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Research Article

Comparative Analysis of Inflammatory Markers in Rheumatic Heart Disease: Pre-operative *vs* Post-operative States

Shivapriya NR[1], B. Senthil Kumar[2*], Sakkarai Jaya Gandhi[3], S. Sangeetha[4]

[1]*Vinayaka Mission's Research Foundation (Deemed to be University), Salem, Tamil Nadu, India.*
[2]*Departmentof Anatomy, Vinayaka Mission's Kirupananda Variyar Medical College and Hospitals, Vinayaka Mission's Research Foundation (DU), Salem, Tamil Nadu, India.*
[3]*Department of Anatomy, PIMS Medical College & Hospital, Pondicherry, India.*
[4]*Department of Community Medicine, Vinayaka Mission's Kirupananda Variyar Medical College and Hospitals, Vinayaka Mission's Research Foundation (DU), Salem, Tamil Nadu, India.*

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ABSTRACT

Present study intends to ascertain the relationship between the serum inflammatory markers in patients with rheumatic heart disease (RHD), which includes interleukin-6, C-reactive protein, NT-proBNP and troponin I (TnI). 108 RHD patients were assessed, who visited Dhanya Cardiac Centre for regular check-ups. The patient's concern regarding the use of their samples for this study has been acknowledged. Quantitative analysis of biomarkers such as IL-6, CRP, NT-pro BNP, and troponin I was performed. The findings revealed a significant upsurge in IL-6 and CRP levels in the pre-operative patients as compared with post-operative patients. Alternatively, NT-pro BNP and troponin I levels didn't show a significant upsurge in pre-operative patients, while these markers were elevated in the initial stage of the post-operative period. Our findings provide insight on numerous factors and biomolecules that might assist as potential markers related to the progression of rheumatic fever (RF) and RHD. Moreover, a follow-up study including a larger population is essential, as it could assist clinicians in predicting any predisposition to RHD.

Introduction

Rheumatic heart disease (RHD) is a foremost acquired cardiovascular condition among young adults and children in middle- and low-income countries, the certain people in higher-income countries are also at risk. RHD affects over 40 million individuals globally and around 3 lakh mortality is noticed annually, especially in developing countries.[1] RHD results from progressive inflammation leading to damage in valves by group A *Streptococcus pneumonia*. This heart disease can be largely mitigated by secondary antibiotic prophylaxis (SAP).[2] Arvind *et al.*, 2022 highlighted the upsurge of RHD and considered it to be a significant substantial health burden in developing countries like India.[3] Universally, there is a noticeable upsurge in the frequency and prevalence rates of RHD among children than adults, commonly in the age group of 10 to 14 years. Moreover, it is noticed that female cases are significantly higher than males during the study period.[4] In reaction to infections and tissue injury, IL-6 is rapidly and temporarily synthesized. It enhances host defense by inducing acute phase responses, hematopoiesis, and an immunological response.[5] Interleukin-6 (IL-6) serves dual roles as both an anti-inflammatory myokine and a pro-inflammatory cytokine. The IL-6 gene in humans encodes it.[6] When certain microbial compounds known as pathogen-associated molecular patterns (PAMPs)

***Corresponding Author:** Dr. B. Senthil Kumar

Address: Departmentof Anatomy, Vinayaka Mission's Kirupananda Variyar Medical College and Hospitals, Vinayaka Mission's Research Foundation (DU), Salem, Tamil Nadu, India.

Email ✉**:** skdrchinu@gmail.com

Tel.: +91-9894398677

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are present, macrophages release IL-6. Since a decade ago, researchers have been trying to determine whether the onset of atrial fibrillation triggers inflammatory consequences or whether an inflammatory condition that already exists encourages the maintenance of atria arrhythmias.[7] Low-grade inflammation has been reported to be both a reaction and a necessary component of the underlying arrhythmic process. High serum levels of interleukin-6 (IL6) and high-sensitivity C-reactive protein (hs-CRP) indicate the presence of a persistent inflammatory condition in individuals suffering from chronic rheumatic valvular heart disease. Secondary protection of rheumatic fever.[8] However, it is unclear how it affects this inflammatory condition. Therefore, we set out to investigate how LAP affected IL-6 and CRP, two inflammatory indicators, in individuals with long-lasting rheumatic heart illness conditions.[9] An international cause of early heart failure is rheumatic heart disease (RHD).[10] Valvular regurgitation, which causes ventricular distention and may result in the production of amino-terminal pro-brain natriuretic peptide (NT-proBNP), is a characteristic of early RHD. Significance troponin I (TnI) serves as an indication for the diagnosis of viral myocarditis and ischemic myocardial damage.[11] Cardiac-specific biomarkers, including BNP (B-type natriuretic peptide) and its precursor NT-pro BNP, are also valid in measuring heart failure extremity often seen in RHD individuals. Furthermore, the incidence of anti-streptococcal antibodies, including anti-streptolysin O (ASO) and anti-DNase B, assists as a signal of recent streptococcal contamination, which can lead to the commencement of rheumatic fever.[12] When combined, these biomarkers provide a holistic strategy to managing RHD, encompassing everything from early detection to tracking the course of the disease and its response to therapy.[13,14] Their varied usefulness in clinical practice, however, emphasizes the need for additional study to confirm their diagnostic and prognostic relevance at various illness stages.[15] The persistence of the present research work is to determine the correlation among the serum levels of inflammation indicators in individuals with RHD, which includes interleukin-6, NT-pro BNP, C-reactive protein, and troponin I (TnI).

Materials And Methods

Selection of Patients

We included 108 patients who visited Dhanya Cardiac Centre, Alagapuram, Salem, Tamil Nadu, for regular check-ups. The patient's concern regarding the use of their samples for this study has been acknowledged. Pre-operative and post-operative groups were created from all of the patients. The patients were split into two groups: Group C, which consisted of ten healthy persons, and group A, which consisted of 45.4% pre-operative patients with RHD and group B, which consisted of 54.6% patients with the same condition. Every patient underwent a thorough physical examination, ECG and medical history. The research adheres to guidelines from the Institutional Ethical Committee, Vinayaka Mission's Kirupananda Variyar Medical College and Hospitals for human subject research, ensuring informed consent and confidentiality of participants. Approval reference number (VMKVMC&H/IEC/21/008) has been granted for the study's duration.

Experimental Design

The basis for this research is a retrospective analysis of clinical data that was gathered prospectively. The study included patient candidates for heart operations over a four-year period (February 2018 - February 2023), with the following exclusion criteria not applying: emergency surgery, congenital heart diseases, deep hypothermia, presence of tumors or autoimmune diseases, and clinical signs of infections. Trained staff members prospectively gathered the clinical data and entered the min into the electronic database of the Dhanya Cardiac Center. Staff members prospectively gathered the clinical data and entered them into the electronic database of the Dhanya Cardiac Center.

Clinical Examination and History

Every patient who visits for a routine check-up has a preliminary examination performed and a complete history collected.

Echocardiography Data

Echocardiography has been demonstrated to be more accurate and sensitive than auscultation. Echocardiography detects subclinical RHD even when there is no pathological heart murmur.[16] A safe, painless procedure that doesn't expose the patient to dangerous radiation is portable echocardiography. We collected samples from individuals who had been clinically diagnosed with right ventricular hypertrophy (RHD) based on the results of echocardiography. These patients were divided into two groups: pre-operative and post-operative. The valvular lesions have affected both groups. In 90% of cases are mitral valves, 10% are tricuspid valves, and there are many valvular abnormalities.

Biochemical Parameters

In 2 mL of serum were extracted from venous blood samples, processed under aseptic conditions, and kept at minus 20°C in preparation for ELISA.[15] ELISA kits for human inter leukin-6, high-sensitivity C-reactive protein, and benzathine benzyl penicillin were used for the ELISA procedures.[17] While enzyme-linked immunosorbent assays (ELISA) offer the maximum sensitivity and specificity, the current CRP and IL-6 testing methods, such as latex cohesion, radial immune diffusion and nephelometry, have the common drawback of low sensitivity.[18]

Analysis of C-Reactive Protein

Quantitative analysis of CRP C-reactive protein (CRP) is measured using latex-enhanced nephelometry in this approach. The foundation of particle-enhanced assays is the interaction of a soluble analyte with the matching antigen or antibody attached to polystyrene particles. Particles with a polystyrene core and a hydrophilic shell are utilized to covalently bond anti-CRP antibodies in order to quantify CRP. Fluid particles that are covered with mouse monoclonal anti-CRP antibodies are assorted with a diluted test sample. The CRP existing in the test sample will interrelate with the latex substance, which results in the development of an antigen-antibody composite. After six minutes, light scattering is measured through a nephelometric process, with the consequence being directly compared to the absorption of the sample analytes. An automated blank subtraction is also performed. A calibration curve is used to determine CRP concentrations. For the calibration curve, a storable logit-log function is used to reduce the amount of data. A Behring Nephelometer is used for these assays in order to determine the quantitative level of CRP.[19]

N-terminal Prohormone of Brain Natriuretic Peptide (NT-proBNP) Analysis

Before being tested for NT-pro BNP using approved radioimmunoassay, the plasma was kept at-80°C. Using electro chemiluminescence (Elecsys NT –pro BNP, Roche Diagnostics) as the signal, serum NT-pro BNP was evaluated using a double antibody sandwich approach. The intra-assay constant of disparity was below 6% for both elevated as well as normal and levels. Age and gender determine the normal reference values, which range in mean from 3.5 pmol/l for men under 50 to 8.4 pmol/l for women between 50 and 65.[11]

Cardiac Troponin Test

The purpose of the cardiac troponin I CLIA Kit is to quantitatively assess the quantity of human high-sensitivity cardiac troponin I (hs-cTnT) in serum samples. The assay makes use of two antibodies that bind to distinct hs-cTnT epitopes using a two-site "sandwich" approach. Assay calibrators, controls or patient serum samples are immediately introduced to a reaction vessel together with biotin-lated hs-cTnT polyclonal antibody and streptavidin-coated magnetic particles. In the form of "magnetic particles–biotin hs-cTnT antibody-hs-cTnT-acridinium ester hs-cTnT antibody," the biotin antibody and an immune complex are captured by the magnetic particles. While unbound materials are washed away, materials bound to the solid beads are kept in a magnetic field. Subsequently, the reaction vessel is filled with trigger solutions, and the ECL100 analyzer is used to monitor the light emission. The concentration of hs-cTnT in the sample is proportional to the relative light units (RLU). Serumhs-cTnT concentration is the measure of the analyte content in the sample, which is obtained using a multi-point calibration curve that is stored.[20]

Statistical Analysis

The data that were collected were studied by version SPSS 23. To regulate statistical significance, the examination employed Fisher's exact test or the Chi-square test for unconditional variables, whereas independent t-tests were applied to assess continuous outcomes. A *p-value* > 0.05 was considered statistically significant.

Results

Relationship Between Plasma C-Reactive Protein and Interleukin-6 Concentrations: Valvular Inflammation and Impairment

Our research indicates a significant correlation between plasma levels of C-reactive protein and interleukin-6, as detailed in Table 1. This finding suggests that there is a persistent chronic inflammation affecting the cardiac valves. Furthermore, patients exhibiting a more pronounced inflammatory response tend to experience a quicker progression of valvular dysfunction. The levels of C-reactive protein and interleukin-6 are interconnected and associated with the inflammatory processes observed in patients suffering from chronic rheumatic heart disease. Additionally, the average levels of C-reactive protein and interleukin-6 were notably elevated in individuals diagnosed with chronic rheumatic heart disease, as presented in Table 2.

Changes in C-Reactive Protein Levels from Pre-operative to Post-operative Status

The investigation exposed a significant connotation between CRP levels and the status of patients (pre-operative vs. post-operative) with a *p-value* of 0.001. (Fig. 1) Among pre-operative patients, 40 (81.6%) had CRP levels<=5, while only 9 (18.4%) had CRP levels >5. In contrast, among post-operative patients, 30 (50.8%) had CRP levels<=5, and 29 (49.2%) had CRP levels>5. A closer examination of the data indicates a notable shift in CRP levels from pre-operative to post-operative status. Specifically, there was a decrease in the proportion of patients with CRP levels <=5 (from 81.6% pre-operatively to 50.8% post-operatively) and a corresponding increase in the proportion of patients with CRP levels >5 (from 18.4% pre-operatively to 49.2% post-operatively). According to these results, CRP levels may be useful biomarkers for rheumatic heart disease (RHD), which could have an impact on pre-operative evaluation and post-operative monitoring. The CRP has been regularly measured in relation to the investigation of the hazards of endocarditis and post-operative infections. Patients in our hospital before heart valve surgery. CRP is tested in individuals

Table 1: Statistical correlation of CRP pre-operative & post-operative group

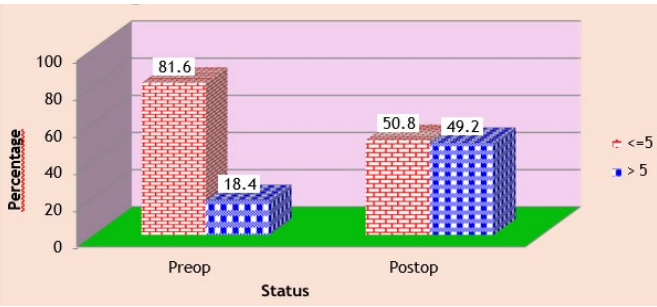
			CRP		*Total*	*p-value*
			<=5	*>5*		
Status	Pre-operative	Count	40	9	49	
		%within status	81.6%	18.4%	100%	0.001
	Post-operative	Count	30	29	59	
		%within status	50.8%	49.2%	100%	
Total		Count	70	38	108	
		%within status	64.8%	35.2%	100.0%	

Statistical correlation of C-reactive protein (CRP) levels in pre-operative and post-operative groups. Table 1 illustrates the statistical correlation analysis between pre-operative and post-operative CRP levels in patients. The columns include mean CRP levels (pre-operative and post-operative), standard deviation (SD), correlation coefficient (r), and the *p-value*. The correlation coefficient indicates the strength of the relationship between CRP levels before and after surgery, with a significant *p-value* of 0.001. This suggests a strong and statistically significant association between CRP levels across the pre-operative and post-operative periods, reflecting the influence of surgical intervention on inflammation.

Table 2: Comparison 6 in preoperative and post-operative

			IL6pgml7		*Total*	*p-value*
			<=7	*>7*		
Status	Pre-operative	Count	33	16	49	
		%within status	67.3%	32.7%	100%	
	Post-operative	Count	3	56	59	0.002
		%within status	5.1%	94.9%	100%	
Total		Count	36	72	108	
		%within status	33.3%	66.7%	100%	

Comparison of level of IL-6 in pre-operative and post-operative groups: Table 2 compares IL-6 among pre and post-operative patient groups. The columns display the mean IL-6 levels, standard deviation (SD), and statistical values, including the *p-value*. The comparison reveals a statistically significant difference in IL-6 levels between the two groups, with a *p-value* of 0.002. This indicates that IL-6 levels significantly changed following surgery, reflecting the body's inflammatory response to the surgical procedure.



The bar graph illustrates the percentage distribution of C-reactive protein (CRP) levels before (pre-operative) and after surgery (post-operative) on the x-axis. The y-axis represents the percentage of patients in each CRP category. CRP levels were measured preoperatively and post-operatively, with the data categorized into low, moderate, and high CRP levels. Differences in CRP levels between pre-operative and post-operative statuses highlight the potential impact of surgical intervention on inflammation as indicated by CRP percentages.

Fig. 1: Association between pre-operative and post-operative status and levels of c-reactive protein

who underwent complex valve surgery following their procedure. More obliquely, we discovered that a large number of patients exhibited noticeable pre-operative elevations in CRP levels. According to our research, elevated CRP levels may be as sign of the evolution of valve lesions and may have significant therapeutic ramifications. This is because treatments aimed at lowering CRP levels may help avoid subclinical inflammation and provide insight into the course of the disease.

Outcome of IL-6 Levels as Biomarkers in Pre-operative and Post-operative RHD

The analysis revealed a substantial association between IL-6 levels and the status of patients (pre-operative vs. post-operative) with a *p-value* of 0.002 (Table 2). Among pre-operative patients, 33 (67.3%) had IL-6 levels <=7, while 16 (32.7%) had IL-6 levels >7. In contrast, among post-operative patients, only 3 (5.1%) had IL-6 levels <=7, while 56 (94.9%) had IL-6 levels>7. A notable

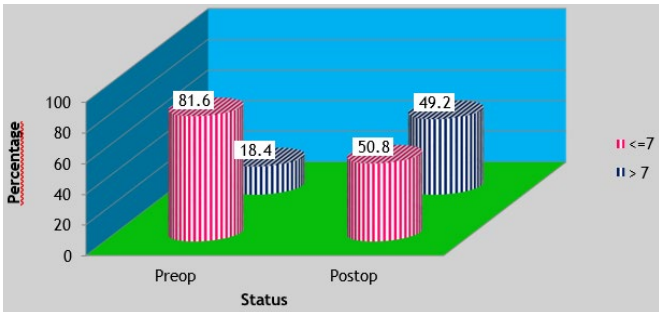
trend emerges when comparing IL-6 levels between pre-operative and post-operative status. There was a substantial decrease in the proportion of patients with IL-6 levels <=7 (from 67.3% pre-operatively to 5.1% post-operatively) and a corresponding increase in the proportion of patients with IL-6 levels >7 (from 32.7% pre-operatively to 94.9% post-operatively) (Fig. 2). Henceforth, there is a notable elevation shown in the pre-operative case. These findings underscore the potential utility of IL-6 levels as biomarkers for rheumatic heart disease (RHD), highlighting their relevance in both pre-operative assessment and post-operative monitoring.

Outcome of Troponin I Levels and Their Limited Role in Differentiating Pre-operative and Post-operative RHD

Numerous prior investigations have assessed the connection between biomarker increases and mortality in individuals after heart surgery. In our investigation, the median peak troponin I measurement in post-operative patients 48 hours after surgery was 2810 ng/liter. The analysis revealed no significant association between troponin I levels and the status of patients (pre-operative vs. post-operative) with a *p-value* of 0.594 (Table 3). Among pre-operative patients, 44 (89.8%) tested negative for troponin I, while only 5 (10.2%) tested positive. Similarly, among post-operative patients, 51 (86.4%) tested negative for troponin I, while 8 (13.6%) tested positive. (Fig. 3) There was a slight difference in the proportion of patients testing positive for troponin I between pre-operative and post-operative status (10.2 vs. 13.6%, respectively), but this difference was not statistically significant. These results simply that troponin I level in individuals with rheumatic heart disease (RHD) could not be a reliable biomarker to differentiate between pre-operative and post-operative conditions. It serves as a marker for cardiac damage in the post-operative state.

NT-pro BNP Levels and Their Limited Diagnostic Value in Pre-operative vs. Post-operative RHD

The analysis revealed no significant association between NT-pro BNP levels and the status of patients (pre-operative vs. post-operative) with a *p-value* of 0.203 (Table 4). Among pre-operative patients, 46 (93.9%) tested negative for NT-pro BNP, while only 3 (6.1%) tested positive. Similarly, among post-operative patients, 51 (86.4%) tested negative for NT-pro BNP, while 8 (13.6%) tested positive. Although there was a slight difference in the proportion of patients testing positive for NT- pro BNP between pre-operative and post-operative status (6.1 vs. 13.6%, respectively), this difference was not statistically significant (Fig. 4). These findings suggest that NT-pro BNP levels may not be reliable biomarkers for distinguishing between pre-operative and post-operative states in patients with RHD.

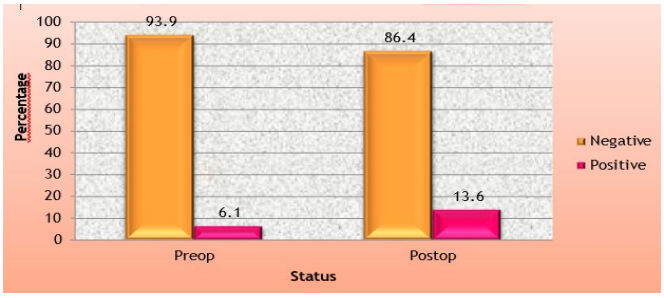


The bar graph presents the percentage distribution of patients according to Interleukin C (IL-C) levels in pre-operative and post-operative statuses, shown on the x-axis. The y-axis represents the percentage of patients in each category. Patients are grouped based on IL-C levels (low, moderate, and high) measured before (pre-operative) and after surgery (post-operative). This figure highlights the variation in IL-C levels in relation to surgical intervention, providing insights into immune response changes.

Fig. 2: Distribution of patients, by levels of Interleukin C

The bar graph displays the percentage distribution of patients with varying levels of Troponin I before (pre-operative) and after surgery (post-operative), represented on the x-axis. The y-axis shows the percentage of patients in each Troponin I category (normal, elevated, and high). The figure illustrates the relationship between operative status and troponin I level, indicating changes in cardiac stress or damage due to surgical intervention. Differences in troponin I level across the two operative statuses provide insights into perioperative cardiac function.

Fig. 3: Association between operative status and levels of troponin I



The bar graph illustrates the percentage distribution of patients with varying levels of NT-proBNP (N-terminal pro B-type Natriuretic Peptide) before (pre-operative) and after surgery (post-operative) on the x-axis. The y-axis represents the percentage of patients in each NT-proBNP category (normal, elevated, and high). This figure highlights the association between surgical intervention and changes in NT-proBNP levels, which reflect cardiac stress and heart function, showing differences in pre-operative and post-operative NT-proBNP status.

Fig. 4: Association between operative status and levels of NTproBNP

Table 3: Shows comparison of troponin I in two groups

			Troponin I		*Total*	*p-value*
			Negative	*Positive*		
Status	Pre-operative	Count	44	5	49	0.594
		%Within status	89.8%	10.2%	100.0%	
	Post-operative	Count	51	8	59	
		%Within status	86.4%	13.6%	100.0%	
Total		Count	95	13	108	
		%within Status	88.0%	12.0%	100.0%	

Comparison of Troponin I Levels in two groups: Table 3 describes troponin I levels between two groups: pre-operative and post-operative. The columns provide the mean troponin I level, standard deviation (SD), and statistical data, including the *p-value*. The analysis shows no statistically significant difference in Troponin I levels between the two groups, with a *p-value* of 0.594, indicating that surgical intervention did not result in a notable change in Troponin I levels across the two groups.

Table 4: Shows the comparison of NTProBNP in pre-operative and post-operative groups

			NTProBNP		*Total*	*p-value*
			Negative	*Positive*		
Status	Pre-operative	Count	46	3	49	0.203
		%within Status	93.9%	6.1%	100%	
	Post-operative	Count	51	8	59	
		%within Status	86.4%	13.6%	100%	
Total		Count	97	11	108	
		%Within status	89.8%	10.2%	100%	

Comparison of NT-proBNP Levels in pre-operative and post-operative groups: Table 4 demonstrates NT-proBNP (N-terminal pro B-type Natriuretic Peptide) levels between pre-operative and post-operative groups. The columns display the mean NT-proBNP levels, standard deviation (SD), and relevant statistical values, including the *p-value*. The comparison shows no statistically significant difference in NT-proBNP levels between the two groups, with a *p-value* of 0.203. This suggests that NT-proBNP levels did not significantly change following surgery, indicating no major alteration in cardiac stress across the two periods.

Discussion

The purpose of this study is to clarify the function of novel biomarkers in patients suffering from RHD. Specifically, the levels of c-reactive protein (CRP), interleukin-6 (IL-6), troponin I, and NT-proBNP were examined, along with their relationships to patient demographics and surgical outcome. The patients in this analysis had a mean age of 47.5 years, and 57.4% of them were men. The gender distribution is significant because it is consistent with epidemiological data indicating that RHD affects both sexes, albeit to differing degrees and at different ages of beginning. The fact that RHD patients range in age from 15 to 78 years old suggests that the condition is persistent and affects people of all ages. Elevated CRP levels are linked to both acute and chronic inflammatory conditions, and it is a recognized indicator of inflammation. The average CRP level in this study was 4.5 mg/L, while a sizable percentage of individuals (64.8%) had CRP levels ≤5 mg/L. These levels, however, had an average of 2.7 mg/L (p<0.05) and were substantially higher in post-operative patients than in pre-operative ones. This implies that a surgical procedure might cause a systemic inflammatory response, which would raise CRP levels. Increased CRP levels after heart surgery have also been reported in the past; these levels are associated with inflammation and possible side effects such as infection or tissue damage. [14,21] Another important indicator of inflammation and the immune system is IL-6. The study discovered that the mean IL-6 levels were 17.5 pg/mL. Post-operative patients had considered ably greater levels of IL-6 (median 10.0 pg/mL) than pre-operative patients (p <0.05). This fits with IL-6's function in the severe stage response, where it is released in response to tissue infection and injury, which are frequently observed after surgery.[18] IL-6 has the potential to be a marker for tracking surgical recovery and identifying individuals at risk for problems or protracted inflammation, as evidenced by the significant difference in levels between pre-operative and post-operative patients.[22] This study revealed a noteworthy association among IL-6 and CRP levels and the status of patients pre-operative vs. post-operative. The pre-operative patients showed a corresponding increase in the proportion of values.

One well-known biomarker for myocardial damage is troponin I. In this study, the mean level was 9.9 ng/L

and 88% of the individuals had positive troponin I tests. Keller *et al*. found no substantial alteration in raised troponin I levels among patients before and after surgery (p>0.05). This specifies that troponin I level might not assist as an operative marker for distinguishing between two groups in the context of RHD.[23] Contrary to this conclusion, troponin levels have been shown to have a critical role in the diagnosis and prognosis of acute myocardial infarction.[24] On the other hand, regardless of the surgical status, myocardial fibrosis and chronic stress may result in persistently high troponin levels in the context of chronic RHD. A sign of cardiac stress and heart failure is NT-pro BNP. In this investigation, the average NT-pro BNP level was 202.6 pg/mL. As with troponin I, there was no discernible difference in NT-pro BNP levels between individuals who underwent surgery and those who did not (p>0.05). This is an interesting finding because, according to Januzzi *et al*.(2006), NT-pro BNP levels are characteristically higher in heart failure cases and are related to the harshness of the condition and its projection.[25] Maizel *et al*. propose that the nonappearance of a prominent alteration related to operative status might be accredited to the continuing cardiac restoration and continued ventricular pressure existing in RHD individuals, circumstances that are not quickly transformed by surgical interference.[11] Biomarkers like CRP and IL-6 display fluctuating expression levels in patients before and after an operation, signifying their important role in pre-operative management. Augmented status of the above markers in individuals recovering from surgery may be assigned to increased inflammatory responses, which could help doctors treat patients more precisely with anti-inflammatory medications or keep a closer eye on them to reduce complications. On the other hand, the absence of a discernible fluctuation in troponin I and NT-pro BNP implies that these indicators may represent persistent myocardial strain instead of sudden modifications associated with surgery.[26] Consequently, these indicators may have a limited function in the perioperative care of RHD despite their importance in other cardiac diseases.
Overall, this study emphasizes how critical it is to comprehend how different biomarkers function differently when it comes to RHD. Owing to their notable fluctuations in relation to surgical conditions, CRP and IL-6 become valuable indicators for post-operative care. On the other hand, while crucial for long-term cardiac evaluation, troponin I and NT-pro BNP might not offer further perioperative information for patients with RHD. The analysis revealed no significant association between troponin I and NT Pro BNP levels and the status of Pre-operative patients. Positive correlations were seen in postop patients in the acute phase of surgery.

Conclusion

In conclusion, our research highlights key biomolecules as potential markers for the development of RF/RHD, though further studies in larger populations are needed. Post-surgery, CRP levels typically rise but return to normal within 7 to 10 days; deviations from this pattern may indicate infection or thromboembolic complications. Cardiac troponins T and I are now the “gold markers” for myocardial injury, aiding in non-invasive diagnosis of myocarditis, cardiac contusion, and monitoring treatment efficacy. Understanding the inflammatory response can help mitigate disease severity, guide vaccine selection, and improve preparedness for future outbreaks.

Limitations

Sample Size and Heterogeneity

Although 108 patients were selected in this biomarker study, limitations persist in size of the sample and heterogeneity of disease stages. Further validation of the results requires larger, multi-center research.

Confounding

The biomarker levels of pre-operative and post-operative patients differed significantly, according to the study. It did not, however, take into consideration any confounding variables that can affect biomarker levels, such as the use of medications, coexisting diseases, or the harshness of lesions in valvular.

Restricted Range

The study concentrated on a small number of biomarkers, possibly ignoring further crucial pertinent markers that would have added more information about the pathogenesis and prognosis of RHD. In order to fully reflect the intricate nature of RHD, future research should incorporate a larger panel of biomarkers.

Author Contribution Statement

Dr. Shivapriya NR played a significant role in the design of the study, as well as in the analysis and interpretation of the data. Dr. B. Senthil Kumar assisted in drafting the manuscript and offered essential revisions regarding the intellectual content. Dr. S. Sangeetha contributed by helping with statistical analysis. Dr. Sakkarai Jaya Gandhi managed the overall project and ensured adherence to ethical standards. All authors have reviewed and approved the final version of the manuscript.

References

1. Watkins DA, Johnson CO, Colquhoun SM, Karthikeyan G, Beaton A, Bukhman G, Forouzanfar MH, Longenecker CT, Mayosi BM, Mensah GA, Nascimento BR, Ribeiro ALP, Sable CA, Steer AC, Naghavi M, Mokdad AH, Murray CJL, Vos T, Carapetis JR, Roth GA. Global, Regional, and National Burden of Rheumatic Heart Disease. NEnglJMed. 2017;377(8):713-722. https://www.nejm.org/doi/10.1056/NEJMoa1603693
2. Beaton A, Okello E, Rwebembera J, Grobler A, Engelman D, Alepere J, Canales L, Carapetis J, DeWyer A, Lwabi P, Mirabel M, Mocumbi AO, Murali M, Nakitto M, Ndagire E, Nunes MCP, Omara IO, Sarnacki

R, Scheel A, Wilson N, Zimmerman M, Zühlke L, Karthikeyan G, Sable CA, Steer AC. Secondary Antibiotic Prophylaxis for Latent Rheumatic Heart Disease. N EnglJ Med. 2022;386(3):230-240. https://doi.org/10.1056/NEJMoa2102074.
3. Arvind B, Saxena A. Rheumatic Heart Disease in India: Has It Declined or been Forgotten? Indian J Pediatr. 2022;89:637-638. http://dx.doi.org/10.1007/s12098-022-04188-y
4. Mao C, Sun X, Long D, Zhang M, Xu X, Gao X, Lin Y, Wang X. Epidemiological study of pediatric rheumatic heart disease: An analysis from the Global Burden of Disease Study 2019. Int J Cardiol. 2024;400:131705.
5. Chopra P, Gulwani H. Pathology and pathogenesis of rheumatic heart disease. Indian J PatholMicrobiol. 2007;50(4):685-697.
6. Engelmann JH. Svendsen Inflammation in the genesis and perpetuation of atrial fibrillation 50 years on nature. Eur Heart J. 2005;26:2083-2092.https://doi.org/10.1093/eurheartj/ehi350
7. Van Leeuwen M, Van Rijswijk MH. Acute phase proteins in monitoring inflammatory disorders. J Bailliere's Clinical Rheumatology. 1994;8:531-552.https://doi.org/10.1016/s0950-3579(05)80114-1
8. Roberts WL *et al*. Evaluation of four automated high-sensitivity C-reactive protein methods: implications for clinical and epidemiological applications. J Clinical Chemistry. 2000; 46(4):461-468.http://dx.doi.org/10.1093/clinchem/46.4.461
9. Attar A, Marzban P, Moaref A, Aghasadeghi K. The association of plasma high- sensitivity C-reactive protein level with rheumatic heart disease: the possible role of inflammation. Indian Heart J. 2018;70(3):346-349.https://doi.org/10.1016/j.ihj.2017.08.017
10. Golbasi Z, Ucar O, Keles T, Sahin A, Cagli K, Camsari A. Increased levels of highly sensitive C-reactive protein in patients with chronic rheumatic valve disease: evidence of ongoing inflammation. Eur J Heart Fail. 2002;4(5):593-595. https://doi.org/10.1016/s1388-9842(02)00102-2
11. Maisel AS, Krishnaswamy P, Nowak RM. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. N. Engl. J. Med. 2002;347:161-167.https://doi.org/10.1056/nejmoa020233
12. Stollerman GH, Rusoff JH, Hirschfeld I. Prophylaxis against group A streptococci in rheumatic fever; the use of single monthly injections of benzathine penicillin G. N Engl J Med.1955;252(19):787-792. https://doi.org/10.1056/NEJM19550512252190
13. Atzeni F, Turiel M, Hollan I, Meroni P, Sitia S, Tomasoni L. Usefulness of cardiovascular biomarkers and cardiac imaging in systemic rheumatic diseases. Autoimmunity reviews. 2010;9(12):845-8. https://doi.org/10.1016/j.autrev.2010.08.001
14. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. J Clin Invest. 2003;111(12):1805-12.https://doi.org/10.1172/jci18921
15. Jayanthi S. Cardiac Biomarkers: A Beneficial Tool in the Diagnosis and Prognostication in Heart Failure-A Focus on Rheumatic Heart Disease. EC Cardiology. 2020;7:36-48.https://doi.org/10.31080/eccy.2020.07.00559
16. Gardezi SK, Coffey S, Prendergast BD, Myerson SG. Serum biomarkers in valvular heart disease. Heart. 2018;104(4):349-58. https://doi.org/10.1136/heartjnl-2016-310482
17. Kazahura PT, Mushi TL, Pallangyo P. Prevalence and risk factors for subclinical rheumatic heart disease among primary school children in Dar es Salaam, Tanzania: a community based cross-sectional study. BMC Cardiovasc Disord. 2021;21:610.https://doi.org/10.1186/s12872-021-02377-9
18. Mihara M, Hashizume M, Yoshida H, Suzuki M, Shiina M. IL-6/IL-6 receptor system and its role in physiological and pathological conditions. ClinSciLond. 2012;122(4):143-59.https://doi.org/10.1042/cs20110340
19. Roberts WL, Sedrick R, Moulton L, Spencer A, Rifai N. Evaluation of four automated high-sensitivity C-reactive protein methods: implications for clinical and epidemiological applications. J Clinical Chemistry. 2000;46(4):461-468. http://dx.doi.org/10.1093/clinchem/46.4.461
20. Keller T, Zeller T, Peetz D, Tzikas S, Roth A, Czyz E. Sensitive troponin I assay in early diagnosis of acute myocardial infarction. N Engl J Med. 2009; 361(9):868-77. https://doi.org/10.1056/nejmoa0903515
21. Santonocito C, Sanfilippo F, DeLocker I, Chiarenza F, Giacomo C,NjimiH. C- Reactive protein kinetics after cardiac surgery: A retrospective multi-center study. Ann Card Anaesth. 2022;25(4):498-504.https://doi.org/10.4103/aca.aca_141_21
22. Scheller J, Chalaris A, Schmidt-Arras D, Rose-John S. The pro-and anti-inflammatory properties of the cytokine interleukin-6. Biochim Biophys Acta. 2011;1813(5):878-88. https://doi.org/10.1016/j.bbamcr.2011.01.034
23. Mauermann E, Bolliger D, Fassl J. Post-operative high-sensitivity troponin and its association with 30-day and 12-month, all-cause mortality in patients undergoing on- pump cardiac surgery. Anesth Analg. 2017;125:1110-1117. https://doi.org/10.1213/ane.0000000000002023
24. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA. Fourth Universal Definition of Myocardial Infarction. J Am Coll Cardiol. 2018; 72(18):2231-64. https://doi.org/10.1016/j.jacc.2018.08.1038
25. Januzzi JL, Van Kimmenade R, Lainchbury J, Bayes-Genis A, Ordonez-Llanos J, Santalo-Bel M. NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure: an international pooled analysis of 1256 patients: the International Collaborative of NT-proBNP Study. Eur Heart J. 2006;27(3):330-7. https://doi.org/10.1093/eurheartj/ehi631
26. McKie PM, Cataliotti A, Lahr BD, Martin FL, Redfield MM, Bailey KR. The Prognostic Value of N-Terminal Pro–B-Type Natriuretic Peptide for Death and Cardiovascular Events in Healthy Normal and Stage A/B Heart Failure Subjects. Journal of the American College of Cardiology. 2010;55(19):2140-7. https://doi.org/10.1016/j.jacc.2010.01.031

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