Journal of Cardiovascular Disease Research
ISSN: 0975-3583,0976-2833 VOL 14, ISSUE 3, 2023

ROLE OF TCF7L2 RS7903146 POLYMORPHISM IN SUSCEPTIBILITY TO TYPE 2 DIABETES MELLITUS: A CASE-CONTROL STUDY IN BIHAR

Dr. Rajiv Kumar Jha[1], Dr. Javed Khan[2], Dr. Rajnish Kumar[3], Dr. Jatin Prajapati[4]

[1] Assistant Professor, Department of General Medicine, Netaji Subhas Medical College & Hospital, Bihta, Patna, Bihar, India.
[2] Assistant Professor, Department of General Medicine, American International Institute of Medical Sciences, Udaipur, Rajasthan, India.
[3] Assistant Professor, Department of General Medicine, Prathima Institute of Medical Sciences, Karimnagar, Telangana, India.
[4] Post Graduate Student, Department of Community Medicine, RNT Medical College, Udaipur, Rajasthan, India. (ORCID: https://orcid.org/0009-0004-7298-4499)

Corresponding Author: Dr. Rajiv Kumar Jha

Address: Department of General Medicine, Netaji Subhas Medical College & Hospital, Bihta, Patna, Bihar, India.

ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease characterized by periods of remission and exacerbation. Accurate identification of factors associated with increased disease activity is essential for optimizing patient management and preventing long-term organ damage. However, data regarding predictors of disease activity in Indian patients remain limited.

Objectives: To assess disease activity among patients with systemic lupus erythematosus and identify clinical and laboratory predictors associated with increased disease activity in a tertiary care hospital in Bihar.

Methods: A hospital-based observational analytical cross-sectional study was conducted from August 2022 to December 2022 in a tertiary care teaching hospital in Bihar. Forty-two adult patients with established SLE were enrolled using consecutive sampling. Demographic, clinical, and laboratory data were collected using a structured case record form. Disease activity was assessed using the Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K). Patients were categorized into low/moderate and high disease activity groups. Associations between clinical and laboratory variables and disease activity were evaluated using appropriate statistical tests. A p-value <0.05 was considered statistically significant.

Results: The mean age of participants was 31.8 ±9.4 years, and females constituted 90.5% of the study population. High disease activity was observed in 17 (40.5%) patients. Lupus nephritis and hematological involvement were significantly associated with high disease activity ($p<0.05$). Among laboratory parameters, anti-dsDNA positivity, low complement C3 and C4 levels, proteinuria, elevated erythrocyte sedimentation rate, and lower hemoglobin levels demonstrated significant associations with increased disease activity. Patients with active disease showed a higher prevalence of immunological abnormalities and renal involvement compared with those having low to moderate disease activity.

Conclusion: Lupus nephritis, hematological involvement, anti-dsDNA positivity, hypocomplementemia, proteinuria, elevated ESR, and anemia were significant predictors of disease

activity in patients with SLE. Routine assessment of these parameters may assist clinicians in identifying high-risk patients and implementing timely interventions to improve disease outcomes and reduce organ damage.

Keywords: Systemic lupus erythematosus; Disease activity; SLEDAI-2K; Anti-dsDNA antibodies; Complement levels; Lupus nephritis; Predictors.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune disease characterized by loss of immunological tolerance, production of autoantibodies, immune complex deposition, and inflammation affecting multiple organs and tissues. The disease exhibits a highly heterogeneous clinical presentation, ranging from mild mucocutaneous manifestations to severe renal, neurological, hematological, and cardiovascular involvement. Owing to its relapsing-remitting course and unpredictable disease behavior, SLE remains a major cause of morbidity and impaired quality of life worldwide [1]. Advances in diagnostic techniques and therapeutic strategies have improved survival rates over recent decades; however, disease flares and persistent activity continue to contribute significantly to organ damage and healthcare burden [2].

Globally, the prevalence and incidence of SLE vary considerably across geographical regions and ethnic groups. The disease predominantly affects women of reproductive age, with a female-to-male ratio approaching 9:1. Genetic susceptibility, hormonal influences, environmental exposures, and immunological factors are believed to contribute to disease pathogenesis and activity [3]. Despite substantial progress in understanding disease mechanisms, predicting periods of increased disease activity remains a major clinical challenge. Disease activity in SLE is dynamic and can fluctuate over time, necessitating regular monitoring to prevent irreversible organ damage and optimize therapeutic interventions [4].

Several clinical, serological, and laboratory parameters have been investigated as potential predictors of disease activity. Traditional biomarkers such as anti-double stranded DNA (anti-dsDNA) antibodies, complement components C3 and C4, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) are frequently used in routine clinical practice. However, their predictive value varies among patients and across disease manifestations [5]. Studies have suggested that demographic characteristics, disease duration, renal involvement, hematological abnormalities, and immunological markers may independently influence disease activity and flare occurrence [6]. Identifying reliable predictors is therefore essential for risk stratification and individualized patient management.

In Asian populations, including India, SLE often presents with greater disease severity and a higher frequency of major organ involvement compared with Western cohorts [7]. Lupus nephritis, hematological manifestations, and constitutional symptoms are common contributors to disease burden in Indian patients. Furthermore, delayed diagnosis, socioeconomic factors, limited access to specialized care, and variations in treatment adherence may influence disease outcomes and activity patterns in resource-constrained settings [8].

Bihar represents a region with a substantial burden of autoimmune diseases managed at tertiary care centers. Although several Indian studies have described the clinical and immunological profile of SLE patients, evidence regarding factors associated with current disease activity remains limited. Most available data originate from heterogeneous populations, varying disease activity indices, and larger multicenter cohorts, making extrapolation to local hospital-based populations challenging [9]. Moreover, there is a need to evaluate the relationship between routinely available clinical and laboratory parameters and disease activity in real-world tertiary care settings where advanced biomarkers may not be readily accessible.

Understanding predictors of disease activity can assist clinicians in identifying high-risk patients, guiding monitoring strategies, optimizing therapeutic decisions, and preventing long-term organ damage. Such evidence is particularly relevant in developing countries where healthcare resources must be utilized efficiently and where disease-related complications contribute substantially to morbidity and healthcare expenditure [10]. Therefore, the present study was undertaken in a tertiary care hospital in Bihar to assess disease activity among patients with systemic lupus erythematosus and to identify clinical and laboratory predictors associated with increased disease activity. The specific objective was to evaluate demographic, clinical, and serological factors associated with active disease using standardized disease activity assessment measures.

METHODOLOGY

Study Design: This hospital-based observational analytical cross-sectional study was conducted to identify clinical and laboratory predictors of disease activity among patients diagnosed with systemic lupus erythematosus (SLE). The study was designed and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Study Setting: The study was conducted in the Department of Medicine/Rheumatology of a tertiary care teaching hospital in Bihar. The hospital serves as a major referral center catering to patients from urban and rural regions of the surrounding states.

Study Duration: The study was conducted over a period of five months from August 2022 to December 2022.

Study Population: The study population comprised patients with established systemic lupus erythematosus attending the outpatient and inpatient services of the tertiary care hospital during the study period. Diagnosis of SLE was based on accepted classification criteria and confirmed by the treating rheumatologist/physician.

Inclusion Criteria

Patients aged ≥18 years.
Patients diagnosed with systemic lupus erythematosus according to established classification criteria.
Patients willing to participate and provide written informed consent.
Patients attending follow-up or admitted during the study period with complete clinical and laboratory records.

Exclusion Criteria

Patients younger than 18 years of age.
Patients with overlap connective tissue disorders.
Patients with active malignancy.
Patients with severe concurrent infections that could influence inflammatory markers and disease activity assessment.
Pregnant women.
Patients unwilling to provide informed consent.
Patients with incomplete clinical or laboratory data.

Sample Size: The sample size was calculated using the formula for estimation of a proportion in a descriptive observational study:

$n = Z^2 \times p \times q / d^2$

Where:

n = required sample size
Z = 1.96 at 95% confidence level
p = anticipated prevalence of active disease among SLE patients (50% taken for maximum sample size estimation in the absence of precise local data)
q = 1 − p = 50%
d = allowable error of 15%

$n = (1.96)^2 \times 50 \times 50 / (15)^2$
$n \approx 42$
Accordingly, a minimum sample size of 42 participants was considered adequate and included in the study.

Sampling Technique: A consecutive sampling technique was employed. All eligible patients meeting the inclusion criteria during the study period were enrolled consecutively until the required sample size of 42 participants was achieved.

Data Collection Tools and Procedure: After obtaining informed written consent, demographic and clinical information was collected using a predesigned structured case record form. Data included age, sex, disease duration, presenting symptoms, organ involvement, treatment history, and comorbid conditions. A detailed clinical examination was performed for each participant. Laboratory investigations included complete blood count, erythrocyte sedimentation rate (ESR), serum complement levels (C3 and C4), anti-double stranded DNA (anti-dsDNA) antibody status, serum creatinine, and urine examination for proteinuria. Disease activity was assessed at the time of enrollment using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K), a validated instrument widely used for evaluating disease activity in SLE. Patients were categorized into low/moderate and high disease activity groups based on SLEDAI-2K scores for analytical purposes.

Study Variables: The dependent variable was disease activity assessed using the SLEDAI-2K score and categorized according to disease activity status. Independent variables included demographic characteristics (age, sex, disease duration), clinical parameters (renal involvement, mucocutaneous manifestations, arthritis, hematological involvement, hypertension), and laboratory parameters (hemoglobin level, ESR, complement C3 and C4 levels, anti-dsDNA positivity, serum creatinine, and proteinuria). The association of these variables with disease activity was evaluated to identify potential predictors of active disease.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ±standard deviation or median with interquartile range as appropriate, whereas categorical variables were presented as frequencies and percentages. The normality of continuous variables was assessed before analysis. Student's t-test or Mann–Whitney U test was used for comparison of continuous variables, while Chi-square test or Fisher's exact test was applied for categorical variables. Variables demonstrating significant association in univariate analysis were further evaluated using multivariable logistic regression to identify independent predictors of high disease activity. A p-value of <0.05 was considered statistically significant.

Ethical Considerations: Written informed consent was obtained from all participants before enrollment. Confidentiality and anonymity of patient information were strictly maintained throughout the study. Participation was voluntary, and participants were free to withdraw at any stage without affecting their medical care. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and subsequent amendments governing research involving human participants.

RESULTS

A total of 42 patients with systemic lupus erythematosus were enrolled in the study. The majority were females and belonged to the younger age groups, with a mean age of 31.8 ±9.4 years. Mucocutaneous manifestations and arthritis were the most common clinical features, while lupus nephritis was observed in approximately two-fifths of the study population (Table 1)

Table 1. Demographic and Baseline Clinical Characteristics of Study Participants (N = 42)

Variable	Category/Value	n (%)
Age (years)	Mean ± SD	31.8 ± 9.4
Age group	18–30 years	21 (50.0)
	31–40 years	13 (31.0)
	>40 years	8 (19.0)
Sex	Female	38 (90.5)
	Male	4 (9.5)
Disease duration	<2 years	15 (35.7)
	2–5 years	18 (42.9)
	>5 years	9 (21.4)
Hypertension	Present	10 (23.8)
Lupus nephritis	Present	16 (38.1)
Arthritis	Present	24 (57.1)
Mucocutaneous manifestations	Present	28 (66.7)
Hematological involvement	Present	14 (33.3)

The laboratory profile demonstrated a high frequency of anti-dsDNA positivity and reduced complement levels. The mean SLEDAI-2K score indicated overall moderate disease activity within the cohort (Table 2).

Table 2. Laboratory Profile of Study Participants

Parameter	Value
Hemoglobin (g/dL), Mean ± SD	10.6 ± 1.8
ESR (mm/hr), Mean ± SD	42.5 ± 18.7
Anti-dsDNA positive, n (%)	25 (59.5)
Low C3 level, n (%)	19 (45.2)
Low C4 level, n (%)	16 (38.1)
Proteinuria (>500 mg/day), n (%)	14 (33.3)
Elevated serum creatinine (>1.2 mg/dL), n (%)	8 (19.0)
SLEDAI-2K score, Mean ± SD	9.7 ± 4.5

Based on SLEDAI-2K assessment, 17 patients (40.5%) had high disease activity, whereas 25 patients (59.5%) had low to moderate disease activity (Table 3).

Table 3. Distribution of Disease Activity According to SLEDAI-2K Score

Disease Activity Category	SLEDAI-2K Score	n (%)
Low/Moderate activity	≤10	25 (59.5)
High activity	>10	17 (40.5)
Total	-	42 (100.0)

Clinical factors significantly associated with high disease activity included lupus nephritis and hematological involvement. Other clinical manifestations, including arthritis, hypertension, and mucocutaneous involvement, did not show statistically significant associations (Table 4).

Table 4. Association of Clinical Variables with High Disease Activity

Variable	Low/Moderate Activity (n=25)	High Activity (n=17)	p-value
Lupus nephritis, n (%)	6 (24.0)	10 (58.8)	0.024*
Hypertension, n (%)	4 (16.0)	6 (35.3)	0.152
Arthritis, n (%)	13 (52.0)	11 (64.7)	0.416
Mucocutaneous manifestations, n (%)	15 (60.0)	13 (76.5)	0.270
Hematological involvement, n (%)	5 (20.0)	9 (52.9)	0.028*

*Statistically significant ($p<0.05$)

Among laboratory parameters, anti-dsDNA positivity, low complement levels (C3 and C4), proteinuria, elevated ESR, and lower hemoglobin levels were significantly associated with high disease activity. These findings suggest that immunological and renal parameters are important indicators of active disease in patients with SLE (Table 5).

Table 5. Association of Laboratory Parameters with High Disease Activity

Variable	Low/Moderate Activity (n=25)	High Activity (n=17)	p-value
Anti-dsDNA positivity, n (%)	11 (44.0)	14 (82.4)	0.014*
Low C3 level, n (%)	7 (28.0)	12 (70.6)	0.007*
Low C4 level, n (%)	6 (24.0)	10 (58.8)	0.022*
Proteinuria, n (%)	5 (20.0)	9 (52.9)	0.027*
ESR (mm/hr), Mean ± SD	35.8 ± 14.2	52.4 ± 18.3	0.003*
Hemoglobin (g/dL), Mean ± SD	11.1 ± 1.5	9.9 ± 1.8	0.031*

*Statistically significant ($p<0.05$)

DISCUSSION

The present hospital-based observational study evaluated clinical and laboratory predictors of disease activity among 42 patients with systemic lupus erythematosus attending a tertiary care hospital in Bihar. Approximately two-fifths of the study population demonstrated high disease activity based on SLEDAI-2K assessment. The principal findings indicated that lupus nephritis, hematological involvement, anti-dsDNA positivity, hypocomplementemia (low C3 and C4 levels), proteinuria, elevated ESR, and lower hemoglobin levels were significantly associated with higher disease activity.

The demographic characteristics observed in the present study are consistent with the established epidemiology of SLE. The predominance of young females reflects the recognized influence of hormonal and genetic factors in disease susceptibility and progression [3,7]. Similar demographic patterns have been reported in Indian and international cohorts, where women of reproductive age constitute the majority of affected individuals [8,9].

Disease activity assessment remains a cornerstone of SLE management because persistent activity contributes substantially to cumulative organ damage and reduced quality of life [2,10]. In the current study, 40.5% of patients exhibited high disease activity. This proportion is comparable to observations from longitudinal lupus cohorts where a substantial subset of patients experiences moderate-to-severe disease activity despite ongoing treatment [6]. Variations in disease activity frequencies across studies may be attributed to differences in disease duration, referral patterns, treatment exposure, and the disease activity instruments employed.

One of the most important findings of the present study was the significant association between lupus nephritis and high disease activity. Renal involvement is recognized as one of the most severe manifestations of SLE and frequently reflects systemic immune dysregulation. Previous studies have consistently demonstrated that patients with active lupus nephritis exhibit higher disease activity scores and increased risk of disease flares [5,11]. Proteinuria, which was also significantly associated with high disease activity in our study, serves as a readily measurable marker of renal inflammation and ongoing immune complex-mediated injury. These findings reinforce the importance of regular renal monitoring in patients with SLE.

Hematological involvement was another clinical predictor associated with increased disease activity. Hematological abnormalities, including anemia, leukopenia, and thrombocytopenia, are common manifestations of active lupus and often reflect immune-mediated destruction or bone marrow suppression [12]. The significant association observed in this study supports previous reports indicating that hematological abnormalities frequently parallel systemic disease activity and may serve as useful clinical indicators during routine follow-up.

Among laboratory predictors, anti-dsDNA positivity and reduced complement levels demonstrated strong associations with disease activity. These findings are biologically plausible and align with the established pathophysiology of SLE. Anti-dsDNA antibodies contribute to immune complex formation and tissue injury, while complement consumption reflects ongoing immune activation [13]. Numerous studies have reported that rising anti-dsDNA titers and declining complement levels are associated with disease flares and increased disease activity, particularly in patients with renal involvement [14,15]. Consequently, these biomarkers remain integral components of routine disease monitoring.
Elevated ESR was significantly associated with higher disease activity in the present study. Although ESR lacks disease specificity, it frequently correlates with systemic inflammation and has been incorporated into clinical assessment strategies for SLE [16]. Conversely, lower hemoglobin levels were associated with increased disease activity, likely reflecting chronic inflammation, autoimmune hemolysis, renal disease, or bone marrow involvement. Similar associations between anemia and active disease have been documented in previous studies evaluating disease activity indices in lupus populations [12,16].

The findings of this study have important clinical implications. Identification of readily available predictors such as proteinuria, anti-dsDNA positivity, complement levels, ESR, and hematological abnormalities may facilitate early recognition of patients at risk for heightened disease activity. This can enable closer monitoring, timely therapeutic adjustments, and potentially reduce irreversible

organ damage. Such approaches are particularly relevant in resource-limited settings where advanced biomarkers may not be routinely available.

The strengths of the present study include the use of a standardized disease activity assessment tool (SLEDAI-2K), inclusion of both clinical and laboratory parameters, and evaluation of patients in a real-world tertiary care setting. However, several limitations should be acknowledged. The relatively small sample size may have limited statistical power and generalizability. The cross-sectional design precludes assessment of temporal relationships and causality. Furthermore, the study was conducted at a single center, which may limit external validity. Longitudinal multicenter studies with larger sample sizes are warranted to validate these findings and identify additional predictors of disease activity in Indian patients with SLE.

CONCLUSION

Systemic lupus erythematosus is a heterogeneous autoimmune disorder characterized by fluctuating disease activity and variable organ involvement. In the present study, a substantial proportion of patients demonstrated high disease activity as assessed by the SLEDAI-2K index. Clinical factors such as lupus nephritis and hematological involvement were significantly associated with increased disease activity. Among laboratory parameters, anti-dsDNA positivity, reduced complement levels (C3 and C4), proteinuria, elevated ESR, and lower hemoglobin levels emerged as important indicators of active disease.These findings highlight the value of routinely available clinical and laboratory markers in identifying patients at greater risk of heightened disease activity. Early recognition of such patients may facilitate closer surveillance, timely therapeutic interventions, and prevention of irreversible organ damage. The study underscores the importance of comprehensive disease monitoring in tertiary care settings. Future multicenter prospective studies with larger sample sizes are recommended to validate these predictors and enhance risk stratification strategies for patients with systemic lupus erythematosus.

DECLARATIONS

Funding: No external funding was received for this study.
Conflict of Interest: The authors declare that there is no conflict of interest related to this study.
Informed Consent: Written informed consent was obtained from all participants before enrollment in the study.
Acknowledgment: The authors acknowledge the support of the faculty, residents, laboratory personnel, and all study participants who contributed to the successful completion of this research.

REFERENCES

1. Tsokos GC. Autoimmunity and organ damage in systemic lupus erythematosus. Nature immunology. 2020 Jun;21(6):605-14.
2. Fan Y, Hao YJ, Zhang ZL. Systemic lupus erythematosus: year in review 2019. Chinese medical journal. 2020 Sep 20;133(18):2189-96.
3. Rees F, Doherty M, Grainge MJ, Lanyon P, Zhang W. The worldwide incidence and prevalence of systemic lupus erythematosus: a systematic review of epidemiological studies. Rheumatology. 2017 Nov 1;56(11):1945-61.
4. Petri M, Orbai AM, Alarcón GS, Gordon C, Merrill JT, Fortin PR, Bruce IN, Isenberg D, Wallace DJ, Nived O, Sturfelt G. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis & Rheumatism. 2012 Aug;64(8):2677-86.
5. Bertsias GK, Tektonidou M, Amoura Z, Aringer M, Bajema I, Berden JH, Boletis J, Cervera R, Dörner T, Doria A, Ferrario F. Joint European League Against Rheumatism and European Renal

Association–European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis. Annals of the rheumatic diseases. 2012 Nov 1;71(11):1771-82.
6. Mina R, Brunner HI. Update on differences between childhood-onset and adult-onset systemic lupus erythematosus. Arthritis research & therapy. 2013 Aug 21;15(4):218.
7. Pons-Estel GJ, Alarcón GS, Scofield L, Reinlib L, Cooper GS. Understanding the epidemiology and progression of systemic lupus erythematosus. InSeminars in arthritis and rheumatism 2010 Feb 1 (Vol. 39, No. 4, pp. 257-268). WB Saunders.
8. Malaviya AN, Chandrasekaran AN, Kumar A, Shamar PN. Occasional series—lupus around the world systemic lupus erythematosus in India. Lupus. 1997 Nov;6(9):690-700.
9. El-Khalawany M, Shaaban D, Aboeldahab S. Immunotherapy of viral warts: myth and reality. Egyptian Journal of Dermatology and Venerology. 2015 Jan 1;35(1):1-3.
10. Lateef A, Petri M. Managing lupus patients during pregnancy. Best practice & research Clinical rheumatology. 2013 Jun 1;27(3):435-47.
11. Almaani S, Meara A, Rovin BH. Update on lupus nephritis. Clinical Journal of the American Society of Nephrology. 2017 May 1;12(5):825-35.
12. Giannouli S, Voulgarelis M, Ziakas PD, Tzioufas AG. Anaemia in systemic lupus erythematosus: from pathophysiology to clinical assessment. Annals of the rheumatic diseases. 2006 Feb 1;65(2):144-8.
13. Liu CC, Ahearn JM. The search for lupus biomarkers. Best practice & research clinical rheumatology. 2009 Aug 1;23(4):507-23.
14. Ter Borg EJ, Horst G, Hummel EJ, Limburg PC, Kallenberg CG. Measurement of increases in anti-double-stranded dna antibody levels as a predictor of disease exacerbation in systemic lupus erythematosus. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 1990 May;33(5):634-43.
15. Esdaile JM, Abrahamowicz M, Joseph L, MacKenzie T, Li Y, Danoff D. Laboratory tests as predictors of disease exacerbations in systemic lupus erythematosus. Why some tests fail. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 1996 Mar;39(3):370-8.
16. Mosca M, Bombardieri S. Assessing remission in systemic lupus erythematosus. Clinical and experimental rheumatology. 2006 Nov 1;24(6):S99.