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EVALUATION OF D-DIMER LEVELS AMONG ANTI-CCP-POSITIVE RHEUMATOID ARTHRITIS SUDANESE PATIENTS IN RIVER NILE STATE, 2024

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ABSTRACT

Background: Rheumatoid arthritis (RA) represents a systemic autoimmune condition characterized by chronic inflammation and an elevated predisposition to hypercoagulability. This study evaluated plasma D-dimer concentrations among anti-CCP-seropositive RA subjects compared to healthy individuals and analyzed potential associations with demographic and clinical variables.

Methods: A hospital-based case-control evaluation was conducted involving 100 participants (50 anti-CCP-seropositive RA subjects and 50 age- and sex-matched non-RA controls). Circulating D-dimer levels were quantified using a fluorescence immunoassay platform (ichroma™). Analytical evaluations were performed utilizing SPSS (v.23), applying parametric tests and correlation models.

Results: Circulating D-dimer concentrations were significantly higher in RA subjects relative to controls (1.3 ± 0.4 µg/mL vs. 0.4 ± 0.1 µg/mL, $p < 0.001$). Pearson correlation demonstrated a robust positive association between D-dimer levels and patient age ($r = 0.762$, $p = 0.03$). Conversely, no statistically significant association was identified with disease duration ($r = -0.168$, $p = 0.34$) or gender distribution ($p = 0.16$).

Conclusion: Anti-CCP-seropositive RA subjects exhibit marked elevations in circulating D-dimer, denoting an active prothrombotic state governed by inflammatory activity and age-dependent vascular factors.

Keywords: Rheumatoid Arthritis; D-Dimer; Anti-CCP; Thrombosis; Biomarkers

1 INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune condition characterized by synovial inflammation, joint breakdown, and systemic complications [1, 2]. Global epidemiological estimates indicate an adult prevalence ranging from 0.5% to 1.0% [1, 3]. A main feature of chronic autoimmune arthritis is the link between immune system activation and blood clotting mechanisms [4, 5]. Sustained secretion of inflammatory mediators accelerates procoagulant cascades while concurrently blunting physiological anticoagulant pathways [5, 6].

Plasma D-dimer—a specific degradation fragment generated via plasmin-mediated cleavage of cross-linked fibrin—serves as a sensitive biomarker for intravascular fibrin formation and secondary fibrinolysis [7, 8, 9]. While contemporary clinical paradigms in RA prioritize controlling articular disease activity, systemic inflammatory stress substantially increases patient vulnerability to hypercoagulable states, venous thromboembolism, and cardiovascular death [8, 9]. Despite these documented thromboembolic risks, the routine clinical monitoring of coagulation end-products such as D-dimer remains underutilized within standard rheumatoid arthritis management frameworks [9, 10].

While disease activity varies over the clinical course, the specific contribution of non-modifiable demographic variables—notably patient age and chronological disease duration—to circulating D-dimer dynamics remains insufficiently characterized, particularly among seropositive populations in East Africa, including Sudan [11, 12]. Elucidating baseline D-dimer patterns in anti-CCP-seropositive RA individuals and establishing their relationship with age and disease chronicity is necessary for refining early thromboembolic risk stratification and optimizing clinical management strategies [13, 14]. Accordingly, this study quantified plasma D-dimer concentrations among anti-CCP-seropositive RA subjects compared to non-RA controls in River Nile State, Sudan, evaluating potential correlations with patient age and disease duration [10, 15

2 MATERIAL AND METHODS

This hospital-based case-control study enrolled 100 individuals, comprising 50 anti-CCP-seropositive RA subjects and 50 age- and sex-matched healthy controls. Individuals exhibiting overlapping autoimmune disorders, malignant tumors, active infectious diseases, diabetes mellitus, renal impairment, or ongoing corticosteroid treatment were omitted from the cohort.

Blood samples (5 mL) were obtained via venipuncture into sodium citrate tubes and promptly subjected to centrifugation (1500×g, 15 min) to yield platelet-poor plasma. D-dimer concentrations were determined through a sandwich fluorescence immunoassay approach (ichroma™) in strict accordance with the manufacturer's protocol.

Computational statistical evaluation was conducted via SPSS software (v.23). Parametric data were summarized using mean ± standard deviation (SD). Differences between the study groups were analyzed using independent sample t-tests, whereas Pearson correlation assessed associations between D-dimer levels, patient age, and disease duration. Statistical significance was inferred at p-values below 0.05.

3 RESULTS

The patient cohort consisted of 35 female (70%) and 15 male (30%) individuals, exhibiting a mean age of 54.2 ± 2.7 years and an average illness duration of 12.3 ± 0.9 years. The healthy comparison group demonstrated a comparable mean age of 53.2 ± 1.9 years, with a similar sex distribution (68% female, 32% male). Regarding demographic background, active tobacco smoking was noted in 30% of RA subjects, while 32% documented a positive family background of rheumatoid condition.

Table 1: Descriptive Statistics of the study group.

	N	Minimum	Maximum	Mean ± SD
Age (case)	50	30	75	54.2 ± 2.7
Duration of disease (case)	50	2	28	12.3 ± 0.9
BMI (Cases)	50	22	28	27.3 ± 0.1
Age (control)	50	27	69	53.2 ± 1.9
BMI (control)	50	21	26	25.3 ± 0.2

Table 2: Mean and SD D dimer among the study group.

	Cases	Control	P-value
D-dimer ug/ml	1.3 ± 0.4	0.4 ± 0.1	0.00 *

*Significant

Table 3: Mean and SD of D dimer among males and females.

	Males	Females	P-value
D-dimer ug/ml	1.2 ± 0.6	1.3 ± 0.1	0.16 **

**Insignificant

Table 4: Correlation between D dimer with age and duration of disease

	Variable	R	P-value
D dimer	**Age**	0.762	0.03*
	Duration of disease	-0.168	0.34**

* Significant **Insignificant

4 DISCUSSION

Rheumatoid arthritis (RA) represents a complex systemic autoimmune disorder wherein persistent articular and extra-articular inflammation frequently induces a prothrombotic state. Prolonged systemic inflammatory stress triggers sustained release of pro-inflammatory cytokines—primarily interleukin-6 (IL-6), interleukin-1 (IL-1), and tumor necrosis factor-alpha (TNF-α). This continuous cytokine activity disrupts basal hemostasis by upregulating tissue factor expression on endothelial surfaces and circulating monocytes, thereby accelerating extrinsic coagulation and microvascular fibrin accretion. Simultaneously, endogenous anticoagulant mechanisms, including protein C and antithrombin pathways, undergo downregulation, alongside impaired plasminogen activation. Plasmin-mediated degradation of these widespread intravascular and intra-articular fibrin aggregates yields substantial circulating D-dimer fragments. Thus, plasma D-dimer serves as a surrogate biomarker reflecting both active fibrinolysis and the intensity of underlying inflammatory joint disease [4, 5, 8, 9].

The marked elevation of plasma D-dimer concentrations observed among anti-CCP-seropositive RA subjects compared to non-RA controls in this cohort [9, 10] aligns with the premise that active rheumatoid inflammation drives systemic thrombin generation and secondary fibrinolysis [4, 5, 12]. These findings parallel observations reported across diverse international cohorts. For instance, Xue et al. [9] and Qiang et al. [12] identified higher D-dimer concentrations in patients with high disease activity. Similarly, regional and global studies, including Babikr et al. [10] in Sudan and Mori et al. [13] in Japan, confirmed elevated fibrin turnover markers within active RA populations [6, 7].

Notably, our analysis demonstrated a strong positive association between patient age and circulating D-dimer levels ($r = 0.762$, $p = 0.03$) [14, 15], pointing toward an age-related amplification of hypercoagulability in rheumatoid individuals. In contrast, disease duration exhibited no statistical correlation with D-dimer levels ($p = 0.34$) [13, 16], implying that ongoing biological disease activity—rather than elapsed chronological time since diagnosis—primarily governs the prothrombotic state.

Several study limitations warrant consideration, including the single-center case-control design and a modest cohort size. Additionally, inflammatory parameters such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were not evaluated concurrently, restricting multi-parameter regression models.

5 CONCLUSION

In summary, anti-CCP-seropositive RA subjects exhibit markedly increased plasma D-dimer concentrations relative to non-RA controls, with hypercoagulable markers demonstrating an age-dependent escalation. Integrating routine plasma D-dimer assessment into standard rheumatoid arthritis clinical management could facilitate early risk stratification for thromboembolic complications in high-risk patient subgroups.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

Statement of informed consent

Ethical approval was granted by the institutional ethical committee, and informed consent was obtained from all individual participants included in the study.

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