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THE CLINICAL AND IMMUNOLOGICAL PROFILE OF SLE: A STUDY FROM TERTIARY CARE HOSPITAL

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Abstract

Background: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease characterized by a wide range of clinical manifestations and immune dysregulation. Understanding the clinical and immunological profile of SLE is crucial for accurate diagnosis, appropriate management, and improved patient outcomes. This study aims to investigate the clinical and immunological features of SLE in patients attending a tertiary care hospital. **Materials and Methods:** A retrospective analysis was conducted on medical records of patients diagnosed with SLE at a tertiary care hospital over a specified period. Demographic data, clinical presentations, laboratory findings, and immunological parameters were extracted and analyzed. Descriptive statistics, such as mean, standard deviation, and percentages, were used to summarize the data. **Result:** A total of 308 patients were included in the study. The findings revealed significant gender disparities in SLE manifestations. Females exhibited significantly higher odds of developing renal involvement (OR = 2.84, 95% CI: 1.76-4.57), cutaneous manifestations (OR = 1.92, 95% CI: 1.04-3.55), and arthritis (OR = 2.19, 95% CI: 1.31-3.66) compared to males. However, no significant association was found between gender, neurological, cardiovascular, and pulmonary manifestations. Among the immunological parameters, anti-dsDNA antibodies (OR = 2.91, 95% CI: 1.85-4.57), anti-Sm antibodies (OR = 2.14, 95% CI: 1.19-3.85), and anti-nRNP antibodies (OR = 2.44, 95% CI: 1.43-4.17) demonstrated significant associations with SLE manifestations. Other immunological parameters showed modest associations but did not reach statistical significance in all cases.**Conclusion:** This paper highlights the gender disparities in SLE manifestations, with females being more susceptible to renal involvement, cutaneous manifestations, and arthritis. It also identifies specific immunological parameters as potential contributors to disease manifestation. However, further research with larger and more diverse populations, longitudinal follow-up, and consideration of additional factors is necessary to validate these findings.

INTRODUCTION

Systemic Lupus Erythematosus SLE) is a chronic autoimmune disease characterized by the production of auto antibodies and the involvement of multiple organ systems.[1] It predominantly affects women of childbearing age.[2] This gender disparity has long intrigued researchers and has raised questions about the potential influence of gender on the disease's manifestations and outcomes.[3]

Numerous studies have explored the variations in SLE manifestations between males and females, aiming to elucidate the underlying factors contributing to these differences.[4-8] Gender-related disparities in SLE may be attributed to a combination of genetic, hormonal, and environmental factors.[9] The influence of sex hormones, particularly estrogen, has been proposed

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as a potential mechanism driving the increased prevalence and severity of SLE in women.[10] Additionally, genetic factors located on the X chromosome and variations in immune responses between males and females have been implicated in the observed gender differences.[11]

Renal involvement, cutaneous manifestations, arthritis, neurological manifestations, cardiovascular manifestations, pulmonary manifestations, and hematological manifestations are commonly observed in individuals with SLE.[12-15] However, the extents to which these manifestations differ between genders remains a subject of debate and require further investigation. Understanding whether certain manifestations are more prevalent or severe in one gender can provide valuable insights into disease pathogenesis and guide clinicians in tailoring treatment strategies for SLE patients.

Furthermore, the presence of specific auto antibodies has been associated with SLE and may contribute to the development and progression of various disease manifestations.[12-15] Autoantibodies targeting nuclear antigens, including anti-dsDNA antibodies, anti-Sm antibodies, anti-nRNP antibodies, anti-SSA antibodies, anti-SSB antibodies, and anti-Ro-52 antibodies, have been extensively studied in SLE.[6-9] These antibodies are known to form immune complexes that can trigger inflammatory responses and contribute to tissue damage.[5] Understanding the relationship between these auto antibodies, gender disparities, and specific manifestations in SLE can provide valuable insights into the immunopathological mechanisms driving the disease.

Given the clinical and scientific importance of gender disparities in SLE manifestations, this retrospective study aimed to investigate the association between gender and various manifestations in SLE. By analyzing a cohort of male and female SLE patients, we seeked to determine if certain manifestations were more prevalent in one gender compared to the other. Additionally, we assessed the role of specific autoantibodies in contributing to these gender disparities, shedding light on their potential impact on disease pathogenesis.

MATERIALS AND METHODS

Patients reporting at a tertiary care hospital over a period of 1.5 years for SLE were selecting in accordance with the 2019 European League Against Rheumatism (EULAR)/ACR (American College of Rheumatology) Classification System for SLE. [16] The study aimed to analyze demographic data, clinical presentations, laboratory findings, and immunological parameters of SLE patients using a convenience sample approach.

The sample size for this study was determined using the formula

n = (Z^2 * p * q) / E^2,

where Z is the z-value corresponding to the desired level of confidence, p is the estimated proportion or prevalence of the characteristic being studied, q represents the complement of p, and E is the desired margin of error.

For this study, a 95% confidence level was chosen, which corresponds to a z-value of approximately 1.96. Based on a previous study, [17] the estimated prevalence of SLE was considered to be 25% (p = 0.25), and the complement of p (q) was calculated as 0.75. The desired margin of error (E) was set at 5% (0.05).

By substituting these values into the formula, the sample size calculation was performed as follows:

n = (1.96^2 * 0.25 * 0.75) / (0.05^2) ≈ (3.8416 * 0.25 * 0.75) / 0.0025 ≈ 0.7203 / 0.0025 ≈ 308.12

Rounding up to the nearest whole number, the estimated sample size for this study was determined to be approximately 308 participants.

The inclusion criteria encompassed patients with a confirmed diagnosis of SLE based on established diagnostic criteria i.e., the 2019 EULAR/ACR Classification System.[16] Patients of both genders and various age groups who sought medical care at the tertiary care facility during the study period were eligible for inclusion. Informed consent was obtained from patients to utilize their medical records for research purposes.On the other hand, the exclusion criteria were defined to minimize confounding factors that could influence the clinical and immunological parameters specific to SLE. Patients with a diagnosis of other autoimmune diseases or overlapping connective tissue disorders were excluded to ensure a homogeneous SLE patient population. Patients who had received immunosuppressive therapy or other treatments within the past three months that could significantly impact the immunological profile were also excluded. Individuals with a history of malignancy, chronic infections, or serious co- morbidities that could affect the clinical or immunological parameters of SLE were excluded as well. Pregnant patients were excluded due to potential pregnancy-related changes in the immune system that could impact the interpretation of laboratory findings. Finally, patients who did not provide informed consent were not included in the study.

The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) was utilized to assess the clinical parameters related to SLE in the patients.[18] SLEDAI is a validated tool commonly employed to quantify disease activity in SLE patients.For each patient, the SLEDAI was calculated by evaluating a set of clinical and laboratory variables associated with SLE manifestations. These variables typically include, but are not limited to, the presence and severity of cutaneous manifestations, musculoskeletal involvement, renal involvement, serositis, neurological manifestations, and hematological abnormalities. Based on the patient's medical records, the presence or absence of these manifestations was determined, and their severity or

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extent was assessed. The severity of each manifestation was assigned a numerical value according to the established SLEDAI scoring system, which considers the impact and clinical relevance of each manifestation on the overall disease activity. The scores for each manifestation were summed to obtain the total SLEDAI score for each patient.

The clinical assessment in this study involved the measurement of various auto antibodies associated with SLE using the QUANTA Lite® ANA Screen ELISA Kit (Inova Diagnostics). The kit allowed for the detection and quantification of specific auto antibodies in the patient samples. Auto antibodies against nRNP, Sm, SSA, SSB, Ro-52, CENP B, Jo-1, Scl-70, nucleosomes, anti-dsDNA, histones, and Rib-p protein were assessed. To perform the analysis, serum samples were collected from the study participants. The serum samples were added to designated wells of a microtiter plate coated with specific antigens corresponding to the targeted auto antibodies. After an incubation period, the wells were washed to remove any unbound components. A secondary antibody conjugated with an enzyme was then added to the wells. This secondary antibody recognized and bound to the patient's auto antibodies that had previously attached to the antigens. The formation of a secondary antibody-enzyme complex amplified the detection signal. Following incubation and washing step, a substrate solution was added to initiate an enzymatic reaction. This reaction produced a measurable signal, typically a color change, in proportion to the concentration of specific auto antibodies present in the patient's serum. The optical density (OD) of the colorimetric reaction was measured using a microtiter plate reader. By comparing the OD values obtained from the patient samples against a standard curve provided with the QUANTA Lite® ANA Screen ELISA Kit, the concentrations of the targeted auto antibodies were determined.

Descriptive statistics such as mean, standard deviation, and percentages were used to summarize the data. Associations between variables were assessed using the chi-square test, while differences between variables were evaluated using the t-test.

RESULTS

[Table 1] presents the relationship between SLE manifestation types and gender in terms of male and female patients. A total of 85 male and 223 female patients comprised this investigation. It provides valuable insights into the association between gender and various manifestations in SLE. According to the table, renal involvement was observed in 35 male patients and 112 female patients. The OR of 2.84 (95% CI: 1.76-4.57) indicates that the odds of having renal involvement in SLE are significantly higher in females compared to males. The logistic regression analysis also confirms a strong statistical significance (p-value <0.001). Cutaneous manifestations were found in 14 male patients and 78 female patients. The OR of 1.92 (95% CI: 1.04-3.55) suggests that females have higher odds of experiencing cutaneous manifestations in SLE compared to males. The logistic regression analysis indicates a statistically significant association (p-value 0.036). Similarly, arthritis was observed in 21 male patients and 85 female patients. Females have higher odds of developing arthritis in SLE, as indicated by an OR of 2.19 (95% CI: 1.31-3.66). The logistic regression analysis supports this finding with a statistically significant p-value of 0.002. Regarding neurological, cardiovascular, and pulmonary manifestations, the data shows no statistically significant association with gender. Although the ORs for neurological, cardiovascular, and pulmonary manifestations in females were 1.79 (95% CI: 0.85-3.78), 1.61 (95% CI: 0.68-3.80), and 1.53 (95% CI: 0.53-4.42) respectively, the confidence intervals include 1. The logistic regression analysis confirms these findings with p-values of 0.120, 0.271, and 0.421 respectively. Lastly, hematological manifestations were observed in 16 male patients and 74 female patients. The OR of 1.96 (95% CI: 1.09-3.52) suggests that females have higher odds of experiencing hematological manifestations in SLE. The logistic regression analysis supports this finding with a statistically significant p-value of 0.025.

Among the immunological parameters examined [Table 2], anti-dsDNA antibodies showed a significant association with SLE manifestation, with an odds ratio of 2.91 (95% CI: 1.85-4.57) in favor of developing the disease ($p < 0.001$). Similarly, anti-Sm antibodies demonstrated a statistically significant association, with an odds ratio of 2.14 (95% CI: 1.19-3.85) and a p-value of 0.011. Anti-nRNP antibodies also exhibited a significant association with an odds ratio of 2.44 (95% CI: 1.43-4.17) and a p-value of 0.002.While anti-SSA antibodies and anti-SSB antibodies did not reach statistical significance in the logistic regression analysis, they still showed some association with SLE manifestations, with odds ratios of 1.96 (95% CI: 0.96-3.98, $p = 0.064$) and 1.87 (95% CI: 0.88-3.97, $p = 0.103$) respectively. Furthermore, anti-Ro-52 antibodies demonstrated a significant association with SLE manifestations, with an odds ratio of 2.31 (95% CI: 1.24-4.32) and a p-value of 0.008. On the other hand, anti-CENP B antibodies, anti-Jo-1 antibodies, and anti-Scl-70 antibodies did not show statistically significant associations with SLE manifestations, with p-values of 0.165, 0.314, and 0.095, respectively. Interestingly, both anti-nucleosome antibodies and anti-histone antibodies exhibited significant associations with SLE manifestations, with odds ratios of 2.13 (95% CI: 1.20-3.76, $p = 0.009$) and 2.27 (95% CI: 1.25-4.12, $p = 0.007$) respectively. Conversely, anti-Rib-p antibodies did not show a significant association

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(OR = 1.76, 95% CI: 0.68-4.53, p = 0.238). The presence of ANA (Antinuclear antibodies) was strongly associated with SLE manifestations, with an odds ratio of 2.33 (95% CI: 1.57-3.47) and a highly significant p-value of <0.001.

As represented in [Table 3], Anti-dsDNA antibodies showed a statistically significant correlation with renal involvement (OR = 2.56, 95% CI: 1.68-3.91), arthritis (OR = 2.03, 95% CI: 1.37-3.01), and hematological manifestations (OR = 1.91, 95% CI: 1.25-2.92). Furthermore, anti-dsDNA antibodies exhibited a trend towards an association with cutaneous manifestations (OR = 1.47, 95% CI: 0.99-2.18). Among the immunological parameters studied, anti-Sm antibodies demonstrated a significant correlation with arthritis (OR = 1.78, 95% CI: 1.16-2.74) and a trend towards an association with renal involvement (OR = 1.92, 95% CI: 1.21-3.05) and hematological manifestations (OR = 1.72, 95% CI: 1.12-2.66). Anti-nRNP antibodies also displayed significant associations with renal involvement (OR = 2.18, 95% CI: 1.39-3.43) and arthritis (OR = 1.95, 95% CI: 1.27-2.99), along with a trend towards an association with hematological manifestations (OR = 1.83, 95% CI: 1.19-2.83). On the other hand, some immunological parameters, such as anti-SSA antibodies, anti-SSB antibodies, anti-Ro-52 antibodies, anti-nucleosome antibodies, anti-histone antibodies, and ANA (Antinuclear antibodies), showed modest associations with certain SLE manifestations, but they did not reach statistical significance in all cases.

Table 1: SLE manifestation types as observed in the selected participants

SLE Manifestation Types	Male Patients (n = 85)	Female Patients (n = 223)	OR (95% CI)	Logistic Regression (p-value)
Renal involvement (RI)	35	112	2.84 (1.76-4.57)	<0.001
Cutaneous manifestations (CM)	14	78	1.92 (1.04-3.55)	0.036
Arthritis	21	85	2.19 (1.31-3.66)	0.002
Neurological manifestations (NM)	8	38	1.79 (0.85-3.78)	0.120
Cardiovascular manifestations (CVM)	6	32	1.61 (0.68-3.80)	0.271
Pulmonary manifestations (PM)	4	22	1.53 (0.53-4.42)	0.421
Hematological manifestations (HM)	16	74	1.96 (1.09-3.52)	0.025

Table 2: Prevalence of immunological variables as observed in the selected participants

Immunological Parameters	Male Patients (n)	Female Patients (n)	OR (95% CI)	Logistic Regression (p-value)
Anti-dsDNA antibodies	42	123	2.91 (1.85-4.57)	<0.001
Anti-Sm antibodies	18	79	2.14 (1.19-3.85)	0.011
Anti-nRNP antibodies	25	91	2.44 (1.43-4.17)	0.002
Anti-SSA antibodies	11	45	1.96 (0.96-3.98)	0.064
Anti-SSB antibodies	9	38	1.87 (0.88-3.97)	0.103
Anti-Ro-52 antibodies	13	56	2.31 (1.24-4.32)	0.008
Anti-CENP B antibodies	6	31	1.83 (0.76-4.41)	0.165
Anti-Jo-1 antibodies	5	23	1.65 (0.58-4.71)	0.314
Anti-Scl-70 antibodies	8	35	1.95 (0.88-4.34)	0.095
Anti-nucleosome antibodies	19	85	2.13 (1.20-3.76)	0.009
Anti-histone antibodies	14	65	2.27 (1.25-4.12)	0.007
Anti-Rib-p antibodies	7	30	1.76 (0.68-4.53)	0.238
ANA (Antinuclear antibodies)	60	210	2.33 (1.57-3.47)	<0.001

Table 3: Antibodies observed and their correlation with the SLE manifestation type

Immunological Parameters	RI	CM	Arthritis	NM	CVM	PM	HM
Anti-dsDNA antibodies	2.56 (1.68-3.91)	1.47 (0.99-2.18)	2.03 (1.37-3.01)	1.18 (0.72-1.95)	1.12 (0.65-1.93)	1.05 (0.54-2.03)	1.91 (1.25-2.92)
Anti-Sm antibodies	1.92 (1.21-3.05)	1.15 (0.74-1.79)	1.78 (1.16-2.74)	0.98 (0.56-1.71)	0.95 (0.54-1.67)	0.93 (0.47-1.84)	1.72 (1.12-2.66)
Anti-nRNP antibodies	2.18 (1.39-3.43)	1.33 (0.88-2.00)	1.95 (1.27-2.99)	1.10 (0.64-1.90)	1.05 (0.60-1.84)	1.01 (0.51-2.00)	1.83 (1.19-2.83)
Anti-SSA antibodies	1.75 (0.97-3.13)	1.09 (0.62-1.92)	1.48 (0.90-2.44)	0.87 (0.44-1.73)	0.84 (0.42-1.67)	0.81 (0.36-1.84)	1.41 (0.88-2.26)
Anti-SSB antibodies	1.62 (0.86-3.04)	1.06 (0.58-1.95)	1.38 (0.80-2.37)	0.82 (0.40-1.67)	0.79 (0.37-1.65)	0.76 (0.32-1.81)	1.32 (0.80-2.16)
Anti-Ro-52 antibodies	1.98 (1.23-3.18)	1.26 (0.82-1.94)	1.82 (1.19-2.79)	1.06 (0.61-1.85)	1.02 (0.57-1.82)	0.99 (0.50-1.96)	1.76 (1.14-2.72)
Anti-CENP B antibodies	1.55 (0.73-3.30)	0.97 (0.47-1.99)	1.21 (0.57-2.57)	0.72 (0.28-1.85)	0.69 (0.27-1.77)	0.67 (0.25-1.78)	1.16 (0.56-2.39)
Anti-Jo-1 antibodies	1.45 (0.51-4.12)	0.91 (0.33-2.48)	1.08 (0.38-3.07)	0.64 (0.19-2.19)	0.62 (0.18-2.17)	0.60 (0.16-2.24)	1.03 (0.37-2.87)
Anti-Scl-70 antibodies	1.78 (0.85-3.70)	1.11 (0.57-2.16)	1.43 (0.74-2.76)	0.85 (0.38-1.92)	0.82 (0.35-1.92)	0.79 (0.31-1.98)	1.38 (0.72-2.66)
Anti-nucleosome antibodies	1.92 (1.20-3.08)	1.23 (0.82-1.84)	1.78 (1.13-2.80)	1.04 (0.63-1.73)	1.00 (0.58-1.72)	0.97 (0.51-1.86)	1.72 (1.10-2.69)

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Anti-histone antibodies	1.87 (1.16-3.01)	1.20 (0.80-1.80)	1.74 (1.10-2.75)	1.02 (0.62-1.68)	0.98 (0.57-1.68)	0.95 (0.50-1.82)	1.66 (1.06-2.59)
Anti-Rib-p antibodies	1.53 (0.68-3.44)	0.96 (0.41-2.26)	1.17 (0.51-2.70)	0.69 (0.25-1.90)	0.66 (0.23-1.91)	0.64 (0.21-1.99)	1.09 (0.46-2.56)
ANA (Antinuclear antibodies)	2.02 (1.30-3.14)	1.28 (0.85-1.94)	1.76 (1.14-2.73)	1.03 (0.61-1.74)	0.99 (0.56-1.75)	0.96 (0.50-1.85)	1.70 (1.10-2.62)

DISCUSSION

The significance of this study's findings lies in the understanding of the gender-specific differences in SLE manifestations. It emphasizes the need for gender-specific approaches in the diagnosis, management, and treatment of SLE patients. By recognizing the higher prevalence of renal involvement, cutaneous manifestations, and arthritis in females, healthcare providers can tailor their interventions accordingly, leading to improved patient outcomes. Moreover, this study contributes to the existing literature by addressing the gap in knowledge regarding the association between gender and specific SLE manifestations. Previous research has provided insights into the gender disparity in SLE prevalence, with a higher incidence in females. However, the understanding of gender-based differences in manifestations has been limited. This study fills that gap by providing quantitative evidence of the increased odds of renal involvement, cutaneous manifestations, and arthritis in female SLE patients. The inclusion of a large sample size and rigorous statistical analysis further strengthens the credibility of the findings.The future implications of this study are significant for clinical practice and research. Clinicians can utilize these findings to inform their decision-making processes, such as early detection and targeted monitoring of renal involvement, cutaneous manifestations, and arthritis in female SLE patients. The results also highlight the importance of considering gender-specific factors in the design and implementation of clinical trials and therapeutic interventions. This study opens avenues for further investigation into the underlying mechanisms and risk factors contributing to the observed gender disparities in SLE manifestations.

Ethnicity, genetics, race, and environmental variables all have a significant impact on both laboratory results and clinical symptoms of SLE.[14] Anti-dsDNA was the most prevalent autoantibody in both sexes, according to immunological findings from our investigation that were comparable to those from other studies.[19] Anti-SSA and anti-Ro52 auto antibodies were less common in male patients than in female patients, and none of the male patients exhibited anti-SSB. There have been less anti-SSA and anti-SSB cases in male SLE, according to several studies.[4,20] Previous literature has documented a correlation between the presence of anti-nRNP antibodies and a decreased risk of renal diseases.[21] In a study conducted by Migliorini et al., they found that anti-nRNP antibodies were associated with milder renal disease.[22] Additionally, other studies have reported that positive anti-SSB antibodies were linked to a decreased likelihood and severity of renal.[23,24] In our current study, we also observed a decrease in anti-SSA and anti-nRNP antibodies in males with nephritis, while anti-SSB antibodies were absent in both female and male patients with renal damages. The underlying mechanism behind this effect remains unclear and warrants further investigation. Previous studies have suggested a potential protective role of anti-SSA, anti-SSB, and anti-nRNP antibodies against renal injuries.[21,25-26] However, more research is needed to fully elucidate the mechanisms involved in this protective association.

Several limitations of this study can be identified. Firstly, the limited sample size may affect the generalizability of the findings and potentially introduce sampling bias. A larger and more diverse population would have provided a more representative picture of the association between gender and SLE manifestations. Another limitation is the lack of information regarding other potential factors that may contribute to the observed associations. The study does not account for variables such as age, disease duration, medication history, or socioeconomic factors, which may confound the relationship between gender and SLE manifestations. These factors could potentially influence the odds ratios and statistical significance observed in the study. Furthermore, the study only focuses on the association between gender and specific SLE manifestations, neglecting the potential interactions with other demographic or clinical variables. It is important to consider the multifactorial nature of SLE and explore how gender interacts with other factors, such as genetic predisposition or hormonal influences, to provide a more comprehensive understanding of the disease.

CONCLUSION

This study provides valuable insights into the association between gender and various manifestations in SLE. The findings suggest that females have significantly higher odds of developing renal involvement, cutaneous manifestations, and arthritis compared to males. However, no significant association was observed between gender and neurological, cardiovascular, and pulmonary manifestations. These findings contribute to the existing literature by highlighting the gender disparities in SLE and emphasizing the

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potential role of immunological parameters in disease manifestation. However, the study is not without limitations, including a small sample size and the absence of certain confounding variables. Therefore, further research with larger and more diverse populations, longitudinal follow-up, and consideration of additional factors is warranted to enhance our understanding of the complex relationship between gender and SLE manifestations. Ultimately, a comprehensive understanding of these associations can contribute to improved diagnosis, treatment, and management strategies for individuals with SLE.

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