

Factors influencing mortality in ICU hospitalized patients with severe sepsis: A systematic review and meta-analysis

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Received 19 April 2023; revised 05 July 2023

Sepsis is one of the primary causes of mortality in the world. When the sepsis develops into acute organ dysfunction it is considered severe. Severe sepsis increases the economic burden by means of potential treatment for inflammatory responses and multiple organ failure. Several factors, including age, inappropriate use of antibiotics, comorbidities, multiple organ dysfunction, and site of infection, are considered to increase mortality risk in severe septic patients. This systematic review analyses various factors influencing mortality in ICU-hospitalized patients with severe sepsis. A systematic search for relevant articles up to September 2022 was carried out on 6 electronic databases, including Scopus, MEDLINE, PubMed, ScienceDirect, Embase and Google Scholar. Of 1078 articles, only nine studies were reviewed after meeting the inclusion criteria. Meta-analysis of three studies reveal significantly more fatality in older patients than the younger (OR; 2.28: 1.65, 3.15: 95% CI: $I^2 = 11\%$, $P < 0.00001$). The number of organ failure also significantly influences the mortality with the mortality rate being higher for patients with ≥ 4 organ failures (OR; 0.19: 0.11, 0.30: 95% CI: $I^2 = 93\%$: $P < 0.00001$). The mortality rates for hospital-acquired, community-acquired and ICU-acquired infections were 0.41 (95% CI; 0.18, 0.69), 0.40 (95% CI; 0.20, 0.63), and 0.42 (95% CI; 0.44, 0.53), respectively. Gender shows no significant difference on mortality rates (OR; 1.05: 0.95, 1.16: 95% CI: $I^2 = 27\%$: $p = 0.35$). Age, the number of organ failures, and the acquisition sites seem to significantly influence the mortality, while gender has an insignificant influence on the mortality of ICU-admitted severe septic patients.

Keywords: Comorbidity, Multiple organ dysfunction

Sepsis is one of the leading causes of mortality in the world. The world health organization estimated that about 27% of hospitalized and 42% of intensive care unit (ICU) patients die of sepsis¹. Sepsis is known to place a substantial burden on healthcare resources. It often requires intensive medical interventions, including diagnostic tests, therapeutic interventions, and specialized care. Also, it necessitates extended hospitalization, particularly in intensive care units (ICUs) and survivors may experience long-term consequences that affect their health-related quality of life^{2,3}. Similarly, sepsis causes a huge economic burden to most countries since the funds that would have been used in other development activities is diverted to developing and evaluating potential treatments and studying the inflammatory responses and multiple organ failure due to severe sepsis. In the United States, the cost of dealing five years ago with severe sepsis was \$25000 per patient⁴.

Generally, when sepsis develops into acute organ dysfunction it is considered severe. Patients with severe sepsis are usually cared for in the ICU. Abe *et al.*⁵ reported that most patients of severe sepsis were admitted in 1 out of 15 of ICU centers. Additionally, data from a previous European study of sepsis occurrence in acutely ill patients revealed that about 30% of intensive care unit admission was due to severe sepsis⁶. Several factors contribute to the high mortality rates observed in severe sepsis cases. Initially, the early recognition of sepsis remains a key challenge. Delayed diagnosis and initiation of appropriate treatment can significantly impact patient outcomes, leading to increased mortality rates. Therefore, efforts should focus on enhancing sepsis awareness among healthcare providers, implementing effective screening protocols, and promoting rapid intervention⁷⁻¹⁰.

Over the years, the treatment of sepsis has evolved beyond the conventional approach of antibiotics and supportive care. Emerging evidence from clinical trials has identified additional methods

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that have shown promise in improving patient outcomes. Three notable interventions are aggressive directed therapy, stress-dose steroids and drotrecogin alfa¹¹⁻¹³.

Supportive care measures play a crucial role in the management of critically ill sepsis patients. Among these measures, mechanical ventilation, blood transfusion, nutrition support, and glucose control have been identified as interventions that can potentially improve survival rates¹⁴⁻¹⁶. The optimal approach to supportive care may vary depending on the patient's specific condition, comorbidities, and overall clinical picture. Multidisciplinary collaboration and adherence to evidence-based guidelines are crucial for delivering effective and personalized supportive care to septic patients, ultimately improving survival rates and patient outcomes.

Various factors influence mortality in severe sepsis patients. Some risk factors associated with sepsis-related mortality include age, inappropriate use of antibiotics, comorbidities, multiple organ dysfunction, and site of infection. Information from published documents shows that gender can also influence the mortality rates of severe sepsis patients. Consequently, this systematic review and meta-analysis discusses the effects of various factors on mortality of severe septic patients.

Methodology

Literature search

The systematic literature search for relevant articles was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines¹⁷. The search was conducted on six electronic databases, including Scopus, MEDLINE, PubMed, ScienceDirect, Embase, and Google Scholar. The search strategy employed in these electronic databases to identify the relevant articles was indexed to all studies up to 2022 using the following combination of keywords and Boolean expressions; (Sepsis OR severe sepsis) AND (intensive care unit OR ICU) AND (risk factors OR factors) AND (case-control study OR cohort study OR prospective study). Additionally, a manual search involving scouring the reference lists of the included studies was performed to identify additional studies. To enhance rigorous scientific research, grey and unpublished literature were not retrieved.

Eligibility criteria

Once all the relevant articles were retrieved, the task of screening articles based on the inclusion and exclusion criteria was independently performed by two reviewers. The inclusion criteria used for this systematic review were studies (i) included patients admitted to the ICU with severe sepsis; (ii) published in English and whose full texts were present; (iii) included only human subjects; (iv) evaluated risk factors associated with severe sepsis related mortality; and (v) included adult patients (>18 years) with severe sepsis.

The exclusion criteria were studies (i) published in a non-English language (to avoid direct translation of scientific terms, leading to loss of meaning and context); (ii) that were unable to distinguish the mortality of severe septic patients from septic shock and septic patients; (iii) conducted on animal subjects; (iv) with abstracts but without evidence of the full text; (v) that included pediatric patients (<18 years); and (vi) other systematic reviews, letters to the editors, and case reports.

Data extraction

Articles that met the eligibility criteria were independently screened by two reviewers tasked with extracting the relevant data. The main data retrieved from the studies included; Author ID (First author name and year of publication), type of ICU, study design, patients' characteristics, Country/location, and the study's main outcomes. The patients' characteristics were subdivided into age, sex, and the sample size. The main outcomes of this systematic review were factors affecting the mortality of ICU hospitalized patients with severe sepsis. Any discrepancies in the retrieved data were reconciled by consulting a third reviewer.

Quality assessment

The studies included in this systematic review were non-randomized; therefore, the Newcastle Ottawa scale was used for the methodological quality assessment¹⁸. All the studies were assigned a score of 0 to 8 based on the three assessment criteria (selection, comparability, and outcomes). Studies with a score of ≥ 7 were considered high methodological quality, while a score of between 4 and 6 meant that the study was of moderate methodological quality¹⁸. Studies that scored between 0 and 3 were considered low quality.

Data analysis

The meta-analysis of the pooled data from various studies was performed using Review Manager

(RevMan version 5.4.1) and R-studio (version 4.2.1). Due to the varied sample size and data heterogeneity, we implemented a random-effect model. The I^2 statistics was also used to measure the data heterogeneity, of which heterogeneity values of 25, 50 and above 70% were considered low, moderate, and substantial, respectively¹⁹. A significant difference was indicated by a p-value of less than 5% ($P < 0.05$). The analyzed data for all outcomes in this systematic review and meta-analysis were discrete; therefore, the effect size was calculated using the odds ratio (OR) and the results of the meta-analysis presented in forest plots.

Observations

Search results

The search strategy yielded a total of 1078 articles from all electronic databases. The retrieved articles were then scrutinized, and all the duplicates removed. Titles and abstracts of the remaining 985 articles were screened which led to the exclusion of 621 articles. Of the remaining 364 articles, 322 were not retrieved. The remaining articles were then assessed using the eligibility criteria of which only 9 articles were included for review. The basis of excluding the 33 articles is outlined as follows; 2 were published in languages other than English, 19 were unable to distinguish patients that were admitted to ICU with either sepsis, severe sepsis or septic shock, 1 was

conducted on animal species, 5 were abstracts without full texts, 2 included pediatric patients and 4 were either systematic reviews, case reports or letters to the editor. The full selection criteria are presented in Fig. 1 and Table 1²⁰⁻²⁸ provides detailed characteristics of the studies included for analysis.

Quality assessment results of the studies

After analyzing the methodological quality of each study using the Newcastle-Ottawa scale for cohort studies, 8 studies had moderate methodological quality while only 1 study was considered high quality. The scores on each element (selection, comparability and outcomes) are presented in Table 2²⁰⁻²⁸.

Risk factors of mortality in severe sepsis

Age

Three studies included in this systematic review and meta-analysis investigated the influence of age on the mortality rate of severe septic patients. The meta-analysis revealed a significant association between age and mortality in severe sepsis ($Z = 4.96$, $P < 0.00001$). Older patients had a higher risk of mortality compared to younger patients (Total 95% CI 2.28, 1.65 to 3.15). The heterogeneity among the included studies was low ($I^2 = 11\%$). The analysis included 513 older patients and 355 younger patients (Fig. 2A).

Gender

The effect of gender on mortality rate in severe septic patients was discussed in 5 studies. There was no significant association between gender and mortality in severe sepsis ($Z = 0.94$, $P = 0.35$). The total effect estimate indicated a marginal effect size with a confidence interval close to unity (Total 95% CI 1.05, 0.95 to 1.16). The heterogeneity among the included studies was low ($I^2 = 27\%$). The analysis included 12,078 male patients and 9,192 female patients (Fig. 2B).

Number of organ failure

The pooled data from three included studies also shows that mortality is independently influenced by organ dysfunction. The meta-analysis revealed a significant association between the number of organ failure and mortality in severe sepsis ($Z = 6.72$, $P < 0.00001$). Patients with less than 4 organ failures had a lower risk of mortality compared to those with 4 or more organ failures (Total 95% CI 0.19, 0.11 to 0.30). The heterogeneity among the included studies was substantial ($I^2 = 93\%$). The analysis included 16,524 patients with less than 4 organ failures and 3,340 patients with 4 or more organ failures (Fig. 3).

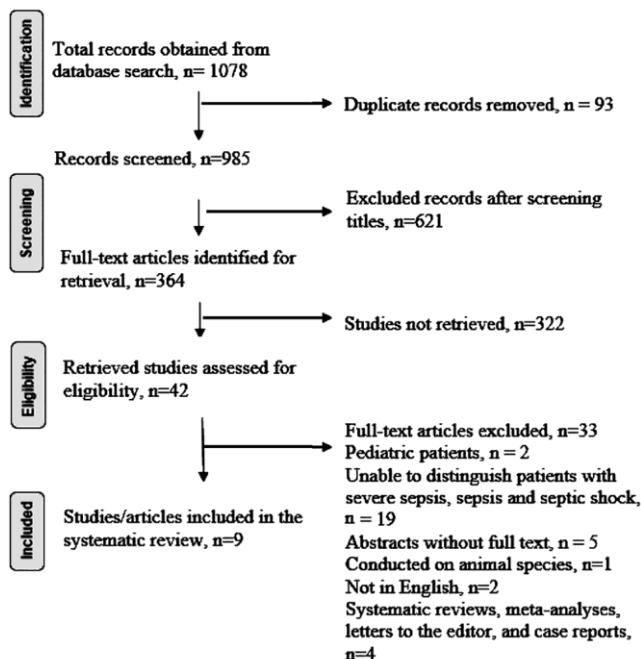


Figure 1 — PRISMA flow diagram

Table 1 — Study characteristics²⁰⁻²⁸

Author ID	Study design	Country	Patients' characteristics	Type of ICU	Main outcomes
Karlsson <i>et al.</i> ²⁰	Prospective study	Finland	470 severe sepsis patients (315 male and 155 female) with a mean age of 59.6 ± 15.2 years.	General	15.5 and 28.3%, ICU and hospital mortality, respectively. The mortality rate was strongly influenced by the number of organ failures (11.5 and 34.0% for 1 and 3 organ dysfunctions, respectively). Older patients displayed high mortality (40.2% for the age group 55-64 years).
Cheng <i>et al.</i> ²¹	Prospective observational study	China	318 severe sepsis patients (206 male and 112 female) with a mean age of 69 ± 21.7 years	Surgical	The mortality rate was 44.7% (142 of 318 severe sepsis patients). Gender had insignificant influence on mortality (51.5% vs. 43.8%, p = 0.198, men and women respectively). Cardiovascular and renal dysfunction showed high mortality rates.
Martin <i>et al.</i> ²²	Prospective observational study	Canada	1238 severe sepsis patients	Medical/surgical	The overall mortality rate recorded was 38.1%. Hospital-acquired infection showed more deaths. Older patients recorded a high mortality rate.
Blanco <i>et al.</i> ²³	Prospective observational study.	Spain	311 severe sepsis patients (208 male and 103 female) with a median age of 68 years (54.9 – 74.5).	Medical/surgical	The 28-day mortality rate was 47.9%. More patients with community-acquired infection died than patients with post ICU admission infection (25.6% vs. 0%, P < 0.001). The univariate analysis shows that age, sex, chronic alcohol abuse, hematological, neurological, and liver factors significantly influenced the hospital mortality rate.
Padkin <i>et al.</i> ²⁴	Prospective observational study	England, Wales, and Northern Ireland	15362 patients (8336 males and 7026 females) with severe sepsis.	surgical	The overall hospital mortality rate was 47.3%. Slightly fewer deaths were observed in female patients (42.7% vs. 51.2%, for women and men respectively). Older patients had a higher mortality rate than younger patients (64.4% vs. 17.4% for age groups 16-19 and >85 years, respectively).
Mohamed <i>et al.</i> ²⁵	Prospective observational study	India	80 patients (57 male and 23 female) with severe sepsis	medical	Death rates increased with age (79.5% vs. 52.5% for patients >60 and <60 years, respectively). More male patients succumbed to severe sepsis than female patients (73.7% vs. 52.2%, respectively). Invasive mechanical ventilation was associated with significantly higher death rate than patients treated without invasive mechanical ventilation (85.7% vs. 25.0%, respectively).
Umegaki <i>et al.</i> ²⁶	Multicenter cross-sectional study	Japan	4196 severe sepsis patients (2575 male and 1621 female).	General	18.8% ICU mortality was recorded. The mortality rate for patients with more than 4 organ dysfunction was higher than for patients with single organ dysfunction (38.9% vs. 8.9%). Cardiovascular and neurologic dysfunctions showed no significant influence in ICU mortality (19.5% (p = 0.178) and 20.5% (p = 0.703), respectively)
Sakr <i>et al.</i> ²⁷	Prospective multicenter observational study	Italy	3902 severe sepsis patients (2479 male and 1423 female)	Medical/surgical/trauma	20% ICU mortality recorded. Significantly more female patients died than in male patients (63.5% vs. 46.4%, p = 0.007, respectively).
Adrie <i>et al.</i> ²⁸	Prospective observational study	France	1692 severe sepsis patients (1061 males and 631 females)	General	The male and female patients showed an insignificant difference in the ICU mortality rates (29% vs. 26%, p = 0.23, respectively). The mortality rate for patients aged <50 years showed an insignificant difference between male and female patients (OR; 1.33; 95% CI: p = 0.36). The mortality rate for female patients aged >50 years was significantly higher than that of male patients aged >50 years (OR, 0.69; 95% CI, 0.52 to 0.93; p = 0.014).

Table 2 — Methodological Quality using the Newcastle Ottawa Scale for cohort studies²⁰⁻²⁸

Author ID	Selection (Maximum 4)	Comparability (Maximum 1)	Outcome (Maximum 3)	Total Score	Quality
Karlsson <i>et al.</i> ²⁰	3	1	2	6	Moderate
Cheng <i>et al.</i> ²¹	3	1	2	6	Moderate
Martin <i>et al.</i> ²²	2	1	2	5	Moderate
Blanco <i>et al.</i> ²³	3	1	1	5	Moderate
Padkin <i>et al.</i> ²⁴	2	1	1	4	Moderate
Mohamed <i>et al.</i> ²⁵	4	1	2	7	High
Umegaki <i>et al.</i> ²⁶	3	1	2	6	Moderate
Sakr <i>et al.</i> ²⁷	2	1	2	5	Moderate
Adrie <i>et al.</i> ²⁸	3	1	2	6	Moderate

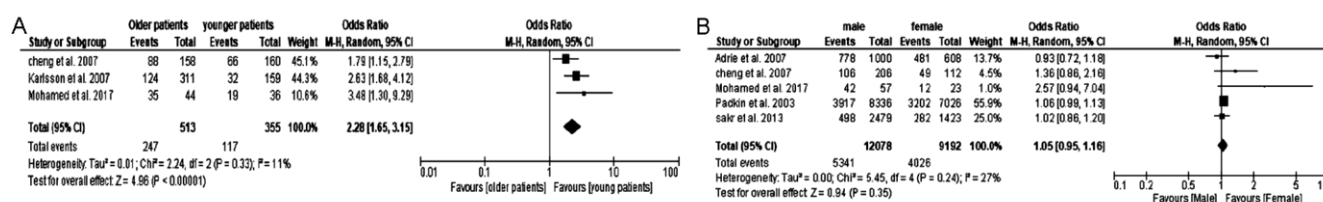


Figure 2 — Forest plot comparing the mortality rates between (A) young and old patients; and (B) female and male patients

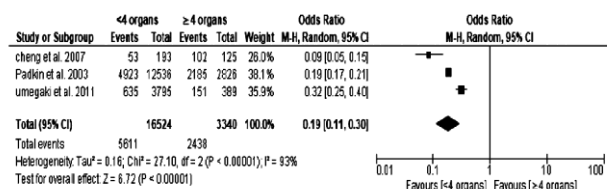


Figure 3 — Forest rate comparing mortality rates for patients <4 and ≥4 organ failures

Acquisition sites

The other factor that independently influenced the mortality among patients with severe sepsis was the acquisition site for infection. The meta-analysis of three studies demonstrated a significant association between ICU-acquired infection and mortality in severe sepsis. Patients with ICU-acquired infections had a higher risk of mortality (Total 95% CI 0.42, 0.28 to 0.57). The heterogeneity among the included studies was moderate (I² = 81%). The analysis included 561 patients (Fig. 4A).

Figure 4B is the meta-analysis indicating a significant association between hospital-acquired infection and mortality in severe sepsis. Patients with hospital-acquired infections had an increased risk of mortality (Total 95% CI 0.41, 0.18 to 0.69). The heterogeneity among the included studies was high (I² = 96%). The analysis included 559 patients. According to Fig. 4C, the meta-analysis revealed a significant association between community-acquired infection and mortality in severe sepsis. Patients with community-acquired infections had a higher risk of

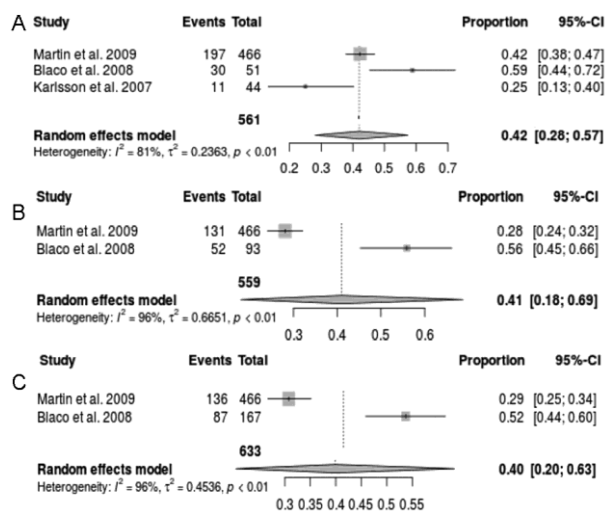


Figure 4 — Forest plot showing mortality rate for patients with (A) ICU-acquired infection; (B) Hospital-acquired infection; and (C) Community-acquired infection

mortality (Total 95% CI 0.40, 0.20 to 0.63). The heterogeneity among the included studies was high (I² = 96%). The analysis included 633 patients.

Overview

The present meta-analysis evaluates the factors that influence the mortality of severe sepsis patients admitted to ICUs. The main factors analyzed included; gender, age, number of organ dysfunction, and the acquisition site of infection. The meta-analysis shows that age, number of organ dysfunction, and acquisition site are independent factors

influencing the mortality of severe septic patients. However, results show that gender is not an independent factor influencing the mortality of severe septic patients due to its insignificant impact.

Meta-analysis of the present study shows that young people have a significantly lower mortality rate compared to older people. For the basis of this meta-analysis, patients aged less than 60 years were considered young, while patients aged ≥ 60 years were considered old. These results are supported by the results from a study Wichmann *et al.*²⁹ which documented that the mortality of patients with severe sepsis or septic shock was affected by age. Patients aged above 60 years showed high mortality rates compared to patients below 60 years (the mortality rate of male and female patients aged between 60-79 years were 70.4 and 67.3%, respectively, and patients aged above 80 years showed the highest mortality rate of 76.7 and 82.1% among men and women respectively). Though eligibility criteria of the present study only allowed for the inclusion of studies conducted on patients over 18 years, previous studies have also shown the influence of different age groups on mortality in pediatric patients with severe sepsis. A Japanese study reported that the death rates were significantly higher among patients in the children and adolescent age groups (26% and 25%, respectively) and significantly lower in neonates and infants with severe sepsis (13% vs. 26%, respectively)³⁰. Contradictory results on the influence of age on the mortality rates among severe sepsis patients have also been documented. For example, a study conducted in Thailand reported that it was unable to establish that age was a factor associated with increased mortality among patients with severe sepsis³¹. However, it is explained that the presence of comorbidities and acute respiratory distress syndrome (APACHE II) score may have erased the effect of age. Age in that study was used to derive APACHE II scores, while older patients were associated with comorbidities.

Additionally, a meta-analysis in the present study has revealed that gender does not influence the mortality of ICU-admitted severe septic patients. Results of this systematic review are supported by a previous German prospective study which reported that despite the high incidences of severe sepsis in male patients, the mortality of ICU-admitted sepsis patients was independent of gender (65.7% vs. 64.9% for male and female patients, respectively)²⁰.

Similarly, a previous study analyzing the epidemiology of sepsis in the US from 1979 to 2000 reported no difference in mortality according to sex (22% vs. 21.8% for men and women, respectively)³². However, Thompson *et al.*³³ presented some contradictions to the results of the present study. According to that study, higher mortality rates were observed among male septic patients as opposed to female septic patients (70% vs. 26%, respectively). Sakr *et al.*²⁷ also reported significantly higher mortality rates in women with severe sepsis than in men (63.5% vs. 46.4%, $P = 0.007$). More recent evidence on the influence of gender among mixed populations with nosocomial infections in the ICU has shown that higher ICU mortality rates are observed in the female gender population³⁴. It is important to note that some of the gender differences observed in the mortality of severe septic patients can be attributed to age. Adrie *et al.*²⁸ reported that for patients with >50 years, the mortality was significantly higher among male patients than female patients (OR, 0.69; 95% CI, 0.52 to 0.93, $P=0.014$). However, patients with ≤ 50 years showed no statistically significant difference in the mortality rates.

On the other hand, the number of failing organs was also associated with the ICU mortality rates among severe septic patients. The meta-analysis particularly shows that an increasing number of organ dysfunction was associated with increased ICU mortality. Martin and colleagues also documented that organ failure cumulatively contributed to mortality after analyzing data of septic patients from 1979 to 2000. The study reported over 70% of deaths in severe septic patients with more than three organ failures³². Similarly, a Canadian national analysis study reported high mortality rates in patients with more than three organ failures (62.0% vs. 52.8% vs. 39.1% for 3, 2, and 1 organ failures, respectively)³⁵. A prospective study of severe sepsis and septic shock patients also reported that the mortality rate at the first 24 hours was 24.3% for patients with a single organ failure and rose to 82.9% in patients with more than 4 organ failures. Based on the evidence supported by these studies, it is essential to note that the number of organ failures greatly influences the mortality rates witnessed in severe septic patients. Even though this review did not distinguish the different organ failures increasing the mortality of severe septic patients, evidence shows that mortality is also affected by the type of organ dysfunction. For instance, Umegaki *et al.*²⁶

reported that hepatic dysfunction was highly associated with increased mortality accounting for about 32.2% of deaths out of 59 patients with hepatic dysfunction. However, other dysfunction such as cardiovascular and neurologic were considered not significant factors for ICU mortality ($P = 0.178$ and $P = 0.703$, respectively). Similarly, Husak and colleagues reported high mortality rates among hepatic dysfunction patients (70% mortality rate). Low mortality rates were witnessed among patients with cardiovascular and central nervous dysfunctions (45.8 and 44.7%, respectively)³⁵.

This systematic review and meta-analysis also shows that the acquisition site significantly influences the mortality outcomes among patients with severe sepsis. The incidence of infections leading to sepsis has varied in different studies. Martin *et al.*²² reported that out of 1238 cases of severe cases of sepsis, community-acquired infections were higher compared to hospital-acquired, early ICU-acquired, and late ICU-acquired (458 vs. 305 vs. 195 vs. 280, respectively). Similarly, Blanco and colleagues noted that a high number of severe sepsis were from community-acquired infections (167 cases), while intra-ICU-acquired infections accounted for the least cases (51 cases)³¹. Meta-analysis of data from our results shows that ICU-acquired recorded a significantly higher mortality rate than both hospital-acquired and community-acquired infections. However, results from some of the included studies show some contradictory results. For instance, results from 311 severe septic patients showed that community-acquired infection had a higher mortality rate than ICU-acquired infection (87% vs. 30%). However, the difference did not reach statistical significance ($P = 0.655$). Therefore, these results show that the acquisition is not independently associated with mortality. The difference in the results of that study and the presented study can be attributed to the patients' sample size analyzed.

Apart from the factors analyzed in this systematic review, other factors such as pre-existing comorbidities, site of infection, and treatment methods influence the mortality of ICU-admitted severe septic patients. Blanco *et al.*²³ reported that patients with an infection on the abdomen had a significantly higher mortality rate [62.4% (63/101)], $P = 0.008$). The results also show that patients with urinary tract infections had significantly lower

mortality [20% (4/20), $P = 0.008$]. Similarly, the multivariate logistic regression analysis of Sakr and colleagues revealed that abdominal site of infection significantly influenced the mortality of severe septic patients (OR; 2.51: 1.15, 5.44:95% CI: $p = 0.02$)²⁷. Karlsson *et al.*²⁰ also show that infections on the intra-abdominal site are associated with high hospital mortality rates [32% (48/150)]. Several studies have also investigated the influence of pre-existing comorbidities on the mortality of severe septic patients admitted to the ICU. A multivariate logistic regression analysis of data from 3902 severe septic patients revealed that patients with pre-existing chronic obstructive pulmonary disease (COPD) were significantly susceptible to death (OR; 1.03: 1.01, 1.05:95% CI: $P = 0.002$)²⁷. Another multivariate analysis showed that patients with comorbidity of malignant neoplasm were significantly vulnerable to death (OR; 4.60: 1.83, 11.55:95% CI: $P = 0.001$)²¹.

Additionally, a previous Thailand study reported that metastatic cancer and hematological malignancy have a significant influence on the death of severe septic patients ($P < 0.001$ and $P = 0.045$, respectively)³¹. Behavioral factors such as chronic alcohol abuse also influence severe septic patients' mortality. Data analysis from 311 severe septic patients showed that chronic alcohol abuse was associated with an increased risk of death. However, the 95% CI interval of the variables included 1, which means that the association with mortality remains uncertain³². Additionally, treatment methods used when treating or caring for patients with severe sepsis may also affect the mortality rates. Mohamed *et al.*²⁵ reported that patients treated with invasive mechanical ventilation (IMV) had a significantly higher mortality rate than patients treated without the IMV (85.7% vs. 25.0%, $P = 0.001$, respectively).

Limitations of the study

This review was also subject to several limitations. First, this review eliminated all studies published in languages other than English. This elimination of related studies may have led to the omission of some relevant information or data that would have been used to improve the scientific research of this systematic review. Secondly, high heterogeneity was observed in the meta-analysis of factors such as the number of organ failures and the acquisition site. The high heterogeneity can be attributed to the varying sample size, ICU types, and definitions of severe

sepsis. Nevertheless, the high heterogeneity did not alter the results of our meta-analysis. Thirdly, some of the studies included in this systematic review were observational in nature, therefore, introducing the biasness that comes with observational studies. However, the quality assessment using the Newcastle-Ottawa scale shows that majority of the studies had good quality (8 moderate and 1 high, Table 2), meaning that bias was low. This systematic review also included studies conducted in university hospitals. This poses a challenge since patients in these hospitals may not be a true reflection of patient populations in other types of medical centers. Lastly, the systematic review distinguished young patients to ≤ 60 years while old patients to be > 60 years. However, some of the studies used different age groups in determining the effect of age on mortality which may have introduced some biased results in the present study.

Conclusion

The present review-cum-meta-analysis reveals that age significantly influences the mortality rates of patients with severe sepsis admitted to the ICUs. The outcomes of the meta-analysis have shown that older people (> 60 years) are more likely to succumb to severe sepsis than young people (≤ 60). Similarly, the acquisition site and the number of organ failures significantly influenced the mortality rates of ICU-hospitalized severe sepsis patients. However, contradictory results on the effect of the acquisition site have been documented. Therefore, more research on the influence of acquisition sites on the mortality of patients with severe sepsis should be conducted to understand this factor's effect better. On the other hand, there was no significant influence of gender on mortality. However, some studies have documented that gender can influence the mortality of ICU-hospitalized patients with severe sepsis. Due to these contradictions, there is a need for more research work to evaluate whether gender alone influences the mortality of patients with severe sepsis.

Conflict of interest

Authors declare no competing interests.

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