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Original Article

Dickkopf 1 Protein Level as a Possible Biomarker of Functional Disability and Disease Activity in Patients with Rheumatoid Arthritis

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic multisystem autoimmune disease affecting the synovial joints. It can lead to joint destruction, deformities and reduce quality of life. Dickkopf-1 (DKK-1) is recognized as endogenous inhibitory factor in the wingless-related integration site (Wnt) signaling done via its binding to the (LRP5/6) co-receptor, which is essential element in bone homeostasis, various tumors and autoimmune diseases.

Objectives: The aim of the current study was to assess the serum DKK-1 protein level among RA patients and to study its relation with the functional disability and disease activity and severity of RA.

Methods: This case control study was carried out on 120 subjects, 60 RA patients and 60 healthy control subjects. All subjects were for DKK-l protein serum level and for RA patients Disease Activity score (DAS28), Steinbrocker's grading system and Rheumatoid Arthritis Severity Scale (RASS) were estimated.

Results: Serum DKK-1 protein levels were significantly greater among RA patients (5888 ± 1868) than the control subjects (1524 ± 430) with P value <0.001. Higher DKK-1 serum level was significantly correlated with increased DAS-28 scores ($p < 0.001$) and C reactive protein (CRP) levels ($p = 0.049$), erythrocyte sedimentation rate (ESR) ($p < 0.001$), rheumatoid factor (RF) ($p = 0.043$), and anti-cyclic citrullinated peptide (Anti-CCP) antibody levels ($p = 0.001$). DKK-1 showed a sensitivity as well as a specificity of 98.33%, 88.33% respectively, at a cut-off of 2068.65 pg/ml.

Conclusions: Serum DKK-1 level could be a valuable biomarker in RA patients. Higher DKK-1 level showed significant correlation with functional impairment, disease activity and severity of RA.

Keywords: Serum Dickkopf 1 Protein, Functional Disability, Disease Activity, Rheumatoid Arthritis.

INTRODUCTION

Rheumatoid arthritis is a chronic autoimmune inflammatory disorder mainly affecting the synovial membrane lining the joints. The disease has a progressive nature whereby, without treatment, the patient suffers from joint degeneration and deformity that can culminate in disability and reduce quality of life [1]. Environmental factors, like smoking, exposure to dust, and alteration of gut microbiome, are also very important in RA pathogenesis along with genetic and epigenetic factors [2]. Approximately around one percent of the population is affected by this disease, with women being more affected than men.

However, as age increases, the difference between the genders becomes smaller [3].
Rheumatoid arthritis is defined by the presence of many pro-inflammatory cytokines, like tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6), which activate inflammation and stimulate osteoclasts, resulting in joint destruction and erosion of bone [4].
The Dickkopf (DKK) protein family consists of four types of glycoproteins, each featuring a distinct cysteine-rich domain at the N-terminus and a conserved cysteine-rich domain at the C-terminus [5]. Among them, Dickkopf-1 (DKK-1) is a natural inhibitor of the wingless-related integration site (Wnt) signaling pathway, which regulates numerous biological actions like cell proliferation, bone metabolism, embryonic development, as well as the tissue homeostasis [6]. Disruption in Wnt signaling has been linked to various conditions, including congenital malformations, degenerative diseases, diabetes mellitus, and malignancies [7].
Due to its impact on T-cell growth and immunological modulation, Dickkopf-1 has also been linked to autoimmune diseases like rheumatoid arthritis, systemic sclerosis (SSC), systemic lupus erythematosus (SLE) in addition to the ankylosing spondylitis (AS) [8].
Inflammation is brought on by the tumor necrosis factor-alpha, a major inflammatory cytokine among patients who had RA. It is known to upregulate DKK-1 by synovial fibroblasts [9]. DKK-1 is likely to have significant roles in joint remodeling, for instance, enhancing the resorption of bone and inhibiting the new bone formation and repair within joints undergoing inflammation [10].
Recent research shows a clear association between the increased DKK-1 levels with higher rates of structural joint damage in addition to the higher disease activity among rheumatoid arthritis patients [11]. Therefore, this work aimed to assess the serum DKK-1 protein level among the RA patients and to study its correlation with the functional disability and severity in addition to the disease activity.

METHODS

This case-control work was conducted in the Department of Rheumatology and Rehabilitation, of Zagazig University Hospitals in period between August 2024 and February 2025. Laboratory investigations were carried out by the Clinical Pathology Department.
Informed consent was obtained from all participants, confirming their voluntary participation.
The research ethics board of the Faculty of Medicine at Zagazig University gave its approval to the study, and all participants gave written informed consent. As a component of the Code of Ethics for Research Involving Humans, the Declaration of Helsinki ensures that the work was performed in compliance with its provisions. Before this study could begin, we obtained approval from the Institutional Review Board (IRB: 101012-13/8/2023).
The sample size was calculated using open epi at 80% power and 95% CI, assuming the mean DKK-1 were 6707.18± 2943.83 vs 5127.03 ± 2931.78 in RA patients vs control group respectively. The estimated sample size for the current case control study was 120 participants, with 60 individuals in each group.
Inclusion criteria: Group I included 60 patients with confirmed diagnosis of RA with reference to the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria. [12]. All patients were aged between 18 and 50 years. Group II consisted of 60 age- and sex-matched healthy participants who served as the control group.
Exclusion criteria: Subjects suffering from any other autoimmune disease, cardiovascular, Diabetes mellitus, liver or renal diseases were excluded. Patients who had any type of malignancies or Infections were also excluded
Patient assessment: All patients diagnosed with rheumatoid arthritis underwent a full history taking, thorough clinical evaluation and laboratory investigations including DKK-1

level, ESR, CRP, CBC, RF, Anti-CCP2, as well as the liver and kidney functions.

Radiographic assessment included plain X-rays for both hands and wrists for detection of joint space narrowing, erosions, or deformities consistent with RA-related structural damage.

Disease activity was evaluated by utilizing the Disease Activity Score in 28 joints with erythrocyte sedimentation rate (DAS28-ESR), that combines the number of swollen, tender joints, ESR values, and a visual analogue scale for patient-reported global health status [13].

Functional disability was classified according to the Steinbrocker grading system, which ranges from Class I (complete functional ability) to Class IV (severe functional limitation with confinement to bed or wheelchair) [14].

Overall disease severity was determined utilizing the Rheumatoid Arthritis Severity Scale (RASS), a brief physician-rated tool that combines aspects of physical function, disease activity, in addition to the damage of joints to provide a global severity score [15].

Laboratory investigations: 7 ml of whole blood were collected under complete aseptic condition and divided into: 2 ml on EDTA tube for CBC, 2 ml in ESR (BD vacutainer) for ESR and the last 3 ml were collected in serum separator vacutainer and allowed to clot before centrifugation for 20 minutes at approximately 1000×g. supernatant serum was divided into 2 aliquots: First aliquot was utilized for CRP, RF, Anti CCP, Liver and kidney function tests and Second aliquot was stored at -80C for later assess DKK-1 protein by enzyme-linked immunosorbent assay (ELISA).

The CBC was performed using a Sysmex XN 2000 Hematology analyzer (Sysmex, Kobe, Japan). The ESR was assessed using a Vision-B analyzer (YHLO Biotech Co., Ltd., Shenzhen, China). CRP and RF were assessed using the Cobas 6000-c501 Modular Analyzer (Roche, Germany). Anti-CCP2 antibodies were detected using the Elecsys anti-CCP kit on Cobas E411 (Roche, Germany). Liver and kidney function tests were measured using Cobas 8000 Modular Analyzer Series/c702 (Roche Diagnostics, Mannheim, Germany).

Serum DKK-1 protein level: The level of DKK-1 was estimated utilizing a Human ELISA Kit, we followed the manufacturer's instructions of Develop Company (A3-South, 100# shuigoutou, renminxi Rd, Wuxi, Jiangsu,214031, China).A standard curve was generated using the concentrations of the provided standards and their corresponding the optical density (OD) values. The OD readings of the samples were then matched to this curve to determine their concentrations. DKK-1 protein levels were expressed in picogram per millilitre (pg/mL).

STATISTICAL ANALYSIS

We used SPSS version 23 (SPSS Inc., Chicago, IL, USA) to analyze the data. Categorical info was shown as numbers and percentages. For numerical data, we checked if it followed a normal distribution using the Shapiro-Wilk test. Normally distributed data was shown as mean ± standard deviation; skewed data is shown as median and range. To compare groups, we used Chi-square for categories, t-test or ANOVA for normal data, and Mann-Whitney or Kruskal-Wallis for non-normal data. Correlations were checked using Pearson or Spearman tests, depending on the data type. We used multiple linear regression to see what factors affected DKK-1 levels, and ROC curve analysis to find the best DKK-1 cut-off for identifying disease activity. A p-value below 0.05 was considered significant.

RESULTS

This study comprised 120 subjects, divided into two equal groups. Group I comprised 60 RA patients, 56 patients (93.3%) were females while 4 patients (6.7%) were males, with a mean age of 41.1 ± 7.20 years. The disease duration ranged between 1 and 25 years. Group II (control group) included 60 apparently healthy volunteers, (81.7%) were females and (18.3%) were males, with a mean ± SD of 39.8 ± 7.57 years.

According to the assessment of RA patients, RASS score ranged from 5 to 19 with mean ± SD of 11.3 ± 3.41 and range of DAS-28 score was from 1.9 to 7.7 with mean ± SD of 4.84 ±

1.54 with (48.3%) of the cases had a high disease activity followed by moderate activity (33.3%). According to Steinbrocker functional grading system (55%) were classified as class III while 45% were classified as class II **(Table 1)**.

Patients had significantly elevated DKK-1 protein levels than controls (P < 0.001) (with mean of 5888 ± 1868pg/mL versus 1524 ± 430pg/ml) **(Table 2)**.

No statistically significant correlations were found between DKK-1 protein serum level and different demographic or clinical history among RA patients (P>0.05) except for deformity where (P=0.02) **(Table 3)**.

Serum DKK-1 protein level was significantly correlated with acute phase reactants (ESR, CRP), RF and Anti-CCP. Also, positive significant correlations were found between clinical parameters including VAS, morning stiffness, NSJ, NTJ, DAS-28 and RASS score with its subscales with DKK-1 levels (P<0.05) **(Table 4)**.

Multiple linear regression analysis exhibited that DKK-1 protein levels were positively correlated with DAS28 (β =1867.4, P < 0.001), RF (β = -0.85, P = 0.04), Anti-CCP (β = -0.565, P = 0.001), ESR (β = -26.37, P < 0.001), CRP (β = 16.58, P = 0.05) **(Table 5)**.

Receiver operation Curve (ROC) was done to reveal the optimal cut-off value of DKK-1 protein serum level. At cut-off point (2068.65 pg/ml) AUC was (0.967) with sensitivity (98.33%) and specificity (88.33%) **(Table 6, Figure 1A)**. As regards the ability of DKK-1 protein to detect disease activity among RA patients, ROC curve analysis showed AUC (.985), sensitivity (98.18%) and specificity (100%) **(Table 6, Figure 1B)**.

Table 1: Rheumatoid Arthritis Severity Scale (RASS), DAS-28 score and Steinbrocker functional grading system in the RA group.

Variables		RA group (n=60)
RASS score	**Mean ± SD**	**11.3 ± 3.41**
	Range	**(5 – 19)**
DAS-28 score	**Mean ± SD**	**4.84 ± 1.54**
	Range	**(1.9 – 7.7)**
	Remission	**5 (8.3%)**
	Low activity	**6 (10%)**
	Moderate activity	**20 (33.3%)**
	High activity	**29 (48.3%)**
Steinbrocker functional grading system	**Class I**	**0 (0%)**
	Class II	**27 (45%)**
	Class III	**33 (55%)**
	Class IV	**0 (0%)**

RA; rheumatoid arthritis, **DAS28**; disease activity score 28, **RASS**; Rheumatoid Arthritis Severity Scale.

Table 2: DKK-1 protein serum level among studied groups

Variables		RA group (n=60)	Control (n=60)	P Value
DKK-1 serum level (pg/ml)	**Mean ± SD**	**5888 ± 1868**	**1524 ± 430**	**<0.001***
	Median (IQR)	**6488 (2517)**	**1579 (547)**	
	Range	**(1985 – 8092)**	**(511 – 2274)**	

DKK-1; Dickkopf 1, Significant: P ≤0.05

Table 3: Relation between demographic, clinical history and DKK-1 protein serum level in the RA group

Variables		**Serum DKK-1 (pg/ml) Mean ± SD**	**P value**
Sex	Male	6512 (2589)	0.73
	Female	6069 (806)	
Smoking	Non-smokers	6512 (2535.8)	0.73
	Smokers	6128 (73.4)	
Family history	Negative	6467 (2424)	0.29
	Positive	7400 (3254)	
Deformity	Absent	6110 (2688)	**0.02***
	Present	7320 (1134)	
Subcutaneous nodules	Absent	6509 (2475)	0.67
	Present	5060 (4629)	
Dry eye	Absent	6509 (2609)	0.67
	Present	6010 (2373)	
Dry mouth	Absent	6415 (2619)	0.49
	Present	6515 (1159)	

Non-significant: P >0.05, Significant: P ≤0.05

Table 4: Correlation between serum DKK-1 protein level and clinical and laboratory parameters in the RA group

Variable	**Serum DKK-1**	
	R	***P***
Age	0.027	0.84[1]
Disease duration	0.228	0.08[2]
Visual analogue scale (VAS)	0.807	**<0.001**[2]
Morning stiffness	0.551	**<0.001**[1]
Number of swollen joints	0.593	**<0.001**[1]
Number of tender joints	0.832	**<0.001**[1]
DAS-28	0.960	**<0.001**[2]
RASS score (total)	0.876	**<0.001**[2]
Disease activity subscale	0.890	**<0.001**[1]
Function impairment subscale	0.804	**<0.001**[1]
Physical damage subscale	0.435	**<0.001**[2]
ESR	0.498	**<0.001**[2]
CRP	0.640	**<0.001**[2]
RF	0.473	**<0.001**[2]
Anti-CCP	0.478	**<0.001**[2]

VAS; Visual analogue scale **ESR**; erythrocyte sedimentation rate**, CRP**; C-reactive protein **RF**; rheumatoid factor, **Anti-CCP**; Anti-cyclic citrullinated peptide, **RA**; rheumatoid arthritis, **DAS28**; disease activity score 28, **RASS**; Rheumatoid Arthritis Severity Scale. *Significant: P ≤0.05*
[1]Pearson correlation, [2]Spearman rank correlation test, **r:** correlation coefficient Significant: P ≤0.05

Table 5: The multiple linear regression analysis between DKK-1 protein serum level and different parameters among RA patients

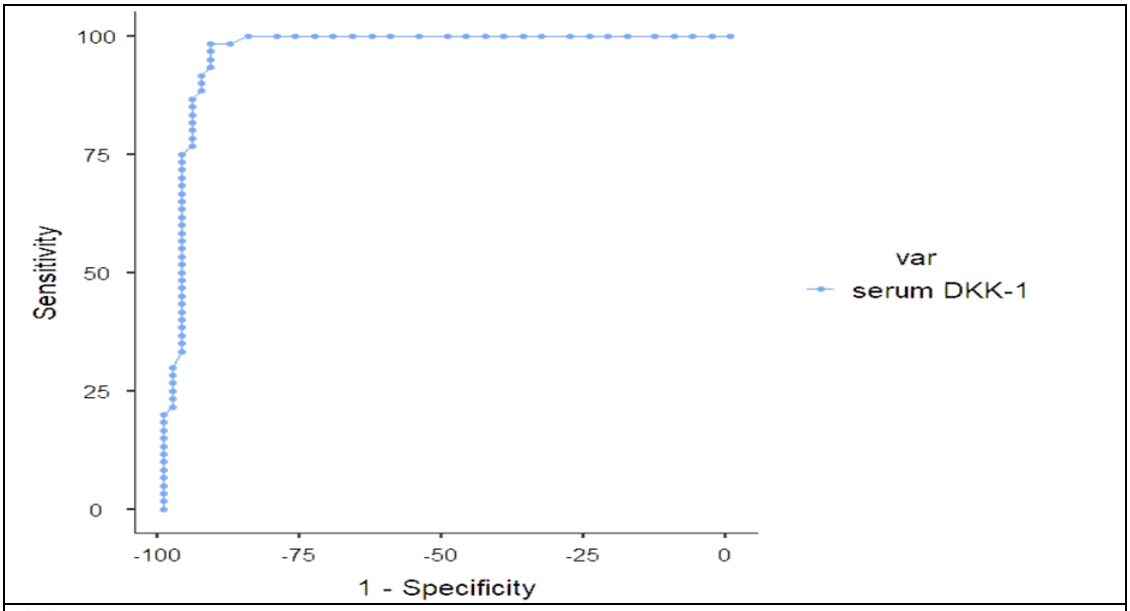
Model Fit Measures	**R=0.987**	**R^2=0.975**	
Model Coefficients	**Estimate**	**T**	**P**
Age	-6.951	-0.784	0.439
Disease duration	5.787	0.384	0.704
DAS-28	1867.405	9.778	**<0.001**
ESR	-26.370	-3.924	**<0.001**
CRP	16.577	2.04	**0.049**
RF	-0.852	-2.101	**0.043**
Anti-CCP	-0.565	-1.115	**0.001**
Steinbrocker classification	158.536	0.7847	0.438
RASS score	323.368	1.384	0.175

VAS; Visual analogue scale **ESR**; erythrocyte sedimentation rate**, CRP**; C-reactive protein **RF**; rheumatoid factor, **Anti-CCP**; Anti-cyclic citrullinated peptide, **RA**; rheumatoid arthritis, **DAS28**; disease activity score 28, **RASS**; Rheumatoid Arthritis Severity Scale. *Significant: P ≤0.05*

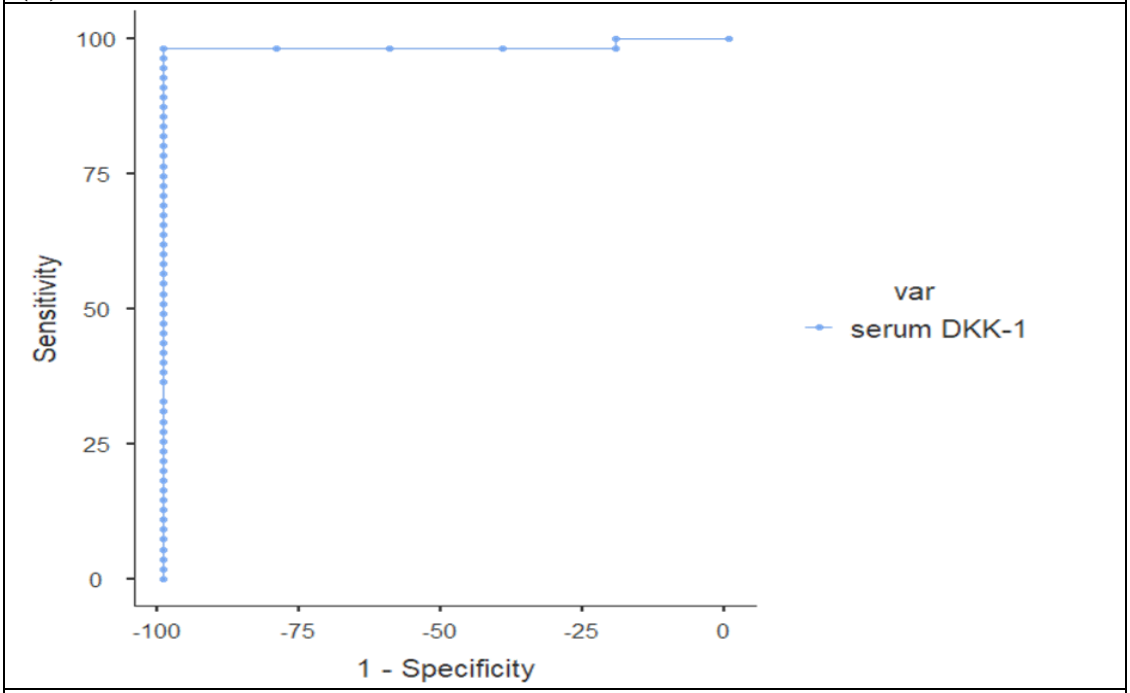
Table 6: Serum DKK-1 protein level in RA patients and DKK-1 protein level as a marker of disease activity.

Serum DKK-1 protein level in RA patients and controls			
Cut-off point	**Sensitivity (%)**	**Specificity (%)**	**AUC (%)**
2068.64	98.33%	88.33%	0.967
Serum DKK-1 protein level as a marker of **disease activity**			
Cut-off point	**Sensitivity (%)**	**Specificity (%)**	**AUC (%)**
2726.97	98.18%	100%	0.985

AUC: area under the curve, **ROC;** Receiver operation Curve



(A)



(B)

Figure 1: ROC curve analysis of (A): DKK-1 protein level in RA patients, (B): DKK-1 protein level as a marker of disease activity.

DISCUSSION

In rheumatoid arthritis, the immune-mediated process elicits a chronic synovitis from which pain, swelling, and progressive joint erosion arises. Although joints are the main and usually first sites affected, it is an extra-articular disease and can affect other organs and systems away from the musculoskeletal system-the lungs, heart, skin, and eyes. The ongoing inflammation, if left uncontrolled, may destroy the structures of the joint, leading to deformities, restricted range of motion, and persistent functional impairment. The impairment has far-reaching effects on daily living and is, therefore, a significant burden upon the patients' quality of life [16].

It is increasingly agreed upon by a majority in the medical community that recognition of rheumatoid arthritis in its earliest stages, alongside a thorough evaluation of disease activity and severity, is a key factor in effective management. By initiating the necessary therapies promptly within this critical early window, they can significantly reduce or halt the progression of joint destruction. An early intervention preserves joint structure and function and decreases the disability of the patient, leading to improved prognosis and quality of life [17].

The Dickkopf family of proteins includes the DKK-1 through DKK-4 which play an important role in cellular growth and communication with respect to the Wnt signaling pathway. These proteins share a common structure with high cysteine content. Among these, DKK-1 is particularly important for the blockade of Wnt signaling through binding to certain receptor proteins present on the cell surface that are called LRP5 /6. Upon binding DKK-1 to its receptors, it triggers the internalization and subsequent degradation of these receptors, thereby shutting down Wnt signaling by means of the lessening of receptor interactions with Wnt signaling [18].

Researchers have recognized DKK-1 as being one of the crucial proteins in the onset and the progressive deteriorating course of different joint disorders like rheumatoid arthritis (RA), ankylosing spondylitis (AS), and osteoarthritis (OA) [9]. High levels of DKK-1 perhaps relate to more severe articular damage in these diseases due to its role in bone and joint repair processes. The current study aimed to evaluate the levels DKK-1 in serum from individuals with RA and determine whether there is an association between it and the activity, severity, and disability caused by the disease.

In the current work, the RA patients exhibited a significantly higher DKK-1 level of 5888 ± 1868 pg/mL, whereas the control group showed a markedly lower level of 1524 ± 430 pg/mL ($P < 0.001$). These findings are in line with the results discovered by Ali et al. [11], who also documented a substantial elevation in serum DKK-1 among RA patients, with a mean value of 5383.80 ± 2973.45 pg/mL, in contrast to 1102.42 ± 758.29 pg/mL among healthy inviduals ($p = 0.001$). This also was in agreement with Wang et al. [19] and Singh et al. [20], both of whom reported significantly higher DKK-1 levels in RA populations compared to healthy individuals ($p<0.05$), reinforcing the proposed association between DKK-1 overexpression and RA pathogenesis. Interestingly, not all studies have shown high levels of DKK-1 among rheumatoid arthritis. In research by Diarra et al. [21], the RA patients who were being treated with anti-TNF medications actually had much lower levels of DKK-1. This finding suggests that TNF-alpha—a protein known to drive inflammation in RA—might also be responsible for increasing DKK-1 production. When TNF-alpha is blocked by medication, DKK-1 levels seem to drop as well. This supports the idea that controlling inflammation through targeted treatments might also help limit some of the damage RA can do to the joints.

In the current study, serum DKK-1 levels exhibited a strong and positive correlation with multiple clinical indicators of rheumatoid arthritis. Interestingly, higher DKK-1 levels were strongly linked to more pain on the VAS ($r = 0.807$, $P < 0.001$), prolonged morning stiffness ($r = 0.551$, $P < 0.001$), and greater numbers of both swollen joints ($r = 0.593$, $P < 0.001$) and tender joints ($r = 0.832$, $P < 0.001$). Higher DKK-1 levels were found to be significantly linked to joint deformities ($P = 0.02$). The strongest connection was with disease activity measured by the DAS-28 score ($r = 0.960$, $P < 0.001$), suggesting DKK-1 could be a useful indicator of overall disease activity. On top of that, DKK-1 levels showed clear positive relationships with several laboratory markers of inflammation and autoimmunity, including ESR ($r = 0.498$, $P < 0.001$), CRP ($r = 0.640$, $P < 0.001$), RF ($r = 0.473$, $P < 0.001$), and Anti-CCP antibodies ($r = 0.478$, $P < 0.001$). The current study findings are in line with those of Sadek et al. [22], who also found that higher DKK-1 levels were closely tied to signs of

more active and severe RA. Their study showed strong links between DKK-1 and the DAS-28 score, VAS for pain, morning stiffness duration, and laboratory markers like ESR, CRP, RF, and anti-CCP antibodies. Similarly, Idriss et al. [23] reported significant associations between DKK-1 and clinical features such as swollen and tender joint counts, patient global assessment, DAS-28, ESR, and platelet levels—further supporting DKK-1's role as a marker of inflammation in RA. While Ali et al. [11] did not reveal any significant relation between RF or CRP and DKK-1 levels, they found significant correlations with disease duration, DAS-28, ESR, and anti-CCP.

Additionally, our data revealed a trend toward higher serum DKK-1 concentrations in patients exhibiting more advanced functional impairment. Specifically, individuals classified under Steinbrocker functional class III demonstrated DKK-1 levels ranging from 4689 to 8092 pg/mL. This observation suggests a potential association between elevated DKK-1 expression and the extent of long-term joint damage and disability in rheumatoid arthritis. These findings support the hypothesis that DKK-1 not only reflects current disease activity but may also serve as an indicator of cumulative structural deterioration over the disease course.

Santos et al. [24] observed a significant elevation in serum DKK-1 levels among patients with more advanced functional impairment as classified by the Steinbrocker grading system. Their study reported that individuals in class IV exhibited substantially higher DKK-1 concentrations (7930.6 ± 10,811.3 pg/mL) compared to those in class I (2948.1 ± 2537.8 pg/mL), indicating a possible link between increased DKK-1 expression and progressive joint dysfunction. Supporting this finding, Giraldo-Bustos et al. [25] also reported a strong association between elevated DKK-1 levels and worse functional outcomes, as evidenced by greater disability and reduced functional capacity across the Steinbrocker functional classes. These findings reinforce the utility of DKK-1 as a potential biomarker for long-term disease burden in rheumatoid arthritis.

In the present study, the Rheumatoid Arthritis Severity Scale (RASS) score ranged from 5 to 19. The disease activity subscale ranged from 3 to 8, the functional impairment subscale from 2 to 8, and the physical damage subscale from 0 to 5. Serum DKK-1 levels showed a strong positive correlation with the total RASS score and all its subcomponents ($P < 0.001$), further supporting its association with both functional limitation and disease severity.

Our findings are also supported by the work of Garnero et al. [26], who showed that in patients with early-stage rheumatoid arthritis, rising levels of DKK-1 were linked to a greater likelihood of radiological progression. Specifically, for every standard deviation increase in DKK-1, there was a higher relative risk of developing more severe bone erosion, defined as an annual increase of at least 0.5 units in the Sharp score. In a related study, Ali et al. [11] found that 37.5% of RA patients who showed bone erosions on hand X-rays had significantly higher serum DKK-1 levels than those without any radiographic signs of joint damage, further highlighting the possible connection between DKK-1 and structural joint deterioration in RA.

We also found that DKK-1 performed exceptionally well in distinguishing active disease from remission among the RA patients. Using a cut-off value of 2726.97 pg/mL, it showed a sensitivity of 98.18% and a perfect specificity of 100%. The area under the ROC curve reached 0.985, highlighting its strong potential as a reliable indicator of disease activity in individuals with RA.

These results align with Wang et al. [28], who showed that DKK-1 had high diagnostic value in patients with moderate to high RA disease activity, with an AUC of 0.968 and a sensitivity of 96.5%.

In line with our findings, Idriss et al. [23] also reported a clear association between rising DKK-1 levels and increasing disease activity in RA patients. Their study showed that DKK-1

concentrations were significantly higher in individuals with severe disease activity ($p < 0.001$) compared to those with moderate or low activity, or those in remission.

A key strength of this study lies in its comprehensive clinical and laboratory assessment of RA patients, alongside objective quantification of serum DKK-1 levels. The inclusion of a well-matched control group further supports the validity of the comparative analysis. Future studies should aim to validate these findings in larger, multi-center cohorts and adopt a longitudinal design to evaluate changes in DKK-1 levels over time and their potential role in predicting disease progression, treatment response, or joint damage.

There are a few limitations to our study that should be kept in mind. Because we worked with a relatively small number of participants from just one center, our findings might not fully reflect what would be seen in the wider RA population. Also, we couldn't track how DKK-1 levels change over time or prove any cause-and-effect relationships. Potential variability in treatment regimens and disease duration among participants may have introduced residual confounding factors that could not be fully controlled for, which may have influenced the observed associations.

CONCLUSION

Serum DKK-1 level could be a valuable biomarker in RA patients. Higher DKK-1 level showed significant correlation with functional impairment, disease activity and severity of RA.

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Citation

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