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Original Article

Thyroid Dysfunction in Rheumatoid Arthritis and its Association with Disease Activity: A Cross-Sectional Study from A Tertiary Care Hospital in Central India

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ABSTRACT

Objectives: To determine the prevalence of thyroid dysfunction in rheumatoid arthritis, and whether thyroid status is associated with disease activity.
Methods: Cross sectional study of 77 consecutive adults with rheumatoid arthritis (2010 American College of Rheumatology and European League against Rheumatism criteria) at a tertiary care hospital in central India. We measured thyroid stimulating hormone, free triiodothyronine and free thyroxine, and assessed disease activity with the Disease Activity Score-28.
Results: Thyroid dysfunction was present in 25 of 77 patients (32.5%, 95% confidence interval 23.1 to 43.5): subclinical hypothyroidism in 12 (15.6%), overt hypothyroidism in 10 (13.0%), and hyperthyroidism in 3 (3.9%). Disease activity was higher in these patients (Disease Activity Score-28 6.48 ± 0.48 versus 5.01 ± 0.67; mean difference 1.47, 95% confidence interval 1.21 to 1.73; $p < 0.001$). All 25 patients with thyroid dysfunction were in the high activity category, against 22 of 52 euthyroid patients (42.3%; Fisher exact $p < 0.001$). Tender joint count (13.6 ± 4.4 versus 5.9 ± 4.1) and duration of morning stiffness (85.3 ± 24.9 versus 50.6 ± 17.7 minutes) were also higher (both $p < 0.001$). Thyroid stimulating hormone correlated with the score ($r = 0.420$, $p < 0.001$). Thyroid dysfunction was not associated with age ($p = 0.387$), sex ($p = 0.090$) or disease duration ($p = 0.508$).
Conclusions: One in three patients had thyroid dysfunction, and it tracked closely with disease activity while showing no relation to age, sex or disease duration. Thyroid function should be tested in every patient with rheumatoid arthritis.

Keywords: *Arthritis, Rheumatoid; Thyroid Diseases; Hypothyroidism; Thyrotropin; Severity of Illness Index; India.*

INTRODUCTION

Rheumatoid arthritis is a chronic autoimmune disease that causes persistent synovitis and progressive joint damage. Population surveys carried out in India have reported a prevalence of between 0.28 and 0.7 per cent.[1]

Autoimmune thyroid disease and rheumatoid arthritis have a similar immunopathology. Both involve a loss of self tolerance, autoreactive T cells and autoantibody production, and both are linked to overlapping genetic susceptibility.[2] The two conditions occur together more often than would be expected by chance. A Mendelian randomisation study reported that this relationship is causal in both directions: genetic liability to rheumatoid arthritis raised the risk of hypothyroidism (odds ratio 1.28), and hypothyroidism raised the risk of rheumatoid arthritis (odds ratio 1.68).[3]

Thyroid dysfunction is easily overlooked in these patients. Hypothyroidism causes fatigue, myalgia, stiffness and a raised erythrocyte sedimentation rate, all of which are also features of active rheumatoid arthritis.[4] A patient whose disease activity score is rising may therefore be given further immunosuppression when thyroxine is what is needed. The systemic inflammation of rheumatoid arthritis may in turn disturb thyroid function.[2]

Reported prevalences of thyroid dysfunction in rheumatoid arthritis range from about 15 to 38 per cent, and there is no agreement on whether thyroid status affects disease activity.[6] Some studies have found higher disease activity in patients with thyroid dysfunction.[7,8] Others have found no association.[9] Part of this variation is likely to be methodological, but iodine intake, genetic background and treatment patterns also differ between the populations studied.

Indian data are limited. The available studies are small and single centre, and most report prevalence without examining the relationship between thyroid function and disease activity.

We therefore set out to measure the prevalence of thyroid dysfunction among patients with rheumatoid arthritis attending a tertiary care hospital in central India, and to examine whether thyroid status is associated with disease activity and with demographic and disease characteristics.

MATERIALS AND METHODS

Study design and setting

We conducted a single centre, hospital based, cross sectional study in the department of general medicine of a tertiary care teaching hospital in central India. Patients were recruited consecutively from outpatient and inpatient services over a 12 month period.

Participants

We enrolled 77 consecutive adults with rheumatoid arthritis. Eligible patients were aged over 18 years, of either sex, and satisfied the 2010 classification criteria of the American College of Rheumatology and the European League Against Rheumatism.[10] Those criteria score four domains: joint distribution, serology, symptom duration, and acute phase reactants, with a total of six points or more classifying definite rheumatoid arthritis.

We excluded patients taking any drug known to disturb thyroid function, such as lithium, interferon alfa, or amiodarone; patients with evidence of malignancy; patients with any pre-existing autoimmune disease other than rheumatoid arthritis and hypothyroidism; patients with a collagen vascular disease other than rheumatoid arthritis; and patients unwilling to give informed consent.

Sample size

We calculated the sample size for a single proportion from the formula $n = Z^2 \times p \times (1 - p) / d^2$, where Z is 1.96 for 95 per cent confidence, p is the anticipated prevalence, and d is the absolute precision. We took p as 38.4 per cent, the prevalence of hypothyroidism reported by Joshi and colleagues among 52 patients with rheumatoid arthritis at a tertiary care centre in the same state as our own.[7] With an absolute precision of 11 per cent this gave $n = (1.96)^2 \times 0.384 \times 0.616 / (0.11)^2 = 75.1$, so 76 patients were required. We enrolled 77.

Assessment of thyroid function

We drew 5 ml of venous blood from each participant under aseptic precautions, centrifuged it, and separated and stored the serum until analysis. Thyroid stimulating hormone, free triiodothyronine and free thyroxine were measured by automated immunoassay. The reference intervals used were 0.27 to 4.2 mIU/l for thyroid stimulating hormone, 3.1 to 6.8 pmol/l for free triiodothyronine, and 12.0 to 22.0 pmol/l for free thyroxine.

We classified thyroid status as follows. Euthyroid: normal thyroid stimulating hormone, free triiodothyronine and free thyroxine. Subclinical hypothyroidism: raised thyroid stimulating hormone with normal free thyroxine. Overt hypothyroidism: raised thyroid stimulating hormone with low free thyroxine. Subclinical hyperthyroidism: suppressed thyroid stimulating hormone with normal free thyroxine. Overt hyperthyroidism: suppressed thyroid stimulating hormone with raised free thyroxine.

Assessment of disease activity

Every patient underwent general physical and detailed rheumatological examination. We assessed disease activity with the Disease Activity Score-28, calculated as 0.56 multiplied by the square root of the tender joint count, plus 0.28 multiplied by the square root of the swollen joint count, plus 0.70 multiplied by the natural logarithm of the erythrocyte sedimentation rate, plus 0.014 multiplied by the patient global assessment on a visual analogue scale of 0 to 100.[11] The 28 joints assessed were the shoulders, elbows, wrists, metacarpophalangeal joints one to five, proximal interphalangeal joints one to five, and knees, bilaterally. We categorised disease activity as remission at 2.6 or below, low activity from 2.6 to 3.1, moderate activity from 3.2 to 5.1, and high activity above 5.1.

Other investigations
We measured the erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor, haemoglobin, and total leucocyte count in all participants. We defined anaemia as a haemoglobin below 12 g/dl in women and below 13 g/dl in men. Anti-thyroid peroxidase antibody was measured in a subset of 22 patients only, and we report it separately for that reason.

Data collection
We collected data on a structured case record proforma covering socio-demographic details, clinical history, examination findings, joint counts, laboratory results, disease activity, and thyroid status. Each participant was given a unique reference number. Paper forms were held in a locked cabinet and electronic data on a password protected computer.

Statistical analysis
We summarised continuous variables as mean and standard deviation, and categorical variables as counts with percentages. We compared continuous variables between two groups with the Welch t test, which does not assume equal variances between groups of unequal size. We compared proportions with the chi-squared test, and used the Fisher exact test wherever any expected cell count fell below five, which was the case for every comparison involving the 12 men and the 3 patients with hyperthyroidism. We examined the association between thyroid function and disease activity with the Spearman rank correlation coefficient, because the distribution of thyroid stimulating hormone was markedly skewed. Confidence intervals for proportions were calculated by the Wilson score method. A p value below 0.05 was taken as statistically significant. Analyses were performed in R version 4.5.2.

Ethics
The institutional ethics committee approved the study before recruitment began (reference LNMC&RC/Dean/2024/Ethics/288), and we obtained written informed consent from every participant.

RESULTS

Baseline characteristics
We studied 77 patients. Their mean age was 46.78 ± 11.06 years, and 38 of them (49.4%) were aged between 36 and 50 years. Sixty five (84.4%) were women, giving a ratio of women to men of 5.4 to 1. Fifty two (67.5%) lived in urban areas and 43 (55.8%) were of middle socioeconomic status. Mean disease duration was 44.21 ± 33.38 months, and 32 patients (41.6%) had been ill for between two and five years. Every patient had joint pain, 73 (94.8%) had morning stiffness, 68 (88.3%) had joint swelling, and 57 (74.0%) reported fatigue. Both small and large joints were involved in 51 patients (66.2%). Table 1 gives the full baseline profile.

Inflammatory markers were raised in most patients. The erythrocyte sedimentation rate exceeded 20 mm/h in 68 patients (88.3%), C-reactive protein was positive in 58 (75.3%), and rheumatoid factor was positive in 62 (80.5%). Sixty patients (77.9%) were anaemic. Disease activity was high throughout the cohort: the mean Disease Activity Score-28 was 5.49 ± 0.92, with 47 patients (61.0%) in the high activity category and 30 (39.0%) in the moderate category. No patient was in remission or in the low activity category.

Table 1: Baseline demographic, clinical, disease activity and laboratory characteristics of the study population

Characteristic	Value
Demographic characteristics	
Age, years, mean ± SD	46.78 ± 11.06
Age, years, range	24–68
18–35 years	12 (15.6)
36–50 years	38 (49.4)
51–65 years	22 (28.6)
More than 65 years	5 (6.5)
Female	65 (84.4)
Male	12 (15.6)
Urban residence	52 (67.5)
Rural residence	25 (32.5)
Socio-economic status, lower	18 (23.4)
Socio-economic status, middle	43 (55.8)
Socio-economic status, upper	16 (20.8)
Disease characteristics	
Duration of disease, months, mean ± SD	44.21 ± 33.38
Duration of disease, months, range	6–140
Less than 2 years	28 (36.4)
2–5 years	32 (41.6)
More than 5 years	17 (22.1)

Joint pain	77 (100)
Morning stiffness	73 (94.8)
Joint swelling	68 (88.3)
Fatigue	57 (74.0)
Loss of appetite	45 (58.4)
Small joints only	18 (23.4)
Large joints only	8 (10.4)
Both small and large joints	51 (66.2)
Disease activity	
Tender joint count (28 joints), mean ± SD (range)	8.45 ± 5.52 (0–23)
Swollen joint count (28 joints), mean ± SD (range)	4.69 ± 3.03 (0–15)
Patient global assessment (visual analogue scale 0–100), mean ± SD (range)	59.98 ± 16.38 (23–95)
Disease Activity Score-28, mean ± SD (range)	5.49 ± 0.92 (3.18–7.61)
Remission (2.6 or less)	0 (0.0)
Low (2.6–3.1)	0 (0.0)
Moderate (3.2–5.1)	30 (39.0)
High (more than 5.1)	47 (61.0)
Laboratory investigations	
Haemoglobin, g/dL, mean ± SD	10.64 ± 1.64
Anaemia	60 (77.9)
Erythrocyte sedimentation rate, mm/h, mean ± SD	45.83 ± 21.35
Elevated (more than 20 mm/h)	68 (88.3)
C-reactive protein, positive	58 (75.3)
Rheumatoid factor, positive	62 (80.5)
Total leucocyte count, cells/mm³, mean ± SD	8336 ± 2438
Anti-thyroid peroxidase antibody, positive*	11 of 22 tested

*Values are n (%) unless otherwise stated. SD = standard deviation. Anaemia defined as haemoglobin below 12 g/dl in women and below 13 g/dl in men. *Anti-thyroid peroxidase antibody was measured in only 22 of the 77 patients.*

Prevalence of thyroid dysfunction

Twenty five of the 77 patients had thyroid dysfunction (32.5%, 95% confidence interval 23.1 to 43.5) and 52 (67.5%) were euthyroid. Hypothyroidism accounted for almost all of it, affecting 22 patients (28.6%, 95% confidence interval 19.7 to 39.5): 12 (15.6%) had subclinical hypothyroidism and 10 (13.0%) had overt hypothyroidism. Hyperthyroidism was uncommon, occurring in 3 patients (3.9%, 95% confidence interval 1.3 to 10.8), of whom 2 had overt and 1 had subclinical disease. Mean thyroid stimulating hormone was 2.19 ± 0.71 mIU/l in euthyroid patients and 9.01 ± 5.21 mIU/l in those with thyroid dysfunction. Table 2 sets out the thyroid function values by group.

Table 2: Thyroid function status and thyroid function test values

Thyroid status	N (%)	Thyroid stimulating hormone, mIU/l	Free triiodothyronine, pmol/l	Free thyroxine, pmol/l
Euthyroid	52 (67.5)	2.19 ± 0.71	4.64 ± 0.85	15.95 ± 2.50
Any thyroid dysfunction	25 (32.5)	—	—	—
Hypothyroidism, total	22 (28.6)	10.22 ± 4.28*	4.45 ± 0.97*	13.53 ± 3.24*
Subclinical hypothyroidism	12 (15.6)	7.43 ± 2.45*	4.88 ± 0.97*	15.88 ± 2.25*
Overt hypothyroidism	10 (13.0)	13.57 ± 3.54*	3.94 ± 0.71*	10.71 ± 1.48*
Hyperthyroidism, total	3 (3.9)	0.16 ± 0.03*	6.51 ± 1.53*	23.38 ± 5.48*
Subclinical hyperthyroidism	1 (1.3)	0.13	4.75	17.09
Overt hyperthyroidism	2 (2.6)	0.17 ± 0.02*	7.39 ± 0.18*	26.52 ± 0.90*
Reference range	—	*0.27–4.20*	*3.1–6.8*	*12.0–22.0*

*Thyroid function values are mean ± SD. *p < 0.05 compared with the euthyroid group by Welch t test. The subclinical hyperthyroid group contains a single patient, so no SD is given.*

Thyroid dysfunction and demographic and disease characteristics

Thyroid dysfunction showed no association with any demographic or disease variable we examined. It was present in 24 of 65 women (36.9%) and 1 of 12 men (8.3%), a difference that did not reach significance (Fisher exact p = 0.090). It was present in 4 of 12 patients aged 18 to 35 years (33.3%), 15 of 38 aged 36 to 50 years (39.5%), 4 of 22 aged 51 to 65 years

(18.2%), and 2 of 5 aged over 65 years (40.0%), with no gradient across age bands (p = 0.387). Nor did it vary with disease duration: 7 of 28 patients ill for under two years (25.0%), 11 of 32 ill for two to five years (34.4%), and 7 of 17 ill for over five years (41.2%) had thyroid dysfunction (p = 0.508). Table 3 gives these comparisons.

Table 3: Association of thyroid dysfunction with demographic and disease characteristics

Variable	Euthyroid, n (%)	Thyroid dysfunction, n (%)	p value
Gender			
Female (n = 65)	41 (63.1)	24 (36.9)	0.090
Male (n = 12)	11 (91.7)	1 (8.3)	
Age group			
18–35 years (n = 12)	8 (66.7)	4 (33.3)	0.387
36–50 years (n = 38)	23 (60.5)	15 (39.5)	
51–65 years (n = 22)	18 (81.8)	4 (18.2)	
More than 65 years (n = 5)	3 (60.0)	2 (40.0)	
Duration of disease			
Less than 2 years (n = 28)	21 (75.0)	7 (25.0)	0.508
2–5 years (n = 32)	21 (65.6)	11 (34.4)	
More than 5 years (n = 17)	10 (58.8)	7 (41.2)	

Percentages are row percentages. Sex compared by Fisher exact test because one expected cell count was below five; age group and disease duration by chi-squared test.

Thyroid dysfunction and disease activity

Disease activity was higher in patients with thyroid dysfunction. The mean Disease Activity Score-28 was 6.48 ± 0.48 in the 25 patients with thyroid dysfunction against 5.01 ± 0.67 in the 52 euthyroid patients, a difference of 1.47 (95% confidence interval 1.21 to 1.73; p < 0.001). Every one of the 25 patients with thyroid dysfunction fell into the high activity category, compared with 22 of the 52 euthyroid patients (42.3%). Not one patient with thyroid dysfunction had merely moderate disease, whereas 30 euthyroid patients (57.7%) did (Fisher exact p < 0.001).

Every individual measure of disease activity moved in the same direction. Comparing the 52 euthyroid patients with the 22 who were hypothyroid, the tender joint count was 5.94 ± 4.07 against 13.55 ± 4.55 (p < 0.001), the swollen joint count 3.90 ± 2.61 against 6.00 ± 2.67 (p = 0.004), the erythrocyte sedimentation rate 40.96 ± 19.31 against 55.55 ± 21.86 mm/h (p = 0.010), the patient global assessment 54.62 ± 14.99 against 69.88 ± 13.17 (p < 0.001), and, among the patients who reported morning stiffness, its duration 50.57 ± 17.70 against 85.29 ± 24.94 minutes (p < 0.001). Table 4 gives these comparisons in full.

Thyroid stimulating hormone correlated positively with the Disease Activity Score-28 (Spearman r = 0.420, p < 0.001). It did not correlate with the erythrocyte sedimentation rate (r = 0.151, p = 0.190). Neither free triiodothyronine nor free thyroxine correlated with either measure of disease activity (all p > 0.09). Table 5 gives the correlation coefficients.

Disease activity did not differ significantly between the 12 patients with subclinical hypothyroidism (Disease Activity Score-28 6.33 ± 0.40) and the 10 with overt hypothyroidism (6.57 ± 0.50; p = 0.243).

Table 4: Disease activity and inflammatory markers according to thyroid status

Distribution of disease activity category			
Disease Activity Score-28 category	**Euthyroid (n = 52), n (%)**	**Thyroid dysfunction (n = 25), n (%)**	**p value**
Remission	0 (0.0)	0 (0.0)	< 0.001
Low	0 (0.0)	0 (0.0)	
Moderate	30 (57.7)	0 (0.0)	
High	22 (42.3)	25 (100)	
Disease activity and inflammatory markers, euthyroid versus hypothyroid patients			
Parameter	**Euthyroid (n = 52)**	**Hypothyroid (n = 22)**	**p value**
Disease Activity Score-28	5.01 ± 0.67	6.44 ± 0.46	< 0.001
Tender joint count	5.94 ± 4.07	13.55 ± 4.55	< 0.001
Swollen joint count	3.90 ± 2.61	6.00 ± 2.67	0.004
Erythrocyte sedimentation rate, mm/h	40.96 ± 19.31	55.55 ± 21.86	0.010
Patient global assessment	54.62 ± 14.99	69.88 ± 13.17	< 0.001
Duration of morning stiffness, min†	50.57 ± 17.70	85.29 ± 24.94	< 0.001
C-reactive protein positive, n (%)	42 (80.8)	14 (63.6)	0.143
Fatigue, n (%)	33 (63.5)	21 (95.5)	0.004

Values are mean ± SD unless otherwise stated. Percentages in the upper section are column percentages. Continuous variables compared by Welch t test; proportions by Fisher exact test. Categories compared by Fisher exact test. †Duration of morning stiffness is given for the 49 euthyroid and 21 hypothyroid patients who reported morning stiffness.

Clinical symptoms

Symptoms characteristic of hypothyroidism were commoner in hypothyroid patients. Cold intolerance affected 8 of 52 euthyroid patients (15.4%), 7 of 12 with subclinical hypothyroidism (58.3%), and 6 of 10 with overt hypothyroidism (60.0%) ($p < 0.001$). Constipation and dry skin followed the same pattern (both $p \leq 0.003$). Fatigue affected 33 of 52 euthyroid patients (63.5%), all 12 with subclinical hypothyroidism, and 9 of 10 with overt hypothyroidism (90.0%) ($p = 0.016$). Weight gain and hair loss did not differ between the groups ($p = 0.435$ and $p = 0.396$). Table 5 gives the symptom comparisons.

Table 5: Clinical symptoms by thyroid status, and correlation of thyroid function with disease activity

Clinical symptoms				
Symptom	**Euthyroid (n = 52), n (%)**	**Subclinical hypothyroid (n = 12), n (%)**	**Overt hypothyroid (n = 10), n (%)**	**p value**
Fatigue	33 (63.5)	12 (100)	9 (90.0)	0.016
Loss of appetite	30 (57.7)	7 (58.3)	7 (70.0)	0.765
Cold intolerance	8 (15.4)	7 (58.3)	6 (60.0)	< 0.001
Constipation	8 (15.4)	9 (75.0)	6 (60.0)	< 0.001
Dry skin	20 (38.5)	10 (83.3)	8 (80.0)	0.003
Weight gain	13 (25.0)	5 (41.7)	2 (20.0)	0.435
Hair loss	20 (38.5)	6 (50.0)	6 (60.0)	0.396
Correlation of thyroid function with disease activity (Spearman rank, n = 77)				
Thyroid parameter	**Disease Activity Score-28, r**	**p value**	**Erythrocyte sedimentation rate, r**	**p value**
Thyroid stimulating hormone	0.420	< 0.001	0.151	0.190
Free triiodothyronine	-0.071	0.538	-0.155	0.179
Free thyroxine	-0.193	0.093	0.033	0.776

Percentages are within-group percentages; symptom p values from the chi-squared test across the three groups. Spearman rank correlation is used because the distribution of thyroid stimulating hormone is markedly skewed.

Anti-thyroid peroxidase antibody

Anti-thyroid peroxidase antibody was measured in 22 of the 77 patients, of whom 11 were positive. Positivity was concentrated in patients with abnormal thyroid function: all 7 patients with subclinical hypothyroidism who were tested were positive, as were 2 of the 7 tested with overt hypothyroidism and 2 of the 3 tested with hyperthyroidism, while none of the 5 euthyroid patients tested was positive. Because testing was not performed in the whole cohort and appears to have been directed at patients whose thyroid biochemistry was already abnormal, we cannot express this as prevalence and we draw no inference from it.

DISCUSSION

Thyroid dysfunction was present in one third of our patients and was associated with substantially higher disease activity. Every one of the 25 patients with thyroid dysfunction had high disease activity, compared with 22 of 52 euthyroid patients (42.3%), and not one had merely moderate disease. Thyroid dysfunction was not, however, associated with age, sex or disease duration. Screening for it therefore cannot be limited to any particular demographic group.

Our prevalence of 32.5 per cent sits within the published range, which runs from about 15 to 38 per cent. A meta-analysis of 29 studies and 35,708 patients found rheumatoid arthritis to carry roughly double the odds of hypothyroidism, with a pooled odds ratio of 2.25.[6] Individual series report 38.4 per cent among 52 patients in Indore, in our own state,[7] 32 per cent among 350 patients in Iran,[5] 25.3 per cent among 400 newly diagnosed patients compared with 11.5 per cent in matched controls,[12] and 15.7 per cent in a Danish cohort of 439.[13] As in almost all of these, hypothyroidism dominated and hyperthyroidism was rare, and subclinical hypothyroidism was the single commonest abnormality.

Our finding of an association with disease activity is consistent with most, though not all, of the published work. A series of 250 patients reported significantly higher disease activity in those with thyroid dysfunction, although the swollen joint count did not differ between groups.[8] The Indore study found that thyroid stimulating hormone correlated with both the erythrocyte sedimentation rate and the Disease Activity Score-28.[7] A Pakistani series reached a similar conclusion,[14] and in a Danish cohort of newly diagnosed patients thyroid disorders predicted a poorer initial response to treatment.[13]

In contrast, a case-control study of 58 women found no relationship between thyroid abnormality and disease activity.[9] Our results support a real association, and the effect size was large: every patient with thyroid dysfunction had high disease activity, against fewer than half of those who were euthyroid. Unlike the series of 250 patients, we found that the swollen joint count did differ significantly between groups.

Two of our findings differ from earlier reports. First, thyroid dysfunction was not associated with age, sex or disease duration. In subgroup analysis, the meta-analysis found a higher risk of subclinical hyperthyroidism in patients aged over 50 years.[6] Our cohort contained only 5 patients aged over 65 years and only 12 men, so our negative results for age and sex reflect an absence of evidence rather than evidence of absence. The negative result for disease duration is on firmer ground, as those subgroups were of adequate size. Second, thyroid stimulating hormone correlated with the Disease Activity Score-28 but not with the erythrocyte sedimentation rate, whereas the Indore study reported correlations with both.[7] The erythrocyte sedimentation rate is one of the four components of the score, so the two correlations would be expected to move together. That they did not suggests that the association is driven more by the joint counts and the patient global assessment than by the acute phase response.

A plausible mechanism exists in either direction, or a cross sectional study cannot distinguish between them. Rheumatoid arthritis and autoimmune thyroid disease share genetic susceptibility and the same pro-inflammatory cytokines.[2,6] Thyroid hormones modulate immune function, so hypothyroidism may amplify systemic inflammation. Alternatively, sustained inflammation in rheumatoid arthritis may suppress thyroid function. Mendelian randomisation supports causation in both directions.[3] Our data demonstrate association only, and we make no causal claim.

Our symptom data explain why thyroid function should be tested at diagnosis rather than when clinical suspicion arises. Fatigue was present in 21 of our 22 hypothyroid patients, and cold intolerance, constipation and dry skin were all significantly commoner in them. Each of these features, however, is also produced by active rheumatoid arthritis or is common in the general population, so symptoms alone cannot reliably identify which patients have thyroid dysfunction. This is of particular importance when the disease activity score is rising, since the decision between increasing immunosuppression and starting thyroxine cannot be made on clinical grounds alone.

LIMITATIONS

This study has several limitations. It was cross sectional, so we can demonstrate association but not sequence or cause. There was no control group, so we cannot determine whether thyroid dysfunction is commoner in rheumatoid arthritis than in the general population. The study was conducted at a single tertiary care centre, which may select for more severe disease and limits generalisability. The sample of 77 patients was small for subgroup analysis, and with only 12 men and 3 patients with hyperthyroidism these comparisons were underpowered.

Four further limitations should be noted. Anti-thyroid peroxidase antibody was measured in only 22 patients, and appears to have been requested selectively in those whose thyroid biochemistry was already abnormal, so it cannot support any conclusion about autoimmune overlap in this cohort. We did not record the use of glucocorticoids or disease-modifying antirheumatic drugs; glucocorticoids suppress thyroid stimulating hormone secretion and are therefore a potential confounder of our main exposure. Anti-cyclic citrullinated peptide antibody was not measured. Finally, we performed no multivariable adjustment, so all the associations we report are unadjusted. Our sample size was calculated from the prevalence of hypothyroidism rather than of all thyroid dysfunction, which is a further minor limitation.

CONCLUSION

Thyroid dysfunction was present in 25 of 77 patients with rheumatoid arthritis (32.5%), and hypothyroidism accounted for almost all of it. Patients with thyroid dysfunction had substantially higher disease activity than euthyroid patients, and none achieved remission. Because thyroid dysfunction was not predicted by age, sex or disease duration, screening cannot be restricted to any demographic subgroup. We recommend that thyroid function be tested in every patient with rheumatoid arthritis at diagnosis.

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Conflicts of interest: none declared

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