



Review Article

Worldwide incidence of suicidal thoughts, attempts, and mortality in systemic lupus erythematosus

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ABSTRACT

The presence of suicidal thoughts, attempts, and fatalities in people with systemic lupus erythematosus (SLE) has been reported in various populations, with different studies showing varying rates. This meta-analysis aims to assess the global prevalence of suicidal thoughts, attempts, and deaths among individuals diagnosed with SLE. A comprehensive search of articles was conducted across several literature databases, such as PubMed, Scopus, and ScienceDirect, to identify relevant studies. The literature search was completed on December 6, 2023. The presence of publication bias was assessed using Egger's regression analysis along with funnel plots, while Cochran Q statistics and I square (I²) values were utilized to analyze heterogeneity. All statistical evaluations were performed using the Comprehensive Meta-Analysis Software version 4. According to the inclusion and exclusion criteria, eleven studies encompassing 1,515 SLE patients were analyzed to assess the prevalence of systemic inflammation (SI). The analysis revealed a 16.8 percent prevalence in the studied populations. Similarly, a total of four and six studies enrolled 3196 and 4134 SLE patients for the calculation of SA and actual suicide frequency in SLE patients, respectively, and the analysis revealed a 2.7 percent and 0.9 percent prevalence of SA and suicidal death, respectively. The current meta-analysis indicates that nearly 17% of SLE patients experience suicidal thoughts, 3% have attempted suicide, and about 1% of SLE patients have died by suicide. To prevent suicidal attempts among SLE patients, clinicians must screen their patients for suicidal ideation and refer them to the appropriate mental health providers.

1. Introduction

Systemic lupus erythematosus (SLE) is marked by the development of autoantibodies that affect multiple organ systems, leading to a wide range of organ dysfunction. Patients with SLE exhibit diverse clinical manifestations, with neuropsychiatric SLE (NPSLE) occurring in 6% to 91% of cases (Sarwar et al., 2021). Depression and anxiety are among the primary psychiatric symptoms observed in NPSLE (Zhang et al., 2017; Moustafa et al., 2020). While suicidal tendencies are not recognized as a clinical manifestation of NPSLE, some SLE patients may experience suicidal thoughts or have a background of attempting suicide (Parperis et al., 2022). This may affect mental well-being and enhance the likelihood of suicidal thoughts in individuals with SLE (Lau and Mak 2009).

Annually, more than 7 lakh people worldwide die by suicide, making it the fourth most common cause of mortality among individuals in the age group of 15-29 years (WHO 2021). The impact of suicide extends beyond individuals to families, communities, and nations. In 2019, economically developing countries accounted for 77% of suicides worldwide. SLE patients often experience a lower quality of life due

to chronic pain, fatigue, and organ impairment (Franco et al., 2014; Kawka et al., 2021). The persistent nature of SLE and its impact on daily life can lead to frustration, hopelessness, and despair (Somers et al., 2012). Psychiatric comorbidities, especially major depressive episodes, are commonly linked to SLE and significantly enhance the risk of suicidal ideation (Somers et al., 2012). Approximately one-third of SLE patients are treated with glucocorticoids (Ruiz-Irastorza et al., 2020) that have been associated with mental health issues (Judd et al., 2014; Yatomi et al., 2020; Kazi and Hoque 2021). The prevalence of depression in SLE patients ranges from approximately 20% to 46% across different studies (Dehghan et al., 2023; Hasan et al., 2024) and is a significant contributing factor to suicide risk (Bachmann 2018). Nevertheless, there is a scarcity of evidence that specifically addresses suicidal behaviors in patients with SLE (Palagini et al., 2013; Hajduk et al., 2016). Although the exact frequency of suicides among this group is not clearly defined, research suggests that individuals with SLE face a higher risk of suicide relative to both the general public and those with other long-term health issues (Li et al., 2018; Parperis et al., 2022).

The incidence of suicidal thoughts, attempts, and deaths among individuals with SLE is unclear and varies across studies. Many

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epidemiological studies do not include information on suicidal intentions, attempts, or the count of recorded suicides within the duration of the study. The variations in the prevalence of suicidal ideation may be attributed to the use of different diagnostic criteria across studies. Additionally, genetic factors are known to significantly influence suicidal behavior, and these factors vary across different populations and ethnicities. Meta-analysis is a robust procedure that systematically integrates data from prior studies with comparable findings, calculates the combined results, and draws firm conclusions with increased statistical power. This study aims to address the gap in understanding the global prevalence and patterns of suicidal behaviors among patients with SLE. By conducting a thorough meta-analysis of existing literature, this research seeks to provide accurate estimates of suicidal ideation, attempts, and completed suicides on a global scale. It will synthesize data from various geographical regions and clinical settings, creating a more comprehensive overview of suicidal behaviors in SLE patients and identifying potential risk factors. This information may serve as a basis for developing psychological interventions for SLE patients.

2. Materials and methods

2.1 Literature search

The systematic review adhered to PRISMA guidelines (Panda 2024). Literature searches were performed across multiple databases, including Google Scholar, PubMed, Scopus, and ScienceDirect, using keywords such as "Suicidal ideation in Systemic Lupus Erythematosus," "Suicidal ideation in SLE," "Suicide and Systemic Lupus Erythematosus," "Suicide and SLE," "Suicidal attempt and Systemic Lupus Erythematosus," and "Suicidal attempt and SLE". Two independent researchers reviewed the titles and abstracts of potential studies, and eligible papers meeting the criteria were downloaded for data extraction. The final search concluded on December 30, 2023.

2.2 Inclusion and exclusion criteria

Stringent inclusion and exclusion criteria were established to maintain the data's relevance. The inclusion criteria specified that studies must focus on SLE patients and offer information regarding suicidal thoughts, attempts, or fatalities, with evaluations carried out using validated techniques. Exclusion criteria included data specific to other diseases or presented only in abstracts or conference proceedings, resulting in the exclusion of those data. The research plan has been registered in the PROSPERO database under the registration number CRD42023488976.

2.3 Data abstraction

Data extraction was conducted independently by two authors and included information on suicidal ideation, attempts, and deaths, as well as patient demographics such as age (mean \pm standard deviation or median with range in years) and disease duration (mean \pm standard deviation or median with range in years). The diagnostic criteria for both SLE and suicidal thoughts were also documented. Subsequently, the studies were categorized into three groups: the occurrence of suicidal ideation, the incidence of suicide attempts, and the rate of suicide fatalities among SLE patients.

2.4 Quality assessment

Two researchers independently assessed the risk of bias utilizing the Joanna Briggs Institute checklist 21 for cross-sectional studies, as detailed in Supplementary Table S1a. The quality of non-randomized trials, cohort studies, and case-control studies was evaluated using the Newcastle-Ottawa Scale (NOS) (Wells et al., 2000), as shown in Supplementary Table S1b,c. Additionally, a NOS modified version was utilized in earlier reviews to assess the quality of uncontrolled studies (Murad et al., 2018), as shown in Supplementary Tables S1d and S2. The NOS assessment was conducted under three main categories: i) subject selection (0-4 stars), ii) subject comparison (0-2 stars), and iii) clinical outcomes (0-3 stars) (Wells et al., 2000). Qualitative scores

were indicated by stars, and a report with a total score of five or more stars was considered high quality according to NOS guidelines. When there were differences in the NOS score for a specific study between the two authors, they addressed it through discussion.

2.5 Statistical analysis

The statistical analyses of the data were done using Comprehensive Meta-Analysis software (CMA) v4 by Biostat Inc. USA. Publication bias was examined by Egger's regression analysis and funnel plots. Study heterogeneity was evaluated with Cochrane Q and I square (I^2) statistics, guiding the choice between fixed-effect and random-effect models. Prevalence figures of suicidal ideation, attempts, and deaths were calculated with a cumulative event rate and 95% confidence interval. A sensitivity analysis was also conducted by excluding individual studies to test the accuracy of the results.

3. Results

3.1 Literature search and eligible reports

Searching the various databases using predefined keywords till December 6, 2023, yielded 3310 articles (PubMed=1195, Scopus=859, Science Direct=1256). We found 18 eligible articles, (Kellum and Haserick 1964; Dubois et al., 1974; Wallace et al., 1981; Swaak et al., 1989; Cohen and Li 1992; Ishikura et al., 2001; Karassa et al., 2003; Li-Yu and Navarra 2007; Jarpa et al., 2011; Xie et al., 2012; Zakeri et al., 2012; Mok et al., 2014; Raafat et al., 2015; Tang et al., 2015; Hajduk et al., 2016; Jalenques et al., 2017; Buji et al., 2018; Grover et al., 2023) for inclusion in the current meta-analysis after careful screening using predefined inclusion criteria. Fig. 1 depicts the search strategies in detail. Out of the 18 articles reviewed, 11 provided data on suicidal ideation (Ishikura et al., 2001; Li-Yu and Navarra 2007; Jarpa et al., 2011; Xie et al., 2012; Zakeri et al., 2012; Mok et al.,

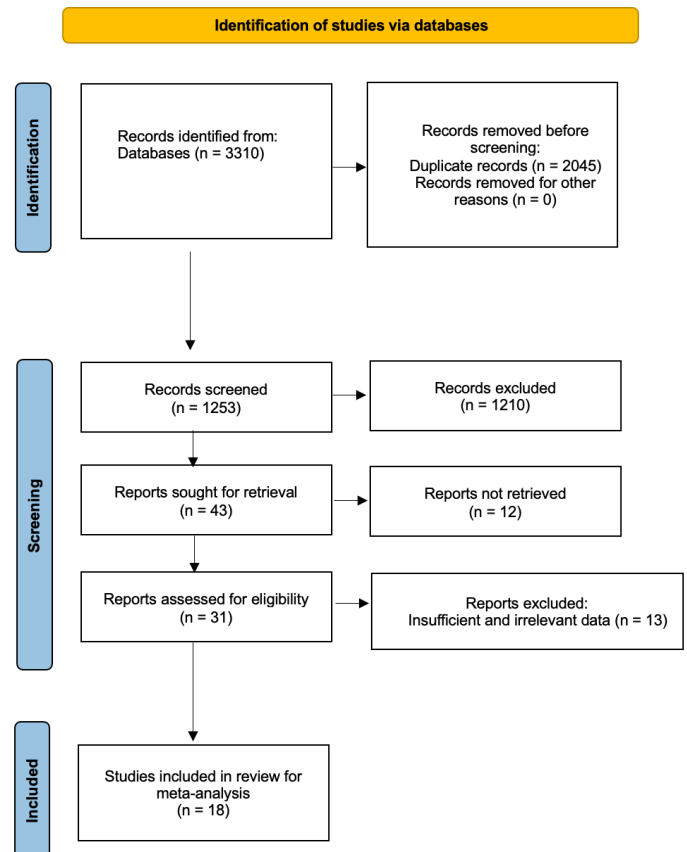


Fig. 1. PRISMA flow diagram outlining the selection of studies included in this meta-analysis.

Table 1.
Preliminary parameters of SLE patients involved in the current study.

Principal author's name & year	Nation	Study type	Total number of SLE patients	Male	Female	Mean age \pm SD/ median (IQR) years	Disease duration \pm SD/ median (IQR) years	Count of patients with suicidal ideation	Count of patients with suicidal attempts	Count of patients suicide (follow-up periods)	SI/SA diagnosis criteria
Grover et al. 2023	India	Cross sectional	79	9	70	30.1 \pm 11.2	3.89 \pm 3.2	35	NR	NR	ICD-10 and PHQ-9
Buji et al. 2017	Malaysia	Cross sectional	130	8	122	37 (18-73)	NR	7	NR	NR	Columbia-Suicidal Severity Rating Scale
Jalenques et al. 2017	France	Case-control	60	13	47	46.8 \pm 13.9	9.7 \pm 7.8	12	4	NR	Mini International Neuropsychiatric Interview (MINI 5.0.0)
Hajduk et al. 2015	Poland	Cross sectional	53	5	48	43.79 \pm 11.66	11.23 \pm 7.74	14	NR	NR	Neuropsychiatric Questionnaire (NP-Q)
Raafat et al. 2015	Egypt	Case-control	50	0	50	27.9 \pm 6.28	5.5 \pm 4.5	10	NR	NR	Beck Suicidal Ideation Scale (BSI)
Tang et al. 2015	Taiwan	Case series	2469	NR	NR	NR	NR	NR	8	NR	NR
Mok et al. 2014	Hong Kong	Cross sectional	367	18	349	40.2 \pm 13	9.3 \pm 7.2	44	45	NR	Beck Scale for Suicidal Ideation (BSSI)
Xie et al. 2012	China	Cross sectional	285	18	267	33.98 \pm 12.98	1.33 (0.21 to 4.96)	98	NR	NR	Beck Depression Inventory (BDI)
Zakeri et al. 2012	Iran	Cross sectional	85	8	77	NR	NR	9	NR	NR	Beck's Depression Inventory (BDI)
Jarpa et al. 2011	Chile	Cross sectional	83	7	76	39 (range 16-72)	5 (0.1 to 40)	8	NR	NR	Mini-Mental State Examination (MMSE) scale
Li-Yu et al. 2007	Philippines	Cross sectional	275	0	275	32.57 \pm 12.26	5.82 \pm 4.98	42	NR	2 (5 months)	Beck Depression Inventory (BDI) II
Karassa et al. 2003	United Kingdom	Case series	300	NR	NR	NR	NR	NR	5	NR	Medical Record Documentation
Ishikura et al. 2001	Japan	Cross sectional	84	0	84	43.1 \pm 12.1	10.9 \pm 6.8	7	NR	NR	Cornell Medical Index (CMI) Health Questionnaire
Cohen et al. 1992	Hong Kong	Retrospective cohort	123	NR	NR	NR	3.1 (0.12 to 15.83)	NR	NR	2 (4 years)	NR
Swaak et al. 1989	Netherland	Prospective cohort	110	16	94	NR	NR	NR	NR	1 (10 years)	NR
Wallace et al. 1981	Los Angeles	Prospective cohort	609	NR	NR	NR	NR	NR	NR	4 (30 years)	NR
Dubois et al. 1974	USA	Case series	249	NR	NR	NR	NR	NR	NR	3 (28 years)	NR
Kellum et al. 1964	USA	Prospective cohort	299	NR	NR	NR	NR	NR	NR	2 (11 years)	NR

Note: Data are presented in number. SD: standard deviation, IQR: inter quartile range, NR: Not reported, SLE: Systemic lupus erythematosus, SI: Suicidal ideation, SA: Suicidal attempts, ICD: International Classification of Diseases, PHQ: Patient health questionnaire.

2014; Raafat et al., 2015; Hajduk et al., 2016; Jalenques et al., 2017; Buji et al., 2018; Grover et al., 2023), four reported suicide attempts (Karassa et al., 2003; Mok et al., 2014; Tang et al., 2015; Jalenques et al., 2017), and six included information on suicide-related deaths among SLE patients (Kellum and Haserick 1964; Dubois et al., 1974; Wallace et al., 1981; Swaak et al., 1989; Cohen and Li 1992; Li-Yu and Navarra 2007) (Table 1). Two studies contained data on both suicidal ideation and attempts (Mok et al., 2014; Jalenques et al., 2017), while one study covered both suicidal ideation and deaths due to suicide in SLE patients (Li-Yu and Navarra 2007). All studies were assessed using NOS, and only those scoring five or more stars were included in the meta-analysis.

3.2 Publication bias

Funnel plots (Fig. 2) and Egger's regression analysis were utilized to assess publication bias in this study. The results indicated no evidence of publication bias for the prevalence of suicidal ideation (intercept: -3.56, 95%CI= -8.83 to 1.70, p=0.16), suicide attempts (intercept: -7.45, 95%CI= -31.76 to 16.86, p=0.31), or completed suicides (intercept: 0.57, 95%CI= -2.89 to 4.04, p=0.66).

3.3 Heterogeneity analysis

The heterogeneity of the included studies was assessed using Cochran Q and I-square (I^2) statistics. Both suicidal ideation and suicide attempts demonstrated significant heterogeneity (Suicidal ideation: Cochran Q=111.09, $P_{\text{heterogeneity}}=0.00$, $I^2=90.00$; Suicidal attempts: Cochran Q=103.60, $P_{\text{heterogeneity}}=0.00$, $I^2=97.10$), leading to the application of a random-effects model for meta-analysis. Conversely, data on the prevalence of completed suicides exhibited homogeneity (Cochran Q=1.62, $P_{\text{heterogeneity}}=0.89$, $I^2=0.00$), supporting the use of a fixed-effects model for the analysis.

3.4 Prevalence of suicidal ideation

A total of 11 reports were found to be eligible for investigating the prevalence of suicidal ideation, comprising data from 1551 SLE patients. The prevalence of suicidal ideation ranges from 5.3%²⁸ to 44%³¹. The combined prevalence of suicidal ideation revealed a worldwide frequency of 16.8% with a 95% confidence interval from 11% to 24.5% (Fig. 3a).

3.5 Frequency of suicidal attempts in SLE patients

The present analysis considered data from four studies involving 3196 patients with lupus to investigate the occurrence of suicide attempts. A meta-analysis conducted using a random-effects model estimated the overall prevalence of suicide attempts at 2.7%, with a 95% confidence interval ranging from 0.4% to 16.1% (as shown in Fig. 3b).

3.6 The Complete suicide rate in SLE patients

Six eligible reports on complete suicide data during the follow-up period were considered to evaluate the prevalence of complete suicide rate among 4,134 SLE patients. Using a fixed-effects model, the meta-analysis determined that the overall prevalence of completed suicides was 0.9%, with a 95% confidence interval of 0.5% to 1.5% (as shown in Fig. 3c).

3.7 Sensitivity analysis

Sensitivity analysis was conducted to evaluate the stability of the meta-analysis by systematic exclusion of one study at a time and comparison of outcomes to the original results. Significant deviations in the sensitivity analysis findings from primary meta-analysis could

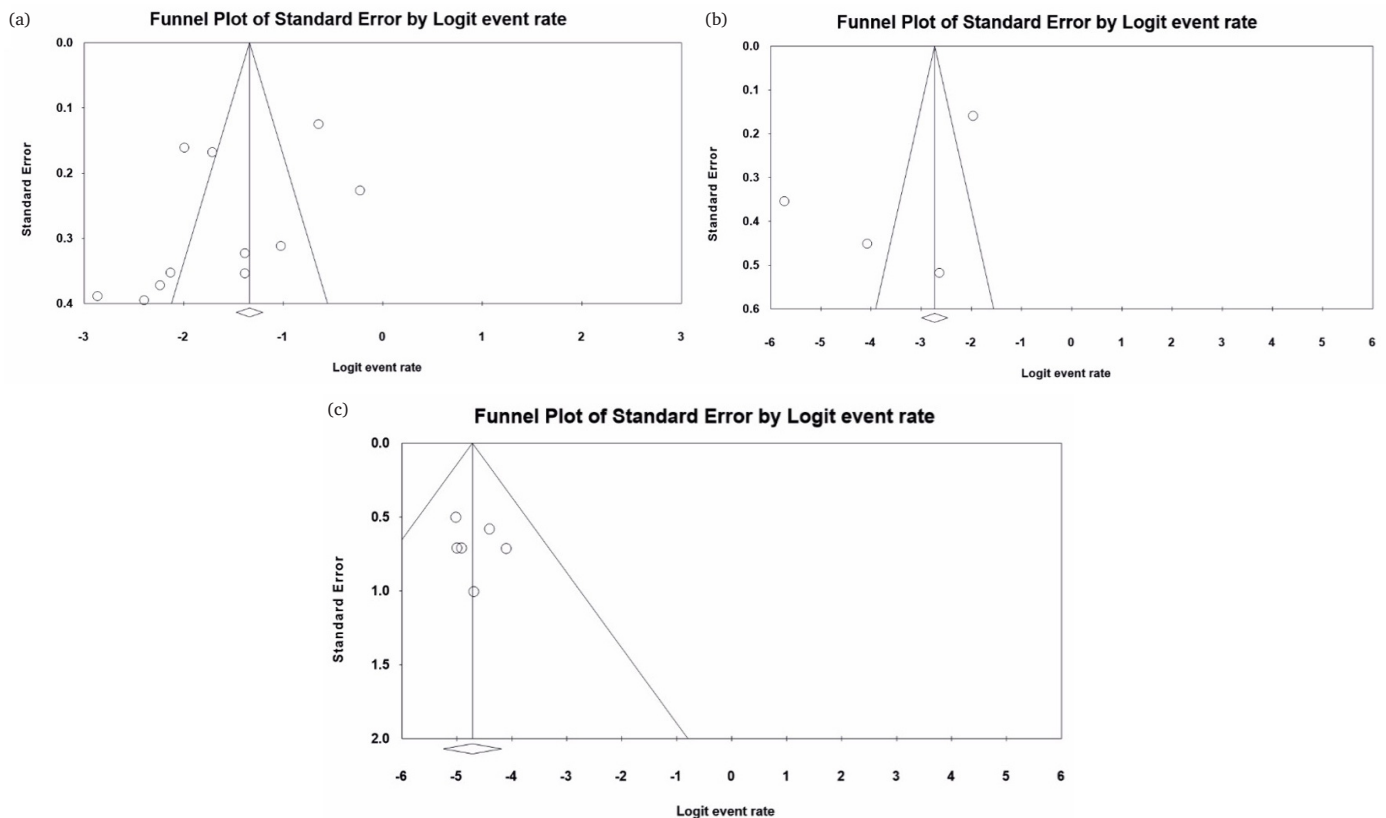


Fig. 2. Funnel plots assessing publication bias in the included studies. The publication bias for the prevalence of (a) suicidal ideation, (b) suicide attempts, and (c) suicide death rates in SLE patients was analyzed using CMA v3. The plots indicated no publication bias in the studies included in the global assessment of suicidal ideation, attempts, and mortality in SLE patients.

indicate weaker conclusions. However, as depicted in Fig. 4, the analyses for the prevalence of suicidal ideation, attempts, and completed suicides showed minimal variations, confirming the robustness of the results.

4. Discussion

The present study explored the worldwide prevalence of suicide ideation, attempts, and actual suicidal death in SLE patients using earlier published articles. It observed about 17% of SLE patients had suicidal ideation, 2.7% had a history of suicidal attempts, and 1% committed suicide during the follow-up period of the investigations. A previous cross-sectional study conducted across 17 countries in the general population found 9.2 percent suicidal ideation and 2.7 percent suicidal attempts (Nock et al., 2008). Although the general population's rate of suicide attempts is comparable to that of SLE patients, suicidal ideation is more common in SLE patients. In addition, a recent report from the World Health Organization showed that 7,03,000 people worldwide attempted suicide in 2019 (WHO 2021), which represents 0.009 percent of the world's population. According to the current analysis, SLE patients have a suicidal death rate that is approximately 100 times higher than the general population. To the best of our knowledge, this research is the first to examine the occurrence of three main types of suicidal behaviors in patients with SLE by utilizing a suitable statistical method.

The specific cause for the increased occurrence of suicidal thoughts in patients with SLE is not known. However, several factors have been attributed to the development of suicidal behaviors in patients. The neuropsychiatric side effects of glucocorticoid administration include psychosis, dementia, mood swings, anxiety, and insomnia (Kazi and Hoque 2021). As glucocorticoids are typically used to treat SLE (Luijten et al., 2013; Porta et al., 2020), patients may experience psychosis and mood disorders, which could increase the likelihood of suicidal thoughts. Additionally, a connection has been noted between suicidal

thoughts in patients with SLE and the activity of the disease in the years leading up to it (Mok et al., 2014). Chronic inflammation may contribute to suicidal behavior through elevated pro-inflammatory cytokines and activation of the kynurenine pathway. Psychosocial stressors like unemployment and social isolation, along with disease-related factors such as organ damage and uncertainty about prognosis, further increase risk. In addition, suicidal behavior was more common in SLE patients who had depression, anxiety, unemployment, a history of psychiatric disorders, or significant life events in the previous months (Mok et al., 2014).

The current meta-analysis has several advantages over previous reports, including considering more reports with more significant patient numbers and considering three crucial parameters: suicidal ideation, attempts, and death during follow-up. An earlier meta-analysis published in 2018 included data on suicidal ideation from nine reports involving 1354 patients with SLE (Li et al., 2018). Although Parperis et al. (2022) considered all three important suicidal parameters, the authors presented their data in a systematic review format. They reported an average prevalence of suicidal ideation (15.7%) and suicidal death (2.3%). However, in the current meta-analysis, we observed a lower number of suicidal deaths (0.9%). The calculation of average prevalence has several drawbacks, and the results are not robust. By integrating findings from multiple reports, meta-analysis overcomes the limitations of individual studies (Curran and Hussong 2009). It provides a more comprehensive and robust assessment of the research question using an appropriate statistical approach (Curran and Hussong 2009). When observational studies merge various designs, methodologies, and characteristics of populations, it can lead to the introduction of errors and biases (Bencko and Chen 2014). Meta-analysis can mitigate those issues using a standardized data collection and analysis approach across multiple reports (Bencko and Chen 2014).

The heightened likelihood of suicidal thoughts among patients with SLE is a critical concern that healthcare professionals need to tackle.

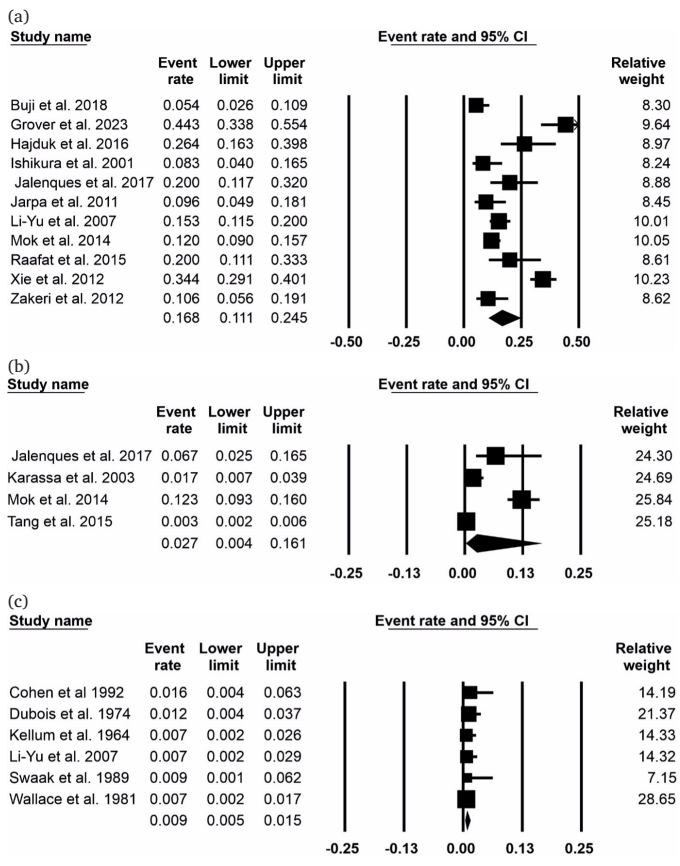


Fig. 3. Forest plots showing the prevalence of suicidal behaviors and death in SLE patients. The pooled event rate and 95% confidence interval were determined for (a) suicidal ideation, (b) attempts, and (c) suicide deaths, with meta-analysis conducted using CMA v3.

Methods to help SLE patients' mental and physical health include routine screenings, easy access to counselling and therapy, and working with interdisciplinary teams (Hanly et al., 2010). By addressing the mental health aspects of SLE, healthcare providers can minimize the suicidal rate and help patients improve their overall well-being and quality of life.

While the present study successfully highlighted the global prevalence of suicidal thoughts, attempts, and completed suicides among individuals with SLE, it also has various limitations that need to be considered. To begin with, the amount of research included in this analysis was somewhat limited due to insufficient data. Second, due to the unavailability of information in the reports considered for the analysis, confounding factors for suicidal behavior in patients with SLE were not considered. Third, the criteria for diagnosing suicidal behavior varied between reports. Fourth, the data used to calculate the prevalence of suicidal ideation and attempts showed heterogeneity, which could be attributed to the adaptation of differential diagnosis criteria for scoring suicidal behaviors, as well as bias in patient selection.

5. Conclusions

The current investigation reveals that 17% of SLE patients experience suicidal ideation, 3% have attempted suicide, and 1% have completed suicide during treatment, highlighting the need for targeted interventions. Healthcare providers should conduct regular mental health assessments for all SLE patients using validated screening tools for suicidal ideation and depression in chronic illness populations. Collaborative care models involving rheumatologists, psychiatrists, and psychologists should be established, with clear referral pathways for at-risk patients. Psychoeducation on the increased risk of suicidal behaviors in SLE should be provided to patients and families. Evidence-

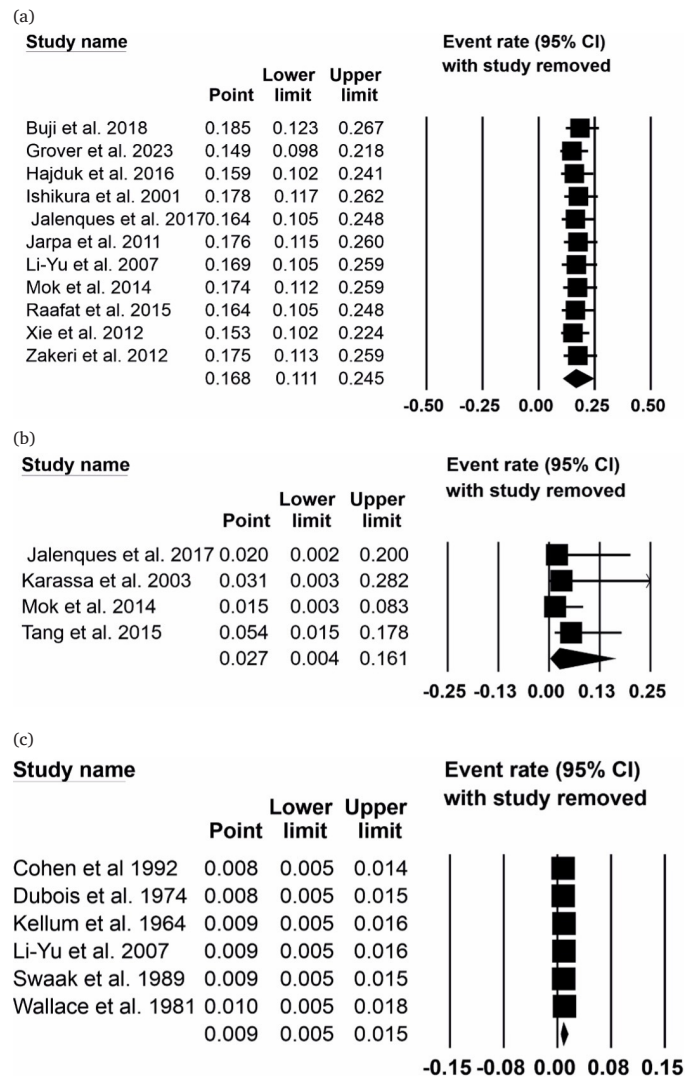


Fig. 4. Sensitivity analysis for suicidal behaviors and death prevalence in SLE patients. The analysis was conducted by sequentially excluding one study at a time and recalculating the meta-analysis. The results demonstrated the robustness of the findings for (a) suicidal ideation, (b) attempts, and (c) suicide death rates.

based psychotherapies, such as cognitive-behavioral therapy, and pharmacological treatments for depression should be considered, with careful monitoring for interactions with SLE medications. Special attention should be given to patients with risk factors like active disease, unemployment, or a history of psychiatric disorders. Implementing these recommendations can help reduce suicidal behaviors and improve the mental health and quality of life for SLE patients.

CRedit authorship contribution statement

Darin Mansor Mathkor: Literature search, data analysis, **Shovit Ranjan:** Literature search, data analysis, **Tapan Kumar Singh Nayak:** Literature search, data analysis, **Aditya K Panda:** Concept, design, manuscript editing, manuscript review, **Ashjan Saeed Babegi:** Data analysis, manuscript preparation, **Raju K. Mandal:** Data analysis, manuscript preparation, **Shafiu Haque:** Concept, design, manuscript editing, manuscript review.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Declaration of Generative AI and AI-assisted technologies in the writing process

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://dx.doi.org/10.25259/JKSUS_47_2024

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