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# The Prevalence of Congenital Heart Diseases and Associated Risk Factors among Neonates Admitted to the NICU of Shahid Sadoughi Hospital, Yazd, Iran from 2022 to 2023: A Cross-Sectional Study

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**ABSTRACT**

**Background:** Congenital heart defects (CHDs) are among the most prevalent congenital defects observed in neonates, leading to structural and functional abnormalities in the heart. This research examines the prevalence of CHDs and its various subcategories among neonates admitted at Shahid Sadoughi Hospital in Yazd, Iran, from 2022 to 2023. The study also aims to assess the presence of risk factors among infants diagnosed with CHDs.

**Methods:** This is a descriptive cross-sectional study, encompassing all neonates diagnosed with CHDs. Echocardiography was conducted to classify the specific type of CHDs, and a questionnaire was administered to the parents of neonates with CHDs to identify potential risk factors.

**Results:** Out of 1149 newborns admitted to the hospital in one year, 29 (2.52%) were diagnosed with CHDs, and 9 of them died from the condition. The prevalence of CHDs and the mortality rate were 2.5% and 0.78%, respectively. The most common defect was atrial septal defect (ASD), affecting 19 newborns (65.5% of cases), and 15 newborns exhibited multiple defects within the subtypes of CHDs.

**Conclusion:** Our research reveals that the incidence of CHDs among newborns in our area was 2.52%, with a mortality rate of 0.78% within a one-year timeframe. More than half of CHD cases were found in offspring of consanguineous unions, suggesting a potential risk factor within the Yazd community, likely linked to the prevalent custom of consanguineous marriages in the region.

## Introduction

Congenital heart defects (CHDs) are structural abnormalities in the heart or great vessels present at birth, affecting 8 to 9 per 1000 live births.[1] They range from harmless to life-threatening, with symptoms like rapid breathing, cyanosis, low weight, and fatigue.[2] Common types include ventricular septal defects (VSDs), atrial septal defects (ASDs), and patent ductus arteriosus (PDA).[3] Severe CHDs like double outlet right ventricle (DORV) and transposition of the great arteries (TGA) can cause serious illness in newborns.[4] CHDs are often the first anomaly in genetic syndromes, with only a third being part of a syndrome. Molecular biology and genetics play an important role in understanding the causes, with some cases linked to Mendelian inheritance or chromosomal anomalies.[5] Advances in diagnosis and treatment, such as echocardiography and stenting, have improved outcomes for CHD patients.[6] Studies indicate that over 1.3 million babies are born annually with CHDs, with the highest incidence in low-income and low-middle income countries.[7] The prevalence of CHD is approximately 9 per 1000 live births globally, affecting various anatomical structures of the heart.[1] Recent systematic reviews show a rising trend in CHD prevalence, with marked differences between regions, such as Africa reporting the lowest and Asia with the highest prevalence rates.[8] The prevalence of severe, moderate, and minor CHDs varies from 4.2 to 8.6 per 1000 live births, underscoring the necessity of a consistent methodological framework for researching CHD occurrence.[9] Numerous studies have shed light on different aspects of CHDs in newborns. In a study by Sanapo et al., a significant link was found between maternal hypertensive disorders and neonatal CHDs, showing a notable increase in the chances of CHDs in babies born to hypertensive mothers.[10] Among environmental risk factors, the strongest association with CHDs is seen in mothers who smoke.[11] Diabetes is a principal contributor to congenital anomalies, affecting 10-30% of pregnancies.[12] Expectant mothers with diabetes are at a 4-5 times higher risk of congenital anomalies compared to non-diabetic mothers.[13] Children of diabetic mothers have a 3-6% higher rate of cardiac anomalies.[12] Babies born to diabetic mothers are five times more likely to develop CHDs than those born to non-diabetic mothers.[14] Concerning cardiovascular anomalies, twins have a higher likelihood of congenital heart issues.[15] Advanced maternal age and the use of Assisted Reproductive Technology (ART) are the primary reasons for twin births. The range of CHD severity varies, with ASD and VSD often going unnoticed until the child is older.[11] Conversely, Tetralogy of Fallot (TOF) and TGA can lead to complications if not treated promptly, emphasizing the need for timely surgical intervention.[15] The incidence of CHDs in Iranian neonates between 2007 and 2011 varied from 4.2 to 8.6 per 1000 live births.[16,17,9] Factors linked to CHDs include maternal age over 30, positive parental consanguinity, and a history of CHDs among siblings.[18] The Persian Registry Of cardio Vascular diseasE (PROVE/CHD) in Isfahan identified 1252 pediatric CHD cases, with VSD as the most common diagnosis.[19] A meta-analysis conducted by Daliri in Iran between 2000 and 2016 revealed an average prevalence rate of 18 per 1000 live births for congenital anomalies, with musculoskeletal disorders and urogenital anomalies being the most common types.[20] Risk factors for CHDs in Iran encompass genetic factors, teratogenic exposure, parental consanguinity, maternal age over 30, history of abortion, and exposure to cigarette smoke during pregnancy.[18,21,22] Factors like low socioeconomic status, low education, unhealthy lifestyle, lack of parental awareness, childhood poverty, inadequate nutrition, and environmental factors such as polluted air also contribute to CHD incidence in Iran.[23] Moreover, the use of specific teratogens during pregnancy, maternal obesity history, and insufficient medical supervision during pregnancy are highlighted as risk factors for CHDs in Iranian children. These results stress

the need for targeted interventions, pre-marital counseling, and enhanced maternal health awareness to manage and prevent CHD in Iran. They underscore the importance of understanding and addressing the burden of CHDs and congenital anomalies in Iran for effective healthcare planning and management. Therefore, this study investigates the prevalence of CHDs and their subgroups in neonates admitted at Shahid Sadoughi Hospital in Yazd in 2022-2023, as well as the prevalence of risk factors in infants with CHDs.

## Materials and Methods

This cross-sectional study was conducted from March 2022 to March 2023. Over twelve months, 1149 newborns were delivered at the medical facility and screened for cardiovascular conditions. Before the research, approval was obtained from the Research Ethics Committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.SPH.REC.1401.034). Written consent was provided by parents of infants diagnosed with CHD before their enrollment in the study. The research involved newborns born at Shahid Sadoughi Hospital in Yazd diagnosed with CHDs, with their parents participating to assess potential risk factors. Cardiac defects were identified using echocardiography and evaluation by a cardiologist. Echocardiographic assessments with Doppler were used to evaluate myocardial thickness, left ventricular myocardial performance index (LVMPI), shortening fraction, right ventricular myocardial performance index (RVMPI), tricuspid flow, and mitral E/A ratio to investigate hereditary cardiac issues in newborns. Patient data was extracted from medical records and documented. A questionnaire was completed by the participant's parents, gathering information on factors such as age, history of miscarriages and stillbirths, maternal diabetes, use of assisted reproductive technologies (ART), exposure to occupational pollutants, pre-pregnancy multivitamin intake, infections during pregnancy, family history of CHDs, and consanguineous marriages. The collected data was then analyzed using appropriate statistical methods, with all variables undergoing descriptive analysis and quantitative variables being presented accordingly.

## Results

***Prevalence of CHDs:*** The investigation involved the admission of 1149 neonates at Shahid Sadoughi Hospital, with 29 (2.52%) diagnosed with CHDs. The prevalence of CHDs was 2.52%. Gender distribution showed a predominance of male patients (18 cases) compared to females (10 cases), with one neonate of indeterminate gender. Also, 17.24% of neonates with CHDs were born to mothers over 35 years old, and 48.27% were born to fathers over 40 years old. The most common CHD type was atrial septal defect (ASD), affecting 19 neonates (65.5%), followed by PDA in 17 neonates (58.6%), and VSD in 7 neonates (24.13%). TOF, TGA, and Tricuspid Atresia each affected one neonate (3.4%). 51.7% of neonates exhibited multiple structural cardiac defects, with a combination of ASD and PDA being the most common. Three neonates had associated syndromes with extracardiac abnormalities, including esophageal atresia and chronic lung disease. The mortality rate within the CHD cohort was 31.03%, contributing to an overall mortality rate of 0.78% among all neonates within one year.

**Table 1.** Prevalence of Various Types of CHDs in neonates admitted to the NICU of Shahid Sadoughi Hospital, Yazd

| Types of CHD (n = 29) | Frequency | Percent |
|---|---|---|
| Atrial septal defect | 19 | 65.5 |
| Patent ductus arteriosus | 17 | 58.6 |
| Atrial septal defect | 7 | 24.1 |
| Transposition of the great arteries | 1 | 3.4 |
| Tetralogy of Fallot | 1 | 3.4 |
| Tricupsid atresia | 1 | 3.4 |

**Table 2.** Number of Neonates with Multiple CHDs

| Combination of Subtype of CHD (n = 15) | Frequency | Percent |
|---|---|---|
| ASD + PDA | 7 | 46.7 |
| ASD + VSD | 3 | 20 |
| VSD + PDA | 2 | 13.3 |
| VSD + TGA | 1 | 6.7 |
| PDA + Tricuspid atresia | 1 | 6.7 |
| PDA + ASD + VSD + TOF | 1 | 6.7 |

***Related risk factors:*** The risk factors associated with CHDs are identified in Table 3 as follows: 69% of mothers of neonates with CHDs used multivitamins before and during pregnancy, while 31% did not. Among neonates with CHDs, 51.7% had parents in consanguineous marriages. Additionally, 48.2% of neonates had fathers over 40 years old, and 17.2% had mothers over 35. Advanced paternal age may be a potential risk factor for CHDs. Some mothers (13.8%) of neonates with CHDs regularly took specific medications during pregnancy, with 10.3% having thyroid disease, mainly hypothyroidism. Only four patients had a family history of CHDs, with most cases being sporadic. Moreover, 10.3% of mothers in the study experienced diabetes and infections during pregnancy.

**Table 3.** Prevalence of Risk Factors among 29 CHDs Cases

| Risk Factors (n = 29) | Yes | No |
|---|---|---|
| Age of mother (>35 years old) | 5 | 24 |
| Age of father (>40 years old) | 14 | 15 |
| History of abortion or stillbirth | 5 | 24 |
| Maternal diabetes | 3 | 26 |
| Use of the ART | 2 | 27 |
| Exposure to the pollutant | 5 | 24 |
| Taking multivitamins before pregnancy | 20 | 9 |
| Infection during pregnancy | 3 | 26 |
| Familial history of CHD | 4 | 25 |
| Consanguine marriage | 15 | 14 |
| Medication use during pregnancy | 4 | 25 |
| Maternal thyroid disease | 3 | 26 |

ART: assisted reproductive technologies

## Discussion

In this study, we offered valuable insights into the prevalence of congenital heart disease (CHD) and its associated risk factors among infants admitted at Shahid Sadoughi Hospital in Yazd. The total prevalence of CHD in infants admitted to our NICU was 2.52%. Gender distribution revealed a higher prevalence of male patients (18%). Additionally, 48.27% of neonates with CHD were born to fathers over 40 years old, while 17.24% had mothers over 35 years old. The predominant anomaly observed in CHD neonates was ASD, aligning with the findings of B. Nikyar et al., which reported an incidence of 2.64 patients per 1000 live births with ASD.[17] Similar to our results, Dadbinpour et al., identified ASD as the most common type of CHD, accounting for 45.2% of cases. In contrast, our study showed that PDA is the second most common type of CHD, while Dadbinpour et al., reported VSD as the second most common with 16.7% of cases in Shahid Sadoughi Hospital of Yazd.[24] The precise prevalence of CHDs remains ambiguous due to a significant number of undiagnosed cases during infancy, as ASD and VSD often evade detection until school age.[25]

Evidence of familial clustering of CHD has been illustrated across various populations and for diverse cardiac abnormalities. The presence of consanguinity, especially among first cousins, poses an additional risk factor for these families, particularly in societies where it is a prevalent cultural norm.[26] In contrast to Nikyar et al.,[17] study, which reported an absence of familial history in CHD neonates, our research revealed that four neonates had a familial predisposition to CHD. As a result, the majority of CHD neonates are considered sporadic cases. The discrepancy between these findings may be attributed to the increased prevalence of consanguineous marriages in Yazd province compared to northern regions of Iran. Our study revealed that 15 (51.7%) of CHDs infants' parents had a familial history of CHD, while Nikyar et al., reported a 39.6%

rate of consanguineous parents with a 0.86% CHD prevalence. In comparison, our study recorded a CHD prevalence of 2.52%, surpassing Nikyar's findings, possibly attributed to the higher frequency of familial unions in Yazd province compared to northern Iran. In the study of Akbari Asbagh, positive parental consanguinity was observed in 502 (39.24%) cases and 386 (32.19%) controls, with a statistically significant difference (P-value < 0.001).[18] The potential role of consanguineous marriages as a risk factor warrants further investigation.

It was observed that a majority of CHD infants' mothers utilized multivitamins pre- and during pregnancy, suggesting this factor may not exert significant risk. Hence, additional investigations into genetic and environmental factors influencing CHD prevalence are warranted. Approximately 10.3% of our patients diagnosed with CHD exhibited extracardiac abnormalities, a percentage notably lower than the 28% prevalence of extracardiac anomalies reported by Son Chang et al., in 2021 for CHD patients in Seoul, Korea.[27] Consequently, the majority of individuals with CHDs manifest an isolated form of the condition, predominantly affecting the cardiovascular system exclusively. The demographic profile of CHD patients indicates a predominance of male neonates, a trend consistent with studies by B. Nikyar et al., and Taheri et al., although investigations in Saudi Arabia and Iceland have identified a higher proportion of female CHD patients. Our study similarly identified a preponderance of male neonates among those with CHD, echoing the observations of Jahantigh et al.,[28] and Dadbinpour et al.,[24] regarding a heightened occurrence of congenital anomalies in male neonates. Lookzadeh et al., study underscored the significance of managing maternal diabetes to prevent CHDs in newborns. The research revealed that poor control of diabetes in pregnant women could contribute to a high incidence of CHDs in neonates.[12] They demonstrated that the prevalence of CHDs and hypertrophic cardiomyopathy (HCM) in neonates of diabetic mothers was 12.7% and 14%, respectively.[12,29]

The management of maternal health before and during pregnancy is crucial to reduce the occurrence of congenital heart diseases in newborns. A study on premature neonates revealed a higher prevalence of cyanotic congenital heart diseases in males compared to females.[30] This disparity provides insights into potential biological differences affecting heart conditions in neonates. Interventions in preconception healthcare have shown effectiveness in improving neonatal outcomes and reducing the risk of malformations in offspring. Some mothers of neonates with CHD had used specific medications, with studies linking hypertension and antihypertensive drugs to CHD.[31] Exposure to second-hand smoke is recognized as a risk factor for CHDs, although not addressed in this study.[32] Proactive measures before and during pregnancy could significantly impact the frequency of CHDs and other anomalies in neonates. These findings enhance our understanding of the factors influencing the prevalence of CHDs, highlighting the importance of maternal well-being, periconceptional care, and timely interventions in reducing the burden of CHDs in newborns. Further studies on the potential links between paternal age, consanguineous unions, and the risk of CHDs are essential given the high prevalence of CHDs among infants in Yazd.

## Conclusion

Our study reveals that the incidence of CHDs in our participants was 2.52%, with a mortality rate of 0.78% from 2022 to 2023. Furthermore, over half of CHDs cases occurred in children of consanguineous marriages. This underscores the need for genetic education and counseling in our community to improve awareness of the risks associated with consanguinity. By providing support and resources to families, we can work towards reducing the prevalence of CHDs and improving outcomes for affected individuals. Future research should focus on genetic

screening and counseling for families with a CHD history to better understand the causes and preventive strategies. Additionally, public health campaigns to raise awareness about the risks of consanguineous unions could help lower CHD rates in Yazd and similar regions. By addressing these issues proactively, healthcare professionals can enhance the overall health prospects for infants with congenital heart conditions.

## Conflict of Interest

The authors declare no conflicts of interest.

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## Ethical Considerations

The present study was approved by Shahid Sadoughi University Ethics Committee (IR.SSU.SPH.REC.1401.034).

## Author's Contribution

Conceptualization, M.M., N.N. and M.N.; methodology, N.N. and M.M.; formal analysis, N.N. and M.M.; investigation, N.N., M.M., and M.N.; resources, N.N. and M.N.; original draft preparation, N.N.; review and editing, S.E., M.M.; supervision, M.M. and S.E. All authors have read and agreed to the published version of the manuscript.

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