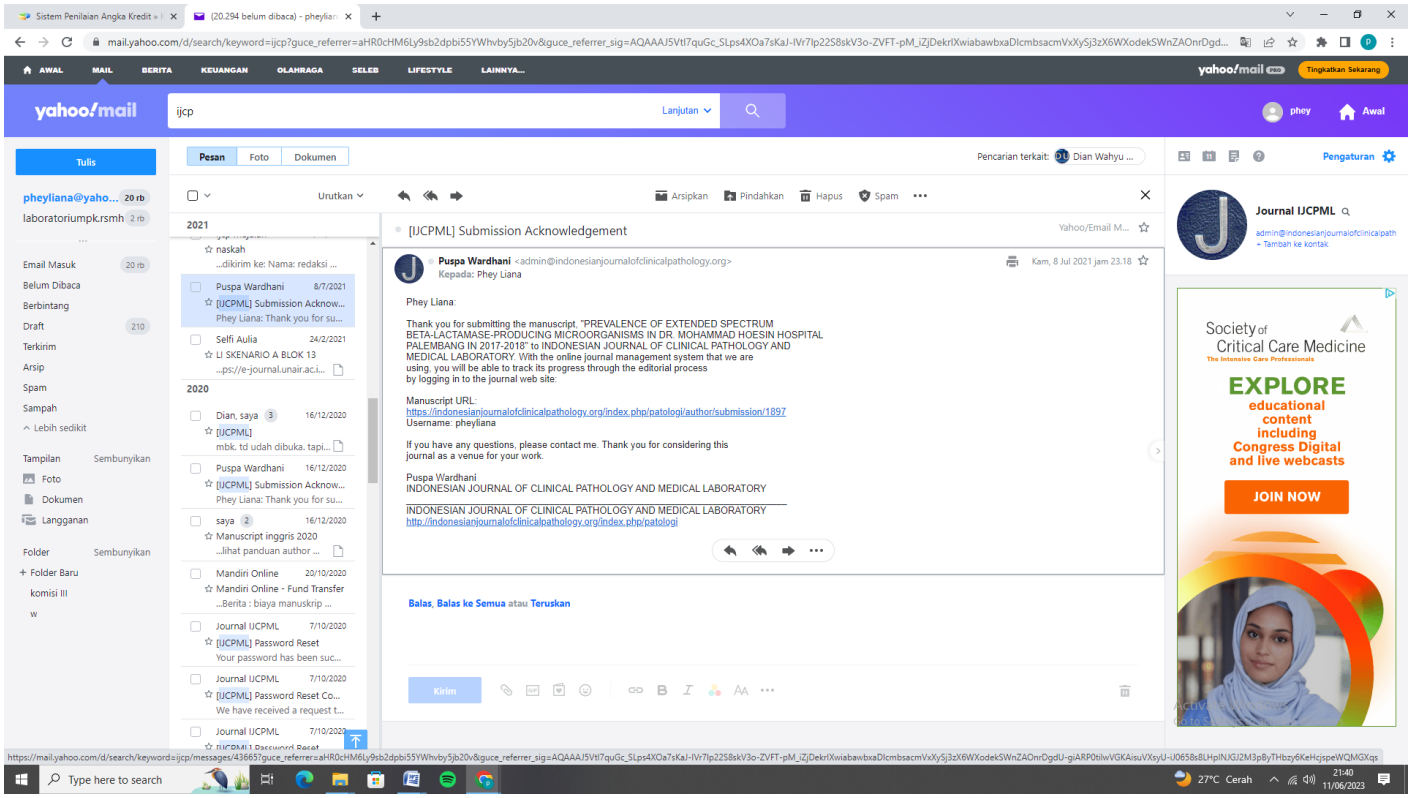
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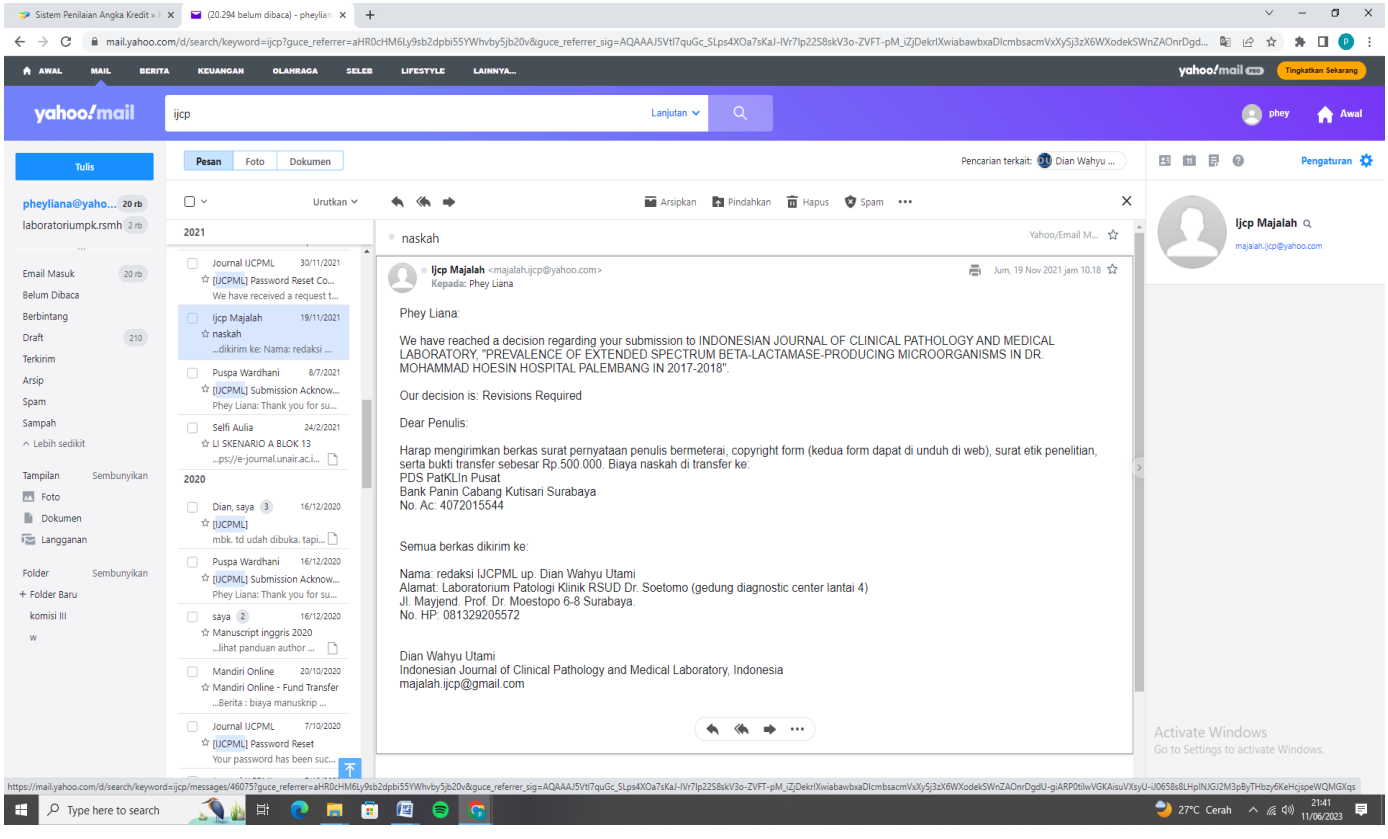
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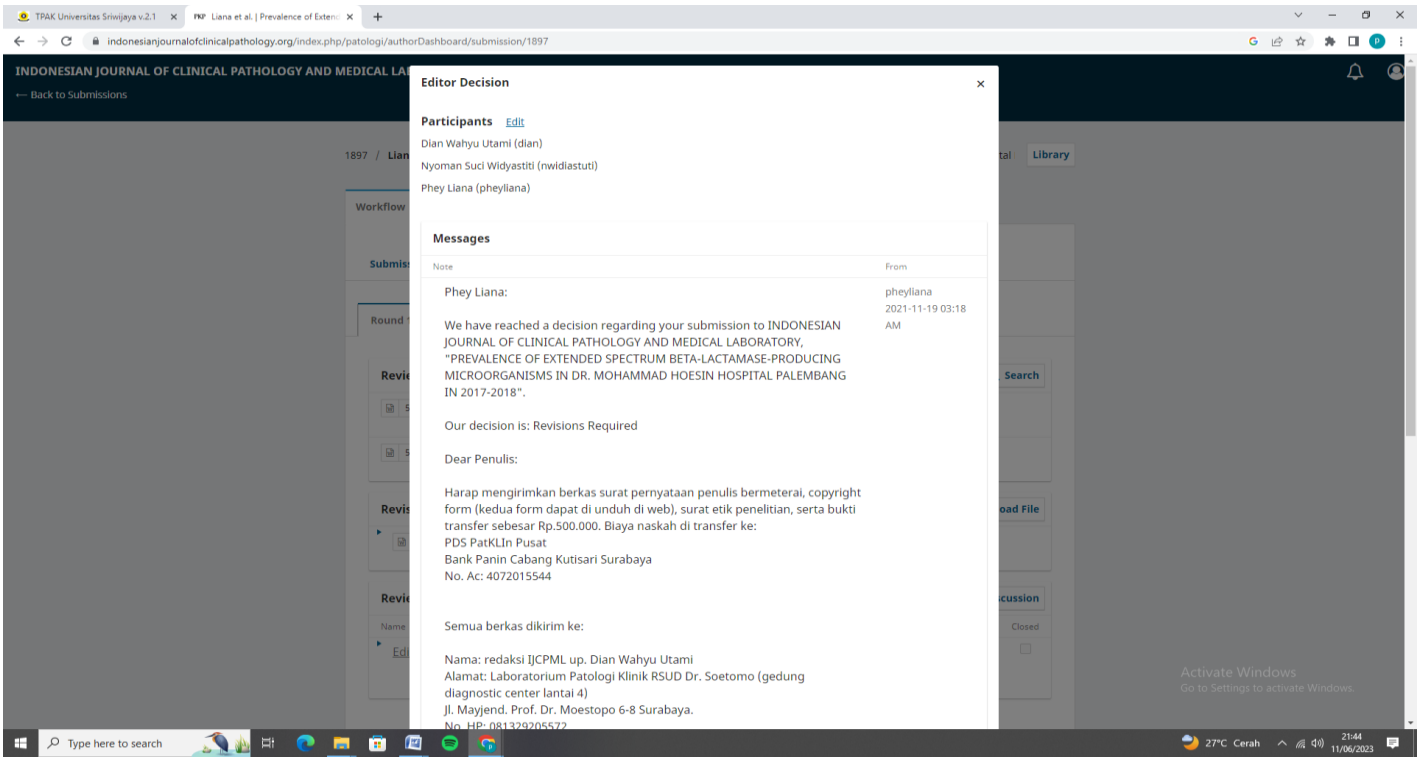
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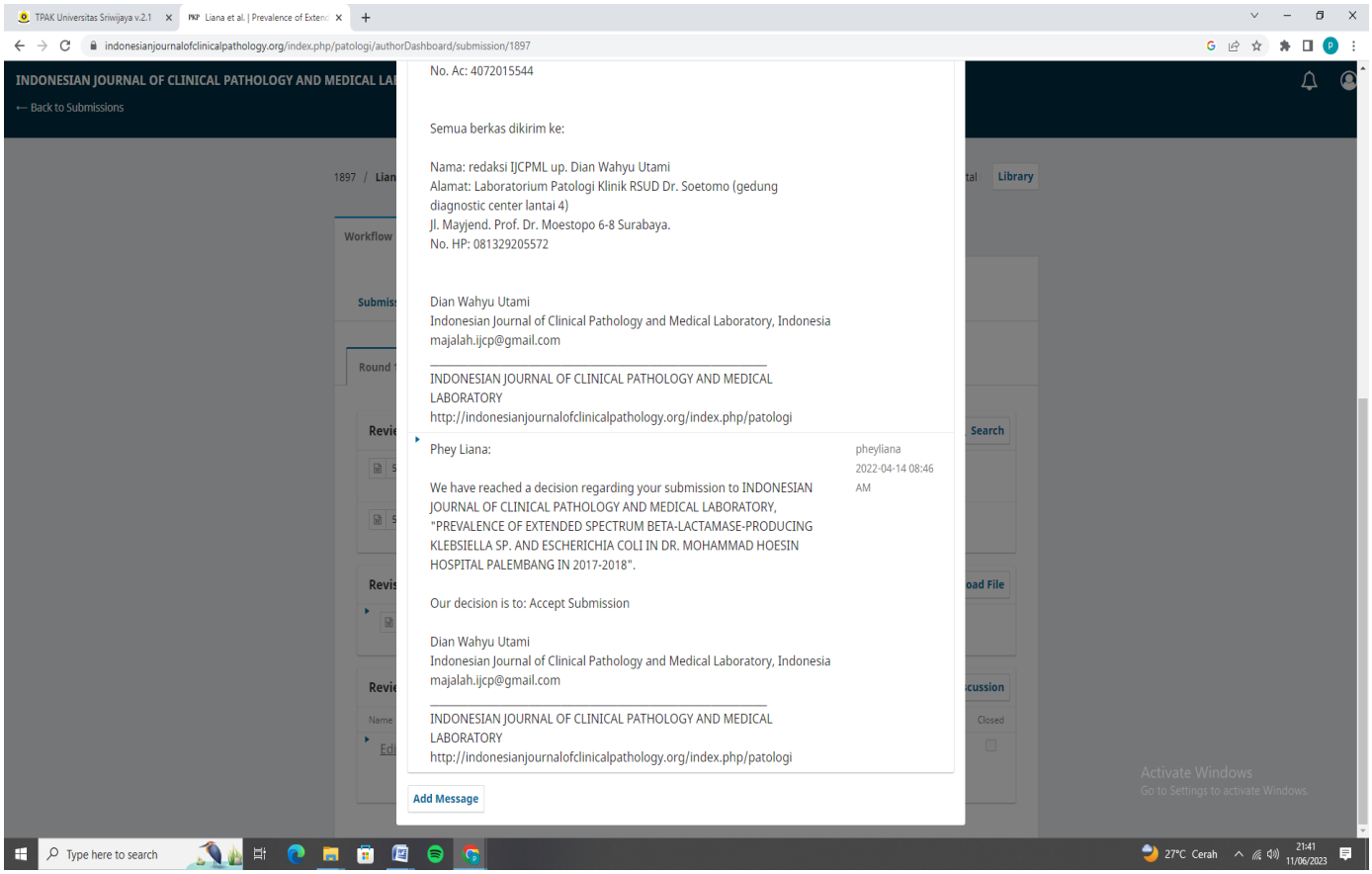
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RESEARCH

PREVALENCE OF EXTENDED SPECTRUM BETA-LACTAMASE-PRODUCING MICROORGANISMS IN DR. MOHAMMAD HOESIN HOSPITAL PALEMBANG IN 2017-2018

(Prevalensi Mikroorganisme yang Memproduksi Extended Spectrum Beta-Lactamase di Rumah Sakit Dr. Mohammad Hoesin Palembang Pada 2017-2018)

Phey Liana[1], Norlaila Binti Chahril[2], Sri Nita[3], Tungki Pratama Umar[1]

ABSTRAK

Produksi Extended Spectrum Beta-Lactamase (ESBL) oleh Enterobacteriaceae terus menjadi masalah penyakit menular terutama di rumah sakit. Penyebab utama kolonisasi bakteri penghasil ESBL adalah infeksi saluran kemih, lama rawat inap di rumah sakit, peralatan medis yang invasif, dan antibiotic. Penelitian ini bertujuan untuk mengetahui perbandingan kejadian ESBL berdasarkan jenis organisme di Rumah Sakit Dr. Mohammad Hoesin Periode 2017 dan 2018. Desain penelitian ~~yang digunakan~~ adalah deskriptif dengan pendekatan cross sectional, yang menggunakan data sekunder di Instalasi Patologi Klinik RSUP Dr. Mohammad Hoesin Palembang. Temuan penelitian ini menunjukkan adanya pola penurunan ~~pada~~ kejadian ESBL pada tahun 2017 dan 2018, namun dengan pola serupa yang didominasi oleh Klebsiella pneumoniae (diikuti Escherichia coli dan Klebsiella ozaenae), pasien rawat inap di bangsal anak, penyakit dalam, dan ruang rawat intensif, serta pada spesimen sputum. Penelitian ini menunjukkan adanya tingkat bakteri penghasil ESBL yang tinggi di RS Dr. Mohammad Hoesin (>60%), yang terutama disebabkan oleh Klebsiella pneumoniae.

Comment [MOU1]: pemakaian

Kata kunci: *Extended-Spectrum Beta-Lactamase,Klebsiella Pneumoniae, Enterobacteriaceae*

ABSTRACT

Production of Extended-Spectrum Beta-Lactamase (ESBL) by Enterobacteriaceae continues to be a problem of infectious diseases, especially in hospitals. The main causes of ESBL-producing bacteria colonization are urinary tract infections, length of hospital stay, invasive medical equipment, and antibiotics. This study aims to compare the incidence of ESBL based on the type of organism in Dr. Mohammad Hoesin Hospital for the 2017 and 2018 periods. The research design used was descriptive with a cross-sectional approach, which used

Comment [MOU2]: antibiotics usage

secondary data at the Clinical Pathology Department of Dr. RSUP. Mohammad Hoesin Palembang. The findings of this study showed a decreasing pattern in the incidence of ESBL in 2017 and 2018, but with a similar pattern which was dominated by *Klebsiella pneumoniae* (followed by *Escherichia coli* and *Klebsiella ozaenae*), inpatients in pediatric wards, internal medicine, and intensive care units, and on sputum specimens. This study showed the presence of high levels of ESBL-producing bacteria (>60%) in Dr. Mohammad Hoesin hospital which was mainly caused by *Klebsiella pneumoniae*.

Keywords: Extended-Spectrum Beta-Lactamase, *Klebsiella Pneumoniae,* Enterobacteriaceae

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INTRODUCTION

Infectious infections are a major issue in developing countries such as Indonesia.[1] In addition to the disease's high prevalence, other issues such as irrational antibiotic use can lead to microorganism resistance. Various surveillance data demonstrate a wide range of irrational antibiotic use, ranging from 35.1% (Ethiopia)[2] to 37.8% (Pakistan)[3] to 68.4% in Indonesia.[4]

Comment [MOU3]: apa maksud kalimat ini?

Antibiotic resistance is a change in bacteria's capacity to diminish the antibiotic action, mediated mostly by upregulation of drug efflux pumps.[5] Resistance initially began in hospitals, but it gradually spread across the community, particularly among *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Escherichia coli*.[6] Multi-resistant bacteria, including Methicilin-Resistant Staphylococcus aureus (MRSA) and Extended-Spectrum Beta-Lactamase (ESBL)-producing bacteria dominated the incidence of resistance, as mentioned by the Antimicrobial Resistance in Indonesia, Prevalence and Prevention (AMRIN) study.[7] Infections caused by bacteria that generate ESBL have increased dramatically in recent years. The ESBL mediates the hydrolysis and inactivation of beta-lactam antibiotics, including third-generation cephalosporins, penicillins, and Aztreonam.[8]

ESBL is produced by mutations of beta-lactamase enzymes Temoneira-1 (TEM-1), Temoneira-2 (TEM-2), and Sulphydryl-1 (SHV-1) which are commonly found in the

Enterobacteriaceae family. Penicillin and first-generation cephalosporins are typically resistant to these enzymes.[9] The family Enterobacteriaceae have many genera such as *Escherichia coli*, *Klebsiella*, *Salmonella*, *Shigella*, *Enterobacter*, *Proteus*, and *Serratia* with about 20-25 species of clinical importance.[10] According to Nazmi, et al., the prevalence of ESBL-producing E.coli and K. pneumoniae infections were 35% and 45%, respectively. In contrast to *K. pneumoniae*, ESBL production in E. coli was mostly found in outpatients.[11] The high occurrence of ESBL-producing bacteria serves as the landscape for this study, which compares the prevalence of ESBL based on the type of organism at the Dr. Mohammad Hoesin General Hospital from 2017 to 2018.

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METHODS

This cross-sectional study used secondary data from Clinical Pathology and Microbiology Department, Dr. Mohammad Hoesin Palembang's Central General Hospital, a tertiary hospital in South Sumatra. Patients who had culture and antibiotic resistance tests (outpatients and inpatients) between July-December 2017 and January-June 2018 were enrolled in this study. The inpatients were originated from 15 wards, including the Emergency Room (ER), Intensive Care Unit/ICU (General, Pediatric, and Neonates), Internal Medicine (Komering), Neurology (Rawas and Brain and Health Center/BHC), Obstetrics and Gynecology (Enim), Oncology (Rambang), Ophthalmology (Kelingi), Otorhinolaryngology (Lematang), Pediatric (Kelingi), Respiratory (Borang), Surgery (Lakitan) and VIP (Musi). Patient data were collected using the total sampling technique, which included culture results and antibiotic resistance tests with ESBL bacteria. A double-disk approximation test was used to identify ESBL strains using the antibiotics cefotaxime, ceftazidime, and cefepime. The study was approved by the institutional review board of Universitas Sriwijaya, Faculty of Medicine, Palembang, Indonesia (Approval Number: 251/kepfkrsmh/2018).

A descriptive analysis of the variables collected was conducted; qualitative variables were expressed as percentages. All statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS®), version 25.0 (IBM SPSS Corp., Armonk, NY, USA) software.

RESULTS AND DISCUSSION

The total ESBL-producing bacteria identified in this study showed decreasing pattern from 78.5% in 2017 to 60.3% in 2018. *Klebsiella pneumoniae* was the most commonly identified organism that produced the most ESBL during the study period (2017 and 2018),

with 244 (49.4%) and 268 (56.0%) cases, respectively. Further bacterial findings followed a similar pattern in the consecutive years, with *Escherichia coli* and *Klebsiella ozaenae* being the second and third-highest organisms in terms of ESBL incidence (Table 1 and Figure 1.).

Table 1. *Extended-Spectrum Beta-Lactamase* (ESBL)Prevalence in 2017 and 2018

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Organisms	ESBL					
	2017			2018		
	ESBL (+), %	ESBL (-), %	% of ESBL (+)	ESBL (+), %	ESBL (-), %	% of ESBL (+)
Escherichia.coli	239, 83.3%	48, 16.7%	48.4	207, 54.0%	177, 46.0%	43.2
Klebsiella pneumoniae	244, 74.2%	85, 25.8%	49.4	268, 53.3%	235, 46.7%	56.0
Klebsiella.ozaenae	11, 85.0%	2, 15.0%	2.2	4, 57.0%	3, 43.0%	0.8
TOTAL	494, 78.5%	135, 21.5%	100%	479, 60.3%	315, 39.7%	100

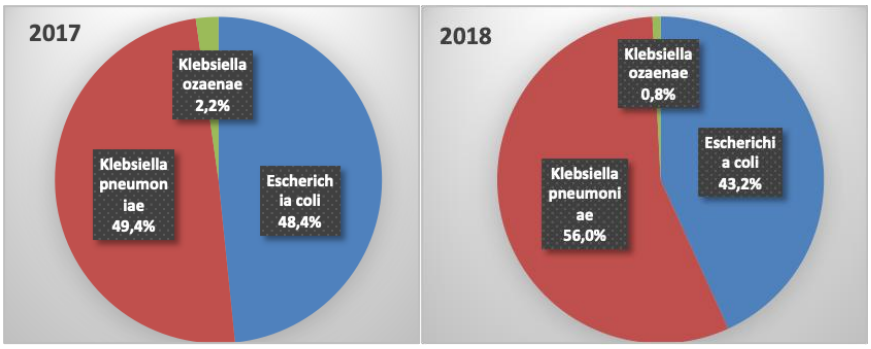

Figure 1. *Extended-Spectrum Beta-Lactamase* (ESBL) Prevalence in 2017 and 2018

The incidence of ESBL caused by *Klebsiella pneumoniae*, *Escherichia coli*, and *Klebsiella ozaenae* bacteria showed findings that were more frequently found in hospitalized cases between 2017 and 2018 (91.9% and 95.0%). Inpatient cases were dominated by *Klebsiella pneumoniae*, while outpatient cases were overtaken by *Escherichia coli*. Table 2 dan Figure 2 displays the details.

Table 2. ESBL Prevalence Between Outpatients and Inpatients

Organisms	2017				2018			
	Outpatients		Inpatients		Outpatients		Inpatients	
	n	%	n	%	n	%	n	%
E.coli	28	70.0	211	46.5	15	62.5	192	42.2
K.pneumoniae	12	30.0	232	51.1	8	33.3	260	57.1
K.ozaenae	0	0.0	11	2.4	1	4.2	3	0.7
TOTAL	40	100	454	100	24	100	455	100

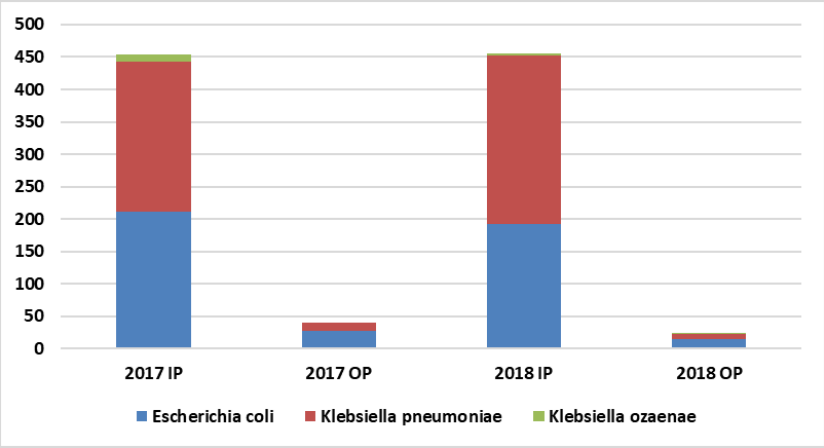

Figure 2. ESBL Prevalence Between Outpatients and Inpatients; (IP= Inpatients, OP=Outpatients)

In detail, the types of ESBL bacteria based on the type of inpatient room can be seen in table 3. The general findings indicated that the internal medicine (Komering), pediatric (Selincah), and intensive care wards (IGD and GICU) were the most common places for ESBL findings, especially for the two dominant microorganisms in this study, *K. pneumoniae*, and *E. coli*. Figures 3-5 displays details the types ESBL bacteria based on treatment wards.

Table 3. ESBL Findings Based on Treatment Wards

Wards	2017						2018					
	E. coli		*K .pneumoniae*		*K. ozaenae*		*E. coli*		*K. pneumoniae*		*K. ozaenae*	
	n	%	n	%	n	%	n	%	n	%	n	%
BHC	9	4.3	7	3.0	1	9.1	6	3.0	7	3.0	0	0
Borang	0	0	0	0	0	0	2	1.0	0	0	0	0
Enim	6	2.8	2	0.9	0	0	5	2.6	3	1.2	0	0
GICU	18	8.5	30	13.0	0	0	9	5.0	52	20.0	0	0
Igd	19	9.0	33	14.2	0	0	29	15.1	23	9.0	1	33.0
Kelingi	8	3.8	16	6.9	1	9.1	7	3.6	19	7.0	0	0
Komering	31	14.7	34	14.7	3	27.2	30	15.6	49	19.0	2	67.0
Lakitan	23	11.0	8	3.4	0	0	20	10.4	10	4.0	0	0
Lematang	10	4.7	10	4.3	1	9.1	9	4.7	3	1.2	0	0
Musi	9	4.3	8	3.4	0	0	9	4.7	6	2.3	0	0
NICU	1	0.5	13	5.6	0	0	0	0	11	4.2	0	0
Ogan	2	0.9	3	1.3	0	0	5	2.6	5	1.9	0	0
PICU	5	2.4	6	2.6	0	0	3	1.6	6	2.0	0	0
Rambang	10	4.7	2	0.9	2	18.2	6	3.0	3	1.2	0	0
Rawas	24	11.4	21	9.0	1	9.1	16	8.3	19	7.0	0	0
Selincah	36	17.0	39	16.8	2	18.2	36	18.8	44	17.0	0	0
TOTAL	211	100	232	100	11	100	192	100	260	100	3	100

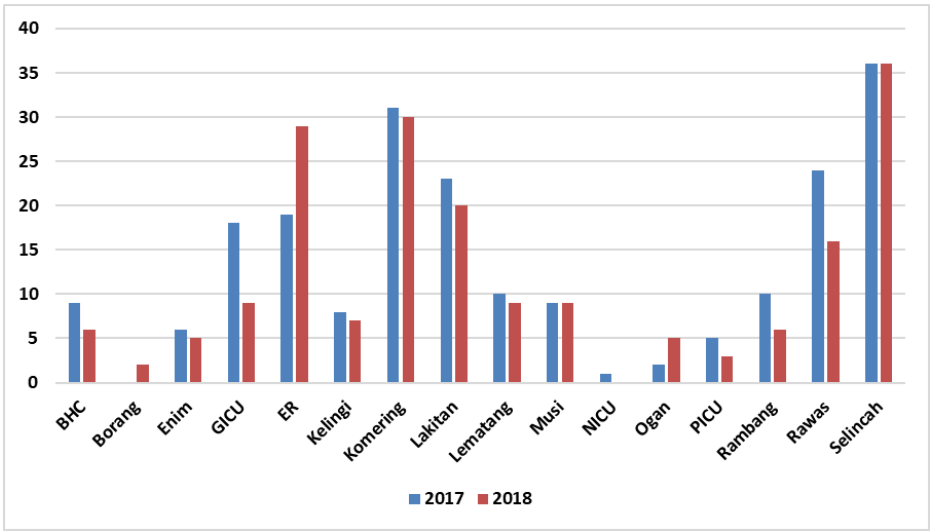

Figure 3. ESBL-producing *Escherichia coli* Findings Based on Treatment Wards

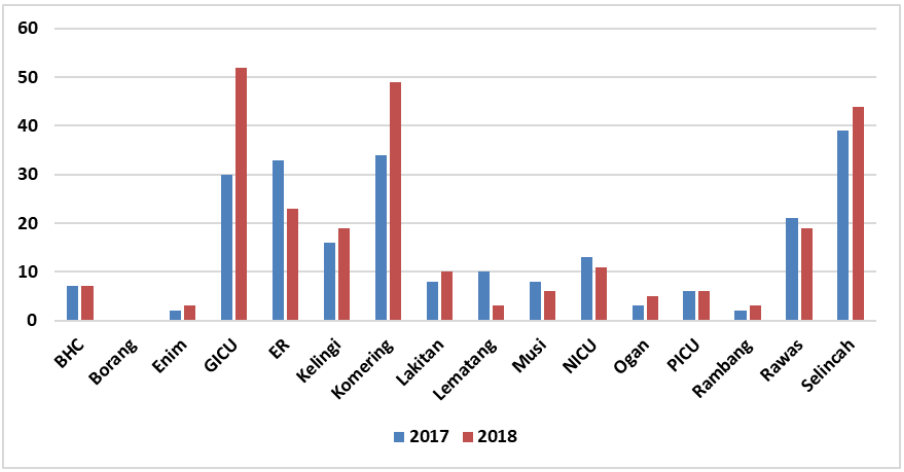

Figure 4. ESBL-producing *Klebsiella pneumoniae* Findings Based on Treatment Wards

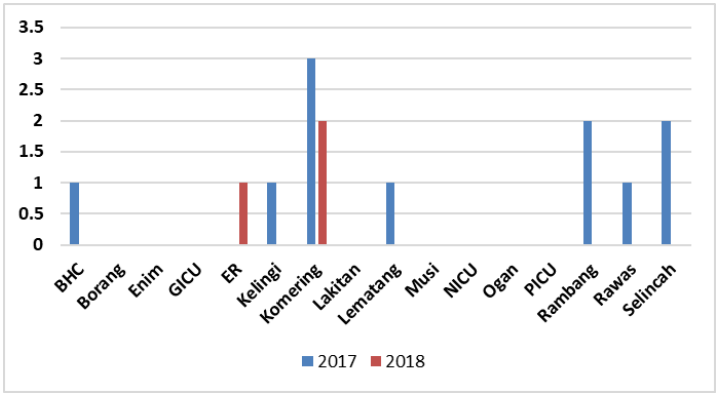

Figure 5. ESBL-producing *Klebsiella ozaenae*Findings Based on Treatment Wards

Urine was the specimen with the most ESBL *E. coli* in both periods (37.2% and 44.0%). Meanwhile, different findings were observed in *K. pneumoniae*, which was frequently found in sputum (48.0% and 45.9%). Meanwhile, in *K. ozaenae*, sputum samples dominated in 2017, and urine samples were overtaken in 2018. Table 4 presented the ESBL distribution based on 2017 and 2018 specimens.

In this study, the incidence of ESBL in Dr. Mohammad Hoesin hospital decreased in 2018 compared to cases in 2017. In Indonesia, accurate data on the prevalence of ESBL-producing bacteria are still scarce.[7] However, some studies stated an increase in the incidence

of ESBL in the Enterobacteriaceae family.[12–14] Nosocomial infections can play a role in this increase.[15]These infections can spread through direct or indirect contact and can originate in hospitals, clinics, or healthcare facilities.[16]

Table 4. Distribution of ESBL Based on Collected Specimens

Specimen Type	*E. coli*				*K. pneumoniae*				*K. ozaenae*			
	2017		2018		2017		2018		2017		2018	
	n	%	n	%	n	%	N	%	n	%	n	%
Sputum	37	15.5	31	15.0	117	48.0	123	45.9	5	46.0	1	25.0
Blood	13	5.4	14	7.0	35	14.3	28	10.4	1	9.0	0	0
Pus	54	23.0	38	18.0	15	6.1	32	12.0	1	9.0	1	25.0
Swab	18	7.5	14	7.0	13	5.3	16	6.0	1	9.0	0	0
Urine	89	37.2	92	44.0	45	18.4	54	20.1	3	27.0	2	50.0
Other Body Fluids	13	5.4	8	4.0	12	5.0	9	3.4	0	0	0	0
Feces	15	6.0	10	5.0	7	2.9	6	2.2	0	0	0	0
Total	239	100	207	100	244	100	268	100	11	100	4	100

In various studies, an increase in the number of ESBL bacteria has been linked to an increase in antibiotic resistance cases.[17] This can have various consequences, including a reduction in the efficacy of antibiotics for exterminating bacteria (due to disruption of the target site, drug entry, and distribution inhibition), as well as a greater economic burden.[18] Inappropriate use of antibiotics in certain clinical situations, such as the administration of antibiotics in the absence of bacterial infection, incorrect antibiotic selection, and inappropriate or excessive doses, can cause transformation in bacterial strains to become more resistant.[19]

In this study, most ESBL cases were found in K. pneumoniae, E. coli, and K. ozaenae organisms, respectively. The prevalence of Klebsiella pneumoniae and E. coli with the ESBL trait was 42.2% and 35.8%, sequentially, according to research published by the Study for Monitoring Antimicrobial Resistance Trends (SMART).[20] Meanwhile, data from Aceh, Indonesia, revealed that Klebsiella pneumoniae was more common than E. coli in terms of ESBL infection (61% vs. 39%).[21] This is consistent with the literature, which states that bacteria from the Enterobacteriaceae family, particularly Klebsiella pneumoniae and Escherichia coli, produce the beta-lactamase enzyme frequently.[22]*Klebsiella pneumoniae* usually infected immunodeficient persons, including alcoholics, diabetes

mellitus, and chronic lung disease sufferers,[23] leading to an increased risk of getting ESBL traits.[24] Meanwhile, ESBL-producing *Escherichia coli* infection was associated with urinary catheterization due to urinary tract infections and irrational antibiotic use particularly Penicillins and first-generation cephalosporins.[25]

Comment [MOU6]: Tambahkan pembahasan mengapa ada penurunan prevalensi ESBL pada 2018.

In this study, inpatients had a higher rate of ESBL than outpatients. These findings were consistent with those from Nigeria, which found that hospitalized patients were more likely to have positive ESBL traits (54.9% vs. 30.2%).[26] A study in Turkey found that the highest prevalence was found for inpatients with ESBL-producing *K. pneumoniae* (25%-60.5%) and the lowest prevalence was found in outpatient ESBL-producing *E. coli* (9.6 %-22.8%).[12] Pediatric wards, internal medicine, and intensive care units were the most commonly affected rooms of inpatients. The findings were similar to those from previous studies, which identified pediatric wards, internal medicine, and intensive care as the most common locations for ESBL-producing bacteria.[27] The high density of patients admitted to the internal medicine and pediatric wards facilitate the horizontal spread of resistant genes through conjugation, transduction, and transformation modes.[28]According to research conducted in Semarang, Indonesia, ESBL-producing bacteria were found eight times more frequently in children than in adults, particularly in the intensive care unit,[29]and are associated with the immature immunity status in children.[30] High rates of antibiotic use and long length of stay in intensive care units also increase the risk of ESBL colonization and infection.[31] According to a study conducted in Makassar, 53.7% of the ICU isolates examined had multi-drug resistant organisms.[32]

ESBL-producing bacteria were found in a variety of specimens, depending on the type of bacteria. Urine specimens were the most common source of *Escherichia coli*, while sputum was the most frequent site of *Klebsiella pneumoniae*. In a previous study in Pekanbaru, the dominance of *K. pneumoniae* in sputum was also demonstrated (43.7%).[33] Previous research in Nepal, Bangladesh, and Indonesia revealed a prevalent *E. coli* profile in urine.[21,34,35]However, another study from Indonesia shows that the majority of *E. coli* was found in pus.[33]

CONCLUSION AND SUGGESTION

The prevalence of ESBL-producing bacteria is quite high at Dr. Mohammad Hoesin hospital, with more than 60% of cases in 2017 and 2018. The most common ESBL-producing bacteria found in inpatients treated at the pediatric wards, internal medicine, and intensive care units is *Klebsiella pneumoniae*. The pattern of ESBL-producing bacteria differed

depending on the specimen, with sputum in *K. pneumoniae* and urine in *E. coli* being the most frequent sites. Additional research could be focused on determining the risk factors for infection with ESBL-producing Enterobacteriaceae in the affected population.

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RESEARCH

PREVALENCE OF EXTENDED SPECTRUM BETA-LACTAMASE-PRODUCING MICROORGANISMS IN DR. MOHAMMAD HOESIN HOSPITAL PALEMBANG IN 2017-2018

Comment [H1]: Klepsiella sp and E. coli

(Prevalensi Mikroorganisme yang Memproduksi Extended Spectrum Beta-Lactamase di Rumah Sakit Dr. Mohammad Hoesin Palembang Pada 2017-2018)

Phey Liana[1], Norlaila Binti Chahril[2], Sri Nita[3], Tungki Pratama Umar[1]

ABSTRAK

Produksi Extended Spectrum Beta-Lactamase (ESBL) oleh Enterobacteriaceae terus menjadi masalah penyakit menular terutama di rumah sakit. Penyebab utama kolonisasibakteripenghasil ESBL adalah infeksi saluran kemih, lama rawat inap di rumah sakit, peralatan medis yang invasif, dan antibiotic. Penelitian ini bertujuan untuk mengetahui perbandingan kejadian ESBL berdasarkan jenis organisme di Rumah Sakit Dr. Mohammad Hoesin Periode 2017 dan 2018. Desain penelitian yang digunakan adalah deskriptif dengan pendekatan cross sectional, yang menggunakan data sekunder di Instalasi Patologi Klinik RSUP Dr. Mohammad Hoesin Palembang. Temuan penelitian ini menunjukkan adanya pola penurunan pada kejadian ESBL pada tahun 2017 dan 2018, namun dengan pola serupa yang didominasi oleh Klebsiella pneumoniae (diikuti Escherichia coli dan Klebsiella ozaenae), pasien rawat inap di bangsal anak, penyakit dalam, dan ruang rawat intensif, serta pada spesimen sputum. Penelitian ini menunjukkan adanya tingkat bakteri penghasil ESBL yang tinggi di RS Dr. Mohammad Hoesin (>60%), yang terutama disebabkan oleh Klebsiella pneumoniae.

Kata kunci: *Extended-Spectrum Beta-Lactamase,Klebsiella Pneumoniae, Enterobacteriaceae*

ABSTRACT

Production of Extended-Spectrum Beta-Lactamase (ESBL) by Enterobacteriaceae continues to be a problem of infectious diseases, especially in hospitals. The main causes of ESBL-producing bacteria colonization are urinary tract infections, length of hospital stay, invasive medical equipment, and antibiotics. This study aims to compare the incidence of ESBL based on the type of organism in Dr. Mohammad Hoesin Hospital for the 2017 and 2018 periods. The research design used was descriptive with a cross-sectional approach, which used

secondary data at the Clinical Pathology Department of Dr. RSUP. Mohammad Hoesin Palembang. The findings of this study showed a decreasing pattern in the incidence of ESBL in 2017 and 2018, but with a similar pattern which was dominated by *Klebsiella pneumoniae* (followed by *Escherichia coli* and *Klebsiella ozaenae*), inpatients in pediatric wards, internal medicine, and intensive care units, and on sputum specimens. This study showed the presence of high levels of ESBL-producing bacteria (>60%) in Dr. Mohammad Hoesin hospital which was mainly caused by *Klebsiella pneumoniae*.

Keywords: Extended-Spectrum Beta-Lactamase, *Klebsiella Pneumoniae,* Enterobacteriaceae

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INTRODUCTION

Infectious infections are a major issue in developing countries such as Indonesia.[1] In addition to the disease's high prevalence, other issues such as irrational antibiotic use can lead to microorganism resistance. Various surveillance data demonstrate a wide range of irrational antibiotic use, ranging from 35.1% (Ethiopia)[2] to 37.8% (Pakistan)[3] to 68.4% in Indonesia.[4]

Antibiotic resistance is a change in bacteria's capacity to diminish the antibiotic action, mediated mostly by upregulation of drug efflux pumps.[5] Resistance initially began in hospitals, but it gradually spread across the community, particularly among *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Escherichia coli*.[6] Multi-resistant bacteria, including Methicilin-Resistant Staphylococcus aureus (MRSA) and Extended-Spectrum Beta-Lactamase (ESBL)-producing bacteria dominated the incidence of resistance, as mentioned by the Antimicrobial Resistance in Indonesia, Prevalence and Prevention (AMRIN) study.[7] Infections caused by bacteria that generate ESBL have increased dramatically in recent years. The ESBL mediates the hydrolysis and inactivation of beta-lactam antibiotics, including third-generation cephalosporins, penicillins, and Aztreonam.[8]

ESBL is produced by mutations of beta-lactamase enzymes Temoneira-1 (TEM-1), Temoneira-2 (TEM-2), and Sulphydryl-1 (SHV-1) which are commonly found in the

Enterobacteriaceae family. Penicillin and first-generation cephalosporins are typically resistant to these enzymes.[9] The family Enterobacteriaceae have many genera such as *Escherichia coli*, *Klebsiella*, *Salmonella*, *Shigella*, *Enterobacter*, *Proteus*, and *Serratia* with about 20-25 species of clinical importance.[10] According to Nazmi, et al., the prevalence of ESBL-producing E.coli and K. pneumoniae infections were 35% and 45%, respectively. In contrast to *K. pneumoniae*, ESBL production in E. coli was mostly found in outpatients.[11] The high occurrence of ESBL-producing bacteria serves as the landscape for this study, which compares the prevalence of ESBL based on the type of organism at the Dr. Mohammad Hoesin General Hospital from 2017 to 2018.Objective of the study?

METHODS

This cross-sectional study used secondary data from Clinical Pathology and Microbiology Department, Dr. Mohammad Hoesin Palembang's Central General Hospital, a tertiary hospital in South Sumatra. Patients who had culture and antibiotic resistance tests (outpatients and inpatients) between July-December 2017 and January-June 2018 were enrolled in this study. The inpatients were originated from 15 wards, including the Emergency Room (ER), Intensive Care Unit/ICU (General, Pediatric, and Neonates), Internal Medicine (Komering), Neurology (Rawas and Brain and Health Center/BHC), Obstetrics and Gynecology (Enim), Oncology (Rambang), Ophthalmology (Kelingi), Otorhinolaryngology (Lematang), Pediatric (Kelingi), Respiratory (Borang), Surgery (Lakitan) and VIP (Musi). Patient data were collected using the total sampling technique, which included culture results and antibiotic resistance tests with ESBL bacteria. A double-disk approximation test was used to identify ESBL strains using the antibiotics cefotaxime, ceftazidime, and cefepime. The study was approved by the institutional review board of Universitas Sriwijaya, Faculty of Medicine, Palembang, Indonesia (Approval Number: 251/kepfkrsmh/2018).

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A descriptive analysis of the variables collected was conducted; qualitative variables were expressed as percentages. All statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS®), version 25.0 (IBM SPSS Corp., Armonk, NY, USA) software.

RESULTS AND DISCUSSION

The total ESBL-producing bacteria identified in this study showed decreasing pattern from 78.5% in 2017 to 60.3% in 2018. *Klebsiella pneumoniae* was the most commonly identified organism that produced the most ESBL during the study period (2017 and 2018),

with 244 (49.4%) and 268 (56.0%) cases, respectively. Further bacterial findings followed a similar pattern in the consecutive years, with *Escherichia coli* and *Klebsiella ozaenae* being the second and third-highest organisms in terms of ESBL incidence (Table 1 and Figure 1.).

Table 1. *Extended-Spectrum Beta-Lactamase* (ESBL)Prevalence in 2017 and 2018

Organisms	ESBL					
	2017			2018		
	ESBL (+), %	ESBL (-), %	% of ESBL (+)	ESBL (+), %	ESBL (-), %	% of ESBL (+)
Escherichia.coli	239, 83.3%	48, 16.7%	48.4	207, 54.0%	177, 46.0%	43.2
Klebsiella pneumoniae	244, 74.2%	85, 25.8%	49.4	268, 53.3%	235, 46.7%	56.0
Klebsiella.ozaenae	11, 85.0%	2, 15.0%	2.2	4, 57.0%	3, 43.0%	0.8
TOTAL	494, 78.5%	135, 21.5%	100%	479, 60.3%	315, 39.7%	100

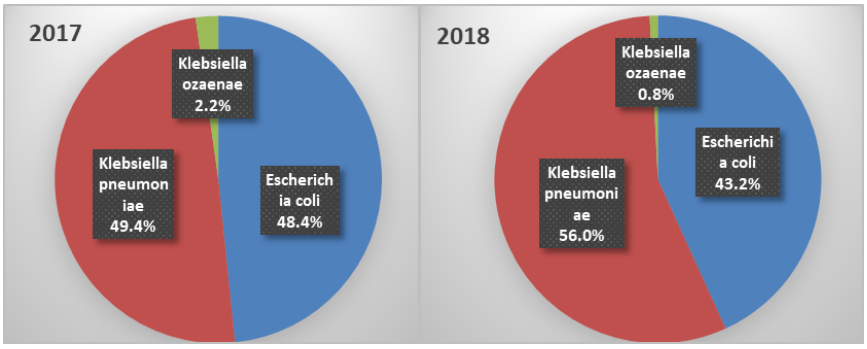

Figure 1. *Extended-Spectrum Beta-Lactamase* (ESBL) Prevalence in 2017 and 2018

Table 1 and figure 1 is redundancy, it should be ovoided!

The incidence of ESBL caused by *Klebsiella pneumoniae*, *Escherichia coli*, and *Klebsiella ozaenae* bacteria showed findings that were more frequently found in hospitalized cases between 2017 and 2018 (91.9% and 95.0%). Inpatient cases were dominated by *Klebsiella pneumoniae*, while outpatient cases were overtaken by *Escherichia coli*. Table 2 dan Figure 2 displays the details.

Table 2. ESBL Prevalence Between Outpatients and Inpatients

Organisms	2017				2018			
	Outpatients		Inpatients		Outpatients		Inpatients	
	n	%	n	%	n	%	n	%
E.coli	28	70.0	211	46.5	15	62.5	192	42.2
K.pneumoniae	12	30.0	232	51.1	8	33.3	260	57.1
K.ozaenae	0	0.0	11	2.4	1	4.2	3	0.7
TOTAL	40	100	454	100	24	100	455	100

Comment [H3]: Prevalence of ESBL producing Klepsiella sp and E. coli in 2017 and 2018

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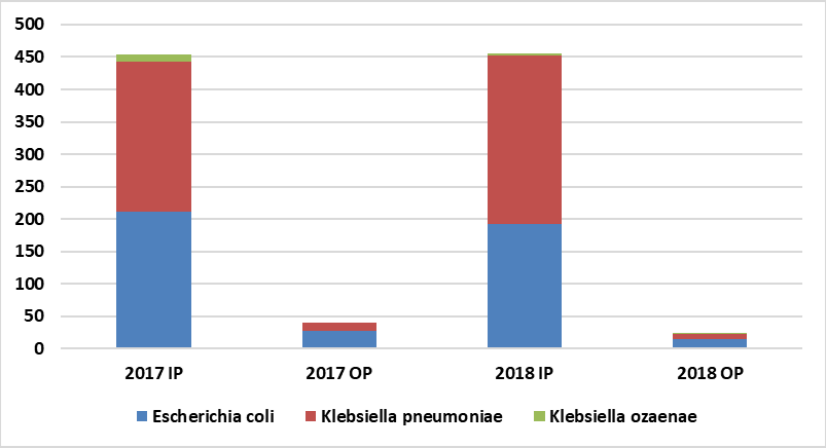

Figure 2. ESBL Prevalence Between Outpatients and Inpatients; (IP= Inpatients, OP=Outpatients)

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In detail, the types of ESBL bacteria based on the type of inpatient room can be seen in table 3. The general findings indicated that the internal medicine (Komering), pediatric (Selincah), and intensive care wards (IGD and GICU) were the most common places for ESBL findings, especially for the two dominant microorganisms in this study, *K. pneumoniae*, and *E. coli*. Figures 3-5 displays details the types ESBL bacteria based on treatment wards.

Table 3. ESBL Findings Based on Treatment Wards

Wards	2017						2018					
	E. coli		*K .pneumoniae*		*K. ozaenae*		*E. coli*		*K. pneumoniae*		*K. ozaenae*	
	n	%	n	%	n	%	n	%	n	%	n	%
BHC	9	4.3	7	3.0	1	9.1	6	3.0	7	3.0	0	0
Borang	0	0	0	0	0	0	2	1.0	0	0	0	0
Enim	6	2.8	2	0.9	0	0	5	2.6	3	1.2	0	0
GICU	18	8.5	30	13.0	0	0	9	5.0	52	20.0	0	0
Igd	19	9.0	33	14.2	0	0	29	15.1	23	9.0	1	33.0
Kelingi	8	3.8	16	6.9	1	9.1	7	3.6	19	7.0	0	0
Komering	31	14.7	34	14.7	3	27.2	30	15.6	49	19.0	2	67.0
Lakitan	23	11.0	8	3.4	0	0	20	10.4	10	4.0	0	0
Lematang	10	4.7	10	4.3	1	9.1	9	4.7	3	1.2	0	0
Musi	9	4.3	8	3.4	0	0	9	4.7	6	2.3	0	0
NICU	1	0.5	13	5.6	0	0	0	0	11	4.2	0	0
Ogan	2	0.9	3	1.3	0	0	5	2.6	5	1.9	0	0
PICU	5	2.4	6	2.6	0	0	3	1.6	6	2.0	0	0
Rambang	10	4.7	2	0.9	2	18.2	6	3.0	3	1.2	0	0
Rawas	24	11.4	21	9.0	1	9.1	16	8.3	19	7.0	0	0
Selincah	36	17.0	39	16.8	2	18.2	36	18.8	44	17.0	0	0
TOTAL	211	100	232	100	11	100	192	100	260	100	3	100

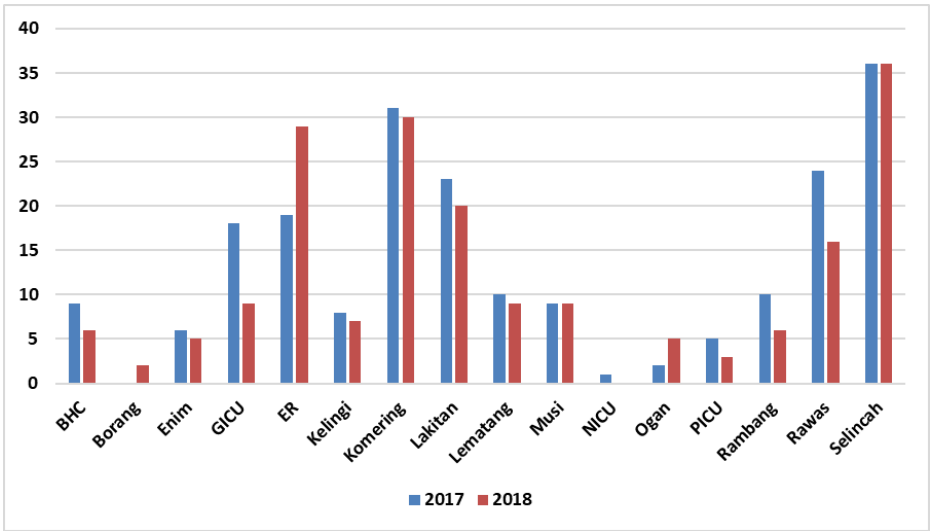

Figure 3. ESBL-producing *Escherichia coli* Findings Based on Treatment Wards

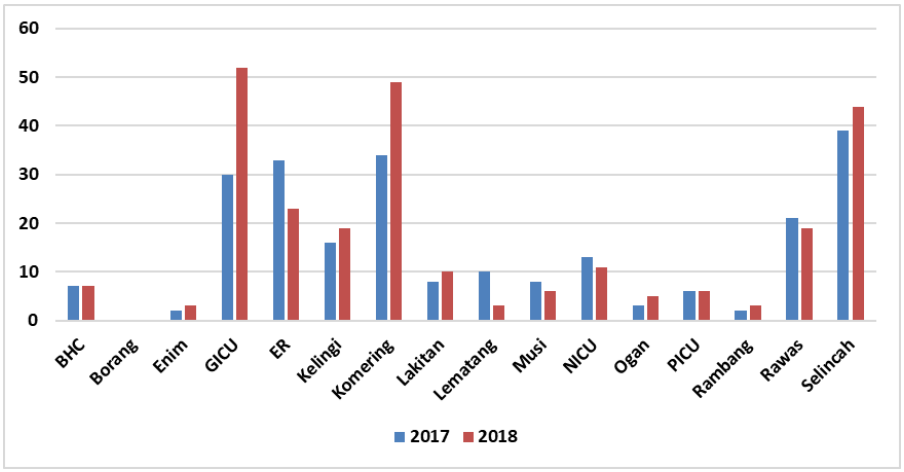

Figure 4. ESBL-producing *Klebsiella pneumoniae*Findings Based on Treatment Wards

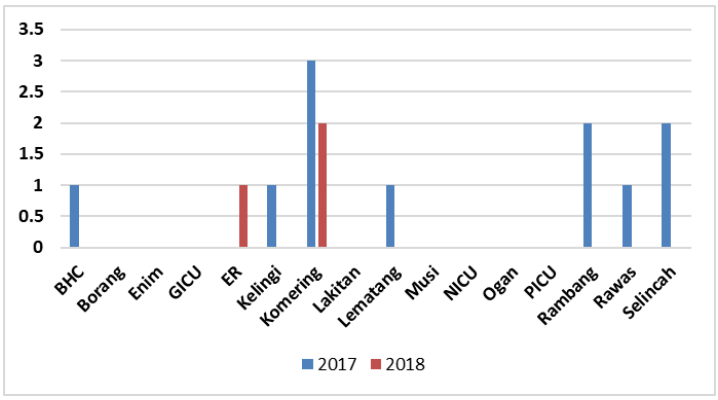

Figure 5. ESBL-producing *Klebsiella ozaenae*Findings Based on Treatment Wards

Table 3 and figure 3, 4, and 5 are redundancy, it should be avoided!!

Urine was the specimen with the most ESBL *E. coli* in both periods (37.2% and 44.0%). Meanwhile, different findings were observed in *K. pneumoniae*, which was frequently found in sputum (48.0% and 45.9%). Meanwhile, in *K. ozaenae*, sputum samples dominated in 2017, and urine samples were overtaken in 2018. Table 4 presented the ESBL distribution based on 2017 and 2018 specimens.

In this study, the incidence of ESBL in Dr. Mohammad Hoesin hospital decreased in 2018 compared to cases in 2017. In Indonesia, accurate data on the prevalence of ESBL-

producing bacteria are still scarce.[7] However, some studies stated an increase in the incidence of ESBL in the Enterobacteriaceae family.[12–14] Nosocomial infections can play a role in this increase.[15]These infections can spread through direct or indirect contact and can originate in hospitals, clinics, or healthcare facilities.[16]

Table 4.Distribution of ESBL Based on Collected Specimens

Specimen Type	*E. coli*				*K. pneumoniae*				*K. ozaenae*			
	2017		2018		2017		2018		2017		2018	
	n	%	n	%	n	%	N	%	n	%	n	%
Sputum	37	15.5	31	15.0	117	48.0	123	45.9	5	46.0	1	25.0
Blood	13	5.4	14	7.0	35	14.3	28	10.4	1	9.0	0	0
Pus	54	23.0	38	18.0	15	6.1	32	12.0	1	9.0	1	25.0
Swab	18	7.5	14	7.0	13	5.3	16	6.0	1	9.0	0	0
Urine	89	37.2	92	44.0	45	18.4	54	20.1	3	27.0	2	50.0
Other Body Fluids	13	5.4	8	4.0	12	5.0	9	3.4	0	0	0	0
Feces	15	6.0	10	5.0	7	2.9	6	2.2	0	0	0	0
Total	239	100	207	100	244	100	268	100	11	100	4	100

In various studies, an increase in the number of ESBL bacteria has been linked to an increase in antibiotic resistance cases.[17] This can have various consequences, including a reduction in the efficacy of antibiotics for exterminating bacteria (due to disruption of the target site, drug entry, and distribution inhibition), as well as a greater economic burden.[18] Inappropriate use of antibiotics in certain clinical situations, such as the administration of antibiotics in the absence of bacterial infection, incorrect antibiotic selection, and inappropriate or excessive doses, can cause transformation in bacterial strains to become more resistant.[19]

In this study, most ESBL cases were found in K. pneumoniae, E. coli, and K. ozaenae organisms, respectively. The prevalence of Klebsiella pneumoniae and E. coli with the ESBL trait was 42.2% and 35.8%, sequentially, according to research published by the Study for Monitoring Antimicrobial Resistance Trends (SMART).[20] Meanwhile, data from Aceh, Indonesia, revealed that Klebsiella pneumoniae was more common than E. coli in terms of ESBL infection (61% vs. 39%).[21] This is consistent with the literature, which states that bacteria from the Enterobacteriaceae family, particularly Klebsiella pneumoniae and Escherichia coli, produce the beta-lactamase enzyme frequently.[22]*Klebsiella*

pneumoniae usually infected immunodeficient persons, including alcoholics, diabetes mellitus, and chronic lung disease sufferers,[23] leading to an increased risk of getting ESBL traits.[24] Meanwhile, ESBL-producing *Escherichia coli* infection was associated with urinary catheterization due to urinary tract infections and irrational antibiotic use particularly Penicillins and first-generation cephalosporins.[25]

In this study, inpatients had a higher rate of ESBL than outpatients. These findings were consistent with those from Nigeria, which found that hospitalized patients were more likely to have positive ESBL traits (54.9% vs. 30.2%).[26] A study in Turkey found that the highest prevalence was found for inpatients with ESBL-producing *K. pneumoniae* (25%-60.5%) and the lowest prevalence was found in outpatient ESBL-producing *E. coli* (9.6 %-22.8%).[12] Pediatric wards, internal medicine, and intensive care units were the most commonly affected rooms of inpatients. The findings were similar to those from previous studies, which identified pediatric wards, internal medicine, and intensive care as the most common locations for ESBL-producing bacteria.[27] The high density of patients admitted to the internal medicine and pediatric wards facilitate the horizontal spread of resistant genes through conjugation, transduction, and transformation modes.[28]According to research conducted in Semarang, Indonesia, ESBL-producing bacteria were found eight times more frequently in children than in adults, particularly in the intensive care unit,[29]and are associated with the immature immunity status in children.[30] High rates of antibiotic use and long length of stay in intensive care units also increase the risk of ESBL colonization and infection.[31] According to a study conducted in Makassar, 53.7% of the ICU isolates examined had multi-drug resistant organisms.[32]

ESBL-producing bacteria were found in a variety of specimens, depending on the type of bacteria. Urine specimens were the most common source of *Escherichia coli*, while sputum was the most frequent site of *Klebsiella pneumoniae*. In a previous study in Pekanbaru, the dominance of *K. pneumoniae* in sputum was also demonstrated (43.7%).[33] Previous research in Nepal, Bangladesh, and Indonesia revealed a prevalent *E. coli* profile in urine.[21,34,35]However, another study from Indonesia shows that the majority of *E. coli* was found in pus.[33]

CONCLUSION AND SUGGESTION

The prevalence of ESBL-producing bacteria is quite high at Dr. Mohammad Hoesin hospital, with more than 60% of cases in 2017 and 2018. The most common ESBL-producing bacteria found in inpatients treated at the pediatric wards, internal medicine, and intensive

care units is *Klebsiella pneumoniae*. The pattern of ESBL-producing bacteria differed depending on the specimen, with sputum in *K. pneumoniae* and urine in *E. coli* being the most frequent sites. Additional research could be focused on determining the risk factors for infection with ESBL-producing Enterobacteriaceae in the affected population.

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