

Sepsis Profil Patients in Internal Medicine Inpatients at Dr. Soetomo Hospital for the Period January 2021 – June 2021

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Abstract

Sepsis is still one of the world's health problems and is also a major cause of death in several countries. A systemic immune response to an infection process in the body that can cause organ dysfunction and death it's sepsis. In 2017 there were 48.9 million cases and 11 million deaths related to sepsis worldwide, accounting for almost 20% of all deaths globally.

Based on this research, the number of sepsis patients hospitalized in internal medicine at Dr. Soetomo Hospital in the period January 2021 - June 2021 was 283 patients, the majority of whom were female (62.5%). The highest age range was 45 - 64 years. The most common comorbidity was diabetes mellitus. A total of 44 patients (36.36%) experienced an increase in procalcitonin values, 169 patients (84.5%) experienced leukocytosis, and 114 patients (57%) had normal platelet values. A total of 132 patients (66%) died during this period. Positive culture results showed that 70 (69.31%) gram-negative bacteria and 31 (30.69%) gram-positive bacteria were found with the highest antibiotic resistance found in cephazolin (48.51%). The number of sepsis patients in the internal medicine inpatient unit of Dr. Soetomo Hospital in the period January 2021 - June 2021 was 283 patients and 132 patients (66%) died during this period.

Keywords: Infection, Sepsis, Dr. Soetomo Hospital

1. INTRODUCTION

Sepsis still being one of the world's health problems and also a major cause of death in several countries. One of the causes of death is due to the delay in early treatment of sepsis, especially when still in the Emergency Unit because of waiting for laboratory results or other supporting examinations related to the diagnosis of sepsis [1]. The condition of sepsis becoming septic shock will increase the risk of death. Delays in administering antibiotics have been shown to increase the death rate of septic shock by 7.6% every hour [2]. The latest scientific publication estimates that in 2017 there were 48.9 million cases and 11 million deaths related to sepsis worldwide, reaching almost 20% of all deaths globally. In 2017, almost half of all global sepsis cases occurred in children, with an estimated 20 million cases and 2.9 million deaths globally in children under the age of five [3].

Sepsis is a systemic immune response to an infection process in the body that can cause organ dysfunction and death [4]. The most common causes of sepsis are gram-negative bacteria (60-70% of cases) and gram-positive bacteria (20-40% of cases) of all sepsis cases. Opportunistic fungi, viruses, or protozoa have also been reported to cause sepsis with a lower incidence [5]. The sepsis diagnostic tool that is often used is the Sequential Organ Failure Assessment (SOFA) scoring [6]. Experts have also proposed new criteria that can be used as a filter for sepsis patients, namely quick SOFA (qSOFA). The three qSOFA criteria are a respiratory rate of more

than or equal to 22 breaths/minute, changes in awareness, and systolic blood pressure of less than or equal to 100 mmHg [5].

The latest scientific publications estimated that in 2017 there were 48.9 million cases and 11 million deaths related to sepsis worldwide which reached almost 20% of all deaths globally. In 2017, almost half of all global sepsis cases occurred in children, with an estimated 20 million cases and 2.9 million deaths globally in children under the age of five [3].

Several factors influence the course of sepsis which are estimated to be used as interpreters of death in sepsis, including clinical factors (age, gender, focus of infection, and APACHE II score), complete blood count (leukocyte count including subtype differentiation and band count, hemoglobin, hematocrit, and platelets) and other laboratory test results (serum lactate levels, glucose, liver transaminases, bilirubin, and creatinine), hemodynamic conditions (systolic blood pressure and heart rate), respiratory parameters (respiratory rate and PaO₂/FiO₂), urinalysis (total urine output), and \pm 3 comorbid diseases (hypertension, diabetes, chronic kidney failure, and malignancy) [7].

The clinical manifestation of sepsis is highly dependent on variables such as the initial site of infection, the causative organism, the important pattern of organ dysfunction, the patient's underlying health status, and the length of time before treatment [8]. The incidence of simple sepsis increases more than 100-fold in the elderly (0.2 / 1000 in children to 5.3 / 1000 in patients aged 60-64 years and 26.2 / 1000 in patients \geq 85) and the death rate increases from 10% in children to 26% in patients 60-64 and 38% in patients \geq 85 [9].

In previous studies, it was stated that the most common cause of death in the elderly was sepsis in second place after stroke. The elderly are more susceptible to infection due to the process of body changes decreased organ function and the presence of comorbid diseases [10]. Previous studies related to comorbidities found that type 2 diabetes mellitus and systemic hypertension were the main comorbidities found in the population. Respiratory disorders, chronic liver and kidney disease, and heart disease were also found in a large number of sepsis patients [11].

In research conducted at Kariadi General Hospital, it was found that most sepsis sufferers were male, namely 34 people (69.4%), and the remaining 15 people (30.6%) were female. Adult patients of the male gender are 2.562 times more at risk of suffering from sepsis compared to adult patients who are female [12]. Angele MK et al in their research showed that steroid hormones in women produce substances that are immunoprotective when trauma or bleeding occurs [13].

Based on the data and explanations above, this research aims to determine the profile of sepsis patients in inpatients of internal medicine at Dr. Soetomo General Hospital for the period January 2021 - June 2021.

2. CONTENTS

2.1 Distribution of Patients by Gender

In this research, it was found that during that period, women were more affected by sepsis compared to men. It was found that there were 125 female sepsis sufferers (62.5%) and 75 male sufferers or 37.5%. The data is supported by research conducted at the Internal Medicine Ward of Sardjito Hospital in 2002, namely 77 female sepsis sufferers (55.4%) and 62 male (44.6%) [14]. This is also following previous studies which obtained results that the number of female sepsis sufferers was greater than that of men [15].

2.2 Distribution of Patients by Age

Based on the results of research in inpatient internal medicine at Dr. Soetomo Hospital, it was found that the group with the largest age range of sepsis patients was in the 45–64-year age group, namely 114 cases (57%). This was followed by the group with an age range of $>$ 65 years (25%). In this research, it was found that the youngest patient was found at the age of 3 years with 1 case and the oldest patient was 91 years with 1 case.

This is by previous research which found that sepsis cases occurred most at the age of 45-74 years compared to younger ages, namely $<$ 45 years [16]. This is also strengthened by other studies which also found that most cases of sepsis were found in the 50–64-year age range, namely 231 patients or 27% followed by the 35-49 age range, namely 209 cases or 24% [17].

2.3 Distribution of Patients Based on Comorbid Diseases

Some data found related to comorbid diseases in sepsis patients in the Internal Medicine Inpatient Unit of Dr. Soetomo Hospital, the most are Diabetes mellitus with 73 patients (52.52%) followed by hypertension with 45 patients (32.38%) then hepatitis b with 4 patients (2.87%) then there are other comorbidities such as leukemia, geriatric, malignancy, pneumonia, liver cirrhosis, pneumonia, cholangiocarcinoma, hypo albumin, hydronephrosis with 18 patients (12.86%).

The results of this research are supported by previous studies which also found the most sepsis comorbidities in diabetes mellitus with 26 samples (32%) and also followed by hypertension with 21 samples (25.9%) [18]. This is following research conducted in 2006 which also found that the most common comorbidity in women was diabetes mellitus [19].

Several previous studies have shown that high blood glucose levels cause defects in neutrophils, namely defects in adhesion, chemotaxis, and intracellular killing, and defects in phagocytosis. The humoral immune response in patients with diabetes mellitus has also been shown to be weaker than in people without diabetes mellitus. Insulin has 2 ways to protect the human body, first by controlling blood glucose so that the effects of hyperglycemia are not continuous, and second by providing direct or indirect effects on the immune system, the result is that disorders in insulin secretion also have an impact on the body's immune system which is also a predisposing factor for experiencing severe infections [20].

2.4 Distribution of Patients Based on Procalcitonin Values

Procalcitonin (PCT) is a specific marker of simple bacteria and can differentiate between sepsis and SIRS (Systemic Inflammatory Response Syndrome). PCT has a sensitivity of 85% and a specificity of 91% and its levels increase the fastest after exposure to bacterial infection compared to other sepsis biomarkers. Procalcitonin measurement as a sepsis biomarker is the most qualified, but the relatively expensive cost of PCT examinations means that some health services do not provide PCT examinations, so many still use laboratory tests such as leukocyte counts or leukocyte differential counts to determine the presence of inflammatory processes [21].

Prospective research of 101 medical intensive care unit (ICU) patients showed that PCT levels were higher in patients with sepsis and positive cultures, with a sensitivity of 0.89 and a specificity of 0.94 for sepsis [22].

2.5 Distribution of Patients Based on Total Leukocyte Value

Leukocytes in the body function to defend the body against foreign agents. An increase in the number of leukocytes in the body can be an indication of an inflammatory process which is a normal response to an infection or inflammation. An increase in the number of leukocytes is a normal response to infection or inflammation that occurs in the body [23].

In sepsis, an infection occurs either due to bacteria, viruses, or fungi that occur in the blood, resulting in an inflammatory response. The majority of sepsis patients hospitalized in internal medicine at Dr. Soetomo Hospital experienced leukocytosis, namely 169 (84.5%).

2.6 Distribution of Patients Based on Platelet Values

This research shows that the majority of sepsis patients hospitalized in internal medicine at Dr. Soetomo Hospital in the period January 2021 - June 2021 had normal platelet examination results. This is evidenced by data taken through medical records, there were 114 patients (57%) who had normal platelet examination results, 44 patients (22%) had thrombocytosis and 42 patients (21%) had thrombocytopenia.

This research is different from the research which explained that Thrombopenia is a common and multifactorial phenomenon that occurs during sepsis [24]. This is also different from previous studies which found that sepsis is associated with thrombopenia. Platelet changes characterized by thrombopenia in the pathophysiology of sepsis occur due to direct platelet activation by endotoxin or proinflammatory cytokines

[25].

Previous studies concluded that there was no relationship between decreased platelets and the incidence of sepsis. The number of platelets in sepsis patients does not decrease drastically or cause bleeding and the lowest point of platelet decline in sepsis patients usually occurs within 48 hours [26].

2.7 Distribution of Patients Based on Mortality

Based on this research, the death rate of sepsis patients was 66% of the total number of patients of 200. This research is different from previous studies which stated that the epidemiology of sepsis in the United States from 1979 to 2000 was respectively 27.8% (1979 - 1984) and 17.95% (1985 - 2000) [27].

2.8 Distribution of Patients Based on Bacterial and Antibiotic Patterns

In this research, the most common type of specimen was urine with 30 samples (29.70%), followed by blood with 29 samples (28.71%), pus with 26 samples (25.74%), and the least obtained was sputum with 16 (15.84%) samples. This is different from the study conducted by the ICU of Haji Adam Malik General Hospital, Medan in 2016 which obtained the most blood specimens, namely 80 specimens (72%) [28].

Blood culture examination is the gold standard in establishing a diagnosis of sepsis, but in this research, blood cultures found growth in 29 specimens (28.71%). Several factors influence blood culture so that bacterial growth is often not found, such as unsuitable time of collection, insufficient blood collection location, and/or antibiotics that have been given before entering the ICU [29].

The most common type of bacteria found in this research was *Acinetobacter baumannii* with 24 samples (23.76%), followed by *Escherichia coli* with 23 samples (22.77%), and *Klebsiella pneumonia* with 9 samples (8.91%). Research conducted at the Intensive Care Unit of Arifin Achmad Hospital in 2017 also had similar results, namely *A. baumannii* with 14 samples (37.85%), followed by *K. pneumoniae* with 9 samples (24.32%), *P. aeruginosa* with 6 samples (16.22%), and *E. coli* with 5 samples (13.51%) [29].

This is also following the results of an epidemiological research which stated that of 4947 ICU patients infected with 118 culture results from 75 countries, 62% of positive isolates were Gram-negative organisms, 47% Gram-positive, and 19% were fungi. The increase in the number of cases of infection caused by Gram-negative bacteria is also due to mutations in some bacteria that cause resistance to antibiotics. These bacteria can live in the hospital environment, especially in the ICU which has a high risk of nosocomial infections [29].

The bacteria obtained in this research were resistant to several antibiotics such as Cephazolin (48.51%), Amoxicillin-clavulanic acid (42.57%), and Ceftriaxone (40.59%) and some bacteria were still sensitive to Amikacin antibiotics (63.37%), meropenem (61.39%) and piperacillin-tazobactam (58.42%).

This research is almost similar to the study conducted at the Intensive Care Unit (ICU) of Arifin Achmad Hospital which also obtained results of bacteria resistant to ampicillin (100%) < cephazolin (94.59%), and ceftriaxone (89.18%) and had high sensitivity to amikacin (72.98%) and tigecyclin (51.36%). Another study conducted at Soemani Hospital Semarang in 2012 also stated that bacteria that cause sepsis have a high level of sensitivity to amikacin [29].

Acinetobacter baumannii has high resistance to Aztreonam, Cephazolin, Chloramphenicol, and Ampicillin and has high sensitivity to Amoxiclav and Nitrofurantoin. This research is almost similar to the study conducted at Dr. M. Djamil Hospital, Padang, which also found the highest antibiotic resistance in *Acinetobacter baumannii* was found in cephazolin at 99.3%. High resistance to Cephazolin is thought to be due to *Acinetobacter baumannii* having the AmpC-type cephalosporinase enzyme which is obtained vertically. This enzyme will hydrolyze cephalosporin antibiotics [30].

Escherichia coli has high resistance to Ampicillin and has a high sensitivity to Amoxiclav, Meropenem, Cefoxitin, Amikacin, Tobramycin, Imipenem, Meropenem, and Teicoplanin. This is following previous research which also found that *E. Coli* bacteria have high resistance to ampicillin. Study conducted by Sulistyaningrum in 2016 on bacterial resistance patterns to antibiotics for the period August 2013-August 2015 also found that *A. Baumannii* bacteria had experienced resistance to Ampicillin by 87.5% [31].

3. CONCLUSION

The conclusion of this research regarding the profile of sepsis patients in the internal medicine inpatients of Dr. Soetomo Hospital from January 2021 to June 2021 is that the number of sepsis patients was 283 cases. The characteristics of sepsis patients are most common in women with an age range of 45-64 years. The most common comorbid disease in sepsis patients is diabetes mellitus followed by hypertension. Laboratory examination of sepsis patients showed an increase in procalcitonin and leukocytes, while platelets did not increase (normal). There were 132 cases of death in sepsis patients during that period. The culture results found the most specimens were urine with a total of 30 samples, followed by blood with 29 samples, pus with 26 samples and the least was sputum with 16 samples. The most common bacteria found were *Acinetobacter baumannii* with 24 samples, followed by *Escherichia coli* with 23 samples, and *Klebsiella pneumoniae* with 9 samples. These bacteria are resistant to several antibiotics such as Cephazolin, Amoxicillin-clavulanic acid, and Ceftriaxone and 57 some bacteria are still sensitive to the antibiotics Amikacin, meropenem, and piperacillin-tazobactam.

Completeness of filling in patient status in medical records is very necessary to support a complete, accurate, and informative approach so that it can improve treatment and can be a reference for further research. Furthermore, more complete and quality research can be conducted on sepsis patients who are treated by considering parameters including diagnostic criteria, complete lab results, and most importantly, germ examination so that the etiology of the instrumental germ can be known. In further study, it is expected to conduct the research with a longer time so that more samples are found.

References

- Putra, I, A. S., 2019, „Update Tatalaksana Sepsis“, CDK-280, 46(11), 683-685.
- Purwanto, D. S. and Astrawinata, D. A. W. (2019) „Pemeriksaan Laboratorium sebagai Indikator Sepsis dan Syok Septik“, *Jurnal Biomedik (Jbm)*, 11(1), p. 1. doi: 10.35790/jbm.11.1.2019.23204.
- World Health Organization, 2020, Global Report on The Epidemiology and Burden of Sepsis, Retrieved: May, 2021 from <https://apps.who.int/iris/bitstream/handle/10665/334216/9789240010789-eng.pdf>
- Umroh, A., 2020, „Tatalaksana Syok Septik“, *Jurnal Penelitian Perawat Profesional*, 2(4), 362.
- Keputusan Menteri Kesehatan Republik Indonesia, Pedoman Nasional Pelayanan Kedokteran Tata Laksana Sepsis, Retrieved: May 10, 2021, from http://hukor.kemkes.go.id/uploads/produk_hukum/KMK_No._HK_.01_.07-MENKES-342-2017_ttg_Pedoman_Pelayanan_Kedokteran_Tata_Laksana_Sepsis_.pdf
- Millizia, A., 2019, „Penatalaksanaan Sepsis“, *Jurnal Kedokteran Nangroe Medika*, 2(3), 29.
- Vivianni, A., Farhanah, N., 2016, „Faktor – Faktor Prediktor Mortalitas Sepsis dan Syok Sepsis di ICU RSUP Dr. Kariadi“, *Jurnal Kedokteran Diponegoro*, 5(4), 505.
- Angus, D. C. & Poll, T. V. D., 2021, „Severe Sepsis and Septic Shock“, *The New England Journal of Medicine*, 369(9), 841.
- Starr ME, Saito H. Sepsis in old age: review of human and animal studies. *Aging Dis.* 2014 Apr 1;5(2):126-36. doi: 10.14336/AD.2014.0500126. PMID: 24729938; PMCID: PMC3966671.
- Wardani, I. S., 2017, „Tatalaksana Sepsis Berat pada Pasien Lanjut Usia“, *Jurnal Kedokteran Unram*, 7(4), 33-39
- Mohamed, A. K. S., Mehta, A. A. & James, P., „Predictors of Mortality of Severe Sepsis Among Adult Patients in The Medical Intensive Care Unit“, *Lung India*, 34(4), 330-335
- Yessica, P. H., 2014, Faktor Risiko Sepsis Pada Pasien Dewasa di RSUP Dr. Kariadi, Retrieved: June 2, 2021 from <https://media.neliti.com/media/publications/139055-ID-faktor-risiko-sepsispada-pasien-dewasa.pdf>
- Angele, M. K., Frantz, M. C. & Chaudry, I. H., 2006, Gender and Sex Hormones Influence The Response To Trauma and Sepsis Potential Therapeutic Approaches, Retrieved: May 20, 2021, from <https://pubmed.ncbi.nlm.nih.gov/17072448/>
- Subroto, Y. and Loehoeri, S. (2003) „Profil Pasien Yang Dididagnosis Dengan Sepsis (ICD X: 41,9) di Bangsal Penyakit Dalam RS Dr. Sardjito Tahun 2022“, *Berkala Ilmu Kedokteran*, 35, pp. 225–238.
- Tambajong, R. N., Lalenoh, D. C., Kumaat, L., 2016, „Profil Penderita Sepsis di ICU RSUP Prof. Dr. R. D. Kandou Manado Periode Desember 2014 – November 2015“, *Jurnal e-Clinic (eCI)*, 4(1), 453.
- Nainggolan, J. J. P., Kumaat, L. T. and Laihad, M. L. (2017) „Gambaran Sumber Terjadinya Infeksi pada Penderita Sepsis dan Syok Septik di ICU RSUP Prof. Dr. R. D. Kandou Manado Periode Agustus 2016 sampai dengan September 2017“, *e-Clinic*, 5(2), pp. 3–7. doi: 10.35790/eci.5.2.2017.18570.
- Ginde, A. A., Blatchford, P. J., Trzeciak, S., Hollander, J. E., Birkhahn, R., Otero, R., Osborn, T. M., Moretti, E., Nguyen, H. B., Gunnerson, K. J., Milzman, D., Gaieski, D. F., Goyal, M., Cairns, C. B., Rivers, E. P. and Shapiro, N. I. (2014) „Age-related differences in biomarkers of acute inflammation during hospitalization for sepsis.“, *Shock* (Augusta, Ga.). United States, 42(2), pp. 99– 107. doi: 10.1097/SHK.0000000000000182.

18. Saputra, F. Y. and Nurul, F. (2015) „Pengaruh Komorbiditas terhadap Angka Mortalitas Pasien Sepsis di RS PKU Muhammadiyah Unit I”. Available at: [https://etd.ums.ac.id/id/eprint/22468/8/Naskah Publikasi.pdf](https://etd.ums.ac.id/id/eprint/22468/8/Naskah_Publikasi.pdf).
19. Esper, A. M., Moss, M., Lewis, C. A., Nisbet, R., Mannino, D. M. and Martin, G. S. (2006) „The role of infection and comorbidity: Factors that influence disparities in sepsis.”, *Critical care medicine*. United States, 34(10), pp. 2576–2582. doi: 10.1097/01.CCM.0000239114.50519.0E.
20. Chodijah, S., Nugroho, A. and Pandelaki, K. (2013) „Hubungan Kadar Gula Darah Puasa Dengan Jumlah Leukosit Pada Pasien Diabetes Mellitus Dengan Sepsis”, *Jurnal e-Biomedik*, 1(1). doi: 10.35790/ebm.1.1.2013.4606.
21. Rahayu, C. and Anjani, M. Y. (2021) „Studi Literatur Gambaran Hasil Pemeriksaan Procalcitonin Sebagai Biomarker Pada Pasien Sepsis”, *Anakes : Jurnal Ilmiah Analisis Kesehatan*, 7(1), pp. 72–82. doi: 10.37012/anakes.v7i1.520.
22. Downes, K. J., Fitzgerald, J. C. and Weiss, S. L. (2020) „Utility of Procalcitonin as a Biomarker for Sepsis in Children.”, *Journal of clinical microbiology*. United 61 States, 58(7). doi: 10.1128/JCM.01851-19.
23. Gita Yustika (2020) „Analisis Parameter Leukosit dalam Diagnosis Awal Sepsis Neonatorum Awitan Dini di RSIA Ananda Makassar”, *Journal of Health Sciences*, 13(2), pp. 204–214. doi: 10.33086/jhs.v13i2.1475
24. Vardon-Boune, F., Ruiz, S., Gratacap, M.-P., Garcia, C., Payrastra, B. and Minville, V. (2019) „Platelets Are Critical Key Players in Sepsis.”, *International journal of molecular sciences*. Switzerland, 20(14). doi: 10.3390/ijms20143494.
25. Arfi, U. (2018) Korelasi Jumlah Trombosit dan Procalcitonin Pada Pasien Sepsis di Intensive Care Unit. Andalas University
26. Siahaan, A. E., Silaen, J. C. and Simanjuntak, L. (2021) „Gambaran Profil Hematologi 63 Dalam 24 Jam Pertama Pada Pasien Sepsis Di Unit Neonatus RSUD Dr. Pirngadi Medan Tahun 2017-2018”, *Nommensen Journal of Medicine*, 6(2), pp. 44–48. doi: 10.36655/njm.v6i2.243.
27. Martin, G. S., Mannino, D. M., Eaton, S. and Moss, M. (2003) „The epidemiology of sepsis in the United States from 1979 through 2000.”, *The New England journal of medicine*. United States, 348(16), pp. 1546–1554. doi: 10.1056/NEJMoa022139.
28. Ahwini, S. H., 2017, Profil Penderita Sepsis di ICU RSUP Haji Adam Malik Medan Pada Tahun 2016, Retrieved: May 28, 2021
29. Wijaksana, D. S., Anggraeni, N. & Endriani, R., „Pola Bakteri dan Resistensi Antibiotik pada Pasien Sepsis di Intensive Care Unit (ICU) RSUD Arifin Achmad Provinsi Riau Periode 1 Januari – 31 Desember 2017”, *JIK*, 13(2), 117-125.
30. Mahdani, W., Hayati, Z. and Yusriadi, T. (2020) „PETA DISTRIBUSI DAN RESISTENSI *Acinetobacter baumannii* DARI SPESIMEN KLINIK DI RSUD DR. ZAINOEL ABIDIN TAHUN 2018”, *AVERROUS: Jurnal Kedokteran dan 62 Kesehatan Malikussaleh*, 6(1), p. 108. doi: 10.29103/averrous.v6i1.2666.
31. Arivo, D. and Dwiningtyas, A. W. (2019) „Pola Kepekaan *Escherichia coli* Penyebab Infeksi Saluran Kemih Terhadap Antibiotik”, *Jurnal Farmasi Malahayati*, 2(1), pp. 12–23.