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Original Research Article

Risk factors in pregnancy with heart disease and their co-relation with adverse feto-maternal outcome

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ABSTRACT

Background: Heart disease complicates 1% to 3% of all pregnancies and is responsible for 10% to 15% of maternal mortality. In India, the predominant heart disease is still RHD (rheumatic heart disease), whereas in the developed countries congenital heart disease is more common.
Methods: This prospective observational study conducted in Department of Obstetrics and Gynecology in carried in PGIMER and Dr. RML Hospital, New Delhi from November 2015 to March 2017. 35 patients with heart disease were included in this study eight risk factors, four non-cardiac (age, parity, BMI and time of reporting to hospital) and four cardiac risk factors (etiology of lesion, type of lesion, prosthetic valve on anticoagulation and associated cardiac complication like atrial fibrillation (AF), pulmonary edema, pulmonary artery hypertension (PAH) were co-related with predefined indicators for adverse feto-maternal outcome. NYHA class, CARPREG score, modified WHO class were also co-related with adverse feto-maternal outcome.
Results: RHD is still more common than CHD in our population. No association was seen between any non-cardiac risk factor and adverse maternal outcome. Among cardiac risk factors, severe MS, severe PAH, NYHA class IV, AF, CARPREG score ≥2 were significantly associated with adverse maternal and fetal outcome. There was no maternal or fetal death in the present study.
Conclusions: Severe MS, severe PAH, AF, NYHA Class IV, CARPREG score ≥2 had positive predictive value for adverse feto maternal outcome in the present study which had no maternal or fetal mortality. Need for Preconceptional counselling which was seen to be totally absent in the present study is emphasized.

Keywords: Adverse fetomaternal outcome, Cardiac risk factors, Heart disease in pregnancy

INTRODUCTION

Heart disease in pregnancy is the leading cause of non-obstetrical maternal death. Heart disease complicates 1% to 3% of all pregnancies and is responsible for 10% to 15% of maternal mortality.[1]

In India, the rheumatic heart disease (RHD) contributes to approximately 70% of heart disease seen in pregnancy with a maternal mortality rate of 7%-10% and a morbidity rate of 30%.[2,3] Heart diseases is the leading cause of admissions in obstetrics intensive care unit (ICU).[4] Severe stenotic lesions, prosthetic valve, NYHA class III/IV, CARPREG score ≥2, WHO class III/IV are all thought to be associated with adverse outcome.

This study aimed at identifying the predictive value of non-cardiac, cardiac risk factors, NYHA risk classification, CARPREG risk score and modified WHO class with feto-maternal outcome in pregnancy with heart disease, as well as validating the existing risk scores in context to our population.

METHODS

This prospective observational study was conducted in PGIMER and Dr. RML hospital, New Delhi, a Government hospital, in the Department of Obstetrics and Gynaecology in collaboration with Department of Cardiology, from November 2015 to March 2017. A total of thirty-five patients, pre-diagnosed or diagnosed with heart disease in current pregnancy were selected from antenatal clinic (ANC) in any trimester of reporting to hospital. Patients with associated chronic medical disorders, multiple gestation, LMP not known or any other complications which could adversely affect fetomaternal outcome were excluded from study.

Four non-cardiac risk factors, four cardiac risk factors, NYHA (New York Heart Association) class (1994), CARPREG (cardiac disease in pregnancy) score (2001) and modified WHO class (2011) was assigned to the study population, at the time of enrolment. The Four non-cardiac risk factors taken were - age, parity, BMI and time of first antenatal visit. The four cardiac risk factors taken were: aetiology of heart disease, severity of lesion, associated cardiac complication (pulmonary artery hypertension (PAH), atrial fibrillation (AF), pulmonary edema) and prosthetic valve on anticoagulant therapy. The risk factors were co-related with adverse feto maternal outcome, which were defined as following. Adverse maternal outcomes were defined as occurrence of one or more of following events: development of congestive heart failure/pulmonary oedema, worsening of NYHA class, need for maternal intensive care unit admission and maternal mortality. Adverse fetal outcome was defined as occurrence of one or more of following-embryopathy, prematurity, LBW (Low birth weight), NICU (neonatal ICU) admission and fetal mortality: IUD (Intrauterine death), stillbirth or early neonatal death.

On enrolment, a detailed history, prior cardiac event, prior cardiac surgery noted, and patients had 12 lead ECG, ECHO, Doppler for outflow measurement and pulmonary artery pressure recorded in cardiology department. Pulmonary oedema was confirmed by X-ray chest. Severe MS (mitral stenosis) was taken as valve <1 cm^2 and severe PAH (pulmonary artery hypertension) was taken as >50 mmHg. Patients were closely followed up in ANC clinic, two weekly till 28 weeks than weekly. Patients in NYHA class III and IV were kept admitted throughout pregnancy. Patients were followed up till 4 weeks of delivery.

Statistical analysis

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean±SD and median. Quantitative variables were correlated using Independent T test/ Mann Whitney test. Qualitative variables were correlated using Chi-Square test /Fisher's exact test. Univariate logistic regression was used to assess the risk factors and co-relate with adverse fetal and maternal outcome. A p value of <0.05 was considered statistically significant. For the purpose of statistical analysis, in patients with multiple lesions most severe lesion was taken as predominant lesion. Analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

Ethical consideration

Present study was approved by the ethical committee of PGIMER and Dr. RML hospital prior to its commencement. Written and informed consent was taken from each participant before enrolment into the study.

RESULTS

Characteristics of study population.

Incidence of heart disease during the period of study in our tertiary care hospital was 2.69%. RHD was seen in 26 cases (74.29%), CHD (Congenital Heart Disease) in 5 cases (14.29%) and cardiomyopathy (CMP) in 4 cases (11.4%) (Figure 1).

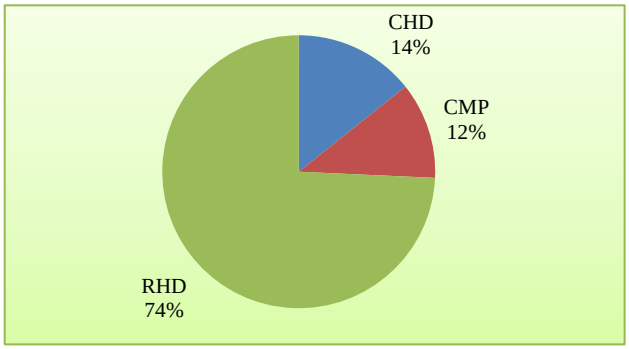

Figure 1: Frequency of etiology of heart disease in study population.

RHD is the still the predominant cardiac disease in developing countries like India. MS (Mitral Stenosis) was the commonest lesion found in patients with RHD and corrected ASD (Atrial Septal Defect) was the commonest lesion found in patients with CHD (Figure 2).

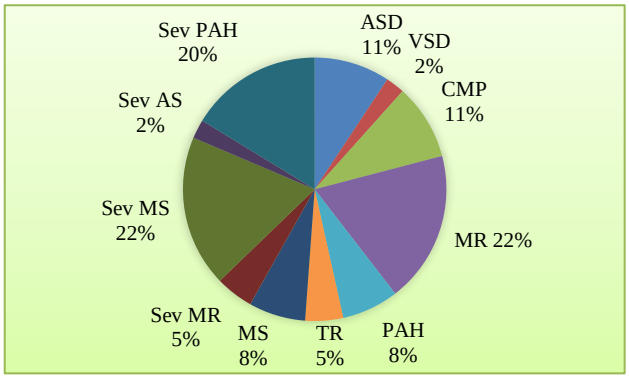

Figure 2: Frequency of predominant lesions in the study population.

Table 1: Various risk factors and co-relation with adverse maternal and fetal outcome in heart disease in pregnancy.

Risk Factor	Total no. of patients	Adverse maternal outcome	Adverse fetal outcome
Age (years)			
<30	30	17/30 (56.66%)	16/30 (53.33%)
>30	05	4/5 (80%)	1/5 (20%)
BMI (Kg/m^2)			
<30	27	13/27 (48.14%)	11/27 (40.74%)
>30	08	3/8 (37.5%)	4/8 (50%)
Parity			
Primigravida	11	5/11 (45.45%)	6/11 (54.54%)
Multigravida	23	11/23 (47.82%)	10/23 (43.47%)
Booking			
<20 weeks	10	2/10 (20%)	4/10 (40%)
>20 weeks	25	13/25 (52%)	11/25 (44%)
Etiology			
RHD	26	13/26 (50%)	12/26 (46.15%)
CHD	05	1/5 (20%)	1/5 (20%)
CMP	04	2/4 (50%)	2/4 (50%)
Severity of lesion			
Severe MS	08	8/8 (100%)	6/8 (75%)
Severe PAH	07	6/7 (85.7%)	5/7 (71.42%)
Associated AF	10	9/10 (90%)	6/10 (60%)
NYHA class			
I	11	1/11 (9.09%)	3/11 (27.27%)
II	19	9/19 (47.36%)	9/19 (47.36%)
III	02	2/2 (100%)	1/2 (50%)
IV	03	3/3 (100%)	3/3 (100%)
CARPREG score			
0	14	3/4 (21.42%)	6/4 (42.85%)
1	13	6/13 (46.15%)	5/13 (38.46%)
≥2	08	8/8 (100%)	6/8 (75%)
WHO class			
I	03	1/3 (33.33%)	2/3 (66.66%)
II	11	5/11 (45.45%)	0%
III	03	0%	2/3 (66.66%)
IV	18	11/18 (61.11%)	11/18 (61.11%)

This has been the finding of other earlier Indian studies.[2-4] There were no patients of maternal cyanotic heart disease and fetal congenital heart disease in the present study group. 18 patients were in WHO class 1V (51.4%), 8 patients had CARPREG score ≥2 (22.8%) and 3 patients were in NYHA class 1V (8.5%). Adverse feto-maternal outcome was seen in 21 patients (60%). In the present study population 17 patients (48.57%) were diagnosed with heart disease prior to pregnancy and 18 (51.42%) were diagnosed during the present pregnancy. None of pre-diagnosed patients in our study had any pre-conceptional counselling.

Mode of delivery

In the present study population, 22 patients delivered vaginally (62.86%). Vaginal delivery is the commonest mode seen in most of heart disease patients in studies.[2-4] However Martin et al had more LSCS than vaginal delivery in their study (55%).[5] In patients with ejection systolic fraction (EF) <30%, severe mitral stenosis and severe PAH, NYHA class IV who remain in failure despite treatment, decision for LSCS on cardiac grounds requires multidisciplinary management as maternal mortality can occur. Graded epidural given by anaesthetist can help to prevent sudden changes in cardiac output during surgery, as in two of our patients, who had "near miss" condition. Vaginal delivery is generally easy in cardiac patients as cervix dilates fast and most deliver safely. In the present study population 13 patients (37.14%) had LSCS. Out of these, only 2 were emergency and rest were elective, 1 had cardiac indication (severe MS + severe PAH) and was in NYHA class IV and the other 12 patients (92.30%) had obstetrical indications for caesarean section. One patient with idiopathic dilated cardiomyopathy had EF of 30 %, would have needed LSCS on cardiac grounds but developed reversal of flow in umbilical artery and had LSCS for obstetrical indication (reversal of umbilical artery flow) at 34 weeks.

Risk factors for adverse maternal outcome

None of the non-cardiac risk factors in the present study were found to be associated with adverse maternal outcome. Severe MS, severe PAH, associated AF, NYHA Class IV, CARPREG score ≥2 were the individual variables found to be significantly associated with adverse maternal outcome (Table 2). Other studies also showed the similar results.[6,7,11-13] Severe MS and severe PAH (Pulmonary artery hypertension) was seen in 8 cases (22.85%) which correlated significantly with adverse fetomaternal outcome. Mild-moderate MS, MR, ASD, VSD and cardiomyopathy were not significantly associated with adverse maternal outcome. Commonest adverse maternal outcome was admission in ICU (37.14%) and commonest adverse fetal outcome was prematurity (22.85%). LSCS became inadvertently a marker of adverse maternal outcome because post LSCS all patients needed ICU care. Prosthetic valve patients

tolerated pregnancy well and prosthetic valve on anticoagulant was not a risk factor, as seen in some studies.[8-10]

There was no maternal mortality in our study population whereas other studies have reported maternal mortality in heart disease in pregnancy.[2,7-11]

Table 2: Univariate regression analysis to correlate risk factors with adverse maternal outcome.

Risk factors	Worsening of NYHA class		ICU admission		PE/CHF	
Noncardiac risk factors	**P value**	**OR**	**P value**	**OR**	**P value**	**OR**
Age	0.321	1.100	0.740	0.969	0.543	0.943
BMI	0.196	1.117	0.266	0.907	0.343	0.921
Parity						
primigravida		1		1		1
multigravida	0.459	0.526	0.279	0.405	0.279	0.405
grandmultipara	0.748	1.667	0.427	0.200	0.427	0.200
Time ofenrollment						
1st trimester				1.000		1.000
2nd trimester	0.487	0.444	0.937	0.900	0.937	0.900
3rd trimester	0.276	0.286	0.605	1.909	0.605	1.909
Cardiac risk factors						
cardiac disease						
CHD		1		1		1
CMP	0.719	0.600	0.427	4.715	0.208	10.997
RHD	0.539	0.538	0.115	7.000	0.284	5.972
Predominant lesion						
VSD	0.914	0.778	0.870	0.681	0.870	0.681
ASD	0.329	2.875	0.343	0.198	.343	0.198
CMP	0.867	0.815	0.769	0.700	0.406	2.444
Mild-mod MR	0.365	0.352	0.215	0.243	0.295	0.300
Mild-mod PAH	0.867	0.815	0.769	0.700	0.343	0.198
Mild-mod TR	0.678	0.447	0.627	0.391	0.627	0.391
Mild-mod MS	0.849	1.278	.941	1.100	0.205	5.111
Sev MR	0.914	0.778	.870	0.681	0.295	0.300
Sev MS	0.230	2.667	0.002	19.250	0.014	8.400
Sev AS	0.914	0.778	0.405	7.046	0.405	7.046
Sev PAH	0.075	4.889	0.020	9.167	0.115	4.000
On AC drug	0.626	0.643	0.334	2.171	0.886	1.125
Associated cardiac complication						
AF/PE	0.230	2.667	<.0001	1186.2	0.002	19.250
NYHA functional class						
I		1		1		1.000
II	0.624	1.552	0.153	9.828	0.119	11.963
III	0.495	3.003	0.157	19.011	0.584	3.797
IV	0.657	0.429	0.035	133.00	0.035	133.012
CARPREG risk score						
0		1		1		1
1	0.165	3.750	0.162	9.667	0.268	3.900
≥2	0.225	3.600	0.004	493.00	0.002	91.000
Modified WHO class						
I		1		1		1
II	0.439	4.200	0.747	1.842	0.571	2.882
III	1.000	1.000	1.000	1.000	1.000	1.000
IV	0.477	3.640	0.282	7.000	0.338	5.667

NYHA functional class and CARPREG Risk score were validated in our study as predictors for adverse maternal outcome Our study had more adverse maternal outcome than CARPREG study, having incidence of adverse maternal outcome as 21.4%, 46.1% and 100% (Table 1) as compared to 1%, 27% and 75% found by Siu et al, in score 0, 1 or ≥2 respectively. This can be explained as all our LSCS patients were shifted to ICU, as per hospital

protocol and admission to ICU was one of the predefined markers for adverse maternal outcome in the present study.

Risk factors for adverse fetal outcome

Non-cardiac risk factors of reporting after 20 weeks of pregnancy and multiparty was found to be associated with adverse fetal outcome. Mild-moderate MS, MR, ASD, VSD and cardiomyopathy were not significantly associated with adverse fetal outcome.

Warfarin embryopathy was noted in one patient with prosthetic valve. Cardiac risk factors like CARPREG risk score ≥2, AF and severe MS was found to be correlated with adverse fetal outcome (Table 3).

Table 3: Univariate regression analysis to correlate risk factors with adverse fetal outcome.

RISK FACTORS	Prematurity		NICU admission		Low birth weight	
Noncardiac risk factors	**P value**	**OR**	**P value**	**OR**	**P value**	**OR**
Age	0.418	0.917	0.542	0.945	0.079	0.832
BMI	0.565	1.050	0.523	0.950	0.653	0.966
Parity						
primigravidae		1		1		1
multigravidae	0.323	0.417	0.089	0.233	0.045	0.157
grandmultipara	0.748	1.667	0.748	0.600	0.501	0.333
First visit						
1st trimester		1		1		1
2nd trimester	0.085	0.083	0.043	0.061	0.083	0.100
3rd trimester	0.535	0.500	0.290	0.267	0.378	0.333
Cardiac risk factors						
Cardiac disease						
CHD		1				1
CMP	0.427	4.714	0.445	2.999	0.803	1.400
RHD	0.207	5.054	0.441	2.500	0.924	1.100
Predominant lesion						
VSD	0.962	0.895	0.786	0.531	0.535	4.261
ASD	0.436	0.263	0.598	0.528	0.455	0.405
CMP	0.972	0.958	0.576	1.818	0.760	1.385
MR	0.962	0.895	0.396	2.000	0.728	0.750
PAH	0.972	0.958	0.270	0.152	0.455	0.405
TR	0.732	0.515	0.537	0.303	0.834	1.357
MS	0.561	0.353	0.376	0.206	0.306	0.161
Sev MR	0.439	3.125	0.471	5.400	0.535	4.261
Sev MS	0.004	15.33	0.043	5.429	0.104	3.778
Sev AS	0.340	9.372	0.471	5.400	0.535	4.261
Sev PAH	0.046	6.133	0.231	2.815	0.398	2.061
On AC drug	0.147	3.360	0.600	1.511	0.104	3.778
AF Associated cardiac complications	0.004	15.33	0.043	5.429	0.104	3.778
NYHA Class						
I		1		1		1
II	0.842	0.824	1.000	1.000	0.627	1.500
III	0.441	3.500	0.661	2.000	0.661	2.000
IV	0.184	7.000	0.327	4.000	0.327	4.000
CARPREG score						
0		1		1		1
1	0.268	03.90	0.475	0.540	0.348	2.143
2	0.015	21.67	0.232	3.000	0.129	4.167
WHO class						
I		1		1		1
II	0.578	0.304	0.063	0.050	0.063	0.050
III	0.406	4.200	0.423	0.250	1.000	1.000
IV	0.199	5.667	0.597	0.500	0.720	0.625

DISCUSSION

Heart disease in pregnancy is a high-risk pregnancy with a risk of mortality or near miss events and adverse feto-maternal outcome. Adverse fetal events closely co-relate with adverse maternal events. This study, which was carried out in a government tertiary level hospital in capital of India, aimed at contemporary assessment of risk factors in our population which still has preponderance of RHD over CHD.

NYHA classification is a functional classification does not take into account structural lesion but despite being old (made in 1928) updated in 1994 has shown significant correlation with feto-maternal outcome. It has been incorporated in CARPREG risk score and modified WHO classification.[7,8] However there are certain discrepancies between the two. NYHA Class III and IV are in WHO Class IV signifying great risk and contraindication to pregnancy, whereas CARPREG gives it score 1 associated with 27 % maternal risk and needs one more risk factor to increase risk to 75%. EF <40% is in WHO Class IV but CARPREG Score of 1 is given to EF <30 %. CARPREG score does not give any individual fetal risk assessment as per scores. However, they found an overall 20% adverse fetal outcome in their study. On the other hand, WHO modified classification has class I and IV well defined but mainly deals with CHD which is more common in west and considers severe valvular lesions in WHO class IV.

WHO class IV does not differentiate between mild or severe PAH. Mitral valve regurgitation (MR) comes in WHO class II-III; with increased maternal risk but clinically MR patients have less adverse outcome. CARPREG score does not include severe PAH as an individual risk, probably because of low incidence in Canadian population. Another risk stratification score Zahara study is used in congenital heart disease with pregnancy would not be useful in our population which still has preponderance of RHD patients. There are very few studies available in India that are prospective, focused particularly on heart disease in pregnancy. Most studies were retrospective. Western literature mainly has pregnancy with congenital heart disease, rheumatic heart disease being very rare in developed nations.

Adverse fetal outcome in the present study with CARPREG score ≥2, was much higher (75%) than 20% found in the multicentric study done by Siu et al in Canada, despite their including twins in the study 4. This can be explained because of high incidence of prematurity (28.57%) in the present study which was taken to be a marker for adverse fetal outcome.

CARPREG score has been validated in many studies.[5,8,12,13] CARPREG Scores though gives a good correlation with adverse fetomaternal outcome does not include PAH and AF in its score which came out to be independent variables significantly associated with adverse outcome. Other studies have found that CARPREG scores overestimated the maternal risk.[8,14]

WHO class did not have significant co-relation to predict adverse maternal outcome in the present study. This is also the finding of large ROPAC Study by van Hagen IM, which concluded that WHO classification is a moderately accurately tool for predicting adverse events in advanced countries but suboptimal in developing nations.[15] Acquired heart disease, seen in developing nations are underrepresented in WHO classification, as found in an African study done in 1914.[15] Studies having preponderance of congenital heart disease subjects show more accuracy of WHO classification for prediction of adverse maternal outcome as the study done by Domenech P et al had 68% CHD but only 16% valvopathies.[16] Another alarming observation was the total lack of pre-pregnancy counseling in all of the study population despite living in capital of India. Pre-pregnancy counseling and adequate risk assessment during pregnancy are essential components in management of this high-risk pregnancy.[17]

The shortcoming of the present study was the small sample size. More multicentric studies are required in India to stratify risk factors in our population.

CONCLUSION

In the present study population in capital of India RHD was still most common aetiology for heart disease followed by CHD and cardiomyopathy, paralleling the prevalence in developing nations. Severe MS and PAH, NYHA class IV, CARPREG risk score ≥2 and AF came out to be the independent cardiac risk factors associated with adverse outcome. There was no co-relation between non-cardiac risk factors and adverse maternal outcome. Optimal outcome in pregnant women with underlying heart disease needs evaluation and monitoring under multidisciplinary approach including obstetrician, cardiologist and anaesthetist. Awareness for peripartum cardiomyopathy and availability of ECHO facilities is required for optimal management. The need for periconceptional counselling in these patients is emphasized.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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