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RESEARCH ARTICLE

Comparative distribution and antibiotic susceptibility of extended-spectrum beta-lactamase- and non-extended-spectrum beta-lactamase-producing *Proteus mirabilis* in wound infections at Zainoel Abidin General Hospital, Banda Aceh, Indonesia

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ABSTRACT

Background and Aim: *Proteus mirabilis*, an opportunistic pathogen of the Enterobacteriaceae family, is frequently implicated in wound infections and exhibits significant antibiotic resistance, particularly through the production of extended-spectrum beta-lactamase (ESBL). This study aimed to determine the occurrence and antibiotic susceptibility of ESBL-producing and non-ESBL *P. mirabilis* isolates in wound infections at Zainoel Abidin General Hospital, Banda Aceh, Indonesia.

Materials and Methods: A cross-sectional study was conducted on wound specimens collected between January 2021 and March 2024. Bacterial identification and antimicrobial susceptibility testing were performed using the VITEK® 2 Compact system. Statistical analyses were conducted using Chi-square or Fisher statistical analyses significance set at $p \leq 0.05$.

Results: A total of 153 *P. mirabilis* isolates were identified, of which 60 (39.22%) were ESBL-producing and 93 (60.78%) were non-ESBL-producing. The highest occurrence was observed in male patients (55% ESBL and 54.84% non-ESBL) and in patients older than 55 years (48.33% ESBL and 38.71% non-ESBL). Antibiotic susceptibility testing revealed that ESBL-producing isolates were highly susceptible to cefoperazone/sulbactam (98.67%), meropenem (98.33%), amikacin (96.67%), and piperacillin/tazobactam (91.67%). Non-ESBL isolates exhibited the highest susceptibility to amikacin (97.85%), cefoperazone/sulbactam (96.77%), piperacillin/tazobactam (91.67%), and ceftazidime (90.32%). Notably, ESBL-producing isolates exhibited resistance to amoxicillin (0%), ampicillin (1.67%), cefotaxime (8.33%), and levofloxacin (10%).

Conclusion: The high occurrence of ESBL-producing *P. mirabilis*, particularly in elderly patients, underscores the need for routine ESBL screening and targeted antibiotic therapy. The observed differences in antibiotic susceptibility between ESBL and non-ESBL isolates highlight the importance of early detection for appropriate antibiotic selection in wound infection management. Continued surveillance and antimicrobial stewardship are crucial in mitigating the impact of antibiotic-resistant *P. mirabilis* in clinical settings.

Keywords: antibiotic resistance, antimicrobial susceptibility, extended-spectrum beta-lactamase, *Proteus mirabilis*, wound infection.

INTRODUCTION

Infectious diseases are still common around the world, and bacterial pathogens remain the most important pathogens with high fatality rates. *Proteus mirabilis* is a pathogenic non-spore-forming Gram-negative (GN) rod clinically important opportunistic pathogen. This facultative anaerobic organism belongs to the group of *Enterobacteriaceae* and is commonly found in the normal intestinal flora of humans and animals. However, it may also become

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pathogenic under certain conditions, especially following common healthcare exposure [1, 2]. Epidemiological studies have shown that *P. mirabilis* poses a burden in recent clinical practice. A significant incidence of *P. mirabilis* was reported in diabetic foot wounds [3]. Our previous investigation with Zainoel Abidin Hospital in Banda Aceh reported that examinations conducted between 2012 and 2018, there were 121 *P. mirabilis* isolates recovered from pus specimens submitted to clinical laboratory [1].

Wounds pose a particularly significant challenge to antibiotic resistance against *P. mirabilis* due to several key factors. First, the wound environment provides optimal conditions for *P. mirabilis* growth, including moisture, tissue damage, and reduced oxygen tension [4]. Second, *P. mirabilis* possesses specific virulence factors that make it especially problematic in wound infections, as its unique swarming ability allows rapid colonization of wound surfaces, whereas its urease production creates an alkaline environment that promotes bacterial growth and impairs wound healing [5]. Third, studies have shown that *P. mirabilis* isolated from wounds has a significantly higher rate of biofilm formation (70%–85%) compared to isolates from other sites, making treatment particularly challenging, as biofilms limit both immune system response and antibiotic effectiveness [6, 7].

It is well-documented that there are extended-spectrum beta-lactamase (ESBL)-producing bacteria in the world, and this has happened in large part because antimicrobial drugs have been misused and overused across hospitals and communities. A previous study by Kwiecinska-Pirog *et al*. [6] described widespread variability in ESBL production in isolates of *P. mirabilis*, with 36.4% of wound swab isolates identified as ESBL producers. Priya and Leela [8] identified ESBL-producing *P. mirabilis* in various clinical specimens, particularly from pus and wound swabs, highlighting the widespread distribution of these resistant strains in healthcare settings.

Given the clinical significance of *P. mirabilis* infections, concerns regarding ESBL-producing organisms, and the urgent need for surveillance to support empirical antibiotic treatment, this study elucidates the occurrence and antibiotic profiles of *P. mirabilis* in Aceh Province, Indonesia. This will help with proper control of *P. mirabilis* in the area, but more generally, it will be useful for infection control, antibiotic stewardship within hospitals, and international monitoring. This study aimed to determine the occurrence and antibiotic susceptibility profiles of ESBL-producing and non-ESBL *P. mirabilis* isolates in wound infections at Zainoel Abidin General Hospital, Banda Aceh, Indonesia, to provide insights into their clinical impact and guide effective antimicrobial treatment strategies.

MATERIALS AND METHODS

Ethical approval

The study was approved by the Health Research Ethics Committee of Zainoel Abidin Hospital (approval no. 278/ETIK-RSUDZA/2023).

Study period and location

The data in the study were collected from January 2021 to March 2024 at the Clinical Microbiology Laboratory, Integrated Laboratory Installation of Zainoel Abidin Hospital, Banda Aceh, Indonesia.

Study design and settings

This retrospective cross-sectional study analyzed laboratory data and bacterial isolates collected during routine clinical care at Zainoel Abidin Hospital, Banda Aceh, Indonesia.

Sample collection, bacterial isolation, observation, and identification

Abscess fluid, swabs, and wound biopsy specimens were collected from patients who had a wound infection and routinely collected using standard microbiology methods. Sterile swabs were used to minimize sample contamination. The samples were inoculated onto blood and MacConkey agar (MCA) media and later incubated at 37°C for 24 h. The pure colonies formed after growth on blood and MCA medium were visually assessed for colony features such as size, shape, color, texture, margins, and elevation. In addition, they were Gram-stained and observed using a light microscope at 1000×.

VITEK® 2 Compact (Biomeriux, Lyon, France) was used to perform bacterial identification and antibiotic susceptibility testing (AST). The VITEK® 2 Compact system (Biomeriux) is an automated platform that utilizes colorimetric reagent cards for bacterial identification and antimicrobial susceptibility testing. The system employs VITEK® 2 GN identification cards containing 64 biochemical tests that measure carbon source utilization, enzymatic activities, and resistance patterns for bacterial identification. The results were obtained by kinetic analysis of the growth patterns measured by optical scanning at 15-min intervals. A single pure strain was streaked out from clinical samples and directly suspended in isotonic saline containing 0.45% NaCl, which was found to be mixed to reach a turbidity of 1.8–2.2 McFarland standard solution. Then, the pure strain was spread into GN cassettes for identification and marched into AST cassettes for determination of antibiotic sensitivity.

Antibiotic sensitivity testing

In antimicrobial susceptibility testing, the system uses AST-GN cards specific for GN organisms containing serial dilutions of antibiotics. The system measures bacterial growth in wells containing different antibiotic concentrations through optical scanning, generates Minimum Inhibitory Concentration values based on

growth patterns, and interprets results as Susceptible, Intermediate, or Resistant according to Clinical and Laboratory Standards Institute breakpoints. Antibiotic sensitivity was tested against a panel of antibiotics, including amoxicillin, ampicillin, amoxicillin/clavulanic, piperacillin/tazobactam, cefoxitin, cefotaxime, ceftazidime, ceftriaxone, cefoperazone/sulbactam, imipenem, meropenem, amikacin, gentamicin, tobramycin, levofloxacin, and doxycycline.

Statistical analysis

Descriptive statistics were used to summarize the occurrence of ESBL-producing and non-ESBL *P. mirabilis* isolates across different patient demographics, including age and gender. Categorical variables are expressed as frequencies and percentages. Associations between ESBL status and categorical variables such as patient gender and age group were analyzed using the Chi-square. Fisher's exact test was applied where expected frequencies in any category were <5. To assess differences in antibiotic susceptibility between ESBL and non-ESBL isolates, Chi-square tests were conducted for each antibiotic tested. Odds ratios with 95% confidence intervals were calculated to evaluate the strength of the association between ESBL production and antibiotic resistance. A Chi-square test for trend was employed to examine temporal variations in ESBL occurrence over the study period. P-value ≤ 0.05 was considered statistically significant. Statistical analyses were performed using the Julius (Caesar Labs, Inc, San Francisco, CA, USA), while Microsoft Excel Version 16.91 (Microsoft Office, Redmond, WA, USA) was used for preliminary data visualization and descriptive statistics.

RESULTS

Over the entire study period from January 2021 to March 2024, 153 *P. mirabilis* isolates were identified from 3545 wound specimens. The colonies exhibited a spreading growth pattern, which was attributed to the swarming phenomenon characteristic of *P. mirabilis*. The gray colonies were round with smooth edges, raised elevation, and a smooth texture (Figure 1a), whereas on MCA media, *P. mirabilis* colonies were colorless with size ranged from 1 mm to 2 mm in diameter (Figure 1b). Microscopic examination following Gram staining revealed that *P. mirabilis* cells appeared as red-stained, short rods arranged either singly or in groups (Figure 1c).

The high number of isolates underscores the significance of *P. mirabilis* as a pathogen in wound infections at our healthcare facility. Of these *P. mirabilis* isolates, 60 (39.22%) isolates were found to be ESBL-producing, whereas 93 (60.78%) isolates were non-ESBL producers (Table 1). The distribution of ESBL and non-ESBL isolates did not appear to be significantly different across the three study periods, as there was no significant association between *P. mirabilis* isolate types and study periods ($\chi^2 = 4.1594$, $p = 0.125$).

Figure 2 shows the frequency (%) distribution of ESBL-producing and non-ESBL *P. mirabilis* isolates recovered from wound specimens according to patient gender. Chi-square analysis was performed to examine the relationship between sex and both ESBL and non-ESBL *P. mirabilis* isolates. Among female patients (n = 69), 27 isolates (39.13%) were ESBL-producing and 42 isolates (60.87%) were non-ESBL-producing. In male patients (n = 84), 33 isolates (39.29%) were ESBL-producing and 51 isolates (60.71%) were non-ESBL-producing. The statistical analysis revealed no significant association between sex and the distribution of either ESBL or non-ESBL isolates ($\chi^2 = 0.000383$, $p = 0.9844$). This finding suggests that sex is not a determining factor in either ESBL production or the overall distribution of *P. mirabilis* strains in wound infections. Likewise, the proportions of non-ESBL isolates were comparable between males (60.71%) and females (60.87%). Although males showed a slightly higher overall number of infections (84 vs. 69), the relative distributions of ESBL and non-ESBL strains remained consistent across both genders.

The frequency distribution of ESBL-producing and non-ESBL-producing *P. mirabilis* isolates from wound specimens based on patients' age groups (0–15, 16–25, 26–35, 36–45, 46–55, and >55) is presented in Figure 3. The statistical test revealed no significant correlation between the distribution of *P. mirabilis* isolates and age

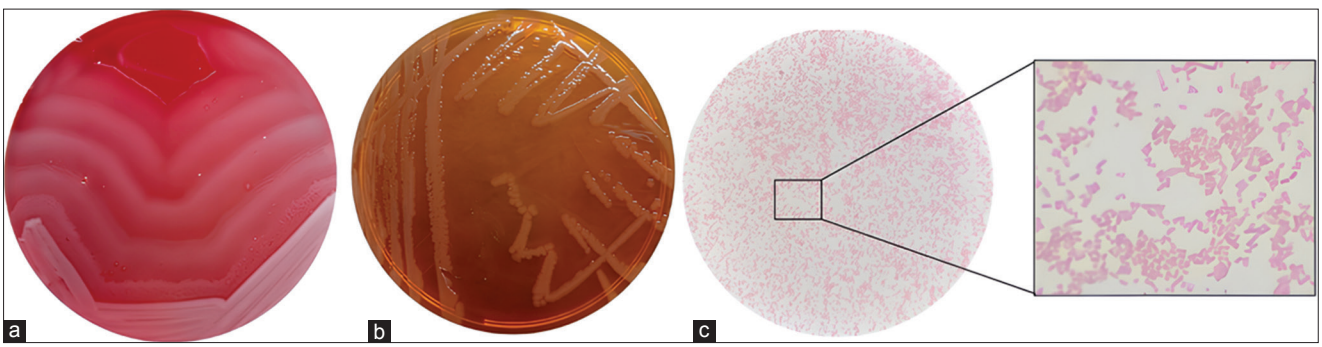

Figure 1: Growth of *Proteus mirabilis* colonies on (a) blood agar, (b) MacConkey agar after 24 h of incubation at 37°C. Characteristics of grayish-white colonies without hemolysis were seen on blood agar, whereas round colorless colonies were observed on MacConkey agar, and (c) Gram staining of *Proteus mirabilis* isolated from wound specimens, showing characteristic Gram-negative short rods with magnification 1000×.

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Table 1: Number of ESBL-producing and non-ESBL-producing *Proteus mirabilis* isolates recovered from abscess fluid, swabs, and wound biopsy specimens at Zainoel Abidin General Hospital from January 2021 to March 2024. Based on the Chi-square test for independence, the isolate type and period were independent (χ^2 = 4.1594, p = 0.125).

Proteus mirabilis phenotype	I (January 2021–January 2022)	II (February 2022–January 2023)	III (February 2023–March 2024)	Total (%)
ESBL	17	15	28	60 (39.22)
Non-ESBL	41	21	31	93 (60.78)
Total	58	36	59	129 (100)

ESBL=Extended spectrum β-lactamase

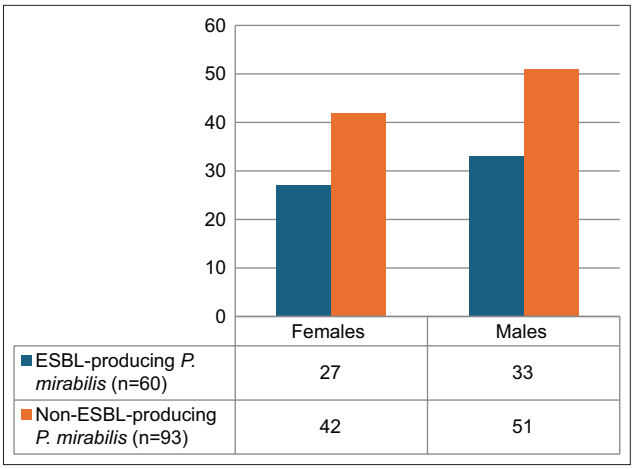

Figure 2: Frequency of occurrence (%) ESBL-producing *Proteus mirabilis* (n = 60) and non-ESBL-producing *Proteus mirabilis* (n = 93) in abscess fluid, swabs, and wound biopsy specimens based on gender at Zainoel Abidin for the period January 2021–March 2024. The numbers above each column show the total number of isolates recovered from each gender. Based on the Chi-square test for independence test, the isolates and the patients' gender were independent (χ^2 = 0.000383, p = 0.9844).

groups (χ^2 = 5.9847, p = 0.3077). This result suggests that the proportions of ESBL and non-ESBL isolates are similar across different age groups. However, Figure 3 also highlights differences in the overall occurrence of *P. mirabilis* isolates according to age group. The majority of isolates were found in older age groups, particularly in patients over 55 years of age, accounting for 65/153 isolates. This age group also had the highest number of both ESBL-producing (n = 29) and non-ESBL-producing (n = 36) *P. mirabilis* isolates.

Table 2 shows the antibiotic susceptibility of ESBL-producing and non-ESBL-producing *P. mirabilis* from January 2021 to March 2024. Among beta-lactam antibiotics, amoxicillin showed significantly different susceptibility between ESBL-producing (0%) and non-ESBL strains (29.03%, p < 0.0001). Similarly, ampicillin demonstrated low effectiveness in both groups (ESBL: 1.67%, non-ESBL: 30.11%). However, the addition of beta-lactamase inhibitors improved effectiveness, with amoxicillin/clavulanic acid showing moderate effectiveness (ESBL: 41.67%, non-ESBL: 50.54%) and piperacillin/tazobactam maintaining high effectiveness in both groups (ESBL: 91.67%, non-ESBL: 91.39%). In the cephalosporin group, its efficacy varied significantly across different generations. Cefoxitin showed variable effectiveness (ESBL: 35.00%, non-ESBL: 84.95%), whereas cefotaxime demonstrated marked differences between the ESBL and non-ESBL strains (8.33% vs. 60.21%). Ceftazidime showed better activity against non-ESBL strains (ESBL: 46.67%, non-ESBL: 90.32%). Cefoperazone/sulbactam maintained excellent activity in both groups (ESBL: 98.67%, non-ESBL: 96.77%). Among carbapenems and aminoglycosides, varying patterns of effectiveness were observed. Meropenem showed high effectiveness (ESBL: 98.33%, non-ESBL: 80.65%), whereas imipenem demonstrated only moderate activity (ESBL: 45.00%, non-ESBL: 55.91%). In the aminoglycoside class, amikacin maintained consistently high effectiveness (ESBL: 96.67%, non-ESBL: 97.85%), whereas gentamicin (ESBL: 68.33%, non-ESBL: 82.80%) and tobramycin (ESBL: 65.00%, non-ESBL: 79.57%) showed moderate to variable activity.

Other antibiotics showed varying degrees of effectiveness. Levofloxacin demonstrated limited effectiveness against ESBL strains (10.00%) but better activity against non-ESBL strains (75.27%). Doxycycline showed poor activity against both groups (ESBL: 6.67%, non-ESBL: 2.15%). Statistical analysis revealed significant differences (p < 0.0001) between ESBL and non-ESBL isolates for most beta-lactam antibiotics and fluoroquinolones. However, newer-generation antibiotics such as piperacillin/tazobactam, cefoperazone/sulbactam, and amikacin maintained consistent effectiveness against both groups, suggesting their potential role as empirical treatment options.

DISCUSSION

In the present study, there were a total of 153 *P. mirabilis* isolates from 3545 wound specimens from January 2021 to March 2024 at Zainoel Abidin Hospital, Banda Aceh. *P. mirabilis* isolates displayed characteristic morphological features on both Blood Agar (BA) and MCA media. On BA, colonies exhibited the distinctive swarming phenomenon with gray coloration, whereas on MCA, they appeared as colorless colonies due to their non-lactose fermenting nature. These morphological characteristics, along with microscopic examination showing GN rods, confirmed the identity of *P. mirabilis* isolates.

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Table 2: Antibiotic susceptibility of ESBL-producing *P. mirabilis* (n = 60) and non-ESBL-producing *P. mirabilis* (n=93) in abscess fluid, swabs, and wound biopsy specimens at Zainoel Abidin from January 2021 to March 2024.

Antibiotic	ESBL-producing *P. mirabilis* (n = 60)		non-ESBL-producing *P. mirabilis* (n = 93)		Chi-square[a]	p-value[b]
	n	%	n	%		
Amoxicillin	0	0	27	29.03	21.1575	<0.0001
Ampicillin	1	1.67	28	30.11	19.2167	<0.0001
Amoxicillin/clavulanic	25	41.67	47	50.54	1.1498	0.3009
Piperacillin/tazobactam	55	91.67	85	91.39	0.0034	0.9536
Cefoxitin	44	73.33	79	84.95	3.1113	0.0879
Cefotaxime	5	8.33	56	60.21	40.9184	<0.0001
Ceftazidime	28	46.67	84	90.32	35.3740	<0.0001
Ceftriaxone	13	21.67	60	64.52	26.7514	<0.0001
Cefoperazone/sulbactam	59	98.33	90	96.77	0.3481	0.6445
Imipenem	20	33.33	41	44.09	1.7618	0.1844
Meropenem	59	98.33	75	80.65	10.4936	0.0012
Amikacin	58	96.67	91	97.85	0.2009	0.6540
Gentamicin	12	20	51	54.84	18.2690	<0.0001
Tobramycin	30	50	72	77.42	12.3387	0.0004
Levofloxacin	6	10	50	53.76	30.1136	<0.0001
Doxycycline	4	6.67	2	2.15	1.9734	0.1601

[a]Chi-square calculation for comparison of susceptibility to ESBL-producing *P. mirabilis* and non-ESBL-producing *P. mirabilis*, [b]p-values generated from the Chi-square, *P. mirabilis*=*Proteus mirabilis*

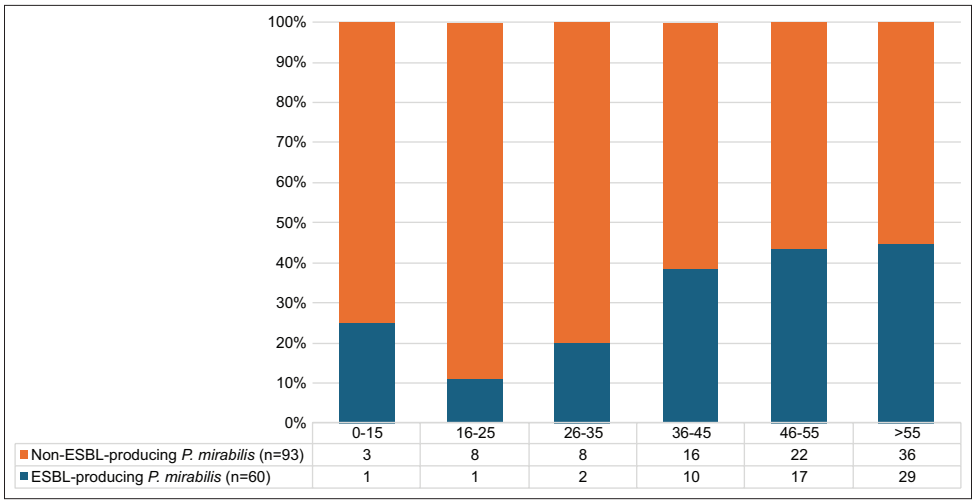

Figure 3: Frequency of occurrence (%) ESBL-producing *Proteus mirabilis* (n = 60) and non-ESBL-producing *Proteus mirabilis* (n = 93) in abscess fluid, swabs, and wound biopsy specimens based on patients; age groups at Zainoel Abidin for the period January 2021–March 2024. The numbers above each column show the total number of isolates recovered from each patient age group. Based on the Chi-square test for independence test, the isolates and the patients' age groups were independent (χ^2 = 5.9847, p = 0.3077).

P. mirabilis in MCA media produced round colonies without color measuring 1–2 mm in diameter with smooth margins, elevated center, and smooth surface. The absence of lactose fermentation by *P. mirabilis* is responsible for the clear appearance of this differential medium. These morphological features assessed in both the BA and MCA media populations are similar to previously documented morphological descriptions of *P. mirabilis* [1]. MCA is a selective and differential medium with the ability to differentiate lactose fermenting from non-lactose fermenting bacillary groups of Enterobacteriaceae. In MCA, the main ingredients, such as lactose, bile salts, and neutral red indicator, are responsible for this differentiation. Bile salts suppress the development of Gram-positive organisms, and neutral red serves as an indicator of lactose fermentation.

A total of 153 *P. mirabilis* isolates were identified from wound specimens. This substantial number of isolates underscores the significance of *P. mirabilis* as a pathogen in wound infections at our hospital. Among these 153 isolates, 60 (39.22%) *P. mirabilis* isolates were identified as ESBL producers, whereas 93 (60.78%) isolates were non-ESBL producers. The occurrence of ESBL-producing *P. mirabilis* was significantly higher in this study than in previous

studies [9, 10]. Alabi *et al*. [9] found 26.8% prevalence in wound swabs, Andrew *et al*. [10] found 1.4% in pus samples, and Kwiecińska-Piróg *et al*. [6] found 36.4% in wound swabs. This difference in prevalence between studies can be attributed to factors ranging from different antibiotic usage patterns to demographics, wound types, and geographic regions of hospitals.

It is interesting to note that of the numerous bacteria, only *P. mirabilis* has been consistently isolated from purulent wounds and overwhelmed tissue injuries. This tendency stems from proteolytic pus, which is both a source of nutrients and allows the virulence factors of the bacteria, such as their proteolytic enzymes, to thrive. Khayyat *et al*. [11] described many virulence factors of *P. mirabilis*, including motility structures such as flagella and fimbriae and many extracellular enzymes and toxins, including protease, urease, and hemolysin. In addition, *P. mirabilis* can form biofilms, especially in ESBL-producing strains, which also increase its virulence and tolerate many antibiotics [6]. Mishu *et al*. [7] reported that 70% of ESBL strains of *P. mirabilis* isolated from pus were biofilm–positive. This finding underscores the risk of treatment with these strains, as biofilm formation increases antibiotic resistance and facilitates the survival and infection of bacteria.

In terms of patients' gender, ESBL production in *P. mirabilis* was not influenced by gender in this study. Although both genders appear to be potentially infected by the pathogens, men had a slightly higher incidence of *P. mirabilis*-related wound infections, as also indicated by other studies. For example, a study found that men had greater infections with *P. mirabilis* than women, especially wound infections [1]. This result is supported by another study finding that of the samples collected, a significantly greater percentage of male patients (n = 40; 8.3%) than female patients (n = 24; 5%) had been infected with *P. mirabilis* [12]. Moreover, there might be many factors at play in this gap, including physical activity, which is also linked to wound infection; younger men tend to participate in more strenuous activities that lead to more injury and later infection [13].

Regarding age groups, ESBL and non-ESBL *P. mirabilis* infections were highest in patients aged >55 years. In particular, 29 isolates (48.33%) of ESBL-producing *P. mirabilis* and 36 strains (38.71%) of non-ESBL *P. mirabilis* were from this age. Infection rates for both ESBL and non-ESBL strains decreased with increasing age. This suggests that age is directly associated with the incidence of *P. mirabilis* infections, particularly among ESBL-producing isolates. *P. mirabilis*-related wound infections, especially ESBL-producing infections, are more common in the elderly for several reasons. These include immunosenescence, in which the body's immunity and ability to resist infection decrease with age [14]. In addition, older patients might have chronic illnesses, such as diabetes, which can increase the susceptibility of wounds to infection and worsen wound healing. Medical exposure is another factor because older patients are more susceptible to nosocomial infections due to prolonged hospitalization and higher healthcare use [15]. This increased exposure to medical settings could lead to the colonization of antibiotic-resistant strains such as ESBL-evolving *P. mirabilis*. Furthermore, older patients tend to have been on antibiotics before and might choose for resistant strains, such as ESBL-producers.

Antibiotic sensitivity tests on *P. mirabilis* isolates revealed very distinct patterns between ESBL and non-ESBL strains. On average, non-ESBL *P. mirabilis* strains were more resistant to antibiotics than ESBL strains. ESBL-producing *P. mirabilis* was most sensitive to cefoperazone/sulbactam (98.67%), meropenem (98.33%), amikacin (96.67%), and piperacillin/tazobactam (91.67%). These results are consistent with studies that demonstrated the efficacy of these antibiotics against *P. mirabilis* [9, 16]. ESBL-producing strains, on the other hand, were least sensitive (resistant) to amoxicillin (0%), ampicillin (1.67%), doxycycline (6.67%), cefotaxime (8.33%), and levofloxacin (10%), as observed for ESBL-producing strains [17].

Non-ESBL P. *mirabilis* isolates were also highly sensitive to amikacin (97.85%), cefoperazone/sulbactam (96.77%), piperacillin/tazobactam (91.67%), ceftazidime (90.32%), cefoxitin (84.95%), and meropenem (80.65%). These findings are in accordance with other publications showing the significant sensitivity of *P. mirabilis* to these drugs [1, 18]. The most sensitive non-ESBL isolates were doxycycline (2.15%), amoxicillin (29.03%), and ampicillin (30.11%). Since ESBL and non-ESBL isolates display significant variations in sensitivity, rapid ESBL detection is critical for selecting appropriate antibiotics. Given the efficacy of cefoperazone/sulbactam, piperacillin/tazobactam, and amikacin against ESBL and non-ESBL *P. mirabilis*, these antibiotics may be considered as first-line agents. Intriguingly, ESBL and non-ESBL isolates differed in sensitivity to carbapenems, showing high sensitivity to meropenem but low sensitivity to imipenem. This observation should be investigated more closely and considered when choosing a carbapenem regimen, as some isolates might lack porins or contain carbapenemase beta-lactamases [17]. The increasing occurrence of ESBL-producing strains, as observed in this study, suggests the importance of continued monitoring and the use of effective antibiotics to combat *P. mirabilis* infections. More molecular analyses of the isolates may include knowledge of the epidemiology and resistance of *P. mirabilis* producing ESBL in this clinical environment.

CONCLUSION

This study provides a comprehensive analysis of the occurrence and antibiotic susceptibility of

ESBL-producing and non-ESBL *P. mirabilis* isolates in wound infections at Zainoel Abidin General Hospital, Banda Aceh, Indonesia. Among the 153 *P. mirabilis* isolates, 39.22% were ESBL producers, with a higher occurrence in male patients and individuals over 55 years of age. AST revealed that ESBL-producing isolates retained high sensitivity to cefoperazone/sulbactam (98.67%), meropenem (98.33%), amikacin (96.67%), and piperacillin/tazobactam (91.67%), while exhibiting complete resistance to amoxicillin (0%) and high resistance to cefotaxime (8.33%) and levofloxacin (10%). Non-ESBL isolates showed significant sensitivity to amikacin (97.85%), cefoperazone/sulbactam (96.77%), and ceftazidime (90.32%), but reduced susceptibility to amoxicillin (29.03%) and ampicillin (30.11%). The findings emphasize the importance of early ESBL detection and antimicrobial stewardship in managing wound infections effectively.

One of the strengths of this study is the inclusion of a large dataset spanning over 3 years, providing robust epidemiological insights into *P. mirabilis* infections. The use of an automated bacterial identification and susceptibility testing system (VITEK® 2 Compact) enhances the accuracy and reproducibility of results. In addition, the study contributes to regional data on antimicrobial resistance patterns, supporting targeted therapeutic strategies.

However, this study has some limitations. It is based on a single tertiary care hospital, which may limit the generalizability of the findings to other healthcare settings. Furthermore, molecular characterization of ESBL genes was not performed, which could have provided deeper insights into the genetic determinants of resistance. In addition, potential confounding factors, such as prior antibiotic exposure and comorbidities, were not analyzed, which may have influenced susceptibility patterns.

Future research should focus on molecular epidemiology to identify specific resistance genes associated with *P. mirabilis* in this region. Longitudinal surveillance studies across multiple healthcare centers would help assess evolving resistance trends. In addition, investigating biofilm formation and its impact on antibiotic resistance could provide valuable insights for infection control strategies. A more detailed analysis of patient comorbidities and clinical outcomes would further strengthen the understanding of *P. mirabilis*-associated wound infections and guide personalized treatment approaches.

AUTHORS' CONTRIBUTIONS

SS: Conceptualized and designed the study, data analysis and interpretation, and drafted and revised the manuscript critically for important intellectual content. ZH: Study design, laboratory work and data collection, and reviewed the manuscript. WM: Microbiological analysis, data interpretation, and reviewed the manuscript. JF: Statistical analysis, data interpretation, and manuscript preparation. All authors have read and approved the final manuscript.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

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