OUTCOMES OF PREGNANT PATIENTS WITH CARDIAC DISEASE AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

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A Dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Obstetrics and Gynaecology

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Johannesburg, 2018

Declaration

I, Dr Maidei Mugwede, declare that this research is my own work. It is being submitted for the Master of Medicine in Obstetrics and Gynaecology in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this and any other University.

Signature.....Mugwede.....

.....2nd..... day of .....DECEMBER..... 2015

DEDICATION

To my mother and father

You are my rock

Love you

ABSTRACT

Introduction: The incidence of cardiac disease in pregnancy ranges between 0.1 – 4.0%. It is the 5th leading cause of maternal deaths in South Africa. Management of pregnant cardiac patients involves pre-pregnancy counselling, with risk assessment and monitoring of the mother and fetus by a multidisciplinary team which includes an obstetrician, materno-fetal medicine subspecialist, cardiologist, neonatologist, geneticist and an anaesthetist.

Objectives: To determine the maternal morbidity and mortality in cardiac patients presenting at Chris Hani Baragwanath Academic Hospital (CHBAH), as well as their neonatal outcomes and to obtain information about specific cardiac conditions in these patients, their obstetric management and the short-term effects of pregnancy on the underlying cardiac lesion.

Methods: This was a prospective descriptive study where post-delivery cardiac patients were approached to enrol in the study from August 2013 to January 2014. Data was collected from the patients' antenatal records and cardiology reports. Patients were also interviewed to determine more detailed information regarding previous pregnancy outcomes and cardiac complications which were not available in the antenatal records. Neonatal information was obtained by follow-up visits to the neonatal wards.

Results: Acquired cardiac conditions accounted for 88.1% of the study patients (Rheumatic Heart Disease (RHD) 42.9% being the most common) while 11.9% were congenital. Most of the patients had a New York Heart Association (NYHA) class of I (85.4%) at antenatal booking. Of the participants in the study, 33.3% were human immunodeficiency virus (HIV) positive. Caesarean section accounted for 66.7% of

the deliveries while 33.3% were by normal vaginal delivery. There were 42.9% of women who experienced morbidities during their pregnancies with 27.5% suffering a decline in their NYHA class. Only eleven patients had a post-partum ECHO, in whom 82% showed a decline in the ejection fraction (EF). Intrauterine growth restriction (IUGR) complicated 44% of pregnancies. The perinatal mortality rate was 7%. There were no maternal deaths.

Conclusion: Rheumatic heart disease is still the predominant underlying cardiac lesion. There is considerable maternal morbidity and perinatal morbidity and mortality in cardiac patients at CHBAH. The multidisciplinary team approach is improving the maternal and perinatal outcome in pregnant women with heart disease at CHBAH.

ACKNOWLEDGEMENTS

My sincere gratitude goes to my supervisor, Dr J Jeebodh for her endless support through the whole period of making this research possible. I will forever be indebted.

To my husband, Edmore, son, Makomborero “Dude” and daughter, Ruvarashe, thank you for your love, patience, and unending support.

Special thanks to the Chief Executive Officer (CEO) of CHBAH and Professor Y Adam, Head of Department of Obstetrics and Gynaecology at CHBAH for their permission to conduct this study. To the staff at the CHBAH and the patients who took part in the study, thank you, without your participation this research would not have been possible.

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ABBREVIATIONS

AIDS – Acquired Immunodeficiency Syndrome

APS – Antiphospholipid Syndrome

ASD – Atrial Septal Defect

ARV – Antiretroviral

AVSD – Atrioventricular Septal Defect

BMI – Body Mass Index

BP – Blood Pressure

CARPREG – Cardiac Disease in Pregnancy

CCF – Congestive Cardiac Failure

CEO – Clinical Executive Officer

CHBAH – Chris Hani Baragwanath Academic Hospital

CHD – Congenital Heart Disease

DCMO – Dilated Cardiomyopathy

DVT – Deep Vein Thrombosis

ECG – Electrocardiography

ECHO – Echocardiography

EF – Ejection Fraction

HB – Haemoglobin

HELLP – Haemolysis Elevated Liver enzymes Low Platelets

HHD – Hypertrophic Heart Disease

HIE – Hypoxic Ischaemic Encephalopathy

HIV – Human Immunodeficiency Virus

INR – International Normalised Ratio

IUFD – Intrauterine Fetal Death

IUGR – Intrauterine Growth Restriction

JVP – Jugular Venous Pressure

kg – kilogram

LMW – Low Molecular Weight

LVEF – Left Ventricular Ejection Fraction

mg – milligrams

MSB – Macerated still birth

NICU – Neonatal Intensive Care Unit

NYHA – New York Heart Association

LSCS – Lower Segment Caesarean Section

PND – Paroxysmal Nocturnal Dyspnoea

PDA – Patent Ductus Arteriosus

PHT – Pulmonary Hypertension

PIH – Pregnancy Induced Hypertension

PMTCT – Prevention of Mother to Child Transmission

PPCM – Peripartum Cardiomyopathy

PPH – Postpartum Haemorrhage

PROM – Prelabour Rupture of Membranes

PPROM – Premature Prelabour Rupture of Membrane

RDS – Respiratory Distress Syndrome

RHD – Rheumatic Heart Disease

SCBU – Special Care Baby Unit

STAH – Subtotal Abdominal Hysterectomy

TICU – Transitional Intensive Care Unit

TOF – Tetralogy of Fallot

VSD – Ventricular Septal Defect

WHO – World Health Organisation

ZAHARA-1 – Zwangerschap bij vrouwen met een Aangeboren HARtAfwijking

(Pregnancy in women with congenital heart disease)

1.0 INTRODUCTION

1.1 Epidemiology of Cardiac Disease in Pregnancy

Cardiac disease in pregnancy has an incidence of between 0.1 – 4.0%.[1, 2] In the 2011 – 2013 triennium Saving Mothers report, medical and surgical conditions were classified as leading indirect causes of maternal deaths in South Africa. Of the 493 medical and surgical cases reported, 169 of these were secondary to underlying cardiac disease (34.3%).[3] The incidence of cardiac disease in pregnant patients in South Africa is about 0.65% and the morbidity and mortality is approximately 9.5%. Some of the highlighted preventable factors are[4]:

1. Uncontrolled fluid infusion
2. Inaccurate assessment of severity of the condition
3. Patient attributable factors:
    - delay in seeking attention
    - lack of antenatal care
4. Problems at secondary/tertiary level:
    - failure to act on the severity of the condition
    - failure to recognise risk during the postpartum period

1.2 Physiological cardiovascular changes in pregnancy

In early pregnancy, due to increased aldosterone secretion, the plasma volume increases from non-pregnant levels of 2600 ml to 3800 ml and remains constant after 32 weeks of gestation. This comprises about 40-50% of the total circulating volume. The red cell mass increases by about 40% due to increased erythropoietin levels. Due to the disproportionate increase of the plasma volume versus the red cell

mass, the haematocrit and haemoglobin levels decrease. The cardiac output increases by about 50%, from 4.5 to 6 l/min. The cardiac output rises till it reaches a plateau between 24-30 weeks of gestation. The heart rate increases by 10%, which results in an increase in stroke volume. Peripheral vasodilatation due to elevated levels of progesterone leads to smooth muscle relaxation with an overall decrease in blood pressure. The diastolic blood pressure decreases from between 12 – 26 weeks but increases again to pre-pregnancy levels by 36 weeks gestation.[5]

In patients with cardiac dysfunction, the normal physiological changes of pregnancy (increased blood volume, increase in heart rate and haemodynamic changes of the puerperium) induce extensive strain on an already diseased heart. Hence the need for pre-pregnancy counselling with risk assessment and close monitoring of the mother and fetus by the management of a multidisciplinary team. The recommendations are that the team should include an obstetrician, materno-fetal medicine specialist, cardiologist, neonatologist, geneticist and anaesthetist.[5]

2.0 LITERATURE REVIEW

2.1 Congenital Heart Disease

In developed countries, advances in surgical treatment and drug management have led to a decline in rheumatic heart disease. With advances in paediatric cardiology and cardiac surgery, more women with congenital heart disease (CHD) are reaching childbearing age.[5, 6] This accounts for 89% of cardiac disease in pregnancy.[1] The incidence of CHD is around 0.8%.[7] The statistics may be higher as some conditions are only diagnosed later in childhood, therefore they are missed in studies focusing on infants only. [8]

Congenital heart lesions comprising 85% of clinical significance include:[8]

i. Ventricular septal defect (VSD)
ii. Atrial septal defect (ASD)
iii. Patent ductus arteriosus (PDA)
iv. Pulmonary stenosis
v. Tetralogy of Fallot (TOF)
vi. Coarctation of the aorta
vii. Aortic stenosis
viii. Atrioventricular septal defect (AVSD)

Children born to mothers with CHD are themselves at risk. The general population has a risk of about 1% compared to the 3 -5% risk of inheriting polygenic cardiac disease. The risk is dependent on the mother's cardiac lesion, being 3% with TOF and as high as 10% with an ASD, aortic stenosis and coarctation of the aorta. In autosomal dominant conditions such as Marfan's syndrome, with a Mendelian mode of inheritance, the recurrence rate is 50%.[2, 5]

In most cases of CHD, the cause is unknown. Known contributory factors may include, genetic causes, chromosomal abnormalities, maternal infections such as rubella infection as well as administration of teratogenic medication or even consanguineous marriages.[8]

2.2 Acquired Cardiac Disease

2.2.1 Peripartum Cardiomyopathy

Peripartum cardiomyopathy (PPCM) presents with heart failure due to left ventricular systolic dysfunction.[9] The incidence ranges from 1 in 1 500 to 1 in 4 000 live births.[10] In Europe it is relatively rare, but more common in West Africa and South Africa (1 in 1000).[11] The highest incidence of 1 in 300 has been reported in Haiti.[12] It usually develops within the last month of pregnancy or the first 5 months post-delivery.[10, 11, 12, 13] Within the first week postpartum 45% of cases present, while 75% present within the first month postprtum.[9]

Table 2.1 Clinical definition of PPCM[7, 11, 13]

1. Heart failure within last month of pregnancy or five months postpartum
2. Absence of prior heart disease
3. No determinable cause
4. Strict echocardiology indication of left ventricular dysfunction:
    - Ejection fraction <45%

      and/or
    - Fractional shortening <30%
    - End-diastolic dimension >2.7 cm per m^2 body surface area

The aetiology of PPCM is still unclear, but postulated causes include:[13]

a. Infectious
b. Immunological
c. Nutritional
d. Drug-induced
e. Familial
f. Impaired cardiac microcirculation

PPCM is associated with maternal age >30 years, black race, multiparity, multiple gestation, use of tocolytic therapy, and pre-eclampsia.[10, 13]

Symptoms in late pregnancy including shortness of breath and pedal oedema often mimic symptoms of early congestive cardiac failure (CCF). Diagnosis of PPCM needs a high index of suspicion. Symptoms and signs include paroxysmal nocturnal dyspnoea (PND), orthopnoea, new regurgitant murmurs, basal pulmonary crepitations, elevated jugular venous pressure (JVP) and hepatomegaly.[10]

Approximately 30 – 50% of patients suffering from PPCM will recover without any complications, with their baseline left ventricular function returning to normal at rest. A poor prognosis is anticipated if, by six months postpartum, the left ventricular function has not returned to normal.[14]

2.2.2 Rheumatic Heart Disease

RHD is the major cardiac disease in developing countries.[1, 2] The prevalence is estimated to be highest in sub-Saharan Africa with a prevalence of 5.7 per 1000, compared to 1.8 per 1000 in North Africa, 2.2 per 1000 in South Central Asia and 0.3% in developed countries.[15] Evidence suggests that RHD occurs at a younger

age and progresses more rapidly in developing compared to developed countries. This may be because of frequent rheumatic fever infections and lack of intervention. A single infection of acute rheumatic fever may lead to RHD, but most cases result from cumulative damage. Those mostly affected are aged between 5 to 18 years of age .[8] The lack of financial support, social and cultural drawbacks as well as lack of information about the risk of pregnancy in women with RHD contribute to the challenges against prevention strategies.[16] The high prevalence of other public health problems which include HIV and acquired immunodeficiency syndrome (AIDS), tuberculosis and malaria have diverted attention from rheumatic fever and RHD.[15]

The most common complication of rheumatic fever is mitral stenosis. A South African study by Nqayana et al. in 2008 reported that 77 of the 95 patients that were recruited had rheumatic heart disease, with the mitral valve being the most commonly affected. Mitral stenosis is graded according to valve area:

- mild >1.5 cm^2
- moderate 1.1 - 1.5 cm^2
- severe <1 cm^2

Symptoms may vary from limited physical activity to signs of pulmonary oedema. The use of beta-blockers and diuretics is recommended in symptomatic patients. Those who do not respond to medical treatment or have severe symptoms will require balloon valvoplasty or valve replacement. Patients with mild to moderate mitral valve stenosis may be allowed to deliver vaginally under epidural analgesia.[13]

Although aortic stenosis may be congenital it may also be of rheumatic origin. Aortic stenosis results in a fixed output state that can be further aggravated during

pregnancy by vena cava occlusion, blood loss, or regional anaesthesia such as spinal or epidural analgesia leading to a decreased cardiac, cerebral and uterine perfusion. Patients with mild or moderate stenosis do not require treatment either medical or surgical while those with severe stenosis benefit from valve replacement. Aortic valve replacement during pregnancy is associated with a fetal mortality risk of 30%. Caesarean section is the preferred mode of delivery for those with severe aortic stenosis.[13]

Valvular incompetence is tolerated better than stenosis. The reduction in systemic vascular resistance improves the forward flow hence limiting the effects of regurgitation. On the other hand, stenosis creates fixed impedance to the increase in cardiac output that occurs during pregnancy and labour, precipitating arrhythmias and heart failure.[10]

2.2.3 Pulmonary Hypertension

Pulmonary hypertension is defined as a mean pulmonary arterial pressure of >25 mmHg at rest or >30 mmHg during exercise.[17] It can be primary or secondary and it can occur in association with cardiac disease or respiratory disorders. Cardiac diseases which lead to pulmonary hypertension include left ventricular failure and chronic left atrial hypertension associated with mitral valve disease while respiratory disorders resulting in pulmonary hypertension include interstitial lung disease, chronic obstructive pulmonary disease and disorders of pulmonary development.[17]

The normal physiological cardiac changes that occur during pregnancy which include increased blood volume, increased cardiac output, decreased vascular resistance and a hypercoagulability state have a negative impact on a patient who has

underlying pulmonary hypertension before or during pregnancy. The risk of maternal mortality lies between 30% and 50% with a high neonatal morbidity resulting from complications of prematurity. Due to the poor tolerance of pregnancy in patients diagnosed with pulmonary hypertension, pregnancy is best avoided. Counselling should be undertaken, and long acting or permanent methods of contraception offered. Should a patient become pregnant or diagnosis occur during pregnancy, termination of pregnancy may be offered though the procedure is not without risk of morbidity and mortality. If pregnancy is allowed to progress there should be the involvement of a multidisciplinary team including a pulmonologist and haematologist.[17]

2.2.4 Hypertrophic Heart Disease

Hypertrophic heart disease (HHD) is defined as an increased ventricular wall thickness in the absence of hypertension or valve disease. Most pregnant women with HHD tend to have a mutation of the sarcomere protein encoding genes that are responsible for the disease, implying an autosomal dominant inheritance. Although about 70% of affected patients have at least one affected family member, the disease maybe sporadic. HHD is primarily diagnosed by echocardiography. Left ventricular outflow tract obstruction is present in 70% of the patients.[18]

Patients with HHD tend to tolerate pregnancy well. The risk of maternal morbidity is higher in patients who are symptomatic prior to pregnancy or with left ventricular outflow tract obstruction. Symptoms that can develop during pregnancy include dyspnoea and chest pain. Atrial fibrillation is one of the common arrhythmias that occurs and has a considerable risk of thromboembolism. Sudden death can occur

especially if there is a corresponding family history, ventricular tachycardia or symptoms of syncope may also occur. Medical treatment is indicated in symptomatic patients and consists of beta-blockers, verapamil and diuretics. Amiodarone is often used for rhythm control and anticoagulation with warfarin or low molecular weight (LMW) heparin warranted in patients with atrial fibrillation. If symptoms persist despite medical treatment surgical myectomy or alcohol septal ablation can be considered. Vaginal delivery is well tolerated under regional anaesthesia.[18]

2.2.5 Dilated Cardiomyopathy

Dilated cardiomyopathy (DCMO) is defined as dilation of the ventricles, left worse than the right, with reduced left ventricular ejection fraction (LVEF) in the absence of valvular, coronary, congenital or systemic diseases that may cause myocardial dysfunction. Patients with LVEF of <30% or moderate to severe left ventricular dysfunction or NYHA class of III or IV are advised against pregnancy. Pregnancy is associated with a negative impact on the clinical course of DCMO. The most common complication of DCMO in pregnancy is cardiac failure which tends to occur in late pregnancy or post-partum. Fetal and/or neonatal complications include first trimester miscarriages, preterm labour, low birth weight and complications of prematurity.[19]

2.3 Prosthetic Heart Valves

Prosthetic heart valves may be either mechanical or bio prosthetic. The types of prosthetic heart valves available include;

1. Mechanical valves,
    - Caged ball

- Monoleaflet
- Bileaflet

2. Bio-prosthetic valves,
    - Stented
    - Stentless
    - Percutaneous

The choice of type of prostheses to use depends on the age, life expectancy, preference, indication or contraindication for warfarin therapy, and the presence of other co-morbidities.[20]

Table 2.2 Bio-prosthetic versus Mechanical valves

Characteristic	**Bio-prosthetic Valve**	**Mechanical Valve**
Durability		Higher
Anticoagulant		Higher
Mortality after 10 years	Higher	
Valve loss	Higher	

Pregnant patients with prosthetic heart valves present with several management challenges.[13]Those that are asymptomatic or have mild symptoms prior to conception often tolerate pregnancy well.[10]

Pregnancy does not cause bio-prosthetic heart valves to degenerate more rapidly.[8]

In young women, the choice of valve prostheses should always be carefully considered as bi- prostheses have a low complication rate during pregnancy, but degeneration will lead to re-operation.[1]

2.4 Anticoagulation

Pregnant women with mechanical prosthetic heart valves are at risk of infection, thromboembolism and haemorrhage because of anticoagulation.[10] The incidence of thrombotic episodes in pregnancy is as high as 45%, while the maternal mortality is around 1-4%. A balance must be reached, as effective anticoagulation is vital to the mother, while reducing the risk of embryopathy and fetal loss.[21] Options available for anticoagulation include;

a. Use of warfarin throughout pregnancy (2.5 – 10 mg daily orally to achieve an international normalised ratio of 2.5 – 3.5) until 36 weeks gestation when warfarin is substituted with unfractionated heparin (±10 000 units 8 hourly subcutaneously to achieve an activated partial thromboplastin time of 2.0 – 2.5 times the control) until post-delivery.
b. Use of unfractionated heparin (±10 000 units 8 hourly subcutaneously) in the first trimester between 4 to 13 weeks gestation, then continuing with warfarin (2.5 – 10 mg daily orally) until 36 weeks gestation, followed by unfractionated heparin (± 10 000 units 8 hourly subcutaneously) from 37 weeks gestation until the post-partum period.
c. Use of unfractionated heparin (± 10 000 units 8 hourly subcutaneously) throughout pregnancy until post-delivery.[22, 23]

Table 2.3 Maternal and fetal risks associated with mechanical valve replacement[21]

Regime	**Maternal thromboembolism (%)**	**Fetal abnormality (%)**	**Fetal loss (%)**
Warfarin until 38 weeks gestation followed by elective LSCS	4	6	30
Heparin for 6-12 weeks gestation, then warfarin till 38 weeks gestation followed by LSCS	9	0	30
Heparin throughout pregnancy	25	0	30

Currently there is no agreement on the most suitable anticoagulant.[10] At present there are no known randomised controlled trials comparing the different anti-coagulation regimens in pregnant women with prosthetic heart valves.[13] A study conducted by Meschengieser et al. followed 92 pregnancies in 59 women between 1986 and 1997. They concluded that oral anticoagulants seem to be safer for the mother than adjusted subcutaneous heparin and that heparin does not offer a clear advantage over oral anticoagulation in the pregnancy outcome.[24]

2.4.1 Warfarin

Warfarin, a coumarin, acts by inhibiting the synthesis of factors II, VI, IX, X, protein C and S.[25] It is the preferred anticoagulant, but poses significant risk of embryopathy when given between the sixth and twelfth week of pregnancy.[2, 24] First trimester embryopathies include abnormal cartilage and bone formation and miscarriages while in the second and third trimester it may cause fetal cerebral haemorrhage, microcephaly and stillbirths.[14] The risk of malformation is estimated to be less than 5%.[24] Risk of teratogenicity with warfarin is dose dependent. While a dose of 5 mg per day is sufficient for most women, the risk of fetal anomalies increases with greater doses.[20, 23] Warfarin overdose has a greater anticoagulant effect on the fetus than the mother, as low levels of vitamin K-dependent clotting factors are synthesised by the immature fetal liver.[23]

2.4.2 Heparin

Heparin, a mixture of sulphated mucopolysaccharides, produces its anticoagulant effect by inactivating thrombin and activated factor X through an antithrombin dependent mechanism.[26, 27] Antithrombin inhibits clotting factor proteases IIa, IXa, and Xa by forming stable equimolar complexes with them. Heparin can be administered as unfractionated or low molecular weight (LMW). Unfractionated heparin has a molecular weight range of 5000 to 30 000 Daltons while low molecular weight heparin has a molecular weight less than 8 000 Daltons. LMW heparin inhibits activated factor X but has less effect on thrombin than unfractionated heparin. Examples of LMW heparins include enoxaparin, dalteparin and tinzaparin. They have the same efficacy as unfractionated heparin, increased bioavailability

from subcutaneous site injection and require less frequent dosing of once or twice daily. Unfractionated heparin can be administered intravenously or subcutaneously but never intramuscularly because of the danger of haematoma formation at the injection site.[27]

Administration of heparin during the first trimester is aimed at reducing the risk of fetal malformations.[24] LMW heparin is usually administered twelve hourly to achieve an antifactory-Xa level of between 0.8 – 1.2 U/ml four hours after administration. If unfractionated heparin is used, activated partial thromboplastin time should be kept at 2.0 - 2.5 times the control value.[24, 27] Older valves require higher levels at least three to four times the normal activated partial thromboplastin time.[10] The risk of fetal loss is not completely eliminated as unfractionated or LMW heparin can cause retroplacental haemorrhage.[14]

At the CHBAH Maternity Department the following regime is used for the management of anticoagulation in pregnancy: [23]

- 4-13 weeks gestation: unfractionated heparin
- 14-36 weeks gestation: warfarin
- 37-42 weeks gestation: unfractionated heparin

Alternatively, LMW heparin (enoxaparin) is used in selected cases in consultation with a cardiologist.[22]

Although the warfarin protocol for use in pregnancy is primarily aimed at avoiding first trimester fetal exposure during the critical period of 6 to 12 weeks gestation, success is dependent on early detection of pregnancy and booking. It is mandatory for patients who use warfarin throughout the first trimester to have a fetal anomaly sonar by the fetal medicine specialist to exclude warfarin embryopathy.

Several other factors can influence the choice of anticoagulation and they include:

i. Type of mechanical valve. First and second-generation valves which include Starr Edwards and Bjork Shirley have a higher risk of thrombosis than newer bi-leaflet valves.
ii. Position of valve replacement. The mitral position is associated with a higher thrombotic risk than the aortic position.
iii. Number of mechanical valves.
iv. Prior history of embolic events.
v. Warfarin dose required to maintain therapeutic international normalised ratio.[14]

Polymorphisms in genes encoding cytochrome P450 2C9 (CYP2C) and vitamin K eposide-reductase complex 1 are known to alter response to warfarin. These polymorphisms explain variability between whites and blacks. In 2013, Green reviewed a genome-wide association study involving black patients who were on stable maintenance doses of warfarin to determine whether blacks had any genetic variants. He observed a single polymorphism (rs12777823) in the CYP2C gene. Oral clearance of warfarin was significantly decreased in homozygotes and heterozygotes versus those without the genotype. He concluded that warfarin doses need to be carefully selected as there is a risk of overdosing or under-dosing and 25% of blacks harbour the rs12777823 polymorphism and would be vulnerable to warfarin toxicity.[26]

2.5 New York Heart Association Classification

NYHA classification is used to assess the functional status of the cardiac patient.[2] The classification lacks in that, it is dependent on the patient's interpretation of her symptoms. It is not reliable in assessing patients with mitral stenosis.[28]

Table 2.4 NYHA Classification[10]

Class I	Patients with cardiac disease but without resulting limitations of physical activity. Ordinary physical activity does not cause fatigue, palpitations, dyspnoea or angina pain.
Class II	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitations, dyspnoea or angina pain.
Class III	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity results in fatigue, palpitations, dyspnoea or angina pain.
Class IV	Patients with cardiac disease resulting in an inability to participate in any physical activity without discomfort. Symptoms of cardiac insufficiency may even be present at rest. If any physical activity is undertaken, discomfort is increased.

Mortality risk of cardiac disease is dependent upon the underlying cardiac lesion and the NYHA functional class.[28]

Table 2.5 Risk of maternal mortality versus cardiac lesion[28]

High **(mortality 25-50%)**	Eisenmenger's complex Cyanotic heart disease Pulmonary hypertension Ischaemic heart disease Hypertrophic obstructive cardiomyopathy Cardiac failure (PPCM)
Moderate to high **(mortality 5-15%)**	Valvular stenosis Coarctation of the aorta History of myocardial infarction Marfan's syndrome Mechanical prosthetic valves
Low **(mortality less than 1%)**	Acyanotic heart disease Mild to moderate regurgitation Mitral valve prolapse Small ventricular and atrial septal defects

2.6 HIV in Pregnant Cardiac Patients

While RHD is the major cause of maternal morbidity in developing countries, HIV serostatus does not modify treatment effects in women with heart disease during pregnancy. Nqayana et al. conducted a study in Durban that looked at the impact of HIV serostatus on pregnancy associated cardiac disease. Their conclusion was that maternal morbidity as well as adverse fetal outcomes was associated with late presentation and problems with anticoagulation, and not with HIV serostatus.[12]

2.7 Fetal Outcomes

The incidence of adverse events such as intrauterine growth restriction, preterm birth and fetal loss occur more often in the pregnant cardiac patient than the healthy pregnant women. Fetal risk depends on the type of underlying cardiac lesion and complexity. The ZAHARA I and CARPREG studies identified multiple pregnancy, smoking, NYHA class III/IV, left heart obstruction, warfarin/heparin use, cyanosis and having a mechanical valve prosthesis as predictors of fetal events such as first trimester miscarriages, preterm delivery and low birth weight.[29]

Watkins et al. in 2012 researched the burden of antenatal heart disease in South Africa. One of their objectives was to determine fetal outcomes by collecting national data on perinatal mortality, which ranged from 8,895 to 23,810 per 100,000 deliveries. Firstly, they confirmed that antenatal heart disease is associated with a higher rate of fetal loss. Women with poor cardiac outcomes had the highest perinatal mortality rates (19.3%) when compared with uneventful pregnancies. Secondly, mitral valve pathology carried the highest risk for the fetus. A study at Dr George Mukhari Hospital by Matlala in 2005, noted a high incidence of low birth

weight deliveries in patients with native stenosis and post-mitral valve repair. Thirdly, indiscriminate prescription of warfarin was associated with a high rate of fetal loss. Soma-Pillay et al. reported a 30% fetal loss in patients taking warfarin. They attributed this increase to the unawareness of patients on warfarin of their pregnancy and a delay in antenatal booking until late in the first trimester.[30]

2.8 Echocardiography and Electrocardiogram

An echocardiogram (ECHO) is a non-invasive sonogram of the heart which can be two or three dimensional. The standard method is transthoracic, but transoesophageal echoes can also be performed. It has become routine in the diagnosis, management and follow up of patients with suspected cardiac disease. It helps to detect cardiomyopathies (hypertrophic or dilated), valvular lesions, location and extent of any tissue damage. It also quantifies the internal chamber size, calculates the cardiac output, ejection fraction and diastolic fraction. Pulsed or continuous wave Doppler ultrasound is used to visualize any abnormal communications between the left and right atria and ventricles, valvular regurgitation and stenosis.

Erbel et al. looked at the sensitivity and specificity of two-dimensional echocardiography in detection of impaired left ventricular function compared with cineventriculography in patients with suspected coronary heart disease, valvular heart disease and congestive cardiomyopathy. They observed a sensitivity of 81% and a specificity of 100% for end diastolic left ventricular volumes.[31]

An electrocardiogram (ECG) is difficult to interpret during pregnancy. Normal physiological changes in pregnancy may mimic cardiac pathology on an ECG. These changes include left axis deviation, ST segment depression, T wave inversion in lead III, V1 and V2, and Q waves in lead III and aVF. Hence, at CHBAH all pregnant cardiac patients have a baseline ECG assessment and ECHO at their first visit. The need for follow up ECGs and ECHO are dependent on the development of cardiac and pregnancy complications. These investigations may also be performed six weeks post-partum and is especially important when cardiac decompensation is diagnosed antenatally or intra-partum.

2.8 Justification

CHBAH has one of the largest obstetric units in South Africa. The hospital's wide referral catchment area allows a representation of the burden of disease in our population. The impact of pregnancy on cardiac disease will provide valuable information in the management and counselling of patients in the future.

3.0 AIMS AND OBJECTIVES

1. To determine the maternal morbidity and mortality in cardiac patients presenting at CHBAH.
2. To determine obstetric outcomes in cardiac patients delivering at CHBAH.
3. To obtain information about specific cardiac conditions in pregnant women and their obstetric management at CHBAH.
4. To determine neonatal outcomes of babies born to mothers with cardiac disease at CHBAH.
5. To determine the short-term effects of pregnancy on the underlying cardiac lesion in cardiac patients presenting at CHBAH.

4.0 MATERIALS AND METHODS

4.1 Setting

The study was conducted at CHBAH, a tertiary hospital located in Soweto, Johannesburg. CHBAH is one of the teaching hospitals associated with the University of the Witwatersrand. The maternity department delivers more than 22 000 babies annually. It serves as a referral centre for patients from Greater Soweto, Orange Farm, Lenasia, Eldorado Park, the Vaal Region and Heidelberg. It also supports Klerksdorp, Natalspruit, Sebokeng and Sedibeng Hospitals.

The obstetric cardiac antenatal clinic adopts a multidisciplinary team approach, which involves obstetricians, fetal medicine specialists and cardiologists in assessment and management of pregnant women with cardiac disease.

4.2 Study Population, Inclusion and Exclusion Criteria

Post-delivery cardiac patients were approached for consent to participated in the study. We also included cardiac patients who demised antenatally, intra-partum or post-delivery after obtaining consent from their families. Those whose families declined consent were excluded from the study. Recruitment took place within a six-month period.

4.3 Sample size

Forty-two (42) patients were recruited during the six-month period.

4.4 Study design

This was a prospective, descriptive study.

4.5 Data Collection

Detailed demographic, obstetric, medical (including drug history specifically noting the use of warfarin in the first trimester and dosage, and HIV status) and surgical history were taken (including the type of cardiac lesion and prior cardiac surgical procedures performed). This information was collected from the patient's antenatal records, ECHO, ECG, and cardiology records. Patients were interviewed to determine more detailed information regarding previous pregnancy outcomes and cardiac complications which were not available in the antenatal records. The NYHA class and haemoglobin level at first visit was noted. Patient confidentiality was maintained at all times and consenting patients were assigned a research number. For patients below the age of 18 years, relevant consent was obtained from the parent/legal guardian. Consent for the use of information of the deceased patients was acquired from the spouse/partner/parent/guardian. Staff (registrars and nurses working in maternity department) were informed about the study verbally and through posters and they alerted the researcher telephonically of any admission of a cardiac patient to the Maternity High Care Area, Ward 64 (high risk postnatal ward), Main Intensive Care Unit or Cardiac Intensive Care Unit. Files of all patients were reviewed for any cardiac or obstetric complications. Cardiac complications were subdivided into primary or secondary events.

A primary event was defined as cardiac death, cardiac arrest, stroke, arrhythmias, or congestive cardiac failure. Decline in NYHA class, pulmonary oedema and pulmonary hypertension were considered secondary cardiac events. Delivery data including gestational age at delivery, mode of delivery, use of assisted delivery, birth weight, fetal or neonatal outcomes was collected.

Obstetric complications included gestational hypertension with or without proteinuria (defined as a blood pressure of 140/ 90 mmHg or more, on 2 occasions at least 4 hours apart), postpartum haemorrhage (defined as estimated blood loss >500ml following vaginal delivery or >1000ml during or after caesarean section or requiring blood transfusion), preterm labour (defined as onset of labour before 37 completed weeks of pregnancy), preterm rupture of membranes (defined as rupture of membranes before the onset of labour prior to 37 completed weeks of pregnancy) and antepartum haemorrhage (defined as bleeding from the genital tract from 24 completed weeks (viability) of pregnancy up to the first stage of labour).

Repeat antenatal ECHO results were compared to ECHO results six weeks postpartum to assess the impact of pregnancy on the underlying cardiac defect.

Neonatal information was obtained by follow up visits to the neonatal ward during the first seven days of admission and consent was obtained from the mother for use of this data. Fetal or neonatal events were defined as:

- Miscarriage (pregnancy loss before 24 completed weeks)
- Intrauterine fetal death (IUFD)
- Warfarin embryopathies which range from mild to moderate (facial, skeletal, central nervous system and cardiovascular anomalies)
- Intracranial bleed secondary to warfarin
- Other structural or chromosomal abnormalities in patients who are not on warfarin.
- Termination of pregnancy
- Intrauterine growth restriction (ultrasound measurement of the abdominal circumference that is less than 5th centile, which is the cut off used by the CHBAH Fetal Assessment Centre)

- Preterm delivery (<37 completed weeks of gestation)
- Respiratory distress syndrome (using Apgar score)
- Admission to Neonatal Intensive Care Unit (NICU) or Transitional Intensive Care Unit (TICU) or Special Baby Care Unit (SCBU) or Ward 66 (medical neonatal ward)
- Early neonatal events (hypoxic ischaemic encephalopathy (HIE) or early neonatal death (occurring between birth and age 7 days of life)
- Low birth weight (<2500g), very low birth weight (<1500g), extremely low birth weight (<1000g)

A Microsoft Excel datasheet was used to capture data corresponding with the patient's research number. This information was kept confidential by the researcher.

4.6 Funding

Most of the requirements for the study were stationery which was funded by the researcher.

4.7 Statistics

Descriptive data were presented as means with standard deviations, and medians with ranges. Analyses were carried out using the Statistical Package for Social Sciences version 13 (SPSS 13)

4.8 Ethics and Consent from Hospital Management

The Human Research Ethics Committee approved the study (Protocol Number M130736).

The CEO of CHBAH gave permission for the study to be conducted at the hospital.

5.0 RESULTS

5.1 Demography

Forty-two patients were recruited into the study. All patients were black and were between the ages of 19 to 42 years. Nine women were of advanced maternal age (> 35years) and one was a teenager. Four of the patients were smokers. The average body mass index (BMI) was approximately 28.3 of the 29 patients who had both weight and height measurements.

One of the 42 pregnancies was a multiple (twin) pregnancy. Five women presented with anaemia (Hb < 11g/dl) on their first antenatal visit. Fourteen patients were HIV reactive, of which twelve were on antiretroviral (ARV) treatment. Thirty patients had fetal anomaly scans. Ten of the patients were primigravid. There was one grand multiparous patient with a parity of 7. One patient had a poor obstetric history of 5 previous IUFDs at 4, 5, 7, 7 and 8 months. She had mitral stenosis secondary to RHD with a valve area of 2.1cm^2.

5.2 Medical History

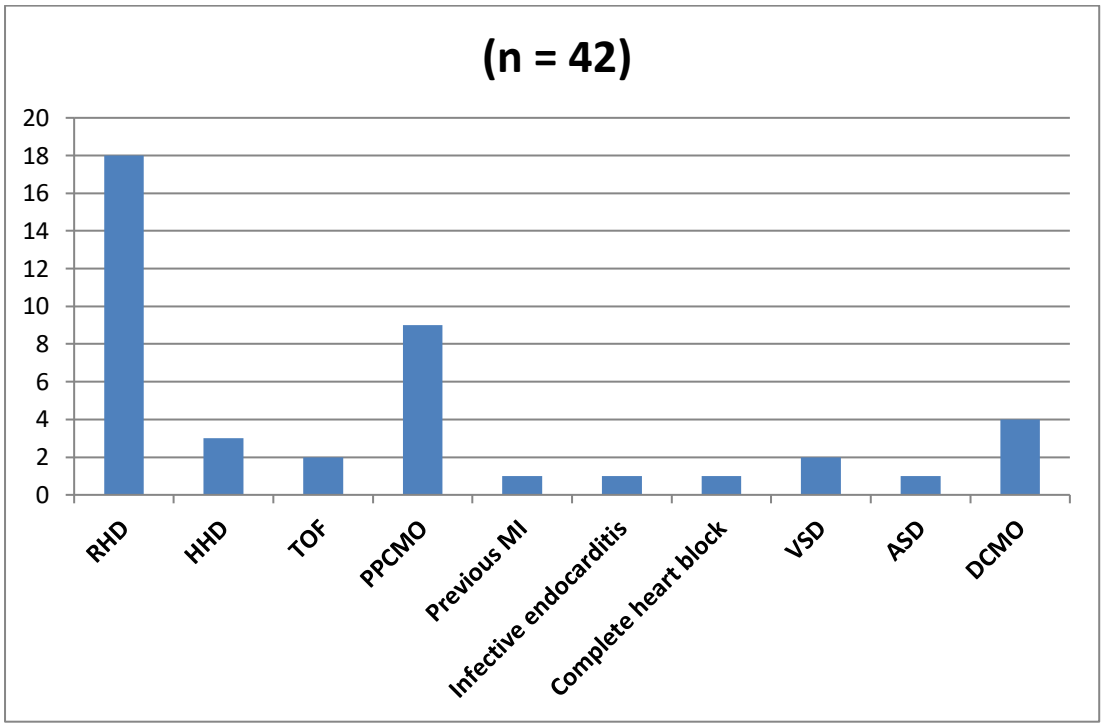

Figure 5.1 Types of cardiac lesions found in women enrolled in our study

Figure 5.1 indicates the distribution of the types of cardiac lesions. RHD was the commonest lesion followed by PPCM. In our study, the mitral valve was the most commonly affected valve in patients with RHD (11 patients). The aortic valve was affected in 3 patients and in 2 patients, both the mitral and aortic valve were affected. Three patients had involvement of both the mitral and tricuspid valves. Two patients had moderate to severe mitral stenosis with valve areas of 1.2 cm^2 and 0.8 cm^2 respectively.

Of the 18 patients with RHD, 4 had metallic valve replacements of the mitral valve and were on warfarin. One patient was on warfarin for atrial fibrillation. Three of these patients were on a dose of 5mg daily while 2 patients were taking 5 mg and 7.5 mg on alternate days.

Nine patients were diagnosed with PPCM. Five of these patients were diagnosed in previous pregnancies and the remaining four were diagnosed during their current pregnancy or post-partum.

Four patients with DCMO were recruited. Two of the patients were diagnosed during their index pregnancy. Three patients presented with newly diagnosed HHD. One of the patients presented in biventricular failure with a NYHA class of II at 36 weeks gestation. Two patients with VSDs were recruited to the study. One of the patients had had a prior VSD repair and pulmonary valvotomy at the time of surgery. She later went on to have pulmonary valve replacement.

Two patients with TOF were recruited. One patient had a repair in childhood while the other patient was newly diagnosed at 35 weeks gestation. One patient with an ASD was recruited. One patient with a complete heart block diagnosed at 33 weeks gestation was enrolled in the study. One patient with a previous history of infective endocarditis and one patient with previous myocardial infarction were also recruited.

Twenty-four patients were on prophylactic doses of furosemide, and of these patients 14 were also on beta-blockers.

5.3 Baseline assessment of cardiac function at first booking or presentation

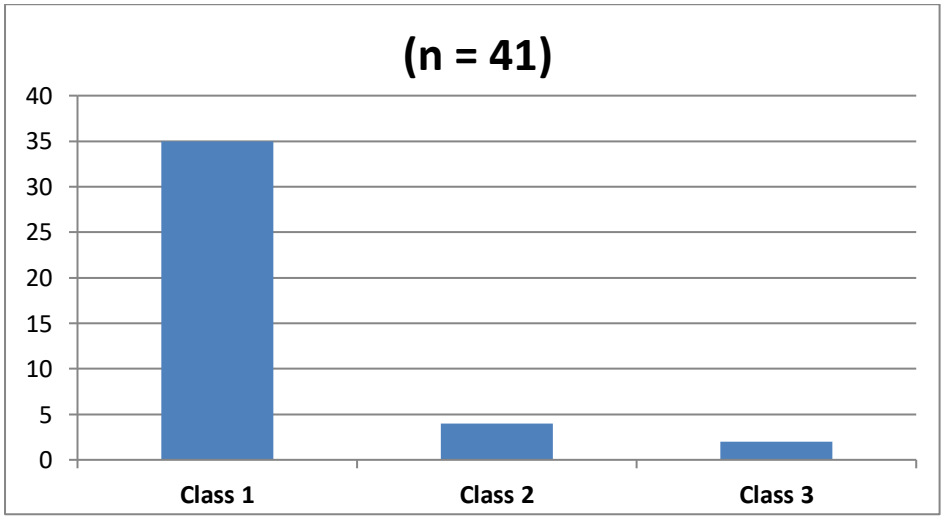

Figure 5.2 Distribution of NYHA class at first antenatal booking

Thirty-five patients booked with a NYHA class of I. One patient with PPCM did not have the NYHA class determined at first presentation.

Table 5.1 Left ventricle Ejection Fraction in women with the various types of cardiac lesions at antenatal booking or first presentation

Cardiac Lesion	n	**Mean ± Standard deviation**	**Minimum**	**Maximum**
RHD	15	60.27 ± 9.98	42.2	77.3
HHD	2	25.50 ± 13.44	16.0	35.0
TOF	1	55.00	55.0	55.0
PPCM	9	43.80 ± 21.67	15.0	82.0
Previous MI	1	56.70	56.7	56.7
Infective endocarditis	1	72.00	72.0	72.0
Complete heart block	1	68.00	68.0	68.0
VSD	2	64.50 ± 6.36	60.0	69.0
ASD	1	45.00	45.0	45.0
DCMO	3	37.00 ± 15.72	20.0	51.0
Total	37	52.15 ± 17.61	15.0	82.0

Patients with PPMC, HHD and DCMO had the lowest Ejection Fractions. (Table 5.1) Patients who had an EF <35% were on therapeutic enoxaparin at 1mg/kg 12 hourly and factor Xa levels were kept between 0.8 – 1.2 U/ml.

Eighteen cardiac patients presented with abnormal ECGs at booking or first presentation. Ten of the patients had underlying RHD, four had PPCM, and two patients had HHD while one patient had TOF.

5.4 Maternal complications

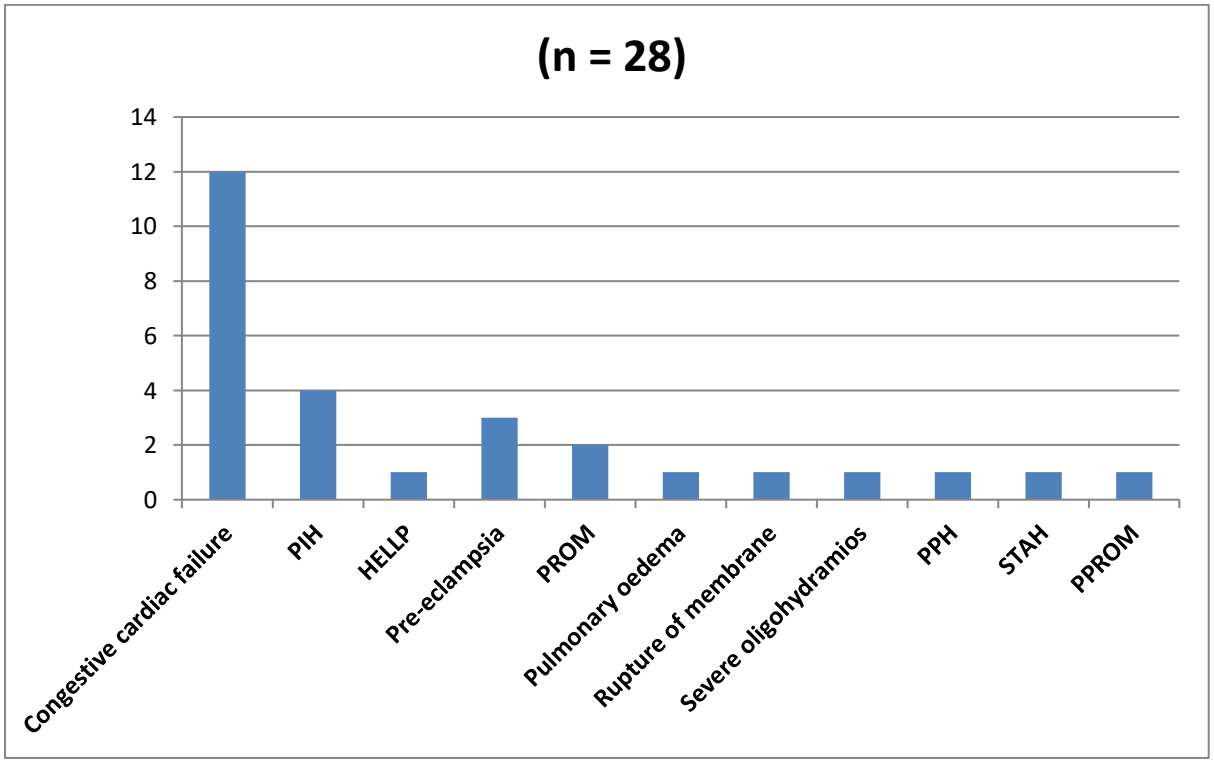

Figure 5.3 Cardiac and Obstetric complications noted in the study participants

Figure 3 indicates that CCF was the predominant complication experienced by pregnant patients with cardiac disease at CHBAH, followed by PIH and pre-eclampsia. Obstetric complications accounted for 57.9 while 42.1% were cardiac related. Three of the patients suffered both obstetric and cardiac complications. A caesarean section performed for obstetric reasons in a patient with RHD (not on

anticoagulation) was complicated by PPH and a subtotal abdominal hysterectomy (STAH) had to be performed.

Three of the patients with PPCM presented with ejection fractions of <20% and required heart transplant. Eleven of the recruited patients suffered deterioration in the NYHA class from functional class II to III. No maternal deaths due to cardiac disease in pregnancy were reported immediately post-delivery (within 7 days).

5.5 Ejection Fraction Comparisons

Table 5.2 Comparisons between antenatal and postnatal Ejection Fractions

Cardiac Lesion	**Antenatal EF (%)** **n=11**	**Postnatal EF (%)** **n=11**
RHD	51.1	49.4
PPCM	62	61.2
RHD	77	62
RHD	60	56.8
Complete Heart Block	60	44.8
VSD	60	50.4
ASD	45	43.2
DCMO	40	42.8
PPCM	56	45
PPCM	55	52.9
RHD	57	57.4

Table 5.2 shows that of the 11 patients who had repeat ECHOs post-partum 9 showed reduction in the EF post-delivery while 2 patients had a slight improvement.

5.6 Pregnancy outcomes

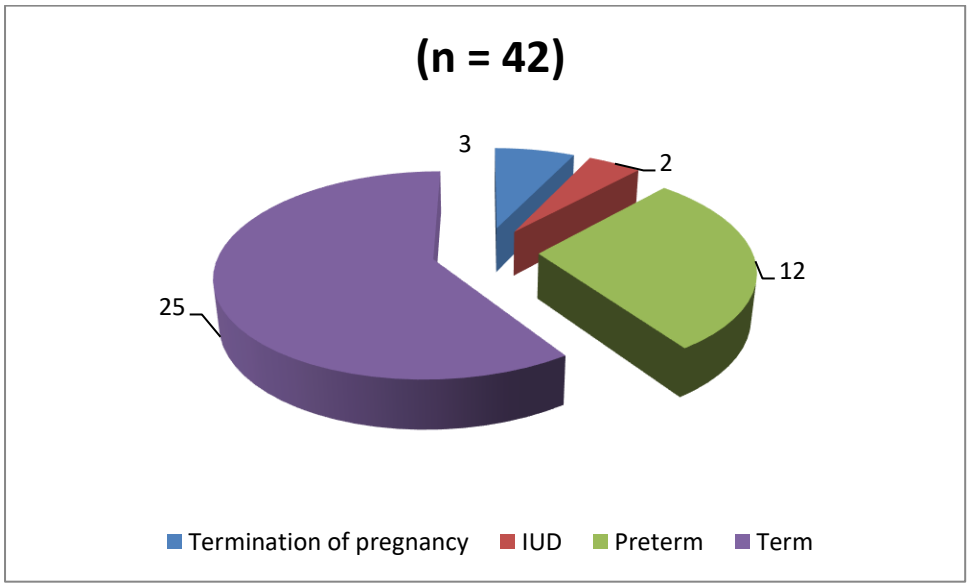

Figure 5.4 Outcomes of pregnancies

Figure 5.4 indicates that most patients had term deliveries. One of the term babies was a macerated still birth (MSB), the remainder were live births. All preterm deliveries were live births. Two patients, who were diagnosed with PPCM in their previous pregnancies, opted for termination of pregnancy at 8 and 11weeks gestation.

Table 5.3 Types of cardiac lesion and pregnancy outcomes

Type of cardiac lesion	**Termination of pregnancy**	**IUD**	**Preterm**	**Term**	**Total**
RHD	0	2	5	11	18
Hypertrophic heart disease	1	0	0	2	3
TOF	0	0	1	1	2
PPCMO	2	0	2	5	9
Previous MI	0	0	0	1	1
Infective endocarditis	0	0	0	1	1
Complete heart block	0	0	0	1	1
VSD	0	0	1	1	2
ASD	0	0	0	1	1
DCMO	0	0	3	1	4
Total	3	2	12	25	42

Table 5.3 shows that two patients with RHD experienced fetal losses. Three terminations of pregnancy were performed. Two patients had PPCMO and opted for first trimester (8 and 11weeks) termination of pregnancy following counselling of the risk of continuing with the pregnancy. The third was a patient with HHD and had a medically indicated termination at 31 weeks and 5 days of pregnancy following a deterioration of NYHA class of I to III complicated by CCF. The baby was stillborn, weighing 850g.

Table 5.4 Type of cardiac lesion and mode of delivery

	NVD	**Caesarean Section**	**Total**
RHD	4	12	16
HHD	2	1	3
TOF	0	2	2
PPCMO	3	5	8
Previous MI	0	1	1
Infective endocarditis	1	0	1
Complete heart block	0	1	1
VSD	1	1	2
ASD	0	1	1
DCMO	2	2	4
Total	13	26	39

Table 5.4 shows that most patients delivered by caesarean section. Of those who had a normal vaginal delivery, 3 were assisted. One delivery was assisted by forceps for a patient with a VSD (EF 69%) at 35weeks gestation while the other two were vacuum deliveries for patients with DCMO (EF 41%) and RHD (EF 65%) at 36 weeks and 40 weeks of gestation respectively. A hysterotomy was performed for a patient who presented at 28 weeks of pregnancy with an IUFD following failed induction of labour with misoprostol. The patient had had a metallic mitral valve.

5.7 Fetal outcomes

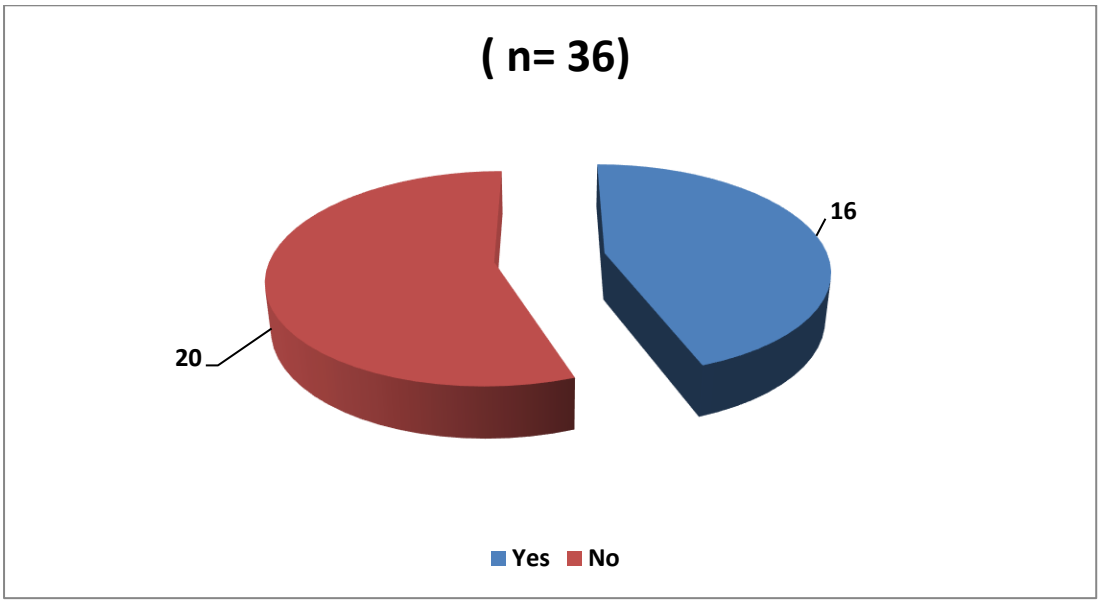

Figure 5.5 Presence of IUGR

Figure 5.5 shows that 16 of the babies born to the women enrolled for the study had IUGR. None of the babies had congenital abnormalities or suffered early neonatal deaths or HIE. Two babies were admitted to NICU. One of the babies had an extremely low birth weight of 850g while the other baby was admitted for very low birth weight (1550g), PDA and RDS. Two other babies were admitted to Ward 66 and had birth weights of 1690 g and 1915 g respectively.

Table 5.5 Fetal Weight Distribution

Birth Weight (g)	**Total number, n=40**
< 500	1
500 – 799	0
800 – 999	2
1000 – 1499	0
1500 – 1999	6
2000 – 2499	7
>2500	24

One fetus with a weight of less than 500 g was an IUFD in a patient on warfarin. (See Table 5.5). In the 800-999 g category, one of the babies was also an IUFD (955 g) delivered via hysterotomy, while the other baby was a live birth weighing 850 g with severe IUGR at 31 weeks of gestation.

Table 5.6 Apgar Scores

		n	Minimum score	Maximum score	Mean score ± Standard deviation
APGAR after 1 minute	RHD	15	4	9	8 ± 1
	Hypertensive heart disease	2	9	9	9
	TOF	2	7	9	8 ± 1
	PPCMO	5	8	9	8 ± 1
	Previous MI	1	9	9	9
	Infective endocarditis	1	8	8	8
	Complete heart block	1	9	9	9
	VSD	2	3	9	6 ± 3
	ASD	1	9	9	9
	DCMO	4	8	9	8 ± 1
	Total	34	3	9	8 ± 2
APGAR after 5 minutes	RHD	14	9	10	9 ± 1
	Hypertensive heart disease	1	10	10	10

	TOF	1	5	5	5
	PPCMO	5	8	10	9 ± 1
	Previous MI	1	10	10	10
	Infective endocarditis	1	10	10	10
	Complete heart block	1	10	10	10
	VSD	2	9	9	9
	ASD	1	10	10	10
	DCMO	4	9	10	9 ± 1
	Total	31	5	10	9 ± 1

Table 5.6 shows Apgar scores at 1 and 5 minutes. Three babies were born with a low one-minute Apgar scores. Their 5-minute scores improved after resuscitation. They had birth weights of 1690 g, 2159 g, and 2255 g respectively. The baby with a weight of 1690 g was admitted to ward 66 for very low birth weight.

6.0 Discussion

Underlying cardiac disease in pregnancy has a significant impact on the maternal and fetal morbidity and mortality. The presence of a multidisciplinary team involved in the management of this group of patients allows for better pregnancy outcomes.

Soweto has a largely black population area as seen by the unbiased recruitment of black patients in the study.

The HIV rate was slightly higher in this small cohort (33.3%) compared to national statistics. In the retrospective study done by Nqayana et al they had a similar figure of 33%.[2] The uptake of antiretroviral medication is a good reflection of the importance of counselling and the Prevention of Mother to Child Transmission (PMTCT) program in preventing vertical transmission. None of these patients had worse outcomes that could be attributed to their HIV status and this was also reflected by Nqayana et al. were the maternal morbidity and adverse fetal outcomes were associated with anticoagulation and late presentation, not with HIV serostatus.[2, 4]. Acquired cardiac lesions accounted for 88.1% of the underlying cardiac lesion in pregnant women delivering at CHBAH. The most common underlying lesion was RHD (42.9 %). This incidence was comparable to the incidence of 36% that was reported of in the Heart of Soweto Study for RHD. Although a higher incidence of 81% was reported by Nqayana et al. in the retrospective review of 95 patients presenting over a period of one year.[1, 2] Most of the Sowetan population are of low socioeconomic status. They experience economic hardships such as overcrowding and poor service delivery. Although health facilities are available, they are not always

readily accessible and appropriate treatment may not always be offered. This may be a contributing factor to the prevalence of RHD in the community.[5]

In the study, the indication for therapeutic anticoagulation was mainly for prosthetic heart valves, atrial fibrillation or an EF <35%. Other subsets of pregnant patients who also require anticoagulation include those suffering from deep vein thrombosis (DVT), pulmonary embolism and antiphospholipid syndrome (APS). Prophylactic doses may be required post caesarean section in high risk (obese or immobile) patients. Maternal and fetal risks and benefits of the different anticoagulants should always be highlighted during counselling of patients on anticoagulants. Warfarin was the preferred anticoagulant for five patients in the study. Two of these patients were on warfarin 5mg alternating with 7.5mg daily. They both experienced fetal losses at 21 and 28 weeks gestation which is consistent with literature if the dose of warfarin exceeds 5mg per day.[2, 23] The cause of the fetal loss at 21 weeks gestation was attributed to hypercoagulation as the patient had an INR of 5.9 on admission. The cause of the fetal loss at 28 weeks of pregnancy could not be established as the maternal INR was within the therapeutic range (2.9), morphologically no warfarin embryopathy was evident on fetal examination and there was no clinical evidence of a retroplacental bleed. On the other hand, three patients on 5 mg of warfarin daily delivered live babies at term. None of the babies showed any signs of warfarin embryopathy which is consistent with literature about its rarity (<5%).[24]

Hameed at el. looked at the effect of valvular heart disease on maternal and fetal outcomes of pregnancy. Although they had a subgroup of 44 patients with predominantly mitral valve disease, they established a clear relationship between the

severity of mitral stenosis and maternal and fetal outcomes. They found a significantly higher incidence of CCF, arrhythmias and hospitalizations in patients who had moderate and severe mitral stenosis. The incidence of preterm birth and IUGR was also high .[32] In our study, there were two patients with mitral stenosis. Due to the severity of their mitral stenosis, secondary cardiac complications had been anticipated during their pregnancies, but both patients did not suffer any secondary cardiac complications. One patient who had severe mitral stenosis with a valve area of 0.8 cm^2 delivered a 1915 g baby at 35 weeks gestation. The other patient with moderate mitral stenosis with a valve area of 1.2 cm^2 delivered a 1690 g baby at 37 weeks. Both babies had low birth weights.

Although the NYHA class is influenced by the patients' perception of symptoms, it is encouraging that most of the study patients booked or presented with a NYHA class of I which tends to favour good outcomes in the patient as well as the fetus. Patients with PPCM, HHD or DCMO tend to have lower EF as the left ventricle is the affected chamber, hence the reduction in the cardiac output leading to CCF.[9, 18, 19] In the study, both patients who presented with a NYHA class of III were diagnosed with PPCM. They had EFs of 20% and 42%. The patient with an EF of 20% warranted therapeutic clexane, lasix and carvedilol. A repeat ECHO showed an improvement in the EF to 41% prior to delivery. With the knowledge that during pregnancy the peripheral vascular resistance decreases in cardiac patients, it is not surprising that an underlying cardiac defect coupled with the abnormalities of placentation can increase the peripheral vascular resistance, further aggravating the cardiac function. This can result in CCF, cardiac arrhythmias and pulmonary oedema among some of the cardiac complications.[21]

Fetal risks depend on the type of underlying maternal cardiac lesion.[33] In this cohort fetal risks increased if the mother had underlying RHD or PPCM. Cardiac patients tend to deliver babies who are small for gestation age as compared to the general population, as can be seen from the results of the study. Although a reduction in the EF can negatively affect uterine perfusion contributing to the pathology of IUGR, another confounding factor is the medication that cardiac patients require. These include diuretics and beta-adrenergic blocking agents which have been also associated with impairment of uterine blood flow hence, increasing the incidence of IUGR which was also observed in the study done by Hua et al.[34] The IUGR rate was 55.6% in our study, while the preterm birth rate was 32% of the babies. Hua et al. observed the presence of IUGR in relation to the NYHA class. The risk of IUGR increased with the worsening of the NYHA class (NYHA class I – 3.4%, II – 5.5%, III – 22.5%, IV – 26.5%).[34] Nqayana et al. only noted the low birth weights and not the presence of IUGR nor the incidence of preterm births hence we were unable to make comparisons with that study.[2]

PPCM had an incidence of 21.4% in the study. Patients with residual left ventricular dysfunction within 6 months and prior to subsequent pregnancy are at an increased risk of worsening cardiac failure (50%) and death (25%) or recurrent PPCM in subsequent pregnancies.[14] Three patients presented with ejection fractions of <20% and required heart transplants. They were discharged after extensive counselling about the poor prognosis as there were no available donors.

Termination of pregnancy is seldom indicated unless a patient has severe cardiac disease in early pregnancy (NYHA class III or IV).[23] Five patients had been diagnosed with PPCM in previous pregnancies. Of these patients, two (both 33 years

old) opted for termination of pregnancy in the first after counselling about the potential risks of the pregnancy on the underlying cardiac disease as they had an EF of 44% and 45% respectively. They had parities of 4 and 1 respectively.

One of the principles of the treatment of PPCM is emphasis on post-partum sterilisation.[35] Due to the substantial risk of pregnancy in cardiac patients only two offspring are permissible.[36] Patients should always be informed about the potential risks in subsequent pregnancies and the need for pre-pregnancy cardiac assessment.[9] A multiparous patient (para 7) previously diagnosed with PPCM presented with an ejection fraction of 36%. Her pregnancy was complicated by a decline in the NYHA class, CCF, severe left ventricular dysfunction with mitral regurgitation. This patient should have been a permanent method of contraception. Contraceptive uptake may be hampered by religious and cultural backgrounds. Limited availability of contraceptive options in the public health facilities and their inconsistent use, contribute to unplanned pregnancies. Women are not always self-empowered about their health and in some African households it is the duty of the husband to make decisions regarding the family's health and family planning issues.

One of the patients, aged 24 years with PPCM and an EF of 43% experienced an IUFD at term. Delivery was by caesarean section following failed induction of labour with misoprostol. The baby had normal morphology, weighed 3745g and no attributable cause could be found.

Grewal et al. highlighted the increased risk of cardiac complications in patients with NYHA class of III or IV and/or moderate to severe left ventricular dysfunction, with an

incidence of 39% of pregnancies.[19] In this study, four patients had DCMO. Two of the patients presented with a NYHA class of III. One of these patients had an initial EF of 21% on presentation and improved to 41%, she also developed PIH and developed of PPROM at 36 weeks of pregnancy. The other patient, with twin pregnancy, had an EF of 42% and went on to have an uneventful caesarean section at 36 weeks of pregnancy. The other two patients had normal NYHA class with EF of 40% and 51%. Their pregnancies were complicated by IUGR. Despite the high risk in this group of women, complications were successfully managed medically and hence, there were no perinatal or maternal adverse effects.

HHD was diagnosed in 7.1% of patients. Oakley et al. had observed good pregnancy outcomes in women with HHD concluding that pregnancy can be well tolerated. However, Elkayam et al. showed worsening of NYHA class (58%) and a cardiac failure rate of 20% in patients with HHD.[36] In this study two of the patients developed severe CCF with a decline in the NYHA class to III. One of these patients developed severe IUGR and the pregnancy was terminated at 31 weeks gestation. The baby weighed 850 g and was admitted to NICU. The third patient with an initial NYHA class of I had an uneventful pregnancy and delivery. She suffered no immediate post-partum complications. The baby was delivered vaginally at 39 weeks gestation with an appropriate for gestational weight of 3565 g.

Three patients who had previous myocardial infarction, previous infective endocarditis and a complete heart block had normal ECHOs. They had uneventful pregnancies and deliveries at term of normal babies with no evidence of IUGR or congenital abnormalities.

Congenital cardiac disease (TOF, VSD and ASD) accounted for 11.9 % of the study patients. When correlating maternal mortality risk to the type of cardiac lesion, all three conditions, including a repaired TOF, are associated with a low maternal mortality risk of <1%. Before repair of TOF was introduced in the 1950s, few patients reached child bearing age and successful pregnancy was uncommon.[37] In this study, the patient with undiagnosed TOF actually reached 35 weeks gestation before complicating with cardiac symptoms. Her pregnancy was complicated by an unexplained thrombocytopenia and right ventricular strain. A planned caesarean delivery at 37 weeks gestation for perceived cardiovascular risk to the mother was uneventful. Residual cardiovascular lesions after TOF repair is always a concern due to the possible progression of right ventricular dysfunction, ventricular or atrial dysrhythmias, thromboembolic phenomena, progressive aortic root dilatation and endocarditis. This can lead to maternal and fetal death in the presence of severe PHT and IUGR.[37] The patient who had TOF repair in childhood had a complicated pregnancy. She developed CCF, severe pre-eclampsia and HELLP syndrome. An induction of labour at 34 weeks gestation failed and she required a caesarean section that was uneventful. Babies born to these patients were diagnosed with IUGR. Veldtman et al. found an incident of 30% of small for gestational age babies in their subgroup analysis of patients who had unrepaired TOF at the time of pregnancy.[37] Nqayana et al. noted one patient with TOF in their study. Comparisons of outcomes could not be made as the patient was in cooperated in the CHD group.[2]

Of the two patients with VSD, one of them had a VSD repair and pulmonary valve replacement six years prior to pregnancy. She had a NYHA class 1 with an EF of 69%. Her pregnancy was eventful as she had preterm prelabour rupture of

membranes (PPROM) at 35 weeks gestation and delivered a baby with a low birth weight of 2255 g via assisted vaginal delivery. The other patient had a normal EF of 60% and had an uneventful pregnancy and caesarean section delivery at 37 weeks. The baby was born with a birth weight of 2630 g.

No prior repair was done for the patient with ASD. She had an EF of 45%. Her pregnancy was uneventful, and she delivered a 2540 g baby at 40 weeks gestation via caesarean section.

In the study caesarean sections were performed for obstetric indications. The caesarean section rate in the study was 66.7% which is comparable with the study done by Nqayana et al., which had a caesarean section rate of 56%. They attributed the high caesarean section rate to the reflection of high-risk obstetric status of patients managed at a tertiary centre which also applies to CHBAH.[2] Labour monitoring was more intensive and frequent to avoid prolonged labour and difficult deliveries,[35] which contributed to the increase in the caesarean section rate in the study cohort. Expedition of the second stage of labour with either vacuum or forceps is also recommended. The choice of either will depend on the skill of the attending obstetrician and the need to prevent the Valsalva manoeuvre.

The benefit of a multi-disciplinary team approach to management of pregnant cardiac patient allows expert ECG interpretation by cardiologists. Hence, all the available ECGs of the study population were interpreted by them.

Due to loss to follow up and transfer back of patients to their respective hospitals, only eleven patients had a post-partum ECHO performed. An alarming 82% had worsened EFs post-partum. The numbers are too small to make a conclusion on the

residual effect of pregnancy on the underlying cardiac function but the negative effect on the EF in this study does suggest the need to counsel patients and advise on future conception.

7.0 LIMITATIONS

- Missing antenatal, intrapartum and post-partum cardiac and obstetric records.
- Failure of the staff to inform the researcher about potential patients, but all patients who were informed about the study, consented to recruitment and minimised inclusion bias.
- Losses to follow-up of patients for the six-week ECHO.
- Patients referred from referral hospitals such as Klerksdorp Hospital were followed up at their respective hospitals and hence, no follow up ECHOs was available at CHBAH.
- Only 42 patients were recruited for the study as the number of cardiac patients who presented was far less than anticipated over the six-month recruitment period.

8.0 CONCLUSION

RHD is still the predominant cardiac lesion among pregnant cardiac patients at CHBAH. There was a high percentage of pregnancies and deliveries without complications allowing us to conclude that pregnancy is possible when a multidisciplinary team is involved.

Pre-pregnancy counselling and education remains the most important intervention to reduce complications. This may be stressed as early as prior to cardiac surgery and at follow up cardiac clinic visits. This is vital for patients on anticoagulation and with poor baseline cardiac function.

It is difficult to establish the appropriate antithrombotic treatment which would be safe for the fetus, while effectively protecting the mother against any possible thromboembolic complications. Although warfarin is contra-indicated in pregnancy, it remains widely used to prevent thromboembolic complications. Patients should be encouraged to plan pregnancies to, prevent first trimester fetal exposure to possible teratogenicity.

The other high-risk group are the patients with poor. Pregnancy may result in worsening cardiac function and should be discouraged in these patients. This leads to the issue of effective contraception in these patients and bilateral tubal ligation is recommended after the second child.

The above interventions may however, be hampered by social and cultural community norms. Disempowerment and financial dependence on partners may worsen the situation.

All pregnant cardiac patients should be referred for first and second trimester screening as well as follow up scans. This is not only suggested for patients on anticoagulation, but all pregnant cardiac patients require close ultrasound surveillance. The high incidence of IURG noted in the study supports the need for this.

9.0 RECOMMENDATIONS

- The World Health Organisation (WHO) contraceptive legibility criteria should assist in the provision of appropriate and effective contraception for cardiac patients.
- Future contraceptive methods should be discussed during the antenatal period or first contact.
- Level three ultrasounds should be included in the routine management protocol for all pregnant cardiac patients to detect early signs of IUGR and allow the appropriate management.
- A multidisciplinary team approach improves management and outcomes of pregnant cardiac patients by early detection of complications or signs and symptoms of deterioration.
- Operative and assisted delivery should be more anticipated in pregnant cardiac patients following the findings in this study.
- The NYHA classification of symptoms remains the best method for patients and doctors to detect clinical stability or deterioration.

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DATA SHEET

Patient's Research Number:

DEMOGRAGHY

Relevent interview questions that may be asked if information is not in the antenatal records

Age (years)
Ethnicity: Black Caucasian Asian Asian Other Specify:
BMI (kg/m2):
Smoker: Yes No If yes, how many a day?

OBSTETRIC HISTORY

Number of fetus: Singleton Multiple
Fetal anomally scan: Yes No
Warfarin embryopathy: Yes No
Type of warfarin embryopathy: Facial Skeletal
Central Nervous System Cardiovascular
Other structural abnormalities not secondary to warfarin specify:
Previous pregnancy outcomes:

	Termination	Miscarriage	Preterm	Term	Birthweight
1					
2					
3					
4					
5					

Was the termination for medical reasons?
Did the doctors tell you what caused the miscarriage?
Did the baby have to stay in hospital because it was small and do you know what the weight was?
Did any of your babies die after delivery?
Did you use warfarin in the first three months of your pregnancy?

MEDICAL HISTORY

Type of cardiac lesion:

When was the heart problem diagnosed?
Were you pregnant when it was diagnosed?
How old were you when it was diagnosed?

NYHA functional class at first antenatal booking:

Current medication and dosage:

Warfarin	Heparin	Lasix	Digoxin
Antiarrthymics		Aspirin	Other Specify:

When was treatment started and doses?
Did you use warfarin in the first 3 months of pregnancy?
If yes, up to what month in the pregnancy?

ECG result at antenatal booking:

ECHO result at antenatal booking:

HIV result: Reactive CD4 count:

On ARVs: Yes No

Nonreactive

Not tested

What is your HIV status?
What is your latest CD4 count?
Are you taking antiretroviral drugs?

Haemoglobin level at antenatal booking:

SURGICAL HISTORY

Prior surgical procedures performed:

How old were you?
Did you have any heart surgery before you fell pregnant?

DATE OF DELIVERY:

PRIMARY CARDIAC EVENTS

Cardiac Death	Cardiac Arrest	Stroke
Cardiac Arrhythmia	Congestive Cardiac Failure	
Other Specify:		

SECONDARY CARDIAC EVENTS

NYHA Class Decline: Yes No

Pulmonary Oedema: Yes No
Pulmonary Hypertension: Yes No
Other Specify:

OBSTETRIC COMPLICATIONS

Gestational Hypertension: Yes No
Gestational Diabetes Mellitus: Yes No
APH: Yes No
Preterm Labour: Yes No
Preterm Rupture of membranes: Yes No
PPH: Yes No
Other Specify:

OUTCOME OF PREGNANCY

Miscarrige (gestational age): Termination of Pregnancy (gestational age):
IUD (gestational age):
Preterm/Term (gestational age): Weight (g):
Mode of Delivery: NVD C/S
Assisted Delivery: Yes Forceps
No
APGAR: 1 minute 5 minutes
Resuscitation: Yes No
Admission to : NICU TICU
Presence of intrauterine growth restriction: Yes No
Intracranial bleed secondary to warfarin: Yes No
Early Neonatal Events: Hypoxic ischaemic encephalopathy: Yes No
Early neonatal death: Yes No

FINDINGS OF POST DELIVERY CARDIOLOGY ASSESSMENT

Echo results 6 weeks post delivery

APPENDIX B

PATIENT INFORMATION CONSENT FORM

My name is Dr Maidei Mugwede. I am a registrar in the Department of Obstetrics and Gynaecology. As part of my training, I am carrying out a research that looks at cardiac disease in pregnancy. The research will look at the effect of the cardiac disease on the pregnant woman and the outcome of the pregnancy.

You are being asked to voluntarily participate in the study as you are specifically suitable to provide data for my study. I will be asking you a few questions which will take about 30minutes of your time and with your permission, have access to your file and the baby's information. All information will be kept confidential. No personal benefits will be obtained for your participation and the standard of care will remain the same.

If you decide to opt out during the course of the study, there will be no repercussion and you and your baby will continue to receive the best of care.

No personal benefits will be obtained for you participation and the standard of care will remain the same.

For more information you can contact me on my mobile number 082 400 8052.

If you have understood and are willing to take part in the research, kindly sign below.

Patient name:

Signature:

Date:

Research Number:

APPENDIX C

PARENTAL INFORMATION AND ASSENT FORM

My name is Dr Maidei Mugwede. I am a registrar in the Department of Obstetrics and Gynaecology. As part of my training, I am carrying out a research that looks at cardiac disease in pregnancy. The research will look at the effect of the cardiac disease on the pregnant woman and the outcome of the pregnancy.

You are being asked to give permission for your daughter to take part in the study as she is specifically suitable to provide data for my study. I will be asking her a few questions which will take about 30minutes of her time and with your permission, have access to her file and the baby's information. All information will be kept confidential. No personal benefits will be obtained for your participation and the standard of care will remain the same.

If on behave of your daughter decide to opt out during the course of the study, there will be no repercussion and your daughter and her baby will continue to receive the best of care.

For more information you can contact me on my mobile number 082 400 8052.

If you have understood and are willing to take part in the research, kindly sign below.

Parent's name:

Signature:

Date:

Research Number:

APPENDIX D

GUARDIAN INFORMATION AND ASSENT FORM

My name is Dr Maidei Mugwede. I am a registrar in the Department of Obstetrics and Gynaecology. As part of my training, I am carrying out a research that looks at cardiac disease in pregnancy. The research will look at the effect of the cardiac disease on the pregnant woman and the outcome of the pregnancy.

You are being asked to give permission for your daughter to take part in the study as she is specifically suitable to provide data for my study. I will be asking her a few questions which will take about 30minutes of her time and with your permission, have access to her file and the baby's information. All information will be kept confidential. No personal benefits will be obtained for your participation and the standard of care will remain the same.

If on behave of your daughter decide to opt out during the course of the study, there will be no repercussion and your daughter and her baby will continue to receive the best of care.

For more information you can contact me on my mobile number 082 400 8052.

If you have understood and are willing to take part in the research, kindly sign below.

Guardian's name:

Signature:

Date:

Research Number:

APPENDIX E

SPOUSE/PARTNER/GUARDIAN/PARENTAL INFORMATION AND ASSENT FORM FOR A DECEASED PATIENT

My name is Dr Maidei Mugwede. I am a registrar in the Department of Obstetrics and Gynaecology. My sincere condolences on the passing of your loved one. As part of my training, I am carrying out a research that looks at cardiac disease in the pregnancy woman and the outcome of the pregnancy.

I believe your loved one had an underlying heart problem and I am kindly asking for your permission to enrol her in the research by having access to her file as well as the baby's information. All information will be kept confidential. No personal benefits will be obtained for her participation.

For more information you can contact me on my mobile number 082 400 8052.

If you understood and give permission for your loved one to be in the study, kindly sign below.

Spouse/Partner/Guardian/Parental name:

Signature:

Date:

Research Number:

APPENDIX F

ETHICS CERTIFICATE

R14/49 Dr Maidei Mugwede

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M130736

NAME: (Principal Investigator)	Dr Maidei Mugwede
DEPARTMENT:	Obstetrics and Gynaecology University of Witwatersrand Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Outcomes of Pregnant Patients with Cardiac Disease at Chris Hani Baragwanath Academic Hospital
DATE CONSIDERED:	26/07/2013
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Jayshree Jeebodh
APPROVED BY:	Professor PE Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	07/08/2013

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 Secretary in Room 10004, 10th floor, Senate House, University.

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.**

Principal Investigator Signature

Date 10/08/2013

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX G

CEO PERMISSION TO CONDUCT RESEARCH

GAUTENG PROVINCE
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE
CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 05 July 2013

TITLE OF PROJECT: Outcomes of pregnant patients with cardiac disease at Chris Hani Baragwanath Academic Hospital

UNIVERSITY: Witwatersrand

Principal Investigator: Dr M Mugwede

Department: Obstetrics and Gynaecology

Supervisor (If relevant): Dr J Jeebodh

Permission Head Department (where research conducted): Yes

Date of start of proposed study: July 2013
Date of completion of data collection: Dec 2013

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Hospital. The CEO /management of Chris Hani Baragwanath 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 July 2013

.....
Approved/Not Approved
Hospital Management
Date: 20130708

APPENDIX H

TURNITIN

Assignments Page 1 of 1

Assignment List MMED Turnitin

MMED Turnitin

No due date was set by the instructor.

Submitted Apr 5, 2016 11:55 AM

Submitted Attachments

MMed Research Final Draft 2015.docx (436 KB) 18%

Assignment Details

Assignment Instructions

Return to List Resubmit Assignment

https://cle.wits.ac.za/portal/tool/4ac3ba8e-453d-4c2e-91e3-856dfd2d2649/student-sub... 2016/05/09