



Incidence of Sepsis Risk Factors in Hospital Research using Vosviewer: A Bibliometrics Study

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ABSTRACT

Risk factors of sepsis have been identified in several points such as chronic health conditions, comorbid diseases (hypertension, diabetes mellitus, HIV, and CKD), old age, male, alcohol users, immunosuppression conditions due to malignancy or use of certain drugs, obesity, length of treatment in hospital, and chemotherapy. This article aims to find out the incidence of sepsis and its risk factors in hospitals, globally in various fields. This study uses literature on the Scopus database from 2011 and Scopus Analyzing Tools. VOS Viewer (version 1.6.17) is used for bibliometrics analysis. Based on visualization results, a total of 430 articles were extracted. Most research was carried out in 2017, with 63 studies. The United States published more articles, amounting to 100 studies. The fields or areas that have been researched related to the incidence of sepsis and its factors the most are medicine. The latest keyword such as length of stay, antibiotic agent, and treatment appeared in 2016. The research trend was determined to have greatly increased in 2017 before declining once more in 2018. This research should be updated in the future to get the latest knowledge on sepsis risk factors in hospitals.

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Kata kunci:

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ABSTRAK

Faktor risiko terjadinya sepsis telah diidentifikasi dalam beberapa poin seperti kondisi kesehatan kronis, penyakit komorbid (hipertensi, diabetes melitus, HIV, dan CKD), usia tua, jenis kelamin laki-laki, pengguna alkohol, kondisi immunosupresi akibat keganasan atau penggunaan obat tertentu, obesitas, lama perawatan yang dijalani di rumah sakit, dan kemoterapi yang sedang dijalani. Artikel ini bertujuan untuk mengetahui bagaimana kejadian sepsis dan faktor risikonya di rumah sakit, secara global di berbagai bidang. Penelitian ini menggunakan literatur pada database Scopus dari tahun 2011 dan dianalisis dengan menggunakan Scopus Analyzing Tools. Vos Viewer (versi 1.6.17) digunakan untuk analisis bibliometrik. Berdasarkan hasil visualisasi, total 430 artikel diekstraksi. Sebagian besar penelitian dilakukan pada tahun 2017, 63 studi. Amerika Serikat menerbitkan lebih banyak artikel, 100 studi. Bidang yang paling banyak melakukan penelitian terkait kejadian sepsis dan faktor risikonya adalah kedokteran. Kata kunci terbaru seperti lama perawatan, agen antibiotik, dan hasil terapi muncul pada tahun 2016. Tren penelitian dipastikan telah meningkat pesat pada tahun 2017 sebelum menurun kembali pada tahun 2018. Penelitian ini harus diperbarui kedepannya untuk mendapatkan pengetahuan terbaru terkait faktor risiko sepsis di rumah sakit.

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INTRODUCTION

Sepsis is the main challenge in healthcare due to its significant cause of morbidity and mortality in healthcare facilities such as Intensive Care Units (ICUs) and is associated with the poor clinical status of patients (Wang *et al*, 2020). Sepsis is an organ dysfunction syndrome caused by an imbalance of the human response to infection. It is mainly characterized by shivering, fever (or hypothermia), palpitations, shortness of breath, and changes in mental status. Sepsis can progress to a more severe sepsis and septic shock. These conditions can cause organ dysfunction, circulatory disorders, and high mortality. Severe organ dysfunction caused by sepsis is a significant cause of death (Zhu *et al*, 2021). By analyzing the factors associated with sepsis organ function injury can provide more clinical prevention and targets of sepsis-related organ function injuries and predict the patient's prognosis (Rogne *et al*, 2021).

The sepsis incidence in patients receiving hospital services worldwide is 132 per 100,000 cases each year, with 17% of them die in hospital. Due to limited treatment options, the sepsis prognosis still remains poor with ICU mortality rates starting to be quite high from between 36.0% to 55.2% (Fathi *et al*, 2019). Meanwhile, in developing countries such as Indonesia, sepsis accounts for a mortality rate of 60-80% of the total cases that occur in hospitals. In a study conducted in a teaching hospital in Yogyakarta, a sepsis incidence rate of 631 was obtained in 2007 with a mortality rate of 48.96% (Yessica, 2014). In addition, sepsis can cost a lot in the hospital leading to increased hospitalization time, morbidity, and mortality (Chowdhury & Chakraborty, 2017).

According to guidelines by the Surviving Sepsis Campaign, timely diagnosis and identification of at-risk patients are recommended to provide aggressive early intervention and improve the prognosis of sepsis patients. Therefore, early detection of sepsis patients with high risk is essential to reduce mortality (Weng *et al*, 2021). In addition, it is necessary to establish a reliable predictive system for doctors to improve patient outcomes given that sepsis is a complex heterogeneous disease related to high morbidity and mortality (Manandhar *et al*, 2021).

According to the latest practice guidelines proposed by the Surviving Sepsis Campaign (SSC), sepsis therapy management that includes serum lactate measurement, blood culture collection, administration of broad-spectrum antimicrobial agents, fluid resuscitation, and vasopressor support should be achieved within an hour after the introduction of sepsis (Yang & Hsu, 2021). The guidelines recommend that for all patients with sepsis, the condition should be managed with a series of interventions, known as *bundles*, in which within 1 hour after the presentation (defined as "triage time in the emergency department or, if called from another treatment site from the earliest graphic explanation consistent with all elements of sepsis). The bundle consists of measuring lactate levels, taking blood cultures before antibiotics, administering broad-spectrum antibiotics giving crystalloids 30 ml per kilogram of body weight if the patient has hypotension or lactate levels higher than 4 mmol per liter, and vasopressor if the patient remains hypotensive despite fluid resuscitation (Chen, 2019).

An important component of the initial management of sepsis is the start of proper antibiotic therapy and proper source control. Choosing the right regimen is often challenging and influenced by a number of determining factors including, but not limited to, previous infections and

accepted antibiotics, local patterns of pathogen activity and antibiotic susceptibility, major clinical comorbidities, and underlying clinical syndromes. The pathogen most commonly associated with sepsis-related death is gram-positive cocci, followed by gram-negative bacillus. Appropriate antibiotic therapy is defined as the use of at least one antibiotic with in vitro activity against the causative bacteria (Gyawali *et al*, 2019).

Recommendations for treatment in patients with sepsis or septic shock are largely based on evidence derived from an adequate set of resources. This causes these recommendations to not be directly generalized to services in conditions with limited resources for several reasons, such as limited human and material resources and concerns about cost and safety. There is even the possibility that the effectiveness of certain strategies differ between an adequate set of resources and a barred resource. Efficacy and effectiveness can depend on the type of sepsis, and it is known that non-bacterial sepsis is much more common in health services with limited resource (Dünser & Schultz, 2019).

Five things need to be considered in the administration of management to sepsis patients related to hemodynamic monitoring of sepsis in health services with limited resources. Due to the introduction of hypoperfusion, the return of normal perfusion, and the detection of fluid responsiveness can avoid less and excessive resuscitation and less and excessive use of vasoactive agents. These five things are (Shawon *et al*, 2021):

1. Affordable tools in bed are required for network perfusion monitoring
2. A better understanding of the ease of passive leg lift tests in sepsis conditions and indications of intravenous fluid administration
3. Suggest which type of intravenous fluid is better to use during fluid resuscitation
4. The amount and timing of intravenous administration of fluid for sepsis shock in the ICU are critical. In addition, it is necessary to pay attention at the time of administration of vasopressor and inotrope and the risks associated with their use
5. Recommendations on indications, titration, and ways of administration in patients with sepsis are indispensable

METHOD

This research use literature from the *Scopus website online* to identify scientific articles or journals with a search strategy using the keywords *risk AND factor AND sepsis AND in AND hospital*, with a year limit of ten years is set, so that the selected scientific articles and journals consist from 2011 to 2021. Authors use Scopus search because it has more journal coverage than other databases, as well as provides services to assess whether a journal has a significant impact or not. With daily updates, current, accurate data that may be used to make decisions, and interdisciplinary abstract and citation databases, Scopus provides the most complete coverage. The results of the literature were subsequently analyzed using the Scopus Analyzing Tools which were analyzed by country, year, subject, author, and source.

To conduct a co-assurance analysis, the VOS Viewer application is used which can be accessed for free, and is

done based on the relationship between scientific publications taken from existing literature to form a network map. Terms are taken from the titles and abstracts of scientific articles and journals taken using the default option in VOS Viewer (binary counting method and there are at least ten occurrences for the listed terms). In the network map the term co-accuracy based on existing data, the circle represents the term, the size of the circle is proportional to the number of articles in which the term is found and the curved line between the circles represents the strength of the interrelation of the two terms.

For terms with a high number of co-occurrences is connected by a thicker line. Terms that are strongly related

to each other form clusters of nodes identified based on modularity-based clustering algorithms implemented in VOS Viewer and represented using different colors. A VOS Viewer application makes it possible to highlight the relationships between two or more nodes and create a distance-based term network map. For each node, the VOS Viewer clustering technique first calculates the normalized strength of associations, then places the nodes on a two-dimensional plane and finally assigns them to a cluster (a group of closely related nodes). The author went through a number of steps in conducting this research, including selecting the research topic, conducting research reviews, disseminating the findings, and processing the data using bibliometrics.

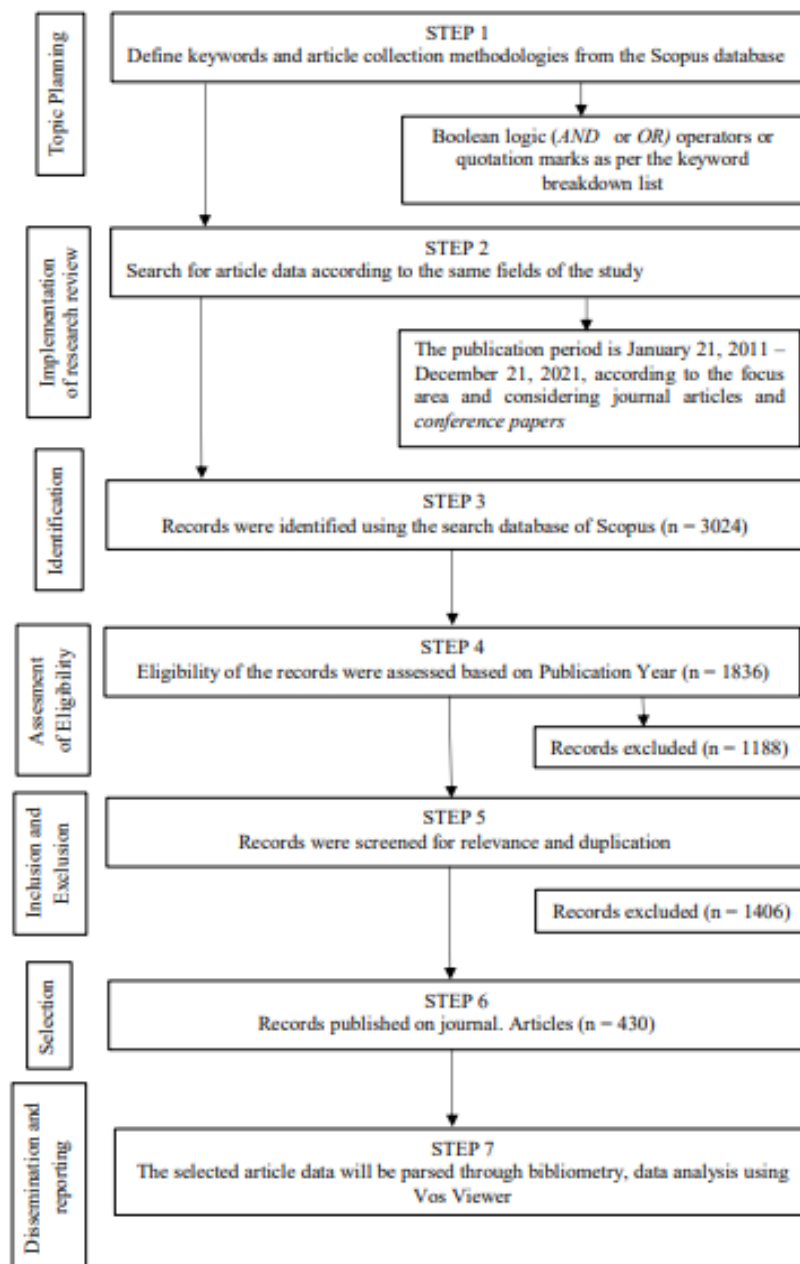


Chart 1. Stages in searching and selection of articles

RESULTS AND DISCUSSION

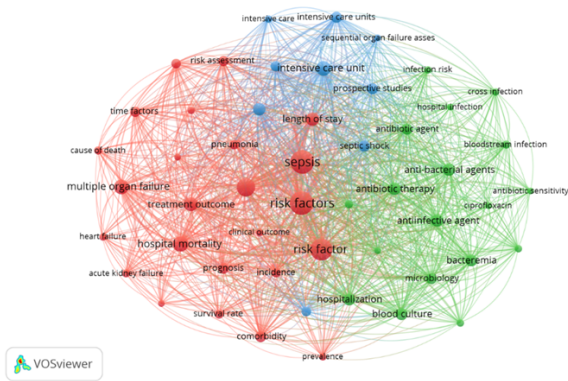


Figure 1. Network Visualization.

Map of incidence terms from studies on risk factor sepsis in hospital

There are 430 documents issued from 2011 to December 2021. The entire document consists of scientific articles originating from many countries. Figure 1 shows a map of the incidence terms from the study of *risk factor sepsis in hospitals* in which the circle represents the term, the size of the circle is proportional to the number of articles in which the term was taken, and the thickness of the line between

the circles represents the strength of the interrelation of the two fields.

Research related to the incidence of sepsis and its risk factors in this hospital can be seen in the visualization of the results of mapping data collected in figure 1. The different color variations are used to separate each list of predominating concepts from the identified clusters in an overview that is provided. This is done to develop a tendency to identify themes that are frequently covered in particular publications. Three clusters that map the research themes of events and risk factors for sepsis in hospitals have been effectively identified from the results of the analysis using VOS Viewer in figure 1. From clusters 1 to 4, each cluster has the color red, green, and blue. Several items from the same category are grouped in each cluster. According to the visualization, each cluster's dominance of subjects is connected to the topics of hospital mortality, length of stay, the risk factor of sepsis, antibacterial agent, and intensive care.

The three main groups of fields that are closely related to each other were identified by VOS Viewer. Red color focus on sepsis, sepsis risk factors, length of treatment, the incidence of sepsis, management, and *outcomes*. Green color focuses on bacteria, antibiotic therapy, blood cultures, and other possible infections in hospital. Meanwhile, blue color focuses on the relation of the risk of infection, septic shock, intensive therapy, hospitalization, and organ malfunction.

Table 1. Cluster

Cluster	Theme	Total (N = 51 (100%))
Cluster 1	Comorbidity, hospital mortality, length of stay, multiple organ failure, severity of illness index, survival rate, treatment outcome, risk factors	N = 24 (47%)
Cluster 2	Anti-bacterial agent, antibiotic agent, bacteremia, blood culture, bloodstream infection, anti-infective agent, microbiology, hospital infection	N = 18 (35%)
Cluster 3	Disease severity, hospital admission, intensive care, septic shock, sequential organ failure, complication	N = 9 (18%)

Researchers, especially those who are just starting, can get a start on their research by using the identification in the form of mapping in Figure 1. With the use of this study, people can read articles about topics that interest them when they come across one in a particular area about which they are curious. A total of 51 articles were retrieved and split into 3 clusters based on the visualization results. In cluster 1, there are 24 articles consisting of several themes such as comorbidity, hospital mortality, length of stay, multiple organ failure, the severity of illness index, survival rate, treatment outcome, and risk factors. For cluster 2, there are 18 articles consisting of several themes such as anti-bacterial agents, antibiotic agents, bacteremia, blood culture, bloodstream infection, anti-infective agent, microbiology, and hospital infection. And then cluster 3 has 9 articles consisting of several themes such as disease severity, hospital admission, intensive care, septic shock, sequential organ failure, and complication. Three clusters were found successfully, which is consist of 51 items displayed in table 1. There is 1 cluster that has a percentage above 20%, namely cluster 1 with 24 items (47%), cluster 2 with 18 items (35%), and cluster 3 with 9 items (18%).

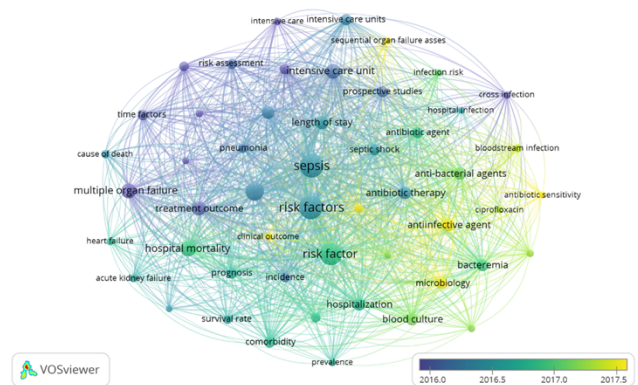


Figure 2. Overlay Visualization

According to the Figure 2 overlay visualization, it can be concluded that around 2015, discussions of terms like risk assessment, the severity of disease index, and intensive care unit increased. In 2016, it is increasingly common to talk about topics including treatment results, sepsis, mortality, antibiotic therapy, length of stay, and septic shock. And then latest themes such as hospital mortality, blood culture, comorbidity, and complication are more often discussed in 2017.

Meanwhile, in 2020, topics related to sepsis and the highest risk factors were mortality rates and clinical

outcomes. The COVID-19 pandemic has significantly changed the way sepsis is discussed in the medical literature. Numerous reports have shown since the beginning of the pandemic that while COVID-19 has some distinct characteristics, many of its early signs are comparable to sepsis brought on by other viruses. Comparing viral sepsis to bacterial sepsis reveals some parallels as well as some differences. In contrast to COVID-19 sepsis, systemic inflammation affecting several organs predominates in bacterial sepsis. Viral illnesses may have a relatively late beginning and chronic course, whereas bacterial sepsis produces an early and rapid onset of clinical deterioration. Finding medicines that will modify the immune response may be aided by considering severe COVID-19 disease as a sepsis syndrome, has relevance and may assist in terms of determining treatments that will modulate the immune response, limit intrinsic damage to tissue and organs, and potentially improve outcome (Al Wadees *et al*, 2021).

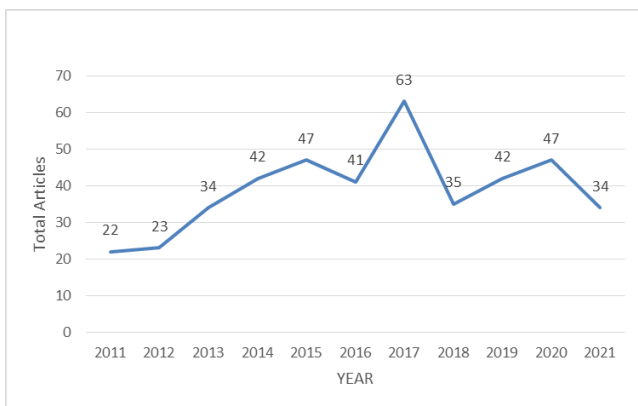


Figure 3. Number of articles published each year

According to the chart above, 430 studies were carried out between 2011 and 2021, including 22 studies in 2011, 23 in 2012, 34 studies in 2013, 42 studies in 2014, 47 studies in 2015, 41 studies in 2016, 63 studies in 2017, 35 studies in 2018, 42 studies in 2019, 47 studies in 2020, and 34 studies in 2021. The research trend was determined to have greatly increased in 2017 before declining again in 2018. However, it tends to be more stable since 2018 until 2021.

Table 2. Distribution of the number of citations by country

Country	Articles	%
United States	100	23,25
China	39	9,06
Germany	39	9,06
Spain	38	8,83
Italy	36	8,37
United Kingdom	31	7,20
France	16	3,72
Japan	16	3,72
Canada	14	3,25
South Korea	14	3,25

Based on the results of article searches on sepsis incidents and risk factors in hospitals from 2011 to 2021, there were 430 Scopus indexed published articles that were successfully identified from the article search strategy based on the main keyword ("risk AND factor AND sepsis AND in AND hospital"). The data is categorized by the number of citations received from each country. It is applied to map the research publications that are most relevant to the problem of sepsis in hospitals. Table 2 shows the ten countries with the most cited publications globally from 2011 to 2021. There are the United States (100), China (39), Germany (39),

Spain (38), Italy (36), United Kingdom (31), France (16), Japan (16), Canada (14), and South Korea (14). With a total of 430 studies, the United States has conducted the most research, according to the number of papers. The next country with the second highest number of studies is China, on par with Germany, with 39 studies. Then, the country with the third highest amount of studies is Spain, with a total of 38 studies. Followed by United Kingdom in the fourth highest of studies, where there are 31 studies. And for the least number of studies, only 14 to 16 studies found in several countries such as France, Japan, Canada, and South Korea.

Researchers visualized the creation of maps of geographical distribution. In the picture, it appears that the country that publishes the most articles on sepsis incidents and risk factors comes from the territory of the United States. Researchers categorize articles based on the number of citations received from each country. It is applied to map published research that is particularly relevant to the incidence and risk factors of sepsis in hospitals. The number of article citations listed as a research sample as a whole comes from international sources.

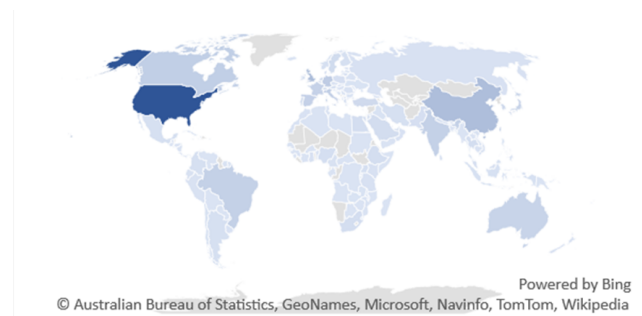


Figure 4. Distribution of research by countries or regions

According to the results of this study, the majority of published articles on sepsis incidences and risk factors in hospitals originated in the United States. This is conceivable since one of the nations with the strongest educational systems in the world is the United States. Researchers are allowed to locate and create the most recent breakthroughs as they see fit. This has led to the high interest of researchers in the United States and various efforts have emerged to find innovations (Romanova *et al.*, 2019).

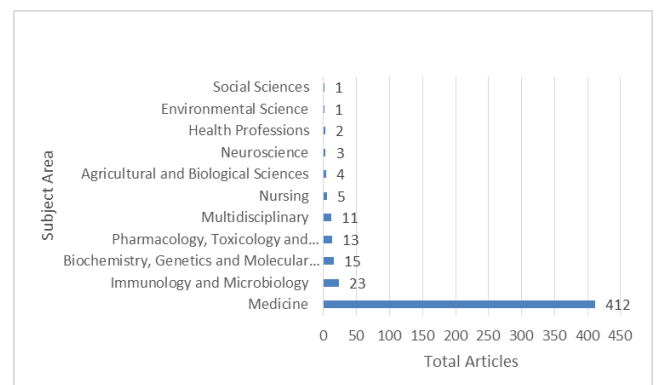


Figure 5. Subject area

Based on the chart above, out of the 430 articles gathered, the disciplines of study that have conducted the most research about the prevalence of sepsis risk factors in hospitals are medicine, with a total of 412 articles, followed by the next immunology and microbiology, as many as 23

articles. Then, other fields of study are followed by biochemistry, genetics and molecular biology with a total of 15 articles. Followed by pharmacology, toxicology, and pharmaceuticals with a total of 11 articles. Most studies related to the incidence of sepsis risk factors in hospitals are predominantly including in *medicine* and *immunology and microbiology* which occupy the two highest positions. Furthermore, other fields of study are followed by multidisciplinary, nursing, agricultural and biological sciences, neuroscience, health professions, environmental science, and social sciences.

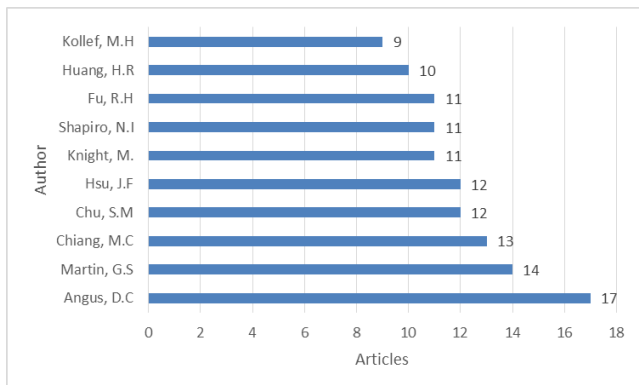


Figure 6. Subject area

Based on the scientific publications contained in the Scopus website that have been accessed, the authors received a total of 159 authors with the highest three details, namely Angus DC with 17 articles, Martin GS with 14 articles, and Chiang MC with 13 articles. In the period between 2011 to 2021, Derek C Angus has published publication articles about the incidence of sepsis and its risk factors which reached 5 articles. Derek C Angus himself is a professor and researcher at the University of Pittsburgh. Scottish-born and trained, associated with the University of Pittsburgh since 1989, he is currently one of the institution's Distinguished Professor and holder of the Mitchell P. Fink Chair at the Department of Critical Care Medicine. In June 2020, dr. Angus was appointed as the first UPMC Chief Healthcare Innovation Officer (CHIO). He has been an editor for JAMA since 2007 (University of Pittsburgh, 2018).

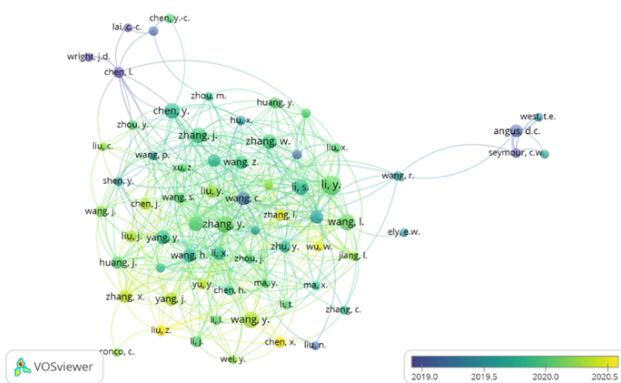


Figure 5. An overview of the relationship between writing scientific publications to writers

Based on figure 5, a total of 67 authors were obtained who were related to each other in the scientific publications carried out. The analysis shows that there are similar studies conducted by several researchers so that later the discussion can be more complex and provide many references.

Patient safety in a hospital environment is a system implemented by the hospital to make patient care safer, which includes risk assessment, identifying and managing matters related to patient risk, reporting and analyzing incidents, minimizing risks, and preventing risks in action taking. Recognizing the importance of this issue, WHO through the East Asti Regional Conference (SEARO 2015), issued a strategy related to *patient safety* in 2016-2025, which includes five strategic objectives with one of them being prevention and infection control on health care which known as *hospital acquired health*. One of the obligations of hospitals is to establish infection risk reduction activities or programs related to hospitals (HALS) in the form of infection prevention and control programs (PPI). The program includes planning, implementation, coaching, education and training, as well as monitoring and evaluation. In realizing infection prevention and control (PPI) in hospitals, the role of hospital management is very important (Agusti et al., 2019).

Hospitals are obliged to create regulations that must be obeyed in efforts to prevent and control infection in hospitals by extracting the principles of PPI management, which consist of standard vigilance and transmission vigilance (Madjid and Wibowo 2017) as follows:

a. Standard Precautions

Standard vigilance applies to all patients, regardless of the type of infection that occurs. Standard vigilance is designed for healthcare workers to reduce the risk of being infected with infectious diseases from known and unknown sources of infection. Standard vigilance consists of:

- 1) Hand hygiene or *hand hygiene personal*
- 2) Protective Equipment (PPE) in the form of gloves, masks, *goggles* (protective glasses), face shields, and dresses
- 3) Decontamination of patient care equipment
- 4) Environmental health control
- 5) Waste
- 6) Patient equipment processing and linen management
- 7) Protection of health workers or employee health workers
- 8) Patient placement
- 9) *Hygiene* respiration or ethics of coughing and sneezing
- 10) Safe inoculating practices
- 11) Practice for lumbar puncture

b. Precautions Based on Transmission

The requirement of breaking the chain of transmission of the infectious cause micro-transmission is intended to be applied to patients who are known or suspected to be infected or the presence of colonization of airborne pathogens, droplets, contact with contaminated skin or surfaces

High infection rate has implications for increased days and treatment costs, antibiotic use leads to increased antibiotic resistance rates, and a high medical burden on costs. Meanwhile, in terms of health service providers, there are various impacts that cause a decrease in the quality and quality of health service facilities. Therefore, it is important for every health care facility to know the risk factors that influence the incidence of sepsis the most in order to make improvements to the specific and efficient infection prevention and control management strategy (Madjid & Wibowo, 2017).

In cluster 1, a study conducted by Chowdury *et al.* named Universal Health Coverage - *There Is More to It than Meets*

the Eye, published in 2017, showed that in general, the predisposing factors of the emergence of an infection consists of genetic factors, age, nutritional status, immune status, comorbidities (chronic diseases, transplants, malignancies, and congenital), and treatment history (steroids, antibiotics, and invasive actions). In addition, gender, race, chronic health status, socioeconomic status, length of hospital, malnutrition, and immunosuppression were also evaluated as the risk factors for infection or sepsis.

The risk factors for sepsis have been identified in several points such as chronic health conditions, comorbid diseases (hypertension, diabetes mellitus, HIV, and CKD), old age, male sex, alcohol users, immunosuppression conditions due to malignancy or use of certain drugs, obesity, length of treatment undergone in the hospital, and chemotherapy that is being undergone (Fathi et al., 2019). The highest cause of sepsis is infection with gram negative bacteria, which produces various products that can stimulate immune cells. The cell will be triggered to release inflammatory mediators (Haque, 2018). Sepsis can lead to death with risk factors such as decreased mobility, failure to detect sepsis early in the Emergency Department (IGD), higher SOFA scores upon entry, and improper administration of antimicrobials (Vucelić et al., 2021)

In cluster 2, an article named Sepsis: The Evolution in Definition, Pathophysiology, and Management by Gyawali *et al.* in 2019 shows the important component of the initial management of sepsis is the start of proper antibiotic therapy and proper source control. Choosing the right regimen is often challenging and influenced by a number of determining factors, such as previous infections and antibiotics received, local patterns of pathogenic activity and antibiotic susceptibility, major clinical comorbidities, and underlying clinical syndromes. The pathogen most commonly associated with sepsis-related death is gram-positive cocci, followed by gram-negative bacillus. Appropriate antibiotic therapy is defined as the use of at least one antibiotic with in vitro activity against the causative bacteria.

In cluster 3, a study conducted by Khilnani *et al.* named Severe Sepsis and Septic Shock, *ICU Protocols: A Stepwise Approach*, the prevalence of severe sepsis is determined by how acute the organ dysfunction is characterized and whether the malfunction is caused by an underlying infection. Because organ dysfunction is frequently defined by the provision of supportive care (e.g., mechanical ventilation), epidemiology studies sometimes count the "treated incidence" rather than the actual incidence. In 2% of hospitalized patients in the US, there is evidence of severe sepsis. These patients make up around 10% of all ICU admissions, with half of them receiving care there. Over 750,000 cases are reported in the United States each year, and the number is reportedly increasing. However, several reasons, including the ICD-9's revised coding guidelines and the fuzziness surrounding the distinction between septicemia and severe sepsis, the increasing capacity to provide intensive care, and increased awareness and surveillance, confound the interpretation of temporal trends (Khilnani, 2012).

LIMITATION OF THE STUDY

The limitation of the study is that it did not use comparable data because it only used the publications found in the Scopus database. Therefore, the following research

must employ a comparative analysis strategy that utilizes both the Scopus and the Web of Sciences (WoS) databases.

CONCLUSIONS AND SUGGESTIONS

This bibliometrics analysis reveals that during the last 5 years, there has been an increase in research on the incidence of sepsis and its risk factors. The quality of studies related to this topic in some countries need to be improved. Research or articles come from a variety of disciplines, with medicine being the one that discusses these pieces the most frequently. The study trend was found to have significantly grown in 2017, but again declined in 2018. In the future, this study should be updated to include the most recent understanding of hospital sepsis risk factors.

This study contributed to mapping studies relating to the incidence of sepsis risk factors in hospitals, which provides an overview of the dominant topics being discussed. In particular, this topic explains how the risk factors of sepsis are present in the hospital and the initial treatment to prevent the occurrence of recurrent sepsis. Good infection prevention and control management is the answer to the reduce of sepsis incidents in hospitals. The suggestion for researchers can use Simago Journal Rank to determine the degree of influence of any existing article (SJR). SJR is used to assess the average scientific impact of journal publications.

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ETHICAL CONSIDERATIONS

Funding Statement

The authors did not receive support from any organization for the submitted work

Conflict of Interest Statement

The authors hereby declare there were no conflict of interest in this study

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