Perinatal Outcome in Pregnant Women with Heart Disease Attending a Combined Obstetric and Cardiology Clinic in a Resource Limited Country

Catherine Elliott[1*], Karen Sliwa[2] and John Anthony[1]

[1]*Department of Obstetrics and Gynaecology, Faculty of Health Sciences, University of Cape Town,Groote Schuur Hospital, South Africa*

[2]*Hatter Institute for Cardiovascular Research in Africa, Department of Medicine, Faculty of Health Sciences, University of Cape Town, South Africa*

Abstract: Previously published literature has shown a clear relationship between adverse perinatal outcome and the presence of maternal heart disease even when demographic and obstetric risk factors have been taken into account. Prospective studies from South Africa or Africa describing pregnancy outcome in mothers with heart disease, where there is a high prevalence of acquired rheumatic heart disease as well as cardiomyopathies and congenital heart lesions, are limited. Perinatal data were collected to describe the perinatal outcome in patients with heart disease.

Objectives: The purpose of this study was to describe the perinatal outcome of pregnancies in women with heart disease attending a multidisciplinary clinic and to compare the perinatal mortality rate with the perinatal mortality rate for the background population. To determine whether there are any other associated adverse outcomes in babies born to mothers with heart disease.

Methods: The first eighty-two consecutive pregnant patients with heart disease attending the weekly combined cardiology and obstetric clinic were studied over eighteen months. Neonatal outcome was recorded. Adverse neonatal outcome was defined as perinatal mortality, the need for delivery room resuscitation and admission to neonatal intensive care unit (NICU).

Results: Perinatal mortality was 12.1 per 1000 live births. Only one stillbirth was documented. Adverse neonatal outcome was 9.7%. Caesarean section rate was 40% with 29% of infants delivered preterm.

Conclusion: Perinatal mortality rate in this cohort was excellent - possibly due to a high level of joint care - but was linked to a high rate of obstetric intervention.

Keywords: Perinatal outcome in pregnant women with heart disease in a resource limited setting.

INTRODUCTION

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 [1-7]. In South Africa, maternal heart disease is one of the leading causes for maternal mortality, prompting continuous efforts to improve screening, diagnosis and management of heart disease.

Previously published literature has shown a clear relationship between adverse perinatal outcome and the presence of maternal heart disease even when demographic and obstetric risk factors have been accounted for [1, 3, 8, 4]. Complications in the fetus and neonate such as preterm delivery, respiratory distress syndrome, birth asphyxia, intrauterine growth restriction, small for gestational age and intraventricular hemorrhage, occur twice as often in mothers with heart disease when compared to mothers without heart disease and the rate of occurrence of neonatal complications is between 17-28% [2, 4, 8].

The perinatal mortality rate (stillbirth and early neonatal death) in this group of patients is between 1-4% in industrialized countries [3] which is significantly higher than in the background population (1%), and 7.6% in sub-Saharan Africa [9]. The most significant cause for perinatal mortality is preterm delivery [2].

This correlation between maternal cardiac disease and adverse perinatal outcome has allowed the identification of predictors of adverse perinatal outcome which include a maternal baseline New York Heart Association functional class>II or cyanosis [4, 8, 10] maternal left heart obstruction [2, 4, 8, 11, 12] the use of oral anticoagulants, mechanical valve prosthesis and symptomatic arrhythmia [4].

*Address correspondence to this author at the Suite 504, The Annex, 162 Longmarket Street, Cape Town, 8001, RSA; Tel: +27214221048;
E-mail: cath@catherine-elliott.co.za

E-ISSN: 2408-9761/15

The potential adverse effect of maternal heart disease on perinatal outcome is amplified if there are concurrent obstetric risk factors including smoking during pregnancy, [4] multiple gestation or advanced maternal age [8].

Data unique to a South African setting are limited and the assessment of risk has been based on available literature from industrialized countries which has been extrapolated to a South African population. Data describing perinatal outcome in South African women with heart disease, where there is a high incidence of both acquired and congenital heart disease, were collected and analyzed to assess differences in and similarities to the described outcomes in an environment that is resource-depleted and in which there is a high prevalence of other medical and obstetric comorbidities.

OBJECTIVES

The purpose of this study was to describe the perinatal outcome of pregnancies in women with heart disease, to compare this outcome with the perinatal mortality rate for the background population and to determine whether there are any other associated adverse outcomes in babies born to mothers with heart disease.

METHODS

Pregnant women with cardiac disease referred to the weekly combined cardiology and obstetric clinic at Groote Schuur Hospital, Western Cape, South Africa, were recruited consecutively between 1 July 2010 and 31 December 2012. The first one hundred patients attending the clinic were analyzed and of those eighty-two had disease. This was a prospective study of consecutive patients who consented to being enrolled. Maternal heart disease was categorized according to the World Health Organization (WHO) classification of maternal risk as outlined in Table **1**. Investigations such as electrocardiograms, echocardiograms, blood tests and fetal ultrasounds were scheduled when clinically indicated according to standard obstetric and cardiology practices. Additional interventions and/or monitoring were provided as indicated according to the nature of the cardiac disease. Spontaneous labour progressing to vaginal delivery was the preferred route of delivery. An operative delivery was deemed preferable in the case of certain cardiac lesions, in which case the mother was counseled accordingly.

Table 1: 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

Adverse neonatal outcome was defined as stillbirth, early neonatal death, the requirement for delivery room resuscitation (bag mask ventilation and/or intubation)

and admission to the neonatal intensive care unit (NICU).

Early neonatal death was defined as death within the first seven days of life.

Preterm delivery was defined as delivery before thirty-seven completed weeks gestation.

Birth asphyxia was defined as a cord pH of less than 7.2 at delivery or a 5-minute Apgar score of less than 7.

Ethics

Ethics approval was obtained from the University of Cape Town Ethics Committee. All patients provided written consent for inclusion in this study.

Data Analysis

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

RESULTS

Maternal Demographics and Delivery Data

Eighty-two patients were included in the study. The average maternal age was twenty-seven years and the median parity was one. Maternal diagnoses included forms of both congenital and acquired cardiac disease. The distribution of diagnoses is listed in Table **2**.

A total of twenty-three patients had WHO class IV disease. The average gestational age at delivery was

Table 2: 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
Bioprothesis		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.

thirty-seven weeks. Thirty-three patients were delivered by caesarean section and one by hysterotomy (termination of pregnancy for a severe fetal anomaly). This represents an operative delivery rate of forty-one percent. The caesarean sections and indications for operative delivery are listed in Table **3**. Table **4** lists the cardiac indications for emergency and elective caesarean section. There were four operative vaginal deliveries (two ventous and two forceps deliveries)

Table 3: Caesarean Section Deliveries

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

Table 4: 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 (Table **5**). 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 on worsening dyspnoea in six 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.

Table 5: Maternal Cardiac Indications for Induction of Labour

Cardiac Indication	Number
Worsening dyspnoea	6
Cardiac arrhythmia	1

Perinatal Outcome

Early Pregnancy Loss and Termination

There was one spontaneous miscarriage and two terminations of pregnancy for fetal indications (a Dandy Walker malformation in one fetus – hysterotomy, and a large ventricular septal defect with overriding aorta in the other).

Perinatal Mortality

There was one stillbirth, no early neonatal deaths and one late neonatal death. The perinatal mortality rate for this study group was one out of eighty-two equating to 12.1 deaths per 1000 live births.

Neonatal Data

Seven babies met the criteria for adverse neonatal outcome (resuscitation at birth and admission to NICU).

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

Stillbirth

The stillborn infant was born at term to a mother with HIV-related cardiomyopathy, managed with β-blockers and diuretics. This patient had an ejection fraction of 54% and was on antiretroviral treatment with a suppressed viral load. Multiple fetal anomalies (hydrocephalus, macrocephaly and a cardiac lesion) were diagnosed by ultrasound examination and the patient declined a termination of pregnancy. A postmortem examination confirmed that the cause of death was due to multiple fetal anomalies and not attributable to any specific syndrome.

Neonatal death

The neonatal death occurred in an infant at one month of age following complications caused by preterm birth. This baby was delivered at thirty-four weeks by caesarean section because the mother had major placenta praevia. The patient was diabetic and had severe mitral regurgitation leading to an episode of acute cardiac failure during the antenatal period which required treatment with furosemide and spironolactone despite having an ejection fraction of 57%. The infant weighed 1800grams at birth and required delivery room resuscitation as well as NICU admission. This infant suffered complications related to preterm delivery including persistent patent ductus arteriosus,

intraventricular haemorrhage, sepsis, persistent acidosis and necrotizing enterocolitis.

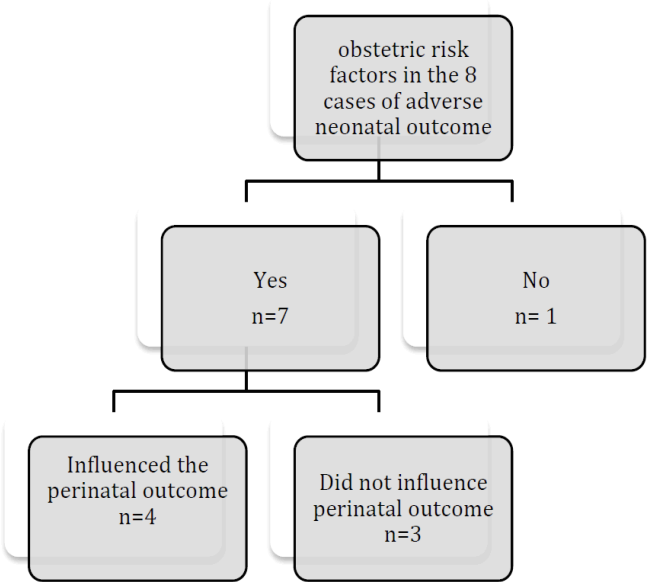
Resuscitation at Birth and Admission to NICU

Three babies suffered birth asphyxia (one required intubation) and three had respiratory distress syndrome (Table **6**).

A total of seven infants required admission to NICU. Two of these seven were not included in this analysis because the NICU admission was for nosocomial sepsis (pneumonia in one and a urinary tract infection in the other). Four babies admitted directly after delivery required resuscitation at birth and demonstrated acidosis on cord blood gas analysis (pH < 7.2, Table **6**). One baby was delivered at an outlying hospital at twenty-seven weeks gestation (weighing 800 grams) and remained in the NICU on site. The details of this delivery are not known, so this baby has been excluded from the analysis.

Obstetric Risk Factors and Adverse Neonatal Outcome

Of the eight cases in which adverse neonatal outcome occurred, seven mothers suffered from one or more of the obstetric risk factors listed in Table **7**. One mother had no additional risk factors. Of the seven mothers with obstetric risk factors, the neonatal outcome was influenced by the obstetric risk factor in four (50%) of the cases (Figure **1**).



Preterm Delivery

Twenty-four patients (29%) delivered before thirty-seven completed weeks gestation. Of these twenty-four patients, fourteen (58%) mothers went onto spontaneous preterm labour. Of these fourteen mothers, four (29%) had worsening cardiac symptoms prior to the onset of labour. The maternal cardiac diagnoses of these four mothers were history of mitral valve replacement and sepsis in two patients, cardiomyopathy and pulmonary edema in one patient and coarctation of the aorta with history of aortic valve replacement in one patient. The remaining ten patients were well at the onset of labour.

Table 6: Neonates Requiring Resuscitation at Birth

GA	Cardiac Indication for Delivery	Maternal Diagnosis	Wt (g)	Apgar 5 Mins	pH	NICU/ Nursery	Outcome
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

GA=gestational age 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.

Table 7: 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

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

Two patients were delivered preterm electively because of cardiac disease.

Congenital Cardiac Disease in the Fetus

The rate of congenital heart disease in the neonates was three out of eighty-two (3.7%). The stillborn baby had multiple fetal anomalies including a cardiac lesion, one pregnancy was terminated for an overriding aorta and a large VSD, and the baby who died at one month of age had a persistent PDA related to prematurity. In all of these cases, the mothers had acquired cardiac disease.

Table 8: Neonatal Outcome and Maternal Primary Diagnosis

Neonatal Outcome	Number	Maternal Primary Diagnosis
Asphyxia	3	Cardiomyopathy; PET induced cardiac failure; Peripartum cardiomyopathy
Respiratory distress syndrome	11	Mitral valve replacement; Peripartum cardiomyopathy Mixed mitral valve disease; Cardiomyopathy (2); PET induced cardiac failure VSD; Pulmonary stenosis; Coarctation of aorta; Severe mitral regurgitation Mitral regurgitation; Severe mitral regurgitation; Palpitations/ arrhythmia
Requiring NICU	7	Peripartum cardiomyopathy; Severe mitral regurgitation VSD; Mitral valve prolapse; PET induced cardiac failure Mitral regurgitation Coarctation of aorta; Aortic valve replacement; VSD; Pulmonary stenosis; Coarctation of aorta
Nosocomial sepsis	8	Mitral valve replacement; Peripartum cardiomyopathy; Severe mitral regurgitation VSD; Mitral valve prolapse; PET induced cardiac failure; Mitral regurgitation VSD; Pulmonary stenosis; Coarctation of aorta; Aberrant coronary artery circulation
Requiring resuscitation	13	Mitral valve replacement; Peripartum cardiomyopathy; Mixed mitral valve disease Cardiomyopathy; Severe mitral regurgitation (2); PET induced cardiac failure Acquired mitral regurgitation; Marfan's syndrome; Portal vein thrombosis; VSD; Pulmonary stenosis; Coarctation of aorta; VSD; Pulmonary stenosis
Weighing 800g	1	Coarctation of aorta; Aortic valve repair
Preterm delivery		Pulmonary arterial hypertension; Mitral valve replacement (2) Severe mitral regurgitation (2); Repaired Tetralogy of Fallot; Cardiomyopathy (2); PET induced cardiac failure; Mitral regurgitation (2); Vasculitis and first degree heart block; Myopathic cardiomyopathy; VSD (2); Coarctation of aorta; Aortic valve replacement; Portal vein thrombosis; HIV cardiomyopathy; VSD; Pulmonary stenosis; Coarctation of aorta Acquired mitral regurgitation; Sarcoidosis and arrhythmias; Familial cardiomyopathy; Aberrant coronary artery circulation; VSD; Atrial fibrillation
Congenital heart disease	3	Severe mitral regurgitation; HIV cardiomyopathy; Bioprosthetic mitral valve

PET=preeclampsia, VSD=ventricular septal defect; HIV=human immunodeficiency virus

DISCUSSION

The reported findings describe a uniquely African data set. Previously published literature describes an association between maternal cardiac disease and perinatal mortality which was not evident in this study. The perinatal mortality rate in this cohort was only 1.2%. This compares favourably to the perinatal mortality rate for the general population from whence this cohort came. The perinatal mortality rate for South Africa was 34 per 1000 during the study period while

perinatal mortality for the Cape Town region was 28.8 per 1000 during the same study period. Spontaneous preterm delivery and prematurity related complications are the most common listed causes of perinatal mortality followed by intrapartum hypoxia, trauma, maternal hypertensive disorders and fetal anomalies. The perinatal mortality rate in this study is better than that reported in the literature for Africa (7.6%) [9] and is more in keeping with industrialized countries (1 - 4%) [3].

Nine percent of the neonates in this study suffered some form of adverse outcome leading to delivery room resuscitation or admission to NICU. This is lower than the previously described rate of 17-28% [2, 4, 8] of neonatal intervention in industrialized countries. The rate of obstetric intervention, that is, operative delivery and preterm delivery, was similarly high, but in the majority of cases (82%) can be ascribed to factors other than cardiac disease.

In 50% of the cases where adverse neonatal outcome (defined as perinatal mortality, the requirement for delivery room resuscitation and admission to the NICU) was documented, additional obstetric risk factors necessitated obstetric intervention and therefore influenced the neonatal outcome.

When the data are analyzed according to the cardiac disease category, the majority of the patients were distributed evenly between congenital heart disease and rheumatic heart disease.

Maternal congenital heart disease had no effect on the perinatal outcome in this cohort. Of the babies delivered to mothers with congenital heart disease who had some form of adverse neonatal outcome, other reasons may be found to account for the adverse outcome, namely sepsis requiring readmission to NICU and spontaneous preterm labour resulting in the need for delivery room resuscitation.

Maternal cardiac disease directly influenced the perinatal outcome in three cases from the rheumatic heart disease group.

Preterm delivery is recognized as a major contributing factor to adverse perinatal outcome. In this study, the average gestational age was thirty-seven 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.

CONCLUSION

The perinatal outcome in this series is better than that previously described for pregnancies in which mothers have heart disease and better than the rate for the general population of the Cape Town region and in the Republic of South Africa. This favourable outcome –possibly related to a high level of joint care - was associated with a high rate of obstetric intervention. Obstetric risk factors alone lead to adverse neonatal outcome in 50% of cases.

This study is limited by the small sample size although the data are unexpectedly different to prior studies. A larger sample size could lead to different conclusions, however, neonatal outcome may also improve when mothers with heart disease are managed intensively in a multidisciplinary clinic. 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 optimal outcome for both mother and infant.

SYNOPSIS

Pregnancies complicated by maternal heart disease managed by a combined obstetric and cardiology clinic in South Africa show good perinatal outcome.

REFERENCES

[1] Pieper PG. Pre-pregnancy risk assessment and counselling of the cardiac patient. Neth Heart J 2011; 19:477-81. http://dx.doi.org/10.1007/s12471-011-0188-z

[2] Khairy P, Ouyang DW, Fernandes SM, Lee-Parritz A, Economy KE, Landzberg MJ. Pregnancy outcomes in women with congenital heart disease. Circulation 2006; 113: 517-24. http://dx.doi.org/10.1161/CIRCULATIONAHA.105.589655

[3] Drenthen W, Pieper PG, Roos-Hesselink JW, *et al*. Outcome of pregnancy in women with congenital heart disease: a literature review. J Am Coll Cardiol 2007; 49: 2303-11. http://dx.doi.org/10.1016/j.jacc.2007.03.027

[4] Siu SC, Sermer M, Harrison DA, *et al*. Risk and predictors for pregnancy-related complications in women with heart disease. Circulation 1997; 96: 2789-94. http://dx.doi.org/10.1161/01.CIR.96.9.2789

[5] Jastrow N, Meyer P, Bouchardy J, Savoldelli GL, Irion O. [Maternal heart disease and pregnancy: a multidisciplinary approach]. Revue medicale suisse 2011; 7: 2070, 2-4, 6-7.

[6] Presbitero P, Somerville J, Stone S, Aruta E, Spiegelhalter D, Rabajoli F. Pregnancy in cyanotic congenital heart disease. Outcome of mother and fetus. Circulation 1994; 89: 2673-6. http://dx.doi.org/10.1161/01.CIR.89.6.2673

[7] Moghbeli N, Pare E, Webb G. Practical assessment of maternal cardiovascular risk in pregnancy. Congenital Heart Disease 2008; 3: 308-16. http://dx.doi.org/10.1111/j.1747-0803.2008.00207.x

[8] Siu SC, Colman JM, Sorensen S, *et al*. Adverse neonatal

and cardiac outcomes are more common in pregnant women with cardiac disease. Circulation 2002; 105: 2179-84. http://dx.doi.org/10.1161/01.CIR.0000015699.48605.08

[9] Diao M, Kane A, Ndiaye MB, *et al*. Pregnancy in women with heart disease in sub-Saharan Africa. Arch Cardiovasc Dis 2011; 104: 370-4. http://dx.doi.org/10.1016/j.acvd.2011.04.001

[10] Siu SC, Sermer M, Colman JM, *et al*. Prospective multicenter study of pregnancy outcomes in women with heart disease. Circulation 2001; 104: 515-21. http://dx.doi.org/10.1161/hc3001.093437

[11] Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, *et al*. ESC Guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). Eur Heart J 2011; 32: 3147-97. http://dx.doi.org/10.1093/eurheartj/ehr218

[12] Hameed A, Karaalp IS, Tummala PP, *et al*. The effect of valvular heart disease on maternal and fetal outcome of pregnancy. J Am Coll Cardiol 2001; 37: 893-9. http://dx.doi.org/10.1016/S0735-1097(00)01198-0

Received on 24-03-2015 Accepted on 05-05-2015 Published on 02-07-2015

http://dx.doi.org/10.15379/2408-9761.2015.02.02.02