PERINATAL OUTCOME IN MOTHERS WITH HEART DISEASE ATTENDING THE COMBINED OBSTETRIC AND CARDIOLOGY CLINIC AT GROOTE SCHUUR HOSPITAL

Catherine Elliott

Supervised by

Professor John Anthony

Dr Catherine Elliott MB ChB (2000), FCOG (2011), MMed (2012)

MP 0540005

Department of Obstetrics and Gynaecology Groote Schuur Hospital

Email: cath@catherine-elliott.co.za

Correspondence Address

PO Box 43908
Fish Hoek
7974

Work: 021 422 1048

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ABSTRACT

Introduction

With the advances made in the management of cardiac conditions, much importance has been placed on the maternal outcome in pregnancies complicated by heart disease. However, to enable attending clinicians to provide suitable counseling and manage the pregnancy appropriately, the potential complications arising in the fetus and neonate also require attention. Adverse neonatal and perinatal outcome is more common in pregnant women with cardiac disease. Analysis of the available data pertaining to the South African population is important, as this population's profile, like that of Africa, differs from that of industrialized countries. The relevance of maternal heart disease is highlighted by the National Committee for the Confidential Enquiries into Maternal Deaths (NCCEMD) in South Africa (http://www.doh.gov.za/docs/reports/2012/Report_on_Confidential_Enquiries_into_Maternal_Deaths_in_South_Africa).

Objectives

To describe the perinatal outcome in women with heart disease and to determine whether there is an associated adverse outcome related to babies born to mothers with heart disease.

Methods

82 patients were collected serially over 18 months. Neonatal outcome was recorded. Adverse neonatal outcome was defined as perinatal mortality, admission to NICU and the need for delivery room resuscitation.

Results

Perinatal mortality rate in this cohort was good, and better than the rate in the general population from whence this cohort came, but was linked to a high rate of obstetric intervention. The rate of adverse neonatal outcome is better than the rate in industrialized countries.

Conclusion

Perinatal outcome is good when mothers with heart disease are managed in a multidisciplinary clinic.

INTRODUCTION

With the advances made in the management of cardiac conditions, much importance has been placed on the maternal outcome in pregnancies complicated by maternal heart disease. However, to enable attending clinicians to provide suitable counseling and manage the pregnancy appropriately, the potential complications arising in the fetus and neonate also require attention.

Previous published literature has shown that a detailed risk analysis allows for improved management during pregnancy and can serve to predict both maternal and neonatal morbidity.[1] Such assessments will enable clinicians to determine the level of surveillance required and allow for informed decisions prior to conception, throughout the pregnancy and in the postpartum period.[2]

Global perspective

Pregnancy in the presence of maternal heart disease remains an important topic for interrogation worldwide. Although mortality from heart disease in pregnancy is low in absolute terms, it remains the leading cause of indirect maternal mortality in developed countries,[1,3-8] whilst in developing countries it remains one of the major indirect causes of maternal death, prompting continuous efforts to improve screening, diagnosis and management of heart disease.

The aetiology of cardiac disease can either be congenital or acquired. Many congenital lesions are described and the prognosis for each may differ, depending on the structural changes within the heart and the progression of the disease.

In developed countries congenital heart disease (CHD) is the most prevalent form of cardiac disease in pregnancy. Due to advances in diagnosis and surgical intervention in infancy and childhood, most women with CHD reach childbearing age. In Europe, CHD makes up 80% of all heart disease in pregnant patients.[1]

The reduction in the number of maternal deaths, as well as the risk of maternal death in pregnancies complicated by heart disease in developed countries over recent years, is largely due to the advancement of interventions and corrective surgery for CHD.[1] However, despite improved survival, significant morbidity remains high.[3,5]

The nature of the presenting lesion, the effect of the lesion on cardiac function and other maternal characteristics, can predict the maternal outcome of cardiac disease during pregnancy. If the mother enters pregnancy with normal cardiac function, the risk of adverse outcome is less. The World Health Organization (WHO) has classified maternal disease into four categories. In this classification, category I has very little effect on the outcome of pregnancy, while category IV is considered a contraindication to pregnancy.[9]

African perspective

In developing countries the prevalence of disease differs significantly from that of developed countries. Congenital heart disease remains prevalent. However, the largest component of maternal cardiac disease in Southern Africa is valvular disease secondary to rheumatic fever. The incidence of rheumatic heart disease is estimated at 13 cases per 100 000 per year.[1,10]

Rheumatic valvular heart disease may involve any of the heart valves, however, mitral stenosis is by far the most common presentation,[10] and carries the greatest risk.[11] Mitral stenosis may not be well tolerated in pregnancy and the presence of maternal mitral stenosis has been described an independent predictor of maternal mortality.[10] Pregnant women with valvular heart disease have a statistically significant risk of cardiac events, clinical deterioration and adverse neonatal outcome.[12] Valvular heart disease is sometimes first diagnosed in pregnancy, making accurate risk assessment and management during pregnancy especially important.

South African perspective

Analysis of the available data pertaining to the South African population is important, as this population's profile, like that of Africa, differs from that of industrialized countries cited in the literature. The relevance of maternal heart disease is highlighted by the National Committee for the Confidential Enquiries into Maternal Deaths in South Africa. (http://www.doh.gov.za/docs/reports/2012/Report_on_Confidential_Enquiries_into_Maternal_Deaths_in_South_Africa). "Medical disorders in pregnancy", are grouped together as one of the top five causes for maternal mortality in South Africa. Within this category, cardiac disease is the most prevalent disorder. Further enquiry into the causes and consequences of heart disease in pregnancy occurring in South African women is necessary in order to improve the clinical outcome. In particular, the analysis of maternal heart disease should focus on severe maternal morbidity as this has been linked to poor perinatal outcome. The risk of a maternal cardiac event or the development of complications can be predicted by assessing baseline criteria of the mother prior to pregnancy and also at the time of the booking visit.[5,9]

The physiological changes in pregnancy

The physiological adaptions in pregnancy, designed to support the pregnancy and placental perfusion include circulatory adaptions. These are usually well tolerated in pregnancy, but may adversely affect cardiac function in the presence of heart disease.

The central adaption is peripheral vasodilatation with a decrease in peripheral vascular resistance. Following this, the cardiac output increases by about 40-50% mostly due to an increase in stroke volume and secondly due to an increase in the heart rate (10- 20 beats per minute) from about 60 bpm to 80 bpm.[13] The blood pressure will decrease due to the drop in peripheral vascular resistance. There is a 40-50% increase in blood volume and another 50% increase at delivery when there is an auto-transfusion of blood from the contracting uterus into the general circulation.[14] These changes can occur as early as the first trimester, and usually return to baseline by 6 weeks postpartum.[15]

The normal heart can tolerate these changes well, and pregnancies remain uncomplicated, however in the case of heart disease, be it structural or functional, the circulatory system may be compromised. The stressors placed on the heart may put the mother at increased risk of a cardiac event and even death, and any

decrease in cardiac output will reduce placental perfusion and result in potential fetal hypoxemia.

Neonatal outcome

Adverse neonatal and perinatal outcome is more common in pregnant women with cardiac disease - even when demographic and obstetric risk factors have been accounted for - and is partly related to maternal cardiac disease.[1,2,4]

The frequency of neonatal complications can be up to twice that of the control group and for each individual complication the risk is higher in the maternal heart disease group. The rate of occurrence of neonatal complications is 17-28%.[2,5] There is a clear relationship between the severity of the cardiac disease and fetal complications.[1,5]

Perinatal outcome can be measured in terms perinatal complications associated with maternal cardiac disease, and these include: premature delivery, (PTD) (prior to 37 completed weeks gestation,) respiratory distress syndrome (RDS), birth asphyxia, intrauterine growth restriction (IUGR), the delivery of babies small for gestational age (SGA) (with birth weight below 3rd percentile), intraventricular haemorrhage (IVH), early neonatal death (ENND) and stillbirth (SB) as well as inherited congenital cardiac lesions and those complications associated with maternal medication such as embryopathy (in the case of warfarin use).[2,3]

The perinatal mortality rate (stillbirths and early neonatal deaths) is between 1 – 4%.[4] This rate was significantly higher than the background population (1%) This may well be accounted for by the high rate of PTD in this group of patients resulting in more early neonatal deaths.

In sub-Saharan Africa the perinatal mortality rate associated with maternal cardiac disease is quoted as 7.6 %.[11] In this region adverse maternal and neonatal outcome appears to be significantly higher - almost double the rate reported by industrialized countries. The most significant cause for perinatal mortality in sub-Saharan Africa is preterm birth[3] with 16% of these deliveries occurring before 34 weeks.[1,4,5]

This is higher than the general background prematurity rate reported in the literature (10%). Iatrogenic preterm delivery may account for this increase because preterm delivery is sometimes indicated by complications arising from severe cardiac

disease. PTD rates are generally higher, the more complex the cardiac disease. In the case of CHD, PTD may occur in 22% of women with cyanotic disease and 65% in Eisenmenger syndrome. In these CHD lesions where PTD was reported to be higher, the perinatal mortality rate increased and in Eisenmenger syndrome it has been quoted as being as high as 27.7%.[4] The sequaele of PTD include RDS, pulmonary haemorrhage and IVH.[5]

Obstetric complications are specifically linked to certain cardiac disease. Coarctation of the aorta, pulmonary stenosis or transposition of the great arteries, have a higher risk of developing preeclampsia, which places the fetus at risk of IUGR, SB and iatrogenic preterm delivery.[4,16]

While there is agreement that cardiac disease in the mother places the fetus and neonate at greater risk than low risk pregnancies, it is important to consider also the likelihood of the pregnancy being successful.[4] The association between maternal cardiac disease and adverse perinatal outcome is highly correlated, and therefore, correct assessment of the maternal risk is necessary in order to provide increased surveillance where indicated. The literature has provided risk analysis frameworks for the assessment of maternal condition. These include the following maternal predictors of adverse neonatal outcome (Table 1).

Table 1: Maternal predictors of adverse perinatal outcome

Baseline NYHA >II or cyanosis
Maternal left heart obstruction
Smoking during pregnancy
Multiple gestation
Use of oral anticoagulants
Mechanical valve prosthesis
Symptomatic arrhythmia

Reasons for the increased rate of neonatal complications associated with the cited maternal risk factors vary.

NYHA >II and cyanosis at booking are independent risk factors for neonatal complications.[5] Fetal cardiac output is adversely affected by fetal hypoxemia resulting from utero-placental insufficiency,[2] a complication of diminished maternal

cardiac output or impaired oxygenation. For each percentage drop in maternal saturation reading, the risk to the fetus increases.[2] Maternal cyanosis similarly leads to IUGR, PTD and SB.[2,4,17]

There is also an increase in the risk of miscarriage to mothers with cyanotic lesions and/or those with poor NYHA functional class.[5] Maternal left heart obstruction can be quantified as a sub-aortic ventricular outflow gradient of >30mmHg.[2,3,5,9]

Even a moderate degree of mitral stenosis will have an adverse effect on the pregnancy as indicated in Table 1.[1]

Hameed *et al* reported that more than half the patients with moderate or severe valvular heart disease suffered some cardiac event with left heart obstruction common among this group of patients.[12]

They were especially at risk of CCF and arrhythmias. These complications led to a greater risk of PTD or the delivery of a neonate with signs of IUGR.[12]

Even events prior to pregnancy, such as arrhythmias, may increase the risk to the fetus and neonate.[5]

In addition, the effect of many cardiovascular drugs, for example β-blockers, have been shown to be related to an IUGR and prematurity.[12]

Smoking in these patients can add additional risk, although the mechanisms behind this are not fully understood. It may be that the advice to cease smoking may be even more critical in the management of these women. One surprising finding was that pulmonary HT was not associated with any fetal complications during pregnancy.[5]

The Addition of Obstetric Risk Factors

If none of the above risk criteria pertain, and there are no obstetric risk factors, the risk of adverse perinatal outcome remains very close to that of controls (about 4% in controls and 5% in cardiac patients). However, the potential adverse effect of maternal cardiac disease on neonatal outcome is amplified if there are concurrent obstetric risk factors (including a maternal age above 35 years).[2]

Early pregnancy loss

The rate of abortion (spontaneous or induced) has been reported to be as high as 20%.[3]

This figure is not significantly different to that of the general population. Although Drenthen *et al* described a miscarriage rate to be higher in patients with cyanosis (such as in the case of pulmonary atresia with VSD). The miscarriage rate in patients with Eisenmenger Syndrome was just over 10%, which is similar to that of a patient with an ASD or VSD. This is lower than the background rate of spontaneous miscarriage in the general population, which is estimated to be between 15-30%. Hence cardiac disease is not associated with an increased risk of miscarriage.[4]

Inheritance

Heritable factors may contribute to adverse perinatal outcome in women with cardiac disease.

In the general population the risk of a congenital cardiac abnormality is 1%. However, the risk to a fetus born to parents with CHD depends on whether the CHD is present in the mother or father or both parents. Generally the risk is slightly higher if the lesion is on the maternal side. Furthermore, the risk of inheritance (3-50%) depends on the type of lesion. A lesion associated with a condition such as Marfan's syndrome - which has an autosomal dominant pattern of inheritance - carries a risk of 50%. However, the final phenotype depends on the penetrance. Samuel *et al* and Khairy *et al*, describe the rate of congenital heart lesions found in offspring born to parents with CHD as approximately 7%. Drenthen *et al* describe an incidence of 0.6-8% depending on the type of lesion.[3,4,17]

Some cardiac lesions carry a far greater heritable trait as they are linked to certain genes. These lesions include coarctation of the aorta and a bicuspid aortic valve, which are highly heritable. *Truncus arteriosus* such as found in Di George syndrome (deletion of 22q11.2) follows an autosomal recessive pattern. ASD and VSD can be isolated lesions but can also be linked to genetic disorders including Holt-Oram, Towes-Brocks and other chromosomal abnormalities.[18]

Cardiac patients should be screened with a nuchal translucency (NT) scan: The risk of CHD in the presence of a normal NT is 1/1000 and the sensitivity of NT screening for cardiac defects is only 40%. Diagnostic accuracy may be increased in pregnant

women with lesions related to a syndrome by means of chromosomal analysis. Direct examination of the fetal heart takes place at 22 weeks when visualization of the heart and outflow tracts is possible.

Fetuses affected by CHD may be at risk of brain injury secondary to changes in fetal blood flow caused by the structural abnormalities of the heart. The blood flow in the fetus preferentially selects the passage of oxygen and nutrients from placenta to the fetal brain and structural defects in the heart associated with CHD may well impair this mechanism. In these cases the fetus may auto-regulate cerebral vascular resistance to increase cerebral flow. There is also an epidemiological association between complex CHD and babies born with small head sizes and IUGR. Postmortem examinations of fetuses who did not survive and ultrasound of the cranium of those neonates born with CHD have shown instances of cerebral atrophy and IVH.[19]

Long-term outcome

An association between neonatal complications and cognitive and neurodevelopmental delay has been demonstrated. This should be disclosed to the patient at the preconception visit and during subsequent antenatal care.

The study proposal and research question

The care of pregnant patients with cardiac disease requires special attention to be paid to accurate diagnosis, treatment and management throughout the pregnancy. This can only be achieved once an accurate assessment of the potential maternal and fetal complications has been made. Counseling is aimed at addressing the risks involved with pregnancy and delivery, and includes future cardiac function, the risk of shortened life expectancy, decreased quality of life, and the implications for the baby and future fertility. The assessment of risk and detailed counseling has been based on the available literature from industrialized countries which has been extrapolated to a South African patient population. Data unique to a South African population are few; clinical circumstance and co-morbidity may therefore remain undisclosed.

A registry of pregnant patients with cardiac disease delivering at Groote Schuur Hospital was initiated to allow the acquisition of South African data.

Patients attending a dedicated multidisciplinary clinic were given counseling and had interventions aimed at limiting the risk of adverse outcomes.

This study was designed to assess perinatal outcome in babies born to South African mothers with cardiac disease who attended this multidisciplinary clinic at Groote Schuur Hospital.

OBJECTIVES

1. To describe the perinatal outcome of pregnancies in women with heart disease.
2. To compare the perinatal mortality rate to the perinatal mortality rate for the background population during the study period.
3. To determine whether there are any other associated adverse outcomes in babies born to mothers with heart disease.

METHODS

This study was a prospective data analysis from 1 July 2010 to 31 Dec 2012.

Participants

Pregnant women with cardiac disease referred to the combined cardiology and obstetric clinic at Groote Schuur Hospital, Western Cape, South Africa were recruited consecutively, starting on the 1 July 2010. All women attending the clinic had either known cardiac disease or suspected cardiac disease. The diagnosis was confirmed or excluded at the first clinic appointment and those with confirmed cardiac disease were included in the study. Referrals to this clinic were accepted from all districts in South Africa. However most patients were resident in the Cape Town area and attended Groote Schuur Maternity Unit. The clinic aimed, to optimize care and provide the necessary support and counseling, as well as to correctly diagnose suspected cardiac disease, or congenital lesions where the diagnosis was not known. Only pregnant women with documented cardiac disease were included in the study.

Management

Patients were interviewed and examined by a cardiologist with a special interest in pregnancy and heart disease and an obstetrician with a special interest in maternal medicine. An echocardiogram was performed on each patient at the first visit.

The primary diagnosis was made or confirmed with additional secondary diagnoses noted. The patient's cardiac condition was classified according to the World Health Organization (WHO) classification of heart disease: class I-IV.

The patient was counseled and informed of any potential adverse outcome or likely complications in the pregnancy. Appropriate medications were prescribed and additional investigations requested if indicated.

Follow up visits were scheduled in the combined clinic as well as the high risk antenatal clinic and repeat echocardiograms were performed and medication administered or adjusted as required.

Fetal ultrasounds were done at booking, at 13 weeks (if the patient presented early enough) and 20 weeks. The first ultrasound (baseline scan) confirmed the

pregnancy. The 13-week ultrasound measured the nuchal translucency and screened for cardiac and chromosomal disorders and the 20-week scan investigated for structural fetal abnormalities. Further scans were requested as indicated, for example ultrasound measurement of fetal growth and weight was often indicated at 28-34 weeks.

Patients delivered at the Groote Schuur Maternity unit. Standard obstetric practices applied and additional interventions or monitoring were provided if indicated depending on the nature of the cardiac disease. Spontaneous labour progressing to a vaginal delivery was preferred and caesarean sections were performed for obstetric indications. In the case of certain cardiac lesions an operative delivery was deemed preferable, in which case the patient was counseled accordingly.

Additional cardiac and/or invasive monitoring was offered in the Intensive Care Unit of the Maternity Center when indicated.

Postnatal follow up appointments were scheduled for 6 weeks after delivery except in cases where closer follow up was indicated.

Definitions

Adverse neonatal outcome was defined as stillbirth, early neonatal death, admission to Neonatal Intensive Care Unit (NICU) or the requirement for delivery room resuscitation.

Neonatal intervention was defined as resuscitation at birth, and or admission to NICU.

Gestational age at term was defined as a delivery at 37-completed week (38 weeks) or beyond.

Preterm delivery was defined as delivery before 37 completed weeks gestation, and very preterm delivery was defined as delivery before 33 completed weeks gestation (34 weeks).

Normal birth weight was defined as an infant birth weight of between 2500 grams and 3500 grams. Low birth weight was defined as infant weight at birth of less than

2500 grams. Very low birth weight was defined as an infant birth weight of less than 1500 grams.

Intrauterine growth restriction was diagnosed after delivery using standard centile charts by the neonatologists. A fetus could have had both low birth weight and growth restriction.

Maternal cardiac disease was classified according to World Health Organization classification (See Table 2).

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Table 2: World Health Organization Classification of Cardiac Diseases

Conditions in which pregnancy risk is WHO I
Uncomplicated small or mild -Pulmonary stenosis -Patent ductus arteriosus -Mitral valve prolapse
Successfully repaired simple lesions (arterial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage)
Arterial or ventricular ectopic beats, isolated
Conditions in which pregnancy risk is WHO II or III
WHO II (if otherwise well and uncomplicated)
Unoperated atrial or ventricular septal defect
Repaired tetralogy of Fallot
Most arrhythmias
WHO II-III (depending on individual)
Mild left ventricular impairment
Hypertrophic cardiomyopathy
Native or tissue valvular heart disease not considered WHO I or IV
Marfan syndrome without aortic dilatation Aorta < 45mm in aortic disease associated with a bicuspid valve
Repaired Coarctation
WHO III
Mechanical valve
Systemic right ventricle
Fontan circulation
Cyanotic heart disease (unrepaired)
Other complex congenital heart disease
Aortic dilatation 40-45mm in Marfan syndrome Aortic dilatation 45-50mm in aortic dissection with bicuspid aortic valve
Conditions in which pregnancy risk is WHO IV (Pregnancy contraindicated)
Pulmonary arterial hypertension of any cause
Severe systemic ventricular dysfunction (LVEF<30%, NYHA III-IV)
Previous peripartum cardiomyopathy with any residual impairment of left ventricular function
Severe mitral stenosis, severe symptomatic aortic stenosis
Marfan syndrome with aorta dilated >45mm Aortic dilatation >50mm in aortic disease associated with bicuspid aortic valve
Native severe Coarctation

Data Collection

All patients consented to have information entered anonymously on a database. Information was recorded on hard copies and transposed into a spreadsheet on a password-protected computer. The entry of the maternal data was made after each visit. The data pertaining to the neonate was extracted at the postnatal follow- up visit or via a folder audit. In cases where the folders could not be located or the patients did not attend the postnatal visit, information was obtained by telephone.

Ethics Approval

Ethical approval was obtained from the University Ethical Committee. Reference number HREC 173/2010.

Data Analysis

Descriptive data were generated comparing adverse perinatal outcome with maternal disease, organized by diagnosis, severity and treatment.

RESULTS

Eighty-two patients were included in the study.

Maternal diagnoses

Maternal diagnoses included all forms of congenital and acquired cardiac disease. The distribution of diagnoses is listed in Table 3 and maternal demographic details described in the text and Tables 4 which follows.

Table 3: Maternal primary diagnosis

Cardiac Disease	Total	Number	Percentage
Congenital Heart Disease	28		34
Uncomplicated/repaired VSD/ASD		7	8.5
VSD/ASD with additional abnormality		7	8.5
Congenital valvular heart disease		3	3.6
Coarctation of Aorta		4	4.8
Transposition of Great Arteries		1	1.2
Tetralogy of Fallot		3	3.6
Coronary/Pulmonary artery malformation		3	3.6
Valvular Heart Disease	25		30
Rheumatic Valvular Heart Disease		18	21.9
Replaced Valves			
Mechanical		6	7.3
Bioprosthesis		1	1.2
Left Ventricular Dysfunction			
Cardiomyopathy	19		23
HIV		2	2.4
Peripartum		7	8.5
Hereditary		2	2.4
Dilated		2	2.4
PET/HT		6	7.3
Other	10		12
Arrhythmias		6	7.3
Marfan Syndrome		1	1.2
IHD		1	1.2
Takayasus		1	1.2
Portal vein thrombosis		1	1.2

VSD=ventricular septal defect; ASD=atrial septal defect; HIV=human immunodeficiency virus PET=Preeclampsia; HT= hypertension; IHD=ischemic heart disease.

Maternal demographics

Table 4: Maternal demographics

	Average	Range
Age (Years)	27	15-43
BMI (kg/m^2)	27	15-44

Age

The average maternal age was twenty-seven years. The oldest was forty-three years old and the youngest fifteen years old.

Parity

The median parity was one. Thirty patients (36%) had two or more children.

Gestational age at booking

The average gestational age at booking was at sixteen weeks. Three patients were unbooked, and one patient presented at the booking clinic acutely unwell at twenty-eight weeks.

Body habitus

The average BMI was 27kg/m^2 .The BMI of seven women had not been recorded. The highest BMI recorded was 44kg/m^2.

WHO class IV cardiac disease

A total of twenty-three patients had cardiac disease classified by the World Health Organization (WHO) as class IV disease.

Twenty-one of the twenty-three patients with WHO class IV disease booked their pregnancies. The average gestational age at booking in these twenty-three patients was sixteen weeks. Six out of the twenty-three, (26%) class IV cardiac patients booked in the first trimester. Two out of the three unbooked patients in this study group had class IV disease.

Of the forty-nine multigravida patients, twelve, (24%) had WHO class IV disease. In some cases the cardiac disease either presented or was diagnosed in the incident pregnancy, however in other cases the diagnosis was known and advice had been given to avoid future pregnancies.

Gestational age at delivery

The average gestational age at delivery was thirty-seven weeks. Of the live born neonates (n=78), fifty-five out of seventy-eight were born at term. Thirteen patients delivered at or after forty weeks, and forty-two patients delivered at thirty-eight or thirty-nine weeks.

One patient suffered a miscarriage at eleven weeks. The most premature delivery was at twenty-seven weeks and the neonate weighed 800g. This patient delivered at George Hospital.

Termination of pregnancy

There were two terminations of pregnancy. Both terminations were indicated for fetal reasons: a Dandy Walker malformation in one and a congenital cardiac lesion (a large VSD) in the other.

Mode of delivery

There were thirty-three patients delivered by caesarean section and one patient was delivered by hysterotomy. This represents an operative delivery rate of forty-one percent. The caesarean sections and the indications for operative delivery are listed in Table 5. Table 6 lists the cardiac indications for emergency and elective caesarean sections.

Table 5: Caesarean section deliveries

Caesarean Section	Number	Indication	Number
Emergency	20	Obstetric	16
		Cardiac	4
Elective	14	Obstetric	9
		Cardiac	5

Table 6: Cardiac indications for Caesarean sections

Elective CS Cardiac Indication	No.	Emergency CS Cardiac Indication	No.
Pulmonary arteriovenous malformation	1	Mitral valve replacement/sepsis	1
Repaired Coarctation of aorta	2	Pulmonary edema	1
Cardiomyopathy	1	Eclampsia CCF and CMO	1
Mixed mitral valve disease	1	Severe MR and CCF	1

CCF=congestive cardiac failure; CMO=cardiomyopathy MR=mitral regurgitation; CS=caesarean section

Ten patients underwent induction of labour (IOL). Of these, seven patients were induced for maternal cardiac indications and three were induced for obstetric indications.

The seven cardiac indications for induction of labour were based upon deteriorating symptoms of dyspnoea in six out of the seven cases. The remaining patient had labour induced electively during working hours because she had an arrhythmia for which intra-partum external cardiac pacing may have been necessary. The induction was timed to allow access to all cardiac and critical care facilities.

For the patients who had an induction of labour based upon worsening dyspnoea, one patient presented at George Hospital at term with pulmonary edema. Labour was induced because of persistent heart failure despite medical treatment. A subsequent diagnosis of peripartum cardiomyopathy was made (Table 7).

The three patients who were induced for obstetric indications delivered three healthy neonates.

Table 7: Maternal cardiac indications for IOL

Cardiac Indication	Number
Worsening dyspnoea	6
Cardiac arrhythmia	1

Neonatal data

Perinatal outcome

There was one miscarriage, one stillbirth, no early neonatal deaths and one neonatal death. The perinatal mortality rate for this study group was 1/82, equating to 12.1 deaths per 1000 live births.
The still birth and neonatal death are described in Appendix A.

Seven babies met the criteria for neonatal intervention as defined by the study protocol (resuscitation at birth, and or admission to NICU).

The composite adverse outcome (as defined as perinatal mortality, resuscitation at birth and admission to NICU) was eight out of eighty-two babies (9.7%)

Need for delivery room resuscitation

Thirteen neonates required some form of resuscitation at birth (Table 8). Twelve infants were resuscitated using a neonatal facemask and ambubag and one infant required intubation and ventilation. Of these, four had low five-minute Apgar scores.

One infant was born at George Hospital and the details of the neonatal condition at birth were not known.

Of these thirteen babies, six were healthy and required no further paediatric care. These six were thus excluded as little intervention in the delivery room was required, they had no evidence of asphyxia, and did not require admission to NICU. Three neonates had respiratory distress syndrome and three had a diagnosis of “birth asphyxia” (Table 8). One infant succumbed to complications of prematurity (neonatal death described in Appendix A).

Clinically diagnosed asphyxia neonatorum

There were three neonates with the diagnosis of birth asphyxia. (Table 8) The details of these babies are to be found in Appendix B.

Table 8: Neonates requiring resuscitation at birth

GA	Cardiac Ind For delivery	Maternal Dx	Wt (g)	Apgar at 5 mins	pH	NICU Nursery	Outcome
35	Yes	MR/ pulm edema/PET	2530	9	7.2	Boarder	Healthy
38	No	Marfan	2480	9	NG	No	Healthy
36	No	Portal vein thrombi	2730	9	NG	Boarder	Healthy
38	No	MMVD	2390	9	7.2	Nursery	Healthy
38	No	VSD/PS Diap/hernia	2580	10	NG	Boarder	Healthy
39	No	MVR	3180	8	7.1	No	Healthy
40	No	Severe MR	2845	6	7.3	Nursery	Mild RDS
34	No	VSD/PDA/ CoA	2260	5	7.08	NICU	TTN/RDS/ LBW
37	Yes	MVR and sepsis	2280	7	7.18	Nursery	RDS/Sepsis
39	No	Eclampsia/ abruption CMO	3125	5	7.2	Nursery	Birth asphyxia/ RDS
30	Yes	PET induced CCF	1230	7	7.1	NICU	PTD/LBW Asphyxia RDS/NNJ
40	Yes	PPCMO	2880	1	6.8	NICU Intubated	HIE/ asphyxia Sepsis
34	No	Severe MR	1800	9	NG	NICU	NND/NEC Persistent Acidosis IVH/Cardiac lesion

VSD=ventricular septal defect; PS= pulmonary stenosis; pulm=pulmonary; MR=mitral regurgitation; MMVD=mixed mitral valve disease; MVR= mitral valve replacement Diap=diaphragmatic hernia; PET=Preeclampsia; HT= hypertension; PDA=persistent ductus arteriosus; CoA= Coarctation of aorta; CMO=cardiomyopathy; PPCMO=peripartum cardiomyopathy

Admission to Neonatal Intensive Care Unit (NICU)

Seven infants required admission to NICU. Four babies admitted to NICU directly after delivery required resuscitation and demonstrated acidosis on cord blood

analysis (pH<7.2) (Table 8) and two were admitted with good Apgar scores and cord pH values, but required intensive care for sepsis (urinary tract infection and pneumonia) and one baby was delivered at George Hospital with extreme prematurity at twenty-seven weeks weighing 800g and remained in NICU at George Hospital.

Two cases of adverse neonatal outcome (admission to NICU for sepsis) developed independently of any pregnancy or maternal-related factors and have not been included in this analysis

Twenty-six other babies were kept in the nursery. Fifteen were admitted for neonatal observation, one for blood glucose level monitoring and ten healthy infants were cared for in the nursery, as the mothers were too unwell to nurse them. All of these babies had a normal outcome.

Obstetric risk factors associated with adverse neonatal outcome

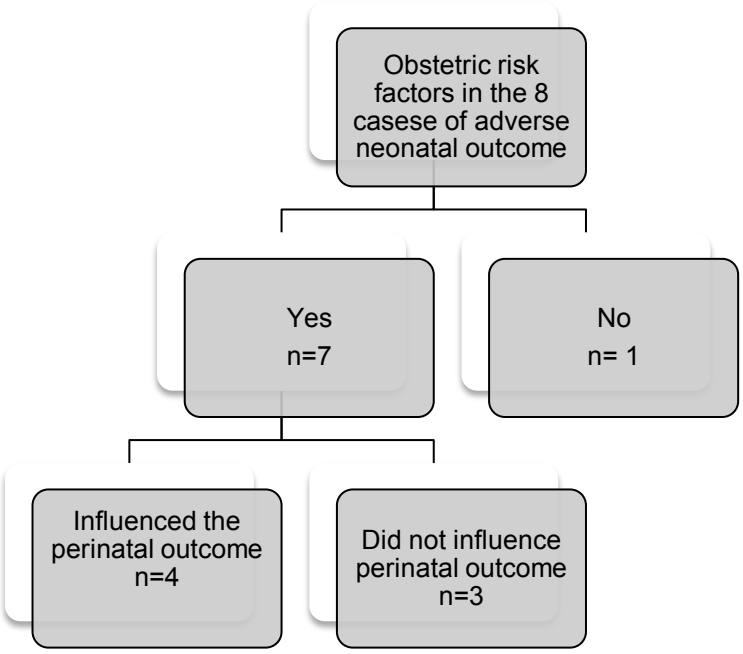
Of the eight cases in which adverse neonatal outcome occurred (including perinatal mortality, the need for delivery room resuscitation or NICU admission) described above, seven mothers suffered from one or more of the obstetric risk factors listed in Table 9. One mother had no additional obstetric risk factors. Of the seven mothers with obstetric risk factors, the neonatal outcome was influenced by the obstetric complication in four cases (Figure 1).

Table 9: Neonatal adverse outcome and associated obstetric risk factors in the 17 pregnancies with adverse neonatal outcome

ORF	No. of mothers affected	No. of neonates with NAO secondary to ORF	NAO associated ORF
HIV	3	none	
BMI >25	0	none	
BMI > 30	2	none	
PET	2	2	Resuscitation NICU
DM	1	1	Resuscitation
Medical conditions	1	none	
Placenta praevia	1	2	Resuscitation
Total		4	

ORF=obstetric risk factor, NAO= neonatal adverse outcome, PTD= preterm delivery (before 37 completed weeks) BMI= body mass index, DM = diabetes mellitus, PET= preeclampsia

Figure 1.



In a total of four out of the eight cases (50%), there was either no obstetric risk factor or the obstetric complication had no influence on the adverse neonatal outcome.

Intrauterine growth restriction

Two neonates were diagnosed to be growth restricted. The details of these babies can be found in Appendix C.

Preterm delivery

Twenty-four patients delivered before thirty-eight weeks (29%). This group includes the NND, SB and intrauterine growth restriction babies described previously.

Of these twenty-four patients, fourteen mothers went into spontaneous preterm labour. Of these fourteen, four mothers had worsening cardiac disease at the onset of labour (mitral valve replacement and sepsis in two mothers, cardiomyopathy and pulmonary edema in one patient and coarctation of the aorta with aortic valve replacement in one patient).

The remaining ten patients were well at the onset of preterm labour.

Two patients were delivered preterm electively because of cardiac disease.

Obstetric intervention

Induction of labour for cardiac indications and adverse neonatal outcome

Of the seven patients induced for cardiac indications, four of the infants were healthy, (all term vaginal deliveries) (Table 10). The three neonates who suffered complications have been described previously (IUGR, PTD, HIE)

Table 10: Indications and outcome for those patients delivered for cardiac indications following IOL

Indication	GA (w)	IOL/CS	MOD	Weight (g)	Apgar at 5 mins	Outcome
Worsening Maternal Dyspnoea	38	IOL	NVD	2800	9	Healthy
Cardiomyopathy	40	IOL	NVD	2870	10	Healthy
Cardiomyopathy	38	IOL	NVD	3700	9	Healthy
Cardiac arrhythmia	38	IOL	NVD	3375	9	Healthy
Maternal CCF	35	IOL	NVD	2075	8	LBW/IUGR
Pulmonary Edema	35	IOL	CS	2530	9	PTD
Worsening maternal cardiac failure	40	IOL	NVD	2880	1	HIE

Delivery by Caesarean Section for cardiac indications and adverse neonatal outcome

Of the patients delivered by caesarean section for cardiac indications, (n=9), three neonates were healthy. Two delivered preterm but were healthy. There was one stillbirth and one neonatal death (described previously). Details of the adverse neonatal outcome in these deliveries are reflected in Table 11.

Table 11: Indications and Outcome in those patients delivered for cardiac indication. CS

Indication for Delivery	GA (w)	IOL/CS	MOD	Weight (g)	Apgar at 5 mins	Outcome
Repaired Coarctation of aorta	38	CS (el)	CS	3090	10	Healthy
Repaired Coarctation of aorta	39	CS (el)	CS	2750	9	Healthy
Mixed mitral valve disease	39	CS (el)	CS	2960	9	Healthy
Pulmonary AV malformation	37	CS (el)	CS	2360	9	PTD/LBW (Healthy)
Maternal det	36	CS (em)	CS	3450	10	PTD (Healthy)
Mitral valve replacement/sepsis	37	CS (em)	CS	2280	7	PTD/LBW/ Sepsis/RDS
Pulmonary edema	30	CS (em)	CS	1230	7	PTD/LBW/Asphyxia/RDS/NNJ
Pre-Eclampsia CCF and CMO	34	CS (em)	CS	1725	9	PTD/IUGR
Cardiomyopathy	35	CS (el)	CS	2234	0	SB/PTD/LBW

Neonates born at Term

Of those neonates who were born at term, twenty-four women required antenatal intervention, which allowed the pregnancy to continue. In most cases, this involved the administration of either a diuretic or β-Blockers or both with increased outpatient surveillance. In one case it involved the diagnosis and management of an arrhythmia.

Congenital cardiac disease in the fetus

The rate of congenital heart disease in the fetus was 3/82 (36%). The stillborn baby had a multiple fetal anomalies including a cardiac lesion, one pregnancy was terminated for Aortic override and a large VSD in the fetus and the baby who passed away at one month of age had a persistent PDA related to prematurity. In all three of these cases, the mothers had acquired cardiac disease.

DISCUSSION

This database describes a unique African program of health care. The combined cardiac and obstetric clinic provided patients with good access to a multidisciplinary team, a reliable triage and referral system and access to neonatal intensive care.

The perinatal outcome (expressed as perinatal mortality) was good. The literature has described an association between maternal cardiac disease and perinatal mortality, which was not evident in this study. The perinatal mortality rates were in the same order as the general perinatal mortality rates in industrialized countries.

The Perinatal Mortality Rate in this cohort was also below the rate for the general population from whence this cohort came. (Perinatal mortality rate for the Metro West is 28.8 per 1000 for the study period). The rate was also below the national rate reported for South Africa. (The perinatal mortality rate for South Africa during 2010 was 34/1000). The perinatal mortality rate for this study cohort is better than that reported for Africa in published literature, (7.6%) and is more in keeping with industrialized countries (1-4%). In addition, one case of a stillborn infant occurred in a child with multiple anomalies and there was no connection with maternal cardiac disease.

Nine percent (8/82) of the neonates in this audit had suffered adverse outcome (perinatal mortality, delivery room resuscitation or admission to NICU). This is lower than similar rates described in industrialized countries. (Sui et al reports a rate of 17-28%) The rate of obstetric intervention, (operative delivery and PTD), was similarly high, but can be ascribed to factors other than cardiac disease. In 50% of cases of adverse neonatal outcome, additional obstetric risk factors necessitated obstetric intervention and therefore influenced the neonatal outcome.

These data are nevertheless too few to allow firm conclusions regarding the influence of maternal cardiac disease on obstetric intervention and outcome.

Preterm delivery is recognized as a major contributing factor to adverse perinatal outcome. In this study, the average gestational age was 37 weeks, and 29% of patients delivered preterm. Although this rate of preterm delivery exceeded the background rate, preterm delivery in this audit was not a major contributing factor to

adverse neonatal outcome (perinatal mortality, delivery room resuscitation or admission to NICU).

When the data are examined from the perspective of cardiac disease, 7 patients required obstetric intervention (induction of labour). Three babies suffered complications partly due to maternal cardiac disease. One baby developed HIE as a consequence of delivering in transit, (an unmonitored and uncontrolled delivery in the air ambulance). The other infant with birth asphyxia was delivered after the mother had labour induced because of pulmonary edema and preeclampsia at 35 weeks. She had severe mitral regurgitation and had been on a diuretic antenatally. The pre-eclampsia may have contributed to the development of pulmonary edema because of left ventricular diastolic dysfunction. This baby had a cord pH of 7.2, and did not require neonatal intensive care. The third had intrauterine growth restriction. This mother had an HIV-related cardiomyopathy and was admitted for a prolonged time antenatally. She was treated with a diuretic, antihypertensive agent and digoxin. She had severe decline in cardiac function in the pregnancy. The baby was healthy and did not require admission to the NICU.

Of the 9 babies born for cardiac indications by caesarean section, three of the remaining 4 babies who had neonatal complications did have maternal cardiac disease that may have contributed to the subsequent outcome (that of the mitral valve replacement and sepsis and cardiomyopathy delivered at 33 weeks and the delivery at 30 weeks for preeclampsia and pulmonary edema).

In summary, in all categories of cardiac disease in which obstetric intervention was considered necessary, there was only one seriously affected child, namely the baby born in the air ambulance, where the circumstances of obstetric care were probably more responsible for the subsequent outcome than the underlying maternal condition itself.

When the data is analyzed according to the different categories of cardiac disease, the distribution was evenly distributed between congenital heart disease and rheumatic fever, as well as a much smaller group of other diagnoses.

The maternal congenital heart disease had no effect on the perinatal outcome. Of the babies delivered to mothers with congenital heart disease who had adverse neonatal outcome, other reasons may have contributed to the any adverse outcome namely:

sepsis requiring readmission NICU and spontaneous preterm labour resulting in the need for delivery room resuscitation.

In the rheumatic heart disease group, the majority of cases, the maternal cardiac disease had no influence on the perinatal outcome. In only three cases from this group where adverse neonatal outcome was documented, could the maternal cardiac disease have had a direct effect on this outcome.

The rate of neonatal congenital heart disease was 3/82 (36%), which is higher than recorded in the literature and influenced the rate of adverse outcome. Not one of these three cases was inherited cardiac disease, as in all three cases the maternal cardiac disease was acquired.

The data also shows that women with severe disease present in pregnancy, and book at a late gestation, despite previous advice to avoid pregnancy. Despite the presence of WHO IV disease, no mothers decided to terminate on the basis of maternal cardiac disease alone. The inability to reproduce has significant social implications in the South African setting and consent to a medically indicated termination may be withheld on this account.[20,21]

CONCLUSION

The perinatal mortality is better than that quoted in the literature, and better than the rate for the service as a whole, however there was a high rate of obstetric intervention noted in this study group. The complication rate for adverse neonatal outcome is better than the rate cited in the literature for industrialized countries, although prematurity rates were high. Obstetric risk factors influenced the rate of adverse neonatal outcome in 50% of cases.

Neonatal outcome is improved when mothers with heart disease are managed in a multidisciplinary clinic, but this sample size is small and continuous data collection and analysis would be helpful in assessing the degree of surveillance required in pregnancies complicated by maternal heart disease to allow the best outcome for both mother and infant.

APPENDIX A

Stillbirth and neonatal death

The stillborn infant was born to a mother with HIV-related cardiomyopathy (CMO). She booked at 15 weeks. An echo revealed an ejection fraction of 54% with diastolic dysfunction. Her CD4 count was 242 and she was taking antiretroviral treatment and had a suppressed viral load at the time of delivery. A renal biopsy prior to pregnancy had shown HIVAN (HIV associated nephropathy). Her BMI was 21kg/m^2 and she was not diabetic. The CMO was managed with a diuretic and a β-blocker. Multiple fetal anomalies were diagnosed in the fetus (Hydrocephalus, cardiac lesion and macrocephaly amongst others). This patient declined a termination of pregnancy. The caesarean delivery was indicated for macrocephaly. The post mortem described multiple anomalies, attributable to any specific syndrome.

One infant died at 1 month of age. This mother delivered at 34 weeks because she had a major placenta praevia. The mother was 37 years old and had two children. She booked at 12 weeks. She had severe mitral regurgitation (WHO III) leading to an episode of cardiac failure during the antenatal period. She required treatment with a diuretic and spironolactone, despite an ejection fraction of 57%. She also suffered from diabetes mellitus and was on insulin for the duration of the pregnancy. The mother was admitted for a total of 40 days prior to delivery and required intubation for the caesarean section. The infant weighed 1800 grams and required resuscitation with bag-mask ventilation due to respiratory stress syndrome. The five-minute Apgar score was 9/10. However, the baby required admission to the NICU. The neonate suffered the following complications associated with prematurity: persistent PDA, intraventricular haemorrhage, sepsis, persistent acidosis, necrotizing enterocolitis and died at age one month.

APPENDIX B

Cases of clinically diagnosed asphyxia neonatorum

There were three babies with birth asphyxia. One infant suffered hypoxic ischemic encephalopathy (HIE). This baby was delivered vaginally at 40 weeks and weighed 2880 grams. The baby delivered in the air ambulance on route to Groote Schuur Hospital because labour had been induced at George Hospital prior to transportation. The Apgar score at 5 minutes was 1/10 and the neonate was intubated and ventilated before admission to the neonatal intensive care unit (NICU).

The second infant was born at 30 weeks by emergency CS weighing 1230 grams. This mother had severe preeclampsia and pulmonary edema. She was admitted for 3 days prior to delivery for stabilization, and required admission to the intensive care unit (ICU). She had an ejection fraction of 39%. The pulmonary edema was attributed to preeclampsia, rather than an underlying cardiac lesion. This mother recovered normal cardiac function postpartum (postpartum ejection fraction of 55%). This preterm infant had a 5 minute Apgar score of 7/10, and a cord blood gas of 7.18. The baby subsequently developed septicemia, RDS and neonatal jaundice (NNJ) requiring admission to the NICU, although intubation was not required. This infant was discharged at 1 month old.

The third infant was delivered at 40 weeks and weighed 3125 grams. The mother had eclampsia, abruptio placentae and a peripartum cardiomyopathy, diagnosed on the basis of reduced ejection fraction, measured during the puerperium. This neonate was born by emergency caesarean section. Chest compressions and ventilatory support via a neonatal facemask and ambubag were required and the infant responded well.

APPENDIX C

Intrauterine growth restriction

One infant was born at 35 weeks. This mother had an HIV-related cardiomyopathy and preexisting hypertension. Her ejection fraction was 24%. She was placed on a diuretic, digoxin and antihypertensive medication antenatally. She was not treated with β-blockers. She was admitted for 37 days prior to delivery. She had two episodes of cardiac failure at 32 and 35 weeks and labour was induced at 35 weeks. The infant weighed 2075 grams.

The second neonate was delivered at 34 weeks because the mother developed preeclampsia. This infant weighed 1725 grams and was admitted to the nursery. There were signs of intrauterine growth restriction. In addition to preeclampsia, this mother had a dilated cardiomyopathy, developing congestive cardiac failure at 33 weeks. Deteriorating renal function developed as a complication of the pre-eclampsia, leading to elective preterm delivery.

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