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DISTRIBUTION AND CHARACTERISTICS OF BACTERIA CULTURED IN CELLULITIS PATIENTS AT RSUP SANGLAH DENPASAR FROM 2016 TO 2021

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ABSTRACT

Cellulitis is an infectious disease of the skin and soft tissues involving the dermis layer and fatty connective tissue of the skin. Prompt and appropriate antibiotic administration is important in the management of cellulitis. Appropriate antibiotic therapy can lead to improvement in the patient's clinical condition within 48 hours of receiving therapy. This study is a descriptive cross-sectional study using medical record data of patients with cellulitis who were hospitalized at Prof. Dr. IGNG Ngoerah Hospital, Denpasar in 2016-2021. The aim of this study is for describing the distribution of cultured bacteria in cellulitis patients in Indonesia, and Bali in particular, along with their antibiotic sensitivity. In this study, it was found that the most common bacteria found in the results of wound bed smear culture, tissue culture, and blood culture in cellulitis patients at Prof. Dr. IGNG Ngoerah Hospital were *S. aureus*, *E. coli*, *Acinetobacter baumannii*, *P. aeruginosa*, and *coagulase-negative Staphylococcus* and most often have susceptibility to antibiotics including aminoglycosides (gentamicin and amikacin), fluoroquinolones (ciprofloxacin), sulfa (trimethoprim/sulfamethoxazole), macrolides (clindamycin), and penicillins (ampicillin). It is necessary to conduct a prospective study to examine the distribution of bacteria, and their antibiotic susceptibility, in patients with cellulitis at Prof. Dr. IGNG Ngoerah Hospital by collecting primary data on the results of wound bed smear culture, tissue culture, blood culture, and urine culture. Further assessment is needed regarding the suitability of empirical antibiotics recommended by PERDOSKI for the management of cellulitis in the local context at Prof. Dr. IGNG Ngoerah Hospital.

Keywords : cellulitis., culture., bacterial characteristic

PENDAHULUAN

Cellulitis is an infectious disease of the skin and soft tissues involving the dermis and fatty connective tissue layers of the skin characterized by erythema lesions with indistinct boundaries accompanied by an opening that becomes the point of entry for the bacteria causing the infection[1].

The pathophysiology of cellulitis is divided into purulent and non-purulent based on the pus production found in the lesions which depends on the cause of infection. Purulent cellulitis is often caused by *Streptococcus pyogenes*, while *Staphylococcus aureus* is more common in non-purulent cellulitis[2]. The bacteria that cause cellulitis can spread hematogenically and lymphogenically. Hematogenic spread risks causing bacteremia and sepsis. Meanwhile, lymphogenic spread can lead to incubation of bacteria in the lymph nodes which then facilitates recurrent cellulitis[3].

The incidence of cellulitis is high, reaching approximately 200 cases per 100,000 person-years[2]. The epidemiology of cellulitis is dominated by the older population. This may be related to systemic risk factors for cellulitis such as obesity and diabetes mellitus (DM). Meanwhile, skin injury is primarily a local risk factor for cellulitis, acting as a point of entry for infectious bacteria and facilitating the onset of the pathophysiologic process in cellulitis[4].

Prompt and appropriate antibiotic administration is important in the management of cellulitis. Appropriate antibiotic therapy can lead to improvement in the patient's clinical condition within 48 hours of receiving therapy. In contrast, antibiotic failure and increased morbidity, length of hospitalization, and complications are closely associated with antibiotic selection errors accompanied by antibiotic therapy failure[5].

Given the important role of antibiotics in the management of cellulitis, there is a need for regular research on the distribution of bacteria that cause cellulitis. Clinical practice guidelines on cellulitis emphasize the importance of considering the distribution of these bacteria in a local context, at a national or even sub-national level[2,6]. The importance of local distribution can be seen from the different first-line antibiotic recommendations in Indonesia

compared to those in the Netherlands or the UK[6–8]. However, few studies have reported on this distribution in Indonesia or Bali in particular. Therefore, this study was conducted with the aim of describing the distribution of cultured bacteria in cellulitis patients in Indonesia, and Bali in particular, along with their antibiotic sensitivity.

CELLULITIS AND THE DISTRIBUTION OF CAUSATIVE BACTERIA

Cellulitis

Cellulitis is a bacterial infection of the skin characterized by indistinctly demarcated erythema, edema, warmth and tenderness. Although common, cellulitis can often present diagnostic and therapeutic challenges[3].

Cellulitis is relatively common and occurs most frequently in middle-aged and older adults. The incidence of cellulitis is relatively high (199 cases per 100,000 person-years) and comparable to other medical conditions that often require hospitalization or substantial expenditure of healthcare resources[9]. Another study found the incidence of cellulitis was increasing and could not only be explained by an aging population, and most cases had no underlying risk factors. It was found that the incidence increased by 4.7% per year during this period to reach 204.8 (95% CI 198.6-211.1) cases per 100,000 population in 2013. However, although incidence was highest in the elderly (aged 85 years and above), incidence increased by only 1.8% per year in this age group compared to 7.5% per year for young adults (16-24 years)[10].

Similar results were found in studies in Southeast Asia. One study in Thailand found of the 970 adult cellulitis patients included, 20.6% were hospitalized and 79.4% were outpatients. The mean age of the patients was 60.6 ± 18.5 years, 75.4% had at least one underlying disease, and 55% were female. Eighty-six percent of patients had community-acquired infections. Amoxicillin-clavulanate, dicloxacillin, ceftriaxone plus clindamycin, and ceftriaxone alone were the most commonly prescribed antibiotics. Ninety-seven percent of patients had good clinical outcomes. The overall mortality rate was 2.0%, and the cellulitis-related mortality rate was 0.3%. Inpatients had a significantly lower proportion of favorable clinical outcomes than outpatients[11]. However, there are still few similar studies reported in Indonesia.

Studies on risk factors for cellulitis suggest that a previous history of cellulitis and a history of safenectomy are major predisposing factors for cellulitis and that foot lesions or toe tissues colonized or infected by potential pathogenic bacteria are significant entry sites for causative organisms[14,15]. A recent case-control study of risk factors for lower extremity cellulitis reported that excess body weight, history of cellulitis, chronic foot edema, skin barrier disorders and toe dermatophytosis were independent risk factors[14].

Patients affected by cellulitis of the lower limbs are a heterogeneous group, with regard to risk factors. Young healthy individuals who develop cellulitis after trauma differ from middle-aged patients whose comorbid conditions may predispose to recurrent attacks, with or without a clear site of pathogen entry. Predisposing factors do not necessarily cause bacterial cellulitis. The role of various predisposing factors, such as previous cellulitis, leg edema, and saphenectomy in the pathogenesis of cellulitis, has not been elucidated. Although these factors do not cause infection, they may facilitate its development by impairing local defense mechanisms[16].

Skin lacerations appeared to be a consistent risk factor across studies. Lesions involving tearing of the skin on the foot and instep were significantly associated with cellulitis in our study. As lesions were not systematically sampled, it is not possible to estimate the extent of bacterial carriage and its relative role in infection[14,16].

These results were confirmed in a more recent systematic review that found obesity was the only systemic risk factor identified. Local risk factors included skin barrier disruption, leg edema, presence of intertrigo between fingers, lymphedema, cosmetic depigmentation practices, and traumatic wounds. Complications occur in 8.9%-47.4% of cellulitis cases, which include abscesses, necrotizing fasciitis, boils, hemorrhagic lesions, phlebitis, and diabetic ketoacidosis. On the other hand, nicotine addiction, delay in antibiotic treatment for 10 days or more, use of non-steroidal anti-inflammatory drugs or antibiotics before consultation, and accelerated ESR on admission are associated with these complications[4].

Cellulitis is a skin infection usually triggered by the entry of bacteria through a gap in the skin barrier. Its pathogenesis and clinical manifestations largely depend on the organism causing the infection. *Streptococcus pyogenes* is the most common cause of non-purulent cellulitis. Non-purulent cellulitis usually has no culturable wound source. *Staphylococcus aureus* can also cause non-purulent cellulitis and is the most common cause of purulent cellulitis. Cellulitis can be caused by *methicillin-resistant S. aureus* (MRSA) *or methicillin-susceptible S. aureus* (MSSA), which can be difficult to distinguish clinically without wound culture and sensitivity testing and has implications for antibiotic selection. The incidence of MRSA has increased in the community, and many patients with MRSA infection present without risk factors. Furthermore, risk factors for MRSA colonization include previous antibiotic use, recent hospitalization or surgery, long-term stay in a healthcare facility, human immunodeficiency virus (HIV) infection, intravenous drug use, incarceration, military service, sharing sports equipment, and sharing razors[2,6].

Other potential pathogens besides *S. pyogenes* and *S. aureus* are less common and should be considered based on

clinical context. Cellulitis at the site of a dog or cat bite can be caused by organisms, such as *Pasteurella, Neisseria*, or *Fusobacterium*, whereas organisms to consider in human bites are *Eikenella corrodens* or *Veillonello*. Cellulitis in the setting of aquatic injuries may include *Vibrio, Aeromonas*, or *Mycobacterium*. In immunosuppressed patients, it is important to investigate the etiology whenever possible, including non-bacterial causes. *Helicobacter cinaedi* can cause cellulitis in patients with HIV infection or with a recent history of chemotherapy. Patients with systemic lupus erythematosus are prone to *Streptococcus pneumoniae* cellulitis. Obtaining a relevant patient history with cellulitis infection can elucidate potential casual microorganisms and promote appropriate antibiotic selection and management[2,6].

The diagnosis of cellulitis is made based on complaints and clinical findings with supporting investigations can be done electively if required. The classic presentation of rubor, dolor, tumor and callus is the hallmark of cellulitis. The spectrum of severity ranges from localized erythema in systemically well patients to rapidly spreading erythema and fulminant sepsis seen with necrotizing fasciitis. Pain that is not proportional to the clinical signs, in particular, if accompanied by a history of rapid progression should be immediately considered for necrotizing fasciitis. The timing and evolution of skin findings can differentiate cellulitis from some conditions with a more chronic clinical course. Recent antibiotic exposure and hospital contact should prompt consideration of antibiotic resistance in the causative organism[8,17].

Supportive examination is not mandatory in the diagnosis and management of cellulitis. Instead, patients with suspected cellulitis can immediately start empirical antibiotic therapy. However, supporting examination in the form of tissue culture is recommended to increase the effectiveness of antibiotic therapy and to avoid antibiotic resistance. In addition, biopsy is also recommended for patients suspected of cellulitis but with non-typical lesions[7].

The aggressiveness of antibiotic therapy for cellulitis patients can be determined based on an assessment of the risk of complications as well as the severity of the cellulitis. In patients with signs of sepsis, such as high fever, tachypnea, extreme tachycardia, hypotension, or decreased consciousness, hospitalization is recommended. However, other than that, patients can still be treated on an outpatient basis[7,8,18].

Regardless of inpatient or outpatient treatment, cellulitis patients are advised to receive systemic antibiotic therapy, either oral or intravenous, according to the treatment method. Empiric antibiotic therapy for cellulitis is localized and should take into account the recommendations of each country or even province[8]. For example, UK CREST recommends agents with anti-streptococcal and anti-staphylococcal activity, such as flucloxacillin as first-line antibiotics in the UK[8]. Similarly, in the Netherlands, the preferred small-spectrum agent that covers *methicillin-susceptible S. aureus* and *Streptococcus ß-haemolyticus* is fluoxacillin[6]. However, PERDOSKI recommendations for first-line antibiotic therapy in cellulitis are cloxacillin/dicloxacillin, amoxicillin and clavulanic acid, or cephalexin[7].

If clinicians promptly identify cellulitis and start treatment with the appropriate antibiotics, patients can expect to see improvement in signs and symptoms within 48 hours. A systematic review compiled results from 20 randomized controlled trials published 260 comparing antibiotic regimens for the treatment of cellulitis. Among, treatment failure rates ranged widely, from 6% to 37%, despite the fact that all regimens included agents active against streptococcus[5].

Proper identification and prompt treatment of cellulitis is necessary. There is a low but real risk of subsequent bacteremia, more frequent in cases of streptococcal disease relative to staphylococcal or gram-negative infections. Endocarditis, glomerulonephritis, osteomyelitis, toxic shock, and elephantiasis verrucosa nostra may also develop. Cellulitis can damage the lymphatics, and subsequent lymphedema makes the patient susceptible to recurrent episodes of cellulitis. The risk of death in uncomplicated non-purulent cellulitis is very low, even in hospitalized patients[3].

However, cellulitis can spread through the bloodstream and lymphatic system. A retrospective case study of people hospitalized with cellulitis found that systemic symptoms, such as fever and elevated white blood cell count, were present in 42% of cases[19]. Lymphatic involvement can lead to obstruction and damage to the lymphatic system which predisposes to recurrent cellulitis. Recurrence may occur rapidly, or after months or years.

Recurrent cellulitis is common, with 22-49% of patients who have cellulitis reporting at least 1 previous episode of the disease. Recurrence occurs in about 14% of cellulitis cases within 1 year and in 45% of cases within 3 years. It tends to occur in the same location. When hospitalized, patients with recurrent cellulitis require a longer hospital stay compared to non-recurrent cellulitis patients. When recurrent disease occurs, identification and treatment of predisposing conditions such as edema, obesity, eczema, venous insufficiency, and toe space abnormalities should be done to help prevent recurrent infection[3].

Distribution of Bacteria Causing Infection in Cellulitis

Bacterial findings from cultures in cellulitis patients vary by region and culture specimen. A Dutch study found differences in the distribution of bacteria found from blood cultures and wound smear cultures in cellulitis lesions. Lesion smear cultures have been reported to be positive in up to 72-75% of all patients cultured. This is much higher than culture of other tissue specimens such as blood cultures which were only found to be positive in 2-4% of patients

cultured. These results suggest that bacteremia is rare in cellulitis except in those with complications and/or at high risk due to comorbidities[6].

In addition, there are differences in the distribution of bacterial species based on different culture specimens. *Staphylococcus aureus* was found to be the predominant bacterial species in cultures of lesion specimens, both smears and biopsies with 70-75% of patients with positive cultures. However, blood cultures were more likely to find other streptococci as the dominant bacterial species in positive blood culture results[6].

These results are similar to those reported by two other studies in Italy and Taiwan. Wound or lesion tissue culture tends to find *Staphylococcus aureus*, either as the only bacteria in the culture (monomicrobial) or accompanied by bacteria of other species (polymicrobial)[20]. Meanwhile, culture from lymphatic tissue around the lesion found results more similar to blood culture, which is dominated by bacteria of the *Streptococcus* genus that vary and cannot be specifically identified[21].

Identification of the bacterial etiology of infection is a very important part of the management of infectious diseases, especially pyogenic bacterial infections. The identification of microbial epidemiology is especially useful in determining empirical therapy that can be used in patients who require rapid antibiotic treatment. However, our literature search had difficulty finding academic literature that reported the types of bacteria found in cellulitis patients in Indonesia.

Distribution of Antibiotic Resistance in Bacteria Causing Cellulitis Infection

Cellulitis caused by MRSA is a real concern. One literature review reported that the proportion of MRSA found in cellulitis patients is increasing every year[2]. In the Netherlands, MRSA is also one of the most common types of bacteria found from culture, as many as 20-25% of patients with positive culture results[6].

However, one American study reported that the overall age- and sex-adjusted incidence of cellulitis for 1999 was 216.0 per 100,000, exceeding the corresponding rate of 176.6 per 100,000 reported for 2013 (p=.045). This suggests that the incidence of cellulitis is not increasing, and may even be decreasing, despite an increase in the prevalence of MRSA infections over the previous years[12].

In contrast, cellulitis caused by MRSA is increasingly found in community settings in Indonesia. The penetration of hospital-acquired MRSA clones in community settings may be mediated by undetected nosocomial bacterial carriers into the community, which requires increased awareness of public health authorities. Promoting household hygiene in general and proper hand hygiene in particular may be a simple and cost-effective method to contain the spread of MRSA in the community; however, further investigation should be conducted. Simultaneously reducing the use of antibiotics in ambulatory care will synergize with such efforts[22].

MATERIALS AND METHODS

This study utilized a descriptive cross-sectional design. Data were collected from the medical records of patients with cellulitis who underwent hospitalization at Prof. Dr. IGNG Ngoerah Hospital, Denpasar in 2016-2021. Medical record data collected included demographic characteristics, clinical characteristics, and bacterial culture results on cellulitis lesions.

Inclusion criteria included diagnosed cellulitis based on doctor's diagnosis and undergoing hospitalization at Prof. Dr. IGNG Ngoerah Hospital, Denpasar with exclusion criteria in the form of incomplete medical record data for the required variables. The subjects were recruited using non-random total sampling method.

This study has obtained ethical approval of the protocol from the Ethics Committee of Prof. Dr. IGNG Ngoerah Hospital Denpasar.

Data analysis in this study included descriptive analysis, bivariate analysis, and multivariate analysis with a significance cut-off point set at <0.05 for all types of analysis. Analysis of normality of distribution using the Kolmogorov-Smirnov test.

RESULTS

Medical record searches identified 68 patients who met the inclusion and exclusion criteria during the data collection period. This number consisted of 43 (61.94%) males and 25 (38.06%) females. The age of the patients was found to be normally distributed (Kolmogorov-Smirnov test p>0.05) with a mean age of 50.94 ± 18.08 years. The youngest patient was 7 years old and the oldest was 87 years old.

Comorbidity search found that 38 (53.69%) patients had comorbidities other than cellulitis and 11 (17.14%) of them had more than one comorbidity. Diabetes mellitus was the most common comorbidity and was found in 19 (25.58%) patients. Frequent comorbidities were coronary heart disease (23.38%) and chronic renal failure (18.56%). In addition, there were 4 (6.88%) patients with sepsis and 1 (1.65%) patient with HIV co-morbidity.

An examination of the hematological characteristics of the patients found that hemoglobin levels tended to be normal with a mean of 11.82 ± 2.53 g/dL. However, as can be expected in patients with acute infections, elevated leukocytes, neutrophils, and platelets were found with an abnormal distribution and median of 14.15 (10.15 - 19.42) × 103 cells/mL, 11.25 (7.03 - 16.63) × 103 cells/mL, and 258.40 (155.05 - 370.45) × 103 cells/mL, respectively.

The culture specimen most frequently used in the examination was the wound bed culture obtained using a smear. This specimen was examined in 42 (61.22%) patients. Furthermore, blood culture was performed in 27 (40.13%) patients, and tissue culture in 18 (26.09%) patients. There were 34

(50%) patients who underwent culture examination of more than one specimen.

Positive culture results, defined as microbiota growth from at least one specimen, were found in 47 (66.59%) patients. Most positive culture results were found from tissue specimens (100%) followed by wound bed (75.28%).

Table 1. Patient demographic and clinical characteristics

Characteristics (n = 68)	
Age (year), mean ± SD	50.94 ± 18.08
Sex, n (%)	
Male	43 (61.94)
Female	25 (38.06)
Co-morbidity, n (%)	
DM	19 (25.58)
Coronary artery disease	15 (23.38)
Chronic kidney disease	
Sepsis	13 (18.56)
Stroke	4 (6.88)
HIV infection	3 (3.57)
	1 (1.65)
Hb (g/dL), meand ± SD	11.81 ± 2.53
Leucocyte (10^3/mL), median (IQR)	14.15 (10.15 – 19.42)
Neutrophil (10^3/mL), median (IQR)	11.25 (7.03 – 16.63)
Lymphocyte (10^3/mL), mean ± SD	1.62 ± 0.95
Platelet (10^3/mL), median (IQR)	258.40 (155.05 – 370.45)

A total of 38 species of bacteria and fungi were found from 47 patients with positive culture results. A total of 26 patients were found with more than one species of microbiota in their culture results. The most common species found from the culture results was *S. aureus* which was found in 10 (14.70%) patients. Furthermore, *E. coli* was found in 8 (11.76%) patients and *Acinetobacter baumannii*, *P. aeruginosa*, and *coagulase-negative Staphylococcus* were each found in 7 (10.29%) patients. In addition, several fungal species were also found in the culture results, such as *Candida albicans* and *Candida parapsilosis*. There was no MRSA found in the patient's culture results.

Antibiotic sensitivity examination identified 49 types of antibiotics and antifungals that were effective on at least one type of bacteria in one of the patients found with positive cultures. Figure 2 shows the frequency distribution of antibiotic sensitivity in bacteria found in patients. The results found gentamicin is the type of antibiotic that is most often found sensitive, namely in 31.1% of examinations. The 6 types of antibiotics most often found sensitive include representatives of the aminoglycoside group (gentamicin and amikacin), fluoroquinolones (ciprofloxacin), sulfa (trimethoprim/sulfamethoxazole), macrolides (clindamycin), and penicillins (ampicillin).

Table 2. Culture examination characteristics

Characteristics (n = 68)	
Culture specimens, n (%)	
Wound bed	42 (61.22)
Blood	27 (40.13)
Tissue	18 (26.09)
Culture results, n (%)	
Negative	21 (33.41)
Positive	47 (66.59)

Conversely, culture analysis also found a list of the most common antibiotics found with resistance in cultured microbiota. Cultured bacteria were most commonly found with ampicillin resistance, which was found in 27.2% of

cultured bacteria. In addition, cultured bacteria were also frequently found resistant to ciprofloxacin, ampicillin/sulbactam, and trimethoprim/sulfamethoxazole. Interestingly, antibiotics that are often found to be effective, such as gentamicin and siflofloxacin, are also often found with resistance in cultured bacteria.

DISCUSSION

The demographics of cellulitis patients found in this study were predominantly male (61.94%) with a mean age of 50.94 ± 18.08 years. These characteristics are in accordance with previous studies that describe the characteristics of cellulitis patients. One of the previous studies in Perth, Australia also reported that cellulitis patients were mainly over 50 years old. However, the study found a more equal gender distribution of 58% male and 42% female[10]. In contrast, a study in Thailand found that cellulitis patients were more female (55%) although they agreed that the average age of patients tended to be middle-aged or elderly with a mean of 60.6 ± 18.5 years[11].

Furthermore, regarding comorbidities, this study found DM to be the most common comorbidity in cellulitis patients. Other metabolic diseases, such as coronary heart disease and chronic renal failure, were also common. This result is consistent with previous studies that reported metabolic diseases, especially DM, as risk factors for cellulitis. A systematic review in Africa found that chronic diseases, such as DM, chronic renal failure, hypertension, and obesity act as risk factors for cellulitis[4]. Similar results were also reported from a cohort study in South Korea that found DM and obesity as risk factors for cellulitis[23].

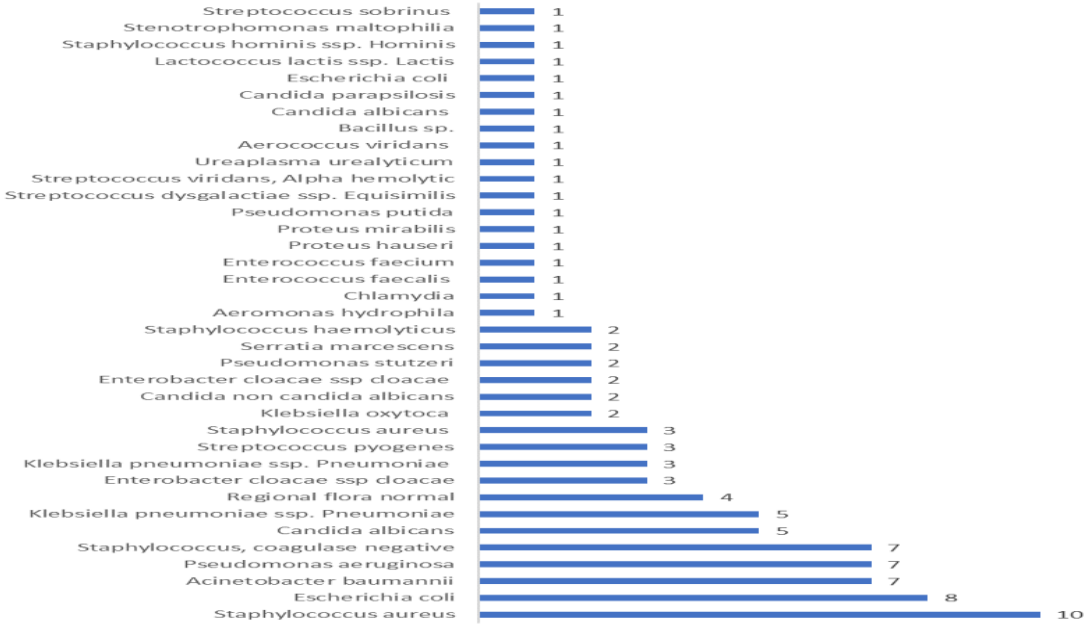

Figure 1. Bacterial and fungal species found from culture results

The clinical hematological characteristics found in this study are also in line with what was previously known about cellulitis. This study found hematological abnormalities characterized by leukocytosis and neutrophilia. This result was also found by a previous study in Brazil that found cellulitis patients had increased neutrophils and neutrophil-lymphocyte ratio[24]. Previously, an elevated neutrophil count was known as one of the signs of acute bacterial infection[25].

The main finding of this study was the characteristics of the culture examination results. This study found positive culture results in 66.59% of cellulitis patients overall with the most common positive results found in wound tissue specimen culture (100%) and wound tissue surface smear culture (75.28%). These results are in agreement with some previous studies, although there are a few details that differ. A literature review by Cranendonk et al. (2017) reported that culture of tissue biopsy specimens and lesion smears were most commonly found with positive results compared to other specimens such as blood. However, this literature review reported tissue smear culture results with the most frequent positive results at 72-75% followed by biopsy results (24%). Two other studies reported slightly lower positive tissue culture results, ranging from 30-60%[26,27].

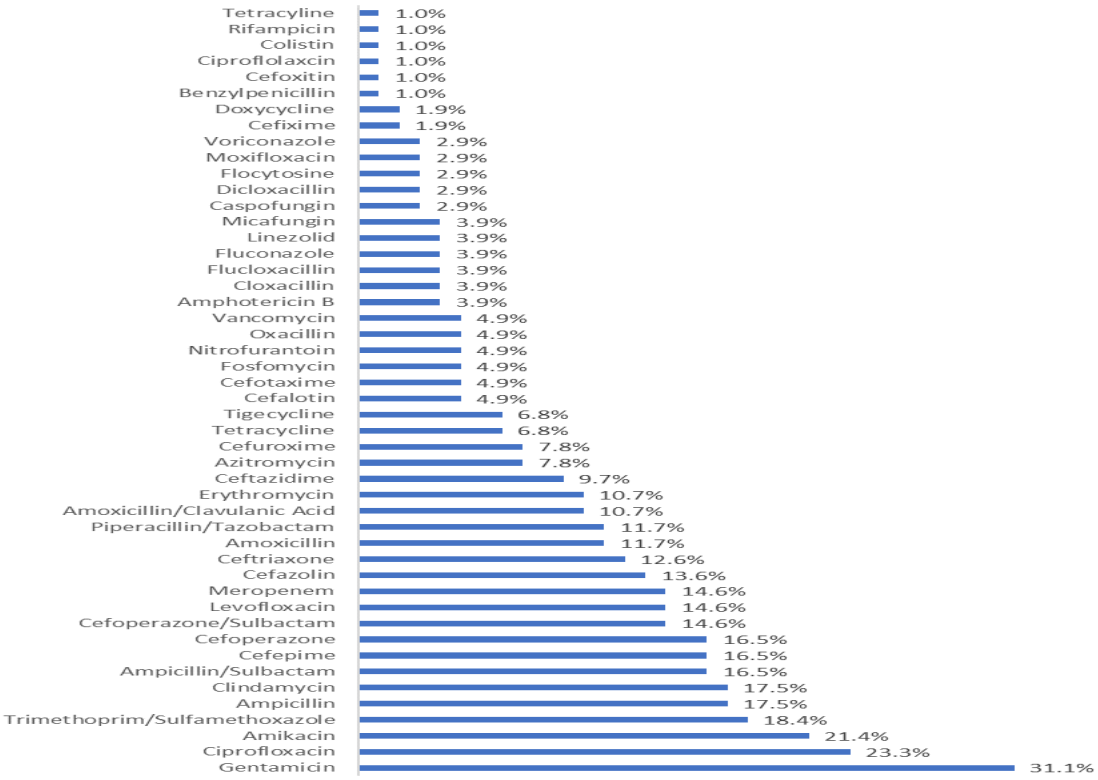

Figure 2. Distribution of antibiotic sensitivity from culture results

This study also found a positive blood culture yield of 45.96%, much higher than that reported in previous studies. A literature review reported a much lower blood culture positivity of 4-9%[6]. Another systematic review reported a similar result, finding a blood culture positivity of 7.9%[28]. The highest positive blood culture result was reported by Serdar et al. (2011) which was 18.8%.

These results indicate that tissue smear is one of the best specimen collection options for cellulitis patients. In addition to high sensitivity, tissue culture is also less invasive than taking tissue specimens through biopsy. Meanwhile, the difference in positive culture results found in this study may imply that the incidence of bacteremia in cellulitis patients in Bali is higher than reported by other studies. However, positive culture results may also result from contamination in the process of specimen collection, shipment, or storage that occurred outside the scope of this study.

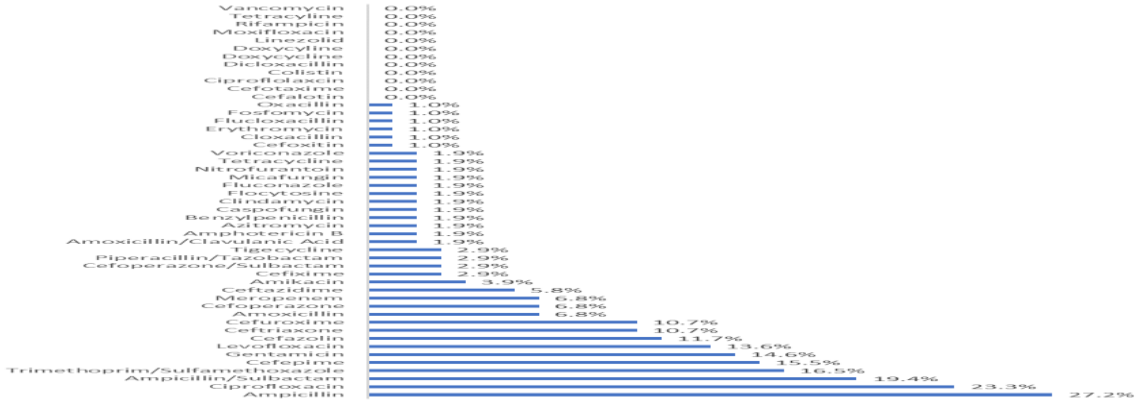

Figure 3. Distribution of antibiotic resistance from culture results

Furthermore, regarding the characteristics of the microbiota found from the culture itself, this study found that the most common bacteria found was *S. aureus* which was found in 14.71% of patients or 21.27% of patients with positive culture results. This result is in accordance with previous studies. Cranendonk et al. (2017) reported that *S. aureus* was the most commonly found bacteria, especially from wound tissue smear cultures. Meanwhile, another systematic review reported that *S. aureus* was the second most common bacteria found in blood cultures, after group A *Streptococcus*[28].

The antibiotic sensitivity examination found that bacteria in patients were most often found to be sensitive to aminoglycosides, especially gentamicin (31.1%). In addition, not many bacteria were found with sensitivity to cephalosporin and penicillin antibiotics (except ampicillin). These results are in contrast to previous findings and standards of cellulitis therapy. Research in the United States found that cellulitis bacteria, especially S. aureus, were most often found to be sensitive to linezolid, trimethoprim-sulfamethoxazole, and tetracycline[29]. Meanwhile, a literature review in the Netherlands recommended flucosacillin, a penicillin group antibiotic, as first-line therapy for cellulitis[6]. The PERDOSKI recommends clloxacillin, dicloxacillin, or amoxicillin-clavulanic acid as first-line therapy[7].

In contrast, the cultured bacteria found in this study were often found to be resistant to penicillin-type antibiotics, such as ampicillin and ampicillin/sulbactam. In addition, cultured bacteria were also often found to be resistant to ciprofloxacin, trimethoprim/sulfamethoxazole, and cefepime. Different results were found in two previous studies in Pakistan and India. The Pakistani study found cultured bacteria were most often resistant to basitrasin, an aminoglycoside antibiotic[30]. Meanwhile, a study in India found that cultured bacteria most often showed resistance to penicillin antibiotics[31].

The difference in the types of empirical antibiotics found in this study compared to previous recommendations must be addressed carefully. There are several possible reasons for this difference. Firstly, there may be differences in the antibiotic sensitivity profiles found locally in this study compared to studies with wider target populations at the national level or in other countries. In addition, some recommendations tend to rely on empirical antibiotics against *S. aureus* while this study reported the antibiotic susceptibility of cellulitis patients broadly, regardless of the type of bacteria. The antibiotic susceptibility for *S. aureus* found in this study included gentamicin (100%), clindamycin (100%), and cefazolin (90.9%).

Despite the interesting findings above, this study is not free from shortcomings. First of all, the limited sample size in this study limits the depth of the data obtained. Despite using the total sampling method, this study only identified 68 people who met the inclusion and exclusion criteria. This number is insufficient for an in-depth description of antibiotic susceptibility for all types of bacteria and microbiota found in cellulitis patients considering that many species are only found in 1 or 2 patients (Figure 1).

In addition, the use of secondary data limits the ability of researchers to control and observe the culture examination process, from collection to transportation to specimen storage. As mentioned above, these processes are important and contamination can occur that affects the culture results. However, this weakness has been mitigated through the adherence to standard operating procedures by health workers during medical services, maintaining the integrity of results recorded in medical records.

CONCLUSIONS AND SUGGESTIONS

The most common bacteria found in the results of wound bed smear culture, tissue culture, and blood culture in cellulitis patients at Prof. Dr. IGNG Ngoerah Hospital were *S. aureus*, *E. coli*, *Acinetobacter baumannii*, *P. aeruginosa*, and *coagulase-negative Staphylococcus*. Bacteria found in wound bed culture, tissue culture, and blood culture in cellulitis patients at Prof. Dr. IGNG Ngoerah Hospital were found to most often have susceptibility to antibiotics including aminoglycosides (gentamicin and amikacin), fluoroquinolones (ciprofloxacin), sulfa (trimethoprim/sulfamethoxazole), macrolides (clindamycin), and penicillins (ampicillin).

It is necessary to conduct a prospective study to examine the distribution of bacteria, and their antibiotic susceptibility, in patients with cellulitis at Prof. Dr. IGNG Ngoerah Hospital by collecting primary data on the results of wound bed smear culture, tissue culture, blood culture, and urine culture. Prospective research with primary data can confirm the findings of bacterial distribution and susceptibility based on medical records that have been described in this study. Further assessment is needed regarding the suitability of empirical antibiotics recommended by PERDOSKI for the management of cellulitis in the local context at Prof. Dr. IGNG Ngoerah Hospital. Differences in bacterial distribution and antibiotic susceptibility are very likely to occur. In this situation, empirical antibiotics given should adjust to local scientific evidence

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