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Review Article

Epidemiology of systemic lupus erythematosus in Korea

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Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by diverse organ system disabilities, predominantly affecting young females. The clinical manifestations of SLE encompass various organs, including the kidney, cardiovascular system, and central nervous system. Young females with SLE experience higher mortality rates than the general population, making it imperative to gain insights into the disease patterns and associated factors. The current review examines the epidemiological studies to analyze the prevalence, incidence, and mortality trends of SLE in Korea and compares them with the findings from other countries. We aim to identify potential similarities, differences, and factors contributing to the burden of SLE in different populations by exploring the comparative epidemiological aspects. The knowledge derived from this comparison would aid in advancing the overall management of SLE in Korea.

Keywords: Systemic lupus erythematosus, Epidemiology, Mortality

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that manifests with a wide range of organ system disabilities, predominantly affecting young female [1-3]. The clinical manifestations of SLE involve various organs, such as the kidney, cardiovascular system, and central nervous system [4-6]. SLE poses a significant mortality risk among young female, with a mortality rate of 2.6 to 5.0 times higher compared with that in the general population [7-9].

In this review, we scrutinize the prevalence, incidence, and mortality trends of SLE in Korea to gain valuable insights into the dynamic nature of the disease in this population. Additionally, we explore the association of comorbidities like cardiovascular disease (CVD), malignancy, and infection with increased mortality rates among SLE patients. We sought to identify potential similarities, differences, and factors contributing to the burden of SLE in diverse populations worldwide by delving into the comparative epidemiological aspects.

The knowledge derived from this comprehensive analysis holds the potential to advance the overall management of SLE on a global scale. Furthermore, this review's findings would deepen the understanding of SLE, leading to improved treatment outcomes for affected individuals. Altogether, the insights garnered may serve as valuable guidance for the development of a tailored national healthcare system, addressing the specific needs of SLE patients in Korea and beyond.

MAIN SUBJECTS

Prevalence and incidence of SLE

The prevalence and incidence rates of SLE vary depending on race and ethnicity. Over the past years, several epidemiological studies have been conducted specifically focusing on SLE patients in Korea [10-14]. Table 1 provides an overview of the prevalence and incidence of SLE among Korean patients. A pop-

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Table 1. The studies of prevalence and incidence of SLE patients in Korea

Study	Database	Prevalence (/100,000 PYs)	Number of prevalent cases of SLE	Incidence (/100,000 PYs)	Number of incident cases of SLE	Female/male ratio	Age (yr)	Study period
Ju et al. [10]	HIRA	18.8-21.7	2,000	-	-	8.4	All age group	2004~2006
Chung et al. [11]	NHI	77.07	12,756	8.18	4,487	Female	20~44	2009~2016
Bae et al. [12]	NHI	28.02	14,049	3.72	1,849	9.9	All age group	2005~2015
Shim et al. [13]	NHI	20.6-26.5	10,080-13,316	2.5-2.8	1,260-1,398	6.5	All age group	2006~2010
Kim et al. [14]	NHI	30.4-38.0	15,287-19,441	-	-	10	All age group	2012~2016

SLE: systemic lupus erythematosus, HIRA: Health Insurance Review and Assessment, PYs: person-years, NHI: National Health Insurance.

ulation-based cohort study, which utilized the Korean National Health Insurance (NHI) database and employed an operational definition of SLE based on diagnostic codes, medications, and laboratory tests, reported a prevalence rate ranging from 20.6 to 26.5 per 100,000 person-years (PY), with an incidence rate ranging from 2.5 to 2.8 per 100,000 PY between 2006 and 2010 [13]. Another Korean study, using a definition of SLE based on diagnostic codes, revealed slightly increased prevalence and incidence rates of 28.02 per 100,000 PY and 3.72 per 100,000 PY, respectively, between 2005 and 2015 compared to those of previous studies [12]. Notably, among female SLE patients in Korea, the highest prevalence (77.07 per 100,000 PY) and incidence (8.18 per 100,000 PY) were observed during the childbearing ages [11].

A recent systematic review of epidemiological studies on SLE patients demonstrated that the highest estimates of prevalence (241 per 100,000 PY) and incidence (23.2 per 100,000 PY) were reported in North America. The lowest prevalence was observed in Northern Australia (0 cases in a sample of 847 individuals), and the lowest incidence was reported in Africa and Ukraine (0.3 per 100,000 PY) [15]. There were notable variations in the published studies across different countries. Most studies comparing ethnic differences indicated higher SLE incidence and prevalence rates in Black populations, lower rates in White populations, and intermediate rates in Hispanic and Asian populations [16]. Among Asian ethnicity, the prevalence of SLE in Korea was lower than that in China (30 per 100,000 PY) [17] or Taiwan (67.4 per 100,000 PY) [18]. However, a comprehensive data comparison should be conducted cautiously because most reports from Asia used information from hospital records or community surveys, except for Taiwan.

Major organ involvement in patients with SLE

Major organ involvement in SLE typically includes the kidney, cardiovascular system, and central nervous system, while minor organ involvement may affect the skin, joints, and hematopoietic system. Race and ethnicity play a significant role in the manifestation and outcomes of SLE, with Black, Asian, and Hispanic individuals having more severe disease and poorer outcomes [19]. Black individuals have the highest risk of developing SLE, followed by South Asians, East Asians, and other non-White groups compared to White individuals. Moreover, non-White populations tend to experience more severe disease and faster damage accumulation.

1) Renal involvement

Studies have reported that approximately 40% to 60% of SLE patients could develop signs and symptoms of kidney disease during the course of their illness [20,21]. Renal manifestation and prognosis of SLE may be influenced by various factors such as age, gender, ethnicity, and high disease activity [22]. Renal involvement in SLE is more common in female and younger patients [21]. In Korea, the risk of chronic kidney disease (CKD) and mortality rate were increased in patients aged over 50 years [23]. Otherwise, the nationwide cohort study in Taiwan reported that those with juvenile-onset SLE had the highest mortality risk, whereas SLE patients aged under 50 years had a higher risk of end-stage renal disease [24]. Thus far, the renal involvement or renal outcome of patients with SLE has been found to vary depending on their ethnicity and country. In Korea, approximately 15.5% of patients diagnosed with lupus nephritis developed CKD within 10 years [25]. A cohort study using the NHI database in 2000~2008 unraveled that the adjusted hazard ratio of end-stage renal disease for Korean SLE patients was 18.2 (95% CI 5.7~58.2) compared to the non-SLE group [26]. African American and Hispanic patients are known to have worse renal outcomes and mortality than Caucasian patients [27,28], while Asians, including Korean SLE patients [29], have shown

higher rates of renal involvement than Caucasians.

2) Neuropsychiatric involvement

Neuropsychiatric systemic lupus erythematosus (NPSLE) is a complex manifestation of SLE that affects the central nervous system, leading to various neurological and psychiatric symptoms. These manifestations vary widely, including cognitive dysfunction, seizures, psychosis, mood disorders, and cerebrovascular events [30]. In addition, previous studies have reported varying prevalence rates of NPSLE due to differences in study populations, diagnostic criteria, and disease heterogeneity [31,32]. The neuropsychiatric manifestations differed from the age of SLE onset. Late-onset SLE showed lower frequencies of neuropsychiatric SLE, seizures, and psychosis but a higher prevalence of peripheral neuropathy than early-onset SLE [33]. A study in Korea observed NPSLE in a significant portion (38.3%) of SLE patients with an increased risk of mortality (HR 3.09, 95% CI 1.03~9.21) [34]. The Swiss SLE cohort study showed that the prevalence rate of NPSLE was 28.1% [35]. Otherwise, a single-center study in the UK reported that approximately 60% of SLE patients developed neuropsychiatric manifestations [36]. Large-scale multi-center studies were crucial to process large and diverse sample sizes and increasing generalizability. In this regard, an international prospective study conducted by the Systemic Lupus International Collaborating Clinics reported that 52% of SLE patients developed neuropsychiatric events, indicating the substantial burden of NPSLE within the SLE population [37]. These studies provide critical insights into the prevalence, clinical course, and outcomes of NPSLE.

3) Diffuse alveolar hemorrhage and pulmonary hypertension

Diffuse alveolar hemorrhage (DAH) and pulmonary hypertension (PH) are potential complications in SLE patients that contribute to life-threatening conditions [38]. DAH refers to bleeding within the lungs, especially in the small blood vessels, and PH refers to elevated blood pressure in the pulmonary arteries of the lungs [39]. They could be developed as a consequence of chronic inflammation, immune dysregulation, and vascular damage [40]. The incidence rates of DAH in SLE patients vary from 0.5% to 5% [41,42]. In previous studies involving Asian populations, the reported incidence rates were 0.52% in Taiwan [43] and 2.0% in China [44], while Korean SLE patients exhibited a lower incidence rate (1.38%) of DAH compared to the Chinese population [45]. The prognosis of SLE patients with DAH depends on various factors, such as thrombocytopenia, renal failure, and mechanical ventilation [46]. In a previous multivariable analysis, a severe condition requiring mechanical ventilation was maintained as an independent risk factor [47].

Although the exact incidence rate of PH in SLE is difficult to determine, incidence rates have been reported to range from 2% to 14% [48,49]. The incidence of PH depend on the diagnostic tool, as well as disease duration and severity [50,51]. Two studies demonstrated varying incidence rates of PH in SLE patients, ranging from 3.8% among Chinese patients [52] to 14% among Korean patients [53]. Another study involving Korean SLE patients reported that the prevalence of PH was 4.3%, with a higher mortality rate [54]. Understanding the epidemiology of PH in SLE patients can support early detection and treatment strategies to improve patient prognosis.

Comorbidities of SLE patients

SLE patients have an increased risk of comorbidities, such as CVD and cancers [55]. They could affect the long-term outcomes and all-cause mortality of SLE patients. Therefore, several epidemiologic studies on comorbidities in SLE have been conducted.

1) Cardiovascular disease in SLE

CVD remains the leading cause of death among SLE patients [56]. Recent studies have reported an increased risk of ischemic heart disease, heart failure, and stroke in SLE patients [57,58]. Previous research conducted in the US, Sweden, and Canada has consistently shown a 2- to 3-fold higher incidence of CVD in individuals with SLE than in the general population (Table 2) [58-65]. A Korean cohort study that utilized the NHI database also reported similar findings, with SLE patients exhibiting an increased risk of myocardial infarction (MI) (HR 2.74, 95% CI 2.28~3.37), stroke (HR 3.31, 95% CI 2.84~3.86), and heart failure (HR 4.60, 95% CI 3.96~5.35) [64]. In addition, another study evaluating newly diagnosed SLE patients indicated a significantly higher risk of MI (IRR 2.19, 95% CI 1.30~3.68) and ischemic stroke (2.41, 95% CI 1.84~3.15) compared to the general population [66]. Furthermore, incident SLE patients aged over 40 years had a substantially higher CVD risk (HR 1.99, 95% CI 1.66~2.38) compared with that of patients with diabetes mellitus (DM) (HR 1.39, 95% CI 1.22~1.58) [67].

Table 2. The studies of cardiovascular disease in SLE patients

Study	Database	Hazard ratio (95% CI)	Outcomes	Study population	Comparator	Country	Study period
Tornvall et al. [58]	Swedish NPR, CDR, and SCAAR	1.6 (1.4, 1.7)	MI	Prevalent SLE patient	General population	Sweden	1996~2015
Bartels et al. [59]	MESA	1.8	CVD combined MI, stroke and heart failure	Incident SLE patient	Matched population	United States	1991~2008
Barbhaiya et al. [60]	US MAX	2.67	CVD combined MI and stroke	Prevalent SLE patient	General population	United States	2007~2010
Bengtsson et al. [61]	Multi-center	1.27 (0.82, 1.87)	CVD combined MI and stroke	Prevalent SLE patient	General population	Northern Sweden	2000~2007
Chen et al. [62]	US Medicaid	2.7 (2.3, 3.1)	Heart failure	Prevalent SLE patient	General population	United States	2007~2010
Magder et al. [63]	Hopkins Lupus Cohort	2.66	CVD combined MI, thrombotic stroke, clinically definite angina, percutaneous coronary intervention, a coronary bypass procedure, or claudication	Prevalent SLE patient	General population	Unites State	1987~2010
Lim et al. [64]	NHI	2.74 (2.28, 3.37) 3.31 (2.84, 3.86) 4.60 (3.96, 5.35) 3.98 (3.61, 4.39)	MI Stroke Heart failure Cardiac death	Prevalent SLE patient	General population	Korea	2008~2015
Yafasova et al. [65]	Danish administrative registries	1.93 (1.46, 2.55) 3.53 (1.82, 6.84) 6.88 (3.53, 13.4)	MI Ischemic stroke HF	Prevalent SLE patient	General population	Denmark	1996~2018
Han et al. [66]	NHI	2.40 (1.88, 3.05) 2.19 (1.30, 3.68) 2.41 (1.84, 3.15)	MACE combined MI and stroke MI Stroke	Incident SLE patient	General population	Korea	2008~2018
Han et al. [67]	NHI	1.39 (1.22, 1.58)	CVD combined MI, stroke, and cardiac arrest	Incident SLE patient	General population	Korea	2008~2018

SLE: systemic lupus erythematosus, CI: confidence interval, MESA: Marshfield Epidemiologic Study Area, MI: myocardial infarction, MAX: Medicaid Analytic eXtract, NHI: National Health Insurance, NIR: National Inpatient Register, CDR: cause of death register, SCAAR: Swedish Coronary Angiography and Angioplasty Register.

Importantly, differences in definitions across studies should be carefully considered while comparing epidemiological studies on CVD. For example, the risk of heart failure was reported to be 1.7 times higher in Korean SLE patients than in US patients [61,64]. However, this difference may be attributed to variations in the heart failure definition. In the US study, heart failure was defined based on diagnostic codes with hospitalization, whereas the Korean study included diagnostic codes with both hospitalization and outpatient visits.

2) Cancer in SLE

It is well known that SLE can be associated with specific types of cancer. Table 3 depicts a few studies on cancer risk in SLE patients [68-75]. A recent study reported that the standardized incidence ratio (SIR) of overall cancer in SLE patients was 1.14 (95% CI 1.05~1.23) [76]. A meta-analysis identified SLE as a risk factor for most cancers, except for prostate cancer and cutaneous melanoma [77]. In a previous study involving female SLE patients, the increased rate of cervical intraepithelial neoplasia was documented in SLE patients treated with intravenous cyclophosphamide [78]. However, there has been no clear explanation for the etiology and pathogenesis of cancer development in SLE patients. Immunosuppressive drugs, chronic inflammation and damage, and genetic susceptibility could be related to an increased risk of cancer development in SLE [79,80].

Several studies have been performed in Korea to determine the risk of cancer in SLE. A nationwide cohort study performed in Korea using NHI data demonstrated an increased risk of overall cancer (SIR 1.75, 95% CI 1.63~1.87), solid cancer (SIR 1.65, 95% CI 1.53~1.77), and hematologic cancer (SIR 5.85, 95% CI 4.48~7.27) [70]. In another Korean study based on the NHI database, Korean patients with SLE showed an increased risk of overall cancer (SIR 1.44, 95% CI 1.33~1.56) [71]. For Asian ethnicity, SLE patients in Taiwan had similar incidence rates of cancer development [69]. The cohort study identified an increased risk of overall cancer (SIR 1.76, 95% CI 1.74~1.79), vulva/vagina cancer (SIR 4.76, 95% CI 4.24~5.33), kidney cancer (SIR 3.99, 95% CI 3.74~4.27), nasopharyngeal cancer (SIR 4.18, 95% CI 3.93~4.45), and hematologic cancer (SIR 4.96, 95% CI 4.79~5.14). It is important to conduct multiple studies to provide valid and generalizable information to physicians and patients. Therefore, further studies should be focused on verifying the heterogeneity of a cancer type and preventable risk factors for cancer.

3) Serious infection in SLE

SLE patients have a higher risk of experiencing severe infections, including the first infection requiring hospitalization, a

Table 3. The studies of malignancies in SLE patients

Study	Database	Overall SIR (95% CI)	Site-specific cancer	Study population	Country	Study period
Hsu et al. [68]	NHI	-	Breast, haematological, colorectal, lung, and hepatobiliary	Prevalent SLE patient	Taiwan	2001~2013
Chen et al. [69]	NHI	1.76 (1.74, 1.79)	Haematological, vagina/vulva, nasopharynx, and kidney	Prevalent SLE patient	Taiwan	1996~2007
Han et al. [70]	NHI	1.75 (1.63, 1.87)	Haematological, head and neck, larynx, bladder, and liver	Prevalent SLE patient	Korea	2012~2014
Bae et al. [71]	NHI	1.44 (1.33, 1.56)	Haematological, cervical, ovarian, oral, thyroid	Prevalent SLE patient	Korea	2008~2014
Kang et al. [72]	Korea National Cancer Registry	1.45 (0.74, 2.16)	Haematological, cervical, and bladder	Prevalent SLE patient	Korea	1997~2007
Björnådal et al. [73]	National Swedish Cancer Register	1.25 (1.14, 1.37)	Haematological, lung, and squamous cell skin	Prevalent SLE patient	Sweden	1964~1995
Westermann et al. [74]	Danish Cancer Registry	1.45 (1.30, 1.62)	Haematologic, hepatobiliary, and nasopharynx	Prevalent SLE patient	Denmark	1995~2014
Dey et al. [75]	UCLH Lupus Clinic	1.05 (0.52, 1.56)	Cervical, prostate, and pancreatic	Prevalent SLE patient	UK	1978~2010

SLE: systemic lupus erythematosus, SIR: standardized incidence ratio, CI: confidence interval, NHI: National Health Insurance, UCLH: University College London Hospital.

greater total number of severe infections, and infection-related mortality compared to the healthy individuals [81]. A study in Korea revealed that 11.2% of SLE patients experienced frequent hospitalizations, and major cause was disease flare (71.2%) and infection (17.1%) [82]. Another study revealed that infection was one of the major causes of death among SLE patients, highlighting the importance of managing infection risk in this population [83]. And, a population-based study in British reported that SLE patients had an increased risk of severe infection (HR 1.82, 95% CI 1.66~1.99) and infection-related mortality (HR 1.61, 95% CI 1.24~2.08) [84].

It was recognized that the infection risk in SLE patients was associated with various factors, such as immunosuppressive agents, comorbidities, and disease activity [85]. A cohort study in Japan suggested that the above 5 mg of prednisolone could pose an infection risk in SLE patients [86]. In Spain, incident SLE patients showed a 2~4 folds risk of severe infection, especially with azathioprine initiators [87]. In another study, the difference in infection risk based on SLE patients' treatment was not evident. A few factors, including prednisolone dose, hypogammaglobulinemia, and comorbidities, significantly impacted serious infections [88]. While the heterogeneity of study design, patient population, and varying definition of infection makes direct comparison challenging, SLE patients experience a substantially higher risk of infections compared to the general population.

Mortality of SLE patients

The prognosis of SLE patients has shown significant improvement compared to previous years, with the persistence of low disease activity. However, due to various contributing factors, their mortality rate is still higher than the general population [89]. Mortality among SLE patients is high across all racial and ethnic groups; nevertheless, it is especially pronounced in Asian populations. In Korea, Chun et al. [90] showed that SLE patients had an increased death risk with a crude mortality rate of 596.0 per 100,000 PY and a standardized mortality ratio (SMR) of 3.02. This was slightly lower than the SMR of 3.8 in Asian groups from a US registry (CLSP), and it was higher than the SMR of white (2.3) and black (2.0) individuals [91]. Another multi-center retrospective cohort study reported that the cumulative 5-year survival rate was 96% among Korean SLE patients [83]. A cohort of SLE patients in a single center in China showed a 5-year survival rate of 93.8% [92], and an Egyptian study reported that the overall cumulative survival rate was 82.9% at 5 years after SLE diagnosis [93], which were lower than that in Korea. Further information on mortality and causes for 20, 30, and 40 years would be helpful to ensure a higher quality of life in patients.

CONCLUSION

The overall prevalence and incidence of SLE have increased in Korea. Several studies have been conducted on SLE patients to assess it as an independent risk factor for cancer, CVD, and other diseases, which may affect the mortality rate. In addition, it is worth noting that variations in population structure, study design, and diagnostic criteria across different studies could contribute to result variations. Recent population-based studies conducted in Korea using the NHI database have significantly contributed to our understanding of SLE. These findings can potentially establish guidelines for diagnosing and treating Korean patients with SLE.

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CONFLICT OF INTEREST

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AUTHOR CONTRIBUTIONS

Y.K.S. and J.Y.H. were involved in the conception and study design. Y.K.S., S.K.C., and J.Y.H. were responsible for the data acquisition, analysis, and interpretation processes. Y.K.S., S.K.C., and J.Y.H were involved in revision of submitted manuscript. All authors approved the final version of submitted manuscript.

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REFERENCES

1. Becker-Merok A, Nossent HC. Damage accumulation in systemic lupus erythematosus and its relation to disease activity and mortality. J Rheumatol 2006;33:1570-7.
2. Biazar C, Sigges J, Patsinakidis N, Ruland V, Amler S, Bonsmann G, et al. Cutaneous lupus erythematosus: first multicenter database analysis of 1002 patients from the European Society of Cutaneous Lupus Erythematosus (EUSCLE). Autoimmun Rev 2013;12:444-54.
3. Li Z, Xu D, Wang Z, Wang Y, Zhang S, Li M, et al. Gastrointestinal system involvement in systemic lupus erythematosus. Lupus 2017;26:1127-38.
4. Ward MM. Premature morbidity from cardiovascular and cerebrovascular diseases in women with systemic lupus erythematosus. Arthritis Rheum 1999;42:338-46.
5. Danchenko N, Satia JA, Anthony MS. Epidemiology of systemic lupus erythematosus: a comparison of worldwide disease burden. Lupus 2006;15:308-18.
6. Renau AI, Isenberg DA. Male versus female lupus: a comparison of ethnicity, clinical features, serology and outcome over a 30 year period. Lupus 2012;21:1041-8.
7. Yen EY, Singh RR. Brief report: lupus-an unrecognized leading cause of death in young females: a population-based study using nationwide death certificates, 2000-2015. Arthritis Rheumatol 2018;70:1251-5.
8. Bultink IEM, de Vries F, van Vollenhoven RF, Lalmohamed A. Mortality, causes of death and influence of medication use in patients with systemic lupus erythematosus vs matched controls. Rheumatology (Oxford) 2021;60:207-16.
9. Lee YH, Choi SJ, Ji JD, Song GG. Overall and cause-specific mortality in systemic lupus erythematosus: an updated meta-analysis. Lupus 2016;25:727-34.
10. Ju JH, Yoon SH, Kang KY, Kim IJ, Kwok SK, Park SH, et al. Prevalence of systemic lupus erythematosus in South Korea: an administrative database study. J Epidemiol 2014;24:295-303.
11. Chung MK, Park JS, Lim H, Lee CH, Lee J. Incidence and prevalence of systemic lupus erythematosus among Korean women in childbearing years: a nationwide population-based study. Lupus 2021;30:674-9.
12. Bae EH, Lim SY, Han KD, Jung JH, Choi HS, Kim HY, et al. Trend of prevalence and incidence of systemic lupus erythematosus in South Korea, 2005 to 2015: a nationwide population-based study. Korean J Intern Med 2020;35:652-61.
13. Shim JS, Sung YK, Joo YB, Lee HS, Bae SC. Prevalence and incidence of systemic lupus erythematosus in South Korea. Rheumatol Int 2014;34:909-17.
14. Kim H, Cho SK, Kim JW, Jung SY, Jang EJ, Bae SC, et al. An increased disease burden of autoimmune inflammatory rheumatic diseases in Korea. Semin Arthritis Rheum 2020;50:526-33.
15. 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 (Oxford) 2017;56:1945-61.
16. Li S, Gong T, Peng Y, Nieman KM, Gilbertson DT. Prevalence and incidence of systemic lupus erythematosus and associated outcomes in the 2009-2016 US Medicare population. Lupus 2020;29:15-26.
17. Li R, Sun J, Ren LM, Wang HY, Liu WH, Zhang XW, et al. Epidemiology of eight common rheumatic diseases in China: a large-scale cross-sectional survey in Beijing. Rheumatology (Oxford) 2012;51:721-9.
18. Chiu YM, Lai CH. Nationwide population-based epidemiologic study of systemic lupus erythematosus in Taiwan. Lupus 2010;19:1250-5.
19. Lewis MJ, Jawad AS. The effect of ethnicity and genetic ancestry on the epidemiology, clinical features and outcome of systemic lupus erythematosus. Rheumatology (Oxford) 2017;56(suppl_1):i67-77.
20. Pons-Estel BA, Catoggio LJ, Cardiel MH, Soriano ER, Gentiletti S, Villa AR, 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.
21. Hanly JG, O'Keeffe AG, Su L, Urowitz MB, Romero-Diaz J, Gordon C, et al. The frequency and outcome of lupus nephritis: results from an international inception cohort study. Rheumatology (Oxford) 2016;55:252-62.
22. Parodis I, Tamirou F, Houssiau FA. Prediction of prognosis and renal outcome in lupus nephritis. Lupus Sci Med 2020;7:e000389.
23. Kang JH, Park DJ, Lee KE, Lee JS, Choi YD, Lee SS. Comparison of clinical, serological, and prognostic differences among juvenile-, adult-, and late-onset lupus nephritis in Korean patients. Clin Rheumatol 2017;36:1289-95.
24. Chen YM, Lin CH, Chen HH, Chang SN, Hsieh TY, Hung WT, et al. Onset age affects mortality and renal outcome of female systemic lupus erythematosus patients: a nationwide population-based study in Taiwan. Rheumatology (Oxford) 2014;53:180-5.
25. Jeon H, Lee J, Ju JH, Kim WU, Park SH, Moon SJ, et al. Chronic kidney disease in Korean patients with lupus nephritis: over a 35-year period at a single center. Clin Rheumatol 2022;41:1665-74.
26. Yu KH, Kuo CF, Chou IJ, Chiou MJ, See LC. Risk of end-stage renal disease in systemic lupus erythematosus patients: a nationwide population-based study. Int J Rheum Dis 2016;19:1175-82.
27. Maningding E, Dall'Era M, Trupin L, Murphy LB, Yazdany J. Racial and ethnic differences in the prevalence and time to onset of manifestations of systemic lupus erythematosus: the California Lupus Surveillance Project. Arthritis Care Res (Hoboken) 2020;72:622-9.
28. Adler M, Chambers S, Edwards C, Neild G, Isenberg D. An assessment of renal failure in an SLE cohort with special reference to ethnicity, over a 25-year period. Rheumatology (Oxford) 2006;45:1144-7.
29. Jakes RW, Bae SC, Louthrenoo W, Mok CC, Navarra SV, Kwon N. 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.
30. Hanly JG, McCurdy G, Fougere L, Douglas JA, Thompson K. Neuropsychiatric events in systemic lupus erythematosus: attribution and clinical significance. J Rheumatol 2004;31:2156-62.

31. Ainiala H, Loukkola J, Peltola J, Korpela M, Hietaharju A. The prevalence of neuropsychiatric syndromes in systemic lupus erythematosus. Neurology 2001;57:496-500.
32. Sibley JT, Olszynski WP, Decoteau WE, Sundaram MB. The incidence and prognosis of central nervous system disease in systemic lupus erythematosus. J Rheumatol 1992;19:47-52.
33. Pamuk ON, Raza AA, Hasni S. Neuropsychiatric lupus in late and early onset systemic lupus erythematosus patients: a systematic review and meta-analysis. Rheumatology (Oxford) 2023 Jun 21 [Epub]. DOI: 10.1093/rheumatology/kead297
34. Ahn GY, Kim D, Won S, Song ST, Jeong HJ, Sohn IW, et al. Prevalence, risk factors, and impact on mortality of neuropsychiatric lupus: a prospective, single-center study. Lupus 2018;27:1338-47.
35. Meier AL, Bodmer NS, Wirth C, Bachmann LM, Ribi C, Pröbstel AK, et al. Neuro-psychiatric manifestations in patients with systemic lupus erythematosus: a systematic review and results from the Swiss lupus cohort study. Lupus 2021;30:1565-76.
36. Sanna G, Bertolaccini ML, Cuadrado MJ, Laing H, Khamashta MA, Mathieu A, et al. Neuropsychiatric manifestations in systemic lupus erythematosus: prevalence and association with antiphospholipid antibodies. J Rheumatol 2003;30:985-92.
37. Hanly JG, Urowitz MB, Gordon C, Bae SC, Romero-Diaz J, Sanchez-Guerrero J, et al. Neuropsychiatric events in systemic lupus erythematosus: a longitudinal analysis of outcomes in an international inception cohort using a multistate model approach. Ann Rheum Dis 2020;79:356-62.
38. Quadrelli SA, Alvarez C, Arce SC, Paz L, Sarano J, Sobrino EM, et al. Pulmonary involvement of systemic lupus erythematosus: analysis of 90 necropsies. Lupus 2009;18:1053-60.
39. Segal AM, Calabrese LH, Ahmad M, Tubbs RR, White CS. The pulmonary manifestations of systemic lupus erythematosus. Semin Arthritis Rheum 1985;14:202-24.
40. Al-Adhoubi NK, Bystrom J. Systemic lupus erythematosus and diffuse alveolar hemorrhage, etiology and novel treatment strategies. Lupus 2020;29:355-63.
41. Jiang M, Chen R, Zhao L, Zhang X. Risk factors for mortality of diffuse alveolar hemorrhage in systemic lupus erythematosus: a systematic review and meta-analysis. Arthritis Res Ther 2021;23:57.
42. Kazzaz NM, Coit P, Lewis EE, McCune WJ, Sawalha AH, Knight JS. Systemic lupus erythematosus complicated by diffuse alveolar haemorrhage: risk factors, therapy and survival. Lupus Sci Med 2015;2:e000117.
43. Chang MY, Fang JT, Chen YC, Huang CC. Diffuse alveolar hemorrhage in systemic lupus erythematosus: a single center retrospective study in Taiwan. Ren Fail 2002;24:791-802.
44. Sun Y, Zhou C, Zhao J, Wang Q, Xu D, Zhang S, et al. Systemic lupus erythematosus-associated diffuse alveolar hemorrhage: a single-center, matched case-control study in China. Lupus 2020;29:795-803.
45. Kwok SK, Moon SJ, Ju JH, Park KS, Kim WU, Cho CS, et al. Diffuse alveolar hemorrhage in systemic lupus erythematosus: risk factors and clinical outcome: results from affiliated hospitals of Catholic University of Korea. Lupus 2011;20:102-7.
46. Martínez-Martínez MU, Abud-Mendoza C. Predictors of mortality in diffuse alveolar haemorrhage associated with systemic lupus erythematosus. Lupus 2011;20:568-74.
47. Kim D, Choi J, Cho SK, Choi CB, Kim TH, Jun JB, et al. Clinical characteristics and outcomes of diffuse alveolar hemorrhage in patients with systemic lupus erythematosus. Semin Arthritis Rheum 2017;46:782-7.
48. Prabu A, Patel K, Yee CS, Nightingale P, Situnayake RD, Thickett DR, et al. Prevalence and risk factors for pulmonary arterial hypertension in patients with lupus. Rheumatology (Oxford) 2009;48:1506-11.
49. Chen HA, Hsu TC, Yang SC, Weng CT, Wu CH, Sun CY, et al. Incidence and survival impact of pulmonary arterial hypertension among patients with systemic lupus erythematosus: a nationwide cohort study. Arthritis Res Ther 2019;21:82.
50. Pérez-Peñate GM, Rúa-Figueroa I, Juliá-Serdá G, León-Marrero F, García-Quintana A, Ortega-Trujillo JR, et al. Pulmonary arterial hypertension in systemic lupus erythematosus: prevalence and predictors. J Rheumatol 2016;43:323-9.
51. Tselios K, Gladman DD, Urowitz MB. Systemic lupus erythematosus and pulmonary arterial hypertension: links, risks, and management strategies. Open Access Rheumatol 2017;9:1-9.
52. Li M, Wang Q, Zhao J, Li Z, Ye Z, Li C, et al. Chinese SLE Treatment and Research group (CSTAR) registry: II. Prevalence and risk factors of pulmonary arterial hypertension in Chinese patients with systemic lupus erythematosus. Lupus 2014;23:1085-91.
53. Min HK, Lee JH, Jung SM, Lee J, Kang KY, Kwok SK, et al. Pulmonary hypertension in systemic lupus erythematosus: an independent predictor of patient survival. Korean J Intern Med 2015;30:232-41.
54. Kim JS, Kim D, Joo YB, Won S, Lee J, Shin J, et al. Factors associated with development and mortality of pulmonary hypertension in systemic lupus erythematosus patients. Lupus 2018;27:1769-77.
55. Arnaud L, Tektonidou MG. Long-term outcomes in systemic lupus erythematosus: trends over time and major contributors. Rheumatology (Oxford) 2020;59(Suppl5):v29-38.
56. Björnådal L, Yin L, Granath F, Klareskog L, Ekbom A. Cardiovascular disease a hazard despite improved prognosis in patients with systemic lupus erythematosus: results from a Swedish population based study 1964-95. J Rheumatol 2004;31:713-9.
57. Guraieb-Chahín P, Cantú-Brito C, Soto-Mota A, Guerrero-Torres L, Flores-Silva F, Chiquete E, et al. Stroke in systemic lupus erythematosus: epidemiology, mechanism, and long-term outcome. Lupus 2020;29:437-45.
58. Tornvall P, Göransson A, Ekman J, Järnbert-Pettersson H. Myocardial infarction in systemic lupus erythematosus: incidence and coronary angiography findings. Angiology 2021;72:459-64.
59. Bartels CM, Buhr KA, Goldberg JW, Bell CL, Visekruna M, Nekkanti S, et al. Mortality and cardiovascular burden of systemic lupus erythematosus in a US population-based cohort. J Rheumatol 2014;41:680-7.
60. Barbhaiya M, Feldman CH, Chen SK, Guan H, Fischer MA, Everett BM, et al. Comparative risks of cardiovascular disease in patients with systemic lupus erythematosus, diabetes mellitus, and in general medicaid recipients. Arthritis Care Res (Hoboken) 2020;72:1431-9.
61. Bengtsson C, Ohman ML, Nived O, Rantapää Dahlqvist S. Cardiovascular event in systemic lupus erythematosus in northern Sweden: incidence and predictors in a 7-year follow-up study. Lupus 2012;21:452-9.
62. Chen SK, Barbhaiya M, Fischer MA, Guan H, Yoshida K, Feldman

CH, et al. Heart failure risk in systemic lupus erythematosus compared to diabetes mellitus and general medicaid patients. Semin Arthritis Rheum 2019;49:389-95.
63. Magder LS, Petri M. Incidence of and risk factors for adverse cardiovascular events among patients with systemic lupus erythematosus. Am J Epidemiol 2012;176:708-19.
64. Lim SY, Bae EH, Han KD, Jung JH, Choi HS, Kim HY, et al. Systemic lupus erythematosus is a risk factor for cardiovascular disease: a nationwide, population-based study in Korea. Lupus 2018;27:2050-6.
65. Yafasova A, Fosbøl EL, Schou M, Baslund B, Faurschou M, Docherty KF, et al. Long-term cardiovascular outcomes in systemic lupus erythematosus. J Am Coll Cardiol 2021;77:1717-27.
66. Han JY, Kim HY, Jeon YN, Kang GE, Jung SY, Jang EJ, et al. Increased cardiovascular risk in patients with systemic lupus erythematosus: population-based cohort study in Korea. J Rheum Dis 2022;29 Suppl 1:116.
67. Han JY, Cho SK, Jeon Y, Kang G, Kim H, Jung SY, et al. Comparative cardiovascular risk in patients with older-onset systemic lupus erythematosus: a nationwide retrospective cohort study in Korea. Lupus Sci Med 2023;10(Suppl 1):A66-7.
68. Hsu CY, Lin MS, Su YJ, Cheng TT, Lin YS, Chen YC, et al. Cumulative immunosuppressant exposure is associated with diversified cancer risk among 14 832 patients with systemic lupus erythematosus: a nested case-control study. Rheumatology (Oxford) 2017;56:620-8.
69. Chen YJ, Chang YT, Wang CB, Wu CY. Malignancy in systemic lupus erythematosus: a nationwide cohort study in Taiwan. Am J Med 2010;123:1150.e1-6.
70. Han JY, Kim H, Jung SY, Jang EJ, Cho SK, Sung YK. Increased risk of malignancy in patients with systemic lupus erythematosus: population-based cohort study in Korea. Arthritis Res Ther 2021;23:270.
71. Bae EH, Lim SY, Han KD, Jung JH, Choi HS, Kim CS, et al. Systemic lupus erythematosus is a risk factor for cancer: a nationwide population-based study in Korea. Lupus 2019;28:317-23.
72. Kang KY, Kim HO, Yoon HS, Lee J, Lee WC, Ko HJ, et al. Incidence of cancer among female patients with systemic lupus erythematosus in Korea. Clin Rheumatol 2010;29:381-8.
73. Björnådal L, Löfström B, Yin L, Lundberg IE, Ekbom A. Increased cancer incidence in a Swedish cohort of patients with systemic lupus erythematosus. Scand J Rheumatol 2002;31:66-71.
74. Westermann R, Zobbe K, Cordtz R, Haugaard JH, Dreyer L. Increased cancer risk in patients with cutaneous lupus erythematosus and systemic lupus erythematosus compared with the general population: a Danish nationwide cohort study. Lupus 2021;30:752-61.
75. Dey D, Kenu E, Isenberg DA. Cancer complicating systemic lupus erythematosus--a dichotomy emerging from a nested case-control study. Lupus 2013;22:919-27.
76. Bernatsky S, Ramsey-Goldman R, Labrecque J, Joseph L, Boivin JF, Petri M, et al. Cancer risk in systemic lupus: an updated international multi-centre cohort study. J Autoimmun 2013;42:130-5.
77. Song L, Wang Y, Zhang J, Song N, Xu X, Lu Y. The risks of cancer development in systemic lupus erythematosus (SLE) patients: a systematic review and meta-analysis. Arthritis Res Ther 2018;20:270.
78. Ognenovski VM, Marder W, Somers EC, Johnston CM, Farrehi JG, Selvaggi SM, et al. Increased incidence of cervical intraepithelial neoplasia in women with systemic lupus erythematosus treated with intravenous cyclophosphamide. J Rheumatol 2004;31:1763-7.
79. Bashir S, Harris G, Denman MA, Blake DR, Winyard PG. Oxidative DNA damage and cellular sensitivity to oxidative stress in human autoimmune diseases. Ann Rheum Dis 1993;52:659-66.
80. Lin YJ, Wan L, Huang CM, Chen SY, Huang YC, Lai CH, et al. Polymorphisms in the DNA repair gene XRCC1 and associations with systemic lupus erythematosus risk in the Taiwanese Han Chinese population. Lupus 2009;18:1246-51.
81. Petri M, Genovese M. Incidence of and risk factors for hospitalizations in systemic lupus erythematosus: a prospective study of the Hopkins Lupus Cohort. J Rheumatol 1992;19:1559-65.
82. Lee JW, Park DJ, Kang JH, Choi SE, Yim YR, Kim JE, et al. The rate of and risk factors for frequent hospitalization in systemic lupus erythematosus: results from the Korean lupus network registry. Lupus 2016;25:1412-9.
83. Koh JH, Park EK, Lee HN, Kim Y, Kim GT, Suh YS, et al. Clinical characteristics and survival of 413 patients with systemic lupus erythematosus in southeastern areas of South Korea: a multicenter retrospective cohort study. Int J Rheum Dis 2020;23:92-100.
84. Goldblatt F, Chambers S, Rahman A, Isenberg DA. Serious infections in British patients with systemic lupus erythematosus: hospitalisations and mortality. Lupus 2009;18:682-9.
85. Jung JY, Yoon D, Choi Y, Kim HA, Suh CH. Associated clinical factors for serious infections in patients with systemic lupus erythematosus. Sci Rep 2019;9:9704.
86. Abe K, Ishikawa Y, Kita Y, Yajima N, Inoue E, Sada KE, et al. Association of low-dose glucocorticoid use and infection occurrence in systemic lupus erythematosus patients: a prospective cohort study. Arthritis Res Ther 2022;24:179.
87. Simard JF, Rossides M, Gunnarsson I, Svenungsson E, Arkema EV. Infection hospitalisation in systemic lupus in Sweden. Lupus Sci Med 2021;8:e000510.
88. Rodziewicz M, Dyball S, Lunt M, McDonald S, Sutton E, Parker B, et al. Early infection risk in patients with systemic lupus erythematosus treated with rituximab or belimumab from the British Isles Lupus Assessment Group Biologics Register (BILAG-BR): a prospective longitudinal study. Lancet Rheumatol 2023;5:e284-92.
89. Kang KY, Kwok SK, Ju JH, Park KS, Cho CS, Kim HY, et al. The causes of death in Korean patients with systemic lupus erythematosus over 11 years. Lupus 2011;20:989-97.
90. Chun BC, Bae SC. Mortality and cancer incidence in Korean patients with systemic lupus erythematosus: results from the Hanyang lupus cohort in Seoul, Korea. Lupus 2005;14:635-8.
91. Gianfrancesco MA, Dall'Era M, Murphy LB, Helmick CG, Li J, Rush S, et al. Mortality among minority populations with systemic lupus erythematosus, including Asian and Hispanic/Latino persons - California, 2007-2017. MMWR Morb Mortal Wkly Rep 2021;70:236-9.
92. Wang Z, Li M, Wang Y, Xu D, Wang Q, Zhang S, et al. Long-term mortality and morbidity of patients with systemic lupus erythematosus: a single-center cohort study in China. Lupus 2018;27:864-9.
93. A Mohammed RH, Lotfy Fayed H, Ibrahim Emara N. Mortality and disease related comorbidities in systemic lupus erythematosus: data from an Egyptian cohort. Lupus 2022;31:628-36.