the change in hydrogen ion concentration and large changes in the H^+ concentration might show only a small change in pH. The proportion of the bicarbonate buffer that has been used for the extra H^+ or the base deficit/excess is therefore a much better parameter to measure the degree of acidosis, it has a linear correlation with the H^+ concentration.

The venous cord blood pH is always higher than the arterial cord blood pH, a pathologically low venous cord blood pH means that the arterial pH will also be abnormal, however it is possible to have a severely acidotic neonate with a normal venous cord blood pH. However, several studies have shown that venous cord blood pH can accurately predict acidosis. [32, 33, 34]

In the third trimester the (Base Deficit) BD is around 2 mmol/l in arterial cord blood and remains unchanged in latent phase of labour. With increasing contractions during the active phase of labour, the BD increases by 1 mmol/l every 3 to 6 hours and in the second stage of labour the BD increases by 1 mmol/l every hour. [35] Thus the normal BD in arterial cord blood is 4mmol/l and 5mmol/l in venous cord blood.

In the case of an acute event obstructing the placental perfusion, CO_2 accumulates with simultaneous reduction in O_2. This will lead to increased PCO_2 and cause respiratory acidosis which is easily cleared when the circulation is restored. If the event persists then metabolic acidosis develops due to anaerobic metabolism and accumulation of lactic acid. Respiratory acidosis rarely lasts more than 30 minutes, after this the picture is a mixed acidosis and eventually a metabolic acidosis. [18, 36]

It is possible to calculate the pH of the fetus before an acute event and thus determine if the event is responsible for the neonatal status using the equation by Eisenberg: for every 10mmHg of PCO_2 above the normal, the pH is reduced by 0.008. [18] In acute events there are large differences in the parameters between the arterial and venous cord blood compared to chronic acidosis. In cases of complete cord occlusion, the arterial umbilical cord base deficit increases by 1 mmol/L every two minutes and the PCO_2 increases by 7mmHg for every one minute. [19]

Lactate is a result of anaerobic metabolism and a high lactate level indicates metabolic acidosis. The level of lactic acid associated with poor neurological outcome has not been established. [37, 38] A study at a district hospital in the Eastern Cape in 2015 showed that healthcare workers were positive of the benefits and supported introduction of universal umbilical cord blood assessment for fetal acidosis. [39]

Problem statement

To counter the rise of malpractice claims, a change in practice is needed. Apart from practicing evidence-based medicine, we need to have medical records to assist in defence of medico-legal

claims. Having a normal umbilical blood gas could assist in defending malpractice claim for a neurologically impaired child alleged to be a result of an intrapartum event is lodged. Cord blood gas is also useful for management of the depressed neonate and for learning purposes as it can give feedback on interpretation of CTG tracing patterns. [19] SASOG has recommended the use of routine cord blood gas at birth. [26] We investigated the feasibility of this approach in a busy tertiary hospital.

2 AIMS AND OBJECTIVES

2.1 Aim

The aim of this study was to assess the utility of universal umbilical cord blood gas analysis of live births at Charlotte Maxeke Johannesburg Academic Hospital.

2.2 Objectives

2.2.1 To determine the proportion of babies who had umbilical cord blood gases done.

2.2.2 To compare the outcome of babies with abnormal umbilical cord blood gas parameters with outcomes of those babies with normal umbilical cord blood gases.

2.2.3 To describe barriers that impacts on the use of umbilical cord blood gas.

2.2.4 To describe the short-term neonatal outcomes of babies who were sampled for umbilical cord blood.

2.2.5 To describe the short-term maternal outcome of mothers whose babies had umbilical cord blood gas sampled.

3 METHODS

This was a prospective cross-sectional study whose aim was to assess the utility of universal umbilical cord blood gas analysis of live births at Charlotte Maxeke Johannesburg Academic Hospital. We assessed live births from 01 February 2019 to 10 April 2019. The objectives were; to determine the proportion of babies who had umbilical cord blood gases done, to compare the outcome of babies with abnormal umbilical cord blood gas parameters with outcomes of those babies with normal umbilical cord blood gases, to describe barriers that impacts on the use of umbilical cord blood gas, and to describe the short-term neonatal and maternal outcomes of babies who were sampled for umbilical cord blood.

Charlotte Maxeke Johannesburg Academic hospital is a tertiary teaching hospital attached to the University of the Witwatersrand, in Johannesburg South Africa. The obstetrics unit delivers approximately 9000 babies annually, and serves as a referral hospital for high risk obstetric patients from several secondary hospitals, Midwife Obstetric Units (MOU) and Community clinics. There are also many low risk walk-in patients from the surrounding community.

The study population were women over 18 years of age who delivered a live birth at Charlotte Maxeke Johannesburg Academic Hospital within the study period. Women with a fetus with a known major congenital abnormality, or who delivered a non-viable fetus, i.e. fetus that weighs less than 800 grams at birth and does not survive for more than 24 hours were excluded. All study participant gave written consent for inclusion in the study. (Appendix 1)

Materials and methods

During the period preceding the study, presentations to nurses and doctors on cord blood gas sampling and analysis were done, emphasizing its importance in cases of obstetric litigation, the role of intrapartum asphyxia in cerebral palsy/neurological handicap. Practical training sessions were also held in the labour ward on how to sample, analyse and interpret umbilical cord blood gas at birth. We encouraged cord blood gas analysis for all women who delivered a live birth (delivery of neonate who is ≥ 26 weeks gestation and/or ≥ 800grams birth weight) i.e. Universal umbilical cord blood gas testing. There were constant reminders to do the cord blood gases in our daily audit meetings, but doing cord blood gas was not mandatory. The participants were then prospectively followed up till discharge.

Sampling method

A section of the umbilical cord was double clamped immediately the baby was born and kept aside for sampling within 30 minutes, samples collected up to 60 minutes after birth were acceptable for analysis. The sampling was done into pre-heparinized syringes recommended by the supplier of the blood gas machine. The arterial sample was obtained first followed by the venous sample whose volume would be higher. The sample could be kept at room temperature for up to 60 minutes, if delayed analysis was anticipated for any reason then the sample was refrigerated.

The analysis was done using a critical point of care blood gas analyser machine that was situated in the High care area of the labour ward. The machine was a Stat Profile Prime® serial number P07614300 by Nova Biomedical Corporation, Waltham, MA, USA. The maintenance of the point of care machine was provided by The Scientific Group, Randburg, South Africa. The Stat Profile Prime® uses Microsensor Card™ technology and automatically self-calibrates and runs quality controls at intervals set by the user (once daily at CMJAH).

The Stat Profile Prime® directly measures the pH, PCO_2, PO_2 and calculates the HCO_3^-, base excess in blood (BE_b), base excess in extracellular fluid (BE_{ECF}). The machine also measures K^+, Na^+, Cl^-, Ca^{2+}, glucose, lactate and haematocrit. This information was recorded in the cord blood gas form to be left in the patients' clinical records (Appendix 3).

Data was collected on a data sheet (Appendix 2), it included patient demographics, booking status and blood results, obstetric and medical history, mode of delivery and indications, cord blood gas results, short term neonatal and maternal outcome. Poor neonatal outcomes included were; need for supplemental oxygen, CPAP, intubation and ventilation, HIE, admission to TU, NICU admission, and early neonatal death. Poor maternal outcomes included were the presence of any complication including; blood transfusion, post-partum haemorrhage (PPH), sepsis, laparotomy, hysterectomy, High-care or ICU admission and death. The data was collected from the maternal records after the patient had consented, the information required was obtained from the maternal case records, the labour ward and theatre registers and neonatal case records in the Transitional Unit (TU), Neonatal ICU (NICU) and in the neonatal records. The cord blood gas analysis results were collected by the delivery team and recorded on a data sheet provided. Barriers to use of cord blood identified by the delivery team were recorded (this was an open-ended question).

Statistical analysis

Data on a total of 207 cord blood gas pairs were analysed using Stata® 14.0 software, StataCorp LLC (2015). A sample size of 534 was calculated using HIE prevalence at CMJAH of 3.6 per 1000 live births [34]. The maternal and foetal characteristics were summarised as frequency and proportions/percentage calculations. Inferential statistics were done using Pearson Chi-square test and logistic regression. To compare blood gas and neonatal intervention/ Apgar score Pearson chi-square test was applied. Odds ratios and 95% confidence intervals were reported. Statistical significance level was taken as p-value <0.05.

Ethics

Ethics clearance for the study was granted by the Human Research Ethics committee (Medical) of the University of the Witwatersrand. Ethics clearance certificate number M180360 (Appendix 4). The research was registered with National Health Research Database. Permission to conduct research was also granted by the CEO of CMJAH (Appendix 5).

4 RESULTS

There were 1719 total births from 1672 deliveries (including two sets of triplet and 43 twin births) from the 01 February 2019 to 10 April 2019. There were 811(48.6%) caesarean sections. There were 41(2.4%) stillbirths, of which 14(0.8%) were fresh stillbirths and 27(1.6%) were macerated stillbirths. Eleven deliveries were non-viable and included two hysterotomies and nine miscarriages (one pair of twins).

There were 1666 live births, one baby had congenital anomalies thus 1665 live births were eligible for inclusion. Of these only 218 (13%) had cord blood gas at birth, 11 did not give consent for inclusion in the study. Thus only 207 cord blood gases from 199 deliveries were included in the study, they consisted of 191 (96%) singletons, seven twins (3.5%) and one set (0.5%) of triplets (one of the triplet was a stillbirth and was not eligible for inclusion). See Figure 4.1

The baseline characteristics of the mothers who participated in the study are shown in Table 4.1, 195 (98%) were Black Africans while 151 (75.9%) were aged between 20 and 35 years and 40 (20.1 %) were older than 35 years. In terms of Body Mass Index (BMI) at first antenatal booking visit 69 (40.1 %) were obese and 14 (8.1 %) had class III obesity. There were 52 (26.1%) HIV positive mothers, 36 (73.5 %) of them had viral load which was lower than detectable (LTD) and 45 (91.8 %) had a Viral load of less than 1000 copies/mL. The CD4 count was available in 45 patients and 18 (40 %) had a CD4 of less than 350 cells/mL. Anaemia defined as Haemoglobin of less than 11 g/dL was present in 57 (29.2 %) of the mothers. There were only nine (4.5 %) who were Rhesus factor negative. The majority of the deliveries 161 (77.8%) were at term gestation (37 weeks and more), 27 (13%) were between 34 and 36 weeks of gestation, 17 (8.2%) were between 28 and 34 weeks and two (1%) were below 28 weeks.

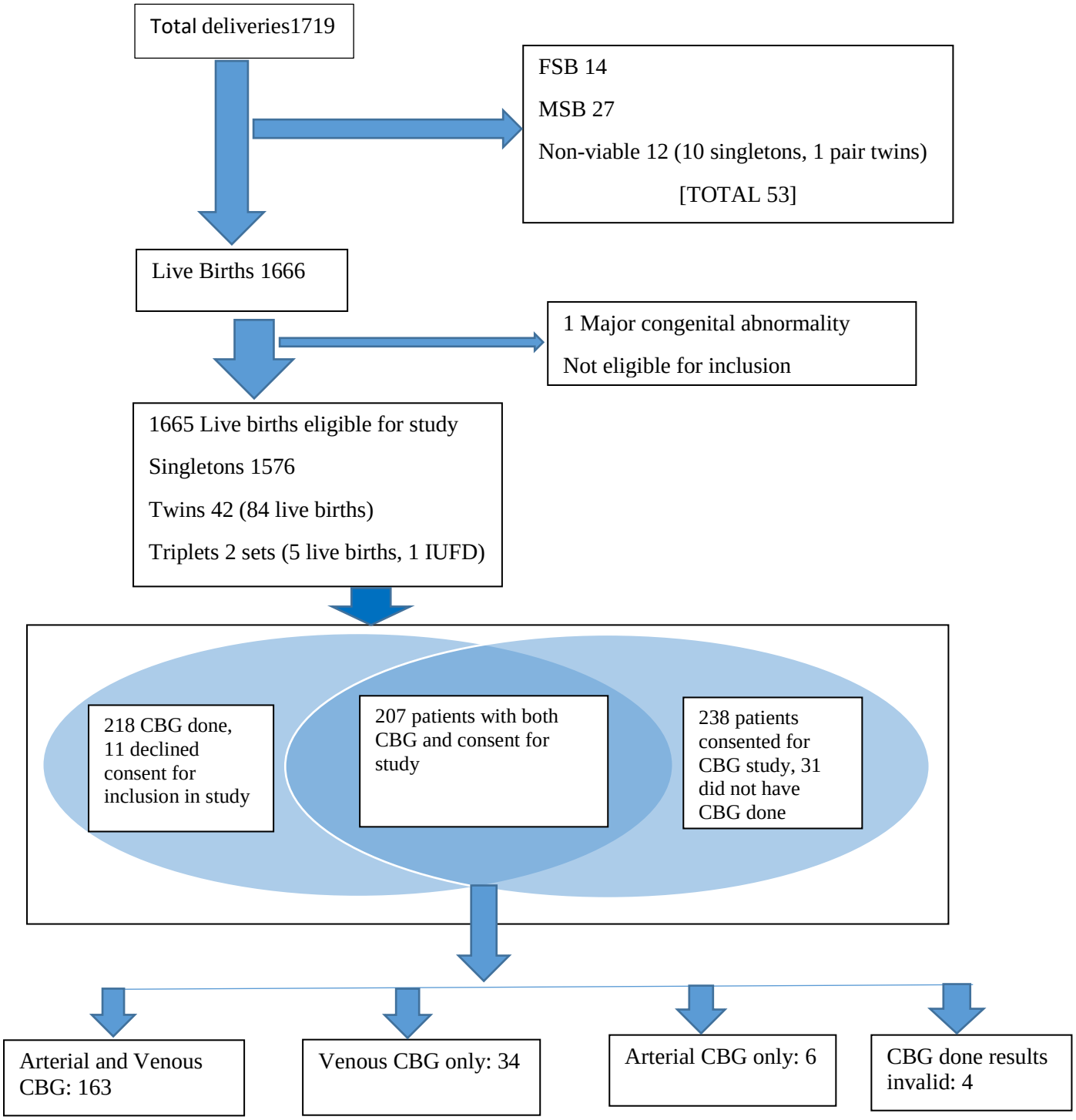

Figure 4.1: Flow chart showing the recruitment of subjects for umbilical cord blood gas at birth.

CBG – cord blood gas, FSB – Fresh stillbirth, IUFD – Intrauterine fetal death, MSB – Macerated stillbirth

Table 4.1: Maternal characteristics of deliveries that had cord blood gas analysis at birth. N= 199

Maternal characteristics	Frequency	
	Number	**Percentage %**
Age (Mean 30.2 years, SD 6.2)		
< 20 years	8	4.0
20-35 years	151	75.9
>35 years	40	20.1
Parity		
0	39	19.3
1	81	40.7
2	53	26.1
3 or more	26	13.1
Gravidity		
Primigravida	36	18.1
Multigravida	148	74.4
Grand multigravida	15	7.5
Race		
African	195	98.0
Coloured	1	0.5
Indian	1	0.45
White	2	1.0
Body Mass Index (kg/m^2) n= 172		
Underweight, <18.5	0	0
Normal weight, BMI 18.5 – 24.9	50	29.1
Overweight, BMI 25 – 29.9	53	30.8
Obese class I, BMI 30 – 34.9	36	20.9
Obese class II, BMI 35 – 39.9	19	11.1
Obese class III, BMI > 40	14	8.1
HIV status, n = 199		
Negative	147	73.9
Positive	52	26.1
Viral Load (copies/mL) n = 49		
LTDL	36	73.9
50 – 999	9	18.4
1000 or greater	4	8.1
CD4 (cells/mL) n=45		
Less than 100	3	6.7
100 – 349	15	33.3
350 and greater	27	60.0
RPR n = 199		
RPR Negative	188	94.5
RPR Positive	3	1.5
RPR Unknown	8	4.0
Haemoglobin (g/dl), n = 195		
Normal (11 or greater)	138	70.8
Anaemia (Less than 11)	57	29.2

Maternal outcome

There were no maternal complications in 174 (87.4%) patients of the 199 deliveries, while 24 (12.1%) had complications that included; one (0.5%) maternal death in ICU after a caesarean section and hysterectomy for placenta praevia accreta that was complicated by bowel injury and sepsis, 11 (5.5%) patients needed blood transfusion two of whom had PPH. There were four (2%) laparotomies, 2 for hysterectomy, one for intra-abdominal sepsis and one for wound sepsis. There were five (2.5%) patients with wound sepsis. High care admission was needed in nine (4.5%) patients and one required ICU. Other complications in six other patients were spinal anaesthetic complications, urinary tract infection, pelvic diasthesis, pyrexia and tachycardia.

Neonatal characteristics

The characteristics of neonates who had cord blood analysis is shown in Table 4.2. Caesarean section delivery was performed in 143 patients with 53 (25.6%) were elective caesareans while 90 (43.5%) were emergency caesarean sections. There were 63 (30.4%) normal vaginal deliveries and one assisted vacuum delivery.

The birth weight was as follows, with 163 (78.7%) having a birth weight of 2500 grams or more, and 10 (4.8%) with a birth weight of less than 1500 grams.

A retro-placental clot was reported in six (2.9%) of placentas and a two vessel cord was recorded in three (1.5%) neonates.

Neonatal outcome

The majority of the neonates 136 (65.7%) were well at birth and were discharged to the mother, while 71 (34.3%) neonates required resuscitation, of which 61 (29.5%) were admitted to the Transitional unit and 10 (4.8%) required NICU admission.

The eventual neonatal outcomes were as follows; 201 (97%) were discharged to the mother, there was one (0.5%) neonatal death, one (0.5%) was transferred for palliative care, another one (0.5%) was transferred to a secondary hospital for continued care while discharge records could not be traced for three (1.45%) neonates.

Table 4.2: Foetal characteristics of deliveries that had cord blood gas analysis at birth. N = 207

Foetal characteristics	Frequency	
	Number	%
Mode of delivery		
Elective CS	53	25.6
Emergency CS	90	43.5
Normal vaginal delivery	63	30.4
Assisted Vaginal delivery	1	0.5
Apgar score at 5 minutes		
Normal (7 or more)	202	97.6
Low score (Less than 7)	4	1.9
Unknown	1	0.5
Birth weight (grams)		
Extremely LBW <1000g	4	1.9
Very LBW <1500g	6	2.9
LBW <2500g	34	16.4
Normal 2500g or greater	163	78.7
Gender		
Female	113	54.6
Male	94	45.4
Retro-placental clot		
No	193	93.2
Unknown	8	3.9
Yes	6	2.9
3 vessel cord		
No	3	1.5
Unknown	6	2.9
Yes	198	95.7
Neonatal outcome		
NICU admission	10	4.8
TU admission	61	29.5
Normal ward	136	65.7

CS – Caesarean section delivery, g – Grams, LBW – low birth weight, NICU – Neonatal intensive care unit, TU – Transitional care unit

Neonatal resuscitation

Neonatal resuscitation was derived at the three different levels defined as follow; No neonatal intervention 134(64.7%), need for admission to the neonatal Transitional unit for any reason 59 (28.5%) and if the neonate required NICU admission for any reason including intubation and ventilation 14(6.8%).

Cord blood gas results

The cord blood gas results analysis included in the study, 169 neonates had arterial cord blood gas pH, 142 (84%) had a normal arterial pH of >7.2 and only two (1.2%) had a pathological arterial pH of <7.0. There were 154 arterial cord blood gas samples with BE results, of these 142 (92.4%) had a normal BE of > -12, and 12 (7.7%) had a pathological BE of < -12. Venous cord blood gases pH was analysed in 197 neonates of which 169 (85.8%) were normal with pH>7.2, and two (1%) were pathological with a venous pH <7.0, 183 cord blood venous BE results were available, 172 (94%) had a normal BE of > -12 and 11 (6%) were pathological with BE of < -12.

Analysis of 154 neonates who had complete arterial cord blood gas results, 128 (83.1%) had normal pH and BE, while 16 had one abnormal parameter; 14 (9.1%) had abnormal pH and two (1.3%) had abnormal BE. Both parameters were abnormal in 10 (6.5%) neonates.

Cord blood gas and neonatal resuscitation

Analysis of the arterial cord blood gas results show that neonatal resuscitation was significantly associated with pH < 7.2, p-value = 0.012. The relationship between BE < -12 and neonatal resuscitation was not significant, p-value = 0.05. When either the arterial cord blood gas pH or both pH and BE were abnormal the significant relation with neonatal resuscitation persisted, p-value = 0.008. See Table 4.3

Table 4.3: Arterial blood gas results versus neonatal resuscitation of neonates that had cord blood gas analysis at birth.

Arterial pH **(n = 169)**	Neonatal resuscitation		
	No n (%)	Yes n (%)	p-value
>7.2	101 (89.4)	41 (73.2)	0.012
7.2 – 7.1	10 (8.8)	12 (21.4)	
>7.1 – 7.0	2 (1.8)	1 (1.8)	
< 7.0	0 (0.0)	2 (3.6)	
Arterial base excess (BE) **(n = 154)**	Neonatal resuscitation		
	No n (%)	Yes n (%)	p-value
Normal (-12 or greater)	101 (95.3)	41 (85.4)	0.050
Abnormal (less than -12)	5 (4.7)	7 (14.6)	
Arterial pH + arterial BE **(n = 154)**	Neonatal resuscitation		
	No n (%)	Yes n (%)	p-value
Normal Arterial pH + normal BE	95 (89.6)	33 (68.8)	0.008
Abnormal Arterial pH + normal BE	6 (5.7)	8 (16.7)	
Normal Arterial pH + abnormal BE	1 (0.9)	1 (2.1)	
Abnormal Arterial pH + abnormal BE	4 (3.8)	6 (12.5)	

A similar relationship was found on analysis of the venous cord blood gas and neonatal resuscitation, venous pH < 7.2 was significantly associated with the need for neonatal resuscitation, p-value = 0.021, venous BE < -12 was significantly associated with neonatal resuscitation, p-value = 0.046, and there was a significant association with the need for neonatal resuscitation when either the venous cord blood gas pH or BE are abnormal, or when both were abnormal, p-value = 0.001. See Table 4.4.

Table 4.4: Venous blood gas results versus neonatal resuscitation of neonates that had cord blood gas analysis at birth.

	Neonatal Resuscitation		
Venous pH **(n = 197)**	No Number (%)	Yes Number (%)	p-value
>7.2	117 (90.7)	52 (76.5)	0.021
7.2 – 7.1	7 (5.4)	9(13.2)	
>7.1 – 7.0	5 (3.9)	5 (7.4)	
< 7.0	0 (0.0)	2 (2.9)	
	Neonatal resuscitation		
Venous base excess (BE) **(n = 183)**	No Number (%)	Yes Number (%)	p-value
Normal (-12 or greater)	117 (96.7)	55 (88.7)	0.046
Abnormal (less than -12)	4 (3.3)	7 (11.3)	
	Neonatal Resuscitation		
Venous pH + venous BE **(n = 183)**	No n (%)	Yes n (%)	p-value
Normal venous pH + normal venous BE	111 (91.7)	44 (71)	0.001
Abnormal venous pH + normal venous BE	6 (5)	11 (17.7)	
Normal venous pH + abnormal venous BE	0 (0.0)	2 (3.2)	
Abnormal venous pH + abnormal venous BE	(3.3)	5 (8.1)	

Cord Blood gas and Apgar score

The cord blood analysis at birth was compared to the Apgar score, there was no significant relationship between the arterial pH (p = 0.411), arterial BE (p = 0.217) and the Apgar score < 7 at 5 minutes. No significant relationship was seen between the venous pH (p = 0.059) nor with venous BE (p = 0.22) and Apgar score < 7 at 5 minutes.

Challenges with umbilical cord blood gas analysis

Reasons that were given when a component of the CBG results were missing included inability to get sample in 16 (6.8%) cases, problems with the machine in six (2.9%) cases, other issues included lack paper strips in one case (0.5%) and lack of the correct syringes in two cases (1%).

Problems that were logged by the midwifes and doctors were as follows; the blood gas analyser cartridge was reported to be faulty for a total period of six days during the study period, on three other days there were no blood gas syringes this included one of the days when the cartridge was faulty. Therefore, no CBG could be done during these eight days of the study period.

There were 31 patients who gave consent for the study but they did not have the CBG, Figure 4.1. No reasons were given in 26 (84%) of the patients, two (6.5%) were due to the blood gas machine not working, another two (6.5%) were due to lack of syringes and in one (3.2%) there was delay of more than 45 minutes to sampling.

The quality of the available results from 207 neonates is shown in Table 4.5. There were no quality issues in 31 cord blood gases i.e. 62 blood gas samples (15%) of the 207 (414 blood gas samples) cord blood gases. There were 420 quality issues identified in the remaining 176 neonatal cord blood gases (352 blood gas samples).

There was no sampling time recorded in 126 (30%) blood gas sampling forms, however it is possible to pick up delay in analysis from the recorded time of birth. Delay in analysis of the blood gas was present in four samples, two (0.5%) for more than 30 minutes from sampling and two (0.5%) for more than 60 minutes from sampling. The other issue picked up was when the analysis time was not indicated on the blood gas form in 100 (23.8%) instances, in these cases the time on the results strip printout was used, this is not always correct as it depends on whether the blood gas time calibration is updated. It was not possible in 15 neonates to determine the analysis time.

Other issues in sampling were: only venous gas done due to technical difficulties in 33 neonates and only arterial sample in seven neonates. In addition to these 14 neonates had similar venous and arterial results, thus probably the sample was venous in these cases as it's more difficult to obtain an arterial sample. In 52 neonates the strips were not labelled correctly as either venous or arterial and this was picked up on analysis of the results.

In terms of recording there were no paper strip printout in 10 neonates and the results were recorded manually, a further 31 blood gas samples had incomplete results, due to the machine not being calibrated. In two blood gas strips the information was unclear and could not be analysed. A different blood gas machine was used in six neonates when the Stat Profile Prime® blood gas machine was not working.

Table 4.5: Quality issues encountered with umbilical cord blood gas analysis at birth at Charlotte Maxeke Johannesburg Academic Hospital.

Quality Issues	**N=420**	
	Frequency	**Percent**
No issues (n=207)	***31***	***15***
No sampling time	126	30
Time on strip used	100	23.8
Wrong labelling (A/V)	52	12.4
Venous sample only	33	7.9
Incomplete results	31	7.4
Did not differentiate A or V	21	5
No analysis time	15	3.6
A & V similar	14	3.3
No Paper strips	10	2.7
Arterial gas sample only	7	1.7
Different gas machine	6	1.4
Delay >60 minutes to analysis	2	0.5
Unclear information	2	0.5
Delay > 30 minutes to analysis	1	0.2
Total	420	100.00

A – Arterial cord blood gas, V – Venous cord blood gas

5 DISCUSSION

There has been an increase in medical litigation in South Africa and pay-outs resulting from these claims have been substantial, many of these cases are due to neurological damage from alleged birth asphyxia. [11, 12, 13, 20] Birth asphyxia may be responsible for a large proportion of CP cases in South Africa and other LMIC [6, 7] unlike in the developed countries where it is responsible for less than 10% of CP cases. [4, 5] Suggestions to help in defence of these cases have included routine cord blood gases at birth, since this is an accurate and objective assessment of the neonate's condition immediately before birth. SASOG is advising universal routine cord gas analysis on all births, [25, 26] while other institutions like the ACOG advocate for selective sampling and analysis. [40]

Only 13% of the 1665 eligible live births had a CBG. This low percentage suggests that it is not feasible to offer routine CBG at birth in our setting as it is currently. However; where the CBG at birth were done, the neonates included; preterm, term, vaginal deliveries, emergency and elective caesarean sections, singleton and multiple pregnancies including triplets. Analysis of the CBG results at birth showed that abnormal CBG results (pH < 7.2 or BE < -12 mmol/L) was significantly associated with the need for neonatal resuscitation.

The study did not explore why cord blood gases were not done in 85% of eligible deliveries. We postulate that the lack of policy/guidelines on CBG analysis, coupled with the workload might be contributory. The CBG analysis showed a statistically significant association between abnormal pH and/or BE in both venous and arterial blood with neonatal resuscitation, however the association between abnormal arterial CBG BE on its own and neonatal resuscitation did not reach statistical significance.

We are not able to explain why the uptake of CBG was so poor, the study did not ask doctors and midwifes to give a reason where the CBG was not performed. Of the CBG done 11 patients declined to give consent to be included in the study, however, 31 patients who had consented to be included in the study did not have the CBG performed. No reason was given for not performing the CBG for the majority 26 (84%) of them. The main problems encountered were with maintenance of the blood gas machine (cartridge not working) or lack of syringes which resulted in no CBG being done for eight days within the study period.

Clear and strict guidelines and rules on when to perform CBG, training, continuing education and emphasising the role and importance of CBG at birth are needed. Review of the CBG at birth on all adverse neonatal outcomes during M&M meetings would help in increasing the uptake of CBG at birth. Maintenance and availability of the necessary supplies is also crucial to ensure uptake. A study in Eastern Cape showed that healthcare workers are supportive of introduction of CBG analysis at birth for Lactate. [39]

There was no difficulty encountered in the process of performing CBG in the majority of the cases (89%). Difficulties encountered were difficulty in sampling (collapsed vessels or inability to obtain arterial cord blood) in 6.8% and logistic problems like machine not calibrated and lack of supplies in 4.3%. These problems would be addressed by training.

There were a number of minor quality issues like incorrect labelling and time recording. There were 33 CBG where only the venous blood was done (the two samples were similar or only one sample analysed), demonstrating the need for further training to emphasise the importance of proper recording of time and the importance of obtaining both arterial and venous samples. Venous cord blood is technically easier to obtain and sometimes arterial cord blood is not obtained. Cantu et al [32] and Swanson et al, [34] found that venous pH and venous BD to be highly predictive of arterial pH and arterial BD, and can be used to evaluate the likelihood of fetal academia in the absence of umbilical arterial cord blood gas values. This mirrors our finding that abnormal venous CBG pH and/or BD were significantly associated with neonatal resuscitation as were the arterial CBG pH and/or BD. A venous CBG is still useful in cases where it is not technically possible to obtain an arterial CBG.

In routine sampling all live births are sampled while in selective sampling only neonates at risk of poor outcome are sampled. The selective sampling criteria recommended by ACOG are; an intrapartum event (e.g. abruption placenta, cord prolapse, CTG changes), all non-elective CS deliveries, 5 min Apgar < 3, Severe IUGR, intrapartum fever, maternal thyroid disease and multiple gestation. [40] The case for routine sampling is that the results are available if needed, its cost effectiveness has been documented, there are cases of vigorous baby with academia who have been shown to be at higher risk of neonatal morbidity and that it also facilitates learning and feedback on FHR tracings. [19, 41] Due to the poor uptake selective sampling maybe the appropriate way to introduce CBG at birth and then scale it up gradually to routine sampling.

Lactate in CBG is directly measured, and is the end product of metabolic acidosis, however the threshold for prediction of poor neonatal outcome is not known. Westgren et al, 1995 [37] found that lactate in CBG was predictive of neonatal outcome. Tuuli et al, 2014, [38] found that lactate was a more discriminatory measure of neonatal morbidity at term than arterial pH and calculated a threshold 3,90mmol/L (sensitivity of 83,9% and specificity 74.1%) compared to arterial pH 7.25 (sensitivity 0f 75% and specificity of 70.6%) in predicting neonatal morbidity.

Knutsen et al, 2015 [41] dealt with the question of whether the use of the BD and lactate added any more information over arterial CBG pH. They concluded that in acidemic term infants the metabolic component of cord gases as measured by the arterial BD does not add prognostic information over and above arterial pH level for neonatal outcomes.

WHO recommends delayed cord clamping in vigorous neonates, delayed cord clamping has been defined by various institutions as a delay of 30 – 60 seconds before cord clamping or till cord pulsations stop. Delayed cord clamping in term neonates results in increased Hb and iron stores, but also increased NNJ, and therefore is not recommended if facilities to monitor and treat NNJ are not available. In preterm neonates delayed cord clamping is associated with improved transitional circulation, RBC volume and decreased need for blood transfusion, reduced NEC and IVH, it is also thought to result in increased transfer of Immunoglobulin and stem cells to the neonate. In terms of maternal safety, it is not associated with increased PPH. [42]

Delayed cord clamping results in decreased arterial cord blood pH, increased Pco_2, Po_2, and BD. [27, 43] This is due to the phenomenon of hidden acidosis, the magnitude of changes in the cord blood gas parameters are not significant in vigorous new-borns, [44] however might cause abnormal results in borderline cases, with medico legal implications.

Immediate cord clamping is advised for; to facilitate neonatal resuscitation, if the placental circulation is not intact, maternal haemorrhage or unstable maternal circulation. Milking of the umbilical cord has shown similar benefits to delayed cord clamping and is an alternative in preterm births. [26, 45]

HIE as a cause of cerebral palsy is well established. However, it is important to exclude other causes of neonatal encephalopathy like prematurity, intrauterine fetal infections,

chorioamnionitis, congenital cerebral abnormalities, placental pathology causing chronic hypoxia, jaundice and metabolic disorders. Investigations therefore should include microbiology and cultures, serology, placental pathology (histology and culture), imaging cranial ultrasound and MRI of the brain, and where appropriate available chromosomal analysis. [12] Salafia et al found a significant relationship between placental histological features and CBG parameters in preterm neonates. [46] Placental histology can also reveal lesions associated with adverse neurological outcomes more so in chronic than in acute insults. [47, 48]

Limitations of this study was the small sample size. There were only two pathological arterial cord blood gases with a pH of less than 7.0 and one of them declined to be included in the study. We were therefore unable to look at the important short term outcome which is the diagnosis of HIE. The study did not look at cerebral palsy as an outcome and medical litigation arising thereof. These outcomes and other important non-cerebral palsy neurological adverse outcomes could require larger population based studies with long term follow up. Not all patients had complete records.

6 CONCLUSIONS

Cord blood gas analysis is accurate and more objective than Apgar score in determining the neonate's condition at birth, and can be useful for management of the neonate and for medico legal purposes. However, the low rate of CBG uptake in this study suggests that routine CBG is not feasible in our setting. Secondly routine use of CBG is associated with quality issues with material impact on the utility of routine CBG. This is possibly due to high patient workload. A policy needs to be developed in the department that will guide the development of guidelines on CBG and their implementation. Training in how to sample, analyse and interpret the cord blood gases should help in implementation. Due to the heavy workload, I could advocate for selective sampling and analysis in high risk deliveries or where the neonate has low Apgar scores, a practical way could be to set aside a clamped section of cord and then sample and analyse within 30 minutes of delivery should the criteria be met.

Larger studies, systematic reviews and meta-analyses on the link of HIE and CP and/or other neurological outcomes are needed. The role of placental histology in HIE and cerebral palsy needs to be studied further. Cost-effectiveness studies in our setting (tertiary academic) and other settings, including community health clinics are needed so as to determine cord blood gas analysis is feasible and whether routine or selective sampling and analysis is appropriate.

7 REFERENCES

1. Schifrin BS, Longo LD. William John Little and cerebral palsy. A reappraisal. Eur J Obstet Gynecol Biol. 2000;90(20):139-144.
2. Osler W. Cerebral Palsies of Children. 1987. Wiley and Sons Inc. ISBN:978-0-901260-38-3
3. Kaman LA, Smith BP, Shift JS. Cerebral Palsy. The Lancet. 2004;363:1619-1631.
4. Blair E, Stanley FJ. Intrapartum asphyxia a rare cause of cerebral palsy. J Paeditr. 1988;112:515-519.
5. Pschirrer RE, Yeomans ER. Does asphyxia cause cerebral palsy. Semin Perinatol 2000;24(3):215-220.
6. Rhoda NR, Velaphi S, Gebhardt GS, Kauchali S, Barron P. Reducing neonatal deaths in South Africa: Progress and challenges. S Afr Med J 2018;108 (3Suppl 1):S9-S16. DOI:10.7196/SAMJ.2018.v10813.12804. Accessed 30/12/2020.
7. Cooper P. Cerebral palsy in SA: Perinatal factors and later neurological handicap in infants born at or near term. S Afr J Child Health 2015;9(4):107. DOI:0.7196/SAJCH.2015.v914.1064. Accessed 30/12/2020.
8. Cowan F. Origin and timing of brain lesions in term infants with neonatal encephalopathy. Lancet 2003;361:736-742.
9. Shevell MI. The "Bermuda Triangle" of Neonatal Neurology: Cerebral Palsy, Neonatal Encephalopathy, and Intrapartum Asphyxia. Sem Pediatr Neurol 2004;11(1):24-30.
10. Sarnat HB, Sarnat MS. Neonatal Encephalopathy Following Fetal Distress. A Clinical and Electroencephalographic Study. Arch Neurol. 1976;33(10):696-705. doi:10.1001/archneur.1976.00500100030012. Accessed 31/12/2020
11. Blumenthal I. Cerebral Palsy – Medicolegal aspects. J R Soc Med 2001;94:624-627.
12. Hankins GDV, Speer M. Defining the pathogenesis and pathophysiology of neonatal encephalopathy and cerebral palsy. Obstet Gynaecol 2003;102:628-636.
13. Johnson SL, Blair E, Stanley FJ. Obstetric malpractice litigation and cerebral palsy in term infants. J Foren Legal Med 2011;18:97-100
14. Kumar S, Paterson-Brown S. Obstetric aspects of hypoxic ischaemic encephalopathy. Earl Hum Dev 2010;86:339-344. http://doi:10.1016/j.earlhumdev.2010.05.009.
15. Herrera CA, Silver RM. Perinatal asphyxia from obstetric standpoint. Diagnosis and interventions. Clin Perinatol 2016;43:423-438.

16. Saling E. Fetal blood analysis during labour. Am J Obstet Gynecol 2005;5:896-899. Online at http://doi:10.1016/j.ajog.2005.05.065.
17. Thorp JA, Dildy GA, Yeomans ER, Meyer B, Parisi V. Umbilical cord blood gas analysis at delivery. Am J Obstet Gynecol 1996;175:517-522.
18. Blickstein I, Green T. Umbilical blood gases. Clin Perinatol. 2007;34:451-459.
19. Ross MG. How and when umbilical cord gas analysis can justify your obstetric management. OBG management [Obstet Gynecol Man] 2017;29(3):39-46.
20. S. Bown. Counting the costs of litigation. Casebook 2012;20(1):9-11.
21. Malherbe J. Counting the cost: The consequences of increased medical malpractice litigation in South Africa. S Afr Med J 2013;103(2):83-84.
22. Masweneg K. Medical lawsuits posing financial risk to healthcare in Gauteng: Ramokgopa. Available at http://www.timeslive.co.za>south-africa Accessed 17/10/2017.
23. 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;105:298-303.
24. Padayachee N, Ballot DE. Outcomes of neonates with perinatal asphyxia at a tertiary academic hospital in Johannesburg South Africa. S Afr J CH 2013;7(3):89-94. DOI:10.7196/SAJCH.574.
25. Bhorat I, Pistorious L, Soma-Pillay P, Smuts I. The case for the routine use of Umbilical Cord pH in all deliveries. O & G Forum 2017;27:33 – 35.
26. Geerts L, Soma-Pillay P, Pistorius L, Mashiloane C, Van Waart J, Bhorat I. The case for universal cord blood gas analysis. SASOG: BetterObs^{TM} Protocols and Guidelines. September 2020.
27. Amstrong L, Stenson BJ. Use of umbilical cord blood gas analysis in the assessment of the newborn. Arch Dis Child Neonatal Ed 2007;92:F430-F434. doi:10.1136/adc.2006.099846.
28. Helwig JT, Parer JT, Kilpatrick SJ, Laros RK. Umbilical cord blood acid base state: what is normal? Am J Obstet Gynecol 1996;174:1807-14.
29. Van den Berg PP, Nelen WLDM, Jongsma HW, Nijland R, Kollé LAA, Nijhuis JG et al. Neonatal complications in newborns with umbilical artery pH < 7.00. Am J Obstet Gynecol 1996;175:1152-1157.

30. Shedev HM, Stamilio DM, Macones GA, Graham E, Morgan MA. Predictive factors for neonatal morbidity in neonates with umbilical arterial cord pH less than 7.00. Am J Obstet Gynecol 1997;177:1030-1034.
31. Low JA, Lindsay BG, Derrick JE. Threshold of metabolic acidosis associated with newborn complications. Am J Obstet Gynecol 1997;177:1391-1394.
32. Cantu J, Szychowski JM, Li X, Biggio J, Edwards RK, Andrews W et al. Predicting fetal acidemia using umbilical venous blood gas parameters. Obstet Gynecol 2014;124:926-932,
33. Gopinath R, Jacobs AS, Gangadharan A, Aslesh OP. Correlation between umbilical venous blood gas at birth and comorbidities in preterm babies – A cohort study. Indian J Child Health 2017;4:231-234.
34. Swanson K, Whelan AR, Grobman WA, Miller ES. Can venous cord gas values predict fetal acidemia? Am J Obstet Gynecol 2017;217:364 e1-5.
35. Wiberg N, Källén K, Olofsson P. Base deficit estimation in umbilical blood is influenced by gestational age, choice of fetal fluid compartment and algorithm for calculation. Am J Obstet Gynecol 2006;195:1651-1656.
36. Westgate J, Greene KR. Umbilical cord blood gas analysis at delivery: a time for quality data. BJOG 1994;101:1054-1063.
37. Westgren M, Divon M, Horal M, Ingermarsson I, Kublicks M, Shimojo N et al. Routine measurement of umbilical artery lactate level in the prediction of perinatal outcome. Am J Obstet Gynecol 1995;173:1416-22.
38. Tuuli MG, Stout MJ, Shanks A, Odibo AO, Macones GA, Cahill AG. Umbilical cord arterial lactate compared with pH for predicting neonatal morbidity at term. Obstet Gynecol 2014;124:756-61.
39. Allanson ER, Grobicki K, Pattinson RC, Dickinson JE. Attitudes towards the implementation of universal umbilical artery lactate analysis in a South African district hospital. BMC Pregnancy and Childbirth 2016;16:166. DOI 10.1186/s12884-016-0968-y published online 18/07/2016.
40. American College of Obstetricians and Gynecologists committee on obstetric practice. Umbilical cord blood gas and acid-base analysis. ACOG committee opinion no.:348. Obstet Gynecol 2006; 108:1319-22.
41. Sabol BA, Caughey AB. Acidemia in neonates with 5-minute Apgar score of 7 or greater – What are the outcomes. Am J Obstet Gynecol 2016;215:486.e1-6. Accessed 04/07/2017.

42. Knutzen L, Svirko E, Phil D, Impey L. The significance of base deficit in acidemic term neonates. Am J Obstet Gynecol 2015;213:373.e1-7.
43. Delayed cord clamping after birth. Committee opinion no. 648. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;129: e5-10.
44. Wiberg N, Källén K, Olofsson P. Delayed Umbilical cord clamping at birth has effects on arterial and venous blood gases and lactate concentrations. BJOG 2008;115:697-703.
45. Mokarami P, Wiberg N, Olofsson P. Hidden acidosis: an explanation of acid–base and lactate changes occurring in umbilical cord blood after delayed sampling. BJOG 2013;120:996–1002.
46. Shirk SK, Manolis SA, Lambers DS, Smith KL. Delayed clamping vs milking of umbilical cord in preterm infants: a randomised controlled trial. Am J Obstet Gynecol 2019;220(5) P485 e1-e8. Accessed 05/01/2021
47. Salafia CM, Minior VK, Lopez-Zeno JA, Whittington SS, Pezzullo JC, Vintzileos AM. Relationship between placental histologic features and umbilical cord blood gases in preterm gestations. Am J Obstet Gynecol 1995;173:1058-64.
48. Baergen RN. The Placenta as witness. Clin Perinatol 2007;34.393-407.
49. Stanek J. Hypoxic patterns of injury. A review. Arch Pathol Lab Med 2013;137:706-720. Doi:10.5858/arpa.2011-0645-RA. Accessed 05/01/2021.
50. Ayres-de-Compos D, Spong CY, Chandarahan E, for the FIGO intrapartum fetal monitoring consensus panel. FIGO consensus guidelines on intrapartum fetal monitoring. Carditocography 2015. Accessed online at http://www.jsog.org.jp/international/pdf/CTG.pdf accessed 30/10/2017

8 APPENDICES

8.1 APPENDIX 1: PATIENT INFORMATION AND CONSENT FORM

Patient Information Sheet

Title of the study: Umbilical Cord Blood Gas in a Tertiary Public Hospital in Johannesburg.

Study location: Charlotte Maxeke Johannesburg Academic Hospital. Departments of Obstetrics & Gynaecology, and Paediatrics and Child Health, the University of the Witwatersrand.

Principal investigator: Dr RB Nyakoe

Supervisors: Dr HL Chauke, and Professor D Ballot

Study related telephone numbers:

(011)4883179, Dr RB Nyakoe, principal investigator, Department of Obstetrics & Gynaecology

(011)4884385, Dr HL Chauke, Head of Department/ supervisor, Obstetrics & Gynaecology

Telephone (after hours): 0825601340, Dr RB Nyakoe

Dear Madam

My name is Dr Robert Nyakoe, I am a specialist doctor and I am also training further in Maternal and Fetal Medicine. You are being invited to take part in a study that is being done here at Charlotte Maxeke Johannesburg Academic Hospital. The study will try to analyse whether introduction of routine sampling of blood from the baby's umbilical cord immediately after the baby is born and analysing the levels of oxygen, carbon dioxide and acid will assist us to understand the condition of the baby at birth and whether this information could be useful in making decisions on treatment of the babies after birth. I am undertaking this project as part of my training.

What is being tested?

After the baby is born a small section (around 10cm in length) of the umbilical cord will be clamped and kept aside. Once you and the baby are stable and safe, the doctor will take two blood sample from the isolated cord, one from the artery and another from the vein. These samples will be analysed for levels of oxygen, carbon dioxide and acid. This will be done using a blood gas analyser.

What is the purpose of these study and why was I chosen?

The study wants to see whether analysing the cord blood gases of the baby immediately at birth will give us more information about the baby's condition and whether this information would be helpful in the treatment of the new born baby.

What will happen to me and my baby if I take part in the study?

By taking part in this study you will not experience any uncomfortable or painful procedures. A sample of your babies cord blood will be obtained as explained above and analysed for the oxygen, carbon dioxide and acids. Your medical records will also be analysed for your medical and personal information.

What are the risks and disadvantages of taking part?

There are no anticipated risks or disadvantages if you decide to take part in this study, the standard of care that you and your baby will receive will be the same as all the other patients in the ward.

What are the possible benefits?

There will be no monetary or material compensation e.g. money or food for your participation in the study. There will be no extra cost to you for participation in the study. If there is abnormality in the cord blood gas the paediatrician (the doctor who takes care of babies) will be informed immediately and will assess your baby.

Do I have to take part?

Your participation in this study is voluntary. If you do not wish to take part in this study your treatment will not be affected in any way, you and your baby will still receive the appropriate care that you are entitled to. If you decide to take part in the study you can still change your mind at any time and this will not affect your treatment in any way.

On taking part in this study will my information be kept confidential?

Your personal and medical information will be kept confidential at all times, you will be allocated a study number and your identity will be known only to me and my supervisor if necessary. Your information might be made available to university representatives who might want to review the validity of the research findings.

What will happen to the results of the study?

The results of the study will be disseminated to other medical professional through publication in medical journals, and presentation in academic meetings and medical conferences.

Who has reviewed the study?

The study has been reviewed and approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, the study will be conducted in accordance to the South African Good Clinical Practice guidelines.

Whom do I call if I have questions or concerns about the study?

You can contact the principal investigator, Dr Robert Nyakoe at any time in connection with the study, he can be contacted at 0825601340.

You can also contact Dr. Chauke the supervisor and Head of Department of Obstetrics & Gynaecology during working hours (08:00 to 16:00) at (011)4884385 or (011)4883179.

You can also contact the Human Research Ethics Committee (Medical) of the University of the Witwatersrand on (011) 717-1234/2656/2700, if you wish to get more details on research conducted at this University.

Informed consent form

Title of the study: Umbilical Cord Blood Gas in a Tertiary Public Hospital in Johannesburg.

Study location: Charlotte Maxeke Johannesburg Academic Hospital. Departments of Obstetrics & Gynaecology, and Paediatrics and Child Health, the University of the Witwatersrand.

Principal investigator: Dr RB Nyakoe

Supervisors: Dr HL Chauke, and Professor D Ballot

I confirm that I have read and understood the information sheet about the above study and have been had the opportunity to ask questions. Alternatively the contents of the information sheet have been explained to me and I have been given an opportunity to ask questions about the study.

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without affecting my medical care or legal rights.

I understand that my medical records might be looked at by the supervisors of this study or by representative from the University of the Witwatersrand as might be necessary to conduct the research. I give permission for these individual to access my medical records.

I agree to participate in the study named above.

Patient name and surname: _____

Patient signature: _____

Date: _____ (DD/MM/YYYY)

Name of Doctor/Nurse: _____

Doctor/Nurse signature: _____

Date: _____ (DD/MM/YYYY)

8.2 APPENDIX 2, DATA COLLECTION SHEET

1; Demographics

Study number:

Age: Parity: Gravidity: Race:

Weight (Kg): Height (m): BMI (Kg/m^2):

2: Antenatal

Booking status: 01: [Yes] 00: [No] 99: [Unknown]

HIV: 00: [Negative]

01: [Positive] Viral Load: CD4 count:

99: [Unknown]

RPR: 01: [Positive] 00: [Negative] 99: [Unknown]

Hb (g/dL):

Rhesus: 01:[Positive] 00:[Negative] 99: [Unknown]

Previous Obstetric History

Year	Gestation	Mode of delivery	Gender	Birth weight grams	Outcome	complications

Medical conditions:

01. [Hypertension]
02. [Diabetes Mellitus]
03. [Cardiac]
04. [Other Medical condition]: Specify:

Medications specify:

3: Antenatal Obstetric complications:

00. None
01. Pregnancy Induced Hypertension
02. Preeclampsia
03. Gestational Diabetes
04. Ante-Partum Haemorrhage: [Abruptio] [Placenta Praevia] [Unknown]
05. IUGR
06. PROM
07. Premature labour
08. Postdates
09. Induction of labour [Misoprostol] [Prostaglandins] [Mechanical]
10. Other Specify:

4: Intrapartum

CTG: 01: [Normal] 02: [Suspicious] 03: [Pathological]

00: [Not interpreted] 99: [CTG not available/not done]

Rupture of Membranes; Duration (HH/MINS) [Intact] [Unknown]

Latent phase of labour

Start: Date: Time:

End: Date Time: Duration: _____ Hrs _____Mins

Active Phase of Labour

Start: Date: Time:

End: Date Time: Duration: _____ Hrs _____Mins

Second stage of Labour

Start: Date: Time:

End: Date Time: Duration: _____ Hrs _____Mins

Third Stage of Labour

Start: Date: Time:

End: Date Time: Duration: _____ Hrs _____Mins

Intrapartum Complications

00. None
01. Prolonged latent phase of labour
02. Prolonged active phase of labour partogram to the right of the alert line
03. Oxytocin augmentation of labour
04. MSL: [Thin] [Thick] [Unknown]
05. APH
06. Cord prolapse
07. Eclampsia
08. Ruptured of uterus or suspected rupture
09. Pyrexia >38^{o}C
10. Other Specify

7: Mode of Delivery: Date: Time: Gestation:

01: [Normal Vaginal Delivery]

02: [Assisted Vaginal Delivery]: [Vacuum] [Forceps]

Indication:

03: [Caesarean Section]: [Emergency Caesarean section] [Elective Caesarean section]

Indication:

8: Neonatal Outcome

APGAR:

Birth Weight: Sex: Placenta weight:

Retro-placental clot: 01: [Yes] 00: [No] 99: [Unknown]

Three vessel cord: [01: Yes] 00: [No] 99: [Unknown]

Neonatal intervention:

00. None
01. Oxygen

02. NICU admission
03. TU admission
04. Ventilation
05. CPAP
06. Head cooling
07. Other specify

Complications:

00. Nil
01. Respiratory Distress Syndrome
02. Transient Tachypnea
03. Neonatal Jaundice
04. Neonatal Sepsis
05. Hypoglycaemia
06. Intraventricular Haemorrhage
07. Necrotising Enterocolitis
08. Other specify

10: Umbilical cord blood gas results

Sampling time: Analysis time:

Sample	pH	PO_2	PCO_2	HCO_3	Lactate	Base Excess	Hct
Venous							
Arterial							

Interpretation: (tick as appropriate)

Venous	Acidosis:	Respiratory	Metabolic	Mixed	Not interpreted
Arterial	Alkalosis:	Respiratory	Metabolic	Mixed	Not interpreted

If any component of Umbilical Cord Blood Gas was not done give reason:

Neonatal outcome:

[Discharge to Mom] [Oxygen] [Intubated] [TU] [NICU] [ENND]

11: Maternal outcome

00. No complications
01. PPH
02. Blood and blood products
03. Chorioamnionitis
04. High Care Admission
05. ICU admission
06. Laparotomy
07. Hysterectomy
08. Maternal death
09. Other specify

8.4 APPENDIX 3, BLOOD GAS COLLECTION TOOL

Name: *OR PATIENT STICKER* Hospital number:

Age: Parity: Gravidity:

CTG: [Normal] [Suspicious] [Pathological]

[Not interpreted] [CTG not available/not done]

Delivery: Date: Time:

[Normal Vaginal Delivery]

[Assisted Vaginal Delivery]: [Vacuum] [Forceps]

Indication:

[Caesarean Section]: [Emergency Caesarean section] [Elective Caesarean section]

Indication:

APGAR:

Birth Weight: Sex:

Placenta weight: Retro-placental clot: [[Yes] [No] [Unknown]

Three vessel cord: [Yes] [No] [Unknown]

Umbilical cord blood gas results

Sampling time: Analysis time:

sample	pH	PO_2	PCO_2	HCO_3	Lactate	Base Excess
Venous						
Arterial						

Interpretation: (tick as appropriate)

Venous	Acidosis:	Respiratory	Metabolic	Mixed	Not interpreted
Arterial	Alkalosis:	Respiratory	Metabolic	Mixed	Not interpreted

If any component of Umbilical Cord Blood Gas was not done give reason:

Neonatal outcome:

[Discharge to Mom] [Oxygen] [Intubated] [TU] [NICU] [ENND]

8.5 APPENDIX 4: ETHICS CLEARANCE CERTIFICATE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Robert Nyakoe et al

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M180360

NAME: (Principal Investigator)	Dr Robert Nyakoe et al
DEPARTMENT:	Obstetrics and Gynaecology Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	Umbilical cord blood gas analysis in a tertiary public hospital in Johannesburg
DATE CONSIDERED:	06/04/2018
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Lawrence Chauke
APPROVED BY:	Prof C Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	02/07/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 301, Third floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in March and will therefore be due in the month of March each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

8.6 APPENDIX 5: CMJAH CEO PERMISSION

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

Enquiries:
Ms. N. Mzila
Office of the Clinical Director
Email:Nolwazi.Mzila@gauteng.gov.za
Tell: (011): 488-4812
16 March 2018

Dear Dr. R. Nyakoe

STUDY TITTLE: Umbilical Cord Blood Gas in a Tertiary Public Hospital in Johannesburg.

Permission to conduct the above mentioned study is provisional approved. Your study can only commence once Ethics approval is obtained. Please forward a copy of your Ethics Clearance Certificate as soon as the study is approved by the Ethics Committee for the CEO's office to give you the final approval to conduct the study.

Supported / not supported

pp
Dr. M.I. Mofokeng
Clinical Director
DATE: 19/03/2018

Approved / not approved

Ms. G. Bogoshi
Chief Executive Officer
DATE: 20.03.2018

8.7 APPENDIX 6: CTG CLASSIFICATION CRITERIA[49]

	Normal	Suspicious	Pathological
Baseline	110-160 bpm	Lacking at least one characteristic of normality but with no pathological features	<100
Variability	5-25 bpm		Reduced variability >50 mins Increased > 30 mins Sinusoidal pattern >30 mins
Decelerations	No repetitive decelerations		Repeated late or prolonged decelerations during > 30 mins or 20 mins if reduced variability, or one prolonged deceleration with more than 5 mins
interpretation	Fetus with no hypoxia/acidosis	Fetus with low probability of hypoxia/acidosis	Fetus with high probability of having hypoxia/acidosis
Clinical management	No intervention necessary to improve fetal oxygenation state	Action to reverse reversible causes if identified, close monitoring or additional method to evaluate fetal oxygenation	Immediate action to correct reversible causes, additional methods to evaluate fetal oxygenation, or if this is not possible to expedite delivery, in acute cases (cord prolapse, uterine rupture, abruptio placenta) immediate delivery should be accomplished

Table of CTG classification criteria, interpretation and recommended management. The presence of accelerations denotes a fetus that does not have hypoxia/acidosis, but their absence during labour is of uncertain significance. Decelerations are repetitive when associated with more than 50% of uterine contractions.

[1] Schifrin BS, Longo LD. William John Little and cerebral palsy. A reappraisal. Eur J Obstet Gynecol Biol. 2000;90(20):139-144.
[2] Osler W. Cerebral Palsies of Children. 1987. Wiley and Sons Inc. ISBN:978-0-901260-38-3
[3] Kaman LA, Smith BP, Shift JS. Cerebral Palsy. The Lancet. 2004;363:1619-1631.
[4] Blair E, Stanley FJ. Intrapartum asphyxia a rare cause of cerebral palsy. J Paeditr. 1988;112:515-519.
[5] Pschirrer RE, Yeomans ER. Does asphyxia cause cerebral palsy. Semin Perinatol 2000;24(3):215-220.
[6] Rhoda NR, Velaphi S, Gebhardt GS, Kauchali S, Barron P. Reducing neonatal deaths in South Africa: Progress and challenges. S Afr Med J 2018;108 (3Suppl 1):S9-S16. DOI:10.7196/SAMJ.2018.v10813.12804. Accessed 30/12/2020.
[7] Cooper P. Cerebral palsy in SA: Perinatal factors and later neurological handicap in infants born at or near term. S Afr J Child Health 2015;9(4):107. DOI:0.7196/SAJCH.2015.v914.1064. Accessed 30/12/2020.
[8] Cowan F. Origin and timing of brain lesions in term infants with neonatal encephalopathy. Lancet 2003;361:736-742.
[9] Shevell MI , The "Bermuda Triangle" of Neonatal Neurology: Cerebral Palsy, Neonatal Encephalopathy, and Intrapartum Asphyxia. Sem Pediatr Neurol 2004;11(1):24-30.
[10] Sarnat HB, Sarnat MS. Neonatal Encephalopathy Following Fetal Distress. A Clinical and Electroencephalographic Study. *Arch Neurol.* 1976;33(10):696-705. doi:10.1001/archneur.1976.00500100030012. Accessed 31/12/2020
[11] Blumenthal I. Cerebral Palsy – Medicolegal aspects. J R Soc Med 2001;94:624-627.
[12] Hankins GDV, Speer M. Defining the pathogenesis and pathophysiology of neonatal encephalopathy and cerebral palsy. Obstet Gynaecol 2003;102:628-636.
[13] Johnson SL, Blair E, Stanley FJ. Obstetric malpractice litigation and cerebral palsy in term infants. J Foren Legal Med 2011;18:97-100
[14] Kumar S, Paterson-Brown S. Obstetric aspects of hypoxic ischaemic encephalopathy. Earl Hum Dev 2010;86:339-344. http://doi:10.1016/j.earlhumdev.2010.05.009.
[15] Herrera CA, Silver RM. Perinatal asphyxia from obstetric standpoint. Diagnosis and interventions. Clin Perinatol 2016;43:423-438.
[16] Saling E. Fetal blood analysis during labour. Am J Obstet Gynecol 2005;5:896-899. Online at http://doi:10.1016/j.ajog.2005.05.065.
[17] Thorp JA, Dildy GA, Yeomans ER. Umbilical cord blood gas analysis at delivery. Am J Obstet Gynecol 1996;175:517-522.
[18] Blickstein I, Green T. Umbilical blood gases. Clin Perinatol. 2007;34:451-459.
[19]Ross MG. How and when umbilical cord gas analysis can justify your obstetric management. OBG management [Obstet Gynecol Man] 2017;29(3):39-46.
[20] S. Bown. Counting the costs of litigation. Casebook 2012;20(1):9-11.
[21] Malherbe J. Counting the cost: The consequences of increased medical malpractice litigation in South Africa. S Afr Med J 2013;103(2):83-84.
[22] Masweneg K. Medical lawsuits posing financial risk to healthcare in Gauteng: Ramokgopa. Available at http://www.timeslive.co.za>south-africa Accessed 17/10/2017.
[23] 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;105:298-303.
[24] Padayachee N, Ballot DE. Outcomes of neonates with perinatal asphyxia at a tertiary academic hospital in Johannesburg South Africa. S Afr J CH 2013;7(3):89-94. DOI:10.7196/SAJCH.574.
[25] Bhorat I, Pistorious L, Soma-Pillay P, Smuts I. The case for the routine use of Umbilical Cord pH in all deliveries. O & G Forum 2017;27:33 – 35.
[26] Geerts L, Soma-Pillay P, Pistorius L, Mashiloane C, Van Waart J, Bhorat I. The case for universal cord blood gas analysis. SASOG: BetterObs™ Protocols and Guidelines. September 2020.
[27] Amstrong L, Stenson BJ. Use of umbilical cord blood gas analysis in the assessment of the newborn. Arch Dis Child Neonatal Ed 2007;92:F430-F434. doi:10.1136/adc.2006.099846.

[28] Helwig JT, Parer JT, Kilpatrick SJ et al. Umbilical cord blood acid base state: what is normal? Am J Obstet Gynecol 1996;174:1807-14.
[29] Van den Berg PP, Willianne PP, Nelen MD et al. Neonatal complications in newborns with umbilical artery pH < 7.00. Am J Obstet Gynecol 1996;175:1152-1157.

[30] Shedev HM, Stamilio DM, Macones GA, Graham E, Morgan MA. Predictive factors for neonatal morbidity in neonates with umbilical arterial cord pH less than 7.00. Am J Obstet Gynecol 1997;177:1030-1034.
[31] Low JA, Lindsay BG, Derrick JE. Threshold of metabolic acidosis associated with newborn complications. Am J Obstet Gynecol 1997;177:1391-1394.
[32] Cantu J, Szychowski JM, Li X, Biggio J, Edwards RK, Andrews W et al. Predicting fetal acidemia using umbilical venous blood gas parameters. Obstet Gynecol 2014;124:926-932,
[33] Gopinath R, Jacobs AS, Gangadharan A, Aslesh OP. Correlation between umbilical venous blood gas at birth and comorbidities in preterm babies – A cohort study. Indian J Child Health 2017;4:231-234.
[34] Swanson K, Whelan AR, Grobman WA, Miller ES. Can venous cord gas values predict fetal acidemia? Am J Obstet Gynecol 2017;217:364 e1-5.
[35] Wiberg N, Källén K, Olofsson P. Base deficit estimation in umbilical blood is influenced by gestational age, choice of fetal fluid compartment and algorithm for calculation. Am J Obstet Gynecol 2006;195:1651-1656.
[36] Westgate J, Greene KR. Umbilical cord blood gas analysis at delivery: a time for quality data. BJOG 1994;101:1054-1063.
[37] Westgren M, Divon M, Horal M, Ingermarsson I, Kublicks M, Shimojo N et al. Routine measurement of umbilical artery lactate level in the prediction of perinatal outcome. Am J Obstet Gynecol 1995;173:1416-22.
[38] Tuuli MG, Stout MJ, Shanks A, Odibo AO, Macones GA, Cahill AG. Umbilical cord arterial lactate compared with pH for predicting neonatal morbidity at term. Obstet Gynecol 2014;124:756-61.
[39] Allanson ER, Grobicki K, Pattinson RC, Dickinson JE. Attitudes towards the implementation of universal umbilical artery lactate analysis in a South African district hospital. BMC Pregnancy and Childbirth 2016;16:166. DOI 10.1186/s12884-016-0968-y published online 18/07/2016.
[40] American College of Obstetricians and Gynecologists committee on obstetric practice. Umbilical cord blood gas and acid-base analysis. ACOG committee opinion no.:348. Obstet Gynecol 2006; 108:1319-22.

[41] Knutzen L, Svirko E, Phil D, Impey L. The significance of base deficit in acidemic term neonates. Am J Obstet Gynecol 2015;213:373.e1-7.

[42] Delayed cord clamping after birth. Committee opinion no. 648. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;129: e5-10.

[43] Wiberg N, Kallen K, Olofsson P. Delayed Umbilical cord clamping at birth has effects on arterial and venous blood gases and lactate concentrations. BJOG 2008;115:697-703.
[44] Mokarami P, Wiberg N, Olofsson P. Hidden acidosis: an explanation of acid–base and lactate changes occurring in umbilical cord blood after delayed sampling. BJOG 2013;120:996–1002.
[45] Shirk SK, Manolis SA, Lambers DS, Smith KL. Delayed clamping vs milking of umbilical cord in preterm infants: a randomised controlled trial. Am J Obstet Gynecol 2019;220(5) P485 e1-e8. Accessed 05/01/2021
[46] Salafia CM, Minior VK, Lopez-Zeno JA, Whittington SS, Pezzullo JC, Vintzileos AM. Relationship between placental histologic features and umbilical cord blood gases in preterm gestations. Am J Obstet Gynecol 1995;173:1058-64.
[47] Baergen RN. The Placenta as witness. Clin Perinatol 2007;34.393-407.
[48] Stanek J. Hypoxic patterns of injury. A review. Arch Pathol Lab Med 2013;137:706-720. Doi:10.5858/arpa.2011-0645-RA. Accessed 05/01/2021.
[49] Ayres-de-Compos D, Spong CY, Chandarahan E, for the FIGO intrapartum fetal monitoring consensus panel. FIGO consensus guidelines on intrapartum fetal monitoring. Carditocography 2015. Accessed online at http://www.jsog.org.jp/international/pdf/CTG.pdf accessed 30/10/2017