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Original Article

Correlation of Haematological Parameters and DAS-28 Score among Rheumatoid Arthritis Patients

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a complex inflammatory disorder with diverse clinical manifestations. While haematological parameters have long been suggested as potential surrogates for RA disease activity, their direct relationship with the DAS-28 score remains to be thoroughly charted.

Objective: To elucidate the correlation between specific haematological markers and RA disease activity, benchmarked against the DAS-28 score, and to determine the potential diagnostic value of these indices in RA monitoring and management.

Methods: In a cross-sectional survey spanning six months at Sheikh Zaid Hospital, Lahore, 104 RA patients were enrolled. Based on disease activity, participants were segmented into four groups. Comprehensive data capture encompassed demographics, clinical specifics, and haematological indicators. Advanced statistical processing, using SPSS, incorporated correlation computations, ANOVA, and ROC curve methodologies.

Results: DAS-28 scores aligned with disease severity, with averages of 2.13, 2.88, 3.98, and 5.61 for remission, low, moderate, and high activity levels respectively. Haemoglobin demonstrated a significant negative correlation with the DAS-28 score (Pearson's R =-0.485, $p < 0.001$). Conversely, RDW (%) (Pearson's R = 0.749, $p < 0.001$), Neutrophils (%) (Pearson's R = 0.691, $p < 0.001$), and NLR (Pearson's R = 0.617, $p < 0.001$) all reflected robust positive correlations. Lymphocytes (%) showed a negative trend (Pearson's R =-0.475, $p < 0.001$). MPV (fl) and platelet count, however, did not indicate significant correlations.

Conclusion: Key haematological parameters, especially RDW, neutrophils, NLR, and inversely, haemoglobin and lymphocytes, manifest marked correlations with the DAS-28 score in RA patients. These indices could serve as valuable ancillary tools in assessing RA disease activity, particularly in settings with limited access to advanced diagnostic modalities.

Keywords: Rheumatoid arthritis, DAS-28 score, haematological markers, RDW, neutrophils, NLR, lymphocytes, disease activity.

INTRODUCTION

Rheumatoid Arthritis (RA) is a pervasive autoimmune disease affecting approximately 0.5% to 1% of the global adult population (1-4). The disease is characterized by systemic inflammation, primarily targeting synovial membranes in the joints, resulting in debilitating and, often, irreversible damage. RA arises from a myriad interplay of genetic predisposition, environmental triggers, and anomalous immunological responses (5-7). These factors collectively induce inflammation and synovial hypertrophy, ushering in the development of the hostile pannus tissue (8, 9). The pannus, in turn, ravages cartilage, bone, and ligaments, which leads to joint deformities and functional impairment. Beyond its musculoskeletal manifestations, RA exhibits systemic ramifications, encompassing extra-articular manifestations, such as rheumatoid nodules, pulmonary and cardiovascular issues, and ocular complications (6, 10). In Pakistan, the prevalence and manifestation of RA have unique presentations, influenced by genetic markers, environmental exposures, and socio-cultural dynamics (11, 12).

At the molecular helm, the intricate genetic architecture of RA emerges, with the HLA-DRB1 locus standing out for its significant association with the disease (13). Environmental triggers, like smoking and certain infections, further accentuate the risk of RA development. Concurrently, a disturbed immune response signifies the inception of RA, evident from the emergence of autoantibodies like the Rheumatoid Factor (RF) and Anti-Citrullinated Protein Antibody (ACPA), indicating the immune system's attack on its tissues (14).

Central to RA's pathogenesis are the cascades of cytokines, chemokines, and immune cells, which converge to instigate inflammation in the synovial tissue. Haematologically, RA engenders alterations in several parameters. Anaemia of inflammation, changes in WBC counts, thrombocytosis, and adjustments in indices such as Neutrophil-to-Lymphocyte Ratios (NLRs) and Mean Platelet Volume (MPV) allude to the systemic nature of the disease. Established markers like Erythrocyte Sedimentation Rate (ESR) and C-reactive Protein (CRP) remain indispensable for diagnosis and monitoring (15).

Within the recent scientific discourse, several investigations have ventured into exploring the correlation between haematological markers and RA disease activity. Notably, the Disease Activity Score of 28 joints (DAS28) has emerged as a focal point for these inquiries. For instance, Talukdar et al. (2017) unveiled disparities in haematological parameters like platelet count, MPV, and Hb levels among newly diagnosed RA patients based on disease activity. Patients with higher disease activity often manifested with decreased Hb levels but exhibited increased platelet counts and MPV (16).

Similarly, research by Tekeoğlu et al. (2016) emphasized the link between RA disease activity and NLR, discovering a positive association between the two (13). Concurrently, lower MPV values were prominent in patients with elevated disease activity, suggesting NLR as a prospective marker for RA's acute phase. Novel markers have also been brought into the limelight. Yang et al. (2018) pivoted towards the albumin to fibrinogen ratio (AFR) and C-reactive protein to albumin ratio (CAR) (17). Their findings disclosed that patients with active RA presented with diminished AFR levels and heightened CAR levels, providing a new horizon for RA assessment (18-21).

In the quest for more comprehensive markers, Abd-Elazeem & Mohamed (2018) underscored the Neutrophil–Lymphocyte Ratio (NLR) and Platelet–Lymphocyte Ratio (PLR) as budding biomarkers. Their work illuminated the elevated NLR and PLR values in patients with active RA, thereby consolidating the significant role of these haematological indicators in RA's landscape. Additionally, newer insights by Farouk et al. (2023) dissected haematological parameters to discern if they could be indicative of RA's disease activity (22). Their revelations portrayed that RA patients had altered blood profiles, and a positive correlation was evident between specific haematological parameters, such as WBCs and neutrophils, and the severity of RA (23).

Building upon the introduction provided, it's evident that the intricacies of Rheumatoid Arthritis (RA) are not confined merely to the synovial layers or the cellular realms. Instead, they pervade the broader systemic horizon, dictating the haematological dynamics of affected individuals. The systemic implications of RA, ranging from synovial inflammation to a myriad of haematological shifts, underscore the disease's complexity and the necessity for comprehensive analyses (24).

The rationale for the current investigation is embedded in the acknowledgment that haematological parameters are not just bystanders in the RA narrative. These parameters intertwine dynamically with the clinical progression of RA, potentially reflecting the disease's activity. However, while the significance of these haematological indices is acknowledged, the depth of their relationship with RA's clinical spectrum remains to be thoroughly charted. Can they reliably predict disease activity? Might they offer an affordable avenue for monitoring RA's trajectory, especially in settings where high-end diagnostic tools are scarce? These questions remain paramount.

Moreover, there is an evident gap in the current literature. While markers like the Neutrophil-to-Lymphocyte ratio (NLR) have generated considerable interest as potential indicators of systemic inflammation, their consistent relevance in the RA landscape is yet to be universally recognized. Some studies hail NLR's correlation with established markers like CRP, while others cast doubt on its consistent association with composite indices like DAS-28. The influence of treatment modalities on these haematological parameters further muddies the waters, necessitating a rigorous and comprehensive inquiry (25-27). Thus, the study's driving objective crystallizes: to navigate the vast haematological landscape of RA patients, categorize them based on various clinical criteria, and discern the potential relationships between these haematological markers and RA's disease activity, as indicated by the DAS-28 score. In achieving this, the research hopes to shed light on potential diagnostic and therapeutic avenues, enhancin the management of RA.

MATERIAL AND METHODS

A cross-sectional study was conducted over six months at the Department of Rheumatology at Sheikh Zaid Hospital, Lahore. Targeting individuals diagnosed with Rheumatoid Arthritis, the study comprised 104 participants, categorized into four groups based on disease activity, with each group hosting 26 individuals. This division was derived from expected mean NLR values in accordance with the DAS-28 criteria, as cited from a referenced study (28). The Power of Precision 3.0 software was employed to arrive at this sample size, ensuring an equal distribution of participants across all groups.

For sampling, a non-probability and convenient approach was chosen. Eligible participants were those aged 18 or older, of any gender, diagnosed with RA but not yet treated. Exclusions were made for those diagnosed with other autoimmune disorders, pre-existing haematological conditions, infections, recent childbirth (within the last six months), or known malignancies and endocrine disorders (29).

Data collection was methodical: demographic and clinical details, a complete blood count (CBC), DAS-28, and other vital haematological parameters were recorded for each participant using an automated hematology analyzer. The Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) were evaluated immediately after blood collection. The gathered data were statistically analysed using the SPSS software 25.0. Variables were presented as mean ± SD or median with interquartile ranges based on their distribution. Correlation coefficients were applied to identify potential relationships between DAS-28 scores and haematological markers. Comparisons between groups were facilitated through ANOVA methods, with the ROC curve assessing the discriminative power of haematological indices among RA activity groups. Statistical significance was set at p-values less than 0.05. This structured methodology aimed to uncover insights into the association between haematological parameters and RA disease activity.

RESULTS

Table 1 Disease Activity Levels with Haematological Parameters

Disease Activity	Gender (M/F%)	Age (Yrs, M ± SD)	DAS-28 (M ± SD)	Hgb, g/dl, (M ± SD)	RDW (%) (M ± SD)	MPV (fl, M ± SD)	PLT (10^9/L, M ± SD)	Neuts (%) (M ± SD)	Lymphs (%) (M ± SD)	NLR (M ± SD)
Remission	46.2/53.8	36.04 ± 8.10	2.13 ± 0.23	14.27 ± 1.33	12.35 ± 1.13	9.80 ± 1.11	278.62 ± 87.38	50.96 ± 5.77	30.42 ± 5.87	1.74 ± 0.38
Low	30.8/69.2	32.23 ± 7.50	2.88 ± 0.16	13.85 ± 1.45	12.77 ± 0.86	9.89 ± 1.22	328.42 ± 77.43	53.85 ± 6.34	31.08 ± 6.88	1.82 ± 0.46
Moderate	53.8/46.2	36.65 ± 7.17	3.98 ± 0.28	13.01 ± 1.22	14.04 ± 0.77	10.30 ± 1.40	294.42 ± 113.44	60.38 ± 5.20	23.77 ± 7.23	2.77 ± 0.83
High	30.8/69.2	34.46 ± 8.56	5.61 ± 0.25	12.41 ± 1.20	15.00 ± 0.85	10.05 ± 1.24	301.27 ± 140.72	66.62 ± 7.14	21.69 ± 6.01	3.39 ± 1.27

M/F%, Male/Female Percentage; Yrs, Years; M ± SD, Mean plus-minus Standard Deviation; DAS-28, Disease Activity Score-28; Hgb, Haemoglobin; RDW, Red Cell Distribution Width; MPV, Mean Platelet Volume; PLT, Platelets; Neuts, Neutrophils; Lymphs, Lymphocytes; NLR, Neutrophil to Lymphocyte Ratio.

In the study, gender distribution varied across disease activity levels: in remission, it was 46.2% male and 53.8% female; in low activity, 30.8% male and 69.2% female; in moderate, 53.8% male and 46.2% female; and in high activity, 30.8% male and 69.2% female.

The mean ages were 36.04 (± 8.10) for remission, 32.23 (± 7.50) for low activity, 36.65 (± 7.17) for moderate, and 34.46 (± 8.56) for high activity. DAS-28 scores correspondingly increased with disease severity: 2.13 (± 0.23) for remission, 2.88 (± 0.16) for low, 3.98 (± 0.28) for moderate, and 5.61 (± 0.25) for high activity.

The study's statistical analysis reveals varying significance levels across different variables. Age (F=1.642) and measures like MPV (F=0.788) and platelet count (F=0.970) showed no significant association with p-values of 0.184, 0.503, and 0.410, respectively. In stark contrast, DAS-28 Score exhibited profound significance with an F-value of 1094.876, mirrored by its p-value of 0.000*. Similarly, haemoglobin (F=10.682), RDW (F=45.684), neutrophils percentage (F=33.557), lymphocytes percentage (F=13.583), and NLR (F=24.486) all showcased a significant relationship, with each marked by a p-value of 0.000*. These results suggest a substantial influence of certain variables on the studied outcome, emphasizing their potential importance in the context of the research.

Table 2 Showcasing F-value and Significance.

Variable	F-value	P Value
Age	1.642	0.184
DAS-28 Score	1094.876	0.000*
Haemoglobin (g/dl)	10.682	0.000*
RDW (%)	45.684	0.000*
MPV (fl)	0.788	0.503
Platelet (10 ^ 9/L)	0.970	0.410
Neutrophils (%)	33.557	0.000*
Lymphocytes (%)	13.583	0.000*
NLR	24.486	0.000*
Values marked with an asterisk () indicate significance, typically at a level of p < 0.05		

Table 3 Correlation Analysis

Haematological Parameter	Pearson's R	Pearson's P-value	Spearman Correlation	Spearman P-value
Haemoglobin (g/dl)	-0.485	<0.001*	-0.459	<0.001*
RDW (%)	0.749	<0.001*	0.737	<0.001*
MPV (fl)	0.076	0.446	0.088	0.373
Platelet (10^9/L)	0.034	0.729	0.051	0.606
Neutrophils (%)	0.691	<0.001*	0.664	<0.001*
Lymphocytes (%)	-0.475	<0.001*	-0.439	<0.001*
NLR	0.617	<0.001*	0.626	<0.001*
Values marked with an asterisk () indicate statistical significance, typically at a level of p < 0.05.				

The correlation analysis of haematological parameters yielded insightful results, delineating the varying degrees of association each parameter shares with the disease activity levels in rheumatoid arthritis. Haemoglobin exhibited a negative correlation, with Pearson's R at -0.485 and Spearman correlation at -0.459, both significant at $p < 0.001$*. RDW (%) demonstrated a strong positive correlation with Pearson's R at 0.749 and Spearman correlation at 0.737, underlining its significance with p-values of <0.001*. Neutrophils (%) also revealed a notable positive correlation, with Pearson's R of 0.691 and Spearman at 0.664, both marked with $p < 0.001$*. Lymphocytes (%) displayed a negative correlation (Pearson's R =-0.475, Spearman =-0.439), achieving significance at $p < 0.001$*. NLR reflected a significant positive correlation, with Pearson's R at 0.617 and Spearman at 0.626, both established at $p < 0.001$*. In contrast, MPV (fl) and platelet count did not exhibit significant correlations, with p-values exceeding 0.05, suggesting a weaker association with the disease activity levels in this context.

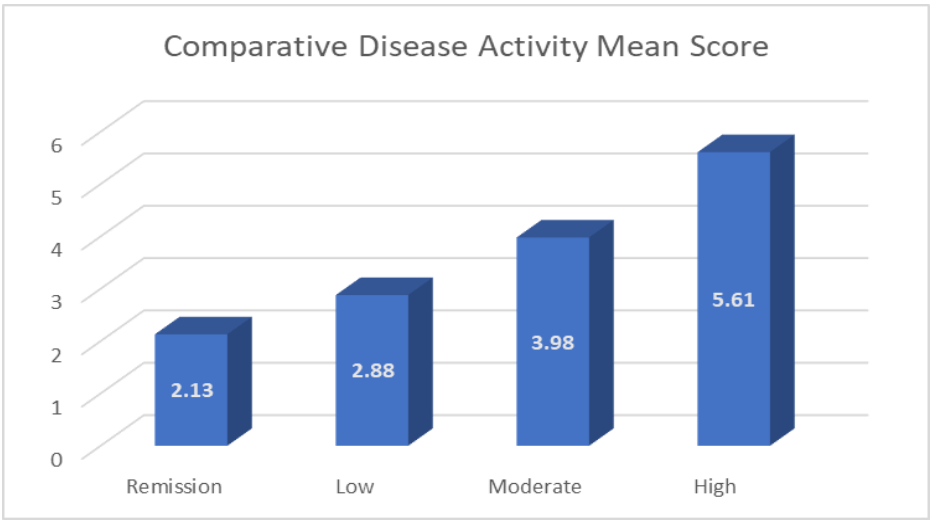

Figure 1 Disease Activity Score-28 (DAS-28)

DISCUSSION

The relationship between gender, age, and disease activity levels in rheumatoid arthritis (RA) remains at the crossroads of medical research, promising to illuminate nuanced aspects of this multifaceted ailment. Central to this discourse is the DAS-28 score, a cornerstone in gauging disease activity. Its remarkable significance (p-value of 0.000) reiterates its status as a linchpin in comprehending RA's intricacies, guiding clinical decisions, and tailoring therapeutic strategies.

However, the landscape is further enriched when observed through the prism of gender dynamics. Preliminary data underscores a potential predisposition of females to certain disease activity levels, based on their heightened representation. Yet, the absence of p-values for low, moderate, and high activity levels leaves these observations open to critique. Critics rightly highlight the need for rigorous statistical substantiation before drawing gender-centric conclusions. For instance, the data's assertion of a balanced gender distribution at remission and moderate levels challenges the notion of gender-based disparities. Without comprehensive gender-focused studies, these observations remain within the realm of speculation, underscoring the need for more granular analyses. Age, often a cornerstone in various disease investigations, intriguingly does not wield pronounced influence over disease activity levels in this context. Despite age variability across different levels, the p-value of 0.184 suggests its role is peripheral, directing our attention to other potentially more influential variables.

Delving deeper into the interplay between haematological markers and disease activity levels unveils a rich tapestry of correlations. Haemoglobin, RDW percentages, neutrophils, lymphocytes, and especially the Neutrophil to Lymphocyte Ratio (NLR), with their significant p-values, resonate prominently in this narrative. These markers, especially the heightened significance of neutrophils and lymphocytes, open new avenues for exploration, suggesting a central role of the immune response in modulating disease activity levels. Contrastingly, MPV and platelet count, often linked with inflammation and coagulation, surprisingly lack the gravitas in this landscape. Their p-values (0.503 and 0.410 respectively) intimate their peripheral role, prompting a re-evaluation of their significance in the RA context.

The presented synthesis emphasizes the inherent complexities surrounding RA, with each parameter offering a piece of the puzzle. These findings should act as a foundation for future investigations (27). Gender-specific research, zeroing in on potential hormonal or genetic influences, might shed light on any predispositions (30). Although age does not significantly correlate with disease activity in this study, its role warrants continuous exploration, potentially within more diversified populations or specific age brackets (31).

Furthermore, as the DAS-28 score remains seminal in understanding RA, the potential of haematological markers, especially those with pronounced significance, cannot be ignored. Their application in patient stratification, guiding therapeutic interventions, and enhancing disease management strategies could revolutionize RA care (16).

Concluding, the quest to elucidate RA's intricacies is ongoing. This study, combined with past research, offers invaluable insights, but the path ahead demands further exploration, robust validation, and adaptability (32). Embracing a holistic, integrative approach ensures that the trajectory of RA research remains progressive, patient-centric, and poised for groundbreaking discoveries (33).

CONCLUSION

The intricate interplay between gender, age, and haematological markers profoundly influences the understanding of rheumatoid arthritis (RA) disease activity. The findings underscore the pivotal role of the DAS-28 score and certain haematological parameters, while questioning traditionally held beliefs about age and some markers. As research progresses, gender-specific studies and the nuanced exploration of these parameters become paramount. The insights gained suggest the potential for personalized, data-driven therapeutic approaches in RA, promising transformative patient outcomes. The challenge ahead lies in harnessing this knowledge for both deeper comprehension and optimized patient care.

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