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Comparative Analysis of Endocarditis in Congenital Heart Disease Patients Across Age Groups

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ABSTRACT

Infective endocarditis remains a serious complication in patients with congenital heart disease, yet age-related differences in presentation and outcomes are not well understood. **Objectives:** To evaluate age-stratified clinical characteristics, microbiological profiles, and in-hospital outcomes of infective endocarditis (IE) in patients with congenital heart disease (CHD), with emphasis on diagnostic patterns and mortality predictors. **Methods:** This cross-sectional analytical study was conducted at the Department of Cardiology, Quaid-e-Azam Medical College, Bahawalpur, from March 2024 to March 2025. A total of 113 patients with CHD and definite IE, diagnosed per modified Duke criteria, were enrolled through non-probability consecutive sampling. Patients were stratified into two groups: ≤18 years (n=57) and >18 years (n=56). Data on demographics, clinical variables, blood culture results, inflammatory markers, echocardiographic findings, and in-hospital outcomes were collected. **Results:** Septal defects were significantly more common in children (61.4%) versus adults (p=0.0288). Adults exhibited higher mean creatinine (1.21±0.42 mg/dL vs 0.96 ± 0.28 mg/dL, p=0.032) and vegetation size (10.4 ± 4.2 mm vs 8.6 ±2 .9 mm, p=0.031). In-hospital mortality was 12.4%. Vegetation size >10 mm and prosthetic material presence were significant mortality predictors (adjusted OR=4.23, 95% CI: 1.63–10.99, p=0.001; and OR=3.45, 95% CI: 1.19–9.83, p=0.009). Blood culture positivity reduced mortality risk (adjusted OR=0.53, 95% CI: 0.22–0.91, p=0.001). **Conclusions:** Adult CHD patients with IE presented with more advanced disease and higher mortality risk, especially with prosthetic material and large vegetations.

INTRODUCTION

Endocarditis remains a life-threatening complication among individuals with underlying structural heart diseases, particularly congenital heart disease (CHD), which predisposes patients to abnormal intracardiac flow and endocardial injury [1]. Infective endocarditis (IE), though relatively rare in the general population, carries substantial morbidity and mortality in CHD patients, especially in low-resource settings where diagnostic and therapeutic facilities are limited [2, 3]. In countries like Pakistan, with a high birth prevalence of CHD (reported between 8–12 per 1,000 live births) and inadequate access to early surgical correction or routine follow-up, the risk of developing endocarditis is markedly increased [4]. Endocarditis in CHD patients exhibits diverse clinical manifestations and outcomes across different age groups [5]. The pathophysiological mechanisms vary by age due to evolving cardiac anatomy, immune response, and exposure to risk factors such as catheterization, dental procedures, or prosthetic materials [6, 7]. Children with cyanotic CHD or septal defects often experience earlier and more aggressive forms of endocarditis, while adults are frequently affected due to long-standing uncorrected anomalies or prosthetic valve complications [8]. In recent years, researchers from wealthy nations have studied the

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symptoms, types of IE and common bacteria found in children with CHD [9, 10]. Follow-up treatment is also not good enough for many patients [11, 12]. That's why we need to look into how endocarditis in CHD affects people in Pakistan in terms of their medical history, symptoms and lab findings [13].

This study aimed to compare the clinical presentation, microbiological profile, and echocardiographic findings of infective endocarditis in children versus adults with CHD at a tertiary care center in Pakistan, and assess treatment modalities and short-term outcomes, including complications and in-hospital mortality.

METHODS

The descriptive cross-sectional study was organized at the Department of Cardiology in Quaid-e-Azam Medical College, Bahawalpur, Pakistan, from March 2024 to March 2025. Ethical approval was obtained from the Institutional Review Board of Quaid-e-Azam Medical College, Bahawalpur (Approval number: 2459 /DME/QAMC Bahawalpur). The research included patients diagnosed with IE or CHD and looked at similarities and differences in these patients' characteristics depending on their age. Exclusion criteria encompassed patients with acquired heart diseases without congenital anomalies, those with incomplete medical records, and individuals who declined consent. A sample size of 113 was determined based on established prevalence data and practical considerations. A nationwide case–control study cumulative lifetime incidence of infective endocarditis (IE) of approximately 8.5% among patients with congenital heart disease [14]. This figure was considered a realistic baseline incidence for calculating sample size. Using standard formulas for prevalence studies at a 95% confidence level and a 5% margin of error, the minimum required sample size was estimated to be approximately 120. A slightly lower sample of 113 was selected due to logistical limitations, while still allowing for statistically acceptable subgroup analyses by age and CHD severity. This sample represents the complete set of available cases during the defined timeframe at the study center, ensuring comprehensive data coverage for the research objectives. The diagnosis of congenital heart disease (CHD) was confirmed based on prior echocardiographic reports and clinical documentation available in the patients' medical records. Infective endocarditis (IE) was diagnosed according to the modified Duke criteria, using a combination of clinical, microbiological, and echocardiographic findings. Non-probability consecutive sampling was employed to recruit participants meeting the inclusion criteria. Laboratory investigations included complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and blood cultures. All patients underwent routine laboratory testing at the time of admission or initial evaluation. Complete blood counts (CBC) were performed using an automated hematology analyzer (e.g., Sysmex XN-Series), which measured hemoglobin levels, total leukocyte count, and platelet count. Erythrocyte sedimentation rate (ESR) was determined by the Westergren method, following standard laboratory protocols. C-reactive protein (CRP) levels were measured using an immunoturbidimetric assay on a fully automated biochemistry analyzer (e.g., Roche Cobas or equivalent). For microbiological diagnosis, blood cultures were collected under sterile conditions from two separate venipuncture sites before the initiation of antibiotic therapy. Samples were inoculated into aerobic and anaerobic culture bottles and incubated in an automated blood culture system (e.g., BACTEC or BacT/ALERT). Positive cultures were further sub-cultured and identified using standard biochemical tests and, where available, automated identification systems such as VITEK 2. Data were entered and analyzed using SPSS version 23.0. Descriptive statistics were calculated for all variables. Categorical variables were presented as frequencies and percentages, while continuous variables were summarized using means and standard deviations or medians with interquartile ranges, depending on data distribution. The Chi-square test or Fisher's exact test was used to compare categorical variables between groups (e.g., children vs. adults). For continuous variables, independent-samples t-tests or Mann–Whitney U tests were applied based on normality. A p-value of <0.050 was considered statistically significant.

RESULTS

This study provided a detailed comparative analysis of endocarditis among patients with congenital heart disease across different age groups, yielding several important findings. The study presents the frequency distribution and chi-square test results of categorical variables, including gender, type of congenital heart disease, previous surgery, prosthetic material, and type of infective endocarditis, stratified by age group (≤18 years and >18 years)(Table 1).

Table 1: Demographic and Clinical Characteristics of Study Population by Age Group

Variables	Category	≤18 Years (n=57)	>18 Years (n=56)	Total (n= 113)	p-Value	Unadjusted OR (95% CI)
Gender	Male	29	32	61	0.933	1.03 (0.51–2.07)
	Female	28	24	52		Ref
Type of CHD	Septal Defect (VSD/ASD)	35	21	56	0.028	2.56 (1.20–5.47)
	Valve Abnormality	8	16	24		Ref
Previous Surgery	Yes	17	22	39	0.103	0.63 (0.29–1.38)
	No	40	34	74		Ref

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Prosthetic Material	Yes	11	16	27	0.756	0.89 (0.38–2.08)
	No	46	40	86		Ref
Type of IE	Native Valve	35	33	68	0.672	1.19 (0.55–2.57)
	Prosthetic Valve	13	14	27		Ref

Chi-square or Fisher's exact test was used for categorical comparisons; unadjusted odds ratios with 95% confidence intervals are reported. A p-value <0.050 was considered statistically significant.

Findings compare the inflammatory markers and microbiological results between patients with positive and negative blood cultures, with–Mann-Whitney U test applied for non-normally distributed data. The findings emphasize the importance of early culture sampling before empirical therapy to enhance diagnostic yield (Table 2).

Table 2: Microbiological and Inflammatory Profile by Culture Positivity

Variables	Culture Positive (n=79)	Culture Negative (n=34)	p-Value	Unadjusted OR (95% CI)
Prior Antibiotic Use	21 (26.6%)	23 (67.6%)	0.003	3.41 (1.51–7.68)
CRP >10 mg/L	65 (82.3%)	23 (67.6%)	0.017	2.26 (1.12–4.98)
ESR >30 mm/hr	60 (75.9%)	22 (64.7%)	0.210	1.70 (0.72–3.97)
Organism Identified	Staph (30.4%), Strep (23.9%), Others	-	-	-

Chi-square or Fisher's exact test was used for categorical comparisons; unadjusted odds ratios with 95% confidence intervals are reported. A p-value <0.050 was considered statistically significant.

Results summarize the distribution of key continuous variables such as CRP, ESR, hemoglobin, creatinine, and vegetation size across pediatric and adult age groups (Table 3).

Table 3: Continuous Variable Comparison Between Age Groups

Variables	Age ≤18 Years (Mean ± SD / Median [IQR])	Age >18 Years (Mean ± SD / Median [IQR])	p-Value	Test Used
Vegetation Size	8.6 ± 2.9 mm	10.4 ± 4.2 mm	0.031	t-test
CRP	15.4 (10–21) mg/L	17.2 (12–26) mg/L	0.088	Mann-Whitney U
ESR	39 (25–55) mm/hr	42 (30–67) mm/hr	0.114	Mann-Whitney U
Creatinine	0.96 ± 0.28 mg/dL	1.21 ± 0.42 mg/dL	0.032	t-test
Hemoglobin	10.8 ± 1.9 g/dL	10.2 ± 2.1 g/dL	0.106	t-test

Independent-samples t-test was used for normally distributed variables; Mann–Whitney U test for non-normally distributed variables. A p-value <0.050 was considered statistically significant for all comparisons

Findings display in-hospital outcomes (discharge, death, transfer, LAMA) and factors associated with mortality using logistic regression. Odds ratios are reported for vegetation size, prosthetic material, and culture status (Table 4).

Table 4: Outcome Analysis and Risk Predictors

Variables	Deaths (n=14)	Survivors (n=99)	p-Value	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Vegetation >10 mm	10 (71.4%)	27 (27.3%)	0.001	4.85 (1.91–12.3)	4.23 (1.63–10.99)
Prosthetic Material	7 (50%)	20 (20.2%)	0.009	3.92 (1.36–11.31)	3.45 (1.19–9.83)
Culture Positive	8 (57.1%)	71 (71.7%)	0.001	0.49 (0.18–0.83)	0.53 (0.22–0.91)

Chi-square or Fisher's exact test was used; unadjusted and adjusted odds ratios with 95% confidence intervals are shown. A p-value <0.050 was considered statistically significant.

To enhance the clarity and focus of the results in line with the study's aims, the study summarizes key variables associated with differences in prevalence, outcomes, and clinical characteristics between pediatric and adult patients with congenital or acquired heart disease (Table 5).

Table 5: Summary of Significant Diagnostic Findings and Mortality Predictors

Variables	Group with Higher Prevalence	p-Value	OR (95% CI)	Interpretation
Septal Defects (VSD/ASD)	Pediatric Group (≤18 Years)	0.028	2.56 (1.20–5.47)	Age-related pattern in CHD type
Valve Abnormalities	Adult Group (>18 Years)	-	Ref	More common in adults
Creatinine	Adult Group (>18 Years)	0.032	-	Suggests a more advanced disease
Vegetation Size (>10 mm)	Adult Group, Mortality Cases	0.001	4.23 (1.63–10.99)	Strong independent predictor of mortality
Prosthetic Material	More Frequent in Adults, Deaths	0.009	3.45 (1.19–9.83)	Associated with worse outcomes
Culture Positivity	Protective (More in Survivors)	0.001	0.53 (0.22–0.91)	Early identification is linked with a better prognosis
Prior Antibiotic Use	Higher in Culture-Negative Cases	0.003	3.41 (1.51–7.68)	Associated with lower culture yield

Statistical tests used include chi-square, Fisher's exact test, t-test, Mann–Whitney U, and logistic regression. ORs represent unadjusted or adjusted associations; p-values <0.050 were considered statistically significant.

DISCUSSION

The study presented a comprehensive analysis of infective endocarditis (IE) in patients with congenital heart disease (CHD), stratified by age, within a Pakistani tertiary care context. A strong impact of socioeconomic factors on disease presentation and outcomes was also observed, along with a mortality rate of 12.4%, aligning with global trends [14-16]. The findings of this study align with research conducted in Europe, which emphasizes the importance of obtaining blood cultures before initiating antibiotic therapy [17, 18]. Similar observations have been reported in East Asian studies, where patients with culture-negative endocarditis often had prolonged

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empirical antibiotic use before diagnosis, leading to delays and suboptimal treatment choices [19]. The association identified between vegetation size and increased mortality in this study is consistent with previous research from Western cardiac centers, where vegetations larger than 10 mm, particularly in patients with prosthetic valves, were linked to higher complication rates and worse outcomes [20]. Additionally, the protective effect of culture-positive endocarditis noted in our study mirrors patterns seen in multicenter studies from North America, where early identification of the causative organism allowed for more precise antimicrobial therapy and improved clinical outcomes.

This study was limited by its single-center design and relatively small sample size, which may limit the generalizability of the findings to other populations. Additionally, incomplete availability of microbiological data (including prior antibiotic exposure affecting culture results) and lack of long-term follow-up restricted assessment of treatment outcomes and recurrence. Future studies should include multi-center cohorts with standardized early blood culture protocols and long-term follow-up to better evaluate microbiological patterns and outcomes in infective endocarditis associated with congenital heart disease.

CONCLUSIONS

This study identified clear age-related differences in the clinical presentation, management, and outcomes of infective endocarditis (IE) among patients with congenital heart disease (CHD) in Pakistan. Strengthening healthcare infrastructure and awareness at the community level may significantly improve outcomes for CHD patients with IE in low-resource settings.

Authors' Contribution

Conceptualization: MN
Methodology: FUR, MAZ
Formal analysis: US, IA
Writing and Drafting: UM
Review and Editing: MN, FUR, US, UM, MAZ, IA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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