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Maryam Movahedi[1], Parvin Bahrami[1], Amirreza Sajadieh[1], Minoo Movahedi[2], Shima Mehdipour[3]

THE SPECTRUM AND OUTCOMES OF CARDIAC DISEASE IN PREGNANCY: A RETROSPECTIVE COHORT STUDY

[1]Department of Cardiology, Alzahra University Hospital, Isfahan University of Medical Science, Isfahan, Iran
[2]Department of Obstetrics and Gynecology, Isfahan University of Medical Sciences, Isfahan, Iran
[3]Department of Cardiology, Isfahan University of Medical Sciences, Isfahan, Iran

ABSTRACT

BACKGROUND. Cardiovascular disease (CVD) complicates pregnancies worldwide and remains a major contributor to maternal mortality, particularly in low- and middle-income countries (LMICs).
OBJECTIVE. This study aimed to evaluate the prevalence, clinical profiles, and outcomes of heart disease (HD) among pregnant women referred to the Joint Clinic of Pregnancy and Heart Disease at Al-Zahra Hospital and assess the utility and limitations of the modified World Health Organization (mWHO) risk classification system.
MATERIAL AND METHODS. We analyzed a retrospective cohort of 389 pregnant women with confirmed heart disease managed at the Joint Clinic of Pregnancy and Heart Disease, a tertiary referral centre, Al-Zahra Hospital (Isfahan, Iran), between March 2017 and March 2023. Participants were followed until hospital discharge after delivery or pregnancy termination. Patients were stratified into mWHO risk classes and categorized by disease type, including congenital heart disease (CHD), valvular heart disease (VHD), cardiomyopathy, and other conditions. Clinical outcomes, including maternal mortality, abortion and delivery methods, were examined.
RESULTS. VHD was the most prevalent condition (35.99%), followed by CHD (20.82%). Severe mitral stenosis and prosthetic heart valves were the most common VHD subtypes. Among CHD cases, atrial septal defect was predominant. Class IV mWHO patients comprised 21.85%, highlighting the high-risk population. Cesarean deliveries were common (53%). Maternal mortality was 1.0%, with four deaths mostly due to pulmonary hypertension.
CONCLUSIONS. The observed outcomes in this high-risk cohort compare favourably to those reported in similar LMIC settings, suggesting that structured multidisciplinary care and mWHO-based risk assessment may contribute to improved maternal and fetal management. However, overlapping and unclassified conditions highlight the need to refine current risk stratification frameworks for pregnancy in cardiac patients.

Keywords: *pregnancy, cardiovascular disease, valvular heart disease, cardio-obstetrics, multidisciplinary maternal care*

INTRODUCTION

In 2020, nearly 800 women died every day from preventable causes related to pregnancy and childbirth – a tragedy that occurred almost every two minutes globally (1). Cardiovascular disease complicates 1-4% of pregnancies, accounting for 16% of maternal deaths globally. It is the leading cause of maternal mortality in high-income countries and presents unique challenges in low-and middle-income settings (2,3).

Pregnancy induces major cardiovascular changes to support fetal development, including a 10-30% drop in systemic vascular resistance and a 30-50% increase in cardiac output by mid-pregnancy. Heart rate and stroke volume rise, with plasma volume expanding by up to 45% at term (2). During labor, uterine contractions further elevate cardiac output due to autotransfusion from the placenta, adding strain to the heart through fluctuations in blood pressure and volume. These changes can worsen preexisting conditions and lead to complications such as heart failure, preeclampsia, and arrhythmias. Women with cardiovascular conditions are at greater risk, facing potential complications like intrauterine growth restriction, fetal demise, or low birth weight (4,5).

Despite a 34% reduction in the global maternal mortality ratio (MMR) since 2000, almost 95% of maternal deaths still occur in low- and middle-income countries, highlighting stark disparities in maternal care (1). Risk assessment is crucial for women with

congenital heart disease (CHD), particularly in those with moderate to high-risk cardiac conditions, as pregnancy-related hemodynamic changes – including increased cardiac output and hypercoagulability – can destabilize underlying conditions (6). The latest ESC Guidelines for the management of cardiovascular diseases during pregnancy recommended to "perform risk assessment in all women with cardiac diseases of childbearing age and before conception, using the modified World Health Organization (mWHO) classification of maternal risk" (7). Skilled healthcare professionals before, during, and after childbirth can dramatically reduce maternal mortality and improve outcomes for both mothers and newborns, particularly in resource-limited settings (1).

In light of these alarming trends, the Joint Clinic of Pregnancy and Heart Disease at Al-Zahra Hospital conducted this study to evaluate the prevalence and clinical profiles of heart disease among pregnant women. This research underscores the practical application and limitations of the mWHO risk classification system in real-world settings, particularly for conditions with overlapping or ambiguous criteria. By advancing early risk stratification and integrating multidisciplinary care, we aim to improve outcomes and ensure tailored, life-saving interventions to those who need them most.

METHODS

Study design and setting. This was a retrospective cohort study of 389 pregnant women with confirmed heart disease (HD) managed at the Joint Clinic of Pregnancy and Heart Disease, a tertiary referral centre at Al-Zahra Hospital, Isfahan, Iran. The clinic serves as a national referral hub for complex cardio-obstetric cases, receiving patients from Isfahan province and surrounding regions.

Study population and inclusion criteria. All women with a confirmed diagnosis of HD who were admitted or referred to the clinic between March 2017 and March 2023 were eligible. Referrals came from outpatient cardiology and obstetrics clinics, in-hospital departments, private practices, and external hospitals. Inclusion criteria were:

1. Confirmed diagnosis of structural or functional heart disease by a cardiologist.
2. Pregnant at the time of presentation or immediately postpartum (<6 weeks).
3. Willingness to participate and provision of informed consent.

Exclusion criteria were patients with uncertain diagnoses or incomplete medical records.

Data collection. Data were collected by trained clinicians using standardized data collection forms and chart review of electronic and paper-based records. Collected variables included demographic characteristics, type and severity of cardiac disease, mWHO classification, obstetric data, delivery method, maternal and neonatal outcomes, and complications. Patients were followed until hospital discharge after delivery or pregnancy termination.

mWHO classification. The mWHO classification of maternal risk was used to categorize patients into Class I, II, II–III, III, IV, or "unclassified" when a clear classification was not possible (e.g., right ventricular dysfunction or severe pulmonary stenosis not explicitly defined by current guidelines). Classification was based on comprehensive cardiology and obstetric assessment.

Maternal mortality was defined as the death of a mother during pregnancy or within 42 days after delivery or pregnancy termination.

Statistical analysis. Data were analyzed using SPSS version 25.0 (IBM, Chicago, IL, USA). Continuous variables are presented as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Analyses were descriptive and stratified by mWHO class where applicable.

RESULTS

A total of 389 pregnant women with confirmed heart disease were included in this study. The average age of participants was 26.3 ± 7.2 years, with an average gestational age of 3.02 ± 0.08 months at study entry. All patients were classified according to the mWHO risk classification, revealing a diverse range of cardiac pathologies.

Patients were categorized into five mWHO risk classes (I, II, II–III, III, IV) on the basis of clinical evaluations of their cardiac conditions, as well as pregnancy-related considerations. For cases where a clear classification was not possible, patients were assigned to an "unclassified" category. Most patients fell into moderate- to high-risk groups, with Classes III and IV comprising over half the cohort. This stratification served as the foundation for analyzing maternal and fetal outcomes. Details of the distribution across mWHO classes are summarized in Figure 1.

Cardiac disease types. Cardiac pathologies were grouped into seven major disease categories, and their frequencies are detailed below:

CHD was observed in 20.82% of patients (81 cases). The most common subtypes included unrepaired ASD (20 cases, 5.14%), repaired ASD (18 cases, 4.63%) and TOF (14 cases, 3.60%). Other less common conditions included truncus arteriosus, and the Fontan procedure.

VHD was the most prevalent category, affecting 35.99% of patients (140 patients). High-risk conditions

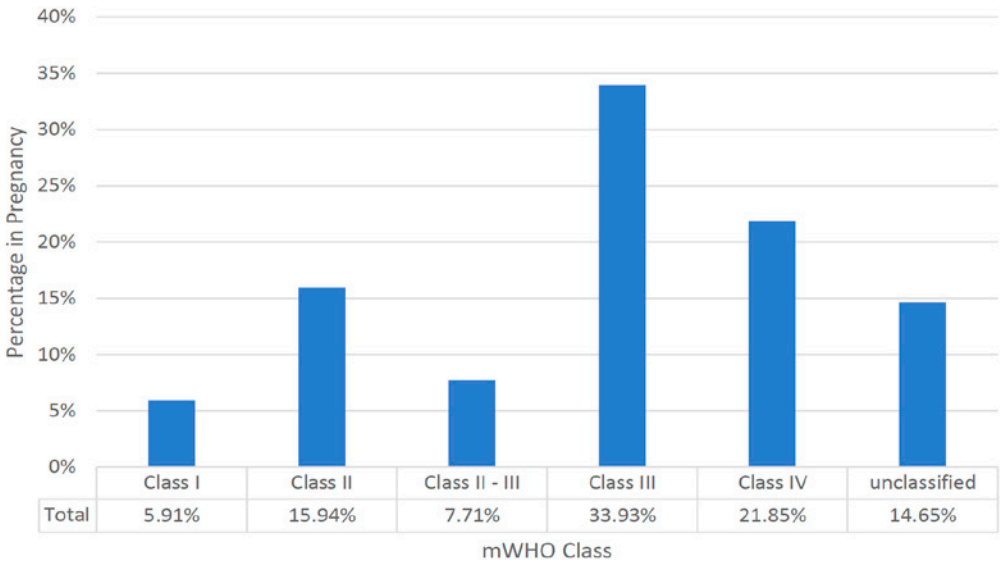


Figure 1. Proportion of patients by mWHO classification (mWHO – modified World Health Organization classification)

(Class IV), including severe MS, severe AS, and severe aortic aneurysms, were observed in 12.60% of the patients (49 patients). Moderate-risk conditions (Class III), such as moderate MS, mechanical prosthetic valves, and moderate aortic aneurysms, were more prevalent, comprising 15.94% of the cases (62 patients). Moreover, mild to moderate-risk conditions (Class II–III), including severe MR, AR, and moderate AS, accounted for 7.73% of the cases (30 patients).

Cardiomyopathy was present in 78 patients (20.05%). The highest-risk group, Class IV, included high risk HCM and LV systolic dysfunction with LVEF <30% (both before and after 30 weeks), affecting 20 patients (5.15% combined). Moderate-risk groups, Class III, comprised the majority, including PPCM and moderate dysfunction (LVEF 30–45%), collectively accounting for 55 patients (14.13%).

Hypertension was observed in a subset of the study population, with gestational hypertension being more common, affecting 3.60% of patients (14 patients). In contrast, chronic hypertension was less frequent, reported in 1.54% of cases (6 patients). The low frequency likely reflects the tertiary referral pattern, where structural and high-risk congenital/valvular disease predominated. Both conditions were unclassified in terms of specific risk categories.

Various pulmonary conditions were noted among the study participants. The most prevalent condition, however, was thromboembolism (unspecified), which occurred in 6.94% of patients (27 patients) but was not assigned a risk classification. Severe PH affected 1.80% of patients (7 patients) and was classified as Class IV, while moderate PH was seen in 2.57% of patients (10 patients) and categorized as Class III.

Less common conditions included severe PI in 1.54% (6 cases) and severe PS in 0.51% (2 cases). Among the cases of PI, two patients had a history of repaired VSD and PS in childhood, three had a history of TOF, and one had undergone valvuloplasty for PS during childhood. These PI cases are categorized as unclassified, with two patients also included in the severe right ventricular dysfunction group as per classification.

Arrhythmias were observed among the study participants, with tachyarrhythmias (such as paroxysmal supraventricular tachycardia, frequent Premature Ventricular Contractions (PVCs)) being the most common, affecting 2.57% of patients (10 patients) and categorized as Class II. Bradyarrhythmia, exclusively complete heart block (CHB), accounted for 0.77% of cases (3 patients) and were not classified by risk. Further details are provided in Table 1 and Figure 2.

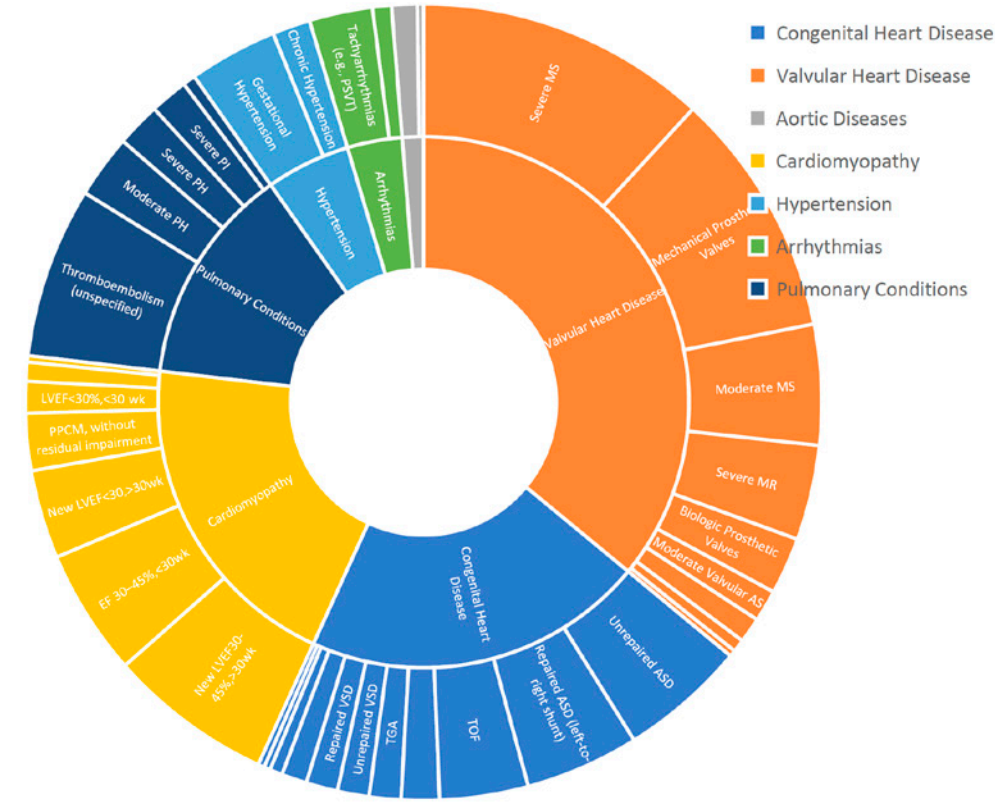
Delivery methods showed a clear trend across mWHO risk categories. Vaginal delivery was more common in lower-risk groups, with Class I and II patients together accounting for over 60 vaginal births and relatively few cesarean sections. In contrast, cesarean delivery became increasingly prevalent in higher-risk classes. Notably, Class IV patients had a markedly high cesarean rate, with nearly five times as many surgical deliveries as vaginal births. Class III showed a more balanced distribution between the two delivery modes, reflecting individualized decision-making based on clinical status. Unclassified cases also leaned toward cesarean delivery. These patterns are illustrated in Figure 3.

Among the high-risk cases, therapeutic abortion was recommended in several instances; however, all patients initially declined the recommendation.

Table 1. Distribution of cardiac disease types, specific conditions, and mWHO classifications among pregnant women

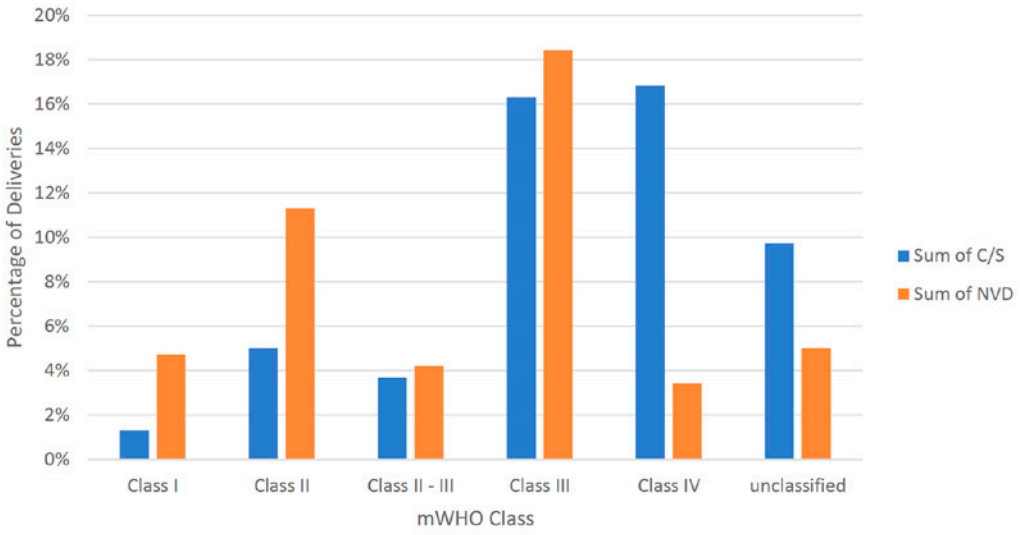
Disease type	Condition	mWHO Class	Frequency (n)	Percentage (%)
Congenital Heart Disease	Repaired ASD (left-to-right shunt)	Class I	18	4.63%
	Unrepaired ASD	Class II	20	5.14%
	Repaired VSD	Class I	5	1.29%
	Unrepaired VSD	Class II	5	1.29%
	TOF	Class II	14	3.60%
	Fontan Procedure, Tricuspid Atresia	Class IV	1	0.26%
	TGA	Class III	5	1.29%
	Severe Ebstein's Anomaly (cyanosis present)	Class IV	6	1.54%
	Severe Uncorrected Coarctation of Aorta	Class IV	2	0.51%
	Repaired Coarctation of Aorta	Class II	4	1.03%
Valvular Heart Disease	moderate MS	Class III	19	4.88%
	Severe MS	Class IV	46	11.83%
	Severe MR	Class II–III	15	3.86%
	Severe AR	Class II–III	4	1.03%
	Moderate AS	Class II–III	5	1.29%
	Severe AS	Class IV	2	0.51%
	Subvalvular AS	Class II–III	1	0.26%
	Mechanical Prosthetic Valves	Class III	39	10.03%
	Biologic Prosthetic Valves	Class II	9	2.31%
Aortic Diseases	Severe Aortic Aneurysm (with or without BAV)	Class IV	1	0.26%
	Moderate Aortic Aneurysm (with or without BAV)	Class III	4	1.03%
Cardiomyopathy	High risk HCM	Class IV	1	0.26%
	HCM with ICD	Class II–III	3	0-77%
	LVEF<30%, <30 wk	Class IV	5	1.29%
	New LVEF<30%,>30 wk	Class IV	14	3.60%
	New LVEF30-45%,>30 wk	Class III	26	6.68%
	EF 30–45%, <30wk	Class III	20	5.14%
	PPCM, without residual impairment	Class III	9	2.31%
Hypertension	Gestational Hypertension	Unclassified	14	3.60%
	Chronic Hypertension	Unclassified	6	1.54%
Arrhythmias	Tachyarrhythmias (e.g., PSVT, PVCs)	Class II	10	2.57%
	Bradyarrhythmia	Unclassified	3	0.77%
Pulmonary Conditions	Severe PH	Class IV	7	1.80%
	Moderate PH	Class III	10	2.57%
	Severe PS	Class II–III	2	0.51%
	Severe PI	Unclassified	6	1.54%
	Thromboembolism (unspecified)	Unclassified	27	6.94%

AR, Aortic Regurgitation; AS, Aortic Stenosis; ASD, Atrial Septal Defect; BAV, Bicuspid Aortic Valve; EF, Ejection Fraction; MR, Mitral Regurgitation; MS, Mitral Stenosis; PH, Pulmonary Hypertension; PPCM, Peripartum Cardiomyopathy; PS, Pulmonary Stenosis; PSVT, Paroxysmal Supraventricular Tachycardia; TGA, Transposition of the Great Arteries; TOF, Tetralogy of Fallot; VSD, Ventricular Septal Defect



AR – Aortic Regurgitation; AS – Aortic Stenosis; ASD – Atrial Septal Defect; BAV – Bicuspid Aortic Valve; EF – Ejection Fraction; MR – Mitral Regurgitation; MS – Mitral Stenosis; PH – Pulmonary Hypertension; PPCM – Peripartum Cardiomyopathy; PS – Pulmonary Stenosis; PSVT – Paroxysmal Supraventricular Tachycardia; TGA – Transposition of the Great Arteries; TOF – Tetralogy of Fallot; VSD – Ventricular Septal Defect

Figure 2. Distribution of cardiac disease types and specific conditions in pregnancy



mWHO – modified World Health Organization classification; NVD – normal vaginal delivery; C/S – cesarean section

Figure 3. Distribution of normal vaginal deliveries and cesarean sections by mWHO risk classification

Additionally, some cases of Class IV cardiac disease were diagnosed after 18 weeks of gestation, when therapeutic abortion was no longer an option. Ultimately, therapeutic abortion was performed in nine high-risk cases following medical decision-making.

Four cases of mortality were documented. Three of these were associated with severe PH: two occurred postpartum, and one followed a therapeutic abortion. The fourth case was attributed to heart failure in a patient diagnosed with an ejection fraction (EF) of 20% at 24 weeks of gestation, who died 17 days after delivery. Other observed complications included pulmonary edema, arrhythmias, and preeclampsia, although these were not individually reported.

DISCUSSION

This study provides a comprehensive analysis of heart disease (HD) in pregnancy at the Joint Clinic of Pregnancy and Heart Disease at Al-Zahra Hospital, focusing on disease types, outcomes, and the challenges associated with management in a low- and middle-income country (LMIC) setting. Our findings reveal that VHD was the predominant diagnosis, followed by CHD, cardiomyopathy, and PH. Comparisons with global and regional data highlight the complexity of HD in pregnancy and emphasize the unique healthcare challenges in low- and middle-income countries (LMICs) (8-12).

VHD was the most prevalent HD type in this cohort, with MS affecting 16.71% of patients, primarily rheumatic in origin. This underscores the enduring impact of rheumatic heart disease (RHD) in LMICs, where limited access to preventive healthcare and early treatment of streptococcal infections persists.

In regional studies, India reported that RHD constituted 56.6% of HD cases in pregnancy, with MS as the leading lesion at 23.3% (11). Similarly, Iraq attributed 34.1% of HD cases to RHD, highlighting the significant burden of rheumatic valvular complications in LMICs (12). The M-PAC registry from India reported a lower proportion of RHD (42%) compared to earlier LMIC studies, where RHD accounted for 71–84% of HD cases in pregnancy, reflecting improved RHD control in some LMIC regions (9).

In contrast to regional findings, data from ROPAC and the U.S. CVD in Pregnancy Trend Study indicate that VHD in pregnancy is less frequently caused by RHD in high-resource settings. In the ROPAC cohort of 5,739 pregnancies across 53 countries, only a minority of VHD cases were rheumatic, and VHD prevalence was lower in developed countries. However, in emerging countries, 55% of VHD cases were RHD-related, consistent with our findings (8-10).

While VHD was most common in our cohort, CHD was also frequently observed, with unrepaired ASD as the most common subtype (5.14%), followed by repaired ASD (4.63%) and TOF (3.60%).

CHD comprised 57% of HD ROPAC cases across developed regions, reflecting the impact of improved pediatric cardiac care that allows CHD patients to reach reproductive age (8). Similarly, the U.S. study documented a 40% increase in CHD prevalence among pregnant individuals over the past decade, primarily due to improved survival rates and older maternal age at pregnancy (10).

In LMICs, where access to early cardiac surgeries may be limited, the prevalence of complex CHD cases may be lower due to reduced survival rates. The M-PAC registry reported CHD in one-third of HD pregnancies, a rate higher than that reported previous LMIC studies but lower than in high-income countries (9). Regional studies in Iraq and India reported lower CHD rates than VHD rates, with CHD accounting for 30.5% and 13.3% of HD cases, respectively, reflecting the limited access to early CHD diagnosis and intervention in these regions.

In our cohort, the high rate of complex CHD presentations, such as TOF, indicates the specialized nature of our tertiary referral center, where more advanced cases are likely to be managed. These findings emphasize the importance of multidisciplinary care in regional centers to handle complex CHD cases in pregnancy, particularly in LMICs where early intervention remains challenging.

The average age of HD patients in our study aligns with findings from the Indian study (mean age 26), which reflect a younger age demographic in LMICs (11). This contrasts with data from the U.S. study, which reported a rising prevalence of HD among older pregnant women due to advanced maternal age and a growing number of CHD survivors (10). The U.S. data demonstrated that older maternal age is a significant related complication, including hypertensive disorders, arrhythmias, and PPCM, and suggests that age should be an essential factor in HD risk stratification for pregnancy (10).

In our cohort, 53% of deliveries were cesarean sections (C/S), compared to 47% normal vaginal deliveries (NVD), reflecting a careful, individualized approach to delivery planning. This higher C/S rate aligns with trends in similar studies, such as ROPAC (48.6%) and M-PAC (39%), where cesareans are often performed in high-risk pregnancies to minimize maternal and fetal complications (8,9). The higher C/S rate in our cohort underscores the severity of cardiac conditions managed in our tertiary center, including cases of pulmonary hypertension and complex CHD,

where precise timing and control during delivery are crucial.

Despite the higher cesarean section rate, our cohort had a relatively low maternal mortality rate, from them three cases recorded among high-risk PH patients: one postpartum death due to PH, one from unrepaired ASD with Eisenmenger syndrome following a therapeutic abortion, and one during cesarean section in a patient with primary PH. These cases reflect the severe risks associated with PH and complex CHD in pregnancy. Comparatively, ROPAC reported a 9% mortality rate for PH patients, and M-PAC observed 4.8%, emphasizing the need for specialized management strategies to reduce these risks (8,9).

Our study reported a maternal mortality rate of 1.0%, significantly lower than the rates reported in the M-PAC (1.9%) and the Indian study (6.4%). This underscores the potential impact of multidisciplinary care, even in resource-constrained settings, in reducing maternal mortality among high-risk populations (9,11). In higher-resource countries, such as those in ROPAC and the U.S., lower mortality rates are often attributed to the presence of cardio-obstetrics teams and structured postpartum care, which emphasizes the potential for similar improvements in lower-resource settings through advanced maternal care models (8,10).

The elevated risks observed in patients with PH and complex CHD underscore the importance of establishing specialized maternal cardiology clinics to address these high-risk pregnancies and enhance maternal and neonatal outcomes. Early risk stratification and focused postpartum monitoring should be prioritized to reduce the impact of complex HD in pregnancy, supporting both maternal survival and improved neonatal outcomes.

This study highlights several key challenges and insights into the classification and management of heart disease in pregnancy. The findings underscore the need for improved risk stratification and highlight areas where current classifications, such as the mWHO risk classification, may fall short.

A subset of patients in our cohort presented with heart failure before 20 weeks of gestation. These cases were more likely related to preexisting cardiomyopathy, such as dilated cardiomyopathy. However, definitive differentiation was challenging without long-term follow-up. This underscores the need for closer postpartum monitoring to confirm the underlying etiology of heart failure and to improve maternal outcomes in future pregnancies.

Severe PS and conditions associated with RV dysfunction, such as TOF and Ebstein's anomaly, presented unique challenges in classification. The current mWHO guidelines do not provide specific criteria for RV dysfunction or severe PS, making it difficult to stratify these patients accurately (7). In our cohort, these cases were few in number, and detailed subgroup analyses were not included here to maintain clarity and focus; however, comprehensive data on echocardiographic parameters, hemodynamic profiles, and maternal-fetal outcomes have been collected and are being analyzed in a separate study currently under submission. Our findings, together with prior literature, suggest that pregnancy in women with RV dysfunction may carry substantial risks, including PH, arrhythmias, and right heart failure (13). While most women with surgically corrected TOF or Ebstein anomaly tolerate pregnancy well, those with pre-existing heart failure are at higher risk for major adverse cardiac events (MACE) during pregnancy and should be counseled accordingly (14,15).

Based on our clinical experience, incorporating echocardiographic RV functional indices, estimated pulmonary artery pressures, and clinical markers of right heart failure into future risk models could improve risk prediction and guide management. The lack of explicit guidance in the current mWHO classification underscores the urgent need for a refined framework that addresses such high-risk yet underrepresented conditions.

A notable proportion of patients in this study were classified as mWHO Class IV, which reflects the high-risk population referred to our center. This group predominantly included patients with clinically significant mitral stenosis with a valve area ≤ 1.5 cm^2. Interestingly, many of these patients had mitral valve areas between 1.2 and 1.5 cm^2 with objective exercise tolerance before pregnancy and experienced favorable pregnancy outcomes with careful management. By contrast, outcomes were significantly worse in patients with mitral valve areas <1 cm^2, highlighting the need for nuanced risk assessment in this group.

It is important to note that some patients in this study had overlapping conditions that required careful consideration in risk classification. For example, patients with combined ASD with PH levels above 60 mmHg were classified in mWHO Class IV, even though ASD alone may not typically qualify for this class. This approach reflects the severity of the combined conditions, ensuring that these patients are not underclassified. These cases highlight the complexity of managing cardiac disease during pregnancy and emphasize the necessity of individualized assessment. We ensured that these patients were allocated to the class with the highest associated risk to avoid double counting or misclassification.

Certain conditions in this study, such as thromboembolism, severe PS, and gestational hypertension, could not be neatly categorized within the existing mWHO framework (7). These ambiguities

highlight the limitations of the current classification system in addressing overlapping or less common conditions. Developing a more inclusive and detailed classification system would enable clinicians to better stratify risks and tailor management strategies for these complex cases.

Our findings suggest that the current mWHO classification does not adequately address some conditions, such as severe PS, RV dysfunction, or MS with valve areas between 1.2–1.5 cm². Given the favorable outcomes in certain high-risk groups receiving specialized care, it may be time to reevaluate the thresholds and criteria used in risk stratification. The incorporation of factors such as RV dysfunction and some forms of severe valvular disease could improve the accuracy and utility of the mWHO classification.

Limitations. While this study offers important insights into the management of cardiac disease in pregnancy, it is not without limitations. Conducted at a single tertiary referral center, the findings may reflect a population with more severe or complex conditions, which could limit their applicability to general obstetric settings. The retrospective design also brings typical challenges, such as inconsistent documentation and the inability to control for confounding variables. In some cases, the modified WHO risk classification lacked sufficient detail to categorize uncommon or overlapping conditions, requiring clinical judgment that may affect consistency. No adjustment was made for socioeconomic status, educational background, or access to prenatal care that can significantly influence maternal outcomes. High risk women were more likely to be referred to the center, potentially leading to an overestimation of complication and mortality rates, while lower risk patients with cardiac disease may have been underrepresented. These factors underscore the need for broader, prospective studies that include diverse clinical settings and a wider spectrum of patient risk profiles.

CONCLUSIONS

These findings emphasize the importance of multidisciplinary maternal cardiology clinics to address high-risk pregnancies effectively. Early risk stratification, comprehensive follow-up, and tailored delivery planning appear to be key components for optimizing outcomes. Moreover, the limitations of the current mWHO classification highlight the need for an updated framework that accounts for conditions such as RV dysfunction and overlapping pathologies. By refining risk assessment and improving access to specialized care, particularly in LMICs, we may help improve outcomes in this high-risk population.

Conflict of interest. The authors declare that they have no competing interests

Ethics approval and consent to participate. The protocol for this study was reviewed and approved by the Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran (IR.MUI.MED.REC.1399.888), in accordance with the Declaration of Helsinki and all applicable institutional and national guidelines governing research involving human participants. Written informed consent was obtained from all participants prior to their inclusion in the study. The study adhered to the ethical standards outlined in these guidelines, ensuring that participants were fully informed of the study's purpose and procedures.

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Authors' contributions. All authors contributed significantly to this work. MaM was responsible for the conceptualization and drafting of the original manuscript. PB provided supervision, project administration, validation, and assisted in reviewing and editing the manuscript. MiM handled methodology, and contributed to reviewing and editing the manuscript. ShM was involved in data collection, statistical analysis, and also contributed to reviewing and editing the manuscript. All authors have read and approved the final version of the manuscript, ensuring its accuracy and integrity.

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Address for correspondence:
Parvin Bahrami
Department of Cardiology, Alzahra University Hospital, Isfahan University of Medical Science, Isfahan, Iran
email: Parvinbahrami194@gmail.com