

Effect of anti-tumor necrosis factor (anti-TNF) alpha therapy versus conventional treatment on Thyroid Autoimmunity and function in Rheumatoid Arthritis patients

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Abstract

Objective: To compare the effects of anti-TNF alpha versus conventional treatment on thyroid gland in rheumatoid arthritis (RA) patients.

Methods: A prospective cohort of 50 adult RA patients was enrolled and allocated into two groups based on treatment line: Group 1 (n=25) comprised anti-TNF naïve patients commencing biologic therapy, while Group 2 (n=25) continued conventional DMARD treatment. All participants underwent thyroid evaluation including function tests (TSH, FT3, FT4), autoantibody profiling (anti-thyroglobulin [ATG] and anti-thyroid peroxidase [ATPO]), and sonographic assessment of the thyroid gland at baseline and after six months.

Results: Baseline serum TSH was significantly elevated in Group 2 relative to Group 1 ($p=0.036$), while thyroid autoantibody profiles and sonographic parameters were broadly similar between cohorts. After six months, complete TSH normalisation was achieved in all subclinically affected Group 1 patients, with autoantibody profiles remaining stable. In the conventional therapy group, 2 patients developed overt thyroid dysfunction and were excluded. Among the remaining 23, TSH status was unchanged but both ATG and ATPO levels rose significantly ($p=0.001$ and $p=0.013$, respectively). TSH status remained unchanged (20 normal, 3 subclinical hypothyroidism), with minor patient level changes (one patient with normal TSH develop subclinical hypothyroidism and one patient with subclinical hypothyroidism became normal). In contrast, significant increase in both ATG and ATPO levels was observed ($p=0.001$, and 0.013 , respectively), with ATG positivity increasing from 3 to 4 patients and ATPO positivity from 5 to 6 patients.

Conclusion: RA patients face a disproportionately high risk of thyroid dysfunction, with subclinical and overt hypothyroidism being the most prevalent forms. Anti-TNF alpha therapy in RA appears to reduce susceptibility to autoimmune thyroid disease.

Keywords: Rheumatoid arthritis; Anti-TNF alpha therapy; Thyroid autoimmunity; Thyroid function tests; Autoimmune thyroid disease; TNF inhibitors

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Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disorder characterized by persistent synovial inflammation and progressive joint destruction, frequently accompanied by extra-articular involvement and a broad spectrum of comorbid conditions.[1,2] Among these, thyroid autoimmunity occupies a particularly prominent position; Hashimoto's thyroiditis and Graves' disease occur at substantially higher rates in RA populations than in the general public, driven by convergent immunological pathways that include shared HLA susceptibility loci, aberrant T-cell regulation, and elevated circulating levels of pro-inflammatory mediators such as TNF-alpha and IL-6. [3-7] The resulting autoantibody milieu and cytokine environment predispose both glandular compartments to concurrent immune-mediated injury.

TNF-alpha is a pivotal mediator of the immune dysregulation underpinning RA, orchestrating

synovial hyperplasia and perpetuating joint destruction through its effects on macrophages, fibroblasts, and osteoclasts. Notably, elevated TNF-alpha expression has been documented in autoimmune thyroid conditions as well, raising the possibility that pharmacological TNF-alpha blockade may exert modulatory effects on thyroid autoimmune activity beyond its primary rheumatological targets. [8,9]

According to current treatment recommendations, escalation to biologic therapy is warranted when RA patients fail to achieve adequate disease control with conventional synthetic DMARDs, or when unfavourable prognostic indicators are identified—including detectable autoantibodies, elevated disease activity, early radiographic erosions, or inadequate response to two or more csDMARDs. Among the expanding armamentarium of biological agents, TNF-alpha inhibitors remain the most widely used class in routine RA management. [10]

This study aimed to evaluate whether anti-TNF therapy differs from conventional DMARDs in its effects on thyroid function and autoimmune thyroid markers in RA patients.

Subjects and methods

The present work was designed as a prospective comparative cohort study enrolling 50 consecutive RA patients from the outpatient clinic of the Rheumatology, Rehabilitation and Physical Medicine Department, Faculty of Medicine, Tanta University Hospitals, over the period from January 2023 through July 2024.

Ethical clearance was granted by the Local Research Ethics Committee, Faculty of Medicine, Tanta University (Approval No. 36221/12/22). All the patients were given their written informed consent to participate in this study.

Participants were stratified into two groups according to their prescribed treatment regimen.

Group I: Comprised 25 patients with persistently active RA despite at least 6 months of conventional DMARDs (methotrexate 15–25 mg/week and/or leflunomide once daily), who were scheduled to initiate anti-TNF therapy; 16 received golimumab and 9 received adalimumab.

Group II: Comprised 25 RA patients maintained on conventional DMARDs administered as monotherapy or in combination.

Inclusion criteria:

1. Age 18 years or above at enrolment.
2. Diagnosis of RA fulfilling the 2010 ACR/EULAR classification criteria. [11]
3. No prior exposure to TNF-alpha inhibitors.
4. Clinically eligible either for initiation of anti-TNF therapy or for continuation of conventional DMARD treatment.

Exclusion criteria:

1. Pre-existing thyroid disease, current thyroid hormone replacement therapy, or any other condition known to alter thyroid function (including pituitary adenoma and pregnancy).
2. Use of medications with recognised thyroid-modifying potential (e.g., interferon-alpha, lithium, amiodarone).
3. History of thyroid surgery or previous radioactive iodine ablation therapy.
4. History of active or latent tuberculosis, malignant disease, current systemic infection, or significant hepatic, renal, or demyelinating disorders.

All enrolled patients underwent the following standardised assessments at two time points: before treatment initiation and after six months:

A. Clinical assessment:

A thorough medical history was taken for each participant, followed by a structured physical

examination with emphasis on the thyroid gland and musculoskeletal system. Duration of morning stiffness and pain intensity, the latter quantified using a 0-10 cm visual analogue scale (VAS), were recorded at each visit.

B. Assessment of disease activity: using the 28-joint Disease Activity Score (DAS28). [12]

C. Functional assessment: using the Modified Health Assessment Questionnaire (MHAQ). [13]

D. Laboratory investigations:

1. Complete blood count (CBC).[14]
2. Erythrocyte sedimentation rate (ESR).[15]
3. C-Reactive Protein (CRP).[16]
4. Rheumatoid factor (RF).[17]
5. Anti-cyclic citrullinated protein antibodies (anti-CCP). [17]

- Laboratory tests of thyroid function:

- Serum free thyroxine level (T4) and free triiodothyronine level (T3).[18]
- Immune-radiometric testing of the Thyroid-Stimulating Hormone (TSH).[18]
- Thyroid autoantibodies (ATG and ATPO).[19]

According to TSH serum levels, thyroid dysfunction was classified as follows:

–Euthyroidism, TSH from 0.4 to 4.0 mU/L.

–Overt hypothyroidism, TSH > 4.0 mU/L and low T4L.

–Subclinical hypothyroidism, TSH > 4.0 mU/L and normal T4L.

– Hyperthyroidism, TSH < 0.4 mU/L. [20]

E. Radiological assessment of the thyroid gland:

Thyroid ultrasonography was performed using a high-resolution B-mode scanner with a 9-MHz transducer. Images were classified according to the ACR Thyroid Imaging Reporting and Data System (TIRADS), which grades nodules from TIRADS 1 (benign) to TIRADS 5 (highly suspicious) based on composition, echogenicity, shape, margin, and echogenic foci, with fine needle aspiration thresholds defined per category and nodule size. Gland parenchymal changes were graded G1–G4 based on the degree of hypoechogenicity and heterogeneity relative to the anterior strap muscle.

- Grade 1 (G1) = diffusely enlarged thyroid gland with normal echogenicity (similar to a normal thyroid gland and hyperechoic to the anterior strap muscle) without heterogeneity.
- G2 = diffusely enlarged thyroid gland with heterogeneity involving less than one third of thyroid gland, while the rest of the gland shows normal echogenicity
- G3 = diffusely enlarged thyroid gland with heterogeneity involving more than one third of

the gland, while the rest of gland shows isoechogenicity compared with the anterior strap muscle; and

- G4=diffusely enlarged thyroid gland with diffuse heterogeneity involving more than one third of the gland with marked hypoechogenicity that is more hypoechoic than the anterior strap muscle.[22]

Statistical analysis:

Data analyses were conducted using IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was applied to evaluate normality of continuous variables, and descriptive statistics were selected accordingly. Intra-group comparisons (baseline vs. six months) used the paired t-test or Wilcoxon signed-rank test. Inter-group comparisons for continuous variables employed the independent t-test or Mann-Whitney U test; for categorical variables, the Chi-square, Fisher's exact, or Monte Carlo exact test was used as appropriate. Results with $p \leq 0.05$ were deemed statistically significant, while $p < 0.001$ denoted high statistical significance.

Results

Baseline demographic, clinical, laboratory, and thyroid parameters for both groups are presented in Table 1. The two cohorts were well-matched at enrolment, showing no significant inter-group differences in age, sex, morning stiffness duration, pain scores by VAS, joint counts, DAS28 disease activity, acute phase reactants, or functional status assessed by MHAQ ($p > 0.05$ for all). Regarding thyroid assessment, the two groups were broadly comparable across thyroid function tests, autoantibody status, and sonographic findings at baseline, with the exception of serum TSH levels, which were significantly higher in the conventional treatment group than in the anti-TNF group ($p=0.036$). TIRADS-based nodule classification also revealed a statistically significant between-group difference ($p=0.029$). At baseline, TSH-based classification revealed euthyroidism in 21 Group 1 patients (with 3 subclinical hypothyroid and 1 subclinical hyperthyroid), and 20 Group 2 patients (with 4 subclinical hypothyroid and 1 subclinical hyperthyroid). Regarding thyroid autoantibodies at enrolment, ATG positivity was present in 2 Group 1 patients and 3 Group 2 patients, while ATPO was detected in 7 patients per group. Thyroid gland sonography at baseline showed Grade 1 (normal) size in 24 Group 1 patients (96.0%) and 19 Group 2 patients (82.6%). TIRADS nodule absence was more frequent in Group 1 ($n=16$, 64.0%) versus Group 2 ($n=10$, 43.5%), with nodule grades spanning TIRADS 1-3 in Group 1 and TIRADS 2-3 in Group 2.

Following six months of treatment, patients in the anti-TNF therapy group exhibited substantial clinical improvement, characterised by reductions in morning stiffness duration, VAS pain ratings, and swollen and tender joint counts, with significant improvements in DAS28 and MHAQ ($p < 0.001$ for all). Parallel reductions were observed in acute-phase markers (ESR and CRP, $p < 0.001$ for both) and immunological markers including declining RF and anti-CCP titres ($p = 0.002$, <0.001 , respectively). Thyroid-specific outcomes in Group 1 were equally favourable. All four patients who had subclinical thyroid abnormalities at enrolment achieved TSH normalisation by six months. ATG levels and positivity rates were unchanged over the study period ($p=0.352$), while ATPO levels declined significantly ($p=0.031$); the number of ATPO-positive patients was unaltered due to reciprocal individual seroconversions. Thyroid sonography also improved: normal gland size was recorded in 24 patients (up from 23), and the proportion with no detectable nodules rose from 15 to 16 patients (Table 2).

During the follow-up period in Group 2, two patients who had subclinical thyroid dysfunction combined with ATPO positivity at baseline progressed to overt thyroid failure requiring hormone replacement and were consequently withdrawn from the analysis; outcomes for the remaining 23 evaluable patients are detailed in Table 3. Within this subgroup, clinically meaningful gains were observed across all musculoskeletal parameters: morning stiffness duration, VAS pain scores, and swollen and tender joint counts all declined significantly ($p < 0.001$ for all), with parallel improvements in DAS28 and MHAQ ($p < 0.001$ and $p = 0.016$, respectively). ESR and CRP were also significantly reduced ($p = 0.003$ and 0.004 , respectively), while RF and anti-CCP titres showed no significant change. Thyroid function by TSH category remained stable overall (20 euthyroid, 3 subclinical hypothyroidism), with individual-level bidirectional changes observed. Conversely, both ATG and ATPO antibody concentrations rose significantly ($p=0.001$ and $p=0.013$, respectively), with ATG positivity advancing from 3 to 4 patients and ATPO positivity from 5 to 6 patients. On thyroid ultrasonography, patients with normal gland size decreased slightly from 21 to 19 ($p=0.099$), TIRADS 3 nodules increased from 8 to 9 ($p < 0.001$), and the nodule-free proportion declined from 11 to 10 patients. At the six-month endpoint, between-group comparisons (Group 1, $n = 25$ vs. Group 2, $n = 23$) are summarised in Table 4. Both cohorts improved relative to baseline; however, superiority of anti-TNF therapy was evident across clinical and inflammatory domains. DAS28 and MHAQ scores were significantly better in Group 1, as were ESR and CRP values, while RF and

anti-CCP titres did not differ significantly between the two groups at this timepoint.

Thyroid hormone levels (FT3 and FT4) were statistically indistinguishable across the two groups. Residual subclinical hypothyroidism was confined exclusively to the conventional treatment arm (n=3, 13.0%), whereas complete euthyroidism was achieved in all anti-TNF-treated patients. Thyroid autoantibody rates were not significantly different between groups (ATG positivity: 8.0% vs. 17.4%, $p=0.407$; ATPO positivity: 28.0% vs. 26.1%, $p=1.000$). Sonographically, normal gland size was more prevalent in Group 1 (96.0% vs. 82.6%). TIRADS nodule assessment revealed a significant inter-group disparity ($p=0.016$), with 64.0% of anti-TNF patients having no detectable nodules versus 43.5% in the conventional treatment arm.

Discussion

Thyroid comorbidity is a recognised feature of RA, with hypothyroidism emerging as the most common thyroid abnormality in affected individuals. The principal thyroid autoimmune entities encountered in RA—namely Hashimoto's thyroiditis and Graves' disease, is the most common cause of various thyroid dysfunctions and is manifested by the production of antibodies against thyroid peroxidase, thyroglobulin or thyrotropin receptor autoantigens.[23]

Shared immunological circuitry between RA and thyroid disease means that drugs designed to interrupt RA pathways may carry secondary consequences for thyroid homeostasis. [24] TNF-alpha inhibitors illustrate this duality: isolated cases of drug-induced subacute thyroiditis have been reported, with a notable clustering during the COVID-19 era [25], while parallel data indicate that TNF-alpha blockade can normalise elevated thyroid autoantibody levels. [26] The present study findings can be summarised as follows.

At enrolment, a statistically significant inter-group difference in TSH levels was identified, whereas thyroid autoantibody profiles and sonographic findings were similar across the two groups. Following six months, Group 1 achieved complete resolution of subclinical thyroid dysfunction with preservation of stable autoantibody status. Group 2, conversely, demonstrated a significant escalation in both ATG and ATPO levels, and two patients progressed to clinically overt thyroid disease requiring pharmacological intervention.

These observations are consistent with accumulating evidence on the thyroid-protective potential of biologic DMARDs. Waldenlind et al. (2024) demonstrated a reduced incidence of thyroxine-treated autoimmune thyroid disease among RA patients receiving biological agents. [27] Nooh et al. (2024) similarly found that TNF-alpha inhibition was safe

from a thyroid standpoint in euthyroid RA patients and, in those with pre-existing hypothyroidism, was linked to measurable recovery of thyroid hormone parameters; the authors proposed that suppression of TNF-alpha's interference with thyroglobulin production and TSH-mediated iodine handling could account for this effect. [28]

Contrasting perspectives exist, however. Chen et al. (2023) [29] reported that methotrexate use correlated with reduced total T4 concentrations in RA patients, while glucocorticoid exposure was linked to lower total T3 levels, suggesting that certain conventional antirheumatic agents may adversely alter thyroid hormone kinetics and thereby contribute to secondary thyroid dysfunction in this population.

Sawicka-Gutaj, et al. (2022)[24] advocated for routine thyroid screening in RA patients, given the heightened prevalence of thyroid abnormalities in this population. Biological therapy for RA may favourably modulate autoimmune thyroid disease through suppression of ATPO antibody levels, though definitive evidence from controlled studies remains limited. TNF inhibitors have been associated with sporadic cases of subacute thyroiditis, necessitating clinical vigilance.

Paschou et al. (2018) [30] noted a mild FT4 decline with anti-TNF treatment in inflammatory bowel disease, with TSH, T3, and thyroid autoantibody levels remaining stable, highlighting the importance of disease context in interpreting such data. Bliddal et al. (2017) [26] likewise documented a trend—albeit statistically non-significant—toward lower thyroid peroxidase and thyroglobulin antibody concentrations and reduced thyrotropin in hypothyroid patients following biological antirheumatic therapy in RA. Taken together, these findings, while derived from a limited body of evidence, suggest that biologic therapy in RA is unlikely to be detrimental to thyroid autoimmunity and can generally be regarded as thyroid-safe.

The TIRADS classification system offers a reliable and reproducible sonographic tool for risk-stratifying thyroid nodules, incorporating nodule composition, echogenicity, margins, shape, and echogenic foci to guide clinical decision-making. [23]

Sonographic reassessment after six months revealed divergent thyroid trajectories between groups: Group 1 demonstrated significant improvement in TIRADS classification, whereas Group 2 showed significant worsening. At the parenchymal level, Group 1 showed significant echotexture improvement whereas Group 2 remained essentially unchanged group 2 at six months. Between-group comparison confirmed significantly superior TIRADS outcomes in Group 1 relative to Group 2, with no significant inter-group difference observed in thyroid gland size.

The sonographic improvements observed in our anti-TNF cohort are consistent with published evidence pointing to a morphologically protective role of TNF-alpha blockade on the thyroid. Bayrak et al. (2023) [31] reported no elevation in thyroid nodule prevalence among 75 axSpA patients on TNF inhibitors, and did not recommend routine pre-treatment nodule screening in this context. Soliman et al. (2024) [32] similarly investigated 75 ankylosing spondylitis patients allocated to NSAIDs ($n = 30$) versus anti-TNF- α biologic therapy. On thyroid ultrasonography, 75.6% of the biologic-treated patients demonstrated a normal gland, compared with 56.6% of the NSAID group, and nodules identified in the biologic cohort were predominantly of benign TIRADS classification. The investigators concluded that anti-TNF biologic agents provided superior suppression of thyroid autoimmunity and nodule development relative to NSAIDs alone.

A dissenting view was offered by Sayiner et al. (2024), [33] who identified a higher burden of thyroid nodules among axial spondyloarthritis patients receiving TNF-alpha inhibitors compared to controls, concluding that pre-treatment thyroid nodule screening and interval surveillance during biologic therapy warrant consideration.

The present investigation carries inherent methodological limitations, most notably the modest cohort size and the restricted six-month observation window, which preclude definitive conclusions regarding long-term immunological trajectories. Adequately powered prospective studies incorporating extended follow-up periods are required to delineate the durable impact of TNF-alpha inhibitor therapy on thyroid autoimmune status in RA.

Conclusion: RA confers an elevated susceptibility to thyroid dysfunction, with hypothyroidism being the most frequently encountered thyroid abnormality in this context. Treatment with TNF-alpha inhibitors appears to confer a degree of protection against the development or progression of autoimmune thyroid disease in RA patients.

Statements and Declarations

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Competing Interests

None of the contributing authors have any financial relationships, affiliations, or non-financial interests that could be perceived as influencing the results or interpretation of this manuscript.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection, and statistical analysis were performed by the first and second authors. The first draft of the manuscript was written by the corresponding author, and all authors reviewed and commented on previous versions. All authors read and approved the final manuscript.

Data Availability

The datasets generated and analysed during the current study are not publicly available due to patient privacy constraints but are available from the corresponding author on reasonable request.

Consent to Participate

Written informed consent was obtained from all individual participants included in the study, in accordance with the Declaration of Helsinki and the regulatory requirements of the local Ethics Committee of Tanta University (Approval No: 36221/12/22).

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Table (1): baseline demographic, clinical, laboratory, thyroid gland assessment of the studied group

		Group 1 (Anti-TNF therapy) (n=25)		Group 2 (Conventional treatment) (n=25)		Test of significance	
Demographic data	Age (years)	50.0 (41.5 – 54.5)		45.0 (37.0 – 52.5)		23 2.0	0.1 18
	Sex	18(72%)		21(84%)		χ^2 1.0 49	0.3 06
	Female Male	7(28%)		4(16%)			
Clinical data	Morning stiffness (min.)	60.0 (60.0 – 120.0)		60.0 (60.0 – 105.0)		U 24 8.0	0.5 63

	VAS for pain	8.0 (7.0 – 8.0)	7.0 (6.0 – 8.5)	U 25 2.0	0.2 23
	SJC	8.0 (4.5 – 10.0)	8.0 (4.0 – 9.0)	U 27 7.0	0.4 88
	TJC	12.0 (10.0 – 17.0)	12.0 (10.0 – 15.5)	U 29 4.0	0.7 16
	DAS28	6.1 ± 0.75	6.3 ± 0.73	T 0.5 57	0.5 80
	MHAQ	1.25 (0.938 – 1.75)	1.25 (0.9375 – 2.125)	U 26 2.5	0.3 30
Acute phase reactants	ESR (mm/hr) (1 st hour)	55.0 (40.0 – 60.0)	55.0 (40.0 – 75.0)	U 28 6.5	0.6 13
	CRP (mg/dl)	24.0 (12.0 – 25.0)	18.0 (13.0 – 38.3)	U 29 2.5	0.6 97
Serological domains	RF titre (IU/ml)	128. 0 (48.0 – 181.5)	50.4 (19.7 – 102.0)	U 24 2.5	0.0 86

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	Anti-CCP titre (IU/ml)	200.0 (107.75 – 250.0)	150.0 (29.5 – 287.0)	U = 262.0	0.326
Thyroid function tests	TSH (μIU/ml)	1.45 (1.105 – 2.305)	2.44 (1.62 – 3.9)	U = 204.5	0.036
	Normal	21(84%)	20 (80%)		
	Subclinical hypothyroid	3(12%)	4 (16%)	$\chi^2 = 0.167$	$p^M_c = 1.000$
	Subclinical hyperthyroid	1(4%)	1(4%)		
	FT3 (pg/ml)	3.2 ± 0.51	3.0 ± 0.49	t = 1.295	0.201
	FT4 (ng/dl)	1.3 ± 0.15	1.33 ± 0.18	t = 1.011	0.317
	ATG (IU/ml)	10.0 (10.0 – 16.45)	10.0 (1.25 – 28.75)	U = 266.0	0.354
	Negative ATG	23 (92.0%)	22(88.0%)	$\chi^2 = 0.222$	$p^{FE} = 1.000$

	Positive ATG	2 (8.0%)	3(12.0%)		
	ATPO (IU/ml)	2.1 (1.0 – 60.8)	3.6 (1.0 – 151.65)	U = 271.0	0.411
	Negative ATPO	18 (72.0%)	18 (72.0%)	$\chi^2 = 0.000$	1.000
	Positive ATPO	7(28.0%)	7 (28.0%)		
Thyroid US findings	Normal	23 (92%)	21(84%)	$\chi^2 = 3.424$	$p^M_c = 0.416$
	Grade 1	2(8%)	1(4%)		
	Grade 2	0	3(12%)		
TIRADS	No nodule	15(60%)	12(48%)		
	TIRADS 1	4(16%)	0(0%)	$\chi^2 = 8.788$	$p^M_c = 0.029$
	TIRADS 2	4(16%)	4(16%)		
	TIRADS 3	2(8%)	9(36%)		

Table (2): clinical, laboratory, thyroid gland assessment of group1 baseline and after 6 months after treatment

	Gro up 1 (Anti- TNF ther apy)	Gro up 1 (Anti- TNF ther apy)	Tes t of sig.
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Effect of anti-tumor necrosis factor (anti-TNF) alpha therapy versus conventional treatment on Thyroid Autoimmunity and function in Rheumatoid Arthritis patients

		(n=25) Before	(n=25) After		
Clinical data	Morning stiffness (min.)	60.0 (60.0 – 120.0)	10.0 (5.0 – 15.0)	4.378	<0.001*
	VAS for pain	8.0 (7.0 – 8.0)	2.0 (1.0 – 2.5)	4.424	<0.001*
	SJC	8.0 (4.5 – 10.0)	0.0 (0.0 – 2.0)	4.383	<0.001*
	TJC	12.0 (10.0 – 17.0)	2.0 (0.0 – 2.0)	4.378	<0.001*
	DAS 28	6.1 ± 0.75	2.8 ± 0.91	Paired t14.266	<0.001*
	MHAQ	1.25 (0.938 – 1.75)	0.9375 (0.375 – 2.03)	Z4.382	<0.001*
acute phase reactants	ESR (mm/hr) (1 st hour)	55.0 (40.0 – 60.0)	15.0 (10.0 – 20.0)	Z4.361	<0.001*

	CRP (mg/dl)	24.0 (12.0 – 25.0)	5.0 (3.0 – 6.5)	Z4.230	<0.001*
serological domains	RF titre (IU/ml)	128.0 (48.0 – 181.5)	64.0 (8.0 – 112.0)	Z3.060	0.002*
	Anti-CCP titre (IU/ml)	200.0 (107.75 – 250.0)	96.0 (51.95 – 165.5)	Z3.920	<0.001*
Thyroid function tests and autoantibodies	TSH (µIU/ml)	1.45 (1.105 – 2.305)	2.12 (1.385 – 3.19)	Z0.888	0.375
	FT3 (pg/ml)	3.2 ± 0.51	3.1 ± 0.50	Paired t0.915	0.369
	FT4 (ng/dl)	1.3 ± 0.15	1.2 ± 0.19	Paired t1.566	0.130
	Normal	21(84%)	25(100%)		
	Subclinical	3(12%)	0(0%)		

Effect of anti-tumor necrosis factor (anti-TNF) alpha therapy versus conventional treatment on Thyroid Autoimmunity and function in Rheumatoid Arthritis patients

	hypothyroid				
	Subclinical hyperthyroid	1(4%)	0(0%)		
	ATG (IU/ml)	10.0 (10.0 – 16.45)	10.0 (10.0 – 15.05)	z 0.931	0.352
	- Negative	23(92%)	23(92%)		
	- Positive	2(8%)	2(8%)		
	Anti ATPO (IU/ml)	2.1 (1.0 – 60.8)	1.0 (1.0 – 59.9)	z 2.158	0.031*
	- Negative	18(72%)	18(72%)		
	- Positive	7(28%)	7(28%)		

	ti v e				
Thyroid US findings	Normal	23(92%)	24(96%)	11.979	<0.001*
	Grade I	2(8%)	1(4%)		
TIRADS	No nodule	15(60%)	16(64%)		
	TIRADS 1	4(16%)	4(16%)	67.578	<0.001*
	TIRADS 2	4(16%)	3(12%)		
	TIRADS 3	2(8%)	2(8%)		

Table (3): clinical, laboratory, thyroid gland assessment of group 2 baseline and after 6 months after treatment

		Group 2 (conventional treatment) (n=23) Before	Group 2 (conventional treatment) (n=23) After	Test of p sig.	
Clinical data	Morning stiffness (min.)	60.0 (60.0 – 105.0)	15.0 (10.0 – 30.0)	4.203	<0.001*
	VAS for pain	7.0 (6.0 – 8.5)	3.0 (2.0 – 7.0)	3.909	<0.001*
	SJC	8.0 (4.0 – 9.0)	2.0 (0.0 – 6.0)	3.909	<0.001*

Effect of anti-tumor necrosis factor (anti-TNF) alpha therapy versus conventional treatment on Thyroid Autoimmunity and function in Rheumatoid Arthritis patients

	TJC	12.0 (10.0 – 15.5)	4.0 (2.0 – 10.0)	3.905	<0.001*
	DAS 28	6.3 ± 0.73	4.2 ± 1.58	Paired t 5.922	<0.001*
	MHAQ	1.25 (0.9375 – 2.125)	0.9375 (0.375 – 2.03)	Z 2.407	0.016*
acute phase reactants	ESR (mm/hr) (1 st hour)	55.0 (40.0 – 75.0)	28.0 (10.0 – 35.0)	Z 3.012	0.003*
	CRP (mg/dl)	18.0 (13.0 – 38.3)	12.0 (5.75 – 13.5)	Z 2.886	0.004*
serological domains	RF titre (IU/ml)	50.4 (19.7 – 102.0)	21.5 (12.0 – 64.0)	Z 1.550	0.121
	Anti-CCP titre (IU/ml)	150.0 (29.5 – 287.0)	125.0 (15.0 – 200.0)	Z 1.912	0.056
Thyroid function tests	TSH (µIU/ml)	2.44 (1.62 – 3.9)	2.2 (1.29 – 3.71)	Z 0.913	0.362
	FT3 (pg/ml)	3.0 ± 0.49	3.2 ± 0.62	Paired t 1.151	0.262
	FT4 (ng/dl)	1.33 ± 0.18	1.28 ± 0.17	Paired t	0.119

				1.623	
	Normal	20	20		
	Subclinical hypothyroid	3	3		
	Subclinical hyperthyroid	0	0		
	ATG (IU/ml)	10.0 (1.25 – 28.75)	10.0 (10.0 – 65.0)	Z 3.249	0.001*
	- Negative	20	19		
	- Positive	3	4		
	ATPO (IU/ml)	3.6 (1.0 – 151.65)	10.0 (1.0 – 98.8)	Z 2.485	0.013*
	- Negative	18(78.26%)	17(73.91%)		

Effect of anti-tumor necrosis factor (anti-TNF) alpha therapy versus conventional treatment on Thyroid Autoimmunity and function in Rheumatoid Arthritis patients

	ti v e				
	- P o s it i v e	5(21.7 4%)	6(26.0 9%)		
Thyr oid US findi ngs	Normal	21(91. 30%)	19(82. 61%)	14. 603	0.09 9
	Grade1	1(4.35 %)	3(13.0 4%)		
	Grade2	1(4.35 %)	0(0%)		
	Decrease in size	0(0%)	1(4.35 %)		
TIR ADS	No nodule	11(47. 83%)	10(43. 48%)	32. 453	<0. 001 *
Increase in size	TIRAD S 1	0(0%)	0(0%)		
	TIRAD S 2	4(17.3 9%)	4(17.3 9%)		
	TIRAD S 3	8(34.7 8%)	9(39.1 3%)		

Table (4): clinical, laboratory, thyroid gland assessment of the studied group 6 months after treatment

Group 1 (Anti -TNF therapy) (n=25)	Group 2 (Conven tional treatment) (n=23)	Test of sig nificance (p)
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Clinic al data	Morning stiffness (min.)	10.0 (5.0 – 15.0)	15.0 (10.0 – 30.0)	U 15 8.5	0.00 7*
	VAS	2.0 (1.0 – 2.5)	3.0 (2.0 – 7.0)	U 15 1.5	0.00 4*
	SJC	0.0 (0.0 – 2.0)	2.0 (0.0 – 6.0)	U 19 1.0	0.03 8*
	TJC	2.0 (0.0 – 2.0)	4.0 (2.0 – 10.0)	U 15 8.5	0.00 7*
	DAS 28	2.8 ± 0.91	4.2 ± 1.58	t 3.8 33	<0.0 01*
	MHA Q	0.937 5 (0.37 5 – 2.03)	0.9375 (0.375 – 2.03)	U 14 5.5	0.00 5*
acute phase reacta nts	ESR (mm/h r) (1 st hour)	15.0 (10.0 – 20.0)	28.0 (10.0 – 35.0)	15 9.0	0.00 8*
	CRP (mg/dl)	5.0 (3.0 – 6.5)	12.0 (5.75 – 13.5)	14 8.5	0.00 1*
serolo gical domai ns	RF titre (IU/ml)	64.0 (8.0 – 112.0)	21.5 (12.0 – 64.0)	24 3.0	0.35 1
	Anti- CCP titre	96.0 (51.9 5 – 200.0)	125.0 (15.0 – 200.0)	27 6.0	0.81 2

Effect of anti-tumor necrosis factor (anti-TNF) alpha therapy versus conventional treatment on Thyroid Autoimmunity and function in Rheumatoid Arthritis patients

	(IU/ml)	165.5)			
Thyroid function tests	TSH (μIU/ml)	2.12 (1.38 – 3.19)	2.2 (1.29 – 3.71)	U 27 3.0	0.76 5
	Normal	25 (100.0%)	20(87.0 %)	χ² 3.4 78	p^{FE} 0.10 2
	Subclinical hypothyroid	0(0.0 %)	3(13.0%)		
	FT3 (pg/ml)	3.1 ± 0.50	3.2 ± 0.62	t 0.4 18	0.67 8
	FT4 (ng/dl)	1.2 ± 0.19	1.28 ± 0.17	t 1.0 75	0.28 8
	ATG (IU/ml)	10.0 (10.0 – 15.05)	10.0 (10.0 – 65.0)	U 26 9.0	0.67 0
	Negative ATG	23 (92.0 %)	19(82.6 %)	χ² 0.9 66	p^{FE} 0.40 7
	Positive ATG	2 (8.0%)	4(17.4%)		

	ATPO (IU/ml)	1.0 (1.0 – 59.9)	10.0 (1.0 – 98.8)	U 22 2.0	0.16 0
	Negative ATPO	18(72.0%)	17(73.9 %)	χ² 0.0 22	p^{FE} 1.00 0
	Positive ATPO	7(28.0%)	6(26.1%)		
Thyroid US findings	Normal	24 (96.0 %)	19(82.6 %)		
	Grade 1	1 (4.0%)	0 (0.0%)	χ² 5.5 08	p^{MC} 0.07 2
	Grade 2	0 (0.0%)	3(13.0%)		
	Decrease in size	0 (0.0%)	1(4.3%)		
TIRADS	No nodule	16 (64.0 %)	10(43.5 %)		
Increase in size	TIRADS 1	4 (16.0 %)	0(0.0%)	χ² 9.9 16	p^{MC} 0.01 6*
	TIRADS 2	3(12.0%)	4(17.4%)		
	TIRADS 3	2(8.0 %)	9(39.1%)		