REVIEW OF FETOCIDES AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL OVER A THREE-YEAR PERIOD.

Research report submitted to the Faculty of

Health Sciences, University of the Witwatersrand,

Johannesburg, in partial fulfilment of the requirements for the degree of Masters in

Medicine (MMed Obstetrics and Gynaecology)

by

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May 2025.

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DECLARATION

I, Gabin Munkita Kiaka, declare that this research is the product of my own work. It has never been presented in this formulation for examination at any of the scientific forums. It is submitted to the University of Witwatersrand in Johannesburg for consideration as part of the requirements for the fulfilment of the degree of Fellowship in Obstetrics and Gynaecology in South Africa.

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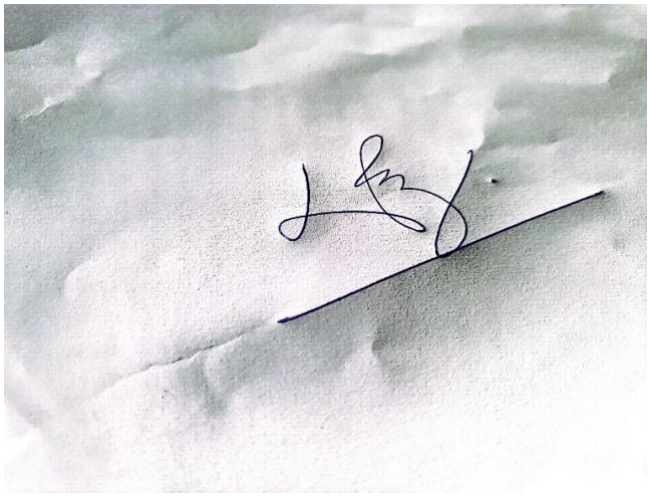

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Dr gabin Munkita Kiaka
Obstetrician and Gynaecologist

DEDICATION

This research report is dedicated to the following important people in my life:

- To my late father, Kiaka Diza Mfumuakanda Magloire, and late mother Ndona Lufiauluisu Lucie, be proud and continue to rest in peace next to the angels.
- To my lovely wife, Sandra Ebali Mbembe, all my children, and my entire family, thank you for being with me through thick and thin. Thank you for all your sacrifices, love, and constant support.

Daddy loves you all.

ACKNOWLEGEMENTS

A special thank you to my supervisor, Dr Jayshree Jeebodh; a phenomenal human being and an incomparable instructor. Thank you for being patient with me and for your guidance and continual assistance in the redaction of this project.

I also wish to express my gratitude to Ms SB Kagodora for the statistical calculations.

To all the members of the Feto Maternal Unit and the Chris Hani Baragwanath Academic Hospital Obstetrics and Gynaecology, I will forever be grateful.

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ABBREVIATIONS AND ACRONYMS

ANC	Antenatal Care
Apr	April.
AVSD	Atrio-Ventricular Septum Defect
CHBAH	Chris Hani Baragwanath Academic Hospital.
CI	Confidence Interval
CNS	Central Nervous System
CVS	Chorionic Villus Sampling
FMU	Feto Maternal Unit
G	Gravidity
G.A	Gestational Age
HIV	Human Immunodeficiency Virus
KCL	Potassium Chloride
NHLS	National Health Laboratory System
OR	Odds ratio
P	Parity
PCR	Polymerase Chain Reaction
QF-PCR	Quantitative fluorescent polymerase chain reaction
RH factor	Rhesus factor
STATA	Statistics and data
TOP	Termination of Pregnancy

ARTICLE

REVIEW OF FETOCIDES AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL OVER A THREE-YEAR PERIOD

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    - **Objectives:** what the study intends to find out
    - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
    - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
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TABLE OF CONTENTS

Abbreviations.

AMA	Advanced Maternal Age.
Apr	April.
CEO	Chief Executive Officer.
CHBAH	Chris Hani Baragwanath Academic Hospital.
CNS	Central Nervous System.
CPAP	Continuous Positive Airway Pressure.
CVS	Chorionic Villus Sampling.
Dec	December
ECHO	Echocardiogram
Feb	February
HICs	High-Income Countries.
HIV	Human Immunodeficiency Virus.
Jan	January
KCL	Potassium Chloride
LMICs	Low-and Middle-Income Countries
Mar	March
NT	Nuchal Translucency
PCR	Polymerase chain Reaction.
POTTER	Pulmonary hypoplasia, Oligohydramnios, twisted skin, Twisted face, Extremity deformities, Renal agenesis.
R.S.A	Republic of South Africa.
RCOG	Royal College of Obstetrics and Gynecology
SARS-2COVID-19	severe acute respiratory syndrome 2 Coronavirus 19.
STATA	Statistics and data
STI	Sexually Transmitted Infection

PROTOCOL OF THE STUDY

Chapter 1.

A. Introduction.

Fetal anomalies may be diagnosed at any stage of pregnancy but most often during a second trimester anatomy scan. The recommended gestational age to perform this type of assessment is between 18 and 23 weeks[1]. The resolution of the ultrasound decreases after 23 weeks which negatively impacts on the diagnosis accuracy in detecting anomalies. Pregnancies are may be dated using the earliest ultrasound scan done by the patient. For the patients who never had an ultrasound before and who are sure of the date of the last normal periods (LNMP), pregnancy may be dated using LNMP.For the patients unsure of the date of their LNMP, Head Circumference (HC) has been used to date the pregnancy.

All patients should ideally be offered a second trimester anatomy scan, but most pregnant women in South Africa will unfortunately, not have such an assessment. Reasons include late booking, no transport money to come to hospital, not referred when initially seen by midwife or doctor at local clinic, flaws in referral routes, inaccurate dating and shortage of expertise in the field of diagnostic sonography with long waiting lists at referral hospitals.

Fetal anomalies can be purely structural, but others might be associated with various chromosomal abnormalities and genetic syndromes. Invasive tests such as amniocentesis and cordocentesis are required for the diagnosis of chromosomal abnormalities. An additional delay in the diagnosis of chromosomal abnormalities is related to laboratory turn-around time. Polymerase chain reaction (PCR) can diagnose trisomy 21, trisomy 13, trisomy 18 and sex chromosomes abnormalities but the average time to await a result is about 2 weeks in state hospitals.

First trimester screening should be performed between 11 and 13 weeks 6 days[1] gestation and should ideally be offered to all pregnant patients. The aim is to diagnose large or lethal structural defects earlier in the pregnancy and confirm chromosomal defects earlier with chorionic villous sampling (CVS). An earlier diagnosis makes the option of termination emotionally easier for the patients and safer from the medical point of view and avoids the need for a fetocide.

Biochemical tests can be combined to the findings of the Nuchal Translucency (NT) scan in order to increase the accuracy of the results[1] but due to the finance constraints these biochemical tests cannot be offered in government hospitals. The utilization of first trimester screening is poor owing once again to lack of knowledge and late booking. Appropriate

counselling of parents is important before performing fetocide. There are many thoughts around fetocide, some validating it and others against it. Cultural, religious, social and ethical considerations do make it difficult to have a uniform view. Already early terminations of pregnancy are controversial in many countries. Late terminations after 20 weeks have opened the door to huge ethical discussions. One of the biggest questions is the ethical status of the fetus as opposed to that of the newborn[2]. There seems to be for the treating obstetrician a conflict between the principle of autonomy of the mother requesting termination and the principle of non -malfeasance[2]. The other ethical consideration is that termination of pregnancy (TOP) for abnormalities attempts to create a discriminatory world without disability.

TOP is governed by the law in South Africa (Choice on termination of pregnancy act 92 of 1996)[3]. In the United Kingdom (U.K) a fetus born alive after TOP for a Fetal abnormality is treated like any other alive child considering published guidance for neonatal practice[4]. The South African TOP act does not stipulate an upper gestational age limit for fetocide, nor does it describe in detail what a severe abnormality is[3]. This does complicate management of non-lethal conditions such Downs Syndrome.

Fetocide avoids a live birth of a severely affected baby, and this can help minimize the stress of parents and healthcare workers having to look after a newborn with almost no chance of survival or with a poor quality of life requiring lifelong care. Despite ethical and cultural challenges, fetocide is a recognized procedure presently in use by many Foeto Maternal units (FMU) worldwide. Protocols differ and may be unique to specific population needs and facility resources. There is, however, limited data on fetocide procedures since only a few countries in the world authorize late termination of pregnancy.

B. Literature Review.

Congenital anomalies may contribute to long term disability while some of them may be‘lethal’ and not compatible with life. It has been reported that an estimated 295 000 newborns die within 28 days of birth every year, worldwide, due to congenital anomalies[4]. This may have significant emotional and socio-economic impact on individuals, families, health-care systems, and societies. Low-income status may be an indirect determinant of congenital anomalies, with a higher frequency among resource-constrained families and countries. It is estimated that about 94% of severe congenital anomalies occur in low-and

middle-income countries (LMICs)[4]. Poor nutrition and increased exposure to infections such as Human Immunodeficiency Virus (HIV) and other Sexually Transmitted Infections (STI)), alcohol and illicit drugs may contribute to the development of congenital anomalies especially among young women. Through the resolutions on birth defects of the 63rd World Health Assembly (2010), member states agreed to promote primary prevention and improve the health of children with congenital anomalies[4]. The frequency of pregnancy termination following prenatal diagnosis of a congenital anomaly is lower in LMICs than High Income Countries (HICs)[4] . This difference is because elective pregnancy termination may be less available in certain LMICs than in HICs.Access to health care or lack of expertise for the diagnosis and procedure does also explain that difference.

Congenital anomalies may be single, multiple, chromosomal or structural and may be caused by genetic factors, environmental factors or a combination of both genetic and environmental factors. Environmental factors include multiple infectious agents such as Rubella, Cytomegalovirus, Syphilis and Toxoplasmosis. Ionizing radiation, hormones, maternal disease like diabetes mellitus and chemical agents such as ethanol are also considered to be environmental factors.

Late maternal age at the time of conception, radiation, chemical agents and viruses are the main determinants of chromosomal abnormalities. Advanced maternal age, defined as being 35 years old or more, is an important risk factor for chromosomal abnormalities including Trisomy 21 known as Down syndrome. The chance of having a child affected by Down Syndrome increases from about 1 in 1 250 for a woman who conceives at age 25, to about 1 in 100 for a woman who conceives at age 40[5]. Errors in meiosis are more likely to happen due to aging process. Besides, Advanced Maternal Age is a known risk factor for diabetes, hypertension and preeclampsia. Mothers with diabetes mellitus, syphilis, rubella and other diseases are at risk of giving birth to babies with congenital anomalies. Some of the antenatally diagnosed fetal defects may not be compatible with life.

Types and prevalence of lethal Fetal abnormality as reported by B. Tosello et al[6].

Central nervous system abnormalities	23.1%
Cardiac abnormalities	17.5%
Other structural birth defects	13.9%
Kidney diseases	12.4%
Trisomy 18	11.2%
Chromosomal abnormalities and genetic disorders	10.8%
Prematurity	6.4%
Hypoplastic left heart syndrome	4.8%

The study listed the following as lethal abnormalities that are not compatible with life:

Lethal Central nervous system abnormalities such as acalvaria, anencephaly, exencephaly, lissencephaly, meningomyelocele, holoprosencephaly.

Lethal cardiac abnormalities such as single ventricle and complex heart disease.

Other structural birth defects including giant omphalocele and syndromic congenital diaphragmatic hernia.

Kidney diseases such as bilateral renal agenesis.

Lethal chromosomal abnormalities and genetic disorders which include trisomy 13, pentalogy of Cantrell, thanatophoric dysplasia and POTTER Syndrome

Prematurity was defined as a gestational age of less than 23 weeks.

It is important to highlight that those babies born with anomalies classified as ‘lethal’may still live for a few hours, few days, few weeks and even a few months before demising. That survival depends on the gestational age at delivery and is increased if some interventions do take place. In settings for example where surgical repair of associated cardiac anomalies of those babies born with ‘lethal’congenital anomalies can be offered, the baby ‘survival has been observed to sometimes approach 1 year of age[4]. The clinician is therefore, advised to be very cautious in the terminology used when counselling pregnant women whose babies suffer major congenital anomalies. Recent research has focused on the diagnosis of fetal abnormalities at an earlier gestation.

While some structural abnormalities will be detected earlier at 11 to 13 weeks and 6 days, the majority will only be identified on an anomaly scan at 18+0 to 23+6 weeks[1]. The overall detection rates for ultrasound screening are 83% for abnormalities incompatible with life,50% for serious abnormalities where survival is possible and 16% for those requiring immediate care after birth[4]. Two-dimensional (2-D) ultrasonography remains the mainstay of non-invasive fetal diagnosis[4]. However new imaging modalities can provide additional information such 3D imaging and Magnetic Resonance Imaging (MRI). These advanced imaging techniques may not be available in most government facilities in South Africa.
The RCOG currently recommends fetocide for terminations over 21 + 6 weeks[4]. The only exception to this rule is when the fetal abnormality itself is so severe as to make early neonatal death inevitable irrespective of the gestational age at delivery[4]. The best example of such a case is a baby with anencephaly.
Statham et al. and Graham et al. have documented for the U.K and Wales differences among fetal medicine specialists concerning abnormalities for which they personally would offer termination even after fetal viability[4]. With respect to decisions about fetocide, Statham et al. reported that the overriding consideration of fetal medicine specialists was staying within the law[4]. However, the study identified specialists who were more flexible about offering fetocide after 21 +6 weeks of gestation where the anomaly was incompatible with survival[4].
Parents must receive sympathetic and supportive counselling before and particularly after the procedure. Decision to terminate a pregnancy especially at an advanced gestational age can be a very traumatic experience for the family and as well for the treating personnel.
Late termination of pregnancy is permitted by the law in South Africa (Act 92 of 1996)[3]. This act states that a termination of pregnancy can be permitted after the 20th week of gestation if by the opinion of the medical practitioner the continuation of pregnancy[3]:

1. Would endanger the woman's life.
2. Would result in a severe malformation of the fetus; or
3. Would pose a risk of injury to the fetus.
4. The medical practitioner must consult another medical practitioner or a registered midwife[3]. Babies born alive should be given the care require considering resources available. Such a decision has to involve a multidisciplinary team, which includes neonatologists, fetal medicine experts, psychologists, psychiatrists and social workers.

At Chris Hani Baragwanath Academic Hospital fetocides are offered for major congenital anomalies diagnosed at and after 24 weeks of gestation. Termination for babies with Downs Syndromes is offered and performed until 24 weeks but if there is a structural abnormality then fetocide is offered up until 28 weeks. Abnormalities with severe disability such as spina bifida or encephaloceles are terminated when the diagnosis is made and the offer of fetocide is accepted by the patient. Sometimes the accurate diagnosis may be difficult and repeat ultrasounds are needed, hence the delay in diagnosis. Further delay can be expected if another specialist opinion is required such as fetal echocardiogram (echo) or in case of a HIV positive patient not on ARVs yet or not suppressed and a confirmatory invasive test cannot be performed, or if the patient wishes to discuss her options with her partner and family.
Viability in SA is not uniform across provinces and medical facilities. At CHBAH viability is around 1000g or 28 weeks gestation owing to our Neonatal Intensive Care Unit (NICU) capabilities. Bara NICU can offer Continuous Positive Airway Pressure (CPAP) from 750g.However, babies born at 24 weeks may survive and suffer a terrible death.
Drugs of choice for fetocides include potassium chloride (KCL), lignocaine and digoxin. Routes of administration include intra-cardiac or the umbilical vein. The choice is dependent on individual preference, access, position of the fetus and gestational age. There is no clear evidence in the literature of the exact dose of each agent that should be administered although a higher dose may be required to ensure a successful procedure, and this may be necessary in fetuses of advanced gestation.
In their study, Statham et al. and Graham et al found that intracardiac potassium chloride is the recommended drug to ensure fetal demise[4]. 2 to 3ml of Kcl 15% is injected into a cardiac ventricle under sonar guidance. A repeat injection may be required if asystole has not occurred after 30 to 60 seconds[4]. Asystole needs to be documented for at least 2min and an ultrasound repeated after 30 to 60 minutes to confirm fetal demise[4]. Intra-amniotic or intrathoracic injection of up to 1mg of digoxin can also induce fetal asystole[4]. Lignocaine1% up to 30mls volume by umbilical venous or intracardiac route can also be used to induce fetal asystole[4]. The practice of fetocide for severe congenital malformations is generally offered to mothers after 24 weeks of gestation. Screening for the major congenital abnormalities should assist in reducing late termination of pregnancies. Fetocide will prevent parents and labour ward staff from facing the agony of neonatal distress and pain.

C. Problem statement and Justification for the study.

The practice of fetocide is not uncommon in the FMU at CHBAH but the data has not been analyzed. International data from developed countries are available but local literature in a typical South African setting on the subject is scanty. The analysis of local data may assist in the understanding of the need to improve screening for major congenital anomalies in the country and to develop regular guidelines on late termination of pregnancy, which considers the unique reasons for late diagnosis of abnormalities.

D. Aims of the study.

The aim of this study is to investigate how many patients with major structural sonographic abnormalities were offered fetocide and the gestational age at which the fetocide was done. We want to establish the interval between the diagnosis and the fetocide procedure. The other aim is to assess the safety of fetocide used on the mother.

E. Objectives of the study.

- To evaluate the indications for fetocide performed at CHBAH during the study period from 01 January 2019 to 31 December 2021.
- To describe the demographics and the number of patients who had fetocide at CHBAH.
- To determine the gestational age when fetocide was performed.
- To assess the techniques of fetocide used to achieve fetal demise at CHBAH during the study period.

Chapter 2.

METHODS

1. Setting.

The FMU at CHBAH. The Unit is staffed with consultants maternal-fetal specialists, fellows in the discipline, Obstetrics and Gynaecology registrars and sonographers. The unit works closely with other high-risk clinics at CHBAH. Patients are referred from twin clinic, poor obstetric history clinic, hematology and HIV clinic, cardiac clinic, diabetic and endocrine clinic. It serves many underprivileged patients of the big township of Soweto. It is a referral center for many clinics around Soweto and for many levels 2 and 3 hospitals in the Gauteng Province. It is also a referral Unit for patients from other provinces including the Northwest Province, Northern Cape and Mpumalanga Province. Patients are also referred from private general practitioners and gynaecologists.

2. Study sample.

All the patients who underwent a fetocide at CHBAH, FMU after 24 weeks of gestation from 01 January 2019 to 31 December 2021.

3. Sample size.

Sample size will be calculated with the assistance of the Statistician; we intend to collect more than 50 patients for this study.

4.Study design.

This is a retrospective cross-sectional study of women offered fetocide for major congenital anomalies at CHBAH FMU.

5.Data collection.

A nursing register is available with daily recordings of all procedures performed in the Unit. Patients will be identified from these registers and their records will be searched for on the viewpoint database in the unit. All the patients will be allocated a study number and data will be entered onto a data collection sheet. Using the names and the hospital number of the patients identified and as well the date when the patient was seen at FMU and the fetocide

procedure performed we will retrieve files of the CHBAH patients from the CHBAH Maternity record department.

6.Data analysis.

Means with Standard Deviations (SD); medians with centiles will be used for our continuous variables such as the patients 'demographics. For our categorical and dichotomous variables, we will make use of frequencies and percentages. This will help to determine the average GA when fetocide was performed The Chi squared test or the Fisher' exact test will also be used in the descriptive analysis of the data collected. This will assist to assess the techniques of fetocide used. The data will be transferred into the STATA program for analysis.

7.Timelines.

	Dec 2021	Jan 2022	Feb 2022	Mar 2022	Apr 2022	May 2022
Protocol development	+					
Protocol submission		+				
correction			+	+		
Ethics application			+	+		
Data collection and analysis				+		
Write up					+	+

8.Permission from the institution.

Permission to conduct this study at FMU CHBAH will be obtained from the CEO of CHBAH and the Head of Department of Obstetrics and Gynaecology.

9.Ethics approval.

Approval for the study will be obtained from the Human Research Ethics Committee of the University of Witwatersrand.

10.Limitations.

Loss of records and incomplete records and as well inadequate notes. Retrieving the files of all the patients selected as some of those patients were referred from various other institutions.

11.Funding.

Any cost for this study will solely be covered by the researcher. The expected cost from conception to printing should vary between R200 and R300 per book. The bill for the statistician who will assist with complex calculations is estimated between R2500 and R3000. R1000 is the estimated additional cost for publication and conference presentation.

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ABSTRACT.

- **Background:** Fetocide is necessary where termination of pregnancy is indicated after 24 weeks. Not many studies have been done particularly in a South African context. It is still regarded as a controversial issue in some countries. An earlier diagnosis allows more time for the counselling of parents and decision-making.

- **Objectives:** To establish the demographics of patients offered fetocides procedures and the indications.
  To determine the gestational age at which the fetocides were performed at the Chris Hani Baragwanath Academic Hospital and the techniques (routes) used.
- **Methods:** Retrospective cross-sectional study of 58 patients who underwent fetocide procedure for severe congenital anomalies at the Chris Hani Baragwanath Academic Hospital Feto maternal Unit. Means with standard deviations (SD) and medians with centiles were used for the continuous variables such as patients' demographics. Frequencies and percentages were used for categorical and dichotomous variables. The chi-square test or Fisher 'exact test were used in the descriptive analysis. The data were transferred into the STATA program for analysis.

- **Results**: Fifty-eight patients underwent fetocide procedure.
  Fifteen percent Potassium chloride was the only agent used. The median age was 30 years (IQR=22-35), the median Body Mass Index (BMI) was 24 kg/m^2, the median Gestational Age (GA) was 29 weeks (IQR=26-32). The umbilical vein route was used in 55% of mothers and the median Potassium Chloride volume used was 20 ml. Central Nervous System anomalies were the leading indication and anencephaly the leading anomaly. A total of 25(66%) fetuses had a normal karyotype result and 13(34%) of the 38 patients who had karyotype had an abnormal karyotype result.

- **Conclusion:** Fetocides are a safe and effective method to induce fetal demise.

Central Nervous System anomalies were the most common with anencephaly the leading one. There was an increasing risk of congenital anomalies with advanced maternal age, particularly above 35 years old. The umbilical vein route was the preferred route used. Further research is needed to explore especially the ethical implications for both the mother and the health care worker.

Keywords: Fetus**;** fetocide; structural congenital anomalies.

INTRODUCTION

The diagnosis of fetal abnormalities has evolved, improved and progressed over the past few decades. The recommended gestational age to perform a detailed anatomy scan is between 18 and 23 weeks 1 day. The resolution of the ultrasound decreases after 23 weeks which negatively impacts on the diagnostic accuracy in detecting anomalies. However, a significant proportion of structural abnormalities may be detected at first trimester screening. An earlier diagnosis allows more time for counselling of parents and decision -making.

One ultrasound scan before 24 weeks' gestation is recommended by World Health Organisation (WHO) for all pregnant women [1]. The average gestational age at booking at local midwifery clinics in Soweto is about 24 weeks [2]. When chromosomal anomalies are suspected, karyotyping can be used. However small anomalies such as deletions or duplications may be missed.
The South African TOP act neither stipulates an upper GA limit for terminating a pregnancy (specifically if maternal life is at risk), nor describes in detail what a severe abnormality is [3].

Opinions may differ when quality of life is an issue and lifelong care is required. There seems to be for the treating obstetrician a conflict between the principle of autonomy of the mother requesting termination of pregnancy and the principle of non-malfeasance. The other ethical consideration is that termination of pregnancy (TOP) for abnormalities attempts to create a discriminatory world without disability. Despite ethical and cultural challenges, fetocide is a recognized procedure presently in use by many FMU worldwide. There is, however, limited data on fetocide procedures as only a few countries in the world authorize late termination of pregnancy.

MATERIALS AND METHODS

1. Setting

The setting of this study was at the FMU at the CHBAH. The Unit is staffed with consultant maternal-fetal specialists, fellows in the discipline, obstetrics and gynaecology registrars and sonographers. The unit works closely with other high-risk clinics at the CHBAH. Patients are referred from the twin clinic, poor obstetric history clinic, haematology and Human Immunodeficiency Virus (HIV) clinic, cardiac clinic, diabetic and endocrine clinic. It serves the underprivileged community of the big township of Soweto. It is a referral centre for many clinics around Soweto and for many levels 2 and 3 hospitals in the Gauteng Province. It is also a referral Unit for patients from other provinces including the North-west Province, as well as the Northern Cape and Mpumalanga Provinces. Patients are also referred from private general practitioners and gynaecologists.

2. Study sample

All the patients who underwent a fetocide procedure at the CHBAH FMU at or after 24 weeks of gestation from 1 January 2019 to 31 December 2021, with one exception.

3. Sample size

A total of 58 patients were recruited for this study.

4. Study design

This was a retrospective cross-sectional study of women who were offered fetocide for severe congenital anomalies at the CHBAH FMU.

5. Data collection

A nursing register is available with daily recordings of all procedures performed in the unit. Patients were identified from these registers and their records searched on the viewpoint database in the unit. All the patients were allocated a study number and a data collection sheet was used.

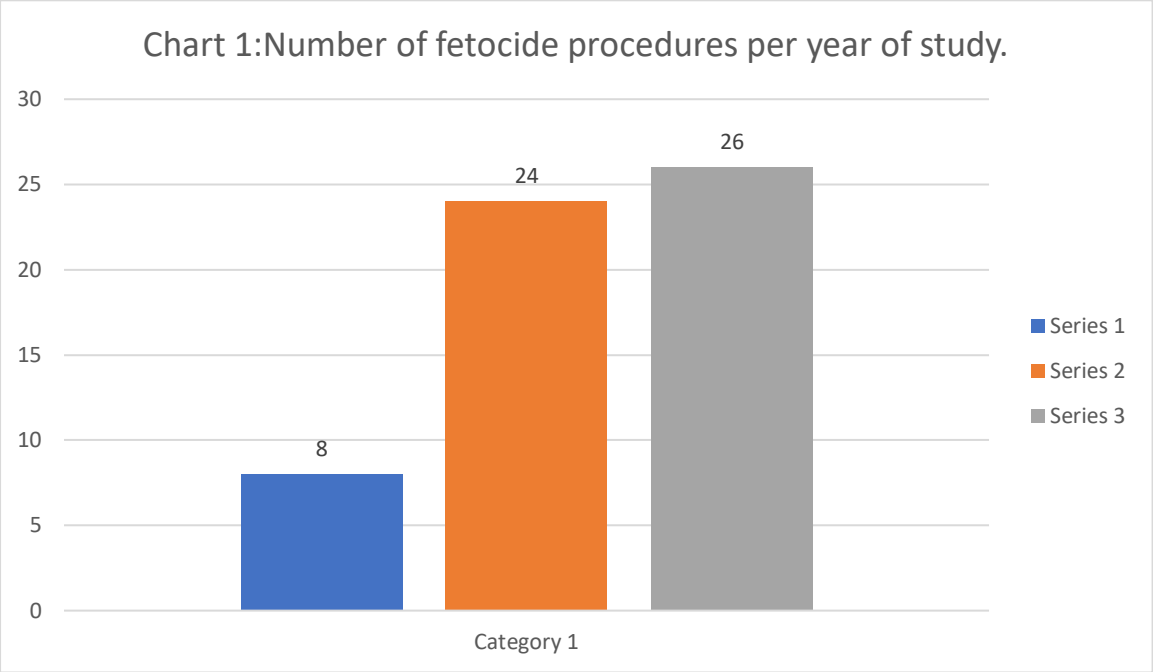
Using the names and the hospital number of the patients identified, as well as the date when the patient was seen at the FMU and the fetocide procedure performed, some files of the CHBAH patients from the CHBAH Maternity Record Department were retrieved.

6. Data analysis

Means with Standard Deviations (SD); medians with centiles were used for the continuous variables such as the patients 'demographics.

For the categorical and dichotomous variables, frequencies and percentages were used. This assisted in determining the average GA when fetocide procedure was performed. The chi-square test or the Fisher 'exact test was used in the descriptive analysis of the data collected. The data were transferred into the STATA program for analysis.

RESULTS



Series 1=procedures done in 2019.

Series 2=procedures done in 2020.

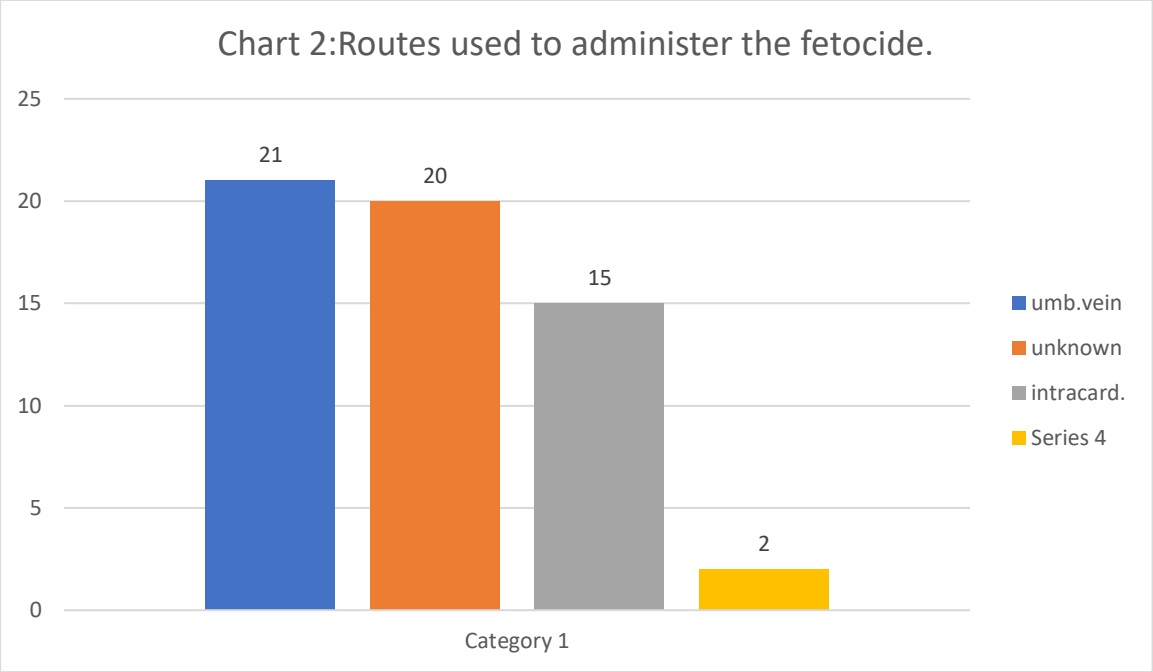
Series 3=procedures done in 2021.

Demographic data.

One patient was 15 years old at the time the fetocide procedure was performed. The indication was severe hydrocephalus. The eldest participant recruited was 44 years old. The indication for a fetocide procedure was severe cardiomegaly with hydrops fetalis. The median age of the women in this study was 30 years old (IQR=22-35). The BMI was available for only 10 of the patients and the median BMI was 24 kg/m^2 (IQR=24-27.3). The median GA was 29 weeks (IQR=26-32).

Table 1: Demographic parameters.

Age (years)	*Frequency N=58 (%)*
<35	**44(76%)**
≥35	**14(24%)**
Gestational age (weeks)	***Frequency N=58 (%)***
24-25	**7 (12%)**
26-30	**32(55%)**
31-35	**14(24%)**
≥36	**5(9%)**
Parity	***Frequency N=58(%)***
P0	**14(24%)**
HIV status	***Frequency N=58 (%)***
HIV positive	**7(12%)**
HIV negative	**17(29%)**
HIV unknown	**34(59%)**
RPR status	***Frequency N=58 (%)***
RPR positive	**0**
RPR negative	**14(24%)**
RPR unknown	**44(76%)**



Series 4=failed intracardiac route and then use of umbilical route.

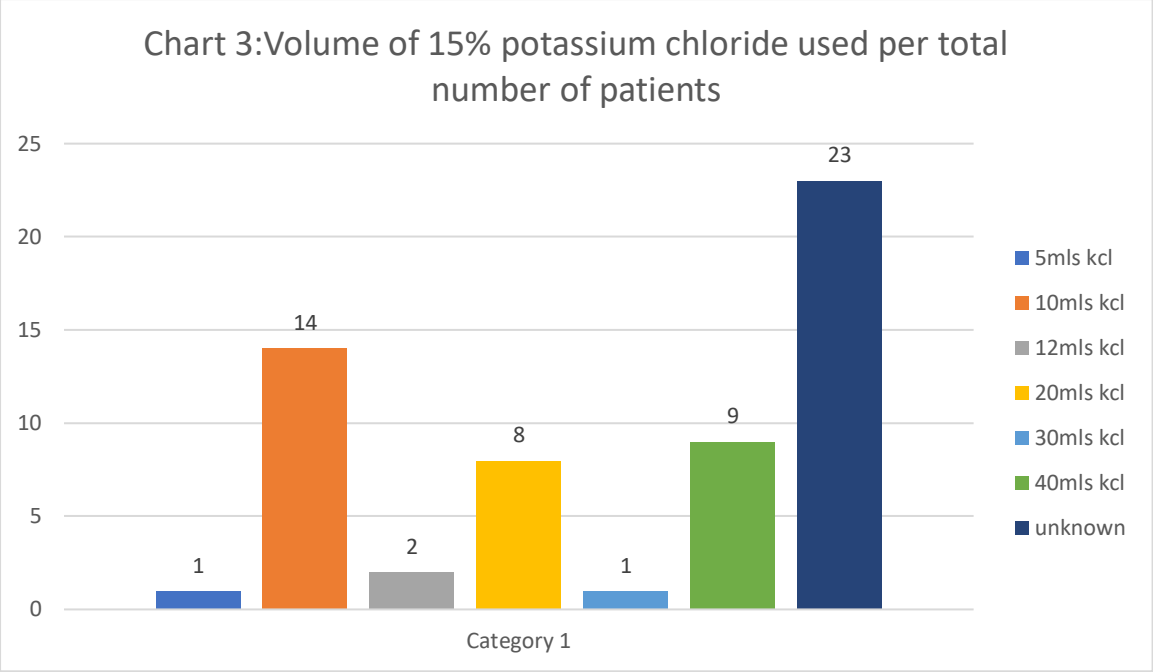
A total of 21(36%) fetocides procedures were performed through the umbilical vein route.

The route was not specified for 20 (34%) patients.

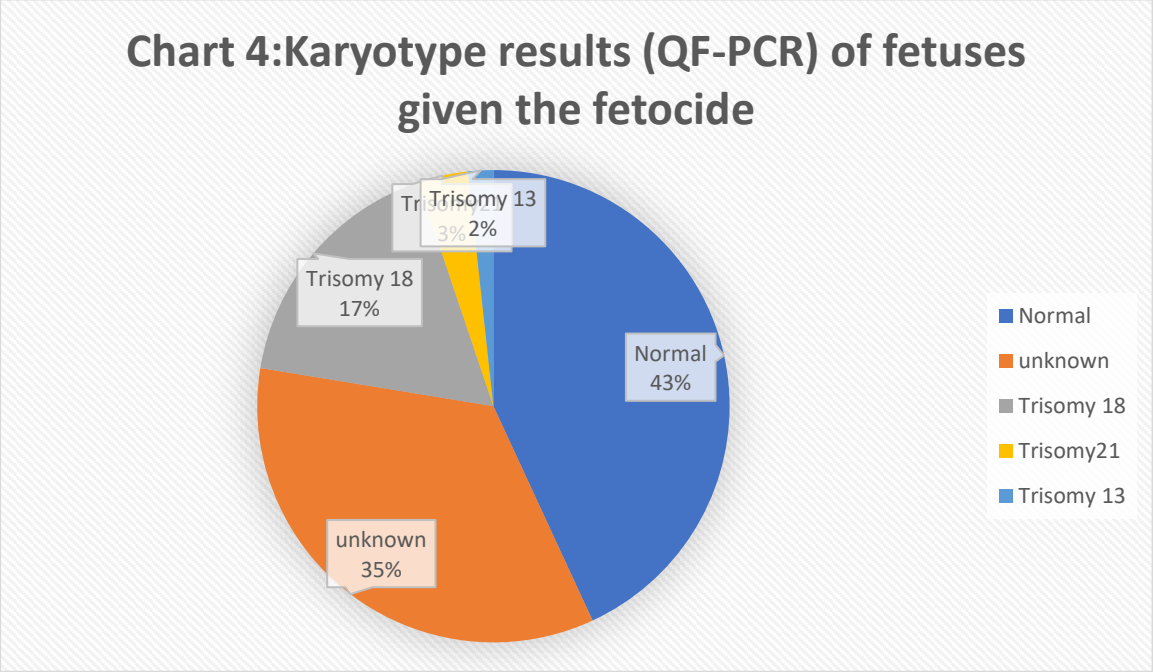
The intracardiac route was used for 15 (26%) patients.

For two (4%) patients, the intracardiac route was initially attempted, but was not successful.

The procedure was successfully repeated few days later through umbilical vein.



Fifteen percent KCl was the only fetocide agent used. The volume of KCl 15% used was not indicated in 23 (40%) of patients. The median amount of KCl used was 20 mls.



Karyotype reports from the National Health Laboratory System database (NHLS) were found for 50(86%) patients.

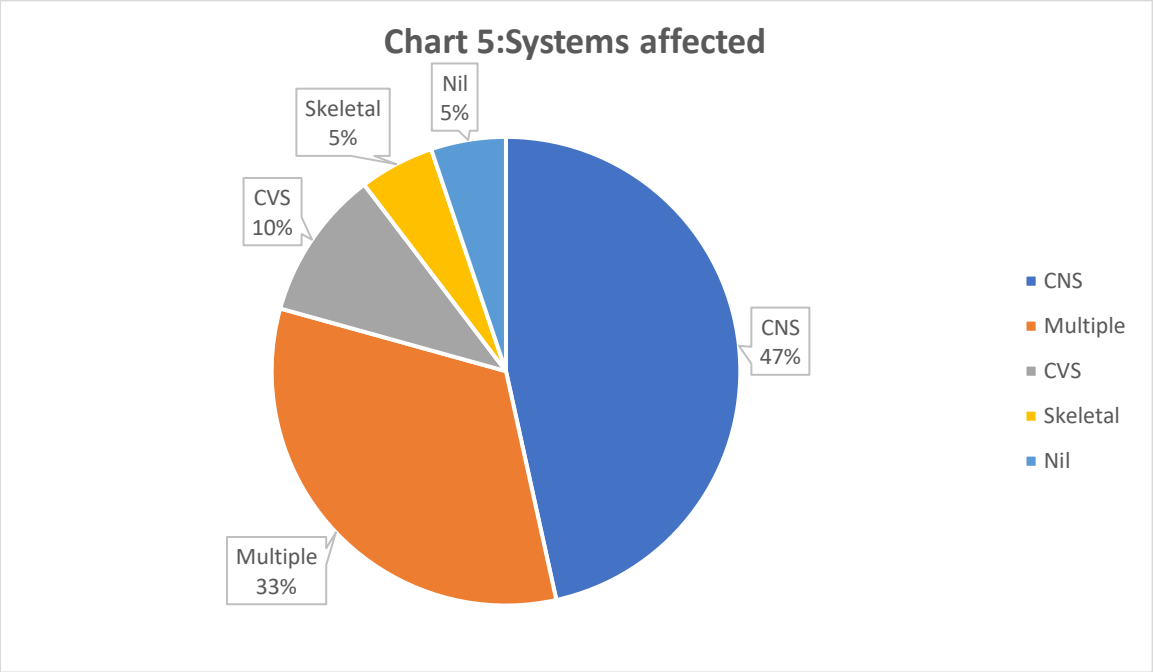


Chart 5:Systems affected
Nil
5%
Skeletal
5%
CVS
10%
CNS
47%
Multiple
33%
CNS
Multiple
CVS
Skeletal
Nil

Table 2: Analysis of Central Nervous System anomalies

Anomaly observed	Number (%)
Anencephaly	6(22%)
Spina bifida	5(19%)
Hydrocephalus	5(19%)
Encephalocele	4(15%)
Holoprosencephaly	3(11%)
Microcephaly	2(7%)
Hydrancephaly	2(7%)

Discussion.

Fetocides at CHBAH are generally offered at or after 24 weeks gestation to patients with fetuses with structural congenital anomalies deemed not compatible with normal life or anticipated to be associated with severe mental and physical challenges. The decision to proceed with a fetocide follows numerous and intensive counselling sessions with a multidisciplinary team. Patients are encouraged to consult their religious leaders and family elders before making their decision.
The study notes an increase in the number of fetocides procedures from 8 in 2019 to 24 in 2020 and 26 in 2021.A possible contributing factor was the covid pandemic with South Africa going into a lockdown in March 2020.In 2019 at the beginning of the pandemic many patients were very reluctant to attend hospitals as not much was known about the SARS COVID 19 Virus.

In this study, it was found that 44 (76%) patients out of 58 were multigravida. This is similar to the report of a Zimbabwean study conducted in 1983 by Caroline Crowther and R. Glyn-Jones: *Lethal congenital malformations in the Greater Harare Obstetric Unit during 1983*.In that study, 72% of patients with lethal structural congenital anomalies were multigravida [20]. The size of the two studies was not the same. The Zimbabwean study had a bigger size, 97vs58.In the same study, it was found that 19 (19.6%) of the patients were nulliparous [4] vs 14(24%) in our study. From this observation, it is clear that even primigravida patients should be referred for anatomy scan and one healthy pregnancy does not guarantee another healthy pregnancy. Every patient should still have an anatomy scan every time they fall pregnant.

With regard to HIV status,17(29%) of the patients were HIV negative. Seven (12%) were HIV positive. Thirty-four (59%) had an undocumented HIV status in their fetal medicine reports. In a study conducted in Kampala (2015-2018) by Linda Barlow-Mosha et al, it was found that 91.1% of babies with Neural tube defects were born to HIV negative mothers and 8.8% to HIV positive mothers [5]. There seems to be a higher prevalence of HIV patients in this study compared to what was found in their study (12%vs 8,8%) but the higher number of patients with unknown HIV results in our study makes it difficult to draw proper conclusion. This study had 58 cases vs 104 in their study.

Only 14(24%) out of the 58 patients in this study had a documented RPR result and all of them had a negative RPR result. This is an unfortunate limitation and we could not draw a proper conclusion regarding the possible link between the occurrence of structural congenital anomalies and syphilis status of the mother.

A total of 14(24%) patients in this study were older than 35 years old. This is higher than what was observed in a cross-sectional study conducted by Bekalu Getachew et al. in Ethiopia in 2018, where only 13% of the mothers carrying fetuses with severe structural congenital anomalies were 35 years old or older than 35 years old [6]. The Ethiopian study had a significantly larger cohort of 754 participants. The possible explanations might be the fact that South Africa may have a higher proportion of women delaying childbearing, the difference in accessing prenatal care, but as well environmental and lifestyle factors such as exposure to alcohol consumption, and khat chewing or use of other substances.
However, our finding is almost similar to the one by Isabelle Scheriff et al. in their study done in England and Wales. Over a period of 8years (2012-2020) ,2 124 (23%) out of 9 310 patients who underwent fetocide procedure for severe congenital anomalies were older than 35 years old [7].

This study had 32(55%) fetocide procedures that were performed between 26 weeks and 30 weeks gestation. Five (9%) were performed after 36 weeks. One was a 26P1G2 who was lost to follow up and reappeared at 36 weeks 4 days. The fetus had skeletal dysplasia. Another patient was a 21POG1 referred from another hospital and seen for the first time at the CHBAH FMU at 38weeks 3days.The fetus had severe hydrocephalus (BPD of 142.3mm), no brain tissue and suspected spina bifida.
In this study, the mean gestation at which fetocide procedure was performed was 29 weeks (IQR=26-32 weeks). This finding is similar to the finding by Sefanyatso in 2012 with his study on '*fetocides at Chris Hani Baragwanath Hospital* [8]'. In his study the mean gestation at which fetocide procedure was performed was 29.67 weeks (range 24-36 weeks)]. Late referrals and poor follow-ups seem to be the main reason of late fetocide procedure. Another factor is the laboratory processing time. It takes two to four weeks to get the report of QF-PCR back from the National Laboratory.
Scheriff et al. reported in their study that 40% of fetocide procedures were performed at 23

weeks gestation. In this specific study only 6% of fetocides procedures were performed at or after 30 weeks gestation [7]. In fact, in England and Wales, fetocides procedures are usually performed from 21weeks 6days, with some of them being performed even at or before 20 weeks gestation.
This is because our viability is different from the viability in most of developed countries and the viability of 500g or lower limit of 22 weeks set by the WHO. South African patients also book late [2].

The route used for the administration of the KCl for 20 (34%) out of 58 of the patients in this study could not be confirmed. The route was known for 38 of these patients, with 21 (55.3%) of them having been administered KCl through umbilical vein;15 (39.4%) through intracardiac route and 2 (5.3%) through a failed intracardiac route and then umbilical vein route. The calculated p-value is 0.51 indicating no statistical difference. Despite this statistical correlation, the umbilical vein route was in this study the most preferred route. This is in contrast with the study conducted by Scherif et al. where the intracardiac route with KCl was used in 67.2% of the patients [7].
The two patients in this study with both intracardiac and umbilical vein routes initially had a failed intracardiac route and a second successful attempt after a few days via umbilical route. The two failed attempts were due to advanced gestation, the position of the baby, and the location of the placenta. With the first case, the patient was 27 weeks, fetus in a breech presentation, back anterior and a posterior placenta. With the second case, the GA was 35 weeks with oligohydramnios and a posterior placenta. The fetus was in vertex presentation.
The choice of agent by the FMU at the CHBAH is 15% KCl.
The volume used was not known for 23 (40%) patients. A total of 10 ml was used in 15 of the patients in this study, but higher volumes were administered in some patients. Seven patients required 40 ml. One was 26weeks 5 days and the remaining 6 between 27 and 30 weeks. The technique and the small number of patients in this study can explain this high number of patients requiring 40 ml of KCl. One patient required only 5ml given via intracardiac route. According to a study done at a tertiary hospital in South Africa and published in the South African Medical Journal (SAMJ), the mean volumes of KCl used were 8ml for GA between 24-25 weeks,10 ml for GA between 26-30 weeks and 13 ml for GA >30 weeks [9].

Twenty-six of the patients in this study who underwent fetocides procedures had a normal karyotype result. Eight of them were diagnosed with Trisomy 18, three had trisomy 21 and

one had trisomy 13.

Comparing the proportions with severe congenital anomalies between the normal and the abnormal groups (group with unknown karyotype result not being considered), both the chi-square and Fisher' exact test yielded a p-value of 0. 040.This difference is statistically significant. The Odds Ratio calculation (O.R) of 0.346 indicates that patients with abnormal karyotype result are about 2.9 times (1/0.346) more likely to have severe congenital anomalies.

One of the patients with Trisomy 21 was a 42-year-old P3G4 who had left pyelectasis, a polydactyly left hand and a flat facial profile on the ultrasound. An amniocentesis was performed at 22 weeks 1 day. The karyotype result was available after two weeks and the patient requested TOP. Fetocide procedure was performed.

A total of 27(47%) out of 58 of the patients in this study had fetocide procedure for CNS anomalies. This percentage does not consider CNS anomalies occurring with anomalies involving other organ systems. The findings correlate with those reported by Scheriff et al., where congenital anomalies of the CNS were found to be the number one leading anomaly (33%) [7]. In their study the cardiovascular system was the second most involved system in contrast with this study where multiple systems were the second leading cause of birth defects requiring fetocides. Anomalies of the cardiovascular system in this study were found to be the third leading cause of structural anomalies requiring fetocide (10%). In this study only 3 (5%) out of 58 patients had anomalies involving the musculoskeletal system requiring fetocide.

Limitations.

Loss of records and incomplete records and as well inadequate notes. Retrieving the files of all the patients selected was not feasible as most of those patients were referred from various other medical institutions. They were referred back to their respective hospitals with their files after the fetocide procedure. The fact that none of the patients in this study had a positive RPR result and many had undocumented RPR result made it difficult to draw proper conclusions regarding the possible role of maternal syphilis infection in the occurrence of severe structural anomalies. Only QF-PCR test is being done at the NHLS. We could therefore not identify possible other small chromosomal anomalies that might have been associated with the structural anomalies observed in this study.

The total number of patients in this study was only 58 and this has to be taken into account when interpreting the statistical results.

Conclusion and recommendations.

In conclusion, fetocides are a safe and highly effective practice to induce fetal demise. It is offered at CHBAH FMU at or after 24 weeks in fetuses diagnosed with severe structural congenital anomalies. The umbilical vein route is very effective to use. CNS structural anomalies have been the most prevalent with anencephaly being the leading one. Abnormal Karyotype result is more associated with severe structural anomalies.
We recommend electronic records keeping to minimize the risk of losing valuable information.
Further research is needed to explore in detail other angles of this exciting topic, especially the ethical implications of fetocides for both mothers and clinicians.

Conflicts of interest

None.

Funding.

None.

Authors' contribution.

All the authors actively participated in the elaboration of this document.

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Annexure 1.

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 5th May 2022

TITLE OF PROJECT:

Review of Fetocides at Chris Hani Baragwanath Academic Hospital Over a Three Year Period.

UNIVERSITY: Witwatersrand

Principal Investigator: Dr G K Munkita

Department: Obstetrics & Gynaecology

Supervisor : Dr J Jeebodh

NHRD Number: GP_

Permission Head Department (where research conducted): Yes

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Academic Hospital. The CEO / management of Chris Hani Baragwanath Academic Hospital is accordingly informed and the study is subject to:-

- **Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.**
- The Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- The MAC will be informed of any serious adverse events as soon as they occur
- Permission is granted for the duration of the Ethics Committee Approval.

Recommended
(On behalf of the MAC)
Date: 05/05/2022

Approved/~~Not Approved~~
Hospital Management
Date: 09/05/2022

Annexure 2

TRREE

Zertifikat Certificado

Certificat Certificate

Promouvoir les plus hauts standards éthiques dans la protection des participants à la recherche biomédicale
Promoting the highest ethical standards in the protection of biomedical research participants

Clinical Trials Centre
The University of Hong Kong

Certificat de formation - Training Certificate

Ce document atteste que - this document certifies that

Munkita Gabin Kiaka

a complété avec succès - has successfully completed

Introduction to Research Ethics

du programme de formation TRREE en évaluation éthique de la recherche
of the TRREE training programme in research ethics evaluation

Release Date: 2022/01/23

Professeur Dominique Sprumont
Coordinateur TRREE Coordinator

FMH

FPH

Annexure 3.

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Munkita Gabin Kiaka

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M220852

NAME: (Principal Investigator)	Dr Munkita Gabin Kiaka
DEPARTMENT:	Obstetrics and Gynaecology Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Review of fetocides at Chris Hani Baragwanath Academic Hospital over a three year period
DATE CONSIDERED:	26/08/2022
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr J. Jeebodh
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	24/10/2022

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 on the 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 **August** and will therefore be due in the month of **August** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

12 Feb 2023
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Annexure 4.

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

29 March 2022
Person No: 2438373
PAG

Dr M Kiaka
14 Wildebees Street
Johanneburg
Alberton
1449
South Africa

Dear Dr Munkita Kiaka

Master of Medicine in Obstetrics and Gynaecology: Approval of Title

We have pleasure in advising that your proposal entitled *Review of fetocides at Chris Hani Baragwanath Academic Hospital over a three year period* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Annexure 5.

Data collection sheet.

Patient no…

1.Age of the patient.

Less than 35 years old	35years old 0 day	More than 35 years old.

2.Parity.

1st pregnancy.	Not 1st pregnancy (pregnancy, no?)

3.Marital status.

Single.	Married.	Divorced.	Widowed.	Not recorded.

4.Booking bloods.

HIV reactive	HIV non-reactive	HIV unknown	RH Positive.	RH Negative.	RH unknown.	RPR Reactive.	RPR non-reactive.	RPR unknown.

5.Major congenital anomaly identified at FMU.

Central nervous system anomalies	Cardiac anomalies	Renal anomalies	Gastrointestinal anomalies.	Musculoskeletal anomalies.	others

6.Gestational age when congenital anomaly diagnosed.

Less than 24 weeks	More than 24 weeks

7.Gestational age when fetocide performed.

24wk+0 - 28wk+0	28wk+1 – 32 wk+0	32wk+1 – 36wk+0	>36wk

8.Body Mass Index (BMI) in kg/m^2

<18.5	18.5-24.9	25-29.9	30-34.9	35-39.9	>/40	Not documented

9.Employment

Employed	Unemployed	Self employed	Informal employment	Not documented

10.On any medications Haematinics excluded.

Yes (which one)	No	Not documented

11.Fetocide offered?

Yes, and accepted	Yes, but declined	Not offered

12.Fetocide agent, technique and total volume used.

Kcl 15%	Lignocaine 1%	digoxin
Umbilical route	Intracardiac route	Other
2mls-4mls of Kcl	4.1mls-6mls of Kcl	>6.1mls of Kcl

13.Karyotyping information.

Karyotyping requested.	Karyotyping not requested.	Karyotyping requested and result available.	Karyotyping requested but result not available.

14.Duration between diagnosis and fetocide procedure.

Less than 4weeks.	More than 4weeks.	4weeks + 0 day.	Not documented.

15.Previous congenital anomaly.

Yes	No	Not documented.

16.Mode of delivery.

Normal vaginal delivery.	Caesarean section delivery.	Assisted delivery.	Not recorded.

17.Place of booking.

Local clinic.	Private general practitioner.	Private Gynaecologist.	Other Hospital.	CHBAH.

18.Habits

Smoker.	Non-smoker.	Alcohol user.	Not alcohol user.	Not documented.

19.Comorbid conditions.

Diabetes mellitus.	Hypertension.	Epilepsy.	Other.	Nil known.	Not documented.

Final MMED DR KIAKA (for submission) (AutoRecovered)3 1.docx

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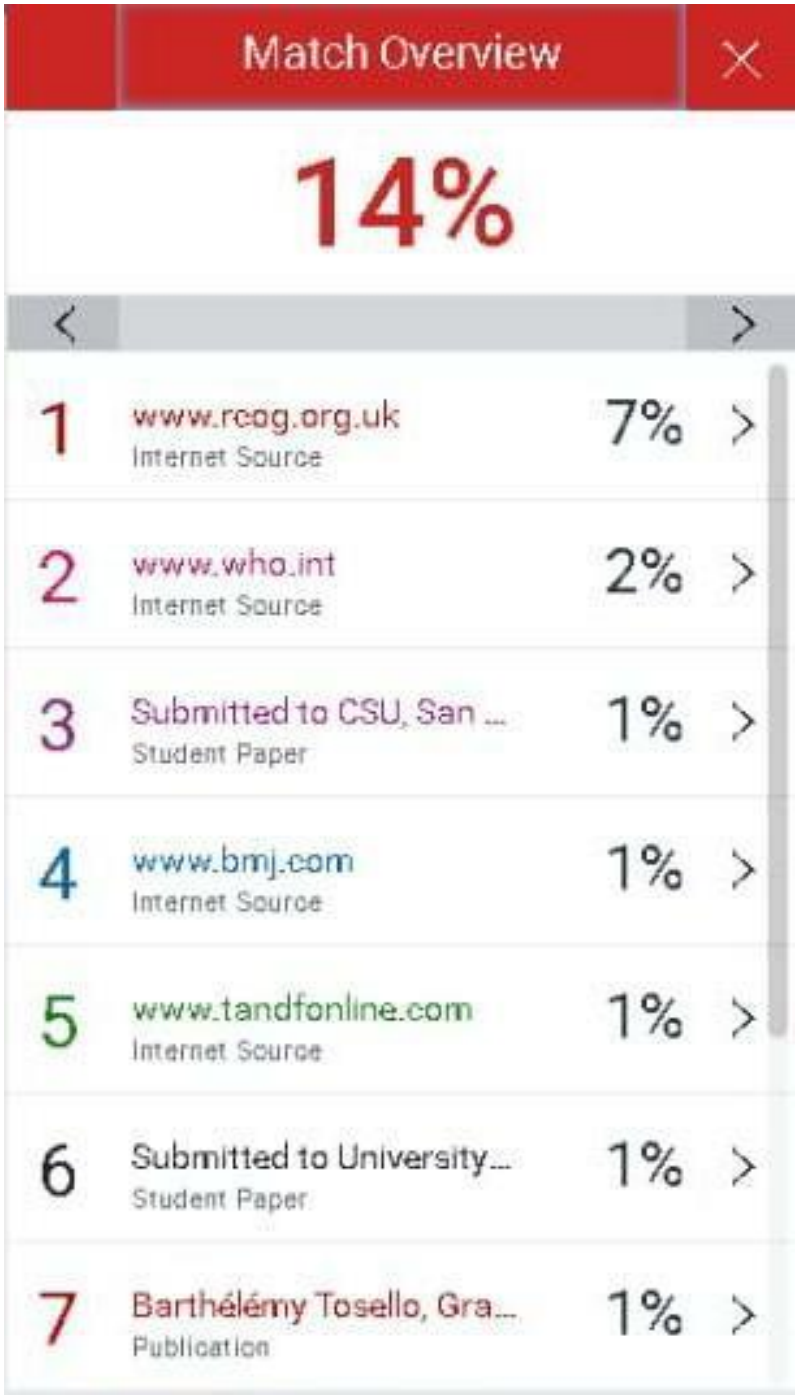

REVIEW OF FETOCIDES AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL OVER A THREE-YEAR PERIOD.