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Artificial Intelligence Assisted Prediction in Acute Rheumatic Fever Patients with Carditis: The Utility of Complete Blood Count and Inflammatory Markers

Karditli Akut Romatizmal Ateşli Hastaların Yapay Zeka ile Tahmini: Tam Kan Sayımı ve Enflamatuvar Belirteçlerin Kullanılması

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Abstract

Objective: Acute rheumatic fever (ARF) is a serious inflammatory disease that results from an autoimmune reaction triggered by a group A beta-hemolytic streptococcal infection, primarily affecting cardiac tissues. It remains the primary etiology of acquired cardiac disorders in children worldwide, especially in developing countries. The present study seeks to examine the potential of inflammatory indices derived from the complete blood count and of machine-learning algorithms for the early diagnosis of the development of carditis associated with ARF.

Methods: In this retrospective study, 68 patients diagnosed with ARF and 71 healthy control subjects were examined between November 2020 and December 2025. Demographic data, blood tests, and transthoracic echocardiography reports were evaluated. Various inflammatory biomarkers, such as the neutrophil-monocyte index, neutrophil-platelet index, neutrophil-lymphocyte ratio, and systemic immune-inflammation index, were calculated. JASP 0.95.2 software and the random forest algorithm were used for data analysis and machine-learning modeling.

Results: As a result of the analyses, notable disparities achieved statistical were found between the control and patient groups in neutrophil (p=0.037), neutrophil-platelet index (p=0.025), neutrophil-lymphocyte ratio (p=0.012), and systemic immune-inflammation index (p=0.016) parameters. The machine-learning random forest model achieved a high test accuracy of 81.5% when using indices with significant p-values. In the feature-importance analysis, parameters such as systemic immune-inflammation index, monocyte, eosinophil and neutrophil were key determinants of the model's classification performance.

Conclusion: This study has demonstrated the potential of inflammatory indices derived from the complete blood count, combined with machine-learning algorithms, to predict, early and with high accuracy, the development of carditis associated with ARF. The significant correlations of markers such as neutrophil-lymphocyte ratio, neutrophil-platelet index, and SII with the presence of carditis, along with the predictive value of machine-learning models, suggest that complete blood count parameters may provide a critical advantage in the diagnosis and early detection of subclinical carditis.

Keywords: Acute rheumatic fever, carditis, inflammatory indexes, machine-learning, artificial intelligent

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Öz

Amaç: Akut romatizmal ateş (ARA), grup A beta-hemolitik streptokok enfeksiyonuna bağlı, kalbi etkileyen ciddi bir otoimmün enflamatuvar hastalıktır ve çocuklarda kazanılmış kalp hastalığının önde gelen nedenidir. Çalışma, tam kan sayımından türetilen inflamatuvar indeksler ve makine öğrenimi algoritmalarıyla ARA ilişkili kardit gelişiminin erken teşhis potansiyelini araştırmayı amaçlamaktadır.

Yöntem: Bu retrospektif çalışmada, Kasım 2020-Aralık 2025 arasında 68 akut romatizmal kalp hastalığı tanılı hasta ve 71 sağlıklı kontrol grubu incelenmiştir. Demografik veriler, kan testleri ve ekokardiyografi raporları değerlendirilmiştir. Nötrofil-monosit indeksi, nötrofil-trombosit indeksi, nötrofil-lenfosit oranı ve sistemik immün-inflamasyon indeksi gibi inflamatuvar biyobelirteçler hesaplanmıştır. Veri analizi ve makine öğrenimi modellemesinde JASP 0.95.2 yazılımı ve random forest algoritması kullanılmıştır.

Bulgular: Analizler, kontrol ve hasta grupları arasında nötrofil (p=0,037), nötrofil-trombosit indeksi (p=0,025), nötrofil-lenfosit oranı (p=0,012) ve sistemik immün-inflamasyon indeksi (p=0,016) parametrelerinde anlamlı farklılıklar ortaya koymuştur. Makine öğrenimi random forest modeli, anlamlı indeksleri kullanarak %81,5'lik yüksek bir test doğruluğu elde etmiştir. Özellik önem analizinde sistemik inflamatuvar indeks, monosit, eosinofil ve nötrofil gibi parametreler modelin sınıflandırma performansında belirleyici rol oynamıştır.

Sonuç: Bu çalışma, tam kan sayımı enflamatuvar indekslerinin ve makine öğrenimi algoritmalarının ARA ilişkili kardit gelişimini erken ve yüksek doğrulukla tahmin etme potansiyelini göstermiştir. Nötrofil-lenfosit oranı, nötrofil-trombosit indeksi ve SII gibi belirteçlerin kardit varlığı ile güçlü korelasyonu ve makine öğrenimi modellerinin öngörücü değeri, tam kan sayımı parametrelerinin subklinik kardit tanısı ve erken tespitinde kritik avantaj sağlayabileceğini düşündürmektedir. Bu hızlı ve düşük maliyetli indeksler, sınırlı kaynaklara sahip klinik ortamlarda bile önemli faydalar sunmaktadır.

Anahtar Kelimeler: Akut romatizmal ateş, kardit, enflamatuvar indeksler, makine öğrenimi, yapay zeka

Introduction

Acute rheumatic fever (ARF) is a multisystemic inflammatory disease that emerges as an autoimmune response to group A beta-hemolytic streptococcal infection in genetically susceptible individuals[1,2]. This condition is an inflammatory process that particularly affects major organ systems such as the heart, joints, brain, and skin[2]. The disease, frequently observed in the 5-15 age group, is recognized as the foremost cause of acquired cardiac disorders among the youth in developing nations and poses a heavy public health burden globally, with a yearly incidence of between 250.000 and 500.000 new cases[3]. The most serious complication of this autoimmune response is rheumatic heart disease, which leads to permanent valve damage and significantly increases morbidity and mortality[4,5]. In particular, Türkiye remains in the medium-high risk countries group[4]. Therefore, the early diagnosis of ARF and especially the prediction of carditis development are of critical importance for halting disease progression and preventing rheumatic heart disease[2,5]. Early diagnosis and treatment of ARF play a vital role in preventing valve involvement during disease progression and reducing the morbidity of rheumatic heart disease[2].

Developing an approach beyond the modified Jones criteria by evaluating inflammatory indices found in the hemogram can provide important preliminary information for the early diagnosis of carditis associated with ARF and for predicting its course[3,4]. In this context, inflammatory markers such as neutrophil (NEU)-to-lymphocyte (LYM) ratio (NLR), platelet (PLT)-to-LYM ratio (PLR), and monocyte (MON)-to-LYM (ML) ratio derived from complete blood count parameters have been found to be significantly higher in patients with carditis compared to those without carditis[6,7]. These findings suggest that these indices should be investigated as potential biomarkers for predicting the development of carditis associated with ARF and examined through new studies in the literature[7].

Machine-learning methods have increasingly been used in the field of medicine. This offers significant potential, particularly in the diagnosis and risk stratification of cardiovascular diseases[8]. In this context, the potential of inflammatory indices derived from complete blood count to predict the development of ARF accompanied by carditis, and the early detectability of this condition using machine-learning algorithms, are of great importance for disease management and improving patient outcomes[9]. This study aims to investigate the capacity of complete blood count parameters and inflammatory indices to predict the development of ARF accompanied by carditis, to facilitate their early diagnosis using machine-learning models, and to determine which inflammatory and hemogram values can be most efficiently utilized in these models.

Materials and Methods

Data Collection and Groups

This retrospective study included 68 newly diagnosed cases of ARF at the Pediatric Cardiology Department of İzmir

Democracy University Buca Seyfi Demirsoy Training and Research Hospital between November 2020 and December 2025 as the patient group (PG) and 71 healthy children as the control group (CG). Patients diagnosed with ARF were evaluated by pediatric cardiologists and diagnosed according to the modified Jones criteria[10]. Demographic data, blood tests, and transthoracic echocardiography reports (Philips Ultrasound Inc./USA) were retrospectively included in the study. Echocardiographic findings and blood test values recorded at initial detection of ARF were included in the study.

The CG consisted of patients who presented to the outpatient clinic with complaints of chest pain or palpitations, in whom no pathology was detected. Echocardiography evaluations for the CG were normal. Retrospectively, only those CG patients whose acute phase reactants [sedimentation, C-reactive protein (CRP), anti-streptolysin O (ASO)] and hemogram were negative were included. Echocardiography report results and acute phase reactants were utilized during data collection to differentiate between the control and PGs. This study received formal ethical clearance from the Non-Interventional Research Ethics Committee of İzmir Democracy University Buca Seyfi Demirsoy Training and Research Hospital (approval no: 2025/531, date: 26.11.2025). The authors further attest that all investigative procedures were carried out in strict adherence to the ethical standards of the Declaration of Helsinki.

Inflamatory Biomarkers

All inflammatory biomarkers used in this study were derived from routine complete blood count parameters measured in peripheral blood. Specifically, the NEU-MON (NM) index was calculated as the product of NEU count and MON count; the NEU-PLT (NP) index was calculated as the product of NEU count and PLT count; and the MON-PLT (MP) index was calculated as the product of MON count and PLT count. Additionally, the NLR, ML ratio, and PLR were determined by dividing the respective absolute cell counts by the LYM count. The systemic immune-inflammation index (SII) was defined as (PLT count×NEU count)/LYM count, and the systemic inflammation response index (SIRI) was computed as (NEU count×MON count)/LYM count. The aggregate index of systemic inflammation (AIRI) was calculated as (PLT count×NEU count×MON count)/LYM count.

Artificial Intelligence and Machine-learning Method

Using JASP 0.95.2 software[11], hemogram data were preprocessed for machine-learning algorithms and appropriate machine-learning model techniques were applied. Among these algorithms, various supervised learning models such as decision trees, support vector machines, and artificial neural networks were utilized to predict the carditis associated with ARF[8]. The performance metrics of each model were evaluated to determine the most suitable model, and the clinical predictive value of this model was investigated.

Optimizing Data Inputs for Machine-learning

Data from the patient and healthy groups were initially evaluated using classical statistical measures. Initially, data with significant p-values were obtained and added to the random forest model. Another aim of this study was to create the machine-learning model that achieved the highest predictive accuracy. For this purpose, starting with data that had significant p-values, all data were manually and sequentially added to and removed from the random forest model. Machine-learning modeling was concluded when the highest "model performance metrics" [hematocrit (HCT), MON, NEU, LYM, eosinophil (EOS), hemoglobin (Hb), NLR, AIRI, SIRI, white blood cell (WBC), PLT, SII] values were obtained (Figure 1). The most efficient random forest model was included in the study.

Statistical Analysis

Data evaluation was conducted using JASP version 0.95.2, an open-source platform integrating both statistical frameworks and machine-learning techniques[11]. For the descriptive analysis, continuous variables were summarized by mean and standard deviation when data were parametric, whereas variables with non-parametric distributions were represented by medians. Categorical factors were summarized as frequencies and corresponding percentages. To verify whether the data followed a normal distribution, the Kolmogorov-Smirnov test was applied. Bivariate associations were determined through simple correlation analyses, and chi-square tests were used to assess differences between categorical variables. To compare quantitative parameters, Student's t-test and one way analysis of variance were applied to normally distributed data, whereas the Mann-Whitney U and Kruskal-Wallis tests were used for variables with non-normal distributions. Statistical significance across all analyses was defined by a p-value threshold of <0.05.

Machine-learning Analyses

The machine-learning component used the random forest algorithm available in the JASP classification module. JASP itself is an open-source initiative developed with structural contributions from the University of Amsterdam and a consortium of institutions, including Utrecht, Nyenrode Business, KU Leuven, and Tilburg University. The dataset was partitioned into a 65% training set, a 20% validation set, and a 15% testing set. Evaluation of the model's performance involved documenting metrics such as accuracy, precision, recall, support, and F1 score, alongside the Matthews correlation coefficient, false positive and false discovery rates, area under the curve, and negative predictive, true negative, and false negative rates. Additionally, feature importance and model dynamics were assessed using mean decrease in accuracy, total increase in node purity, and mean dropout loss.

Power Analyses

Based on the power analysis, a study design utilizing 68 subjects per group provides a minimum probability of 0.89 for identifying effect sizes of $|\delta| \geq 0.5$. This calculation assumes a one-sided detection threshold and a maximum type I error rate of α=0.05.

Results

A total of 139 cases were included. There were 68 patients and 71 cases in the CG. Of these cases, 41 in the PG and 43 in the CG were girls. The median age was 12 years in the PG and 11 years in the CG. The median ASO value measured in the PG was 330 IU/mL. The median CRP value in the PG was 2.69 mg/dL (minimum 0.5 mg/dL, maximum 168 mg/dL). The ASO and CRP values in the CG were selected from negative values. Chorea was present in 2 patients and hemichorea was present in 1 patient. Steroid treatment was administered to 5 patients during hospitalization. Complete atrioventricular (AV) block was present in one patient, and first-degree AV block was present in 6 patients.

According to the hemogram values for the patient and CGs, WBC had a median of 7.06 in CG and 7.37 in PG, with no significant difference. PLT had medians of 287 and 292 for CG and PG, respectively, with no significant difference. The median Hb was 13.3 in both CG and PG, with no significant difference. HCT had a median of 39.5 in CG and 40.0 in PG, with no significant difference. NEU had median values of 3.55 for CG and 4.24 for PG; the difference was statistically significant. LYM had medians of 2.78 for CG and 2.68 for PG, with no significant difference between CG and PG. MONs had medians of 0.55 in CG and 0.47 in PG, with no significant difference between groups. EOS had a median of 0.15 in both CG and PG, with no significant difference. The NM index had a median of 2.07 in CG and 1.93 in PG, with no significant difference between CG and PG. The NP index had medians of 1.016 for CG and 1.175 for PG, and this difference was statistically significant. The MP index had a median of 165 in CG and 138 in PG, with no significant difference between CG and PG. The NL ratio had a median of 1.31 in CG and 1.50 in PG, and the difference between the groups was statistically significant. The ML ratio had medians of 0.208 and 0.179 in CG and PG, respectively, with no significant difference between groups. The PL ratio had a median of 107.2 in CG and 107.3 in PG, with no significant difference. SII had medians of 388.3 in CG and 427.2 in PG; this difference was statistically significant. SIRI had a median of 0.74 for both CG and PG, with no significant difference. AIRI median values were 209.1 for CG and 204.5 for PG; this difference was not statistically significant (Table 1).

Machine-learning Results

According to Table 2, the random forest classification model developed using significant indices was built with 7 trees and 3 features per split and achieved validation, test, and out-of-bag (OBB) accuracies of 65.2%, 81.5%, and 36.6%, respectively. These values indicate that the model has high test performance and has been optimized using the OOB criterion. The confusion matrix in Table 3 shows 9 correct and 0 incorrect predictions for CG, and 13 correct and 5 incorrect predictions for PG. According to Table 4, the model's performance metrics have been calculated for each of the two classes and for the average and total values. Support values are 9 for CG, 18 for PG, and 27 in total. Overall accuracy is 81.5%. Precision is 64.3% for CG, 100.0% for PG, and 88.1% on average. Recall is 100.0% for CG, 72.2% for PG, and 81.5% on average. The false positive rate is 27.8% for CG, 0.0% for PG, and 13.9% on average. The F1 scores are 0.783 for CG, 0.839 for PG, and 0.820 on average. The Matthews correlation coefficient is 0.681 across all classes, indicating a strong positive correlation for the model. The area under the curve is 0.728 for CG, 0.605 for PG, and 0.667 on average. The average negative predictive value, true negative rate, and threat score are 82.1%, 86.1%, and 1.750, respectively. All metrics are calculated for each class against all others, and the model exhibits high performance.

The feature importance of the random forest model developed using significant indices were calculated as the mean decrease in accuracy, the total increase in node purity, and the mean dropout loss. The highest mean decrease in accuracy values are observed for SII, MON, and EOS; for total increase in node purity, MON, NEU, and LYM are prominent. Based on mean dropout loss, MON, EOS, and NEU were determined to be the most effective features; note that dropout loss was calculated based on 50 permutations. These metrics indicate that features such as MON, EOS, NEU, and SII play a decisive role in the model's classification performance (Table 5).

Discussion

Between ARF patients and the CG, the inflammatory hemogram indices presented in Table 1 differed significantly at the $p<0.05$ level. These indices reflect the differences in inflammatory response between groups; for example, ratios such as MON, EOS, and NEU for MONs, EOSs, and NEUs indicate inflammatory processes that play a role in ARF pathogenesis. SII, with its complex structure based on PLTs and NEUs, emphasizes the systemic dimension of the disease. Similarly, it has been reported that NEU, leukocyte, and NLR levels are significantly higher in children with ARF compared to healthy children, and these parameters can be used in the diagnosis of the disease[12]. However, some studies show that full blood parameters such as leukocytes, NEUs, PLTs, and MONs are insufficient in predicting the severity of carditis[12]. Nevertheless, other studies indicate that parameters such as NLR, ML ratio, and PLR are significantly higher in patients with cardiac involvement in ARF, and these indices can be evaluated as potential biomarkers in predicting carditis[7]. These findings suggest that evaluating inflammatory indices in the hemogram of children with ARF may provide important preliminary information for the early diagnosis and determination of carditis. Accordingly, comparing the healthy CG without echocardiographic pathology with patients exhibiting carditis findings due to ARF offers a valuable approach for the early detection of carditis using machine-learning algorithms[2,7,13].

The random forest model, automatically configured by JASP with 7 trees and 3 features per split, emerged as the superior machine-learning algorithm for this classification task, outperforming traditional methods and achieving high test accuracy (0.815). The random forest model was employed due to its superior performance-F1 score and Matthews correlation coefficient exceeding 0.60-among evaluated algorithms for predicting carditis from hemogram parameters, consistent with robust results in pediatric inflammatory conditions (Figure 1)[8,14,15]. The small sample size poses substantial challenges for reliable machine-

Table 1. Descriptive statistics

Descriptive statistics	Groups (CG: 71, PG: 68)	Median (IQR: Q3-Q1)	p-value
WBC	CG	7.06 (8.46-6.15)	0.075
	PG	7.37 (9.52-6.23)	
PLT	CG	287 (342-259)	0.916
	PG	292 (350-256)	
Hb	CG	13.3 (14-12.3)	0.305
	PG	13.3 (13.8-12.3)	
HCT	CG	39.5 (41.7-37.8)	0.410
	PG	40.0 (41.9-37.6)	
NEU	CG	3.55 (4.41-2.93)	**0.037**
	PG	4.24 (5.72-3.07)	
LYM	CG	2.78 (3.23-2.18)	0.107
	PG	2.68 (3.31-2.18)	
MON	CG	0.55 (0.65-0.45)	0.451
	PG	0.47 (0.58-0.39)	
EOS	CG	0.15 (0.24-0.09)	0.316
	PG	0.15 (0.22-0.09)	
NM index	CG	2.07 (2.59-1.32)	0.267
	PG	1.93 (3.58-1.30)	
NP index	CG	1.016 (1.416-781)	**0.025**
	PG	1.175 (1.903-712)	
MP index	CG	165 (216-121)	0.442
	PG	138 (184-110)	
NL ratio	CG	1.31 (1.81-0.98)	**0.012**
	PG	1.50 (2.41-1.06)	
ML ratio	CG	0.208 (0.263-0.159)	0.785
	PG	0.179 (0.248-0.144)	
PL ratio	CG	107.2 (130.1-90.1)	0.786
	PG	107.3 (138.1-78.3)	
SII	CG	388.3 (527.4-269.9)	**0.016**
	PG	427.2 (683-289.8)	
SIRI	CG	0.74 (1.10-0.49)	0.109
	PG	0.74 (1.16-0.46)	
AIRI	CG	209.1 (348.8-143.2)	0.078
	PG	204.5 (368.5-131.6)	

WBC: White blood cell, PLT: Platelet, Hb: Hemoglobin, HCT: Hematocrit, NEU: Neutrophil, LYM: Lymphocyte, MON: Monocyte, EOS: Eosinophil, NM: Neutrophil-monocyte, NP: Neutrophil-platelet, MP: Monocyte-platelet, NL: Neutrophil-to-lymphocyte, ML: Monocyte-to-lymphocyte, PL: Platelet-to-lymphocyte, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, AIRI: Aggregate index of systemic inflammation, CG: Control group, PG: Patient group, IQR: Interquartile range

Table 2. Machine-learning model summary

Model summary: random forest classification							
Trees	**Features per split**	**n (train)**	**n (validation)**	**n (test)**	**Validation accuracy**	**Test accuracy**	**OOB accuracy**
7	3	89	23	27	0.652	0.815	0.366

The model is optimized with respect to the out-of-bag accuracy
OOB: Out-of-bag

Table 3. Machine-learning model prediction

Confusion matrix			
		Predicted	
		0	1
Observed	0	9	0
	1	5	13

Table 4. Machine-learning model performance metrics

Model performance metrics	**0**	**1**	**Average/ total**
Support	9	18	27
Accuracy	0.815	0.815	0.815
Precision (positive predictive value)	0.643	1.000	0.881
Recall (true positive rate)	1.000	0.722	0.815
False positive rate	0.278	0.000	0.139
False discovery rate	0.357	0.000	0.179
F1 score	0.783	0.839	0.820
Matthews correlation coefficient	0.681	0.681	0.681
Area under curve	0.728	0.605	0.667
Negative predictive value	1.000	0.643	0.821
True negative rate	0.722	1.000	0.861
False negative rate	0.000	0.278	0.139
False omission rate	0.000	0.357	0.179
Threat score	0.900	2.600	1.750
Statistical parity	0.519	0.481	1.000

All metrics are calculated for every class against all other classes

Table 5. Machine-learning feature impotance metrics

Feature importance metrics	**Mean decrease in accuracy**	**Total increase in node purity**	**Mean dropout loss**
HCT	-0.026	0.039	0.167
MON	0.040	0.025	0.235
NEU	0.018	0.021	0.180
LYM	0.021	0.011	0.131
EOS	0.040	0.001	0.191
Hb	-0.027	0.001	0.150
NL ratio	0.018	-0.004	0.144
AIRI	0.018	-0.006	0.146
SIRI	0.016	-0.011	0.154
WBC	-2.035×10^{-4}	-0.025	0.177
PLT	0.004	-0.039	0.146
SII	0.072	-0.041	0.170

Mean dropout loss (defined as 1-area under curve) is based on 50 permutations
WBC: White blood cell, PLT: Platelet, Hb: Hemoglobin, HCT: Hematocrit, NEU: Neutrophil, LYM: Lymphocyte, MON: Monocyte, EOS: Eosinophil, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, AIRI: Aggregate index of systemic inflammation

learning results, particularly regarding overfitting, generalizability, and capturing subtle inflammatory patterns like MON, EOS, NEU, and SII in pediatric ARF with carditis[8,16]. Indeed, pediatric cardiology studies affirm random forest's precision and robustness in handling heterogeneous data and imbalanced classes despite such limitations[8,16].

By developing a machine-learning model based on hemogram parameters, high-risk patients can be predicted with high accuracy before the clinical onset of carditis. The development of such models is supported by previous findings suggesting that inflammatory markers, particularly NLR, ML ratio, and PLR, can assist in the diagnosis and prognosis of carditis associated with ARF through serial measurements[1]. This is further corroborated by the feature importance metrics of the random forest model. SII, MON, and EOS rank highest for the mean decrease in accuracy; MON, NEU, and LYM are prominent for the total increase in node purity; and MON, EOS, and NEU play a decisive role in the mean dropout loss. These indices emerge as key biological markers, reinforcing the inflammatory distinction between ARF patients and the CG, and signaling their potential utility in clinical diagnostic processes, given the model's high test accuracy. This advancement holds particular promise for the early diagnosis of cardiac involvement and the management of ARF in children[12]. Accordingly, as supported by the literature, inflammatory indices such as NLR, PLR, and

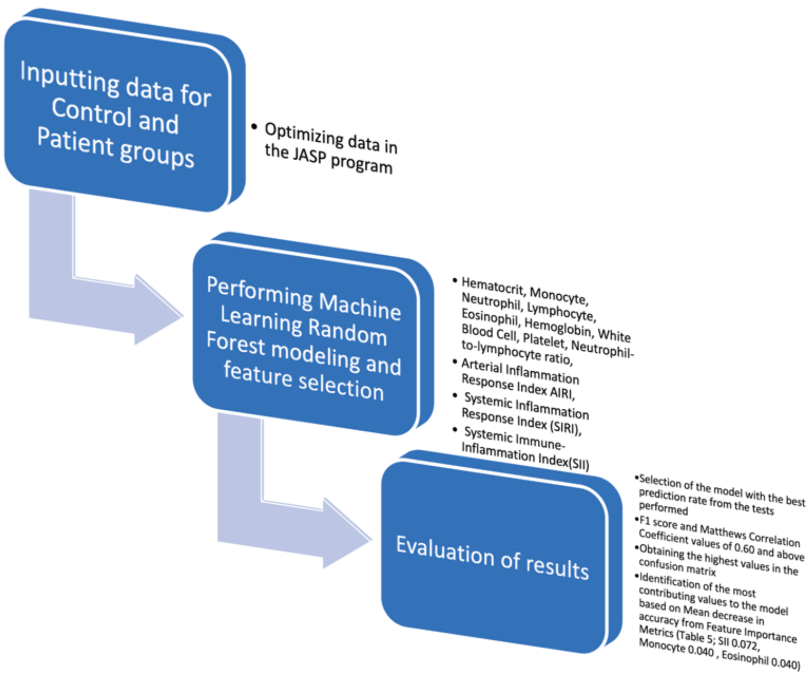

Figure 1. Schematic workflow of the data optimization process for the machine learning model integrating complete blood count parameters and inflammatory biomarkers

ML ratio have been found significantly elevated in patients with cardiac involvement due to ARF[7,9,13-17]. This integration enables the development of clinical decision support systems, particularly for preventing carditis progression and reducing morbidity rates[7,12]. However, some studies indicate that these inflammatory markers, whether used alone or in multiparametric evaluations, are insufficient for predicting carditis severity[7]; conversely, their combined use is thought to enhance diagnostic and prognostic accuracy[7]. In this context, machine-learning models can offer more robust predictive capabilities by integrating novel biomarkers and echocardiographic findings from large datasets of patients diagnosed using standardized Jones criteria[1,2,8].

As an important and innovative approach of our study, we evaluated the potential of p-value significant inflammatory indices and hemogram data using the machine-learning random forest method to predict ARF with findings, and determined that these parameters can predict the risk of ARF with high accuracy[7,14]. Particularly, parameters associated with WBC offer important predictive values in predicting the severity of rheumatic heart disease[8]. This innovative approach emphasizes the predictive potential of inflammatory indices and complete blood count parameters in pediatric patients diagnosed with ARF using Jones criteria, especially in the presence of carditis[18]. These findings suggest that complete blood count parameters may play an important role in the diagnosis of subclinical carditis, given their operator-independent nature and lack of requirement for technical expertise[7]. In this context, markers such as the NLR and ML ratio are reported to be helpful in the diagnosis and prognosis of ARF[7]. This can lead to significant progress, particularly in the early diagnosis of cardiac involvement and in the management of ARF in children. Indeed, while studies indicate that carditis presence in ARF is not associated with CRP, sedimentation, NLR, and PLR indices[9], the literature contains findings that cytokines such as interleukin (IL)-1 and IL-6 can be used as minor criteria in the diagnosis of carditis and arthritis, and anti-cytokine treatments may prevent valvular damage. In this context, machine-learning models offer significant potential for early diagnosis of carditis and for predicting its progression through the combined analysis of these cytokines and other inflammatory markers. We believe that prospective studies incorporating machine-learning models are necessary to obtain more detailed insights into inflammatory biomarkers and indices.

Future research can more thoroughly investigate the extent to which these integrated approaches can successfully predict carditis development and personalize treatment strategies[14]. Additionally, multicenter, prospective studies are required to evaluate the effectiveness of these models in clinical practice[15]. In the future, as machine-learning methods evolve and data availability increases, combining hemogram and simple biochemical values with clinical data will enable more precise and reliable diagnosis of ARF and earlier prediction of complications such as carditis. It is believed that such studies will further enhance their potential in predicting carditis by expanding the use of inflammatory indices found in hemograms[9] alongside next-generation systemic inflammatory indices[19].

Study Limitations

A primary constraint of this investigation is its retrospective methodological framework. Retrospective studies may be more vulnerable to unknown confounding factors and missing data because data are collected retrospectively. Additionally, the single-center design and limited patient population may limit generalizability. Despite the high test accuracy of our machine-learning model, larger-scale, international, multicenter, prospective studies are needed to confirm the validity and applicability of these findings in clinical practice. Furthermore, some conflicting findings in the literature regarding the inadequacy of the examined inflammatory indices-whether used alone or in multiparametric evaluations-for predicting carditis severity underscore the need for additional research to better understand their potential for comprehensive clinical use.

Conclusion

In this study, the potential of inflammatory indices found in the hemogram, together with that of machine-learning algorithms to predict the early development of carditis associated with ARF fever with high accuracy was evaluated. Analyses showed that markers such as the NLR, PLR, and ML ratios were significantly correlated with the presence of carditis and had high predictive value in machine-learning models. These findings suggest that complete blood count parameters may play an important role in diagnosing subclinical carditis, given their operator-independent nature and lack of requirement for technical expertise. Therefore, the rapid and low-cost availability of these indices offers a critical advantage in the management of ARF and in the early diagnosis of cardiac complications, even in clinical settings with limited resources.

Ethics

Ethics Committee Approval: This study received formal ethical clearance from the Non-Interventional Research Ethics Committee of İzmir Democracy University Buca Seyfi Demirsoy Training and Research Hospital (approval no: 2025/531, date: 26.11.2025).

Informed Consent: Retrospective study.

Footnotes

Support for manuscript preparation, specifically for grammatical revisions and minor summarization or translation, was provided by Jenni.ai. The authors declare that the intellectual content of the current work has been thoroughly verified and remains their full responsibility.

Authorship Contributions

Surgical and Medical Practises: O.A., A.Ş., Concept: O.A., A.Ş., Design: O.A., A.Ş., Data Collection or Processing: O.A., A.Ş., Analysis or Interpretation: O.A., Literature Search: O.A., Writing: O.A.

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