Original Article

Study on disease activity of immunological disorders to correlate with thyroid function and other associated correlations

Akash Pawar[1], Prakash Joshi[2], Abhishek Singhai[1]

[1]Department of General Medicine, AIIMS, Bhopal, Madhya Pradesh, India, [2]Department of Medicine, Sri Aurobindo Institute of Medical Sciences and PGI, Indore, Madhya Pradesh, India

Abstract

Background: Organ-specific immunological disorders involving organ/gland like the thyroid, liver, muscles, pancreas, etc., is a result of autoimmunity which can be with or without association with systemic immunological disorders. The thyroid gland is most commonly involved. We evaluated thyroid dysfunction and ESR among various immunological disorders and their correlation with disease activity and hemoglobin respectively. **Material and Methods:** A cross-sectional/observational study was conducted by including 110 patients with different immunological disorders who came in as in-patients and outpatients in our institute for 18 months and various data were collected and evaluated to analyze the targeted parameters among the study group. **Results:** We found a positive correlation between disease activity and thyroid dysfunction in different immunological disorders (only in Rheumatoid arthritis [$P = 0.004$) and Systemic lupus erythematosus (0.009) and not in other immunological disorders] among the study group. A positive correlation was found between ESR (Mean value – 19.63 and Standard Deviation (SD) – 09.473) and disease activity (only in Rheumatoid arthritis $P = 0.0001$) where a negative correlation was found between ESR and Hemoglobin (Mean value – 11.07 and SD – 01.91 ($P = 0.001$) in patients under study. **Conclusion:** Our study demonstrated a positive correlation between thyroid dysfunction and ESR with disease activity, whereas demonstrated a negative correlation between ESR and Hemoglobin in patients with various immunological disorders under study.

Keywords: Anemia, disease activity index, erythrocyte sedimentation rate, immunological disorders, thyroid function

Introduction

Autoimmunity is a result of an abnormal immune response to antigens either by itself or from an external source, which occurs in individuals due to the breakdown of immune regulatory mechanisms tolerability, resulting in possible tissue damage by self-reactivity. Examples of systemic immunological disorders are systemic lupus erythematosus, Ankylosing spondylitis, Systemic sclerosis, Rheumatoid arthritis, etc.[1] Examples of organ-specific autoimmune disorders – Autoimmune thyroiditis, hepatitis, pancreatitis, myasthenia gravis, Type-1 diabetes mellitus, multiple sclerosis, autoimmune hemolytic anemia, etc. These autoimmune disorders (either systemic or organ-specific) can be present in affected patients either alone or in various combinations/overlap among them. Systemic autoimmune disorders can cause or can be associated organ specific autoimmune involvement. The thyroid gland is most commonly involved.

The thyroid gland is a major gland in the endocrine system of the human body and among various etiologies, immunological mechanism is one of the important causes of thyroid gland dysfunction which can present with or without systemic

Address for correspondence: Dr. Akash Pawar, Department of Trauma and Emergency Medicine, AIIMS, Bhopal, Madhya Pradesh, India.
E-mail: pawarakash4141@gmail.com

Received: 25-06-2023 **Revised:** 04-09-2023
Accepted: 07-09-2023 **Published:** 04-04-2024

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_1053_23

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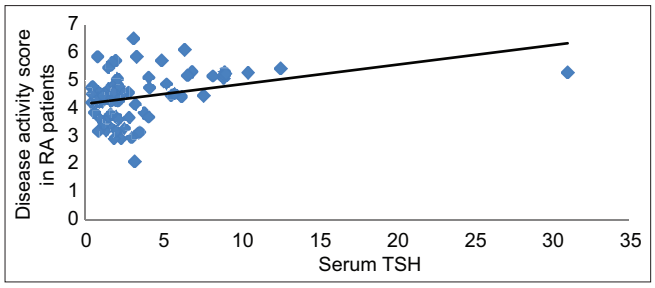
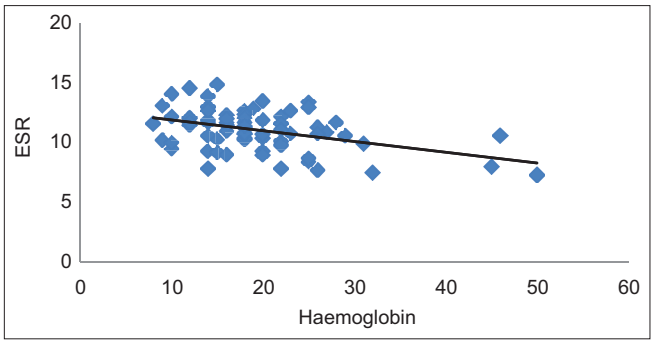
How to cite this article: Pawar A, Joshi P, Singhai A. Study on disease activity of immunological disorders to correlate with thyroid function and other associated correlations. J Family Med Prim Care 2024;13:896-902.



Graph 1: Correlation between TSH and DAS in RA patients



Graph 2: Correlation between ESR and Hemoglobin. A negative correlation was found between ESR and Hemoglobin in the study group

immunological disorders. Autoimmunity involvement of the thyroid gland can cause an increase in thyroid function (Hyperthyroidism) or a decrease/deficiency of thyroid function (Hypothyroidism) by destruction of the thyroid gland.[2]

Systemic or organ-specific autoimmune disorders do have different disease activity responses during the disease course which can be evaluated/demonstrated by various disease activity scores for individual autoimmune disorders. These disease activity scores are important to assess disease activity in patients. Rheumatoid arthritis disease activity score can be assessed by DAS-28-ESR,[2] similarly Systemic lupus erythematosus (SLE) can be assessed by SLE disease activity Index (SLEDAI), for Systemic sclerosis – DAS28-ESR/DAS28-CRP/Simplified disease activity index/Clinical disease activity index, for Ankylosing spondylitis- Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and similar individual scoring index for other autoimmune disorders.

Autoimmunity can involve and cause various tissue/gland destruction and is known to involve and cause thyroid dysfunction with or without associated systemic autoimmune disorder. There are various studies, and literature in the past that evaluated, analyzed, and demonstrated the thyroid gland dysfunction in various individual systemic autoimmune disorders and its association/correlation with disease activity which can cause hypofunctioning or hyperfunctioning of the thyroid gland.[3]

Considering the fact/data that autoimmunity plays a vital role in the pathophysiology of both systemic immunological disorders and organ-related immunological disorders, especially of the thyroid gland and its dysfunction. We did a study on 110 patients with various immunological disorders to estimate and analyze the thyroid function in systemic immunological disorder patients and their disease activity correlations.

Thyroid dysregulation in systemic immunological disorder is considered the most common type of organ-specific immunological disorder.[4]

Methods and Materials

Source of study group

This study is based on the patients who came as outpatients or admitted as in-patients for medical conditions in internal medicine and associated departments in our institute for the study duration of 18 months.

Study design and patient selection

This was a cross-sectional and observational type of study. We have screened 282 patients from outpatient and inpatient departments among which we only included 110 patients who met the diagnostic/classification criteria for their respective diseases, all patients who have met definite diagnostic criteria were included in the study who are newly diagnosed or known cases of systemic immunological disorder or those with clinical and biological features suggestive of systemic immunological disease. The study has been approved by the ethical committee of our institute and written informed consent was taken from all participants under study.

Inclusion criteria

Patients who are newly diagnosed/known cases of systemic immunological disorder and patients with clinical features, and biochemical markers suggestive of systemic immunological disorder. Female and male of age equal to or more than 18 years. Patients who gave written consent for participation in the study.

Exclusion criteria

Patient with known/isolated diagnosed case of any thyroid disorders. Patients who were taking medication that might be affecting their thyroid function. Patients who are known cases of chronic non-immunological systemic disease. Patients who did not give written consent to participate in the study.

Study protocol

All patients and collected patient data in the study group underwent detailed clinical history, physical examination, analysis, and necessary investigations. The study has been approved by the ethical committee of our institute and written informed consent was taken from all participants under study.

Karl pearson correlation test

The Pearson correlation coefficient, often referred to as the Pearson R test, is a statistical formula that measures the strength

between variables and relationships. To determine how strong the relationship is between variables, you need to find the coefficient value, which can range between −1 to +1.[5,6]

Clinical methods and techniques for data collection

a. Disease activity [Table1]:

1) DAS-28-ESR for Rheumatoid arthritis:[3]
   The DAS-28-ESR is a score developed and validated by the EULAR (European League Against Rheumatism) to measure the progress and improvement of RA. DAS-28-ESR is often used in clinical trials for the development of RA.
   'DAS 28 = 0.56 √TJC + 0.28 √SJC + 0.70 (log ESR) + 0.014 GH' Where –
   TJC - Tender Joint Count, SJC - Swollen Joint Count, GH- General Health status as assessed by the patient on a Visual Analog Scale (VAS), subjective assessment with a scale between 0–100 (10) as 0 is no activity and 10 being highest activity possible.
   "28" describes the number of different joints including in the measurement: proximal interphalangeal joints (10 joints), metacarpophalangeal joints (10), wrists (2), elbows (2), shoulders (2), knees (2). When looking at these joints, both the number of joints with tenderness upon touching and swelling are counted. In addition, the erythrocyte sedimentation rate is measured.
2) BASDAI for Ankylosing spondylitis[7] -
   BASDAI is used to assess the disease activity. It consists of six questions related to fatigue (Ql), spine pain (Q2), joint pain/swelling (Q3), enthesopathy (Q4) intensity (Q5), and duration (Q6) of morning stiffness.
3) SLEDAI for Systemic lupus erythematosus (SLE)[8] - It is used to assess disease activity.
4) DAS-28-ESR for Systemic sclerosis (SSc)[9]- DAS-28-ESR is best score to assess disease activity among DAS28-ESR, DAS28-CRP, Simplified disease activity index, Clinical disease activity index. Although there is no definite disease activity score for SSc.[10]
5) Disease activity in polymyositis is assessed by a Health Questionnaire survey
   (SF-36), MYOACT.

Clinical/biological technique and methods

CBC - done by Beckman-Coulter automated analysis method via coulter LH 750 analyzer. The Diluent used is LH-750, differential pack, series pack, and cleaning reagent.[11] Normal value male hemoglobin – 13–17 gm%. Normal value female hemoglobin – 11.5–15.5 gm%.

ESR - Wintrobe method was used to calculate the ESR of patients in the study, transported in EDTA sample vial[12] and age and gender factors were considered while estimating the ESR - Normal value male – 0–9 mm/hr and normal value female – 0–20 mm/hr. ESR level was not used separately to estimate disease activity/remission, but along with disease activity score for individual diseases whenever it's applicable for the same.

Thyroid profile

T3, T4, and TSH samples were taken after eight hours of fasting, which was then ultracentrifuge. Evaluations were done by a solid phase competitive chemiluminescent enzyme immunoassay viz immulite/immulite 1000 – elecsys 2010 fully automated analyzer.[13]

Quantitative determination of T3, T4, and TSH was done by enzyme-linked immunosorbent assay. Normal value: TSH - 0.35–5.5 uIU/mKL, T3-0.8–2.0 ng/ml, T4-5.1–14.1 ug/dl.

Statistical analysis

The data from the customized proforma was entered into the Microsoft Excel sheet and then transferred to the relevant statistical software package for analysis (SPSS 19).

Correlation results among groups were obtained by applying the Karl Pearson correlation coefficient and *P* value of <0.05 was taken as statistically significant.

The final data in this study was represented in the form of tables/charts/text.

Ethical and legal considerations

The protocol of the present study was submitted to the Ethics Committee of our Institute. After getting their due approval, the study was initiated in the institute. A patient information and consent form was given to the patients in his/her local language, when all their queries were satisfactorily answered, the signature of patients was obtained and then only study-related procedures were initiated.

Result

Rheumatoid arthritis was the most common disease and Hypothyroidism was the most common type of thyroid dysfunction among the study group.

1. Descriptive data and Correlation between serum TSH, serum T3, serum T4, ESR (Erythrocyte Sedimentation Rate), and Disease Activity Score/Index (DAI) in various autoimmune disorders under study [Table 2 and 3].

Rheumatoid arthritis (RA) and Parameters - Thyroid profile, ESR, Disease Activity Score (DAS). Disease activity in RA patients – 45 patients had moderate disease activity, 15 patients had severe disease activity, ten patients had mild disease activity and four patients were in remission [Table 1]. A positive correlation was found between serum TSH and ESR with DAS score in Rheumatoid arthritis, which was statistically significant ($r = 0.335$, $n = 74$, $P = 0.004$) [Graph 1]. No correlation was found between T3, T4 with Disease activity in RA. The majority of our patients had sub-clinical hypothyroidism, therefore was positive correlation was found only between disease activity and TSH whereas not with T3 and T4.

Table 1: Disease activity scores and Disease severity for various autoimmune disorders[10,14,15]

Disease severity	Disease activity index/score			
	Rheumatoid Arthritis (DAS-28-ESR)	Systemic Lupus Erythematosus (SLEDAI)	Ankylosing spondylitis (BASDAI)	Systemic Sclerosis (DAS-28-ESR)
Mild	>2.6 to<3.2	<3 to<7	<4	<3.3
Moderate	>3.2 to<5.1	>7 to<12	>4 to<7	>3.3 to<5.1
Severe	>5.1	>12	>7	>5.1

Table 2: Descriptive data of Serum TSH, T3, T4, ESR, and Activity Index in various disorders under study

Parameters	Various disorders descriptive data							
	Rheumatoid arthritis		Systemic lupus erythematosus		Ankylosing spondylitis		Systemic sclerosis	
No. of patients	74		11		19		05	
Disease activity index	DAS-28		SLEDAI		BASDAI		DAS-28-ESR	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Serum TSH	04.22	0.35	11.93	21.24	4.10	2.80	3.56	3.31
Serum T3	01.10	0.29	0.95	0.31	0.94	0.26	1.08	0.08
Serum T4	08.22	01.97			7.94	1.37	9.25	1.74
ESR	19.43	07.91	23.27	09.67	18.37	13.90	20.80	11.735
Activity Index	04.43	0.88	06.09	04.06	4.25	0.66	4.69	0.83316

Table 3: Correlation between Serum TSH, T3, T4, ESR with Activity Index in various disorders under study

Parameters	Various disorders correlation data							
	Rheumatoid arthritis		Systemic lupus erythematosus		Ankylosing spondylitis		Systemic sclerosis	
No. of patients	74		11		19		05	
Disease activity index	DAS-28		SLEDAI		BASDAI		DAS-28-ESR	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Serum TSH	0.33	0.004	0.74	0.009	−0.30	0.42	−0.23	0.70
Serum T3	0.05	0.66	0.006	0.98	−0.58	0.09	−0.07	0.90
Serum T4	−0.19	0.09	--	0.21	−0.36	0.12	0.34	0.56
ESR	0.432	0.0001	−0.148	0.66	0.004	0.98	0.36	0.54

Systemic Lupus Erythematosus (SLE) and Parameters - Thyroid profile, ESR, Disease Activity Score (SLEDAI). A positive correlation was found between serum TSH and SLEDAI score, which was statistically significant ($r = 0.741$, $n = 11$, $P = 0.009$). No correlation was found between T3, T4, ESR, and SLEDAI in SLE patients with *P* values – 0.985, 0.212, and 0.663, respectively.

Ankylosing Spondylitis (AS) and Parameters – Thyroid profile, ESR, and Disease Activity Score (BASDAI). No correlation was found between serum TSH, T3, T4, ESR, and BASDAI in Ankylosing spondylitis patients.

Systemic Sclerosis (SSc) and Parameters – Thyroid profile, ESR, and Disease Activity Score (DAS-28-ESR). No correlation was found between serum TSH, T3, T4, ESR, and disease activity score among systemic sclerosis patients with *P* values – 0.709, 0.900, 0.569, and 0.54, respectively.

Polymyositis – only one patient so no analysis can be/has been done. All RA study patients were seropositive.

2) Descriptive data and Correlation between ESR (Erythrocyte Sedimentation Rate) and Hemoglobin in various autoimmune disorders under study.

Discussion

In our study, we included a total of 110 patients of various diagnosed/newly diagnosed and with symptoms of systemic immunological disorders attending as outpatients or admitted as in-patients for medical conditions in internal medicine and associated departments in our institute for the study duration of 18 months and to study the correlation of thyroid function with Disease activity and ESR with Disease activity and Hemoglobin in patients of different systemic immunological disorders.

Correlation of thyroid dysfunction and ESR with disease activity among individual autoimmune disorders in study group:

Rheumatoid arthritis

A Pearson product-moment correlation was run in data from 74 patients of rheumatoid arthritis patients to determine the correlation between serum TSH, T3, T4, ESR, and DAS-28. A positive correlation was found between serum TSH, ESR, and disease activity score, which was statistically significant ($r = 0.335$, $n = 74$, $P = 0.004$) and ($r = 0.432$, $n = 74$, $P = 0.0001$), respectively, whereas no correlation found between serum T3, T4 with

Table 4: ESR vs. Hemoglobin data and correlation

	Descriptive Statistics		
	Mean	**Std. Deviation**	***n***
ESR	19.63	9.473	110
Hemoglobin	11.074	1.9137	110
Parameter	**Correlations**	**Hemoglobin**	
ESR	Pearson Correlation (*r*)	−0.463	
	Sig. (2-tailed) (*P*)	0.0001	
	Number of patients	110	

disease activity in RA patients. Similar correlations were found in Elatter *et al.*,[2] in 2014, Nadeem Mir *et al.*,[16] in 2017, and Silva *et al.*,[17] in 2010.

Systemic lupus erythematosus (SLE)

A Pearson product-moment correlation was run in data of 11 patients of SLE to determine the correlation between serum TSH, T3, T4, ESR, and disease activity (SLEDAI). A positive correlation was found between serum TSH and SLEDAI score, which was statistically significant (r = 0.741, n = 11, P = 0.009). whereas no correlation was found between serum T3 (P = 0.985), T4 (P = 0.212), ESR (P = 0.663) and disease activity score (SLEDAI). Similar correlations were found in studies – El-Azizi *et al.*,[18] in 2014, Appenzeller *et al.*, in 2009,[19] and Silva Martina *et al.*, in 2017.[20]

Ankylosing spondylitis (AS)

A Pearson product-moment correlation was run in data of 19 AS patients to determine the correlation between serum TSH, T3, T4, ESR, and disease activity (BASDAI). No correlation was found between serum TSH (P = 0.422), T3 (P = 0.095), T4 (P = 0.129), ESR (P = 0.986), and disease activity (BASDAI) among AS patients. Similarly, no correlations were found in studies – Tarhan *et al.,* in 2013,[21] Emmungil *et al.,* in 2014,[22] Pexito *et al.,* in 2013,[23] and Spoorenberg *et al.,*[24] in 2005.

Systemic sclerosis (SSc)

A Pearson product-moment correlation was run on data from five patients of SSc patients to determine the correlation between serum TSH, T3, T4, ESR, and Disease activity (DAS-28-ESR). No correlation was found between serum TSH (P = 0.709), T3 (P = 0.900), T4 (P = 0.0.569), ESR (P = 0.543) and disease activity score (DAS-28-ESR) among systemic sclerosis patients. Hudson *et al.,*[25] in 2007. This relation is difficult to correlate as there is no prompt disease activity score for SSC, and needs larger-scale multi-center studies with effective disease activity parameters/index for SSc. We have not used the Medsger score as it has its limitations, unequal weightage among various factors used in the Medsger score. We have only five patients with systemic sclerosis in the study. We have used DAS-28-ESR for disease activity in systemic sclerosis patients.

Polymyositis – No data can be analyzed due to a smaller number of patients.

Correlation between ESR and Hemoglobin in patients under the study group [Table 4] and [Graph 2]:

ESR was evaluated in each 110 study group patients with a mean value of 19.63 and a standard deviation of 09.473. Hemoglobin (HB) was evaluated in each 110 study group patients with a mean value of 11.074 and a standard deviation of 1.9137. A Pearson product-moment correlation was run to determine the correlation between ESR and Hemoglobin in all patients under study. A negative correlation was found between ESR and hemoglobin, which was statistically significant (r = −0.463, n = 110, P = 0.001). Kanfer *et al.,*[26] in 1997.

Various other findings in our study

Rheumatoid arthritis (67.3%) was found to be the most common autoimmune disorder in patients under study. The female gender is more susceptible to developing autoimmune disorders and anemia than in male gender. We found a high (22.7%) prevalence of thyroid dysfunction in autoimmune disorders as it is 10% in the general population (who do not have autoimmune disorders). Hypothyroidism is the most common and hyperthyroidism is the rarest type among the study group. Anemia was found in 60% of patients under study with female predominance. Anemia found in study patients was attributed to immunological/rheumatological disorders. Primarily type of anemia found in RA patients was anemia of chronic disease. Thyroid dysfunction compounds as a confounding factor for anemia in RA patients. Younger age group patients are more susceptible to developing autoimmune disorders with few exceptions (Rheumatoid arthritis found in comparatively older age group people). No correlation was found between ESR and Disease activity except in RA patients. ESR is an integrated part of the disease activity score (DAS-28-ESR) for RA.

One of the limitations of our study is that it's a cross-sectional and observational study, which is why we were not able to assess the clinical, biochemical, and various drug effects on the follow-up to demonstrate the aftereffect of disease treatment on thyroid dysfunction, hemoglobin, and vice versa. Another limitation is the lesser number of patients in some diseases and also a not well-established disease activity scores for some of the diseases because of which correlation among many parameters could not be evaluated effectively and significantly.

Conclusion

Our study demonstrated that there is a positive correlation between thyroid dysfunction (TSH) and disease activity in most prevalent autoimmune disorders (Rheumatoid arthritis and Systemic lupus erythematosus) and no correlation was found among other autoimmune disorders under study. No correlation was found between T3, T4, and Disease activity among any of the autoimmune disorders in the study. ESR demonstrated good parameters for assessing disease activity only in Rheumatoid arthritis but not in any other autoimmune disorder. Our study demonstrated a negative significant correlation between ESR and Hemoglobin in the study group.

Our findings emphasize the need to raise awareness among General physicians and Family/community healthcare workers regarding the simultaneous screening, and evaluation of ESR, Disease activity, and Thyroid dysfunction in newly diagnosed or pre-diagnosed patients of systemic autoimmune diseases and as we found a negative correlation between ESR and Hemoglobin, so here we also advocating the early and prompt initiation of treatment for disease and thyroid dysfunction to slow down the disease activity/progression which helps to control the disease, improvement in thyroid dysfunction, hemoglobin level (as it is related to one of the parameters for disease activity) and patient general condition/symptoms. General practitioner awareness is of uttermost importance in this regard as to suspect and evaluate the disease, and other associated parameters in the initial stage of symptoms so that patients can be treated accordingly at the earliest which helps to prevent long-term consequences/co-morbidities in the patient of community and at the level of primary health care.

We also emphasize prompt and effective research work for disease activity scoring system for systemic sclerosis and larger scale multi-center follow-up studies for ankylosing spondylitis and systemic sclerosis to effectively evaluate the correlation among disease activity Esr, thyroid dysfunction, Hemoglobin and to follow up the effect of treatment on thyroid status, disease activity, and Hemoglobin.

Financial support and sponsorship

Dr. Prakash Joshi, Dr. Abhishek Singhai, Medicine Department, Colleagues.

Conflicts of interest

There are no conflicts of interest.

References

1. Diamond B, Lipsky PE. Autoimmunity and Autoimmune Diseases | Harrison's Principles of Internal Medicine, 20e | AccessMedicine | McGraw Hill Medical (mhmedical.com), 1933771.2015.
2. Elatter EA, Younes TB, Mobasher SA. Hypothyroidism in patients with rheumatoid arthritis and its relation to disease activity. Egypt Rheumatol Rehabil 2014;41:58-65.
3. Jameson JL, Weetman AP, Disorders of The Thyroid Gland Harrison's Principles of Internal Medicine. New York: McGraw Hill; 2012;2:2913-8.
4. Mousa AA, Ghonem M, Hegazy A, El-Baiomy AA, El-Diasty A. Thyroid function and auto-antibodies in Egyptian patients with systemic lupus erythematosus and rheumatoid arthritis. Trends Med Res 2012;7:25-33.
5. Mukaka MM. A guide to appropriate use of Correlation coefficient in medical research. Malawi Med J 2012;3:24:69-71–.
6. Hazra A, Gogtay N. Biostatistics series module 6: Correlation and linear regression. Indian J Dermatol 2016;61:593-601.
7. Garrett S, Jenkinson T, Kennedy LG, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: The Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994;21:2286-91.
8. Hawker G, Gabriel S, Bombardier C, Goldsmith C, Caron D, Gladman D. A reliability study of SLEDAI: A disease activity index for systemic lupus erythematosus. J Rheumatol 1993;20:657-60.
9. Lóránd V, Bálint Z, Komjáti D, Németh B, Minier T, Kumánovics G, *et al.* Validation of disease activity indices using the 28 joint counts in systemic sclerosis. Br Society Rheumatol 2016;55:1849-58.
10. Chen YH, Huang WN, Chen YM, Lai KL, Hsieh TY, Hung WT, *et al.* The BASDAI Cut-Off for Disease Activity Corresponding to the ASDAS Scores in a Taiwanese Cohort of Ankylosing Spondylitis. Front Med (Lausanne) 2022;9:856654. doi: 10.3389/fmed.2022.856654.
11. Biambo HI, Ejele OA, Nwauche CA. An evaluation of the Beckman-Coulter AcT 3-part differential haematology analyzer in a tertiary hospital laboratory. Niger J Med 2005;14:183-7.
12. Gilmour D, Sykes AJ. Westergren and Wintrobe methods of estimating E.S.R. compared. Br Med J 1951;2:1496-7.
13. Fung AWS, Knauer MJ, Blasutig IM, Colantonio DA, Kulasingam V. Evaluation of electrochemiluminescence immunoassays for immunosuppressive drugs on the Roche cobas e411 analyzer. F1000 Res 2017;1832:6. doi: 10.12688/f1000research.12775.2.
14. Kumar BS, Suneetha P, Mohan A, Kumar DP, Sarma KVS. Comparison of Disease Activity Score in 28 joints with ESR (DAS28), Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire Disability Index (HAQ-DI) & Routine Assessment of Patient Index Data with 3 measures (RAPID3) for assessing disease activity in patients with rheumatoid arthritis at initial presentation. Indian J Med Res 2017;146:S57-62.
15. Arora S, Isenberg DA, Castrejon I. Measures of adult systemic lupus erythematosus: Disease activity and damage. Arthritis Care Res 2020;72(Suppl 10):27–46.
16. Nadeem M, Khaliq A, Bhat MH. Thyroid Dysfunction in Rheumatoid Arthritis. Journal of Medical Science and Clinical Research [Internet] 2017;05(11). Available from: http://www.jmscr.igmpublication.org/home/index.php/archive/144-volume-05-issue-11-november-2017/3836-thyroid-dysfunction-in-rheumatoid-arthritis. [Last accessed 2023 Sep 28].
17. Silva I, Mateus M, Branco JC. Assessment of erythrocyte sedimentation rate (ESR) and C- reactive protein (CRP) on rheumatoid arthritis activity prediction. Acta Rheumatol Port 2010;35:456-62.
18. El-Azizi N, Abd El-baky M, Abdel Mohsen D, Mahammed DF, Mansour HE. AB0541 Thyroid dysfunction in patients with systemic lupus erythematosus correlation with disease activity. Annals of the Rheumatic Diseases 2014;73:985.
19. Appenzeller S, Pallone AT, Natalin RA, Costallat LT. Prevalence of thyroid dysfunction in systemic lupus erythematosus. J Clin Rheumatol 2009;15:117-9. doi: 10.1097/RHU.0b013e31819dbe4c.
20. Ferrari SM, Elia G, Virili C, Centanni M, Antonelli A, Fallahi P. Systemic Lupus Erythematosus and Thyroid Autoimmunity. Front Endocrinol (Lausanne) 2017;8:138. doi: 10.3389/fendo.2017.00138.
21. Tarhan F, Orük G, Niflioğlu O, Ozer S. Thyroid involvement in ankylosing spondylitis and relationship of thyroid dysfunction with anti-TNF α treatment. Rheumatol Int 2013;33:853-7. doi: 10.1007/s00296-012-2438-9.
22. Emmungil H, Erdogan M, Kalfa M, Karabulut G, Kocanaogulları

H, Inal V, *et al.* Autoimmune thyroid disease in ankylosing spondylitis. Clin Rheumatol 2014;33:955-61. doi: 10.1007/s10067-013-2466-1.

23. Peixoto D, Raposo A, Teixeira F, *et al.* THU0454 Thyroid Involvement in Patients with Spondyloarthritis Annals of the Rheumatic Diseases 2013;72:A318.
24. Spoorenberg A, van Tubergen A, Landewé R, Dougados M, van der Linden S, Mielants H, *et al.* Measuring disease activity in ankylosing spondylitis: Patient and physician have different perspectives. Oxford Rheumatol 2005;44:789-95.
25. Hudson M, Steele R; Canadian Scleroderma Research Group (CSRG), Baron M. Update on indices of disease activity in systemic sclerosis. Semin Arthritis Rheum 2007;37:93-8.
26. Kanfer EJ, Nicol BA. Haemoglobin concentration and erythrocyte sedimentation rate in primary care patients. J R Soc Med 1997;90:16-8.