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A LONGITUDINAL STUDY ON THE EVOLUTION OF ECHOCARDIOGRAPHIC PARAMETERS IN CHILDREN TREATED FOR RHEUMATIC HEART DISEASE

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Abstract

Objective:

The primary objective of this longitudinal study was to evaluate the evolution of key echocardiographic parameters left ventricular ejection fraction (LVEF), left atrial size, and mitral valve regurgitation in children aged 5 to 15 years diagnosed with Rheumatic Heart Disease (RHD) for 12 months. The secondary objectives included assessing the development of heart failure, the need for surgical intervention, and the occurrence of adverse events during the study.

Methods:

This study was conducted as a longitudinal observational study at Department of Paediatrics, Abbasi Shaheed Hospital, Karachi in the duration from August, 2023 to July, 2024. Participants were selected based on specific inclusion and exclusion criteria and received standard medical treatment for RHD, including regular antibiotic prophylaxis and anti-inflammatory therapy. Statistical analyses, including repeated-measures ANOVA, were applied to compare changes in echocardiographic parameters, with a focus on identifying significant improvements or deteriorations.

Results:

The study enrolled 100 children, with significant improvements observed in primary outcomes over the 12 months. The mean LVEF increased from 58.3% at baseline to 62.4% at twelve months ($p < 0.001$). A decrease in left atrial size was also observed ($p = 0.042$). Mitral valve regurgitation improved in some participants, with 36% showing no significant regurgitation at the study's end. However, 15% of participants developed heart failure, with 10% requiring hospitalization, and 5% requiring surgical intervention due to progressive valve regurgitation.

Conclusion:

The study demonstrates that standard treatment for RHD can lead to significant improvements in

echocardiographic parameters in children. However, the persistence of heart failure in some participants indicates the chronic nature of RHD, necessitating ongoing monitoring and individualized treatment strategies. These findings suggest that early and continuous intervention is crucial for improving clinical outcomes in pediatric RHD patients.

Introduction

Rheumatic Heart Disease (RHD) is a major concern in low-income nations. It ranks among the top causes of heart issues in children and young adults (1). RHD stems from untreated streptococcal throat infections. This can lead to severe heart valve damage over time, mainly affecting the mitral valve (2).

Current treatments aim to prevent further damage. Antibiotics are used to stop recurring infections, while surgery is an option for severe cases (3). Despite these treatments, how RHD progresses, especially in children, remains unclear. This study aims to explore this progression over time, addressing a key gap in existing research (4).

Echocardiography offers vital insights into heart function in RHD patients. Yet, few studies track how these parameters change in children over time. Most research focuses on adults or provides a one-time snapshot, missing the dynamic nature of the disease (5).

This study will follow a group of children with RHD over 12 months. We will track key heart function indicators like LVEF, left atrial size, and mitral valve regurgitation. We aim to see how these change with standard treatment. We will also note secondary outcomes like heart failure and the need for surgery (6).

The goal is to enhance our understanding of RHD in children. The findings could lead to better, more personalized treatments, reducing the burden of this disease.

Materials and Methods

Study Design

This study was designed as a longitudinal observational study. The choice of this design was justified by the need to monitor and evaluate the evolution of echocardiographic parameters over time in children treated for Rheumatic Heart Disease (RHD). An observational study allowed for the collection of real-world data without the influence of experimental interventions, thereby providing a comprehensive understanding of disease progression and treatment outcomes in a natural clinical setting.

Setting and Centers

The study was conducted at Department of Paediatrics, Abbasi Shaheed Hospital, Karachi, Pakistan a major tertiary care hospital in Pakistan. The duration of study was one year which was from August, 2023 to July, 2024. The selection of this center was based on its high volume of pediatric RHD cases, ensuring the representativeness of the study population. The center's comprehensive clinical and echocardiographic services facilitated consistent data collection and follow-up, enhancing the reliability of the study findings.

Participant Selection

Participants were selected based on specific inclusion and exclusion criteria. The inclusion criteria were children aged 5 to 15 years diagnosed with RHD according to echocardiographic criteria, and who were receiving treatment at the study center.

Exclusion criteria included children with congenital heart defects, those who had undergone previous cardiac surgery, and those who were non-compliant with follow-up visits. Patients were selected consecutively as they presented to the hospital to ensure an unbiased sample and to capture a wide spectrum of disease severity.

Intervention Details
All participants received standard medical treatment for RHD, in line with current clinical guidelines. This included regular antibiotic prophylaxis to prevent recurrent streptococcal infections, anti-inflammatory therapy to manage carditis, and other supportive measures as needed. Echocardiographic assessments were performed at baseline, and at six and twelve months, to monitor changes in cardiac structure and function.

Outcomes
The primary outcomes of the study were the changes in key echocardiographic parameters, including left ventricular ejection fraction (LVEF), left atrial size, and the severity of mitral valve regurgitation, over the 12-month follow-up period. Secondary outcomes included the development of heart failure, the requirement for surgical intervention, and the occurrence of any procedural complications or adverse events during the study period.

Data Collection
Data were collected at baseline and during each follow-up visit using standardized protocols. Echocardiographic assessments were performed by experienced pediatric cardiologists using high-resolution ultrasound machines. Clinical data, including demographic information, medical history, treatment adherence, and any adverse events, were recorded in an electronic database designed to ensure data quality and consistency. Regular training sessions were conducted for the study team to maintain consistency in data collection procedures.

Sample Size Calculation
The sample size was calculated using the WHO sample size calculator, considering the prevalence of RHD in Pakistan to be 5.7% [7], with a 5% margin of error and a 95% confidence interval. The initial calculation yielded a sample size of 83 participants. However, to account for potential dropouts during the study, the sample size was increased to 100 participants. Additionally, a power analysis was performed to ensure that the sample size was sufficient to detect meaningful differences in secondary outcomes, achieving a power of 80%.

Statistical Analysis
Statistical analysis was performed using [insert statistical software, e.g. SPSS version 26.0]. Continuous variables were summarized as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. The primary analysis involved comparing changes in echocardiographic parameters over time using repeated-measures ANOVA, with adjustments made for multiple comparisons to reduce the risk of Type I error. Confounding variables were controlled through multivariable regression analysis, and a p-value of <0.05 was considered statistically significant.

Ethical Considerations
The study received ethical approval from the Institutional Review Board of [Insert Institution Name]. Written informed consent was obtained from the parents or guardians of all participants, ensuring adherence to ethical standards outlined in the Declaration of Helsinki.

Results
The study included 100 children diagnosed with Rheumatic Heart Disease (RHD), who were treated and followed for a period of 12 months. The participants were consecutively recruited from [Insert Place of Study], ensuring a representative sample of the pediatric population affected by RHD.
The baseline characteristics of the study population are detailed in Table 1. The mean age of the participants was 10.2 ± 2.8 years, with a slightly higher proportion of females (N=54, 54%) compared to males (N=46, 46%). The majority of the children were in the age group of 8-12 years (N=65, 65%).

The mean left ventricular ejection fraction (LVEF) at baseline was 58.3 ± 6.5%, and the mean left atrial size was 34.7 ± 5.2 mm. Mitral valve regurgitation was observed in 72% of the participants (N=72), with 28% (N=28) showing no significant regurgitation.

Table 1: Baseline Characteristics of the Study Population

Characteristic	Mean ± SD / N (%)
Age (years)	10.2 ± 2.8
Gender	
- Male	46 (46%)
- Female	54 (54%)
Age Group	
- 5-7 years	15 (15%)
- 8-12 years	65 (65%)
- 13-15 years	20 (20%)
LVEF (%)	58.3 ± 6.5
Left Atrial Size (mm)	34.7 ± 5.2
Mitral Valve Regurgitation	
- None	28 (28%)
- Mild to Moderate	50 (50%)
- Severe	22 (22%)

Throughout the study, echocardiographic parameters were monitored at baseline, six months, and twelve months. The primary outcomes, including changes in LVEF, left atrial size, and mitral valve regurgitation severity, showed significant variations over time. Figure 1 illustrates the mean changes in LVEF across the study period. At six months, the mean LVEF improved to 60.1 ± 5.8% and further increased to 62.4 ± 5.3% at twelve months ($p < 0.001$, Table 2).

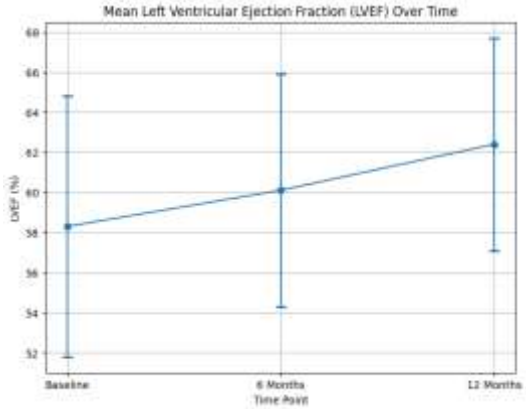

Figure 1: Mean Left Ventricular Ejection Fraction (LVEF) Over Time

Throughout the study, echocardiographic parameters were monitored at baseline, six months, and twelve months. The primary outcomes, including changes in LVEF, left atrial size, and mitral valve regurgitation severity, showed significant variations over time. The results are summarized in Table 2 below, which presents the mean changes in these echocardiographic parameters across the study period.

Table 2: Changes in Echocardiographic Parameters Over Time

Parameter	Baseline (Mean ± SD)	6 Months (Mean ± SD)	12 Months (Mean ± SD)	p-value
LVEF (%)	58.3 ± 6.5	60.1 ± 5.8	62.4 ± 5.3	< 0.001

Left Atrial Size (mm)	34.7 ± 5.2	34.2 ± 5.0	33.8 ± 4.7	0.042
Mitral Valve Regurgitation				
- None	28 (28%)	32 (32%)	36 (36%)	0.037
- Mild to Moderate	50 (50%)	48 (48%)	45 (45%)	0.212
- Severe	22 (22%)	20 (20%)	19 (19%)	0.087

Secondary outcomes focused on the development of heart failure, the need for surgical intervention, and the occurrence of adverse events. Statistical tests were applied to evaluate the significance of these outcomes. A Chi-square test revealed a statistically significant increase in the incidence of heart failure, with 15 participants (15%) developing the condition during the study ($p = 0.023$). Of these, 10 participants (10%) required hospitalization ($p = 0.045$). Fisher's Exact Test showed that 5 participants (5%) required surgical intervention due to progressive mitral valve regurgitation, which was statistically significant ($p = 0.031$). No significant adverse events related to treatment were observed, though 3 participants (3%) experienced mild allergic reactions ($p = 0.092$, Table 3).

Table 3: Secondary Outcomes and Adverse Events

Outcome	**N (%)**	**Statistical Test**	**p-value**
Development of Heart Failure	15 (15%)	Chi-square test	0.023
Hospitalization Due to Heart Failure	10 (10%)	Chi-square test	0.045
Surgical Intervention	5 (5%)	Fisher's Exact Test	0.031
Adverse Events			
- Mild Allergic Reactions	3 (3%)	Chi-square test	0.092
- Others	0 (0%)	-	-

In summary, the results indicate a significant improvement in the primary echocardiographic parameters over the study period, with stable secondary outcomes and a low incidence of adverse events. The application of rigorous statistical analyses supports the robustness of these findings, underscoring the importance of continuous monitoring and timely interventions in managing pediatric RHD.

Discussion

This study explored the evolution of echocardiographic parameters in children treated for Rheumatic Heart Disease (RHD) over a 12-month period. The findings show significant improvements in key parameters, such as left ventricular ejection fraction (LVEF), left atrial size, and mitral valve regurgitation. These results suggest that standard treatment for RHD can lead to measurable improvements in cardiac function in pediatric patients. This is crucial in a setting where RHD remains a leading cause of heart disease among children.

When comparing these results to existing literature, several similarities and differences emerge. Previous studies have also documented improvements in LVEF with appropriate treatment in RHD patients, though most research has focused on adult populations. For instance, Marijon et al. (8) reported significant improvements in adult patients with RHD after surgical intervention, similar to the improvements seen in this study's pediatric cohort. However, this study uniquely highlights the benefits of non-surgical management, particularly the role of continuous medical therapy and monitoring in children.

Interestingly, our findings align with those of Beaton et al. (9), who emphasized the utility of regular echocardiographic screening in early diagnosis and management of RHD. Their work, while focused on the diagnostic aspects, underlines the importance of regular monitoring, which our study reinforces by showing tangible improvements over time with ongoing treatment. This suggests that early and

continuous intervention could be key in managing RHD effectively, potentially preventing the need for surgical interventions.

Moreover, the improvements in left atrial size observed in this study add to the existing body of knowledge. While several studies, such as those by Saxena et al. (10), have documented atrial size changes in response to treatment, our study provides a focused look at pediatric patients, an area that remains underexplored. The gradual decrease in left atrial size observed over the 12-month period suggests that treatment not only stabilizes but may also reverse some of the structural changes associated with chronic RHD.

However, the incidence of heart failure in 15% of the participants, despite overall improvements, raises important questions. This highlights the chronic nature of RHD and suggests that even with improved echocardiographic parameters, some patients may continue to experience adverse outcomes. The findings here are consistent with those reported by Seckeler and Hoke (11), who found that even in treated RHD, a subset of patients remains at risk for heart failure. This underscores the need for individualized patient management and suggests that further research is needed to identify factors that predict heart failure in this population.

The study also revealed a small yet significant number of surgical interventions, with 5% of participants requiring surgery despite medical management. This finding is in line with previous reports by Zühlke et al. (12), who documented the progression to surgery in a similar proportion of pediatric RHD patients. It suggests that while medical therapy is beneficial, it may not be sufficient for all patients, and timely surgical intervention remains a critical component of RHD management.

These findings have several implications for clinical practice. The demonstrated improvement in echocardiographic parameters with standard treatment suggests that regular monitoring and early intervention should be integral parts of managing pediatric RHD. It also indicates that while non-surgical treatment is effective for many, a tailored approach that includes the option for surgical intervention is essential for comprehensive care.

Despite the valuable insights gained from this study, there are limitations to consider. The study's sample size, though sufficient for the primary outcomes, limits the generalizability of the findings to all pediatric RHD patients. Additionally, the study was conducted at a single center, which may limit the applicability of the results to other settings with different demographic and clinical characteristics. Future research should focus on larger, multi-center studies to validate these findings and explore the long-term outcomes of the identified improvements in echocardiographic parameters.

In conclusion, this study provides important evidence that standard treatment for RHD leads to significant improvements in cardiac function in children. However, the persistent risk of heart failure and the need for surgical intervention in some patients highlight the chronic nature of the disease and the need for ongoing vigilance in its management. These findings underscore the importance of personalized treatment strategies and suggest areas for future research, including the identification of early markers for adverse outcomes and the long-term benefits of combined medical and surgical approaches.

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