

Maternal and Neonatal Outcomes in Pregnant Patients with Pre-Existing Cardiac Diseases

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ABSTRACT

Objective: To assess the maternal and fetal outcome in pregnant patients with preexisting cardiac conditions and to determine the prevalence of different cardiac diseases among pregnant patients.

Study Design: Cross sectional study.

Place and Duration of Study: Tertiary Cardiac Care Center in Rawalpindi Pakistan, from Dec 2021 to Apr 2022.

Methodology: This was across sectional study done in a tertiary cardiac care center in Rawalpindi. A total of (n=100) pregnant patients with pre-existing cardiac diseases were included in the study from Dec 2021 to Apr 2022 over a period of 5 months. Prospective data including patients' demographics and their outcomes was collected using preformed proformas. Data was analyzed by SPSS version-23. Prevalence of maternal death, fetal death, maternal complications and neonatal complications were the primary outcomes of study. Descriptive statistics were run to present categorical data in frequencies and percentages. Chi-square and Fisher Exact Test was applied to find the association between study variables at 95% CI and 5% margin of error ($\alpha=5\%$).

Results: A total of (n=100) patients were included in our study which was conducted from Dec 2021 to Apr 2022. Maternal mortality was observed in 6% (n=6) of patients. Maternal outcomes of pulmonary edema were seen in 24% (n=24) of patients and post-partum hemorrhage was seen in 14% (n=14) patients. Three parameters of perinatal outcome were studied i.e., low birth weight, preterm delivery and death. 39% (n=39) neonates were found to have low birth weight, 22% (n=22) were preterm and perinatal mortality was 21% (n=21). The primary results of our study showed 6% (n=6) maternal mortality and 21% (n=21) perinatal mortality.

Conclusion: Overall maternal mortality was 6% while perinatal mortality was 21%. There existed a statistically significant ($p<0.05$) association of age and neonatal outcome with maternal complications. With proper counseling, some of the avoidable maternal and perinatal deaths can be prevented.

Keywords: Low birth weight, Maternal mortality, Pregnancy, Pulmonary edema, Postpartum haemorrhage, Perinatal mortality, Preterm,

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INTRODUCTION

Pregnant women with cardiac diseases are at increased risk of adverse neonatal, obstetric and maternal outcomes. In recent years, due to better health care facilities, advancement in medical treatments and surgical correction of congenital heart disease, more women with cardiac disease are surviving till reproductive age. Incidence of maternal cardiac diseases in pregnancy is approximately 0.2-3% globally. Despite recent advancements, cardiac diseases contribute towards increased fetomaternal morbidity and mortality (10-25%).¹⁻² In our country this is firstly due to increased prevalence of rheumatic heart diseases and secondly due to lack of diagnostic facilities and referral system in rural health care setups. During pregnancy undiagnosed valvular heart diseases become a cause of

significant morbidity due to hemodynamic stress.¹⁻² Over expression of rennin-angiotensin-aldosterone system, decreased peripheral vascular resistance, increased protein synthesis and hematopoiesis and increase in plasma volume all contribute to increase preload and decrease afterload which increases cardiac output.³⁻⁵ Cardiac diseases are the second most prevalent cause of mortality after psychiatric illness in pregnant women. Pregnancy in pre-existing cardiac diseases not only poses a risk of maternal mortality but also significant morbidity including arrhythmias, pulmonary edema, cardiac failure and postpartum hemorrhage. Similarly, neonatal morbidity and mortality increases mainly due to premature births, low birth weights and intrauterine growth restriction.⁶ Neonates of females with cardiac diseases have increased incidence of congenital heart defects; 3-50% as compared to females with no cardiac diseases.⁵ Pregnancy is well tolerated in patients with corrected congenital heart defects. This

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Neonatal Outcomes in Pregnant Patients

study was designed to analyze different types of cardiac diseases pregnant females present with and to evaluate the outcome of pregnancies with cardiac disease in Armed Forces Institute of Cardiology.

Cardiac obstetric patients are an unusual cohort. Armed Force Institute of Cardiology/National Institute of Heart Disease is a tertiary care cardiology and cardiac surgery center, fully equipped to cater this rare group. Fetomaternal outcomes can be helpful in identifying cardiac diseases with poor outcomes to guide patients, provide appropriate obstetric counseling about current and future pregnancies and to anticipate the challenges that can be faced once pregnant patients with cardiac diseases arrive in the hospital.

METHODOLOGY

This was a cross sectional study carried out in a tertiary cardiac care center in Rawalpindi Pakistan, from December 2021 to April 2022, after approval from IERB (letter #26/10/R&D/2021/118)

Sample Size: With reference to 3% prevalence of cardiac diseases in pregnant females¹, the sample size calculated was n=45 at 95% CI and 5% margin of error by using WHO calculator. However, the data collected was of 100 cases to increase the power of study.

Inclusion Criteria: All females fulfilling the inclusion criterion with pre-existing cardiac diseases presenting to healthcare unit for delivery were included. A total of (n=100) patients were included in the study. Informed consent was taken from all patients. Inclusion criteria encompassed booked patients with pre-existing cardiac diseases that were planned for multidisciplinary obstetric, cardiology, anesthesiology and neonatology care and patients with singleton pregnancy.

Exclusion Criteria: Patients with new diagnosis of cardiac diseases, known intra uterine death or miscarriage and twin pregnancies were excluded.

Maternal complications included pulmonary edema, post partum hemorrhage, stuck valves and arrhythmias. Neonatal complications included low birth weight, prematurity and intrauterine death. Demographics of all patients including age, gravidity, parity, co morbidities and family history were assessed. Patients were admitted in female cardiology ward with labor room. Operating theatre facilities were present in the same building on first floor. All patients were reviewed by obstetrician, on call cardiologist and anesthetist for preanesthesia assessment. Patients were followed up on the ward and prospective data was

collected using preformed proformas. Fresh echocardiograms were done to determine status of pre-existing cardiac diseases. Duration of stay of mother and neonate was recorded.

Pre-existing maternal cardiac diseases were defined as known cardiac conditions for which patient had been under care of a cardiologist. Maternal age was defined as age of mother at the time of infant's birth. Post partum hemorrhage was defined as post delivery blood loss of more than 500ml. Pulmonary edema was defined as fluid in the lungs causing decreased oxygen saturations, crackles in lungs and severe dyspnea. Pre term delivery was defined as delivery before 37 weeks of gestation. Low birth weight was defined according to world health organization (WHO) as weight at birth less than 2500 grams. Low birth weight for preterm deliveries was determined according to centile chart specified by WHO.

Prevalence of maternal death, fetal death, maternal complications and neonatal complications were the primary outcomes of study. Data was analyzed by SPSS version-23. Descriptive statistics was run to present categorical data in frequencies and percentages. Chi-square and Fisher Exact Test was applied to find the association between study variables at 95% CI and 5% margin of error ($\alpha=5\%$). *p*-value less than or equal to 0.05 was considered statistically significant ($p\leq 0.05$).

RESULTS

A total of 100 patients were included in our study which was conducted from December 2021 to April 2022. Patients included had mean age of 26.62 ± 4.59 years. About 23% patients were primigravida and 77% patients were multiparous. Cesarean section was done in 68% of patients, 32% had spontaneous vaginal delivery. About 71% patients were in class NYHA I & II and rest 29% were in NYHA III & IV at the time of admission (n=100) (Table-I).

Patients were divided into two main groups namely; rheumatic heart diseases and congenital heart diseases. Most common congenital heart disease identified was Atrial Septal Defect (ASD) with incidence of 7% followed by Ventricular Septal Defect (VSD) 5%. Mitral valve disease was identified to be the most frequent presentation. About 12% (n=12) patients were found to have mitral stenosis which was the commonest rheumatic heart disease, 7% (n=7) were found to have severe mitral regurgitation and 17% (n=17) were found to have metallic mitral valve replacement.

Table-I: Maternal Distribution According to Age, Parity and Mode of Delivery

| Maternal Distribution According to Parity | |
|--|---------------|
| Parity | n(%) |
| Primigravida | 23(23%) |
| Multigravida | 77(77%) |
| Maternal Distribution According to Age | |
| Age (years) | n(%) |
| <20 | 1(1%) |
| 20-29 | 71(71%) |
| 30-34 | 23(23%) |
| 35-39 | 5(5%) |
| Maternal Distribution According to Mode of Delivery | |
| Mode | Frequency (n) |
| Spontaneous Vaginal delivery | 32(32%) |
| Cesarean Section | 68(68%) |
| Maternal Distribution According to NYHA Classification | |
| NYHA I&II | 71(71%) |
| NYHA III&IV | 29 (29%) |

Of note was presentation of mothers with cardiomyopathies. About 8% (n=8) had previously known peripartum cardiomyopathy and 4% (n=4) had dilated cardiomyopathy (Figure-1 & 2).

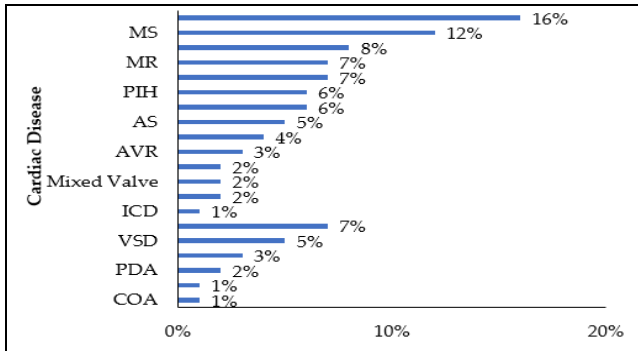


Figure-1: Frequencies of Pre-existing Cardiac Diseases

COA=Coarctation of Aorta; PDA=Patent Ductus Arteriosus; TOF= Tetralogy of Fallot; VSD=Ventricular Septal Defect; ASD=Atrial Septal Defect; ICD= Implantable Cardioverter Defibrillator; IHD= Ischemic Heart Disease; AR= Aortic Regurgitation; AVR=Aortic Valve Replacement; DCM=Dilated Cardiomyopathy; AS=Aortic Stenosis; HTN= Hypertension; PIH=Pregnancy Induced Hypertension; MR=Mitral Regurgitation; PPCM=Peripartum Cardiomyopathy; MS=Mitral Stenosis; MVR; Mitral valve replacement.

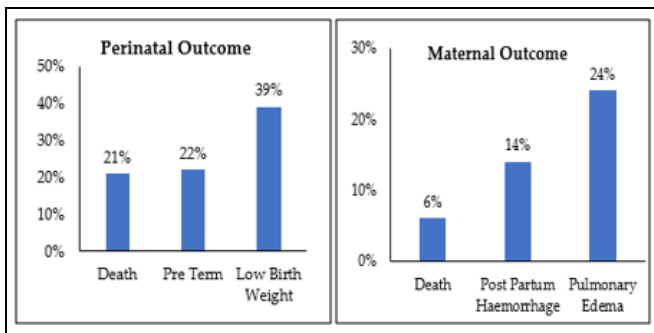


Figure-2: Maternal and Perinatal Outcomes

Maternal mortality was observed in 6% (n=6) of patients. Maternal outcomes of pulmonary edema were seen in 24% (n=24) of patients and post-partum haemorrhage was seen in 14% (n=14) patients whereas pre-eclampsia was seen in 5% (n=5) participants and eclampsia was observed in 1% (n=1) patient. About 20 mothers had prosthetic valve replacements, 17 participants had metallic mitral valve and 3 had metallic aortic valve. Out of these 20 patients, 3 presented with stuck valve and left ventricular failure. A total of 6 mothers encountered complications of arrhythmias. 4% (n=4) had atrial fibrillation with rapid ventricular rate and 2%(n=2) had supraventricular tachycardias. Three parameters of perinatal outcome were studied i.e. preterm delivery, low birth weight and death. 39% (n=39) neonates were found to have low birthweight, 22% (n=22) were preterm. The primary results of our study showed 6% (n=6) maternal mortality and 21% (n=21) perinatal mortality. All mothers who died were classified in NYHA III/IV. Chi-square and Fisher Exact Test results showed insignificant ($p>0.05$) association comorbidities and age with maternal outcomes (Table-II).

Table-II Association Between Comorbidities, Age, NYHA Class and Maternal Outcome

| | Maternal Outcome | | p-value | |
|---------------|------------------|------|---------|-------|
| | Alive | Dead | | |
| Comorbidities | Cholecystectomy | 1 | 0 | 0.610 |
| | AF | 1 | 1 | |
| | AF, TIA | 1 | 0 | |
| | Asthma, AF | 3 | 0 | |
| | HTN | 3 | 0 | |
| | Allergic | 1 | 0 | |
| | Asthma | 2 | 0 | |
| | CVA | 1 | 0 | |
| | MCTD | 1 | 0 | |
| | DM | 2 | 0 | |
| | Nil | 78 | 5 | |
| | Age (years) | <20 | 1 | |
| 20-29 | | 67 | 4 | |
| 30-34 | | 21 | 2 | |
| 35-39 | | 5 | 0 | |

$n=100$; $p\text{-value} \leq 0.05$ = significant; ns =non-significant. $n=100$; $p\text{-value} \leq 0.05$ =significant; ns =non-significant; AF= atrial fibrillatio; TIA= transient ischemic attack; HTN= hypertension; CVA= cerebrovascular accident; MCTD=mixed connective tissue disease; DM= diabetes mellitus

There was statistically significant ($p<0.05$) association of age and neonatal outcome with maternal complications, while insignificant ($p>0.05$) result of age of the mother with neonatal complications (Table-III).

Neonatal Outcomes in Pregnant Patients

Table-III: Association of Age with Maternal and Neonatal Complications

| Age (Years) | Maternal Complications | | | | | | | | | | | | p-value |
|------------------|------------------------|--------------------|----------------------------|-------------|-----|--------------------|-----|-----|-----------------|---------------|-----------------------------------|----------------------------|---------|
| | Nil | Pre-Eclampsia, PPH | PSV, PPH, Pulmonary Edema | AF with RVR | LVF | AF with rapid rate | SVT | PPH | Pulmonary Edema | Eclampsia PPH | Stuck Valve, PPH, Pulmonary Edema | Raised Blood pressure, PPH | |
| <20 | 1 | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.003* |
| 20-29 | 49 | 2 | 0 | 2 | 1 | 1 | 1 | 2 | 12 | 1 | 1 | 0 | |
| 30-34 | 5 | 3 | 2 | 1 | 0 | 0 | 0 | 1 | 7 | 1 | 0 | 2 | |
| 35-39 | 2 | - | 0 | 0 | 0 | 0 | 1 | 0 | 2 | 0 | 0 | 0 | |
| Neonatal Outcome | Nil | Pre-Eclampsia, PPH | PSV, PPH, Pulmonary Oedema | AF with RVR | LVF | AF with rapid rate | SVT | PPH | Pulmonary Edema | Eclampsia PPH | Stuck Valve, PPH, Pulmonary Edema | Raised Blood pressure, PPH | p-value |
| Alive | 50 | 4 | 1 | 2 | 1 | 1 | 1 | 3 | 15 | 1 | 0 | 0 | 0.007* |
| IUD | 7 | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 6 | 1 | 1 | 2 | |
| Age (years) | Neonatal Complications | | | | | | | | | | | p-value | |
| | Nil | | | Preterm | | | | LBW | | | | | |
| <20 | 1 | | | 0 | | | | 0 | | | | 0.092 | |
| 20-29 | 49 | | | 12 | | | | 10 | | | | | |
| 30-34 | 9 | | | 8 | | | | 6 | | | | | |
| 35-39 | 2 | | | 2 | | | | 1 | | | | | |

*PPH=postpartum haemorrhage, RVR=rapid ventricular rate, RSV=pressure support ventilation

DISCUSSION

Pregnancy with cardiovascular diseases poses a challenge for obstetricians and cardiologists. In pregnant population with cardiac diseases in developed countries, congenital heart diseases comprise of around 70-80% of the patients. However, in Pakistan rheumatic heart disease is still the commonest cardiac disease in women of childbearing age.⁷ This is mainly due to lack of education, low socioeconomic status and poor health care facilities in basic health units. However, recent improvements in health care facilities, public awareness and vigilant antenatal surveillance have seen a decline in incidence of rheumatic heart disease in the region of South Asia. Advancements in treatments of valvular heart diseases with percutaneous trans venous mitral commissurotomy (PTMC), valve replacements and early surgical correction of congenital heart diseases is allowing more women to survive till child bearing age. The physiological change in pregnancy leads to haemodynamic stress in presence of cardiac diseases and still increases number of admissions and complications in obstetric patients. According to Geva *et al.* cardiac output raises by 30-50% by third trimester of pregnancy.⁸ During labor, maternal oxygen demand can tripartite. Raised blood pressures during active phase of labor can significantly increase cardiovascular complications. The CARPREG

II study also concluded that most maternal cardiac complications occur during antepartum period.⁹ Current study showed similar population demographics of age and parity with other studies done in this region. Our center had multi-disciplinary approach and input from cardiac anesthetist, cardiologist and obstetrician and mode of delivery was decided beforehand.

The study included 100 patients. Commonest lesion found out was mitral stenosis with incidence of 12%. This was in keeping with Mazhar *et al.* and Pratibha *et al.*^{7,10} This current study showed 32% mothers had spontaneous vaginal delivery and 68% had cesarean section. This is comparable to similar study done by Salam *et al.* in Kashmir, India on similar population which showed 35.6% patients had spontaneous vaginal delivery.¹¹

This study showed that 71% patients were in class NYHA I & II and rest 29% were in NYHA III & IV. This was similar to Liaquat *et al.* who reported these to be 69% & 31% respectively.¹² A study done by Bhatla reported that mothers with dyspnea NYHA I/II not only tend to have better prognosis than those who have NYHA III/IV but their neonates also have better outcomes in terms of survival and birth weight.¹³ This was comparable to our study which showed all maternal deaths were in patients with NYHA III/IV. Javaid *et al.* demonstrated similar results and conclu-

ded that pregnancy in women with preexisting cardiac diseases resulted in increased preterm and low birth weight neonates.⁴ A metaanalysis of 32 articles conducted by Isabel Hardee and survival analysis done by Spector *et al.* showed that neonatal outcomes worsened with worsening severity of maternal congenital heart disease.^{13,14}

Primary outcomes of our study were maternal and fetal outcome. Out of 100 patients, maternal mortality in our study was 6% which was comparable with other studies (2.7-8.1%).^{7,12,15} A study published in European Cardiology Review (ECR) by Poli *et al.* reported maternal death to be slightly higher at 12%.¹⁶ Causes of death were acute pulmonary edema and congestive cardiac failure. In maternal mortality, highest incidence of death was in patients of dilated and peripartum cardiomyopathies. Cardiomyopathies are serious and often fatal cardiac complication in pregnant patients. There were a total of 11 patients with poor ejection fraction (EF \leq 30%) 3 had known dilated cardiomyopathy and 8 had peripartum cardiomyopathy. Out of 11(27%) women in total with both forms of cardiomyopathies, 3 died. This referred to worse outcomes in patients with worsening functional classification of NYHA III/IV. This was demonstrated in a retrospective analysis done by Subbaiah *et al.* in New Delhi, India.¹⁷ Novel treatments for peripartum cardiomyopathy in pregnancy are under research. This involves use of Bromocriptine to inhibit byproducts of prolactin.¹⁸ Maternal mortality in patients of pulmonary hypertension in our study was 16%. This was comparable to Alireza *et al.* which showed maternal mortality of 16.33% in mothers with pulmonary arterial hypertension.¹⁹ Other studies done by Lane and Kiely reported it to be significantly higher between 30-56%. Hesselink *et al.* in registry of pregnancy and cardiac disease (ROPAC) also reported highest complication rate in women with pulmonary arterial hypertension.^{20,21} This was mainly attributed to physiological stress on already poor right ventricle leading to right heart failure. Post-partum hemorrhage occurred in 14% patients with identifiable risk factors of episiotomy, uterine atony and patients being on anticoagulation for atrial fibrillation and metallic heart valves.²²

Perinatal mortality was 21%. There was a high incidence of still births (4 out of 6, 66%) in women with pulmonary hypertension, possibly attributing to lack of understanding of severity of disease in low socio-economic population and lack of counseling to avoid conception. This was comparable to Owens *et al* who

reported that mothers with pulmonary hypertension and cardiomyopathies have significantly increased neonatal complications.²³

LIMITATIONS OF STUDY

This is a single center study with limited sample size, so results cannot be generalized to whole population. Moreover, follow up study for the duration of 5 to 10 years is required to determine the long term cardiac status of study participants.

CONCLUSION

Due to advancements in medical field, more women with cardiac diseases are surviving till child bearing age. Despite these advancements, cardiac diseases remain one of the leading causes of morbidity and mortality in pregnancy. Our study showed comparable results with other studies done in region of Asia. Overall maternal mortality was 6% while perinatal mortality was 21%. Incidence of preterm and low birth weight neonates was high. Women of child bearing age with cardiac diseases should have preconception counseling and advice to avoid pregnancy in certain conditions and on the other hand proper antenatal evaluation and multidisciplinary care once they have conceived. With proper counseling, some of the avoidable maternal and perinatal deaths can be prevented. This warrants multidisciplinary approach in antenatal care to improve maternal and fetal outcomes.

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Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

FUR: Manuscript writing, drafting, concept and editing

MS: Intellectual contribution, concept and final approval

IAK: Study design, concept and critical review

MBS: Intellectual contribution, concept & final approval

HY: Data collection, data entry and review of article

WA: Formatting, critical review and data collection/entry

SIS: Analysis, manuscript writing and proof reading

AK: Analysis, manuscript writing and proof reading

NAS: Proof reading, Intellectual contribution, final approval

NA: Review of article, formatting and critical review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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