

INDONESIAN JOURNAL OF
**CLINICAL PATHOLOGY AND
MEDICAL LABORATORY**

Majalah Patologi Klinik Indonesia dan Laboratorium Medik

EDITORIAL TEAM

Editor-in-chief:
Puspa Wardhani

Editor-in-chief Emeritus:
Prihatini
Krisnowati

Editorial Boards:

Maimun Zulhaiddah Arthamin, AAG Sudewa, Rahayuninggih Dharma, Mansyur Arif, July Kumalawati, Nurhayana Sennang Andi Nanggung, Aryati, Purwanto AP, Jusak Nugraha, Sidarti Soehita, Endang Retnowati Kusumowidagdo, Edi Widjajanto, Budi Mulyono, Adi Koesoema Aman, Uleng Bahrun, Ninik Sukartini, Kusworini Handono, Rismawati Yaswir, Osman Sianipar

Editorial Assistant:
Dian Wahyu Utami

Language Editors:
Yolanda Proboboesodo, Nurul Fitri Hapsari

Layout Editor:
Akbar Fahmi

Editorial Address:

d/a Laboratorium Patologi Klinik RSUD Dr. Soetomo Jl. Mayjend. Prof. Dr Moestopo 6–8 Surabaya, Indonesia
Telp/Fax. (031) 5042113, 085-733220600 E-mail: majalah.ijcp@yahoo.com, jurnal.ijcp@gmail.com
Website: <http://www.indonesianjournalofclinicalpathology.or.id>

Accredited No. 36a/E/KPT/2016, Tanggal 23 Mei 2016

INDONESIAN JOURNAL OF CLINICAL PATHOLOGY AND MEDICAL LABORATORY

Majalah Patologi Klinik Indonesia dan Laboratorium Medik

CONTENTS

RESEARCHS

Molecular Aspect Correlation between Glycated Hemoglobin (HbA1c), Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) on Type 2 Diabetes Mellitus (T2DM) (Aspek molekuler Hubungan Kadar Hemoglobin Terglikasi (HbA1c), Prothrombin Time (PT) dan Activated Partial Thromboplastin Time (APTT) di Diabetes Melitus Tipe 2)	1–6
Indranila KS	1–6
Platelet-Lymphocyte Ratio (PLR) Markers in Acute Coronary Syndrome (Platelet Lymphocyte Ratio (PLR) Sebagai Petanda Sindrom Koroner Akut)	7–11
Haerani Harun, Uleng Bahrun, Darmawaty ER	7–11
The Mutation Status of Kras Gene Codon 12 and 13 in Colorectal Adenocarcinoma (Status Mutasi Gen Kras Kodon 12 dan 13 di Adenocarcinoma Kolorektal)	12–17
Gondo Mastutik, Alphania Rahniayu, Anny Setijo Rahaju, Nila Kurniasari, Reny Ptishom	12–17
Creatine Kinase Related to the Mortality in Myocardial Infarction (Creatine Kinase terhadap Angka Kematian di Infark Miokard)	18–21
Liong Boy Kurniawan, Uleng Bahrun, Darmawaty Rauf, Mansyur Arif	18–21
Application of DNA Methylation on Urine Sample for Age Estimation (Penggunaan Metilasi DNA Dalam Perkiraan Umur Individu di Sampel Air Kemih)	22–26
Rosalinda Avia Eryatma, Puspa Wardhani, Ahmad Yudianto	22–26
Lipid Profile Analysis on Regular and Non-Regular Blood Donors (Analisis Profil Lipid di Pendonor Darah Reguler dan Non-Reguler)	27–30
Waode Rusdiah, Rachmawati Muhiddin, Mansyur Arif	27–30
Percentage of CD3 ⁺ T Lymphocytes Expressing IFN-γ After CFP-10 Stimulation (Persentase Limfosit T-CD3 ⁺ yang Mengekspresso Interferon Gamma Setelah Stimulasi Antigen CFP-10)	31–35
Yulia Nadar Indrasari, Betty Agustina Tambunan, Jusak Nugraha, Fransiska Sri Oetami	31–35
Characteristics of Crossmatch Types in Compatibility Testing on Diagnosis and Blood Types Using Gel Method (Ciri Inkompatibilitas Uji Cocok Serasi Metode Gel terhadap Diagnosis dan Golongan Darah)	36–41
Irawaty, Rachmawati AM, Mansyur Arif	36–41
Diagnostic Values of Mycobacterium Tuberculosis 38 kDa Antigen in Urine and Serum of Childhood Tuberculosis (Nilai Diagnostik Antigen 38 kDa Mycobacterium tuberculosis Air Kemih dan Serum di Tuberkulosis Anak)	42–49
Agustin Iskandar, Leliawaty, Maimun Z. Arthamin, Ery Olivianto	42–49
Erythrocyte Indices to Differentiate Iron Deficiency Anemia From β Trait Thalassemia (Indeks Eritrosit Untuk Membedakan Anemia Defisiensi Besi Dengan Thalassemia β Trait)	50–55
Yohanes Salim, Ninik Sukartini, Arini Setiawati	50–55

HbA1c Levels in Type 2 Diabetes Mellitus Patients with and without Incidence of Thrombotic Stroke (<i>Kadar HbA1c Pasien Diabetes Melitus Tipe 2 Dengan dan Tanpa Kejadian Strok Trombotik</i>) Dafina Balqis, Yudhi Adrianto, Jongky Hendro Prayitno	56–60
Comparative Ratio of BCR-ABL Genes with PCR Method Using the Codification of G6PD and ABL Genes in Chronic Myeloid Leukemia Patients (<i>Perbandingan Angka Banding Gen BCR-ABL Metode PCR Menggunakan Baku Gen Glucosa-6-Phosphate Dehidrogenase dan Gen Abelson Kinase di Pasien Chronic Myeloid Leukemia</i>) Tonggo Gerdina Panjaitan, Delita Prihatni, Agnes Rengga Indrati, Amaylia Oehadian	61–66
Virological and Immunological Response to Anti-Retroviral Treatment in HIV-Infected Patients (<i>Respons Virologis dan Imunologis Terhadap Pengobatan Anti-Retroviral di Pasien Terinfeksi HIV</i>) Umi S. Intansari, Yunika Puspa Dewi, Mohammad Juffrie, Marsetyawan HNE Soesatyo, Yanri W Subronto, Budi Mulyono	67–73
Comparison of sdLDL-C Analysis Using Srisawasdi Method and Homogeneous Enzymatic Assay Method on Hypertriglyceridemia Condition (<i>Perbandingan Analisa sdLDL-C metode Srisawasdi dan Homogeneous Enzymatic Assay di Kondisi Hipertrigliseridemia</i>) Gilang Nugraha, Soebagijo Poegoeh Edijanto, Edhi Rianto	74–79
Pattern of Bacteria and Their Antibiotic Sensitivity in Sepsis Patients (<i>Pola Kuman dan Kepekaan terhadap Antibiotik di Pasien Sepsis</i>) Wahyuni, Nurahmi, Benny Rusli	80–83
The Correlation of Naive CD4 ⁺ T Lymphocyte Cell Percentage, Interleukin-4 Levels and Total Immunoglobulin E in Patients with Allergic Asthma (<i>Kenasaban antara Persentase Sel Limfosit T-CD4⁺ Naive dengan Kadar Interleukin-4 dan Jumlah Imunoglobulin E Total di Pasien Asma Alergi</i>) Si Ngr. Oka Putrawan, Endang Retnowati, Daniel Maranatha	84–89

LITERATURE REVIEW

Antibiogram (<i>Antibiogram</i>) Jeine Stela Akualing, IGAA Putri Sri Rejeki	90–95
---	-------

CASE REPORT

Pancreatic Cancer in 31 Years Old Patient with Normal Serum Amylase Level (<i>Kanker Pankreas di Pasien Usia 31 Tahun Dengan Kadar Amilase Serum Normal</i>) Melda F Flora, Budiono Raharjo, Maimun Z. Arthamin	96–101
--	--------

Thanks to editors in duty of IJCP & ML Vol 23 No. 1 November 2016

Kusworini Handono, Prihatini, Purwanto AP, July Kumalawati, Jusak Nugraha, Ida Parwati,
Adi Koesoema Aman, Edi Widjajanto, AAG. Sudewa, Nurhayana Sennang AN

RESEARCH

PATTERN OF BACTERIA AND ITS ANTIBIOTIC SENSITIVITY IN SEPSIS PATIENTS

(*Pola Kuman dan Kepekaan terhadap Antibiotik bagi Pasien Sepsis*)

Wahyuni, Nurahmi, Benny Rusli

ABSTRAK

Sepsis merupakan masalah serius karena berkebayaan kematian yang tinggi. Penggunaan antibiotik profilaksis telah menjadi tata langkah baku untuk penanganan sepsis, tetapi jika pola kuman dan kepekaan antibiotik tidak diketahui, maka akan memperbesar kemungkinan resistensi kuman terjadi yang selanjutnya akan menyebabkan peningkatan angka infeksi. Penelitian ini bertujuan mengetahui pola kuman dan kepekaannya terhadap antibiotik di pasien sepsis di RS Dr. Wahidin Sudirohusodo Makassar masa waktu Januari 2009–Desember 2010. Metode penelitian yang digunakan adalah observational dengan desain potong lintang. Data penelitian diambil dari hasil kultur dan kepekaan terhadap antibiotik yang tertulis di rekam medis pasien sepsis di RS Dr. Wahidin Sudirohusodo Makassar masa waktu Januari 2009–Desember 2010. Data yang dikumpulkan kemudian dianalisis menggunakan metode statistik sebaran kekerapan. Telitian menunjukkan umur pasien sepsis terbanyak adalah di atas 40 tahun. Infeksi lebih banyak disebabkan oleh bakteri negatif Gram (90,48%). Urutan kuman terbanyak adalah Alkaligenes faecalis (30,16%), Escherichia coli (12,70%), Acinetobacter calcoaceticus (12,70%) dan Staphylococcus aureus (7,94%). Uji kepekaan terhadap 39 jenis antimikroba, terdapat 12 antimikroba yang memperlihatkan persentase resistensi yang tinggi (75% ke atas). Antimikroba yang paling peka yaitu Nitrofurantoin (83,33%). Dapat disimpulkan bahwa bakteri yang terbanyak ditemukan di sepsis adalah Alkaligenes faecalis, Escherichia coli, Acinetobacter calcoaceticus dan Staphylococcus aureus. Antimikroba yang masih peka adalah Nitrofurantoin. Disarankan untuk dilakukan penelitian pola kuman dan kepekaan terhadap antibiotik secara berkala.

Kata kunci: Pola kuman, sensitivitas, sepsis

ABSTRACT

Sepsis is a serious health problem because of high a risk of death. The use of prophylactic antibiotics has become standard procedure for the treatment of sepsis. Nevertheless, if the pattern of bacteria and antibiotic sensitivity is still not known, resistance to other bacteria will increase, leading to increased rates of infections. Therefore, this research aimed to determine the pattern of bacteria and their sensitivity to antibiotics in patients with sepsis in Dr. Wahidin Sudirohusodo Hospital, Makassar from January 2009 to December 2010. The research method used was an observational method with cross-sectional design. First, data were collected from the results of their culture and their sensitivity to antibiotics written in the medical records of those patients with sepsis in Dr. Wahidin Sudirohusodo Hospital, Makassar from January 2009 to December 2010. Second, the data collected were analyzed using statistical methods of frequency distribution. The results show that the sepsis patients were mostly above 40 years. Moreover, infections occurred were mostly caused by Gram negative bacteria (90.48%). The most bacteria found in sequence were Alkaligenes faecalis (30.16%), Escherichia coli (12.70%), Acinetobacter calcoaceticus (12.70%) and Staphylococcus aureus (7.94%). Next, sensitivity test was conducted on 39 kinds of antimicrobials, 12 of which had high resistance percentage (above 75%). Those bacteria were mostly sensitive to Nitrofurantoin (83.33%). Thus, it can be concluded that the majority of bacteria found in sepsis are Alkaligenes faecalis, Escherichia coli, Staphylococcus aureus, and Acinetobacter calcoaceticus. Those bacteria are still sensitive to Nitrofurantoin. Consequently, it is advisable to do research on pattern of bacteria and their sensitivity to antibiotics regularly.

Key words: Pattern of bacteria, sensitivity, sepsis

INTRODUCTION

Sepsis is defined as a systemic inflammatory response to infections. The inflammatory response is a systemic immune response that emerges after the local immune response does not successfully eliminate microbial antigens.¹ Infection is a microbial phenomenon characterized by an inflammatory response against microorganisms invading into the tissue under normal and sterile circumstances.² Acute inflammation is a direct response to the early response to the injury-causing agent and the production/release of a wide variety of chemical mediators. Although types of tissues experiencing lesion are different, mediators released are the same.³

Acute inflammation, moreover, can be local (confined to the place of injury) or widespread with systemic signs and symptoms. Clinical manifestation of the systemic infection is referred as *Systemic Inflammatory Response Syndrome* (SIRS).³ *Systemic inflammatory response syndrome* is a systemic response to a variety of causes, such as massive trauma, burns, pancreatitis, major surgery and infection. *Systemic inflammatory response syndrome* caused by infections is known as sepsis.⁴ The most common etiology of sepsis is bacteria (positive culture results), that can be derived from Gram negative bacteria, Gram positive bacteria or a mixture of both.⁵

Sepsis, furthermore, is considered as a global problem because of its high incidence, mortality and cost of care. The incidence of sepsis around the word reached to 1.8 million cases/year. The incidence of sepsis in the United States in 2000 was 750 000 cases/year, whereas in Europe 90.4 cases/100,000 inhabitants/year. Unfortunately, in Indonesia the incidence of sepsis still has not had accurate data. The incidence of sepsis in some referral hospitals ranged from 15 to 37.2%, with a mortality rate of 37-80%. The incidence of neonatal sepsis in developing countries was various, ranging from 1 to 10 per 100 live births. Mortality ranged from 13% to 50%. The high mortality rate was because of late handling.^{5,6}

Sepsis, therefore, can be considered as a serious problem with a higher risk of death. After the diagnosis of sepsis, blood culture must be conducted to determine kind of organisms infecting, but an antibiotic must be given even before the results of the culture obtained. In the beginning, the antibiotic given is determined by what bacterium is often found in the infected area. Then if the results of the culture have already obtained,

the antibiotic can be replaced with the most effective one for the bacterium causing the infection.⁷

However, excessive use of antibiotics can lead to bacterial resistance to antibiotics. Prospective research on newborns at Cipto Mangunkusumo Hospital from July 2004 to May 2005 shows clinical signs of septicemia, thus, blood cultures are taken. The bacteria most commonly found are *Acinetobacter calcoaceticus* (35.7%), *Enterobacter sp* (7.0%) and *Staphylococcus sp* (6.8%). Most of those bacteria show high levels of resistance to antibiotics often used (*Ampicillin* and *Gentamicin*). They, both Gram negative bacteria and Gram positive bacteria, also have a high level of resistance to *cefalosporin*. Meanwhile, *A. calcoaceticus* (61.7%) and *Enterobacter sp* (45.7%) are sensitive to *ceftazidime*. Gram negative bacteria also show high levels of resistance to *amikacin*, yet *Staphylococcus sp* has a moderate level of resistance. Their resistance to *carbapenem* (*meropenem* and *imipenem*) is also various, from moderate to low one.⁸

Similarly, a research on “Neonatal Bacteremia” in Dr. Kariadi Hospital in 2004 finds that most bacteria causing bacteraemia in neonates are *Pseudomonas sp* (21.6%) and *Enterobacter sp* (12.4%). Those bacteria are resistant to *ampicillin* (97.4%), *gentamicin* (80.6%), and *cefotaxime* (55.6%).⁹ Another research on “Risk factors, pattern of bacteria and their sensitivity, as well as causes of bacteraemia in geriatric patients” at Dr. Kariadi Hospital, Semarang in 2004 also finds that the main causes of bacteraemia are *Staphylococcus*, *Enterobacter* and *Pseudomonas*. Their antibiotic sensitivity is low on *penicillin*, *chloramphenicol*, *cotrimoxazole* and various aminoglycoside.¹⁰ Like the previous ones, a research on “Sepsis in Children” at Dr. Cipto Mangunkusumo Hospital in 2010 finds that bacteria mostly causing sepsis are *Klebsiella pneumoniae* (24%), *Serratia marcescens* (14%) and *Burkholderia cepacia* (14%). They are sensitive to *cefepime* and *levofloxacin*.¹¹

Finally, based on those previous researches, it can be concluded that the high rate of mortality is associated with the presence of various bacteria in sepsis, which is resistant to some antibiotics commonly used. Thus, this research aimed to determine patterns of bacteria in sepsis and their sensitivity to various antibiotics commonly used. Consequently, the results of this research are expected to be used as consideration for the clinicians in determining antibiotics that must be given before getting the results of a sensitivity test for the diagnosis of sepsis in Dr. Wahidin Sudirohusodo Hospital, Makassar.

METHODS

This research was conducted using an observational method with a cross-sectional design. Data were collected from the results of culture and sensitivity to antibiotics written on the medical records of patients with sepsis in Dr. Wahidin Sudirohusodo Hospital, Makassar from January 2009 to December 2010. The research variables were patterns of bacteria and their sensitivity to antibiotics. The data collected were then analyzed using a statistical method of frequency distribution.

RESULTS AND DISCUSSION

There were 63 patients, consisted of 44 males (69.84%) and 19 females (30.16%) with the most age range of 40 years above (60.32%). Data obtained were presented in Table 1 with the sex ratio of 2:1 (male: female).

Table 1. Characteristics of sepsis patients by sex and age

Variables	n (63)	%
Sex		
Male	44	69.84
Female	19	30.16
Age (years old)		
≤10 years old	2	3.17
11–40 years old	23	36.51
>40 years old	38	60.31

Table 2. Kinds and number of bacteria causing infections in sepsis patients

Variable	n(63)	%
Gram		
Negative (-)	57	90.48
Positive (+)	6	9.52

Table 2 shows that infections in those patients with sepsis were mostly caused by Gram negative bacteria. This finding was the same as the results of the previous prospective research on newborns at Cipto Mangunkusumo Hospital from July 2004 to May 2005 that shows clinical signs of septicemia, thus, blood cultures are taken. The research also finds that Gram-negative bacteria have high levels of resistance to amikacin.⁸ In addition, there were 13 kinds of bacteria derived from the culture results of those 63 samples. Percentage of bacteria causing infections in sepsis patients is shown in Figure 1.

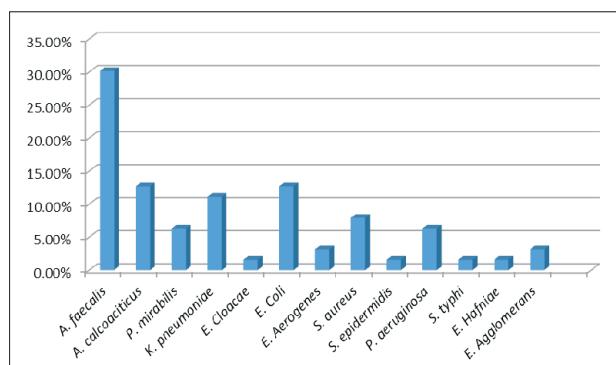


Figure 1. Percentage of bacteria causing infections in sepsis patients.

Table 3. Percentage of antimicrobial sensitivity test results in patients with sepsis

No.	Name of Antibiotics	Sensitivity (%) Sensitive
1.	Amikacin	0
2.	Amoxicillin	4.16
3.	Ampicillin	21.62
4.	Aztreonam	24.44
5.	Bacitracin	8.33
6.	Cefazolin	15.69
7.	Cefepime	33.33
8.	Chloramphenicol	40.35
9.	Cefoperazone	20.83
10.	Cefotaxime	26.32
11.	Cefpirome	42.86
12.	Ceftazidime	31.03
13.	Cefuroxime	25.45
14.	Ceftriaxone	23.08
15.	Ciprofloxacin	14.29
16.	Clindamycin	47.62
17.	Dibekacin	36.36
18.	Doxycycline	32.73
19.	Erythromycin	16.67
20.	Fosfomycin	44.44
21.	Gatrifloxacin	31.58
22.	Gentamycin	36.84
23.	Imipenem	53.66
24.	Levofloxacin	46.34
25.	Meropenem	67.35
26.	Methicillin	41.67
27.	Neomycin	36.59
28.	Netilmicin	33.33
29.	Nitrofurantoin	83.33
30.	Norfloxacin	34.15
31.	Novobiocin	22.22
32.	Ofloxacin	35.14
33.	Sulbactam	33.33
34.	Cotrimoxazole	33.33
35.	Sulfametoxazole	29.63
36.	Tetracycline	16.22
37.	Cefadroxil	33.33
38.	Trimethoprim	30
39.	Vancomycin	40

Figure 1 shows that bacteria mostly causing infections in sepsis were *Alkaligenes faecalis* (30.16%), *Acinetobacter calcoaceticus* (12.70%), and *Escherichia coli* (12.70%). The third bacteria mostly causing infections was *Klebsiella pneumoniae* (11.11%). Similarly, a research conducted at Cipto Mangunkusumo Hospital (from July 2004 to May 2005) finds that bacteria mostly causing *septicemia* are *A. calcoaceticus*.⁸ Another research on “Pediatric Sepsis” at Dr. Cipto Mangunkusumo Hospital in 2010 also finds that bacteria mostly causing sepsis are *Klebsiella pneumoniae* (24%), *Serratia marcescens* (14%) and *Burkholderia cepacia* (14%).¹¹

Table 3 shows the 39 kinds of antimicrobials tested, 12 of which showed the high percentage of antimicrobial resistance (over 75%). Antimicrobials with the high sensitivity were *nitrofurantoin* (83.33%), *meropenem* (67.35%), and *imipenem* (53.66%). Based on these results, it can be said that *nitrofurantoin* is an appropriate antimicrobial that can be used for the treatment of infections in patients with sepsis in Dr. Wahidin Sudirohusodo Hospital, Makassar. Unlike this research, a research conducted on “Pediatric Sepsis” at Dr. Cipto Mangunkusumo Hospital in 2010 found that antimicrobials with the high sensitivity were *cefepime* and *levofloxacin*.¹¹

CONCLUSION AND SUGGESTION

In conclusion, infections in patients with sepsis are mostly caused by Gram negative bacteria. Bacteria mostly found in sepsis are *Alkaligenes faecalis*, *Escherichia coli* and *Acinetobacter calcoaceticus*, and then *Staphylococcus aureus*. Those bacteria are still sensitive to antibiotics, such as *nitrofurantoin*, *meropenem*, and *imipenem*. Thus, *nitrofurantoin* is the best antimicrobial for treatment of infections in

patients with sepsis in Dr. Wahidin Sudirohusodo Hospital, Makassar. Finally, evaluation of the pattern of bacteria and their antibiotic sensitivity should be conducted periodically, particularly in sepsis patients in order to become a reference for clinicians in conducting therapy so that the therapeutic effects are expected to be achieved and drug side effects can be avoided.

REFERENCES

1. Aryana IG, Biran SI. Konsep Baru Kortikosteroid Pada Penanganan Sepsis. DEXA MEDICA. 2006; (4)19: 177–181.
2. Govinda D. W. A. Penanganan Sepsis. DEXA MEDIA. 2006; 19(2): 110–114.
3. Buchori dan Prihatini. Diagnosis Sepsis Menggunakan Procalcitonin. Indonesian Journal of Clinical Pathology, 2006; 12(3): 131–137.
4. Guntur A. H. The Role of Norepinephrine in Septic Shock Patients. DEXA MEDIA. 2008; 21(1): 3–7.
5. Kadir AN. Analisis Eosinofil dan Prokalsitonin pada pasien suspek Sepsis di Intensive Care Unit. Program Pascasarjana. Universitas Hasanuddin. Makassar. 2011; 8.
6. Nurulita A. Analisis Kadar Interleukin 18 dan C-Reaktif Protein pada pasien suspek Sepsis. Program Pascasarjana. Universitas Hasanuddin. Makassar. 2010; 1–2.
7. Setyawati, Dian Ariningrum, Umi S. Intansari, Ekawaty Lutfia. Penampilan Diagnostik Parameter-parameter Hematologi untuk Diagnosis Sepsis Neonatal. Bagian Patologi Klinik. Bagian Ilmu Kesehatan Anak. Fakultas Kedokteran. Universitas Gajah Mada. RSUP Dr. Sardjito. Yogyakarta. Berkala Ilmu Kedokteran. 2006; 38(1): 30–40.
8. Sepsis Klasifikasi dan Bahan-bahan Eksternal ICD-10 A50 – A41.0 ICD 9995.91 Diseases DB 1960 MeSH D018805.
9. Rohsiswatmo R. Resistensi terhadap Bermacam-Macam Obat pada Unit Neonatal & Implikasi Terapeutiknya. Pediatri Indonesia. 2006; 46: 25–31.
10. Deliana, Elly, Farida, Helmia. Pola Kuman dan Kepekaan terhadap Antibiotik pada Pasien Sepsis di Pediatric Intensive Care Unit (PICU)/Neonatal Intensive Care Unit (NICU) RSUP Dr. Kariadi Januari 1999 – Desember 2001. Media Medika Indonesia. Semarang, Fakultas Kedokteran Universitas Diponegoro. 2003; 139–142.