SKRIPSI

POLA SENSITIVITAS BAKTERI *Pseudomonas aeruginosa* TERHADAP ANTIBIOTIK PADA PASIEN RAWAT INAP DI RSUP DR. MOHAMMAD HOESIN PALEMBANG PERIODE MEI 2022 – APRIL 2023

SALWA ADILAH NINGTIYAS

04011182025029

PROGRAM STUDI PENDIDIKAN DOKTER

FAKULTAS KEDOKTERAN

UNIVERSITAS SRIWIJAYA

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Diajukan untuk memenuhi salah satu syarat guna memperoleh gelar
Sarjana Kedokteran (S.Ked)

SALWA ADILAH NINGTIYAS
04011182025029

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FAKULTAS KEDOKTERAN
UNIVERSITAS SRIWIJAYA
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HALAMAN PENGESAHAN

POLA SENSITIVITAS BAKTERI *PSEUDOMONAS AERUGINOSA* TERHADAP ANTIBIOTIK PADA PASIEN RAWAT INAP DI RSUP DR. MOHAMMAD HOESIN PALEMBANG PERIODE MEI 2022 – APRIL 2023

LAPORAN AKHIR SKRIPSI

Diajukan untuk memenuhi salah satu syarat memperoleh gelar
Sarjana Kedokteran di Universitas Sriwijaya

Oleh:

Salwa Adilah Ningtiyas
04011182025029

Palembang, 8 Desember 2023
Fakultas Kedokteran, Universitas Sriwijaya

Pembimbing I

dr. Rizki Andini Nawawi, M.Biomed. .....
NIP. 199312262022032012

Pembimbing II

Masayu Farah Diba, S.Si., M.Biomed. .....
NIP. 199406172019032020

Penguji I

dr. Erizka Rivani, M.Ked.Klin, Sp.MK. .....
NIP. 199112292015042001

Penguji II

dr. Rima Zanaria, M.Biomed. .....
NIP. 199009042015104201

Mengetahui,
Ketua Program Studi
Pendidikan Dokter

dr. Susilawati, M.Kes.
NIP. 197802272010122001

Wakil Dekan I

Dr. dr. Irfannuddin, Sp.KO., M.Pd.Ked.
NIP. 197306131999031001

HALAMAN PERSETUJUAN

Karya tulis ilmiah berupa Laporan Akhir Skripsi ini dengan judul "Pola Sensitivitas Bakteri *Pseudomonas aeruginosa* terhadap Antibiotik pada Pasien Rawat Inap di RSUP Dr. Mohammad Hoesin Palembang Periode Mei 2022 – April 2023" telah dipertahankan di hadapan Tim Penguji Karya Tulis Ilmiah Program Studi Pendidikan Dokter, Fakultas Kedokteran, Universitas Sriwijaya, pada tanggal 12 Desember 2023.

Palembang, 12 Desember 2023

Tim Penguji Karya Tulis Ilmiah berupa Laporan Akhir Skripsi

Pembimbing I

dr. Rizki Andini Nawawi, M.Biomed. .....
NIP. 199312262022032012

Pembimbing II

Masayu Farah Diba, S.Si., M.Biomed. .....
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Ketua Program Studi
Pendidikan Dokter

dr. Susilawati, M.Kes.
NIP. 197802272010122001

Wakil Dekan I

Dr. dr. Irfannuddin, Sp.KO., M.Pd.Ked.
NIP. 197306131999031001

HALAMAN PERNYATAAN INTEGRITAS

Yang bertanda tangan di bawah ini:

Nama	:	Salwa Adilah Ningtiyas
NIM	:	04011182025029
Judul	:	Pola Sensitivitas Bakteri *Pseudomonas aeruginosa* terhadap Antibiotik pada Pasien Rawat Inap di RSUP Dr. Mohammad Hoesin Palembang Periode Mei 2022 – April 2023

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Salwa Adilah Ningtiyas

ABSTRAK

POLA SENSITIVITAS BAKTERI *PSEUDOMONAS AERUGINOSA* TERHADAP ANTIBIOTIK PADA PASIEN RAWAT INAP DI RSUP DR. MOHAMMAD HOESIN PALEMBANG PERIODE MEI 2022 – APRIL 2023

(Salwa Adilah Ningtiyas, 8 Desember 2023, 127 halaman)
Fakultas Kedokteran, Universitas Sriwijaya

Latar Belakang: *Pseudomonas aeruginosa* adalah bakteri Gram-negatif yang menyebabkan infeksi oportunistik dan *healthcare-acquired infections*. Bakteri ini mampu mengembangkan resistensi antibiotik dengan cepat selama pengobatan. Resistensi *P. aeruginosa* terhadap antibiotik akan mempersulit pengobatan dan pemulihan pasien, serta meningkatkan morbiditas dan mortalitas akibat waktu rawat inap lama, perawatan rumit, dan biaya pengobatan tinggi.

Metode: Penelitian deskriptif observasional dengan desain studi *cross-sectional* menggunakan data dari Laboratorium Mikrobiologi Klinik dan Instalasi Rekam Medik RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023. Data dianalisis secara univariat dan disajikan dalam bentuk tabel, diagram, dan narasi deskriptif.

Hasil: *Pseudomonas aeruginosa* ditemukan menginfeksi 465 pasien rawat inap. Angka kematian pada pasien rawat inap sebanyak 26,7%. Pasien dewasa berusia 18–65 tahun mendominasi sebanyak 71%. Pasien mayoritas berjenis kelamin laki-laki sebanyak 51,2%. Spesimen pemeriksaan terbanyak menggunakan sputum sebanyak 40%. Diagnosis klinis paling sering ditemukan adalah infeksi luka operasi, *diabetic foot ulcer*, dan pneumonia. Pasien mayoritas berasal dari ruang non-ICU sebanyak 71%. Pasien sering ditemukan menjalani rawat inap selama 8–14 hari sebanyak 25,2%. Hasil uji sensitivitas menunjukkan hasil terbaik pada amikasin, dan terburuk pada sefazolin dan tigesiklin.

Kesimpulan: Pola sensitivitas *Pseudomonas aeruginosa* terhadap antibiotik menunjukkan bakteri paling sensitif terhadap amikasin (94,2%). Profil resistensi antibiotik pada pasien ditemukan Probable-PDR 0,9%, XDR 6,7%, MDR 24,7%, dan non-MDR 67,7%, serta DTR 2,4% dan non-DTR 97,6%.

Kata Kunci: *Pseudomonas aeruginosa*, Pasien rawat inap, Resistensi antibiotik

ABSTRACT

SENSITIVITY PATTERN OF *PSEUDOMONAS AERUGINOSA* BACTERIA AGAINST ANTIBIOTICS IN HOSPITALIZED PATIENTS AT RSUP DR. MOHAMMAD HOESIN PALEMBANG PERIOD OF MAY 2022 – APRIL 2023

(Salwa Adilah Ningtiyas, December 8th 2023, 127 pages)
Faculty of Medicine, Sriwijaya University

Background: *Pseudomonas aeruginosa* is a Gram-negative bacteria that causes opportunistic and healthcare-acquired infections. It is capable of rapidly developing antibiotic resistance during treatment. The resistance of *P. aeruginosa* to antibiotics will complicate the treatment and recovery of patients, as well as increase morbidity and mortality due to long hospitalization period, complicated treatment, and high medical costs.

Method: Descriptive observational research with a cross-sectional study design using data from the Clinical Microbiology Laboratory and Medical Records Installation of RSUP Dr. Mohammad Hoesin Palembang period of May 2022 – April 2023. The data were analyzed univariately and presented in the form of tables, diagrams, and descriptive narratives.

Results: *Pseudomonas aeruginosa* was found to infect 465 hospitalized patients. The mortality rate in hospitalized patients was 26,7%. Adult patients aged 18–65 years dominated as much as 71%. The majority of patients were male, 51,2%. Most examination specimens used sputum, as much as 40%. The most common clinical diagnoses were surgical wound infection, diabetic foot ulcer, and pneumonia. The majority of patients came from the non-ICU room, as much as 71%. Patients were often found to undergo hospitalization for 8–14 days, as much as 25,2%. The sensitivity test results showed the best results in amikacin, and the worst in cefazoline and tigecycline.

Conclusion: The sensitivity pattern of *Pseudomonas aeruginosa* to antibiotics showed that the bacteria were most sensitive to amikacin (94,2%). The antibiotic resistance profile in patients found Probable-PDR 0,9%, XDR 6,7%, MDR 24,7%, and non-MDR 67,7%, and DTR 2,4% and non-DTR 97,6%.

Keywords: *Pseudomonas aeruginosa,* Hospitalized patients, Antibiotic resistance

RINGKASAN

POLA SENSITIVITAS BAKTERI *PSEUDOMONAS AERUGINOSA* TERHADAP ANTIBIOTIK PADA PASIEN RAWAT INAP DI RSUP DR. MOHAMMAD HOESIN PALEMBANG PERIODE MEI 2022 – APRIL 2023
Karya tulis ilmiah berupa Skripsi, 8 Desember 2023

Salwa Adilah Ningtiyas, dibimbing oleh dr. Rizki Andini Nawawi, M.Biomed. dan Masayu Farah Diba, S.Si., M.Biomed.
Program Studi Pendidikan Dokter, Fakultas Kedokteran, Universitas Sriwijaya

xxiii + 127 halaman, 15 tabel, 23 gambar, 7 lampiran

Pseudomonas aeruginosa adalah bakteri Gram-negatif yang menyebabkan infeksi oportunistik dan *healthcare-acquired infections* pada pasien rawat inap. Bakteri ini mampu memproduksi faktor virulensi yang dapat mengkolonisasi, mempertahankan infeksi, meningkatkan dampak sitotoksik, meningkatkan kelangsungan hidup patogen, dan memodulasi mekanisme imun adaptif sel host. Hal ini menyebabkan *P. aeruginosa* mampu mengembangkan resistensi antibiotik dengan cepat selama pengobatan sehingga meningkatkan risiko kegagalan terapi. Resistensi *P. aeruginosa* terhadap antibiotik akan mempersulit pengobatan dan pemulihan pasien, serta meningkatkan morbiditas dan mortalitas akibat waktu rawat inap lama, perawatan rumit, dan biaya pengobatan tinggi.

Penelitian ini merupakan penelitian deskriptif observasional dengan desain studi *cross-sectional* menggunakan data dari Laboratorium Mikrobiologi Klinik dan Instalasi Rekam Medik RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023 dengan metode *total sampling*. Data dianalisis secara univariat dan disajikan dalam bentuk tabel, diagram, dan narasi deskriptif.

Pseudomonas aeruginosa ditemukan menginfeksi 999 pasien, meliputi 525 pasien rawat jalan dan 474 pasien rawat inap (465 sampel diinklusi dan 9 sampel dieksklusi). Angka kematian pada pasien rawat inap sebanyak 26,7%. Pasien dewasa berusia 18–65 tahun mendominasi sebanyak 71%. Pasien mayoritas berjenis kelamin laki-laki sebanyak 51,2%. Spesimen pemeriksaan terbanyak menggunakan sputum sebanyak 40%. Diagnosis klinis paling sering ditemukan adalah infeksi luka operasi, *diabetic foot ulcer*, dan pneumonia. Pasien mayoritas berasal dari ruang non-ICU sebanyak 71%. Pasien sering ditemukan menjalani rawat inap selama 8–14 hari sebanyak 25,2%. Hasil uji sensitivitas menunjukkan bakteri ini memiliki beragam tingkat sensitivitas terhadap antibiotik, yaitu amikasin (94,2%), gentamisin (86,5%), sefepim (81,7%), siprofloksasin (81,5%), piperasilin-

tazobaktam (78,5%), meropenem (76,6%), seftazidim (75,1%), aztreonam (62,2%), sefazolin (0%), dan tigesiklin (0%).

Oleh karena itu, dapat disimpulkan bahwa pola sensitivitas *Pseudomonas aeruginosa* terhadap antibiotik menunjukkan bakteri ini paling sensitif terhadap amikasin (94,2%) dan gentamisin (86,5%), serta paling resistan terhadap sefazolin (0%) dan tigesiklin (0%). Berdasarkan data tersebut, profil resistensi antibiotik diklasifikasikan berdasarkan jumlah dan golongan antibiotik yang resistan, dan ditemukan Probable-PDR 0,9%, XDR 6,7%, MDR 24,7%, dan non-MDR 67,7%, serta DTR 2,4% dan non-DTR 97,6%.

Kata Kunci: *Pseudomonas aeruginosa*, Pasien rawat inap, Resistensi antibiotik

SUMMARY

SENSITIVITY PATTERN OF *PSEUDOMONAS AERUGINOSA* BACTERIA AGAINST ANTIBIOTICS IN HOSPITALIZED PATIENTS AT RSUP DR. MOHAMMAD HOESIN PALEMBANG PERIOD OF MAY 2022 – APRIL 2023

Scientific paper in the form of Undergraduate Thesis, December 8th 2023

Salwa Adilah Ningtiyas, supervised by dr. Rizki Andini Nawawi, M.Biomed. and Masayu Farah Diba, S.Si., M.Biomed.
Medical Science Department, Faculty of Medicine, Sriwijaya University

xxiii + 127 pages, 15 tables, 23 pictures, 7 attachments

Pseudomonas aeruginosa is a Gram-negative bacteria that causes opportunistic and healthcare-acquired infections in hospitalized patients. This bacteria is capable of producing virulence factors that can colonize, maintain infection, increase cytotoxic impact, increase pathogen survival, and modulate host cell adaptive immune mechanisms. This causes *P. aeruginosa* to rapidly develop antibiotic resistance during treatment, increasing the risk of therapeutic failure. The resistance of *P. aeruginosa* to antibiotics will complicate the treatment and recovery of patients, and increase morbidity and mortality due to long hospitalization times, complicated treatment, and high medical costs.

This research is a descriptive observational study with a cross-sectional design using data from the Clinical Microbiology Laboratory and Medical Records Installation of RSUP Dr. Mohammad Hoesin Palembang period of May 2022 – April 2023 using the total sampling method. The data were analyzed univariately and presented in the form of tables, diagrams, and descriptive narratives.

Pseudomonas aeruginosa was found to infect 999 patients, including 525 out-patient patients and 474 hospitalized patients (465 samples were included and 9 samples were excluded). The mortality rate in hospitalized patients was 26.7%. Adult patients aged 18–65 years dominated as much as 71%. The majority of patients were male, 51.2%. Most examination specimens used sputum, as much as 40%. The most common clinical diagnoses were surgical wound infection, diabetic foot ulcer, and pneumonia. The majority of patients came from non-ICU rooms, as much as 71%. Patients were often found to undergo hospitalization for 8–14 days as much as 25.2%. The results of the sensitivity test showed that these bacteria had various levels of sensitivity to antibiotics, such as amikacin (94.2%), gentamicin (86.5%), cefepime (81.7%), ciprofloxacin (81.5%), piperacillin-tazobactam

(78.5%), meropenem (76.6%), ceftazidime (75.1%), aztreonam (62.2%), cefazoline (0%), and tigecycline (0%).

Therefore, it can be concluded that the sensitivity pattern of *Pseudomonas aeruginosa* to antibiotics shows that this bacteria is most sensitive to amikacin (94.2%) and gentamicin (86.5%), and most resistant to cefazoline (0%) and tigecycline (0%). Based on these data, the antibiotic resistance profile was classified based on the number and class of resistant antibiotics and found to be Probable-PDR 0,9%, XDR 6,7%, MDR 24,7%, and non-MDR 67,7%, and DTR 2,4% and non-DTR 97,6%.

Keywords: *Pseudomonas aeruginosa,* Hospitalized patients, Antibiotic resistance

KATA PENGANTAR

Puji dan syukur penulis panjatkan kehadirat Allah *subhanahu wa ta'ala*, Tuhan semesta alam yang telah melimpahkan rahmat dan pertolongan-Nya kepada penulis sehingga penulis dapat menyelesaikan skripsi yang berjudul "Pola Sensitivitas Bakteri *Pseudomonas aeruginosa* terhadap Antibiotik pada Pasien Rawat Inap di RSUP Dr. Mohammad Hoesin Palembang Periode Mei 2022 – April 2023" tepat pada waktu yang telah direncanakan sebelumnya.

Penulis menyadari bahwa penyelesaian skripsi ini tidak terlepas dari bantuan, bimbingan, serta dukungan dari berbagai pihak. Oleh karena itu, dengan kerendahan hati penulis mengucapkan terima kasih kepada pihak-pihak yang terlibat langsung maupun tidak langsung, terkhusus kepada:

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Penulis menyadari sepenuhnya bahwa masih banyak kekurangan dalam skripsi ini. Oleh karena itu, penulis mengharapkan kritik dan saran yang membangun demi perbaikan dan kesempurnaan di masa mendatang. Penulis berhadap skripsi ini dapat bermanfaat dan berguna dikemudian hari.

Palembang, 8 Desember 2023

Salwa Adilah Ningtiyas

HALAMAN PERNYATAAN PERSETUJUAN PUBLIKASI

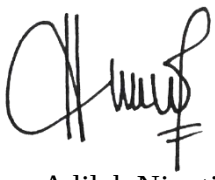
Yang bertanda tangan di bawah ini:

Nama	:	Salwa Adilah Ningtiyas
NIM	:	04011182025029
Judul	:	Pola Sensitivitas Bakteri *Pseudomonas aeruginosa* terhadap Antibiotik pada Pasien Rawat Inap di RSUP Dr. Mohammad Hoesin Palembang Periode Mei 2022 – April 2023

Memberikan izin kepada Pembimbing dan Universitas Sriwijaya untuk mempublikasikan hasil penelitian saya untuk kepentingan akademik apabila dalam waktu 1 (satu) tahun tidak mempublikasikan karya penelitian saya. Dalam kasus ini saya setuju untuk menempatkan Pembimbing sebagai penulis korespodensi (*Corresponding author*).

Demikian, pernyataan ini saya buat dalam keadaan sadar dan tanpa ada paksaan dari siapapun.

Palembang, 8 Desember 2023



Salwa Adilah Ningtiyas

DAFTAR ISI

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DAFTAR GAMBAR

Nomor **Judul** **Halaman**

DAFTAR LAMPIRAN

Nomor **Judul** **Halaman**

DAFTAR SINGKATAN

ASEAN	: *Association of Southeast Asian Nations*
AST	: *Antimicrobial Susceptibility Testing*
ATP	: *Adenosine Triphosphate*
CAIs	: *Community-Acquired Infections*
CAUTI	: *Catheter-Associated Urinary Tract Infection*
CDC	: *Centers for Disease Control and Prevention*
CFTR	: *Cystic Fibrosis Transmembrane Conductance Regulator*
CLSI	: *Clinical and Laboratory Standards Institute*
DNA	: *Deoxyribonucleic Acid*
DTR	: *Difficult-to-Treat*
DTR-PA	: *Difficult-to-Treat Pseudomonas aeruginosa*
GNB	: *Gram-Negative Bacteria*
HABP	: *Hospital-Acquired Bacterial Pneumonia*
HAIs	: *Healthcare-Acquired Infections*
HCW	: *Healthcare Workers*
ICU	: *Intensive Care Unit*
ITIS	: *Integrated Taxonomic Information System*
MAC	: *Membrane Attack Complex*
MDR	: *Multi-Drug Resistant*
MDR-PA	: *Multi-Drug Resistant Pseudomonas aeruginosa*
MDRO	: *Multidrug Resistant Organism*
MIC	: *Minimum Inhibitory Concentration*
OMV	: *Outer Membrane Vesicles*
PAMPs	: *P. aeruginosa Pathogen-associated Molecular Patterns*
PBP	: *Protein Binding Penicillin*
PDR	: *Pan-Drug Resistant*
PER	: *Pseudomonas Extended Resistant*
PPOK	: Penyakit Paru Obstruktif Kronis

QS	: *Quorum Sensing*
RNA	: *Ribonucleic Acid*
RND	: *Resistance-Nodulation-Division*
ROS	: *Reactive Oxygen Species*
RSUP	: Rumah Sakit Umum Pusat
SSP	: Sistem Saraf Pusat
T3SS	: *Type III Secretion System*
VABP	: *Ventilator-Associated Bacterial Pneumonia*
WHO	: *World Health Organization*
XDR	: *Extensively-Drug Resistant*

BAB 1
PENDAHULUAN

1.1 Latar Belakang

Pseudomonas aeruginosa (*P. aeruginosa*) adalah jenis bakteri Gram-negatif yang dapat mengakibatkan infeksi oportunistik pada manusia sehingga memicu berbagai infeksi akut maupun kronis yang mengancam jiwa, terutama pada pasien dengan imunitas lemah.[1,2] Bakteri ini berbentuk *bacillus* (berukuran 0,5 – 3,0 µm), dengan metabolisme aerob dan flagella tunggal yang membantu dalam pergerakan.[3] *P. aeruginosa* dianggap sebagai patogen utama dalam kelompok *Pseudomonas spp.* yang paling sering diisolasi di laboratorium klinis sebagai penyebab penyakit. Bakteri ini tersebar lebih luas di alam dan umumnya ditemukan pada lingkungan lembab di rumah sakit. *P. aeruginosa* mampu mengkolonisasi berbagai bagian tubuh (seperti kulit, selaput lendir, saluran pernapasan, dan saluran perncernaan).[4] Bakteri ini dapat ditemukan di berbagai kondisi kehidupan karena kemampuannya yang sangat fleksibel dalam beradaptasi dan bertahan hidup pada lingkungannya.[5]

Pseudomonas aeruginosa merupakan salah satu penyebab utama *healthcare-acquired infections* (HAIs) yang setiap tahunnya menginfeksi lebih dari 2 juta pasien dan menyebabkan sekitar 90.000 kematian di seluruh dunia.[6] Prevalensi HAIs akibat *P. aeruginosa* mencapai 10% – 15% dan sekitar 10% – 20% berada di unit perawatan intensif (ICU).[7] Strain pada bakteri ini mengakibatkan peningkatan morbiditas dan mortalitas yang sangat signifikan.[3] Menurut *U.S. Centers for Disease Control and Prevention* (CDC), setiap tahunnya terdapat 51.000 kasus infeksi akibat *P. aeruginosa* di fasilitas layanan kesehatan di Amerika Serikat.[8] Bahkan, pasien yang mengalami *multidrug resistance* (MDR) terkait infeksi ini mencapai 13%, dengan angka kematian sebesar 400 jiwa per tahun.[9] Selain itu, berdasarkan penelitian yang dilakukan di RSUP Dr. Mohammad Hoesin Palembang pada tahun 2020, prevalensi *P. aeruginosa* yang mengalami MDR mencapai 34,6%.[10] MDR ini timbul sebagai akibat dari penggunaan antibiotik yang tidak rasional, terputus, terlalu sering, jumlahnya berlebihan, dan dalam jangka waktu lama.[11]

Pseudomonas aeruginosa mampu memproduksi suatu enzim yang disebut *extended spectrum β-lactamase* (ESBL) yang mampu menyebabkan resistensi atau menghidrolisis antibiotik golongan β-laktam dengan cara memutus cincin amida pada cincin beta-laktam sehingga antibiotik menjadi tidak aktif.[12] Bakteri ini juga mampu mengembangkan resistensi antibiotik baru dengan cepat selama pengobatan sehingga meningkatkan risiko kegagalan terapi.[3] *P. aeruginosa* penghasil ESBL ini memproduksi faktor virulensi yang dapat mengkolonisasi dan mempertahankan infeksi pada individu yang mengalami penurunan imunitas, meningkatkan dampak sitotoksik patogen pada jaringan host, meningkatkan kelangsungan hidup patogen, dan memodulasi mekanisme imun adaptif manusia.[1,13] Hal ini dikarenakan *P. aeruginosa* mampu membentuk komunitas yang kebal terhadap antibiotik dan melekat pada permukaan yang dikelilingi oleh matriks polimer yang dikenal sebagai biofilm atau mikrokoloni.[13] Biofilm ini mampu melindungi *P. aeruginosa* dari tekanan lingkungan sekitar dan menghambat fagositosis, yang kemudian memberikan kapasitas untuk melakukan kolonisasi dan persistensi jangka panjang.[14] Selain itu, *P. aeruginosa* memiliki plastisitas genetik yang sangat besar dari patogen bakteri, yang memicu respons spesifik terhadap adaptasi mutasi, perolehan materi genetik, atau perubahan ekspresi gen, yang mengakibatkan resistensi terhadap hampir semua antibiotik dalam praktik klinis.[15]

World Health Organization (WHO), pada tahun 2017, mengklasifikasikan *Pseudomonas aeruginosa* sebagai salah satu bakteri paling berbahaya bagi kesehatan manusia dan termasuk sebagai patogen prioritas untuk penelitian dan pengembangan antibiotik baru.[16] Saat ini, terapi kombinasi antara dua atau lebih antibiotik dari kelas yang berbeda untuk mengatasi infeksi *P. aeruginosa* sangat diragukan karena data menunjukkan kemungkinan efek samping dan resistensi dari kombinasi obat.[17] Resistensi terhadap beberapa kelas antibiotik seringkali dimediasi oleh mekanisme atau regulator yang sama (MexAB, AmpR), yang meningkatkan kemungkinan resistensi silang terhadap antibiotik.[18] Selain itu, bakteri ini memiliki kemampuan yang tinggi dalam memanfaatkan substrat yang berbeda, serta kecenderungan terhadap resistensi antibiotik karena kemampuan adaptasinya yang sangat signifikan.[19]

Pasien terinfeksi *Pseudomonas aeruginosa* umumnya memiliki luaran klinis yang lebih buruk dibandingkan dengan patogen lainnya.[20] Sebuah analisis komprehensif yang diterbitkan pada tahun 2015, meliputi 21 studi kohort, menemukan bahwa *P. aeruginosa* dikaitkan dengan peningkatan risiko peradangan, peningkatan risiko kematian sebesar tiga kali lipat, dan penurunan kualitas hidup pasien. Infeksi *P. aeruginosa* menjadi semakin sulit diobati karena bakteri ini secara alami resistan terhadap berbagai antibiotik, serta jumlah strain yang resistan terhadap berbagai obat dan *pan-drug* meningkat secara global.[13,18] Strain pada bakteri ini diketahui telah resistan terhadap hampir semua kelas antibiotik yang umum digunakan, seperti aminoglikosida, sefalosporin, fluorokuinolon, dan salah satu yang paling banyak dibahas saat ini adalah resistensi terhadap karbapenem.[1] Berdasarkan data Surveilans Resistensi Antibiotik Rumah Sakit di Indonesia tahun 2021 oleh Perhimpunan Dokter Spesialis Mikrobiologi Klinik Indonesia (PAMKI), dari total 3.778 isolat *P. aeruginosa*, sebanyak 1.840 isolat sensitif terhadap karbapenem (48,8%) dan 1.938 resistan terhadap karbapenem (51,2%), dengan spesifikasi 9,8% pada pasien rawat jalan dan 90,2% pada pasien rawat inap.[21] Resistensi *P. aeruginosa* terhadap antibiotik ini tentunya mempersulit pengobatan dan pemulihan pasien, yang dapat meningkatkan morbiditas dan mortalitas akibat waktu rawat inap yang lama, perawatan yang rumit, dan biaya pengobatan yang tinggi.

Data mengenai pola sensitivitas bakteri *Pseudomonas aeruginosa* memerlukan data lokal teraktual, khususnya di Kota Palembang. Oleh karena itu, penelitian ini penting dilakukan untuk mengetahui lebih lanjut mengenai pola sensitivitas *P. aeruginosa* terhadap antibiotik guna mengetahui antibiotik apa yang sensitif dan resistan terhadap bakteri *P. aeruginosa* sehingga dapat menjadi bahan evaluasi terapi selanjutnya dan panduan dalam menentukan strategi pencegahan dan pengobatan yang tepat dan efektif, serta dapat menurunkan morbiditas dan mortalitas pasien rawat inap di RSUP Dr. Mohammad Hoesin Palembang.

1.2 Rumusan Masalah

1. Bagaimana profil demografi dan klinis pasien rawat inap yang terinfeksi bakteri *Pseudomonas aeruginosa* di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023?
2. Bagaimana gambaran pola sensitivitas bakteri *Pseudomonas aeruginosa* terhadap antibiotik pada pasien rawat inap di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023?

1.3 Tujuan Penelitian

1.3.1 Tujuan Umum

1. Mengetahui profil demografi dan klinis pasien rawat inap yang terinfeksi bakteri *Pseudomonas aeruginosa* di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023.
2. Mengetahui gambaran pola sensitivitas bakteri *Pseudomonas aeruginosa* terhadap antibiotik pada pasien rawat inap di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023.

1.3.2 Tujuan Khusus

1. Mengetahui angka kejadian infeksi bakteri *Pseudomonas aeruginosa* di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023.
2. Mengetahui angka kematian pada pasien rawat inap yang terinfeksi bakteri *Pseudomonas aeruginosa* di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023.
3. Mengetahui distribusi usia pada pasien rawat inap yang terinfeksi bakteri *Pseudomonas aeruginosa* di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023.
4. Mengetahui distribusi jenis kelamin pada pasien rawat inap yang terinfeksi bakteri *Pseudomonas aeruginosa* di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023.

5. Mengetahui distribusi jenis spesimen pada pasien rawat inap yang terinfeksi bakteri *Pseudomonas aeruginosa* di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023.
6. Mengetahui distribusi diagnosis klinis pada pasien rawat inap yang terinfeksi bakteri *Pseudomonas aeruginosa* di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023.
7. Mengetahui distribusi ruang perawatan pada pasien rawat inap yang terinfeksi bakteri *Pseudomonas aeruginosa* di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023.
8. Mengetahui distribusi lama rawat inap pada pasien rawat inap yang terinfeksi bakteri *Pseudomonas aeruginosa* di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023.
9. Mengetahui gambaran pola sensitivitas bakteri *Pseudomonas aeruginosa* terhadap antibiotik pada pasien rawat inap di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023.
10. Mengetahui profil resistensi antibiotik pada pasien rawat inap terinfeksi bakteri *Pseudomonas aeruginosa* di RSUP Dr. Mohammad Hoesin Palembang periode Mei 2022 – April 2023.

1.4 Manfaat Penelitian

1.4.1 Manfaat Teoritis

1. Penelitian ini diharapkan dapat berkontribusi memberikan teori dan referensi ilmiah mengenai infeksi bakteri *Pseudomonas aeruginosa* pada pasien rawat inap di RSUP Dr. Mohammad Hoesin Palembang.
2. Penelitian ini diharapkan dapat menjadi landasan ilmiah untuk penelitian selanjutnya mengenai efektivitas pemberian antibiotik pada pasien rawat inap yang terinfeksi bakteri *Pseudomonas aeruginosa* di RSUP Dr. Mohammad Hoesin Palembang.

1.4.2 Manfaat Kebijakan/Tatalaksana

1. Penelitian ini diharapkan dapat memberikan informasi ilmiah kepada tenaga medis mengenai pola sensitivitas bakteri *Pseudomonas aeruginosa* terhadap antibiotik, sehingga dapat menjadi bahan evaluasi terapi selanjutnya bagi pasien rawat inap di RSUP Dr. Mohammad Hoesin Palembang.
2. Penelitian ini diharapkan dapat menjadi panduan dalam menentukan strategi pencegahan dan pengobatan infeksi bakteri *Pseudomonas aeruginosa* yang tepat dan efektif sehingga dapat menurunkan morbiditas dan mortalitas pada pasien rawat inap di RSUP Dr. Mohammad Hoesin Palembang.

1.4.3 Manfaat Pasien/Masyarakat

1. Penelitian ini diharapkan dapat meningkatkan kesadaran pasien yang terinfeksi bakteri *Pseudomonas aeruginosa* dalam mematuhi dan menuntaskan pengobatan dengan antibiotik untuk menghindari risiko terjadinya resistensi antibiotik sehingga meningkatkan potensi kesembuhan pasien rawat inap di RSUP Dr. Mohammad Hoesin Palembang.
2. Penelitian ini diharapkan dapat meningkatkan kesadaran masyarakat agar lebih waspada dalam menjaga kebersihan diri dan lingkungan, guna mencegah infeksi bakteri *Pseudomonas aeruginosa*.

DAFTAR PUSTAKA

1. Moradali MF, Ghods S, Rehm BHA. Pseudomonas aeruginosa Lifestyle: A Paradigm for Adaptation, Survival, and Persistence [Internet]. Vol. 7, Frontiers in Cellular and Infection Microbiology. Gainesville: University of Florida; 2017. p. 39. Available from: https://doi.org/10.3389/fcimb.2017.00039
2. Rezzoagli C, Granato ET, Kümmerli R. Harnessing Bacterial Interactions to Manage Infections: A Review on the Opportunistic Pathogen Pseudomonas aeruginosa as A Case Example [Internet]. Vol. 69, Journal of Medical Microbiology. Oxford: Microbiology Society; 2020. p. 147–61. Available from: https://doi.org/10.1099/jmm.0.001134
3. de Sousa T, Hébraud M, Enes Dapkevicius MLN, Maltez L, Pereira JE, Capita R, et al. Genomic and Metabolic Characteristics of the Pathogenicity in Pseudomonas aeruginosa [Internet]. Vol. 22, International Journal of Molecular Sciences. Basel: MDPI; 2021. p. 12892. Available from: https://doi.org/10.3390/ijms222312892
4. Riedel S, Hobden JA, Miller S, Morse SA, Mietzner TA, Detrick B, et al. Jawetz, Melnick, & Adelberg's Medical Microbiology. 28th ed. New York: McGraw-Hill Education; 2019.
5. Sauvage S, Hardouin J. Exoproteomics for Better Understanding Pseudomonas aeruginosa Virulence [Internet]. Vol. 12, Toxins. Mont-Saint-Aignan: MDPI; 2020. p. 571. Available from: https://doi.org/10.3390/toxins12090571
6. Mulcahy LR, Isabella VM, Lewis K. Pseudomonas aeruginosa Biofilms in Disease. Microb Ecol [Internet]. 2014;68(1):1–12. Available from: https://dx.doi.org/10.1007/s00248-013-0297-x
7. Wisdom Nzubechukwu Obiefu, Nnaemeka Jireh Okolie, Chizaram Winners Ndubueze, Joy Nkeiruka Dike-Ndudim. Antibacterial Effect of Chromolaena odorata (Awolowo Leaf) Aqueous Leaf Extract on Pseudomonas aeruginosa Induced Gastrointestinal Tract Infection in Adult Wistar Rat. GSC Biol Pharm Sci [Internet]. 2021 Jan 30;14(1):055–64. Available from: https://doi.org/10.30574/gscbps.2021.14.1.0006
8. CDC. Antibiotic Resistance Threats in the United States. U.S. Centers for Disease Control and Prevention. Atlanta; 2013.
9. Pires DP, Vilas Boas D, Sillankorva S, Azeredo J. Phage Therapy: A Step Forward in the Treatment of Pseudomonas aeruginosa Infections. J Virol [Internet]. 2015 Aug;89(15):7449–56. Available from: https://dx.doi.org/10.1128/jvi.00385-15
10. Sutrisno VS. Prevalensi dan Pola Sensitivitas Basil Gram-Negatif Multidrug Resistant (MDR) di RSUP Dr. Mohammad Hoesin Palembang. Palembang; 2020.
11. Pratiwi RH. Mekanisme Pertahanan Bakteri Patogen terhadap Antibiotik. J Pro Life [Internet]. 2017;4(3):418–29. Available from:

https://doi.org/10.33541/jpvol6Iss2pp102
12. Laudy AE, Róg P, Smolinska-Król K, Ćmiel M, Søoczynska A, Patzer J, et al. Prevalence of ESBL-Producing Pseudomonas aeruginosa Isolates in Warsaw, Poland, Detected by Various Phenotypic and Genotypic Methods. PLoS One [Internet]. 2017 Jun 1;12(6):1–15. Available from: https://dx.doi.org/10.1371/journal.pone.0180121
13. Palmer GC, Whiteley M. Metabolism and Pathogenicity of Pseudomonas aeruginosa Infections in the Lungs of Individuals with Cystic Fibrosis. Microbiol Spectr [Internet]. 2015 Jul 2;3(4):1–20. Available from: http://dx.doi.org/10.1128/microbiolspec.MBP-0003-2014
14. Žiemytė M, Carda-Diéguez M, Rodríguez-Díaz JC, Ventero MP, Mira A, Ferrer MD. Real-Time Monitoring of Pseudomonas aeruginosa Biofilm Growth Dynamics and Persister Cells' Eradication. Emerg Microbes Infect [Internet]. 2021;10(1):2062–75. Available from: https://dx.doi.org/10.1080/22221751.2021.1994355
15. Rumbaugh KP. Genomic Complexity and Plasticity Ensure Pseudomonas Success [Internet]. Vol. 356, FEMS Microbiology Letters. Lubbock: Blackwell Publishing Ltd; 2014. p. 141–3. Available from: https://dx.doi.org/10.1111/1574-6968.12517
16. Thi MTT, Wibowo D, Rehm BHA. Pseudomonas aeruginosa Biofilms [Internet]. Vol. 21, International Journal of Molecular Sciences. Nathan: Griffith University; 2020. p. 1–25. Available from: https://doi.org/10.3390/ijms21228671
17. Miyoshi-Akiyama T, Tada T, Ohmagari N, Viet Hung N, Tharavichitkul P, Pokhrel BM, et al. Emergence and Spread of Epidemic Multidrug-Resistant Pseudomonas aeruginosa. Genome Biol Evol [Internet]. 2017 Dec 1;9(12):3238–45. Available from: https://dx.doi.org/10.1093/gbe/evx243
18. Balasubramanian D, Kumari H, Mathee K. Pseudomonas aeruginosa AmpR: An Acute-Chronic Switch Regulator [Internet]. Vol. 73, Pathogens and Disease. Oxford: Oxford University Press; 2014. p. 12208. Available from: https://doi.org/10.1111/2049-632X.12208
19. Mielko KA, Jabłoński SJ, Milczewska J, Sands D, Łukaszewicz M, Młynarz P. Metabolomic Studies of Pseudomonas aeruginosa [Internet]. Vol. 35, World Journal of Microbiology and Biotechnology. Wrocław: Politechnika Wrocławska; 2019. p. 178. Available from: https://doi.org/10.1007/s11274-019-2739-1
20. Chai YH, Xu JF. How Does Pseudomonas aeruginosa Affect the Progression of Bronchiectasis? [Internet]. Vol. 26, Clinical Microbiology and Infection. Shanghai: Elsevier B.V.; 2020. p. 313–8. Available from: https://dx.doi.org/10.1016/j.cmi.2019.07.010
21. Kuntaman, Karuniawati A, Gunardi W, Anggaini D, Santosaningsih D, Saptawati L, et al. Surveilans Resistansi Antibiotik Rumah Sakit di Indonesia Tahun 2021 [Internet]. Jakarta: Perhimpunan Dokter Spesialis Mikrobiologi Klinik Indonesia (PAMKI); 2022. Available from: https://pamki.or.id/unduhan-download/
22. Integrated Taxonomic Information System (ITIS). Pseudomonas aeruginosa

Taxonomy [Internet]. International Journal of Systematic and Evolutionary Microbiology (IJSEM). 2023 [cited 2023 Jun 25]. Available from: https://www.itis.gov/servlet/SingleRpt/SingleRpt?search_topic=TSN&search_value=965278#null
23. Batra S. Morphology and Culture Characteristics of Pseudomonas aeruginosa (P. aeruginosa). Paramedics World; 2018.
24. Killough M, Rodgers AM, Ingram RJ. Pseudomonas aeruginosa: Recent Advances in Vaccine Development [Internet]. Vol. 10, Vaccines. 2022. Available from: https://doi.org/10.3390/vaccines10071100
25. Avinash MG, Aishwarya S, Zameer F, Gopal S. Pseudomonas aeruginosa Biofilm and Their Molecular Escape Strategies. J Appl Biol Biotechnol [Internet]. 2023;11(3):28–37. Available from: http://dx.doi.org/10.7324/JABB.2023.36700
26. Halebeedu PP, Kumar GSV, Gopal S. Revamping the Role of Biofilm Regulating Operons in Device-Associated Staphylococci and Pseudomonas aeruginosa. Indian J Med Microbiol [Internet]. 2014;32(2):112–23. Available from: https://doi.org/10.4103/0255-0857.129766
27. Avinash MG, Zameer F, Gopal S. The Propensity of Selected Indian Plant Extracts for Polyphenolics, Antioxidant, and Inhibition of Pseudomonas aeruginosa Biofilms through Type-3 Secretion System. J Appl Biol Biotechnol [Internet]. 2022;10(3):87–96. Available from: https://doi.org/10.7324/JABB.2022.100312
28. Ashwini P, Mn S, Shilpa U V, Mamatha P, Manasa P, Bl D, et al. A Review on Helicobacter pylori: Its Biology, Complications, and Management. Int J Pharm Pharm Sci. 2015;7:14–20.
29. Abrusci P, McDowell MA, Lea SM, Johnson S. Building a Secreting Nanomachine: A Structural Overview of the T3SS. Curr Opin Struct Biol [Internet]. 2014 Apr;25(100):111–7. Available from: https://doi.org/10.1016/j.sbi.2013.11.001
30. Green ER, Mecsas J. Bacterial Secretion Systems: An Overview. Microbiol Spectr [Internet]. 2016 Feb;4(1). Available from: https://doi.org/10.1128/microbiolspec.VMBF-0012-2015
31. Prasad A, Devi AT, Prasad MNN, Zameer F, Shruthi G, Shivamallu C. Phyto Anti-Biofilm Elicitors as Potential Inhibitors of Helicobacter pylori. 3 Biotech [Internet]. 2019 Feb;9(2):53. Available from: https://doi.org/10.1007/s13205-019-1582-2
32. Zameer F, Ms R, Chauhan JB, Khanum SA, Kumar P, Devi AT, et al. Evaluation of Adhesive and Anti-Adhesive Properties of Pseudomonas aeruginosa Biofilms and Their Inhibition by Herbal Plants. Iran J Microbiol. 2016 Apr;8(2):108–19.
33. Onsare J, Arora DS. Antibiofilm Potential of Flavonoids Extracted from Moringa oleifera Seed Coat Against Staphylococcus aureus, Pseudomonas aeruginosa and Candida albicans. J Appl Microbiol [Internet]. 2014 Nov 1;118. Available from: https://doi.org/10.1111/jam.12701
34. Jennings LK, Storek KM, Ledvina HE, Coulon C, Marmont LS, Sadovskaya I, et al. Pel is A Cationic Exopolysaccharide that Cross-Links Extracellular

DNA in the Pseudomonas aeruginosa Biofilm Matrix. Proc Natl Acad Sci U S A [Internet]. 2015 Sep;112(36):11353–8. Available from: https://doi.org/10.1073/pnas.1503058112

35. Deveaux W, Selvarajoo K. Searching for Simple Rules in Pseudomonas aeruginosa Biofilm Formation. BMC Res Notes [Internet]. 2019;12(1):763. Available from: https://doi.org/10.1186/s13104-019-4795-x
36. Monegro AF, Muppidi V, Regunath H. Hospital-Acquired Infections. StatPearls [Internet]. 2023; Available from: http://www.ncbi.nlm.nih.gov/books/nbk441857/
37. Xia J, Gao J, Tang W. Nosocomial Infection and Its Molecular Mechanisms of Antibiotic Resistance. Biosci Trends [Internet]. 2016;10(1):14–21. Available from: https://doi.org/10.5582/bst.2016.01020
38. Haque M, Sartelli M, McKimm J, Bakar MA. Healthcare-Associated Infections – An Overview [Internet]. Vol. 11, Infection and Drug Resistance. Kuala Lumpur: Dove Medical Press Ltd.; 2018. p. 2321–33. Available from: https://dx.doi.org/10.2147/IDR.S177247
39. Voidazan S, Albu S, Toth R, Grigorescu B, Rachita A, Moldovan I. Healthcare Associated Infections — A New Pathology in Medical Practice? Int J Environ Res Public Health [Internet]. 2020 Feb 1;17(3):1–13. Available from: https://dx.doi.org/10.3390/ijerph17030760
40. Valentini M, Gonzalez D, Mavridou DA, Filloux A. Lifestyle Transitions and Adaptive Pathogenesis of Pseudomonas aeruginosa [Internet]. Vol. 41, Current Opinion in Microbiology. Lausanne: Elsevier Ltd; 2018. p. 15–20. Available from: https://dx.doi.org/10.1016/j.mib.2017.11.006
41. Fujii A, Seki M, Higashiguchi M, Tachibana I, Kumanogoh A, Tomono K. Community-Acquired, Hospital-Acquired, and Healthcare-Associated Pneumonia Caused by Pseudomonas aeruginosa. Respir Med Case Reports [Internet]. 2014 Jan 1;12:30–3. Available from: https://doi.org/10.1016/j.rmcr.2014.03.002
42. Destoumieux-Garzón D, Mavingui P, Boetsch G, Boissier J, Darriet F, Duboz P, et al. The One Health Concept: 10 Years Old and A Long Road Ahead. Front Vet Sci [Internet]. 2018;5. Available from: https://doi.org/10.3389/fvets.2018.00014
43. Okello AL, Bardosh K, Smith J, Welburn SC. One Health: Past Successes and Future Challenges in Three African Contexts. PLoS Negl Trop Dis [Internet]. 2014 May 22;8(5):e2884. Available from: https://doi.org/10.1371/journal.pntd.0002884
44. Dulon M, Peters C, Schablon A, Nienhaus A. MRSA Carriage Aamong Healthcare wWorkers in Non-Outbreak Settings in Europe and the United States: A Systematic Review. BMC Infect Dis [Internet]. 2014;14(1):363. Available from: https://doi.org/10.1186/1471-2334-14-363
45. Patel PK, Mantey J, Mody L. Patient Hand Colonization With MDROs Is Associated with Environmental Contamination in Post-Acute Care. Infect Control Hosp Epidemiol [Internet]. 2017/07/11. 2017;38(9):1110–3. Available from: https://doi.org/10.1017/ice.2017.133
46. Otto M. Coagulase-Negative Staphylococci as Reservoirs of Genes

Facilitating MRSA Infection: Staphylococcal Commensal Species such as Staphylococcus epidermidis are being Recognized as Important Sources of Genes Promoting MRSA Colonization and Virulence. BioEssays [Internet]. 2013;35(1):4–11. Available from: https://doi.org/10.1002/bies.201200112
47. Lax S, Gilbert JA. Hospital-Associated Microbiota and Implications for Nosocomial Infections. Trends Mol Med [Internet]. 2015 Jul 1;21(7):427–32. Available from: https://doi.org/10.1016/j.molmed.2015.03.005
48. Christoff AP, Sereia AFR, Hernandes C, de Oliveira LF V. Uncovering the Hidden Microbiota in Hospital and Built Environments: New Approaches and Solutions. Exp Biol Med [Internet]. 2019 Jan 7;244(6):534–42. Available from: https://doi.org/10.1177/1535370218821857
49. Brooks B, Firek BA, Miller CS, Sharon I, Thomas BC, Baker R, et al. Microbes in the Neonatal Intensive Care Unit Resemble Those Found in the Gut of Premature Infants. Microbiome [Internet]. 2014;2(1):1. Available from: https://doi.org/10.1186/2049-2618-2-1
50. Chen LF, Knelson LP, Gergen MF, Better OM, Nicholson BP, Woods CW, et al. A Prospective sStudy of Transmission of Multidrug-Resistant Organisms (MDROs) Between Environmental Sites and Hospitalized Patients. Infect Control Hosp Epidemiol [Internet]. 2018/11/14. 2019;40(1):47–52. Available from: https://doi.org/10.1017/ice.2018.275
51. D'Agata EMC, Horn MA, Ruan S, Webb GF, Wares JR. Efficacy of Infection Control Interventions in Reducing the Spread of Multidrug-Resistant Organisms in the Hospital Setting. PLoS One [Internet]. 2012 Feb 20;7(2):e30170. Available from: https://doi.org/10.1371/journal.pone.0030170
52. Weber DJ, Rutala WA, Miller MB, Huslage K, Sickbert-Bennett E. Role of Hospital Surfaces in the Transmission of Emerging Healthcare-Associated Pathogens: Norovirus, Clostridium difficile, and Acinetobacter species. Am J Infect Control [Internet]. 2010 Jun 1;38(5):S25–33. Available from: https://doi.org/10.1016/j.ajic.2010.04.196
53. Dalton KR, Rock C, Carroll KC, Davis MF. One Health in Hospitals: How Understanding the Dynamics of People, Animals, and the Hospital Built-Environment Can be used to Better Inform Interventions for Antimicrobial-Resistant Gram-Positive Infections. Antimicrob Resist Infect Control [Internet]. 2020;9(1):78. Available from: https://doi.org/10.1186/s13756-020-00737-2
54. Bucior I, Pielage JF, Engel JN. Pseudomonas aeruginosa Pili and Flagella Mediate Distinct Binding and Signaling Events at the Apical and Basolateral Surface of Airway Epithelium. PLOS Pathog [Internet]. 2012 Apr 5;8(4):e1002616. Available from: https://doi.org/10.1371/journal.ppat.1002616
55. Golovkine G, Faudry E, Bouillot S, Elsen S, Attrée I, Huber P. Pseudomonas aeruginosa Transmigrates at Epithelial Cell-Cell Junctions, Exploiting Sites of Cell Division and Senescent Cell Extrusion. PLOS Pathog [Internet]. 2016 Jan 4;12(1). Available from: https://doi.org/10.1371/journal.ppat.1005377
56. Rangel SM, Diaz MH, Knoten CA, Zhang A, Hauser AR. The Role of ExoS

in Dissemination of Pseudomonas aeruginosa during Pneumonia. PLOS Pathog [Internet]. 2015 Jun 19;11(6). Available from: https://doi.org/10.1371/journal.ppat.1004945

57. Lee J, Zhang L. The Hierarchy Quorum Sensing Network in Pseudomonas aeruginosa. Protein Cell [Internet]. 2015 Jan 1;6(1):26–41. Available from: https://doi.org/10.1007/s13238-014-0100-x
58. Curran CS, Bolig T, Torabi-Parizi P. Mechanisms and Targeted Therapies for Pseudomonas aeruginosa Lung Infection. Am J Respir Crit Care Med [Internet]. 2018 Mar;197(6):708–27. Available from: https://dx.doi.org/10.1164/rccm.201705-1043SO
59. Deshpande R, Zou C. Pseudomonas Aeruginosa Induced Cell Death in Acute Lung Injury and Acute Respiratory Distress Syndrome. Int J Mol Sci [Internet]. 2020 Jul;21(15). Available from: https://dx.doi.org/10.3390/ijms21155356
60. Song D, Meng J, Cheng J, Fan Z, Chen P, Ruan H, et al. Pseudomonas aeruginosa Quorum-Sensing Metabolite Induces Host Immune Cell Death Through Cell Surface Lipid Domain Dissolution. Nat Microbiol [Internet]. 2019;4(1):97–111. Available from: https://doi.org/10.1038/s41564-018-0290-8
61. Losa D, Köhler T, Bellec J, Dudez T, Crespin S, Bacchetta M, et al. Pseudomonas aeruginosa–Induced Apoptosis in Airway Epithelial Cells Is Mediated by Gap Junctional Communication in a JNK-Dependent Manner. J Immunol [Internet]. 2014 May 15;192(10):4804–12. Available from: https://doi.org/10.4049/jimmunol.1301294
62. Maurice NM, Bedi B, Yuan Z, Goldberg JB, Koval M, Hart CM, et al. Pseudomonas aeruginosa Induced Host Epithelial Cell Mitochondrial Dysfunction. Sci Rep [Internet]. 2019;9(1):11929. Available from: https://doi.org/10.1038/s41598-019-47457-1
63. Wood S, Goldufsky J, Shafikhani SH. Pseudomonas aeruginosa ExoT Induces Atypical Anoikis Apoptosis in Target Host Cells by Transforming Crk Adaptor Protein into A Cytotoxin. PLOS Pathog [Internet]. 2015 Jul 23;11(5):e1004934. Available from: https://app.dimensions.ai/details/publication/pub.1038381855
64. Wood SJ, Goldufsky JW, Bello D, Masood S, Shafikhani SH. Pseudomonas aeruginosa ExoT Induces Mitochondrial Apoptosis in Target Host Cells in A Manner That Depends on Its GTPase-Activating Protein (GAP) Domain Activity *. J Biol Chem [Internet]. 2015 Nov 27;290(48):29063–73. Available from: https://doi.org/10.1074/jbc.M115.689950
65. Ryu JC, Kim MJ, Kwon Y, Oh JH, Yoon SS, Shin SJ, et al. Neutrophil Pyroptosis Mediates Pathology of P. aeruginosa Lung Infection in the Absence of the NADPH Oxidase NOX2. Mucosal Immunol [Internet]. 2017 May 1;10(3):757–74. Available from: https://doi.org/10.1038/mi.2016.73
66. Pylaeva E, Lang S, Jablonska J. The Essential Role of Type I Interferons in Differentiation and Activation of Tumor-Associated Neutrophils. Front Immunol [Internet]. 2016;7. Available from: https://www.frontiersin.org/articles/10.3389/fimmu.2016.00629

67. Pylaeva E, Bordbari S, Spyra I, Decker AS, Häussler S, Vybornov V, et al. Detrimental Effect of Type I IFNs During Acute Lung Infection With Pseudomonas aeruginosa is Mediated Through the Stimulation of Neutrophil NETosis. Front Immunol [Internet]. 2019;10. Available from: https://www.frontiersin.org/articles/10.3389/fimmu.2019.02190
68. Dar HH, Tyurina YY, Mikulska-Ruminska K, Shrivastava I, Ting HC, Tyurin VA, et al. Pseudomonas aeruginosa Utilizes Host Polyunsaturated Phosphatidylethanolamines to Trigger Theft-Ferroptosis in Bronchial Epithelium. J Clin Invest [Internet]. 2019;128(10):4639–53. Available from: https://doi.org/10.1172/JCI99490
69. Raman G, Avendano EE, Chan J, Merchant S, Puzniak L. Risk Factors for Hospitalized Patients with Resistant or Multidrug-Resistant Pseudomonas aeruginosa Infections: A Systematic Review and Meta-Analysis. Antimicrob Resist Infect Control [Internet]. 2018;7(1):1–14. Available from: https://doi.org/10.1186/s13756-018-0370-9
70. Coates M, Blanchard S, MacLeod AS. Innate Antimicrobial Immunity in the Skin: A Protective Barrier Against Bacteria, Viruses, and Fungi. PLOS Pathog [Internet]. 2018 Dec 6;14(12). Available from: https://doi.org/10.1371/journal.ppat.1007353
71. Elmassry MM, Mudaliar NS, Colmer-Hamood JA, San Francisco MJ, Griswold JA, Dissanaike S, et al. New Markers for Sepsis caused by Pseudomonas aeruginosa during Burn Infection. Metabolomics [Internet]. 2020;16(3):40. Available from: https://doi.org/10.1007/s11306-020-01658-2
72. Weintrob AC, Murray CK, Xu J, Krauss M, Bradley W, Warkentien TE, et al. Early Infections Complicating the Care of Combat Casualties from Iraq and Afghanistan. Surg Infect (Larchmt) [Internet]. 2018 Jan 19;19(3):286–97. Available from: ttps://doi.org/10.1089/sur.2017.240
73. Kollef MH, Chastre J, Fagon JY, François B, Niederman MS, Rello J, et al. Global Prospective Epidemiologic and Surveillance Study of Ventilator-Associated Pneumonia due to Pseudomonas aeruginosa*. Crit Care Med [Internet]. 2014;42(10). Available from: https://doi.org/10.1097/CCM.0000000000000510
74. Mehta AC, Muscarella LF. Bronchoscope-Related "Superbug" Infections. Chest [Internet]. 2020 Feb 1;157(2):454–69. Available from: https://doi.org/10.1016/j.chest.2019.08.003
75. Baidya S, Sharma S, Mishra SK, Kattel HP, Parajuli K, Sherchand JB. Biofilm Formation by Pathogens Causing Ventilator-Associated Pneumonia at Intensive Care Units in a Tertiary Care Hospital: An Armor for Refuge. Brul S, editor. Biomed Res Int [Internet]. 2021; Available from: https://doi.org/10.1155/2021/8817700
76. Kaier K, Heister T, Götting T, Wolkewitz M, Mutters NT. Measuring the in-Hospital Costs of Pseudomonas aeruginosa Pneumonia: Methodology and Results from A German Teaching Hospital. BMC Infect Dis [Internet]. 2019;19(1):1028. Available from: https://doi.org/10.1186/s12879-019-4660-5

77. Restrepo MI, Babu BL, Reyes LF, Chalmers JD, Soni NJ, Sibila O, et al. Burden and Risk Factors for Pseudomonas aeruginosa Community-Acquired Pneumonia: A Multinational Point Prevalence Study of Hospitalised Patients. Eur Respir J [Internet]. 2018 Aug 1;52(2). Available from: https://doi.org/10.1183/13993003.01190-2017
78. Elborn JS. Cystic Fibrosis. Lancet [Internet]. 2016 Nov 19;388(10059):2519–31. Available from: https://doi.org/10.1016/S0140-6736(16)00576-6
79. Rossi E, La Rosa R, Bartell JA, Marvig RL, Haagensen JAJ, Sommer LM, et al. Pseudomonas aeruginosa Adaptation and Evolution in Patients with Cystic Fibrosis. Nat Rev Microbiol [Internet]. 2021;19(5):331–42. Available from: https://doi.org/10.1038/s41579-020-00477-5
80. Waters CM, Goldberg JB. Pseudomonas aeruginosa in Cystic Fibrosis: A Chronic Cheater. Proc Natl Acad Sci [Internet]. 2019 Apr 2;116(14):6525–7. Available from: https://doi.org/10.1073/pnas.1902734116
81. Costas LM, Martí S, Ardanuy C, Liñares J, Santos S, Dorca J, et al. Specific immune response against pseudomonas aeruginosa and haemophilus influenzae in severe COPD. Eur Respir J [Internet]. 2016 Sep 1;48(suppl 60):OA1790. Available from: http://erj.ersjournals.com/content/48/suppl_60/OA1790.abstract
82. Kwok WC, Ho JCM, Tam TCC, Ip MSM, Lam DCL. Risk Factors for Pseudomonas aeruginosa Colonization in Non-Cystic Fibrosis Bronchiectasis and Clinical Implications. Respir Res [Internet]. 2021;22(1):132. Available from: https://doi.org/10.1186/s12931-021-01729-5
83. Baker SM, McLachlan JB, Morici LA. Immunological Considerations in the Development of Pseudomonas aeruginosa Vaccines. Hum Vaccines Immunother [Internet]. 2020;16(2):412–8. Available from: https://doi.org/10.1080/21645515.2019.1650999
84. Mauch RM, Jensen PØ, Moser C, Levy CE, Høiby N. Mechanisms of Humoral Immune Response Against Pseudomonas aeruginosa Biofilm Infection in Cystic Fibrosis. J Cyst Fibros [Internet]. 2018;17(2):143–52. Available from: https://doi.org/10.1016/j.jcf.2017.08.012
85. Moser C, Jensen PØ, Thomsen K, Kolpen M, Rybtke M, Lauland AS, et al. Immune Responses to Pseudomonas aeruginosa Biofilm Infections. Front Immunol [Internet]. 2021;12. Available from: https://doi.org/10.3389/fimmu.2021.625597
86. Sainz-Mejías M, Jurado-Martín I, McClean S. Understanding Pseudomonas aeruginosa-Host Interactions: The Ongoing Quest for an Efficacious Vaccine. Cells [Internet]. 2020;9(12). Available from: http://dx.doi.org/10.3390/cells9122617
87. Lin CK, Kazmierczak BI. Inflammation: A Double-Edged Sword in the Response to Pseudomonas aeruginosa Infection. J Innate Immun [Internet]. 2017;9(3):250–61. Available from: https://doi.org/10.1159/000455857
88. Skopelja-Gardner S, Theprungsirikul J, Lewis KA, Hammond JH, Carlson KM, Hazlett HF, et al. Regulation of Pseudomonas aeruginosa-Mediated

Neutrophil Extracellular Traps. Front Immunol [Internet]. 2019;10:1–13. Available from: https://doi.org/10.3389/fimmu.2019.01670
89. Rada B. Interactions between Neutrophils and Pseudomonas aeruginosa in Cystic Fibrosis. Pathogens [Internet]. 2017;6(1). Available from: https://doi.org/10.3390/pathogens6010010
90. Sirina M, Yasir A, Darryl J, Sonali S, Afrakoma AA, Miguel C, et al. Gamma Interferon and Interleukin-17A Differentially Influence the Response of Human Macrophages and Neutrophils to Pseudomonas aeruginosa Infection. Infect Immun [Internet]. 2019 Jan 24;87(2). Available from: https://doi.org/10.1128/iai.00814-18
91. Toka O, Pascal Z, Erin C, Zhenyu C, Brent J. Mice Lacking γδ T Cells Exhibit Impaired Clearance of Pseudomonas aeruginosa Lung Infection and Excessive Production of Inflammatory Cytokines. Infect Immun [Internet]. 2020 May 20;88(6). Available from: https://doi.org/10.1128/iai.00171-20
92. McIsaac SM, Stadnyk AW, Lin TJ. Toll-like Receptors in the Host Defense Against Pseudomonas aeruginosa Respiratory Infection and Cystic Fibrosis. J Leukoc Biol [Internet]. 2012 Nov 1;92(5):977–85. Available from: https://doi.org/10.1189/jlb.0811410
93. Meenu M, Adam R, S. SL, J. WD. Identification of OprF as a Complement Component C3 Binding Acceptor Molecule on the Surface of Pseudomonas aeruginosa. Infect Immun [Internet]. 2015 Jul 8;83(8):3006–14. Available from: https://doi.org/10.1128/iai.00081-15
94. Domingue JC, Drewes JL, Merlo CA, Housseau F, Sears CL. Host Responses to Mucosal Biofilms in the Lung and Gut. Mucosal Immunol [Internet]. 2020 May 1;13(3):413–22. Available from: https://doi.org/10.1038/s41385-020-0270-1
95. Li Y, Jin L, Chen T. The Effects of Secretory IgA in the Mucosal Immune System. Biomed Res Int [Internet]. 2020;1–6. Available from: https://doi.org/10.1155/2020/2032057
96. Seibold MA. Interleukin-13 Stimulation Reveals the Cellular and Functional Plasticity of the Airway Epithelium. Ann Am Thorac Soc [Internet]. 2018 Apr 1;15. Available from: https://doi.org/10.1513/AnnalsATS.201711-868MG
97. Mensa J, Barberán J, Soriano A, Llinares P, Marco F, Cantón R, et al. Antibiotic Selection in the Treatment Acute Pseudomonas Aeruginosa Guidelines. Rev Esp Quim [Internet]. 2018;31(1):78–100. Available from: https://pubmed.ncbi.nlm.nih.gov/29480677/
98. Kollef MH, Chastre J, Clavel M, Restrepo MI, Michiels B, Kaniga K, et al. A Randomized Trial of 7-day Doripenem vs. 10-day Imipenem-Cilastatin for Ventilator-Associated Pneumonia. Crit Care [Internet]. 2012 Nov;16(6). Available from: https://doi.org/10.1186/cc11862
99. Lodise TP, Bidell MR. Pseudomonas aeruginosa [Internet]. 2nd ed. IDSAP; 2019. Available from: https://www.accp.com/docs/bookstore/IDSAP/id2019b2_sample.pdf
100. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of Adults With Hospital-Acquired and Ventilator-

Associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis [Internet]. 2016 Sep;63(5). Available from: https://doi.org/10.1093/cid/ciw353

101. O'Donnell JN, Rhodes NJ, Lopez J, Jett R, Scheetz MH. Carbapenems vs. Alternative β-lactams for the Treatment of Nosocomial Pneumonia: A Systematic Review and Meta-Analysis. Int J Antimicrob Agents [Internet]. 2018 Oct;52(4):451–8. Available from: https://doi.org/10.1016/j.ijantimicag.2018.04.011
102. Xipell M, Bodro M, Marco F, Losno RA, Cardozo C, Soriano A. Clinical Experience with Ceftazidime/Avibactam in Patients with Severe Infections, including Meningitis and Lung Abscesses, Caused by Extensively Drug-resistant Pseudomonas aeruginosa [Internet]. Vol. 49, International journal of antimicrobial agents. Netherlands; 2017. p. 266–8. Available from: https://doi.org/10.1016/j.ijantimicag.2016.11.005
103. Saderi H, Owlia P. Detection of Multidrug Resistant (MDR) and Extremely Drug Resistant (XDR) P. aeruginosa Isolated from Patients in Tehran, Iran. Iran J Pathol. 2015;10(4):265–71.
104. Grassi L, Di Luca M, Maisetta G, Rinaldi AC, Esin S, Trampuz A, et al. Generation of Persister Cells of Pseudomonas aeruginosa and Staphylococcus aureus by Chemical Treatment and Evaluation of Their Susceptibility to Membrane-Targeting Agents. Front Microbiol [Internet]. 2017;8(OCT):1–12. Available from: https://doi.org/10.3389/fmicb.2017.01917
105. Pachori P, Gothalwal R, Gandhi P. Emergence of Antibiotic Resistance Pseudomonas aeruginosa in Intensive Care Unit: A Critical Review. Vol. 6, Genes and Diseases. 2019. p. 109–19.
106. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-Resistant, Extensively Drug-Resistant and Pandrug-Resistant Bacteria: An International Expert Proposal for Interim Standard Definitions for Acquired Resistance. Clin Microbiol Infect [Internet]. 2012;18(3):268–81. Available from: https://doi.org/10.1111/j.1469-0691.2011.03570.x
107. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, Van Duin D, Clancy CJ. Infectious Diseases Society of America 2022 Guidance on the Treatment of Extended-Spectrum β-lactamase Producing Enterobacterales (ESBL-E), Carbapenem-Resistant Enterobacterales (CRE), and Pseudomonas aeruginosa with Difficult-to-Treat Resistance (DTR-P. Clin Infect Dis [Internet]. 2022;75(2):187–212. Available from: https://doi.org/10.1093/cid/ciac268
108. Morales E, Cots F, Sala M, Comas M, Belvis F, Riu M, et al. Hospital Costs of Nosocomial Multi-drug Resistant Pseudomonas aeruginosa Acquisition. BMC Health Serv Res [Internet]. 2012 May;12:122. Available from: https://doi.org/10.1186/1472-6963-12-122
109. Jadimurthy R, Mayegowda SB, Nayak SC, Mohan CD, Rangappa KS. Escaping Mechanisms of ESKAPE Pathogens from Antibiotics and Their

Targeting by Natural Compounds Elsevier Enhanced Reader. Biotechnol Reports [Internet]. 2022;34. Available from: https://doi.org/10.1016/j.btre.2022.e00728

110. Anggraini D, Yulindra UG, Savira M. Prevalensi dan Pola Sensitivitas Antimikroba Multidrug Resistant Pseudomonas aeruginosa di RSUD Arifin Achmad [Internet]. Vol. 50, Majalah Kedokteran Bandung. 2018. p. 6–12. Available from: http://dx.doi.org/10.15395/mkb.v50n1.1150
111. Dharmayanti IGAMP, Sukrama DM. Karakteristik Bakteri Pseudomonas aeruginosa dan Pola Kepekaannya terhadap Antibiotik di Intensive Care Unit (ICU) RSUP Sanglah pada Bulan November 2014 – Januari 2015. E-Journal Med. 2019;8(4):1–9.
112. Sanseverino I, Navarro A, Loos R, Marinov D, Lettieri T. State of the Art on the Contribution of Water to Antimicrobial Resistance. 2018.
113. Sagar S, Kaistha S, Das AJJ, Kumar R. Antibiotic Resistant Bacteria: A Challenge to Modern Medicine. Antibiotic Resistant Bacteria: A Challenge to Modern Medicine. New York: Springer; 2019. p. 1–179.
114. Chegini Z, Khoshbayan A, Taati Moghadam M, Farahani I, Jazireian P, Shariati A. Bacteriophage Therapy Against Pseudomonas aeruginosa Biofilms: A Review. Vol. 19, Annals of Clinical Microbiology and Antimicrobials. 2020.
115. Etebu E, Arikekpar I. Antibiotics: Classification and Mechanisms of Action with Emphasis on Molecular Perspectives. Int J Appl Microbiol Biotechnol Res [Internet]. 2016;90–101. Available from: https://api.semanticscholar.org/CorpusID:40048022
116. Hong W, Zeng J, Xie J. Antibiotic Drugs Targeting Bacterial RNAs. Acta Pharm Sin B [Internet]. 2014 Aug;4(4):258–65. Available from: https://doi.org/10.1016/j.apsb.2014.06.012
117. Biswas R, Panja AS, Bandopadhyay R. Molecular Mechanism of Antibiotic Resistance: The Untouched Area of Future Hope. Indian J Microbiol [Internet]. 2019;59(2):254–9. Available from: https://doi.org/10.1007/s12088-019-00781-6
118. Motta SS, Cluzel P, Aldana M. Adaptive Resistance in Bacteria Requires Epigenetic Inheritance, Genetic Noise, and Cost of Efflux Pumps. PLoS One [Internet]. 2015 Mar 17;10(3):e0118464. Available from: https://doi.org/10.1371/journal.pone.0118464
119. Qin S, Xiao W, Zhou C, Pu Q, Deng X, Lan L, et al. Pseudomonas aeruginosa: Pathogenesis, Virulence Factors, Antibiotic Resistance, Interaction with Host, Technology Advances and Emerging Therapeutics. Signal Transduct Target Ther [Internet]. 2022;7(1):199. Available from: https://doi.org/10.1038/s41392-022-01056-1
120. Angeletti S, Cella E, Prosperi M, Spoto S, Fogolari M, De Florio L, et al. Multi-drug Resistant Pseudomonas aeruginosa Nosocomial Strains: Molecular Epidemiology and Evolution. Microb Pathog [Internet]. 2018;123:233–41. Available from: https://doi.org/10.1016/j.micpath.2018.07.020
121. Samanta S, Bodrenko I, Acosta-Gutiérrez S, D'Agostino T, Pathania M,

Ghai I, et al. Getting Drugs through Small Pores: Exploiting the Porins Pathway in Pseudomonas aeruginosa. ACS Infect Dis [Internet]. 2018 Oct 12;4(10):1519–28. Available from: https://doi.org/10.1021/acsinfecdis.8b00149

122. Song F, Wang H, Sauer K, Ren D. Cyclic-di-GMP and oprF Are Involved in the Response of Pseudomonas aeruginosa to Substrate Material Stiffness during Attachment on Polydimethylsiloxane (PDMS). Front Microbiol [Internet]. 2018;9. Available from: https://doi.org/10.3389/fmicb.2018.00110
123. Valentini M, Filloux A. Biofilms and Cyclic di-GMP (c-di-GMP) Signaling: Lessons from Pseudomonas aeruginosa and Other Bacteria. J Biol Chem [Internet]. 2016 Jun 10;291(24):12547–55. Available from: https://doi.org/10.1074/jbc.R115.711507
124. Lee J, Patel DS, Kucharska I, Tamm LK, Im W. Refinement of OprH-LPS Interactions by Molecular Simulations. Biophys J [Internet]. 2017 Jan 24;112(2):346–55. Available from: https://doi.org/10.1016/j.bpj.2016.12.006
125. Farjah A, Owlia P, Siadat SD, Mousavi SF, Ardestani MS, Mohammadpour HK. Immunological Evaluation of An Alginate-Based C as A Vaccine Candidate Against Pseudomonas aeruginosa. APMIS [Internet]. 2015 Feb;123(2):175–83. Available from: https://doi.org/10.1111/apm.12337
126. Xian-Zhi L, Patrick P, Hiroshi N. The Challenge of Efflux-Mediated Antibiotic Resistance in Gram-Negative Bacteria. Clin Microbiol Rev [Internet]. 2015 Mar 18;28(2):337–418. Available from: https://doi.org/10.1128/cmr.00117-14
127. Cohen NR, Lobritz MA, Collins JJ. Microbial Persistence and the Road to Drug Resistance. Cell Host Microbe [Internet]. 2013 Jun;13(6):632–42. Available from: https://doi.org/10.1016/j.chom.2013.05.009
128. Maurice NM, Bedi B, Sadikot RT. Pseudomonas aeruginosa Biofilms: Host Response and Clinical Implications in Lung Iinfections. Am J Respir Cell Mol Biol [Internet]. 2018;58(4):428–39. Available from: https://doi.org/10.1165/rcmb.2017-0321TR
129. Pang Z, Raudonis R, Glick BR, Lin TJ, Cheng Z. Antibiotic Resistance in Pseudomonas aeruginosa: Mechanisms and Alternative Therapeutic Strategies. Biotechnol Adv [Internet]. 2019;37(1):177–92. Available from: https://doi.org/10.1016/j.biotechadv.2018.11.013
130. Fisher RA, Gollan B, Helaine S. Persistent Bacterial Infections and Persister Cells. Nat Rev Microbiol [Internet]. 2017;15(8):453–64. Available from: https://doi.org/10.1038/nrmicro.2017.42
131. Rafiee R, Eftekhar F, Tabatabaei SA, Minaee Tehrani D. Prevalence of Extended-Spectrum and Metallo β-Lactamase Production in AmpC β-Lactamase Producing Pseudomonas Aeruginosa Isolates From Burns. Jundishapur J Microbiol [Internet]. 2014;7(9). Available from: https://doi.org/10.5812/jjm.16436
132. Ramirez MS, Tolmasky ME. Aminoglycoside Modifying Enzymes. Drug Resist Updat [Internet]. 2010;13(6):151–71. Available from:

https://doi.org/10.1016/j.drup.2010.08.003
133. Lerminiaux NA, Cameron ADS. Horizontal Transfer of Antibiotic Resistance Genes in Clinical Environments. Can J Microbiol [Internet]. 2018 Sep 24;65(1):34–44. Available from: https://doi.org/10.1139/cjm-2018-0275
134. Aldred KJ, Kerns RJ, Osheroff N. Mechanism of Quinolone Action and Resistance. Biochemistry [Internet]. 2014 Mar;53(10):1565–74. Available from: https://doi.org/10.1021/bi5000564
135. Salam MA, Al-Amin MY, Pawar JS, Akhter N, Lucy IB. Conventional Methods and Future Trends in Antimicrobial Susceptibility Testing. Saudi J Biol Sci [Internet]. 2023;30(3). Available from: https://doi.org/10.1016/j.sjbs.2023.103582
136. Luc M. A Comparison of Disc Diffusion and Microbroth Dilution Methods for the Detection of Antibiotic Resistant Subpopulations in Gram-Negative Bacilli. Thesis [Internet]. 2015; Available from: https://digital.lib.washington.edu/researchworks/bitstream/handle/1773/33070/Luc_washington_0250O_14147.pdf?sequence=1
137. BSAC. BSAC Methods for Antimicrobial Susceptibility Testing [Internet]. Birmingham: British Society for Antimicrobial Chemotherapy; 2015. Available from: https://bsac.org.uk/wp-content/uploads/2012/02/BSAC-disc-susceptibility-testing-method-Jan-2015.pdf
138. Khan ZA, Siddiqui MF, Park S. Current and Emerging Methods of Antibiotic Susceptibility Testing. MDPI J [Internet]. 2019;9(49):65–100. Available from: http://dx.doi.org/10.3390/diagnostics9020049
139. Chiu CT, Lai CH, Huang YH, Yang CH, Lin JN. Comparative Analysis of Gradient Diffusion and Disk Diffusion with Agar Dilution for Susceptibility Testing of Elizabethkingia anophelis. Vol. 10, Antibiotics. 2021.
140. Correa M, Martínez F, Patiño Vidal C, Streitt C, Escrig J, Lopez de Dicastillo C. Antimicrobial Metal-Based Nanoparticles: A Review on Their Synthesis, Types and Antimicrobial Action. Beilstein J Nanotechnol [Internet]. 2020 Sep 25;11:1450–69. Available from: http://dx.doi.org/10.3762/bjnano.11.129
141. EUCAST. EUCAST Disk Diffusion Method for Antimicrobial Susceptibility Testing [Internet]. 11th ed. Basel: European Society of Clinical Microbiology and Infectious Disease; 2023. Available from: http://www.eucast.org
142. OIE Terrestrial Manual. Laboratory Methodologies for Bacterial Antimicrobial Susceptibility Testing [Internet]. OIE Terrestrial Manual. 2012. p. 1–11. Available from: https://www.woah.org/fileadmin/Home/fr/Our_scientific_expertise/docs/pdf/GUIDE_2.1_ANTIMICROBIAL.pdf
143. Khullar S, Rathore L, Khatri PK, Parihar RS, Meena S, Bora A, et al. Identification and Antibiogram of Various Gram-Positive Bacterial Isolates from Pyogenic Samples by VITEK® 2 Compact System. Int J Curr Microbiol Appl Sci [Internet]. 2016;5(2):66–77. Available from: https://doi.org/10.20546/ijcmas.2016.502.007

144. Prihatini, Aryati, Hetty. Identifikasi Cepat Mikroorganisme Menggunakan Alat VITEK-2. Indones J Clin Pathol Med Lab [Internet]. 2018;13(3):129–32. Available from: https://dx.doi.org/10.24293/ijcpml.v13i3.915
145. Wrenn C. Introduction of the VITEK 2 Compact and Implementation of EUCAST Guidelines in A Microbiology Department [Internet]. Royal College of Surgeons in Ireland (RCSI); 2015. Available from: https://core.ac.uk/download/pdf/60777463.pdf
146. Kemenkes RI. Bahaya Resistensi Antibiotik [Internet]. Kementerian Kesehatan RI. 2022. Available from: https://yankes.kemkes.go.id/view_artikel/1411/bahaya-resistensi-antibiotik
147. Kemenkes RI. Keputusan Menteri Kesehatan Republik Indonesia Nomor Hk.01.07/Menkes/1423/2022 tentang Pedoman Variabel dan Meta Data pada Penyelenggaraan Rekam Medis Elektronik [Internet]. Jakarta: Kementerian Kesehatan RI; 2022. Available from: https://yankes.kemkes.go.id/unduhan/fileunduhan_1664868356_130610.pdf
148. Hilda. Pola Kepekaan Pseudomonas aeruginosa terhadap Antibiotik di Laboratorium Mikrobiologi Klinik RSUP Dr. Mohammad Hoesin Palembang Periode Juli 2012 - Juni 2013. Palembang: Universitas Sriwijaya; 2014.
149. Primasari FS, Puspitasari I, Nuryastuti T. Prevalensi Bakteri Resisten Karbapenem di RSUP Dr. Sardjito Periode Januari-Agustus 2020. Maj Farm [Internet]. 2022;18(3):265–71. Available from: https://doi.org/10.22146/farmaseutik.v18i3.65823
150. Sukertiasih NK, Megawati F, Meriyani H, Sanjaya DA. Studi Retrospektif Gambaran Resistensi Bakteri terhadap Antibiotik. J Ilm Medicam [Internet]. 2021;7(2):108–11. Available from: https://doi.org/10.36733/medicamento.v7i2.2177
151. CDC. Pseudomonas aeruginosa in Healthcare [Internet]. Centers for Disease Control and Prevention (CDC). 2019. Available from: https://www.cdc.gov/hai/organisms/pseudomonas.html
152. Hidayat. Analisis Pola Kuman dan Pola Resistensi Antibiotik di Ruangan ICU dan Ruang Perinatologi Rumah Sakit Umum Daerah Dr. H. Abdul Moeloek Provinsi Lampung Tahun 2013. J Med Malahayati. 2016;3(1):1–14.
153. G.Wilson M, Pandey S. Pseudomonas aeruginosa [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557831/
154. Monegoro AF, Muppidi V, Regunath H. Hospital-Acquired Infections [Internet]. Florida: StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441857/?report=reader
155. Rambi E V, Makalew LA, Tumbol MVL, Sunati N, Rahim R, Kesehatan P, et al. Strategi Minimalisasi Risiko Stunting Lewat Gambaran Bakteri Aerob Penyebab Infeksi Nosokomial pada Ruang Rawat Inap Obstetri dan Ginekologi Rumah Sakit Islam Sitti Maryam Manado. e-PROSIDING SEMNAS. 2022;1(2):1–10.

156. Habboush Y, Guzman SNSY, Nilmarie. Infection Control [Internet]. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519017/
157. Ramírez-Estrada S, Borgatta B, Rello J. Pseudomonas aeruginosa Ventilator-Associated Pneumonia Management. Infect Drug Resist [Internet]. 2016;9:7–18. Available from: https://doi.org/10.2147/IDR.S50669
158. Babich T, Naucler P, Valik JK, Giske CG, Benito N, Cardona R, et al. Risk Factors for Mortality Among Patients with Pseudomonas aeruginosa Bacteraemia: A Retrospective Multicentre Study. Int J Antimicrob Agents [Internet]. 2020 Feb;55(2):105847. Available from: https://doi.org/10.1016/j.ijantimicag.2019.11.004
159. Caselli D, Cesaro S, Ziino O, Zanazzo G, Manicone R, Livadiotti S, et al. Multidrug Resistant Pseudomonas aeruginosa Infection in Children Undergoing Chemotherapy and Hematopoietic Stem Cell Transplantation. Haematologica [Internet]. 2010 Sep;95(9):1612–5. Available from: https://doi.org/10.3324/haematol.2009.020867
160. Matos ECO de, Andriolo RB, Rodrigues YC, Lima PDL de, Carneiro IC do RS, Lima KVB. Mortality in Patients with Multidrug-Resistant Pseudomonas aeruginosa Infections: A Meta-Analysis. Rev Soc Bras Med Trop [Internet]. 2018;51(4):415–20. Available from: https://doi.org/10.1590/0037-8682-0506-2017
161. GRAM. Bacterial Infections Linked to One in Eight Global Deaths, According to GRAM Study [Internet]. Global Research on Antimicrobial Resistance. 2022. Available from: https://www.tropicalmedicine.ox.ac.uk/gram/news/bacterial-infections-linked-to-one-in-eight-global-deaths-according-to-gram-study
162. Hwang W, Yoon SS. Virulence Characteristics and An Action Mode of Antibiotic Resistance in Multidrug-Resistant Pseudomonas aeruginosa. Vol. 9, Scientific Reports. 2019.
163. Hosu MC, Vasaikar SD, Okuthe GE, Apalata T. Detection of Extended Spectrum Beta-Lactamase Genes in Pseudomonas aeruginosa Isolated from Patients in Rural Eastern Cape Province, South Africa. Sci Rep [Internet]. 2021;11(1):7110. Available from: https://doi.org/10.1038/s41598-021-86570-y
164. Zhang Y, Li Y, Zeng J, Chang Y, Han S, Zhao J, et al. Risk Factors for Mortality of Inpatients with Pseudomonas aeruginosa Bacteremia in China: Impact of Resistance Profile in the Mortality. Infect Drug Resist [Internet]. 2020;13:4115–23. Available from: https://doi.org/10.2147/IDR.S268744
165. Rizaldi T, Muslim M, Yudaningtyas E. Knowledge Management System untuk Diagnosis Infeksi Nosokomial. J EECCIS. 2014;8(2):105–10.
166. Fabian P, Alimsardjono L, Indiastuti DN. Pola Resistensi Bakteri Pseudomonas aeruginosa dan Acinetobacter baumannii pada Spesimen Darah terhadap Antibiotik Golongan β-laktam dan Aminoglikosida di RSUD Dr. Soetomo periode Januari 2016 – Desember 2016. J Kedokt Syiah Kuala [Internet]. 2020;20(1):31–6. Available from: https://doi.org/10.24815/jks.v20i1.18296

167. Motbainor H, Bereded F, Mulu W. Multi-drug Resistance of Blood Stream, Urinary Tract and Surgical Site Nosocomial Infections of Acinetobacter baumannii and Pseudomonas aeruginosa among Patients Hospitalized at Felegehiwot Referral Hospital, Northwest Ethiopia: A Cross-Sectional Study. BMC Infect Dis [Internet]. 2020;20(1):92. Available from: https://doi.org/10.1186/s12879-020-4811-8
168. Gill JS, Arora S, Khanna SP, Kumar KH. Prevalence of Multidrug-resistant, Extensively Drug-resistant, and Pandrug-resistant Pseudomonas aeruginosa from a Tertiary Level Intensive Care Unit. J Glob iIfectious Dis [Internet]. 2016;8(4):155–9. Available from: https://doi.org/10.4103/0974-777X.192962
169. El Chakhtoura NG, Bonomo RA, Jump RLP. Influence of Aging and Environment on Presentation of Infection in Older Adults. Infect Dis Clin North Am [Internet]. 2017 Dec;31(4):593–608. Available from: https://doi.org/10.1016/j.idc.2017.07.017
170. Martín S, Pérez A, Aldecoa C. Sepsis and Immunosenescence in the Elderly Patient: A Review. Front Med [Internet]. 2017;4:20. Available from: https://doi.org/10.3389/fmed.2017.00020
171. Saputra IPGS, Iswari IS, Pinatih KJP. Prevalensi dan Pola Kepekaan Multidrug Resistance Pseudomonas aeruginosa terhadap Antibiotika pada Pasien Pneumonia di RSUP Sanglah. J Med Udayana [Internet]. 2021;10(12):89–95. Available from: https://doi.org/10.24843.MU.2021.V10.i12.P15
172. Yayan J, Ghebremedhin B, Rasche K. Antibiotic Resistance of Pseudomonas aeruginosa in Pneumonia at a Single University Hospital Center in Germany over a 10-Year Period. PLoS One [Internet]. 2015;10(10):e0139836. Available from: https://doi.org/10.1371/journal.pone.0139836
173. Setianingsih Y, Fadraersada J, Ibrahim A, Ramadhan AM. Pola Resistensi Bakteri terhadap Antibiotik pada Pasien Diabetic Foot di RSUD Abdul Wahab Sjahranie Samarinda Periode Agustus-Oktober 2016. Vol. 4, Prosiding Seminar Nasional Kefarmasian. 2016. p. 20–1.
174. Chung DR, Song JH, Kim SH, Thamlikitkul V, Huang SG, Wang H, et al. High Prevalence of Multidrug-Resistant Nonfermenters in Hospital-Acquired Pneumonia in Asia. Am J Respir Crit Care Med [Internet]. 2011 Dec;184(12):1409–17. Available from: https://doi.org/10.1164/rccm.201102-0349OC
175. Drope J, Schluger N, Cahn Z, Drope J, Hamill S, Islami F, et al. The Tobacco Atlas. 6th ed. American Cancer Society and Vital Strategies. 2018.
176. Tan YL, Dorotheo U. The Tobacco Control Atlas ASEAN Region. 4th ed. Southeast Asia Tobacco Control Alliance. 2018. 1–172 p.
177. Jiang C, Chen Q, Xie M. Smoking Increases the Risk of Infectious Diseases: A Narrative Review. Tob Induc Dis [Internet]. 2020;18(7):1–17. Available from: https://doi.org/10.18332/tid/123845
178. Zhu H, Zhan X, Wang C, Deng Y, Li X, Song L, et al. Causal Associations Between Tobacco, Alcohol Use and Risk of Infectious Diseases: A Mendelian Randomization Study. Infect Dis Ther [Internet].

2023;12(3):965–77. Available from: https://doi.org/10.1007/s40121-023-00775-4
179. WHO. Alcohol [Internet]. World Health Organization. 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/alcohol
180. EuroStat. Alcohol Consumption Statistics [Internet]. European Statistics. 2021. Available from: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Alcohol_consumption_statistics
181. Malherbe DC, Messaoudi I. Transcriptional and Epigenetic Regulation of Monocyte and Macrophage Dysfunction by Chronic Alcohol Consumption. Front Immunol [Internet]. 2022;13. Available from: https://doi.org/10.3389/fimmu.2022.911951
182. Szabo G, Saha B. Alcohol's Effect on Host Defense. Alcohol Res. 2015;37(2):159–70.
183. Hardia L, Djide MN, Arief M, Kunci K. Deteksi Fenotip Isolat Pseudomonas aeruginosa Penghasil Mettalo Beta-Laktamase (MBL) Resisten Karbapenem pada Pasien Infeksi di RSUP Dr. Wahidin Sudirohusodo Makassar. Maj Farm dan Farmakol [Internet]. 2022;26(2):48–51. Available from: https://doi.org/10.20956/mff.v26i2.17871
184. Tosi M, Roat E, De Biasi S, Munari E, Venturelli S, Coloretti I, et al. Multidrug Resistant Bacteria in Critically Ill Patients: A Step Further Antibiotic Therapy. J Emerg Crit Care Med Vol 2 (December 2018) J Emerg Crit Care Med [Internet]. 2018; Available from: https://jeccm.amegroups.org/article/view/4845
185. Trinh TD, Zasowski EJ, Claeys KC, Lagnf AM, Kidambi S, Davis SL, et al. Multidrug-Resistant Pseudomonas aeruginosa Lower Respiratory Tract Infections in the Intensive Care Unit: Prevalence and Risk Factors. Diagn Microbiol Infect Dis [Internet]. 2017 Sep;89(1):61–6. Available from: https://doi.org/10.1016/j.diagmicrobio.2017.06.009
186. Riquelme SA, Wong Fok Lung T, Prince A. Pulmonary Pathogens Adapt to Immune Signaling Metabolites in the Airway. Front Immunol [Internet]. 2020;11. Available from: https://doi.org/10.3389/fimmu.2020.00385
187. Singh S, Sharma A, Nag VL. Bacterial Pathogens from Lower Respiratory Tract Infections: A Study from Western Rajasthan. J Fam Med Prim care [Internet]. 2020 Mar;9(3):1407–12. Available from: https://doi.org/10.4103%2Fjfmpc.jfmpc_994_19
188. Reynolds D, Kollef M. The Epidemiology and Pathogenesis and Treatment of Pseudomonas aeruginosa Infections: An Update. Drugs [Internet]. 2021;81(18):2117–31. Available from: https://doi.org/10.1007/s40265-021-01635-6
189. Williams BJ, Dehnbostel J, Blackwell TS. Pseudomonas aeruginosa: Host Defence in Lung Diseases. Respirology [Internet]. 2010 Oct 1;15(7):1037–56. Available from: https://doi.org/10.1111/j.1440-1843.2010.01819.x
190. Freiberg JA. The Mythos of Laudable Pus Along with An Explanation for Its Origin. J community Hosp Intern Med Perspect [Internet]. 2017 Jul;7(3):196–8. Available from: https://doi.org/10.1080%2F20009666.2017.1343077

191. Gabriel S. Profil dan Pola Kepekaan Bakteri pada Spesimen Pus di RSUP H. Adam Malik Periode Januari – Desember 2019 [Internet]. Medan: Universitas Sumatera Utara; 2019. Available from: http://repositori.usu.ac.id/handle/123456789/30695
192. Kim M, Christley S, Khodarev NN, Fleming I, Huang Y, Chang E, et al. Pseudomonas aeruginosa Wound Infection Involves Activation of Its Iron Acquisition System in R to Fascial Contact. J Trauma Acute Care Surg [Internet]. 2015 Apr;78(4):823–9. Available from: https://doi.org/10.1097%2FTA.0000000000000574
193. Mittal R, Aggarwal S, Sharma S, Chhibber S, Harjai K. Urinary Tract Infections Caused by Pseudomonas aeruginosa: A Minireview. J Infect Public Health [Internet]. 2009;2(3):101–11. Available from: https://doi.org/10.1016/j.jiph.2009.08.003
194. de Sousa T, Hébraud M, Alves O, Costa E, Maltez L, Pereira JE, et al. Study of Antimicrobial Resistance, Biofilm Formation, and Motility of Pseudomonas aeruginosa Derived from Urine Samples [Internet]. Vol. 11, Microorganisms. 2023. Available from: https://doi.org/10.3390/microorganisms11051345
195. Estiningsih D, Puspitasari I, Nuryastuti T. Identifikasi Infeksi Multidrug-Resistant Organisms (MDRO) pada Pasien yang Dirawat di Bangsal Neonatal Intensive Care Unit (NICU) Rumah Sakit. J Manaj dan Pelayanan Farm. 2016;6(3):1–6.
196. Wijaksana DS, 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 [Internet]. Vol. 13, Jurnal Ilmu Kedokteran. 2019. p. 46. Available from: https://doi.org/10.26891/jik.v13i2.2019.46-54
197. Farras Aziz F, Suryadinata H, Wahyudi K. Pola Bakteri Pasien Rawat Inap Pneumonia Komunitas Dewasa Rumah Sakit Hasan Sadikin Bandung Tahun 2018. Indones J Chest. 2020;7(2):8–17.
198. Samirah, Rahayu, Noerwahyono A. Pola Bakteri Penyebab Pneumonia Nosokomial di RS Dr. Soetomo Surabaya Periode Januari 2011 - Maret 2012 [Internet]. Vol. 8, Saintika Medika. 2015. Available from: https://doi.org/10.22219/sm.v8i2.4112
199. Akhi MT, Ghotaslou R, Asgharzadeh M, Varshochi M, Pirzadeh T, Memar MY, et al. Bacterial Etiology and Antibiotic Susceptibility Pattern of Diabetic Foot Infections in Tabriz, Iran. GMS Hyg Infect Control [Internet]. 2015;10:Doc02. Available from: https://doi.org/10.3205/dgkh000245
200. Gellatly SL, Hancock REW. Pseudomonas aeruginosa: New Insights into Pathogenesis and Host Defenses. Pathog Dis [Internet]. 2013 Apr 1;67(3):159–73. Available from: https://doi.org/10.1111/2049-632X.12033
201. Coello Pelegrin A, Palmieri M, Mirande-Meunier C, Oliver A, Moons P, Goossens H, et al. Pseudomonas aeruginosa: A Clinical and Genomics Update. FEMS Microbiol Rev [Internet]. 2021 May 10;45. Available from: https://doi.org/10.1093/femsre/fuab026
202. Ryan KJ, Ray CG. Sherris Medical Microbiology: An Introduction to

Infectious Disease [Internet]. 4th ed. Clinical Infectious Disease. New York: McGraw-Hill Education; 2004. Available from: http://dx.doi.org/10.1036/0838585299
203. CDC. What is Sepsis? [Internet]. U.S. Centers for Disease Control and Prevention. 2023. Available from: https://www.cdc.gov/sepsis/what-is-sepsis.html
204. Taslim E, Maskoen TT. Pola Kuman Terbanyak sebagai Agen Penyebab Infeksi di Intensive Care Unit pada Beberapa Rumah Sakit di Indonesia. Maj Anest dan Crit Care. 2016;34(1):33–9.
205. Rustini, Istiqamah S, Armin F. Penentuan Multi Drug Resisten Pseudomonas aeruginosa (MDRPA) yang Berasal dari Sampel Klinis Pasien RSUP Dr. M. Djamil Padang. In: Prosiding Rakernas dan Pertemuan Ilmiah Tahunan: 88. Padang; 2016.
206. Nair V, Sahni AK, Sharma D, Grover N, Shankar S, Chakravarty A, et al. Point Prevalence and Risk Factor Assessment for Hospital-Acquired Infections in A Tertiary Care Hospital in Pune, India. Indian J Med Res [Internet]. 2017 Jun;145(6):824–32. Available from: https://doi.org/10.4103/ijmr.ijmr_1167_15
207. Matos ECO de, Matos HJ de, Conceição ML, Rodrigues YC, Carneiro IC do RS, Lima KVB. Clinical and Microbiological Features of Infections Caused by Pseudomonas aeruginosa in Patients Hospitalized in Intensive Care Units. Rev Soc Bras Med Trop [Internet]. 2016;49(3):305–11. Available from: https://doi.org/10.1590/0037-8682-0446-2015
208. Boncea EE, Expert P, Honeyford K, Kinderlerer A, Mitchell C, Cooke GS, et al. Association Between Intrahospital Transfer and Hospital-Acquired Infection in the Elderly: A Retrospective Case-Control Study in A UK Hospital Network. BMJ Qual Saf [Internet]. 2021 Jun;30(6):457–66. Available from: https://doi.org/10.1136%2Fbmjqs-2020-012124
209. Parcell BJ, Oravcova K, Pinheiro M, Holden MTG, Phillips G, Turton JF, et al. Pseudomonas aeruginosa Intensive Care Unit Uutbreak: Winnowing of Transmissions with Molecular and Genomic Typing. J Hosp Infect [Internet]. 2018;98(3):282–8. Available from: https://doi.org/10.1016/j.jhin.2017.12.005
210. Kemenkes RI. Peraturan Menteri Kesehatan Nomor 27 Tahun 2017 tentang Pedoman Pencegahan Dan Pengendalian Infeksi di Fasilitas Pelayanan Kesehatan [Internet]. Jakarta: Kementerian Kesehatan RI; 2017. Available from: https://peraturan.bpk.go.id/Home/Details/112075/permenkes-no-27-tahun-2017
211. RSMH. Laporan Kerja (LKJ) RSUP Dr. Mohammad Hoesin Palembang Tahun 2022 [Internet]. Palembang: RSUP Dr. Mohammad Hoesin Palembang; 2022. Available from: https://www.rsmh.co.id/
212. Kristiningrum S, Widyawati IY, Huda N. Identifikasi Infeksi Multidrug Resistant Organism (MDRO) pada Pasien ICU [Internet]. Vol. 5, Journal of Telenursing (JOTING). 2023. p. 180–9. Available from: https://doi.org/10.31539/joting.v5i1.5404
213. Deni J, Pangalila JF. Hubungan Keberhasilan Terapi Pneumonia

Nosokomial Resisten Pseudmonas aeruginosa dan Acinetobacter baumannii dengan Dosis Karbapenem Di ICU RS Royal Taruma Periode 2012-2017. Vol. 1, Tarumanegara Medical Journal. 2019. p. 532–43.

214. Pérez A, Gato E, Pérez-Llarena J, Fernández-Cuenca F, Gude MJ, Oviaño M, et al. High Incidence of MDR and XDR Pseudomonas aeruginosa Isolates Obtained from Patients with Ventilator-Associated Pneumonia in Greece, Italy and Spain as Part of the MagicBullet Clinical Trial. J Antimicrob Chemother [Internet]. 2019 May;74(5):1244–52. Available from: https://doi.org/10.1093/jac/dkz030
215. Sommer LM, Johansen HK, Molin S. Antibiotic Resistance in Pseudomonas aeruginosa and Adaptation to Complex Dynamic Environments [Internet]. Vol. 6, Microbial Genomics. 2020. p. 1–6. Available from: https://doi.org/10.1099/mgen.0.000370
216. El Zowalaty ME, Al Thani AA, Webster TJ, El Zowalaty AE, Schweizer HP, Nasrallah GK, et al. Pseudomonas aeruginosa: Arsenal of Resistance Mechanisms, Decades of Changing Resistance Profiles, and Future Antimicrobial Therapies. Future Microbiol [Internet]. 2015;10(10):1683–706. Available from: https://doi.org/10.2217/fmb.15.48
217. Yaghoubi S, Zekiy AO, Krutova M, Gholami M, Kouhsari E, Sholeh M, et al. Tigecycline Antibacterial Activity, Clinical Effectiveness, and Mechanisms and Epidemiology of Resistance: Narrative Review. Eur J Clin Microbiol Infect Dis [Internet]. 2022;41(7):1003–22. Available from: https://doi.org/10.1007/s10096-020-04121-1
218. Somily AM, Absar MM, Arshad MZ, Al Aska AI, Shakoor ZA, Fatani AJ, et al. Antimicrobial Susceptibility Patterns of Multidrug-Resistant Pseudomonas aeruginosa and Acinetobacter baumannii Against Carbapenems, Colistin, and Tigecycline. Saudi Med J. 2012 Jul;33(7):750–5.
219. King DT, Sobhanifar S, Strynadka NCJ. The Mechanisms of Resistance to β-Lactam Antibiotics. Handb Antimicrob Resist [Internet]. 2017;177–201. Available from: https://dx.doi.org/10.1007/978-1-4939-0694-9_10
220. BPOM. Sefalosporin dan Antibiotik Beta-Laktam Lainnya [Internet]. Badan POM RI; 2021. Available from: https://pionas.pom.go.id/ioni/bab-5-infeksi/51-antibakteri/512-sefalosporin-dan-antibiotik-beta-laktam-lainnya/5121
221. Saderi H, Owlia P. Detection of Multidrug Resistant (MDR) and Extremely Drug Resistant (XDR) P. Aeruginosa Isolated from Patients in Tehran, Iran. Iran J Pathol. 2015;10(4):265–71.
222. Santoro A, Franceschini E, Meschiari M, Menozzi M, Zona S, Venturelli C, et al. Epidemiology and Risk Factors Associated With Mortality in Consecutive Patients With Bacterial Bloodstream Infection: Impact of MDR and XDR Bacteria. Open Forum Infect Dis [Internet]. 2020 Nov 1;7(11):ofaa461. Available from: https://doi.org/10.1093/ofid/ofaa461
223. Sastre-Femenia M, Fernández-Muñoz A, Gomis-Font M, Taltavull B, López-Causapé C, Arca-Suárez J, et al. Pseudomonas aeruginosa antibiotic susceptibility profiles, genomic epidemiology and resistance mechanisms: a

nation-wide five-year time lapse analysis. Lancet Reg Heal - Eur. 2023 Nov 1;34:100736.

224. Spagnolo AM, Sartini M, Cristina ML. Pseudomonas aeruginosa in the Healthcare Facility Setting. Rev Res Med Microbiol [Internet]. 2021;32(3). Available from: https://doi.org/10.1097/MRM.0000000000000271
225. Sader HS, Castanheira M, Duncan LR, Flamm RK. Antimicrobial Susceptibility of Enterobacteriaceae and Pseudomonas aeruginosa Isolates from United States Medical Centers Stratified by Infection Type: Results from the International Network for Optimal Resistance Monitoring (INFORM) Surveillance Program,. Diagn Microbiol Infect Dis [Internet]. 2018;92(1):69–74. Available from: https://doi.org/10.1016/j.diagmicrobio.2018.04.012
226. Sid Ahmed MA, Hassan AAI, Abu Jarir S, Abdel Hadi H, Bansal D, Abdul Wahab A, et al. Emergence of Multidrug- and Pandrug- Resistant Pseudomonas aeruginosa from Five Hospitals in Qatar. Infect Prev Pract [Internet]. 2019 Dec;1(3–4):100027. Available from: https://doi.org/10.1016/j.infpip.2019.100027
227. Lob S, Hackel M, Siddiqui F, Bauer KA, DeRyke CA, Young K, et al. Activity of Imipenem/Relebactam and Comparators Against Gram-Negative MDR and DTR Pathogens from Patients with Respiratory and Bloodstream Infections – SMART United States 2018-2020. Open Forum Infect Dis [Internet]. 2022 Dec 1;9(Supplement_2):ofac492.1301. Available from: https://doi.org/10.1093/ofid/ofac492.1301
228. CLSI. Performance Standards for Antimicrobial Susceptibility Testing, 30th Edition. Clinical and Laboratory Standards Institute. 2020.
229. Kadri SS, Adjemian J, Lai YL, Spaulding AB, Ricotta E, Prevots DR, et al. Difficult-to-Treat Resistance in Gram-negative Bacteremia at 173 US Hospitals: Retrospective Cohort Analysis of Prevalence, Predictors, and Outcome of Resistance to All First-line Agents. Clin Infect Dis [Internet]. 2018 Nov;67(12):1803–14. Available from: https://doi.org/10.1093/cid/ciy378