LUPUS SCIENCE & MEDICINE™

# Systematic review of the reporting of extrarenal manifestations in observational studies of Saudi patients with systemic lupus erythematosus

Fahidah Alenzi ,[1] Roaa Aljohani,[2] Aos Aboabat,[3] Fehaid Alanazi,[3] Haya M Almalag ,[4] Mohammed A Omair[3]

**To cite:** Alenzi F, Aljohani R, Aboabat A, *et al*. Systematic review of the reporting of extrarenal manifestations in observational studies of Saudi patients with systemic lupus erythematosus. *Lupus Science & Medicine* 2025;**12**:e001469. doi:10.1136/lupus-2024-001469

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/lupus-2024-001469).

Received 1 December 2024
Accepted 18 February 2025



For numbered affiliations see end of article.

**Correspondence to**
Dr Fahidah Alenzi; fmalenzi@pnu.edu.sa

## ABSTRACT

**Background** SLE is prevalent in Saudi Arabia, with numerous studies focusing on SLE in adult patients. However, there is a lack of comprehensive studies summarising the extrarenal manifestations of SLE in this population. This study aims to assess the variability in the prevalence rates of extrarenal manifestations of SLE across different cities in Saudi Arabia and to emphasise the need for a national registry to better understand the overall disease burden in the region.

**Methods** We conducted a systematic review of articles with no time restrictions, including studies from databases such as Medline, ScienceDirect, EBSCO and PubMed up to July 2024. The review process involved screening, data extraction and quality assessment in duplicate. Only observational or experimental studies focusing on extrarenal manifestations in adult patients with SLE in Saudi Arabia were included. The review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist for systematic reviews to ensure a rigorous and comprehensive evaluation.

**Results** A total of 35 studies were included, primarily retrospective cohort studies. Riyadh showed the highest number of publications over time. Musculoskeletal involvement in SLE ranged from 2% to 100%, with most studies reporting 46%–85%. Mucocutaneous manifestations, including discoid rash (5%–100%), malar rash (up to 79%) and photosensitivity (6.12%–29.3%), varied widely. Raynaud's phenomenon was noted at 4.5%–15.2%. Constitutional symptoms were more common in early-onset SLE, while serositis and cardiopulmonary issues showed variability. Neuropsychiatric symptoms, especially depression, reached up to 67.6%.

**Conclusion** This study explores the prevalence of extrarenal manifestations of SLE among adult Saudi patients, highlighting significant regional variability in musculoskeletal, dermatological, cardiovascular and neurological symptoms. It addresses a gap in the literature for a region where autoimmune diseases are a growing public health concern. The findings emphasise the need for population-based studies to investigate environmental, genetic and lifestyle factors influencing SLE progression.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ SLE is a complex autoimmune disorder with varied manifestations and delays in diagnosis, impacting patient outcomes and necessitating specialised care.

### WHAT THIS STUDY ADDS

⇒ Understanding the clinical manifestations of SLE in Saudi Arabia holds broader significance, contributing to the global knowledge of this autoimmune disease. They also highlight the urgent need for early diagnosis and specialised care for lupus in Saudi Arabia.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Recommendations for future research and emphasis on appropriate management strategies aim to improve health outcomes for Saudi patients with SLE. Healthcare practitioners should use these insights to enhance diagnostic precision and develop management strategies that are both effective and culturally sensitive.

## INTRODUCTION

SLE is a chronic autoimmune disease characterised by diverse clinical manifestations, potentially involving multiple organs and systems. Due to genetic, environmental or perhaps even ethnic reasons, this disease has high variability and heterogeneity. In Saudi Arabia, the incidence rate of SLE stands at an estimated 19.28 cases in every 100 000 people.[1 2] In this region, SLE is more commonly found among women, indicated by a 12.5 to 1 ratio of males to females.[3] SLE manifestations and symptoms have been studied widely in Saudi Arabia. Such studies have provided crucial insights into SLE diagnosis, management and prognosis in Saudi Arabia. Studies have also reported morbidity and mortality rates

related to SLE in Saudi Arabia, with renal involvement recognised as a significant indicator of poor prognosis.[1–3] While the primary aim of this study is to explore the prevalence and patterns of extrarenal manifestations among Saudi patients, it also indirectly addresses diagnostic delays by highlighting the variability in disease presentation across regions. Understanding these patterns is crucial for improving early recognition, timely diagnosis and management strategies, ultimately reducing the diagnostic gap in this population. Significant delays in diagnosing SLE often occur, primarily because of initial evaluations being conducted by non-specialists and the need for multiple consultations with physicians before patients are referred to a rheumatologist.[4] It is concerning that only 33.4% of patients are able to see a rheumatologist within 1 month of their initial clinical presentation, and some patients have to wait for over a year.[3 4] These delays have been linked to poorer outcomes, particularly in patients with severe organ involvement.[5] In contrast, patients under the care of lupus specialists tend to have less active diseases and receive more effective treatment plans, underscoring the significance of specialised care.[4] Timely diagnosis of SLE is crucial for improving clinical outcomes and is cost-effective, as it helps reduce healthcare costs.[5] By facilitating early and accurate diagnosis, followed by appropriate immunosuppressive therapy, the quality of life can be significantly enhanced, and the development of early damage can be prevented.[4 5] Understanding the clinical manifestations of SLE in Saudi Arabia holds broader significance, contributing to the global knowledge of this autoimmune disease. It is important to consider factors such as diagnosis delay, hospital facilities and the type of city to provide effective care. They also highlight the urgent need for early diagnosis and specialised care. Recommendations for future research and emphasis on appropriate management strategies aim to improve health outcomes for Saudi patients with SLE. Healthcare providers in Saudi Arabia should use these insights to enhance the diagnostic accuracy of SLE and design management strategies that are both effective and culturally appropriate. This study aimed to evaluate the variation in prevalence rates of extrarenal manifestations across Saudi Arabian cities, present findings on extrarenal manifestations from observational studies involving Saudi patients with SLE and highlight the significance of setting up a national registry for a better understanding of overall disease burden in the region.

## METHODS

### Information sources and search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) updated checklist[6] was followed and the extrarenal manifestations of adult Saudi patients with SLE were systematically reviewed in this study. The study used various databases including Medline (via OVID), ScienceDirect, Cochrane Library and PubMed in a search for key words and medical subject headings including 'lupus erythematosus', 'systemic lupus erythematosus', 'lupus', 'SLE', 'Saudi Arabia', 'kingdom of Saudi Arabia' and 'Saudi'. The search was conducted on 11 September 2023, with no time restrictions, incorporating articles from the inception of each database up to July 2024. Article alerts were set in all databases (except for Medline, where a manual search was performed weekly) to capture updates until the manuscript's publication. Studies on SLE in Saudi Arabia from the earliest available data were included in this analysis.

### Inclusion and exclusion criteria

Both Arabic-language and English-language articles that mentioned SLE in the Saudi Arabian context were considered. Specifically, the studies included those that discussed the prevalence of SLE, patient characteristics, disease management, disease flares, disease remission, quality of life, mortality and other outcomes reported by patients or healthcare providers. All articles including observational and experimental studies involving adult human subjects were considered. Books, chapters, case reports and reviews were excluded from the analysis. The search strategy and report can be found in online online supplemental file 1, which is reported in accordance with PRISMA-S guidelines: An Extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews.[7]

### Article screening process

Database searches were exported to Microsoft Excel and stored in a shared Dropbox folder with the research team. Duplicate entries in the database were identified and removed, after which the articles were organised based on their titles and abstracts following the predefined inclusion and exclusion criteria. Finally, the full texts of the studies were examined to determine their eligibility for inclusion in the final study.

### Data extraction

In order to regulate the process of data extraction, an extraction sheet was designed in advance. This sheet contained a variety of information, including author's name, year of publication, study setting, number of patients, their age and sex; diagnostic criteria; any interventions that were implemented; time since diagnosis; important findings relating to extrarenal manifestations of SLE and any additional comments. For accuracy and reliability, multiple authors independently performed data extraction. In this way, any discrepancies that might have arisen during the data extraction process could be identified. The authors involved in this discussion agreed on how to resolve the differences. This was a collaborative effort, and it aimed at improving the overall quality of the extracted data.

### Article quality grading

The quality and risk of bias of the studies that were included were evaluated using relevant tools according to the study design. The Cochrane bias risk assessment tool

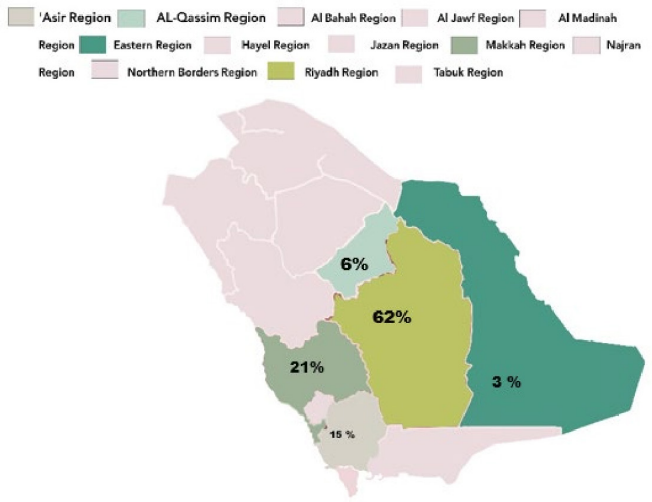


**Figure 1** Distribution of SLE studies by region in Saudi Arabia.

was employed for randomised controlled trials, whereas the National Institute of Health Quality Assessment was used for cohort and cross-sectional studies. The British Medical Journal Quality Assessment tool[8–10] was used for qualitative research. To visualise the distribution of studies across different regions of Saudi Arabia, a map was created using Datawrapper (https://app.datawrapper.de/map/3w1i1/publish) and the data were collected on 29 April 2024 (figure 1).

## RESULTS

### Included articles and studies

A total of 3869 records were obtained. Following the elimination of duplicates and reassessment of the inclusion and exclusion criteria based on article titles and abstracts, 398 reports were selected for full-text reviews. Because of the large number of reports identified, additional categorisation was conducted (adult, paediatric, renal and non-renal). Of the 3869 articles retrieved in the initial search, 35 satisfied the inclusion criteria (figure 2).

### Article quality results

This review examined 35 articles, all of which were observational studies. Of these, 21 followed a retrospective approach, whereas 11 studies adopted a cross-sectional design, and 3 studies employed alternative study designs (figure 3). Two authors independently conducted the literature search and quality assessment. When discrepancies arose, a third author was involved to review the evaluations and assist in resolving differences through discussion and consensus, ensuring a thorough and consistent quality assessment.

Because of differences in measurement methods and sample origin, it was not possible to conduct a meta-analysis.

### Result of extrarenal manifestations of Saudi patients with SLE

The musculoskeletal, mucocutaneous and systemic manifestations of SLE in Saudi patients show considerable variability across studies conducted in different regions and over time (figures 4–6).

### Musculoskeletal manifestations

The degree of joint involvement in Saudi patients with SLE varied greatly between studies. Frequencies ranged from 2% to 100%, with most studies reporting between 46% and 85%. However, joint involvement in Riyadh fluctuated significantly from 87.3%[11] to 22.9%,[12] highlighting substantial regional and temporal variations in musculoskeletal involvement. Moderate rates of 48%[13] and 57.1%[14] were observed in recent studies. These findings indicate the need for standardised criteria to assess musculoskeletal symptoms in Saudi patients with SLE.

### Mucocutaneous manifestations

Mucocutaneous involvement varied significantly between studies conducted in various Saudi Arabian cities and regions from 1988 to 2024. Discoid rash frequencies ranged from 5%[15] (Riyadh) to 100%[16] (Riyadh). While malar rash was reported in up to 79%[17] (Makkah). Photosensitivity rates ranged from 6.12%[14] (Riyadh) to 29.3%[18] (Riyadh), suggesting substantial differences in both regional and methodological factors. These differences emphasise the importance of adopting a more consistent method for evaluating mucocutaneous manifestations in Saudi patients with SLE .

### Raynaud's phenomenon

The frequency of Raynaud's phenomenon among Saudi patients with SLE has shown regional variation. Reported rates range from 4.5%[19] (Riyadh) to 15.2%[20] (Al-Hasa). Alomair *et al*[3] (Abha) reported a frequency of 7.4%, while Al Arfaj *et al*[21] (Riyadh) documented 8.7%. This variability highlights differences in patient populations, study methodologies and disease presentation across regions and time periods.

### Hair loss

The frequency of hair loss among Saudi patients with SLE varies across different studies and regions. In Abha, Alomair *et al*[3] reported a frequency of 26.9%, while Somaily *et al*[22] found a lower rate of 12.24%. In Riyadh, Alsuwayegh *et al*[13] documented a hair loss frequency of 16.07%, and Alhassan *et al*[14] reported the same frequency of 12.24%. Furthermore, Abid *et al*[20] observed a significantly higher frequency of 65.2% in Al-Hasa. These discrepancies suggest that both regional factors and disease severity may contribute to the observed variability in hair loss prevalence among patients with SLE in Saudi Arabia.

### Constitutional symptoms

The prevalence of constitutional symptoms, including fever, fatigue and weight changes, varied significantly across studies. Fever was reported in 18.6%–92% of

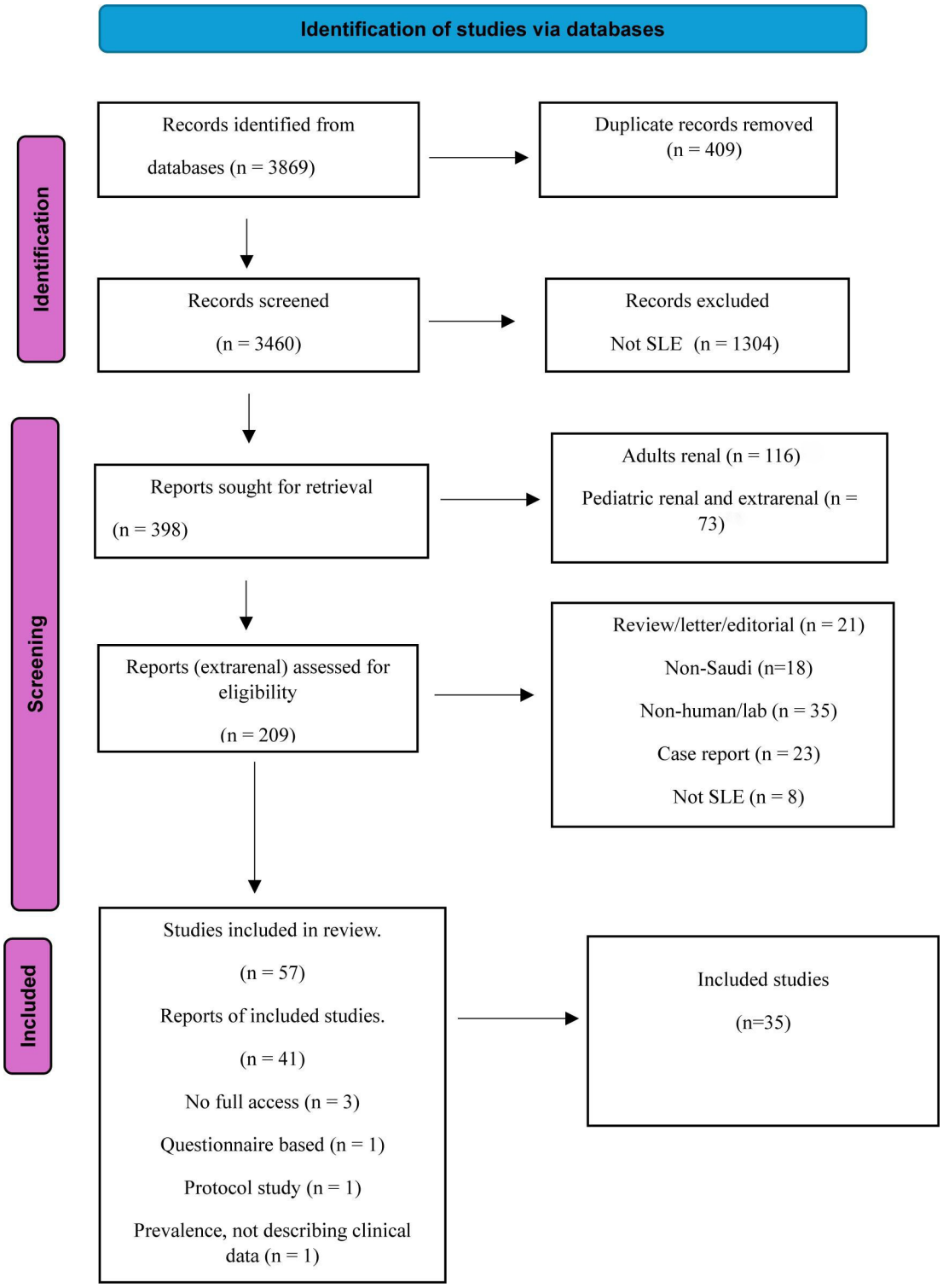


**Figure 2** Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram (Page *et al*[72]).

patients, while fatigue ranged from 40% to 64.8%. Weight changes were less common, with reported frequencies between 16.6% and 27.5%. Patients with early-onset SLE tended to have higher rates of fever and fatigue compared with late-onset cases, indicating potential differences in disease manifestation based on age of onset.

### Serositis and cardiopulmonary involvement

Serositis, including pleuritis and pericarditis, showed considerable variation across regions. The frequency of pleuritis ranged from 7.14%[13] (Riyadh) to 37.3%[19] (Riyadh), with differences in presentation observed based on disease onset. Alrashdi *et al*[15] (Riyadh) highlighted differences based on disease onset, with pleuritis

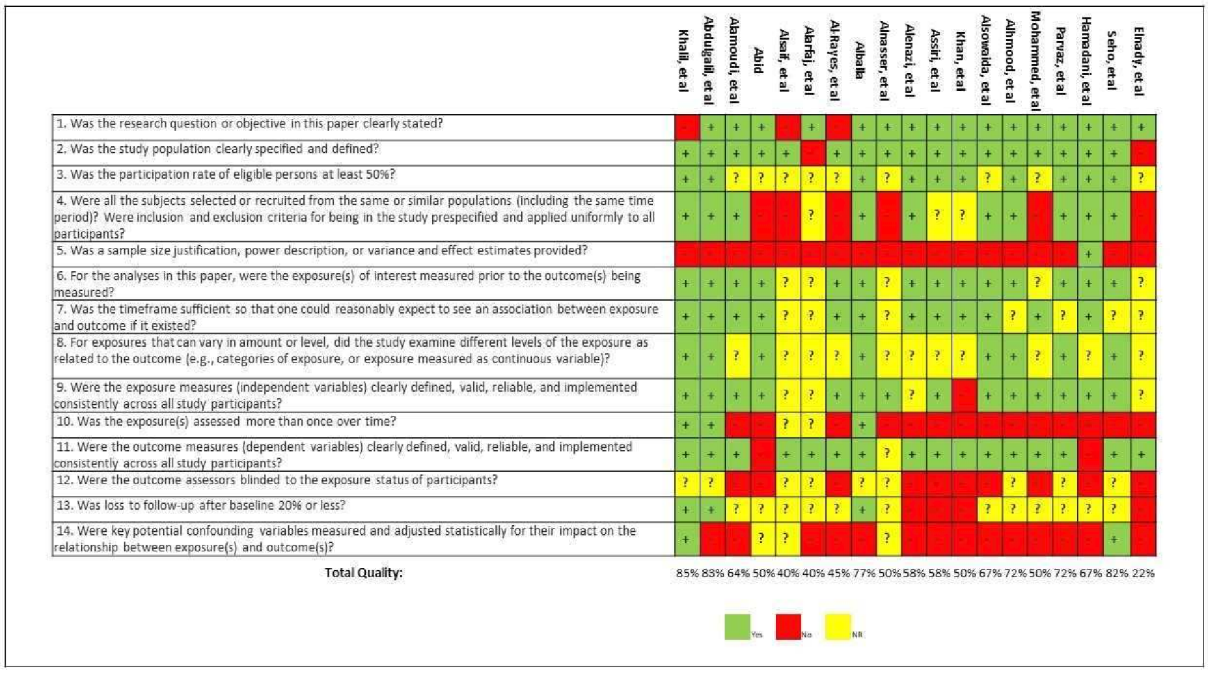


**Figure 3** The quality assessment of articles and evaluation of authors' assessments of the various biases using the NIH risk of bias tool. A green box indicates 'yes/low risk of bias', yellow 'not applicable/not reported' and red 'no/potential risk of bias'.

being more frequent in late-onset cases (25% vs 16.67% in early-onset) and pericarditis being rare (5.2% in early-onset), or absent in late-onset. Additionally, pericarditis being rare highlights the influence of disease onset on serositis manifestation. Abdel Galil *et al* (2016, Makkah) reported a pleuritis frequency of 9%, underscoring the variability in presentation across regions and disease stages. Cardiopulmonary involvement varied widely across cities and regions, with frequencies ranging from 8.33%[3] (Abha) to 37.5% for pulmonary and 31.3% for cardiac manifestations[23] (Riyadh). Common manifestations, such as pleuritis (2.8%–19%), pericardial effusion (5%–32%) and pulmonary hypertension (1.9%–15.5%) were common, with severe complications, such as alveolar haemorrhage, myocarditis and thromboembolic events being reported but with lower frequencies.[24 25] Variability persists between early and late-onset SLE, with late-onset patients showing higher rates of interstitial lung disease (ILD) and pulmonary hypertension (PHTN)[15] (Riyadh). Regional and temporal variations are likely to contribute to these differences.

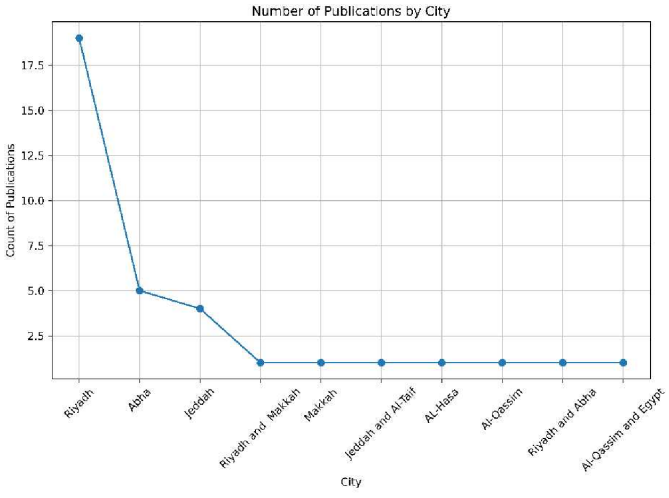


**Figure 4** Number of publications by city.

## Neuropsychiatric involvement

Neuropsychiatric manifestations, such as depression, seizures and psychosis, varied greatly, with reported frequencies ranging from 1.5% to 67.6%[26–28] (Riyadh and Makkah). Depression was the most common neuropsychiatric symptom, with frequencies reaching 67.6%, while seizure and psychosis rates varied from 2.2% to 17.4%; headache from 6.4% to 28.3% and focal deficits from 6% to 64.3%. More severe complications, such as cerebritis, cerebrovascular accident (CVA) and suicidal ideation, have been less frequently reported. These wide discrepancies may be due to differences in diagnostic criteria, patient demographics, methodologies and regional reporting.

## Gastrointestinal involvement

Gastrointestinal (GI) involvement in Saudi patients with SLE has shown variable frequencies across studies conducted between 1988 and 2023 in cities like Abha, Riyadh and Jeddah. Reported frequencies range from 3.7%[3] (Abha) to 29.6%[29] (Riyadh). Common manifestations include gastroesophageal reflux disease (GERD) (3.7%), oesophagitis, peptic ulcer disease, pancreatitis and hepatitis, with frequencies varying between 0% and 20%[15] (Riyadh). Ascites rates were reported at 9% in Jeddah[30] and 8.9% in Riyadh[21], while hepatosplenomegaly

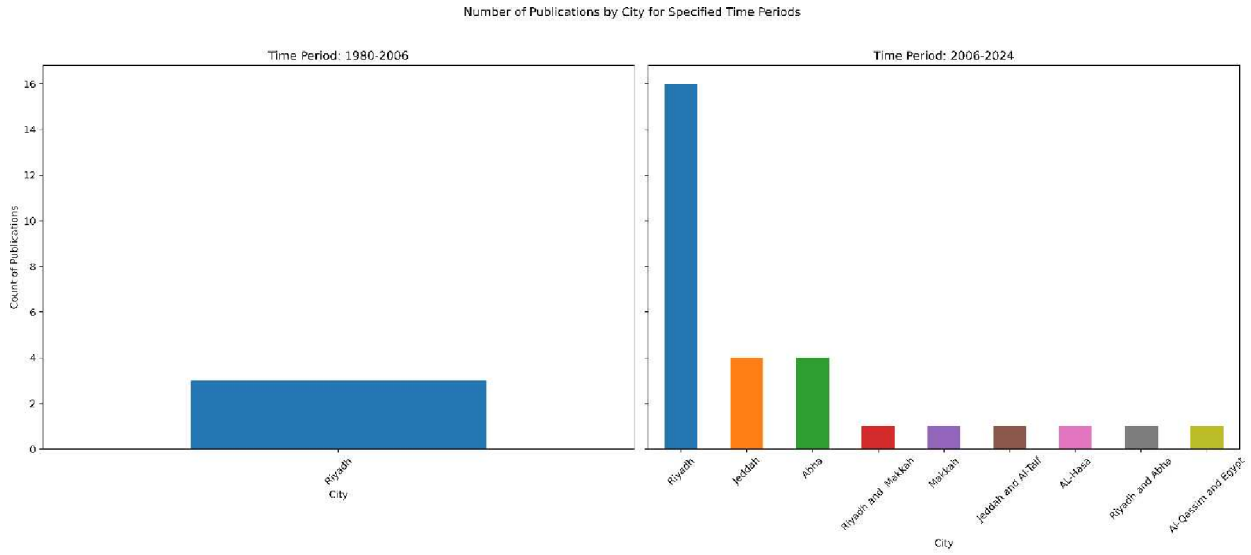


**Figure 5** Number of publications over time.

reached 6.1%. The variation may reflect differences in study design and population characteristics as well as lack of data from the Northern and Eastern regions of Saudi Arabia, highlighting a gap in regional representation.

### Haematological manifestations

Haematological manifestations in Saudi patients with SLE commonly include anaemia, leucopaenia and thrombocytopaenia. Anaemia remains the most frequently reported abnormality, with rates ranging from 5.36%[13] (Riyadh) to 89.1%[20] (Al-Hasa). Leucopaenia was noted in 14%–58.7% of patients, while thrombocytopaenia ranged from 12.5% to 40% across studies. AlShomer *et al* (2024, Al Qassim) highlighted anaemia in 63.5% of patients, thrombocytopaenia in 15%, and leucopaenia in 20%. Alrashdi *et al*[15] (Riyadh) reported a higher anaemia prevalence (82.1%) in early-onset SLE cases compared with 37.5% in late-onset cases. Haemolytic anaemia, lymphopaenia and varying degrees of cytopaenia were also described in several studies. Variations in prevalence were observed based on disease onset and patient subgroups. No studies have been conducted in the Northern regions, highlighting a gap in regional data.

The variability across studies may be attributed to differences in patient demographics, disease severity and methodological approaches.

## DISCUSSION

Several studies have focused on the clinical symptoms and prognoses of patients with SLE from diverse regions, including Saudi Arabia. Although studies undertaken in Saudi Arabia have focused on certain characteristics of SLE, there is a gap in the literature about how frequently extrarenal symptoms arise in Saudi patients with SLE in contrast to patients with SLE worldwide. Our analysis of extrarenal manifestations of SLE in Saudi patients reveals considerable variability in the frequency and presentation of various clinical features. The variability observed across studies from different regions and cities in Saudi Arabia emphasises the influence of regional factors and disease severity, underscoring the need for a standardised approach to assess SLE manifestations in this population. Several studies in the Kingdom of Saudi Arabia have investigated the prevalence of musculoskeletal complaints associated with SLE. Reported frequencies ranged from as low as 2% to as high as 100%, with most studies indicating rates between 46% and 85%. Furthermore, findings from Riyadh varied substantially, with Al-Nasser *et al*[11] reporting a high frequency of 87.3%, while Al Arfaj *et al*[12] documented a much lower rate of 22.9%. More recent studies, such as those by Alsuwayegh *et al*[13] and Alhassan *et al*[14] reported moderate frequencies of 48% and 57.1%, respectively. These findings suggest variability influenced by disease diversity, different disease onset, duration and environmental factors.[3 11 13 14 17–22 30–35] According to a study carried out by Al-Jarallah *et al*,[36] the prevalence of arthritis was 87% in Kuwait, which was almost close to the figures for Europeans (84%) and North Americans (86%), as well as Indians (85%). In Spain, for instance, it was found that SLE had a high occurrence of arthritis in 68.7% of cases.[37] Other extrarenal manifestations in Saudi patients with SLE were reported with considerable variability, with serositis prevalence ranging from 1% to 37.3%. Serositis, including pleuritis and pericarditis, was observed in a significant number of patients, though frequencies differed between studies. Pleuritis appeared more frequently in late-onset cases, suggesting possible differences in disease behaviour between early-onset and late-onset SLE. Cardiopulmonary manifestations, such as pericardial effusion, pleuritis and pulmonary hypertension, also showed regional variation, being more frequent in certain areas while less common in others. This variability may be influenced by differences in regional healthcare infrastructure, diagnostic accessibility and patient referral patterns. Compared with international cohorts, the range observed in Saudi patients was considerably

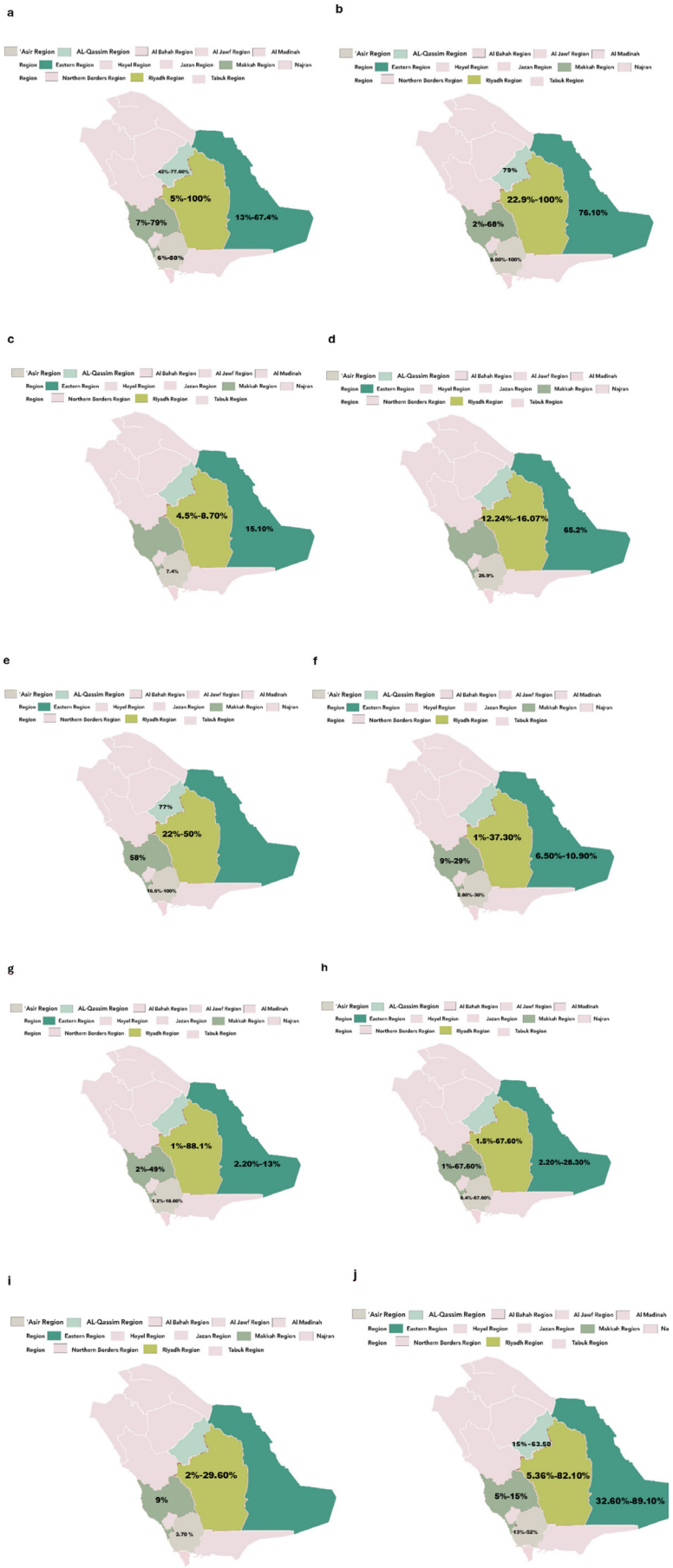


**Figure 6** (a–j) Systemic lupus manifestations observed in Saudi studies.

wider: 20% in Malaysia,[38] 16% in the Euro-Lupus cohort,[39] 22.1% in the Latin American Grupo Latino Americano De Estudio del Lupus (GLADEL) cohort,[40] 16.4% in the Chinese CSTAR cohort,[41] 32.2% in Egypt[42 43] and 19.9% in Hong Kong.[44] The wide range in Saudi research differs from the stable rates seen in these global groups. Saudi patients with SLE exhibit different rates of cardiopulmonary symptoms compared with patients with SLE globally. In Saudi studies, the prevalence of pulmonary hypertension ranged from 1.9% to 23%, whereas it was 3.8% in the Chinese CSTAR cohort,[41] 1.4% in the Latin American GLADEL cohort[40] and up to 14% at the University of Toronto Lupus Clinic.[45] Similarly, the frequency of myocarditis in studies conducted in Saudi Arabia ranges from 1.9% to 5%, which is consistent with the 3% seen in the Latin American GLADEL cohort[40] but lower than the 10.7% recorded in the multiethnic US-based LUMINA cohort.[46] Saudi studies show that the prevalence of interstitial lung disease ranges from 2% to 15%, which is higher than the 4.2% in the Chinese CSTAR group[41] and the 3%–6% range reported in American studies.[47 48]

In several Saudi studies, specific cardiac disorders, such as pulmonary embolism and pulmonary haemorrhage, have greater prevalence rates than other groups. Moreover, AlOmair *et al*[3] reported a pulmonary embolism frequency of 3%, which is higher than the rates of 1.2% in the Latin American GLADEL cohort[40] and 1.62% in the US National Center for Health Statistics data.[49] The prevalence of pulmonary haemorrhage in Saudi studies ranges from 1.9% to 8.6%, with the Latin American GLADEL cohort reporting 1%.[40] In a single US-based tertiary centre, 3.7% of hospital admissions for SLE were due to pulmonary haemorrhage.[50] These differences emphasise the unique characteristics of the Saudi population with SLE.

Neuropsychiatric complications significantly contribute to the morbidity and mortality of patients with SLE, with an unclear aetiology and no definitive diagnostic tests.[51] The reported prevalence of neuropsychiatric SLE (NPSLE) varies widely, ranging from 4% to 91%, due to its complex pathophysiology, genetic polymorphisms and diverse clinical phenotypes.[51] In this analysis, NPSLE occurrence ranged from 1% to 67%, potentially reflecting differences in clinical presentations, patient selection criteria and study populations. These findings are consistent with previous studies.[52–54] Prior research has identified headaches (50%–70%), depression (50%–60%) and cognitive impairment (30%–50%) as the most common neuropsychiatric symptoms.[55–57] Similarly, our study found headache (17%–50%) and depression (8%–67%) to be the most frequently observed symptoms. Less common manifestations included seizures, stroke and acute confusion. Depression remained the most prevalent neuropsychiatric symptom, consistent with global data highlighting mental health challenges in patients with SLE. Though less frequent, seizures and psychosis remain critical manifestations requiring ongoing monitoring. The regional variation in neuropsychiatric symptom prevalence underscores the importance of specialised mental healthcare in SLE management, particularly in regions with higher symptom burden.

GI involvement in Saudi patients with SLE has demonstrated considerable variability across studies conducted between 1988 and 2023 in cities such as Abha, Riyadh and Jeddah. Reported frequencies ranged from 3.7%[3] (Abha) to 29.6%[29] (Riyadh). Common manifestations included GERD (3.7%), oesophagitis, peptic ulcer disease, pancreatitis and hepatitis, with rates varying between 0% and 20%[15](Riyadh). Ascites was noted in 9% of cases in Jeddah[30] and 8.9% in Riyadh[21], while hepatosplenomegaly was reported in 6.1%. These differences may stem from variations in study design, population characteristics and a lack of data from the Northern and Eastern regions, underscoring a gap in regional representation. GI involvement in SLE can range from moderate to severe and, in some cases, may be life-threatening.[58] Systematic studies have shown a global frequency of GI involvement in patients with SLE ranging from 15% to 75%.[59] In contrast, our review indicated a lower prevalence in Saudi Arabia, with rates ranging from 2% to 29.6%.[60] This discrepancy may be due to less emphasis on GI symptoms compared with other organ manifestations, as common symptoms such as anorexia, nausea and vomiting are often underreported or not clearly defined.[61 62] Global estimates for the prevalence of GI manifestations affecting the oesophagus, stomach, pancreas, small intestine and colon range from 0.2% to 13%. Our findings were consistent, with frequencies ranging between 0.7% and 11.6%.

Lupus hepatitis has been reported globally with a prevalence of 9.3%.[63] However, our analysis revealed a higher frequency of 25%, suggesting a greater disease burden in the Saudi population compared with previous international data.[64]

Haematological manifestations are frequently reported in Saudi patients with SLE, with anaemia being the most common, ranging from 5.36%[13] (Riyadh) to 89.1%[20] (Al-Hasa). Leucopaenia was noted in 14%–58.7%, while thrombocytopaenia ranged from 12.5% to 40%[31] (Al Qassim). Early-onset SLE cases showed higher anaemia rates (82.1%) compared with late-onset cases (37.5%)[15] (Riyadh). Haemolytic anaemia, lymphopaenia and varying degrees of cytopaenia were also observed. Variability across studies may be due to differences in study design, disease activity and population characteristics. Haematological abnormalities, often present at disease onset or during flare-ups, are key diagnostic criteria for SLE.[65 66] The variability in Saudi data aligns with international findings, where leucopaenia affects 19%–61% of patients at diagnosis, rising to 67%–87% as the disease progresses.[67] In this review, leucopaenia (14.2%–58.7%) was most prevalent, followed by thrombocytopaenia (12.5%–32.6%) and haemolytic anaemia (14.1%). Conversely, another study reported a higher prevalence of leucopaenia (37.8%) and haemolytic anaemia (21.3%) among patients with lupus compared with the findings in this review, while the frequency of thrombocytopaenia

(20.3%) was comparable.[68] Previous research has shown that approximately half of patients with SLE experience low white blood cell counts, while 10%–25% present with low platelet counts, and around 10%–13% develop autoimmune-related anaemia.[69–71] These findings emphasise the need for standardised diagnostic approaches and broader regional representation in Saudi studies.

### Limitations

While our study provides valuable insights into the clinical presentation of extrarenal manifestation of SLE in Saudi Arabia, with the majority of our reviewed studies being retrospective and observational in nature, rather than prospective. Several limitations must be acknowledged, primarily related to potential biases and methodological inconsistencies across the included studies. This study identified several types of bias that may have influenced the findings. Selection bias could be present as most data were derived from hospital-based studies, which may overrepresent patients with more severe diseases. Reporting bias was noted due to inconsistent data collection and selective documentation of clinical features. Measurement bias may have resulted from differences in diagnostic criteria and laboratory methods across studies. Recall and information bias could affect the accuracy of retrospective data, while regional and referral bias was evident, with specialised centres in major cities potentially overrepresenting complex cases, whereas some regions were under-represented. Confounding bias was also a concern, as variations in disease duration, treatment regimens and comorbidities were not consistently controlled for, potentially affecting the reported frequency of clinical features.

## CONCLUSION

This study highlights the distinct patterns and prevalence of extrarenal manifestations of SLE among adult Saudi patients. By systematically analysing available data, we addressed a significant gap in literature, particularly in a region where autoimmune diseases are increasingly recognised as a public health concern. The findings demonstrate variability in musculoskeletal, dermatological, cardiovascular and neurological manifestations across Saudi regions, offering valuable insights into the regional disease profile. Future research should focus on expanding the scope of population-based studies to better understand the environmental, genetic and lifestyle factors influencing disease progression and outcomes in Saudi Arabia. Such efforts will not only contribute to regional healthcare policy development but also enrich the global understanding of SLE heterogeneity.

**Author affiliations**
[1]Department of Internal Medicine, College of Medicine, Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia
[2]Department of Medicine, College of Medicine, Taibah University, Medinah, Saudi Arabia
[3]Rheumatology Unit, Department of Medicine, College of Medicine, King Saud University, Riyadh, Saudi Arabia
[4]Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

**Acknowledgements** The authors thank Princess Nourah bint Abdulrahman University Researchers Supporting Project number (PNURSP2025R210), Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia.

**Contributors** Conceptualisation: FaA, MAO; methodology: HMA, FaA, MAO; formal analysis and investigation: FaA, RA, AA, FeA, HMA, MAO; writing—original draft preparation: FaA, RA, AA, FeA, HMA MD, MAO; supervision: FaA, MAO. FaA is a guarantor.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.



**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Ethics approval** Not applicable.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information.



**ORCID iDs**
Fahidah Alenzi http://orcid.org/0000-0001-8495-9064
Haya M Almalag http://orcid.org/0000-0001-8531-556X

## REFERENCES

1 Almaghlouth IA, Hassen LM, Alahmari HS, *et al*. National systemic lupus erythematosus prospective cohort in Saudi Arabia: A study protocol. *Medicine (Baltimore)* 2021;100:e26704.
2 Al-Arfaj AS, Al-Balla SR, Al-Dalaan AN, *et al*. Prevalence of systemic lupus erythematosus in central Saudi Arabia. *Saudi Med J* 2002;23:87–9.
3 AlOmair M, AlMalki H, AlShahrani M, *et al*. Clinical Manifestations of Systemic Lupus Erythematosus in a Tertiary Center in Saudi Arabia. *Cureus* 2023;15:e41215.
4 Karremah MF, Hassan RY, Faloudah AZ, *et al*. From Symptoms to Diagnosis: An Observational Study of the Journey of SLE Patients in Saudi Arabia. *Open Access Rheumatol* 2022;14:103–11.
5 Alrashdi MN, Alrasheedi SM, Alkhdairi A, *et al*. Primary Healthcare Practitioners' Knowledge, Attitude, and Practice Toward Systemic Lupus Erythematosus in the Qassim Region, Saudi Arabia. *Cureus* 2022;14:e30297.
6 Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev* 2021;10:89.
7 Rethlefsen ML, Kirtley S, Waffenschmidt S, *et al*. PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. *Syst Rev* 2021;10:39.

8 Higgins JPT, Altman DG, Gøtzsche PC, *et al*. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
9 NIH. Quality assessment tools for observational cohort and cross-sectional studies. quality assessment tools. 2019. Available: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools
10 Mays N, Pope C. Assessing quality in qualitative research. *BMJ* 2000;320:50–2.
11 Al-Nasser A-AN, El-Shabrawy Aboul-Enein M, Al-Aska A-K. Systemic Lupus Erythematosus in Riyadh, Saudi Arabia. *J R Soc Health* 1988;108:90–3.
12 Al Arfaj AS, Khalil N. Pregnancy outcome in 396 pregnancies in patients with SLE in Saudi Arabia. *Lupus (Los Angel)* 2010;19:1665–73.
13 Alsuwayegh A, Almaghlouth IA, Almasaoud MA, *et al*. Cost Consequence Analysis of Belimumab versus Standard of Care for the Management of Systemic Lupus Erythematosus in Saudi Arabia: A Retrospective Cohort Study. *Int J Environ Res Public Health* 2023;20:1917.
14 Alhassan N, Almetri T, Abualsoud S, *et al*. Causes of Hospitalization for Systemic Lupus Erythematosus in Saudi Arabia Compared With the Global Setting: A Retrospective Single-center Observational Study. *Cureus* 2021;13:e18858.
15 Alrashdi M, Alrasheedi S, Alkhdairi A, *et al*. Clinical features, serological findings, and survival rate comparison between early versus late-onset systemic lupus erythematosus from 2000 to 2010, two centers experience. *Int J Health Sci (Qassim)* 2020;14:4–10.
16 Al-Saif FM, Al-Balbeesi AO, Al-Samary AI, *et al*. Discoid lupus erythematosus in a Saudi population: Clinical and histopathological study. *Journal of the Saudi Society of Dermatology & Dermatologic Surgery* 2012;16:9–12.
17 Abdel Galil SM, Edrees AM, Ajeeb AK, *et al*. Prognostic significance of platelet count in SLE patients. *Platelets* 2017;28:203–7.
18 Alsowaida N, Alrasheed M, Mayet A, *et al*. Medication adherence, depression and disease activity among patients with systemic lupus erythematosus. *Lupus (Los Angel)* 2018;27:327–32.
19 Hamdani MA, Saud Al-Arfaj AR, Parvez K, *et al*. Pulmonary manifestations of systemic lupus erythematosus patients with and without antiphospholipid syndrome. *Pak J Med Sci* 2015;31:70–5.
20 Abid N, Khan AS, Al Otaibi FH. Systemic lupus erythematosus (SLE) in the eastern region of Saudi Arabia. A comparative study. *Lupus (Los Angel)* 2013;22:1529–33.
21 Al Arfaj AS, Khalil N. Clinical and immunological manifestations in 624 SLE patients in Saudi Arabia. *Lupus (Los Angel)* 2009;18:465–73.
22 Somaily M, Asiri S, Aseery L. Causes and Outcomes of Hospitalization among Systemic Lupus Erythematosus Patients in Aseer Central Hospital, Saudi Arabia: A Retrospective Study. *Egyptian Journal of Hospital Medicine* 2018;71:2358–64.
23 Alzeer AH, Al-Arfaj A, Basha SJ, *et al*. Outcome of patients with systemic lupus erythematosus in intensive care unit. *Lupus (Los Angel)* 2004;13:537–42.
24 Alhammadi NA, Alqahtani HS, Mahmood SE, *et al*. Pulmonary Manifestations of Systemic Lupus Erythematosus Among Adults in Aseer Region, Saudi Arabia. *Int J Gen Med* 2024;17:1007–15.
25 Almaghlouth I, Bohuliga KG, Alanazi B, *et al*. Prevalence of major adverse cardiovascular events among Saudi patients with systemic lupus erythematosus compared with the general population: updates from the national SLE and PURE cohorts. *Lupus Sci Med* 2024;11:e001158.
26 Khan WA, Zaman GS, Alouffi S, *et al*. Depression and its related parameters increased the production of autoantibodies against 16α-hydroxyestrone-albumin complex in systemic lupus erythematosus. *Int Immunopharmacol* 2019;71:215–23.
27 Al-Homood IA, Omran NE, Alwahibi AS, *et al*. Depression in patients with systemic lupus erythematosus: A multicenter study. *Saudi J Med Med Sci* 2017;5:248.
28 Parvez K, Al-Arfaj AR, Hamdani MA, *et al*. Pattern of MRI brain in neuro-psychiatric SLE. Effect of anti-phospholipid antibodies. A study at a tertiary care teaching hospital. *Pak J Med Sci* 2015;31:1182–7.
29 Al-Rayes H, Al-Swailem R, Arfin M, *et al*. Systemic lupus erythematosus and infections: a retrospective study in Saudis. *Lupus (Los Angel)* 2007;16:755–63.
30 Heller T, Ahmed M, Siddiqqi A, *et al*. Systemic lupus erythematosus in Saudi Arabia: morbidity and mortality in a multiethnic population. *Lupus (Los Angel)* 2007;16:908–14.
31 AlShomar A, Sula I, Alsulmi HA, *et al*. Clinical characteristics of systemic lupus erythematosus in Al Qassim region of Saudi Arabia. *The Egyptian Rheumatologist* 2024;46:121–4.
32 Alamoudi OSB, Attar SM. Pulmonary manifestations in systemic lupus erythematosus: association with disease activity. *Respirology* 2015;20:474–80.
33 Alballa SR. Systemic lupus erythematosus in Saudi patients. *Clin Rheumatol* 1995;14:342–6.
34 Sayeeda A, Al Arfaj H, Khalil N, *et al*. Herpes Zoster Infections in SLE in a University Hospital in Saudi Arabia: Risk Factors and Outcomes. *Autoimmune Dis* 2010;2011:174891.
35 Shahin D. Thrombocytopenia and leukocytosis are independent predictors of hyperprolactinemia in systemic lupus erythematosus patients. *The Egyptian Rheumatologist* 2011;33:77–83.
36 Al-Jarallah K, Al-Awadi A, Siddiqui H, *et al*. Systemic lupus erythematosus in Kuwait—hospital based study. *Lupus (Los Angel)* 1998;7:434–8.
37 Alonso MD, Llorca J, Martinez-Vazquez F, *et al*. Systemic lupus erythematosus in northwestern Spain: a 20-year epidemiologic study. *Medicine (Baltimore)* 2011;90:350–8.
38 Wang F, Wang CL, Tan CT, *et al*. Systemic lupus erythematosus in Malaysia: a study of 539 patients and comparison of prevalence and disease expression in different racial and gender groups. *Lupus (Los Angel)* 1997;6:248–53.
39 Cervera R, Khamashta MA, Hughes GRV. The Euro-lupus project: epidemiology of systemic lupus erythematosus in Europe. *Lupus (Los Angel)* 2009;18:869–74.
40 Pons-Estel BA, Catoggio LJ, Cardiel MH, *et al*. The GLADEL multinational Latin American prospective inception cohort of 1,214 patients with systemic lupus erythematosus: ethnic and disease heterogeneity among "Hispanics". *Medicine (Baltimore)* 2004;83:1–17.
41 Li M, Zhang W, Leng X, *et al*. Chinese SLE Treatment and Research group (CSTAR) registry: I. Major clinical characteristics of Chinese patients with systemic lupus erythematosus. *Lupus (Los Angel)* 2013;22:1192–9.
42 El Hadidi KT, Medhat BM, Abdel Baki NM, *et al*. Characteristics of systemic lupus erythematosus in a sample of the Egyptian population: a retrospective cohort of 1109 patients from a single center. *Lupus (Los Angel)* 2018;27:1030–8.
43 Mohammed AG, Alghamdi AA, ALjahlan MA, *et al*. Echocardiographic findings in asymptomatic systemic lupus erythematosus patients. *Clin Rheumatol* 2017;36:563–8.
44 Mok CC. Epidemiology and survival of systemic lupus erythematosus in Hong Kong Chinese. *Lupus (Los Angel)* 2011;20:767–71.
45 Johnson SR, Granton JT. Pulmonary hypertension in systemic sclerosis and systemic lupus erythematosus. *Eur Respir Rev* 2011;20:277–86.
46 Apte M, McGwin G Jr, Vilá LM, *et al*. Associated factors and impact of myocarditis in patients with SLE from LUMINA, a multiethnic US cohort (LV). [corrected]. *Rheumatology (Oxford)* 2008;47:362–7.
47 Eisenberg H, Dubois EL, Sherwin RP, *et al*. Diffuse interstitial lung disease in systemic lupus erythematosus. *Ann Intern Med* 1973;79:37–45.
48 Estes D, Christian CL. The natural history of systemic lupus erythematosus by prospective analysis. *Medicine (Baltimore)* 1971;50:85–95.
49 Annangi S, Dammalapati TR, Nutalapati S, *et al*. Prevalence of Pulmonary Embolism Among Systemic Lupus Erythematosus Discharges: A Decade of Analysis of the National Hospital Discharge Survey. *J Clin Rheumatol* 2017;23:200–6.
50 Zamora MR, Warner ML, Tuder R, *et al*. Diffuse alveolar hemorrhage and systemic lupus erythematosus. Clinical presentation, histology, survival, and outcome. *Medicine (Baltimore)* 1997;76:192–202.
51 Sato S, Temmoku J, Fujita Y, *et al*. Autoantibodies associated with neuropsychiatric systemic lupus erythematosus: the quest for symptom-specific biomarkers. *Fukushima J Med Sci* 2020;66:1–9.
52 Hanly JG, Urowitz MB, Sanchez-Guerrero J, *et al*. Neuropsychiatric events at the time of diagnosis of systemic lupus erythematosus: An international inception cohort study. *Arthritis Rheum* 2007;56:265–73.
53 Bertsias GK, Boumpas DT. Pathogenesis, diagnosis and management of neuropsychiatric SLE manifestations. *Nat Rev Rheumatol* 2010;6:358–67.
54 Govoni M, Bortoluzzi A, Padovan M, *et al*. The diagnosis and clinical management of the neuropsychiatric manifestations of lupus. *J Autoimmun* 2016;74:41–72.
55 Abdel-Nasser AM, Ghaleb RM, Mahmoud JA, *et al*. Association of anti-ribosomal P protein antibodies with neuropsychiatric and other manifestations of systemic lupus erythematosus. *Clin Rheumatol* 2008;27:1377–85.
56 Brey RL, Holliday SL, Saklad AR, *et al*. Neuropsychiatric syndromes in lupus: prevalence using standardized definitions. *Neurology (ECronicon)* 2002;58:1214–20.

57 Unterman A, Nolte JES, Boaz M, *et al*. Neuropsychiatric Syndromes in Systemic Lupus Erythematosus: A Meta-Analysis. *Semin Arthritis Rheum* 2011;41:1–11.
58 Alharbi S. Gastrointestinal Manifestations in Patients with Systemic Lupus Erythematosus. *Open Access Rheumatol* 2022;14:243–53.
59 Hallegua DS, Wallace DJ. Gastrointestinal manifestations of systemic lupus erythematosus. *Curr Opin Rheumatol* 2000;12:379–85.
60 Ebert EC, Hagspiel KD. Gastrointestinal and hepatic manifestations of systemic lupus erythematosus. *J Clin Gastroenterol* 2011;45:436–41.
61 Takeno M, Ishigatsubo Y. Intestinal manifestations in systemic lupus erythematosus. *Intern Med* 2006;45:41–2.
62 Sultan SM, Ioannou Y, Isenberg DA. A review of gastrointestinal manifestations of systemic lupus erythematosus. *Rheumatology (Oxford)* 1999;38:917–32.
63 Zheng RH, Wang JH, Wang SB, *et al*. Clinical and immunopathological features of patients with lupus hepatitis. *Chin Med J (Engl)* 2013;126:260–6.
64 Piga M, Vacca A, Porru G, *et al*. Liver involvement in systemic lupus erythematosus: incidence, clinical course and outcome of lupus hepatitis. *Clin Exp Rheumatol* 2010;28:504–10.
65 Tan EM, Cohen AS, Fries JF, *et al*. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982;25:1271–7.
66 Petri M, Orbai A, Alarcón GS, *et al*. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum* 2012;64:2677–86.
67 Jakes RW, Bae S-C, Louthrenoo W, *et al*. Systematic review of the epidemiology of systemic lupus erythematosus in the Asia-Pacific region: prevalence, incidence, clinical features, and mortality. *Arthritis Care Res (Hoboken)* 2012;64:159–68.
68 El-Garf K, El-Garf A, Gheith R, *et al*. A comparative study between the disease characteristics in adult-onset and childhood-onset systemic lupus erythematosus in Egyptian patients attending a large university hospital. *Lupus (Los Angel)* 2021;30:211–8.
69 Nossent JC, Swaak AJ. Prevalence and significance of haematological abnormalities in patients with systemic lupus erythematosus. *Q J Med* 1991;80:605–12.
70 Harvey AM, Shulman LE, Tumulty PA, *et al*. Systemic lupus erythematosus: review of the literature and clinical analysis of 138 cases. *Medicine (Baltimore)* 1954;33:291–437.
71 Worrall JG, Snaith ML, Batchelor JR, *et al*. SLE: a rheumatological view. Analysis of the clinical features, serology and immunogenetics of 100 SLE patients during long-term follow-up. *Q J Med* 1990;74:319–30.
72 Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.