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ASSOCIATION BETWEEN DISEASE ACTIVITY SCORE, FUNCTIONAL IMPAIRMENT, AND QUALITY OF LIFE IN RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT HYPOTHYROIDISM

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by joint pain, swelling, and stiffness that predominantly affects women. Hypothyroidism, a common autoimmune comorbidity in patients with RA, involves an underactive thyroid gland and can affect RA disease activity, functional impairment, and quality of life. The objective of this study is to investigate the associations between disease activity, functional impairment, and quality of life in Rheumatoid Arthritis **(**RA) patients with and without hypothyroidism.

Materials and Methods: This cross-sectional study enrolled 100 RA patients at Integral Institute of Medical Sciences, Lucknow, from October 2022 to October 2023. Participants were categorized into groups with/without hypothyroidism. Demographic data, Disease Activity Score (DAS 28-CRP), Health Assessment Questionnaire (HAQ), and Short form-36 (SF-36) were collected and analysed using independent t-tests, Mann-Whitney U tests, and Pearson's correlation.

Results: RA patients with hypothyroidism were younger (mean age 34.08 ± 3.86 years) compared to those without hypothyroidism (mean age 44.92 ± 12.18 years; $p < 0.001$). They also showed a higher BMI (31.24 ± 1.14 vs. 29.49 ± 3.41; $p = 0.014$). Disease activity varied significantly, with hypothyroid patients more often in high disease activity states ($p < 0.001$, Chi-square test) and non-hypothyroid patients more often in low disease activity states (100% below the DAS 28-CRP score of 2.6; $p = 0.001$). The SF-36 revealed lower scores in the physical functioning, role-physical, and role-emotional domains among hypothyroid patients ($p \leq 0.035$). Functionally, hypothyroidism correlated with worse HAQ scores across most domains ($p \leq 0.001$ for DG, arising, eating, and reaching).

Conclusion: RA patients with hypothyroidism exhibit significantly higher disease activity, worse functional impairment, and a reduced quality of life than those without hypothyroidism. These findings underscore the need for comprehensive management strategies that integrate thyroid function monitoring and management into RA care to improve patient outcomes.

Keywords: Rheumatoid arthritis, hypothyroidism, disease activity, functional impairment, quality of life, DAS 28-CRP, HAQ, and SF-36 scores.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease that is characterized by joint pain, swelling, and stiffness. It affects approximately 1% of the global population, with women being the most commonly affected. This disease can lead to

significant functional impairment and decreased quality of life in affected individuals. The association between rheumatoid arthritis and hypothyroidism has been a topic of interest, as both conditions are autoimmune disorders and share common risk factors, such as genetics and hormonal imbalances. Hypothyroidism, characterized by an underactive thyroid gland and decreased production of thyroid hormones, is one of the most common causes of this disease.[1] Hypothyroidism has been found to be more prevalent in patients with rheumatoid arthritis compared to the general population, suggesting a potential connection between these two conditions.[2] The association between the Disease Activity Score (DAS), functional impairment, and Quality of Life (QOL) in patients with RA, both with and without hypothyroidism, reveals a complex interplay influenced by disease activity, functional capacity, and psychological factors. Studies have consistently shown that higher disease activity, as measured by DAS, correlates with greater functional impairment and poorer QOL in RA patients.[3] Functional impairment is often assessed using the Health Assessment Questionnaire (HAQ) and activities of daily living (ADLs), which directly impact patients' QOL by limiting their physical abilities and contributing to psychological distress. Quality of Life, as measured by instruments such as the SF-36, is significantly affected by both the physical and mental components of health, with disease activity and functional impairment being key determinants.[4] Interestingly, even patients who achieve clinical remission or low disease activity (LDA) can experience residual symptoms, such as pain and fatigue, which further deteriorate their QOL.[5] This suggests that traditional measures of disease activity may not fully capture patient's experiences with RA, highlighting the importance of patient-reported outcomes (PROs) in managing the disease.[6] The presence of hypothyroidism in RA patients introduces an additional layer of complexity. Hypothyroidism was associated with higher DAS-28 scores, indicating increased disease activity, potentially exacerbating functional impairment, and diminishing QOL. This relationship underscores the necessity of comprehensive screening and management strategies that address not only the joint manifestations of RA but also coexisting conditions, such as hypothyroidism, that can influence disease outcomes. Moreover, work activity limitations and disease severity are significant factors affecting QOL, with high disease activity and severity being associated with greater work limitations and lower QOL scores. The treat-to-target strategy, which aims to achieve remission, is crucial for improving health related quality of life (HAQ), with studies suggesting that controlling disease activity can lead to better QOL outcomes.[7] However, the association between disease activity and functional capacity is not always linear, indicating that other factors, including mental and general health perceptions, play critical roles in determining the overall impact of RA on patients' lives.[8]

Despite this knowledge, the relationship between the disease activity score, functional impairment, and quality of life in rheumatoid arthritis patients with and without hypothyroidism remains poorly understood.

This knowledge gap highlights the need for further research to elucidate the impact of hypothyroidism on disease activity, functional impairment, and quality of life in patients with rheumatoid arthritis. This study aimed to address this gap by examining the association between the disease activity score, functional impairment, and quality of life in rheumatoid arthritis patients with and without hypothyroidism.

This study not only highlights the intricate relationship between rheumatoid arthritis and hypothyroidism but also paves the way for integrating comprehensive thyroid management into therapeutic strategies for RA, promising a potential boost in patient care and quality of life.

MATERIAL AND METHODS

This cross-sectional study was conducted with 100 patients at the Department of Medicine Integral Institute of Medical Sciences, Lucknow, between October 2022 and October 2023 after obtaining approval from the institutional ethics committee. All participants provided written informed consent and the study adhered to the ethical principles of the Declaration of Helsinki (World Medical Association). Ethical clearance was granted by the Institutional Ethical Committee (IEC/IIMS&R/2022/29) of the Integral University, Lucknow, India.

To determine the appropriate sample size for our study, we used formula n =z2p (1-p) / d2, where, Sample size = ‘n,’’ n” p,’’ p’ =41.6% (Waseem et al), 1-p = ‘q’ =58.4% Confidence level 95%, so ‘z’= 1.96, Absolute error/ Margin of error (‘d’) =10%, on the basis of this calculated sample size = 93, Non response = 7%. The calculation showed that a minimum of 90 participants was necessary to detect a statistically significant difference within our study parameters [9]. To enhance the robustness of our study and mitigate the potential for type II errors, we elected to include 100 participants, who were split into two groups on the basis of RA without hypothyroidism (Group A, n=25) and RA with hypothyroidism (group B, n= 75). The inclusion criteria for this study were that both male and female RA patients were included in each group. Participants had to be above 18 years of age to qualify for either group and be diagnosed according to the 2010 American College of Rheumatology (ACR)/EULAR RA classification criteria.[10] The inclusion criteria for Group A FT3>4.2, FT4>2.3, and TSH<.4. For Group B, the inclusion criteria

were FT3<1.4, FT4<.9, and TSH>5.5. The exclusion criteria for both groups were as follows: patients on medication known to cause thyroid dysfunction, patients already taking thyroxine/neomerazole, patients with concurrent infection, pregnant women, patients who had undergone thyroidectomy, and patients with type 1 Diabetes Mellitus.

Following enrolment, each participant underwent a detailed physical examination, laboratory tests (including FT3, FT4, THS, anti-TPO, RA-factor, anti-CCP, ESR, and CRP), and Disease Activity Score (DAS28) assessment to evaluate disease severity. Based on the thyroid profile, participants were categorized into groups A and B. All participants in Groups A and B were evaluated for DAS 28, HAQ, and SF36.

We measured DAS 28-CRP for both group (RA without hypothyroidism and RA with hypothyroidism) to assess the disease activity score. DAS 28-CRP enumerates the number of proximal interphalangeal joints (PIP), metacarpophalangeal joint (MCP), wrist, elbow, shoulder, knee, and 28 swollen and tender joints of the thumb to the little finger on both sides. Additionally, CRP level and patients' global assessment using the Visual Analog Scale (VAS) were calculated using specific formulas. The DAS28 score was calculated using the following formula, which includes CRP level as a measure of inflammation:

DAS28=0.56×Tender Joint Count+0.28×Swollen Joint Count+0.70×ln (CRP) +0.014×Global Health

This formula integrates both objective inflammation measures and a patient's subjective health assessment to provide a comprehensive view of the disease activity. The DAS28 scoring system, with the inclusion of CRP, remains a robust, reliable, and valid method widely used in clinical research because of its precision in measuring and categorizing disease activity in patients with RA.[11,12] Based on their DAS28 scores, the participants' disease activity was categorized into the following levels: Remission: DAS28 score ≤ 2.6, Low Activity: DAS28 score > 2.6 and ≤ 3.2, Moderate Activity: DAS28 score > 3.2 and ≤ 5.1, High Activity: DAS28 score > 5.1

In this study, we used the Health Assessment Questionnaire (HAQ) to assess functional impairment in both the groups. HAQ is an established tool in clinical research for evaluating physical functional limitations in patients with Rheumatoid Arthritis (RA).[13] It measures a patient's ability to perform everyday tasks through self-reporting, thus reflecting the impact of RA on the quality of life and functional impairment. The HAQ includes a spectrum of functional activities, such as dressing, rising, eating, walking, hygiene, reaching, gripping, and other daily tasks, scored on a scale from 0 (no difficulty) to 3 (unable to do). The questionnaire was adjusted for any aid or device that the patient might use, which could affect their ability to perform these activities.

The SF-36 was used for QOL assessment in both RA groups.[14] This comprehensive health-related QOL scale is commonly used to assess subjective outcome measures. The subscales consisted of eight sections: Physical Function (PF), Role Physical (RP), Body Pain (BP), General Health (GH), vitality (VT), Social Function (SF), Role Emotional (RE), and Mental Health (MH). There are 36 questions. The raw scores for each subscale range from 0 to 100 points. Higher scores indicate a higher QOL. SF-36 has been adapted and translated into several languages, and its validity and reliability established in several countries.[15,16]

2.1 Statistical Analysis

IBM SPSS Statistics software (version 26.0) was used for statistical analysis. Descriptive statistics were used to summarize the data. Independent t-tests were used to analyse differences between the two groups, while baseline characteristics were compared using the chi-square test for categorical variables. For continuous variables that did not follow a normal distribution, we applied the Mann-Whitney U test. The correlation between DAS 28 and the evaluated variables (HAQ and SF-36) was determined using Pearson's correlation coefficient. The significance threshold was set at $p \leq 0.05$.

RESULTS

Table 1 displays the demographic characteristics of patients with rheumatoid arthritis (RA), categorized based on with and without hypothyroidism. The average age of RA patients without hypothyroidism was 44.92±12.18 years, which was significantly older than the average age of 34.08±3.86 years for those with hypothyroidism (p<0.001). Additionally, the body mass index (BMI) was significantly higher in hypothyroidism patients, with an average of 31.24±1.14, compared to RA without hypothyroidism patients, with an average of 29.49±3.41 (p = 0.014). The sex distribution revealed no significant differences in the proportion of male patients. However, a higher proportion of female patients had RA hypothyroidism (76.0%) than those without hypothyroidism (24.0%; p = 0.689, chi-square test). [Table 1]

Table 2 presents a comparison of the Disease Activity Score (DAS 28-CRP) in patient rheumatoid arthritis (RA) patients with and without hypothyroidism. The results indicated that none of the patients in either group was in remission. There was a notable difference in the proportion of patients with low disease activity, as all RA patients without hypothyroidism (100.0%) reported scores below 2.6, whereas none of the RA patients with hypothyroidism had scores within this range (P = 0.001). Additionally, a substantial proportion of RA patients without hypothyroidism showed moderate disease activity compared to RA patients with hypothyroidism (76.4% vs. 23.6%). Furthermore, all

patients with high disease activity (>5.1) were in the hypothyroid group (p < 0.001, chi-square test). [Table 2]

Table 3 compares the SF-36 scores, which indicate the quality of life. Significant differences were noted in the physical functioning (PF), role-physical (RP), and role-emotional (RE) domains in RA patients with hypothyroidism, scoring lower in PF and RE but higher in RP (p = 0.035, 0.035, and 0.004, respectively). General health perceptions and vitality were significantly lower in RA with hypothyroidism (p < 0.001 for vitality), while social functioning (SF) also showed a significant reduction (p = 0.034). Mental health (MH) scores did not differ significantly between the groups. [Table 3]

The Health Assessment Questionnaire (HAQ) scores are summarized in Table 4. Significant differences were found in disability grades (DG), arising, eating, hygiene, reach, grip, and other activities in RA patients with hypothyroidism, who generally showed worse outcomes (p < 0.001 for DG, eating, and reach; p = 0.001 for arising, hygiene, grip, and p = 0.003 for activities). No significant differences were observed during walking. [Table 4]

The correlations between DAS 28-CRP and quality of life measures in patients with RA with and without hypothyroidism are shown in Tables 5 and 6, respectively. Figure 1 and 2 are scatter diagrams that show the correlation of Das 28-CRP with SF-36 and HAQ. Correlation analysis between SF-36 and DAS 28-CRP scores in RA patients without hypothyroidism indicated no significant correlations across most domains, except for a positive correlation in role-physical (RP; r = 0.323, p = 0.005). For HAQ scores, no consistent significant correlations with DAS28-CRP were observed, indicating the varied impacts of disease activity on different aspects of daily living. [Table 5]

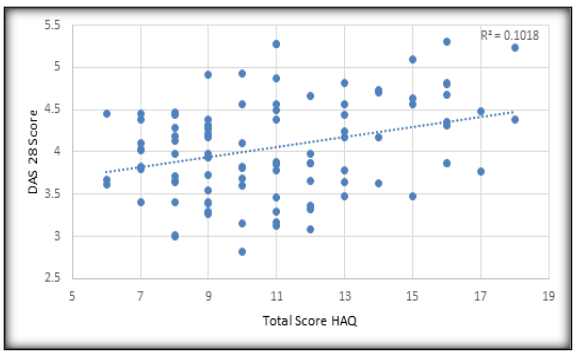

Figure 1: Scatter diagram between total score HAQ and DAS 28 score

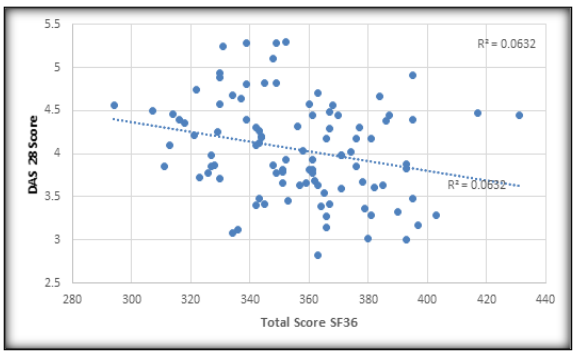

Figure 2: Scatter diagram between total score SF-36 and DAS 28 score

Table 1: Demographic characteristics of RA patients with and without hypothyroidism

Demographic characteristics			RA without Hypothyroidism	RA with Hypothyroidism	P value
AGE	(in years)	Mean	44.92	34.08	<0.001
		SD	12.18	3.86	
HEIGHT	(in Cm)	Mean	165.56	166.40	0.626
		SD	7.26	7.95	
WEIGHT	(in kg)	Mean	80.93	86.60	0.021
		SD	11.24	7.64	
BMI	kg/m 2	Mean	29.49	31.24	0.014
		SD	3.41	1.14	
Gender	Male	n	7	18	0.689@
		%	28.0%	72.0%	
	Female	n	18	57	
		%	24.0%	76.0%	

@chi-square test

Table 2: Comparison of DAS 28-CRP Score in RA patients with and without hypothyroidism

DAS 28-CRP Score	RA without Hypothyroidism	RA with hypothyroidism	P value
	n (%)	n (%)	
Remission	0 (0.0%)	0 (0.0%)	0.001
Low Disease activity (<2.6)	7 (100.0%)	0 (0.0%)	
Moderate Disease activity (<3.2)	68 (76.4%)	21 (23.6%)	
High Disease activity (>5.1)	0 (0.0%)	4 (100.0%)	

Chi square

Table 3: Comparison of SF-36 Score in RA patients with and without hypothyroidism

SF-36	RA without Hypothyroidism		RA with Hypothyroidism		P value
	Mean	SD	Mean	SD	

PF	35.43	13.100	29.40	8.708	0.035
RP	36.07	6.901	39.72	8.696	0.035
RE	45.31	7.048	40.56	6.449	0.004
BP	46.99	7.936	46.52	5.903	0.788
SF	48.59	11.813	43.12	7.976	0.034
MH	51.64	9.977	49.88	7.965	0.426
VITALITY	55.08	7.116	48.80	5.881	<0.001
GH	43.08	8.882	40.40	5.930	0.163

Independent t test

Table 4: Comparison of HAQ Score in RA patients with and without hypothyroidism

HAQ	RA without Hypothyroidism		RA with Hypothyroidism		P value
	Mean Rank	Sum of Ranks	Mean Rank	Sum of Ranks	
DG	44.08	3306.00	69.76	1744.00	<0.001
ARISING	45.63	3422.00	65.12	1628.00	0.001
EATING	44.61	3346.00	68.16	1704.00	<0.001
WALKING	50.77	3808.00	49.68	1242.00	0.861
HYGINE	45.75	3431.50	64.74	1618.50	0.001
REACH	43.93	3294.50	70.22	1755.50	<0.001
GRIP	45.42	3406.50	65.74	1643.50	0.001
ACTIVITIES	45.83	3437.50	64.50	1612.50	0.003

Mann Whitney U test

Table 5: Correlation between SF-36 in RA patients with and without hypothyroidism

SF-36	Pearson correlation	RA without Hypothyroidism	RA with Hypothyroidism
		DAS28 CRP	
PF	r	-.086	.011
	P value	.463	.958
RP	r	.323**	-.117
	P value	.005	.576
RE	r	.017	.245
	P value	.883	.238
BP	r	-.185	.233
	P value	.112	.261
SF	r	-.082	.111
	P value	.486	.598
MH	r	.072	.245
	P value	.538	.237
VITALITY	r	-.113	-.071
	P value	.333	.736
GH	r	-.200	-.103
	P value	.086	.625

**** Statistically significant**

Table 6: Correlation between HAQ and DAS score in RA patients with and without hypothyroidism

HAQ	Spearman's rho	RA without Hypothyroidism	RA with Hypothyroidism
		DAS28 CRP	
DG	r	.102	-.015
	P value	.385	.945
ARISING	r	-.084	.082
	P value	.475	.698
EATING	r	-.019	-.220
	P value	.873	.290
WALKING	r	-.031	.089
	P value	.793	.674
HYGINE	r	.068	.041
	P value	.560	.847
REACH	r	-.107	.088
	P value	.359	.677
GRIP	r	-.139	.053
	P value	.235	.803
ACTIVITIES	r	-.108	-.103
	P value	.354	.625

**** Statistically significant**

DISCUSSION

The results of the study revealed several associations between the disease activity score, functional impairment, and quality of life in rheumatoid arthritis patients with and without hypothyroidism. First, there was a significant difference in age between the two groups, with rheumatoid arthritis patients without hypothyroidism being significantly older than those with hypothyroidism. Second, the study found that patients with hypothyroidism had a significantly higher body mass index compared than those without hypothyroidism. This can be explained by the effects of hypothyroidism on metabolism and weight regulation. Additionally, this study found that patients with hypothyroidism had a higher disease activity score than those without hypothyroidism. This suggests that hypothyroidism may contribute to the increased disease activity in patients with RA. Furthermore, this study found a significant association between functional impairment and hypothyroidism in patients with rheumatoid arthritis. This indicates that patients with hypothyroidism may experience greater difficulty in performing daily activities than those without hypothyroidism. These findings highlight the importance of considering comorbid conditions such as hypothyroidism in the management of rheumatoid arthritis. These findings emphasize the need for healthcare professionals to assess and address the impact of hypothyroidism on disease activity, functional impairment, and quality of life in patients with rheumatoid arthritis. Additionally, it is important to consider the impact of hypothyroidism on medication adherence and overall management of patients with RA.

Previous research has supported these findings. A study by Chung-Ming et al. indicated that hypothyroidism is a common comorbidity in patients with rheumatoid arthritis and may contribute to increased disease severity.[17] Similarly, Shivaprasad et al. suggested that hypothyroidism may exacerbate functional impairment and decrease quality of life in patients with rheumatoid arthritis.[18] These findings align with the results of the current study, highlighting the importance of considering hypothyroidism in the management of rheumatoid arthritis patients. Further research exploring the mechanisms underlying this association may provide insights into targeted and effective treatment strategies.

Several studies have reported similar findings regarding the association between hypothyroidism and rheumatoid arthritis. A study by Yi-Jing et al. demonstrated a significant relationship between hypothyroidism and disease activity in rheumatoid arthritis patients.[19] This aligns with the results of our study, suggesting consistent evidence of the impact of hypothyroidism on the severity of RA.

It is important to compare these results with other findings to establish the strength and consistency of this association. A study conducted in South Asia revealed that patients with RA and concomitant hypothyroidism had increased disease activity, as indicated by higher disease activity scores (DAS-28), suggesting that hypothyroidism could contribute to the functional impairment seen in RA by increasing disease activity.[20] Evidence suggests a significant link between hypothyroidism and functional impairment in RA, primarily through the exacerbation of disease activity and severity, which underscores the importance of screening and managing thyroid dysfunction in RA patients to potentially mitigate functional impairment.

Further research on the mechanisms underlying this association holds promise for developing more effective interventions. Understanding the specific pathways through which hypothyroidism affects disease activity and functional impairment in patients with rheumatoid arthritis could lead to tailored treatment approaches. Additionally, exploring the role of hypothyroidism in medication adherence and overall quality of life may provide valuable insights for improving patient outcomes.

Despite the compelling findings of this study, it is important to acknowledge its limitations. One limitation is the dependence on self-reported data, which may be subject to recall bias and inaccuracies. Additionally, the study design may not have accounted for all potential confounding variables that could have influenced the observed association between hypothyroidism and rheumatoid arthritis.

Furthermore, this study focused on a specific population and may not be generalizable to broader demographics or geographic regions. The sample size and demographic characteristics of the participants may also affect the generalizability of the results.

Another limitation is the cross-sectional nature of the study, which restricts the ability to establish causality between hypothyroidism and the observed outcomes in rheumatoid arthritis. Longitudinal studies and clinical trials are needed to explore the temporal relationships and effects of interventions on these associations.

Moreover, the study did not delve into the specific mechanisms through which hypothyroidism may impact disease activity, functional impairment, and quality of life in rheumatoid arthritis patients. Future studies should aim to elucidate the underlying pathways to better inform targeted treatment strategies.

Future studies should address these limitations to enhance the robustness of the evidence and provide a more comprehensive understanding of the relationship between hypothyroidism and rheumatoid arthritis.

CONCLUSION

In conclusion, our study and supporting literature underscore the importance of considering hypothyroidism as a significant factor in the management of rheumatoid arthritis. The associations between hypothyroidism and disease activity, functional impairment, and quality of life are substantial, and addressing these factors in clinical practice is essential for optimizing patient care and treatment outcomes. Further exploration of this relationship will contribute to more targeted and personalized approaches for managing rheumatoid arthritis in patients with hypothyroidism.

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Institutional Review Board Statement: The study was conducted after obtaining ethical clearance from the Institutional Ethical Committee (IEC/IIMS&R/2022/29) and performed in accordance with the principles of the Declaration of Helsinki.

Informed Consent Statement: All participants' written informed consent was signed and obtained publication of this study.

Data Availability Statement: The datasets analysed in the current study are available from the corresponding author on reasonable request.

Conflicts of Interest: All the authors declare that they have no competing interest.

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