Original article

Clinical characteristics and preoperative outcomes in neonates with severe congenital heart disease at Hue Central Hospital

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Abstract

Background: Approximately 25% of congenital heart disease (CHD) cases present symptoms during the neonatal period. These cases are classified as critical CHD, requiring immediate medical intervention or treatment. Preoperative stabilization plays a pivotal role in determining the prognosis, particularly for neonates. **Subjects and Methods:** This cross-sectional descriptive study with longitudinal follow-up included 39 neonates diagnosed with critical CHD via Doppler echocardiography at Hue Central Hospital from July 2022 to April 2023. **Results:** Ductal-dependent CHD was the most prevalent, accounting for 56.4% of cases, with 41% classified as ductal-dependent pulmonary circulation CHD. The most common clinical manifestations among neonates were cyanosis (51.3%) and heart murmur (46.2%). Prostaglandin therapy to maintain ductal patency was administered in 35.9% of cases. The mortality rate during preoperative stabilization was 25.6%. Risk factors associated with preoperative mortality in neonates with critical CHD included: Birth weight < 2500 grams (OR = 4.71, 95% CI: 1.03–21.65, p < 0.05); Invasive mechanical ventilation (OR = 23.62, 95% CI: 2.56–217.7, p < 0.05; Heart failure treatment (OR = 8.88, 95% CI: 1.56–50.5, p < 0.05); Inotropic support (OR = 8.67, 95% CI: 1.55–48.5, p < 0.05). **Conclusions:** Preoperative mortality risk in neonates with critical CHD is significantly increased by low birth weight (< 2500 grams), the need for invasive mechanical ventilation, heart failure treatment, and inotropic support.

Keywords: *Newborn, critical congenital heart disease, mortality*

1. INTRODUCTION

Congenital heart disease (CHD) is a significant cause of morbidity and mortality in infants. Approximately 25% of newborns with CHD exhibit symptoms during the neonatal period, classified as severe congenital heart disease requiring immediate treatment or intervention [1, 2]. In Europe and the United States, the prevalence of severe CHD is estimated at 2 - 3 per 1000 live births [3, 4]. In Vietnam, research by Vo Duc Tri identified the prevalence of severe CHD as 21.9%, with a mortality rate of 28.8% in this group [5]. Similarly, in Hong Kong, the study by Jacobs E. G. reported a mortality rate of 20% among patients with critical CHD [6].

Preoperative stabilization, especially in neonates, plays a pivotal role in determining the prognosis of CHD. Stabilization measures, such as prostaglandin infusion for ductal-dependent lesions and interventions like patent ductus arteriosus (PDA) stent or balloon pulmonary valvotomy, can be life-saving prior to surgical repair [7].

With the critical importance of early diagnosis, timely intervention, and treatment of severe congenital heart disease in the neonatal period, we conducted the study titled: "Clinical Characteristics and Preoperative Outcomes in Neonates with Severe Congenital Heart Disease at Hue Central Hospital" aiming to achieve two specific objectives: *1. To describe the clinical characteristics and preoperative outcomes of severe congenital heart disease in neonates; 2. To identify factors associated with the preoperative outcomes of severe congenital heart disease in neonates.*

2. MATERIALS AND METHODS

2.1. Inclusion Criteria

- Neonates aged 0 to 28 days presenting with clinical symptoms suggestive of CHD, confirmed by Doppler echocardiography.

- Severe CHD in neonates, defined and classified according to Hoffman J. and Kaplan S. (2002) [8, 9], included:

+ Cyanotic CHD: Transposition of the great arteries, tetralogy of Fallot (including cases with pulmonary atresia), hypoplastic right heart, hypoplastic left heart, single ventricle, double outlet right ventricle,

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truncus arteriosus, and total anomalous pulmonary venous return with symptoms manifesting during the neonatal period.

+ Acyanotic CHD: Complete atrioventricular canal defect, large ventricular septal defect, large patent ductus arteriosus, critical or severe aortic stenosis, critical coarctation of the aorta, and severe pulmonary stenosis with symptoms presenting in the neonatal priod.

- All patients required medical management and/or intervention during the neonatal period.

2.2. Exclusion Criteria

- Infants older than 28 days.

- Neonates with suspected symptoms ruled out as cardiac etiology by Doppler echocardiography.

- Neonates diagnosed with mild or moderate CHD or not requiring treatment during the neonatal period [8].

2.3. Study Time and Location

- Time: From July 2022 to April 2023.

- Location: Neonatal Unit – Neonatal Intensive Care Department, Pediatrics Center, Hue Central Hospital.

2.4. Research Methodology

- Study Design*:* A prospective descriptive clinical study was conducted.

- Sampling Method: convenient sampling.

2.5. Data Analysis Method

- Data were processed using medical statistical methods with SPSS 20.0 software.

- Differences in proportions were compared using the $\chi 2$ test. When theoretical frequencies ≤ 4 were encountered, Yates' correction or Fisher's exact test was applied.

- Odds ratios (OR) with 95% confidence intervals (95% CI) were calculated to assess associations between treatment outcomes of severe CHD and factors such as gestational age, birth weight, invasive mechanical ventilation, inotropic support, heart failure, and others.

2.6. Ethical consideration

This study was an observational, non-interventional study and did not involve any therapeutic intervention. Before enrolling the neonates in the study, written informed consent about the study, and used data in the medical records were obtained from their parents. Participant confidentiality and data anonymity were strictly maintained.

3. RESULTS

A total of 39 neonates with severe congenital heart disease requiring immediate treatment during the neonatal period were included in the study. The male-to-female ratio was 0.86:1. Preterm neonates accounted for 30.8%, and 33.3% of the neonates had a birth weight below 2.500 grams. Chromosomal abnormalities were identified in 7.7% of the neonates.

3.1. Classification and type of Severe Congenital Heart Disease in Neonates

Table 1. Classification and type of Severe Congenital Heart Disease (CHD)

Type of CHD	n	%
Ductal-dependent CHD (56.4%)		
- Ductal-dependent systemic circulation (2.6%)		
Severe aortic valve stenosis	1	2.6
- Ductal-dependent pulmonary circulation (41.0%)		
Pulmonary valve atresia with ventricular septal defect	8	20.5
Single ventricle with pulmonary valve atresia	2	5.1
Pulmonary atresia with intact ventricular septum	5	12.8
Single ventricle with pulmonary valve atresia	1	2.6
- Parallel circulation (12.8%)		
Transposition of the great arteries	5	12.8
Non-ductal-dependent CHD (43.6%)		
Large ventricular septal defect	6	15.4
Single ventricle	2	5.1
Double outlet right ventricle	2	5.1
Total anomalous pulmonary venous return	2	5.1

Truncus arteriosus	1	2.6
Complete atrioventricular septal defect	1	2.6
Large patent ductus arteriosus	2	5.1
Ventricular septal defect with large patent ductus arteriosus	1	2.6
Total	39	100

Ductal-dependent congenital heart disease was more common, accounting for 56.4% of cases. Among these, the majority (41.0%) involved pulmonary circulation dependent on the ductus arteriosus. CHD with ductal-dependent systemic circulation was rare, with only one case (2.6%).

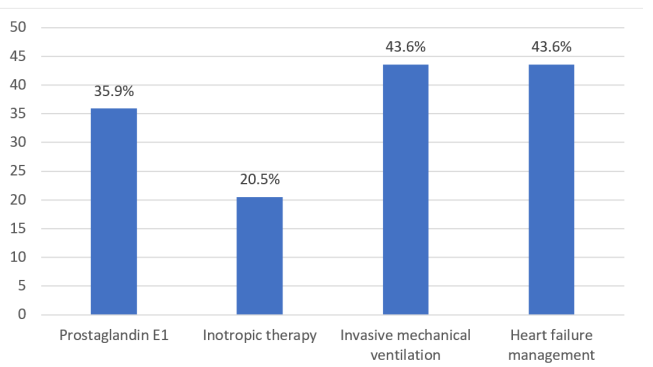
3.2. Symptoms of Severe Congenital Heart Disease in Neonates

Table 2. Symptom Frequency

Symptom		n	%
Chromosomal abnormality	Edward syndrome	1	2.6
	Down syndrome	1	2.6
	Duplication of chromosome 18	1	2.6
Restricted activity (feeding, crying)		12	30.8
Dyspnea		15	38.5
Right-sided apex		4	10.3
Hyperactive precordium		6	15.4
Second heart sound	Loud	2	5.1
	Soft	3	7.7
Heart murmur		18	46.2
Heart rate	Bradycardia	3	7.7
	Tachycardia	0	0
Respiratory rate	Bradypnea	5	12.8
	Tachypnea	5	12.8
Signs of respiratory effort		11	28.2
Cyanosis		20	51.3
Heart failure		17	43.6
Cardiogenic shock		8	20.5
SpO_2(%)	≤ 80	12	30.8
	> 80	27	69.2

The most common symptoms of severe congenital heart disease in neonates were cyanosis (51.3%) and cardiac murmurs (46.2%).

3.3. Preoperative Interventions and Treatments for Severe Congenital Heart Disease in Neonates



Fifure 1. Preoperative Treatments for Severe Congenital Heart Disease

The proportion of neonates requiring invasive mechanical ventilation and heart failure management was relatively high at 43.6%. Additionally, 35.9% of neonates received prostaglandin E1 to maintain ductal patency.

3.4. Preoperative Outcomes in Severe Congenital Heart Disease

Table 3. Preoperative Outcomes

Initial Outcome	n	%
Proceeded to surgery	11	28.2
Outpatient treatment, scheduled for surgery	18	46.2
Mortality	10	25.6
Total	39	100.0

The proportion of patients who were successfully stabilized with medical therapy and subsequently referred for cardiac surgery was 28.2%. However, the mortality rate during the stabilization phase prior to surgery was 25.6%.

3.5. Factors Associated with Preoperative Mortality in Neonates with Severe Congenital Heart Disease

Table 4. Factors Associated with Preoperative Mortality

Factor		Non-survival		Survival		p-value	OR (95%CI)
		n = 10	%	n = 29	%		
Gestational age	Preterm	3	30.0	9	31.0	0.95	0.95 (0.19 - 4.55)
	Fullterm	7	70.0	20	69.0		
Birth weight	< 2500 g	6	60	7	24.1	**< 0.05**	**4.71 (1.03 - 21.65)**
	> 2500 g	4	40	22	75.9		
Prenatal diagnosis	Yes	3	30.0	13	44.8	0.41	0.53 (0.11 - 2.46)
	No	7	70.0	16	55.2		
Time of diagnosis	Within 48 hours of birth	8	80.0	14	48.3	0.08	4.3 (0.77 - 23.7)
	After 48 hours	2	20.0	15	51.7		
Type of CHD	Ductal-dependent	5	50.0	17	58.6	0.64	0.7 (0.17 - 2.99)
	Non-ductal-dependent	5	50.0	12	41.4		
Invasive mechanical ventilation	Yes	9	90.0	8	27.6	**< 0.05**	**23.62 (2.56 - 217.7)**
	No	1	10.0	21	72.4		
Heart failure treatment	Yes	8	80.0	9	31.0	**< 0.05**	**8.88 (1.56 - 50.5)**
	No	2	20.0	20	69.0		
Inotropic therapy	Yes	5	50.0	3	10.3	**< 0.05**	**8.67 (1.55 - 48.5)**
	No	5	50,0	26	89.7		

Key risk factors for preoperative mortality in neonates with severe congenital heart disease included: Low birth weight (< 2500 g): OR = 4.71 (95% CI: 1.03 - 21.65, p < 0.05); Requirement for invasive mechanical ventilation: OR = 23.62 (95% CI: 2.56–217.7, p < 0.05); Heart failure treatment: OR = 8.88 (95% CI: 1.56 - 50.5, p < 0.05); Inotropic therapy: OR = 8.67 (95% CI: 1.55 - 48.5, p < 0.05).

4. DISCUSSION

4.1. Classification of Congenital Heart Disease (CHD) in Neontates

Our study indicates a higher prevalence of ductal-dependent CHD in neonates, accounting for 56.4% compared to non-ductal-dependent CHD (43.6%). This finding aligns with Vo Duc Tri's 2019 study [5], which reported a significantly higher proportion of ductal-dependent CHD (72.6%).

Among ductal-dependent CHD cases, ductal-dependent pulmonary circulation lesions constituted the majority (41%), followed by transposition of the

great arteries (15.4%), and a single case of ductal-dependent systemic circulation (2.6%). Similarly, Vo Duc Tri's study [5] reported 45.4% ductal-dependent pulmonary circulation CHD, and Vo Phan Thao Trang and Pham Diep Thuy Duong (2021) [10] reported 65.4%.

4.2. Clinical Symptoms of Severe CHD in Neonates

The most common clinical symptoms identified in our study were cyanosis and murmurs, observed in 51.3% and 46.2% of cases, respectively. These rates are lower than those reported by Vo Duc Tri [5] (81.8% cyanosis, 90.9% murmurs), which also highlighted a correlation between cyanosis and the severity of CHD. Another study by Mat Bah [9] reported cyanosis in 75.8% of neonates.

Beyond these symptoms, 38.5% of cases presented with dyspnea and 30.8% with poor feeding and/or weak crying. Mat Bah's study [9] found 34.4% of neonates with respiratory failure and 32.6% with heart failure during the neonatal period. These symptoms might be attributed to CHD or other neonatal pathologies, particularly in preterm or critically ill neonates. This emphasize the importance of maintaining a high index of suspicion for CHD when such symptoms arise.

4.3. Preoperative Interventions for Severe CHD in Neonates

Administering prostaglandin E1 (PGE1) to maintain ductal patency is a cornerstone preoperative therapy for neonates with ductal-dependent CHD, particularly in patients with severe cyanosis or shock [11]Romania.
Institute of Cardiovascular Disease and Transplant Tirgu Mureș, Romania.
Department of Neonatal Intensive Care, County Clinical Emergency Hospital Tirgu Mureș, Romania.</auth-address><titles><title>Congenital Heart Disease Requiring Maintenance of Ductus Arteriosus in Critically Ill Newborns Admitted at a Tertiary Neonatal Intensive Care Unit</title><secondary-title>J Crit Care Med (Targu Mures. In our study, 35.9% of neonates required PGE1, a lower proportion than Vo Duc Tri's 2019 study [5], which reported 43.9%.

Other interventions included inotropic support (20.5%), invasive mechanical ventilation (43.6%), and heart failure management (43.6%). By comparison, Zübarioğlu (2020) [12] reported higher rates of inotropic support (44.6%) and mechanical ventilation (56.5%).

4.4. Initial Treatment Outcomes

Preoperative mortality in our study was 25.6%, with the others either proceeding to surgery or being managed as outpatients awaiting surgery. This mortality rate is consistent with other studies: 28.8% in Vo Duc Tri's study (2019) [5], 20% in E.G. Jacobs (2000) [6], 21% in Cheng Henry H. (2011) [13], 32.6% in Lopes S. (2018) [14], and 27% in Zübarioğlu (2020) [12]. The relatively high mortality rates across studies reflect the critical severity of CHD in neonates.

4.5. Factors Associated with Preoperative Mortality in Neonates with Severe CHD

Our findings identified several significant risk factors for preoperative mortality:

- Birth weight < 2500 grams**:** Neonates with low birth weight had a 4.71-fold higher mortality risk than those with a birth weight ≥ 2500 grams (OR=4.71, 95%CI: 1.03–21.65, p<0.05). This is consistent with Lopes S. (2018) [14] (RR=2.33, p=0.0068), Delany [15] (OR=3.8, 95% CI: 3.0–4.7, p<0.01), and Zübarioğlu (p<0.05) [12]. Mat Bah [9] found birth weight < 2000 grams significantly increased mortality risk (HR=2.61).

- Invasive mechanical ventilation**:** This intervention increased mortality risk by 23.62 times (OR=23.62, 95%CI: 2.56–217.7, p<0.05). Similar results were reported by Vo Duc Tri [5], who found a strong association between respiratory failure in intensive care and mortality (OR=4.4, 95% CI: 1.3–15.3, p=0.019).

- Inotropic therapy**:** This increased mortality risk by 8.67 times (OR=8.67, 95%CI: 1.55–48.5, p<0.05). Zübarioğlu's study [12] also reported a higher mortality rate (64%) in neonates requiring inotropes compared to those who did not (37.3%), p<0.05.

- Heart failure**:** Neonates with heart failure had an 8.88-fold increased mortality risk (OR=8.88, 95%CI: 1.56–50.5, p<0.05). Vo Duc Tri's study [5] similarly linked heart failure in intensive care to higher mortality rates (OR=5.0, 95%CI: 1.1–21.9, p=0.034).

Notably, our study found no significant associations between mortality and gestational age, prenatal diagnosis, or type of CHD. This contrasts with other studies, potentially due to our smaller sample size and shorter study duration [9, 12, 15].

5. CONCLUSION

Key preoperative mortality risk factors in neonates with severe congenital heart disease include: Birth weight < 2500 grams, need for invasive mechanical ventilation, heart failure, and requirement for inotropic therapy. These findings highlight the importance of targeted interventions to optimize survival outcomes in this high-risk population.

6. LIMITATIONS

This study has some limitations. The modest sample size may affect the robustness and external validity of the findings. Furthermore, the relatively short study period may limit the assessment of long-term effects. Future studies with larger sample sizes and longer follow-up periods are warranted.

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