INTRODUCTION

Neonatal sepsis is a systemic response that responds to infection in newborns, which is one of the main causes of mortality and morbidity in neonates worldwide. The incidence of neonatal sepsis worldwide reaches around 3 million neonates (22 per 1000 live birth group). The incidence of neonatal sepsis is still relatively high in developing countries, reaching 1.8-18 per 1000 live births. The incidence in several referral hospitals in Indonesia reaches 1.5%-3.7% with a mortality rate of 37.1%-80%. The incidence of neonatal sepsis at Prof Ngoerah Hospital Denpasar in 2010 reached 5% with a mortality rate of up to 30.4%, and in 2011 reached 48% with positive blood culture.

Based on the onset of symptoms, neonatal sepsis is divided into 2: early-onset neonatal sepsis (EONS) and late-onset neonatal sepsis (L.O.N.S.). This systemic infection arises due to various causative pathogens such as viruses, bacteria, or fungi that can be detected in blood culture, and the most frequent is bacteria. Pathogenic bacteria differ from one country to another or between hospitals and impact the choice of antibiotic therapy. Excessive use of antibiotics can increase the consequences of increased morbidity, mortality, costs, and length of stay in the hospital, and the use of antibiotics is quite high, closely related to the increase in the problem of antibiotic resistance.

Until now, the empirical antibiotics used for neonatal sepsis patients at Prof Ngoerah Hospital, Bali, are ampicillin and gentamicin. Based on the description above, this study aims to evaluate the bacterial patterns and antibiotic susceptibility in neonatal sepsis at Prof Ngoerah Hospital, Bali. The results can be used as a reference as the basis for giving empirical antibiotics for neonatal sepsis.

METHODS

This observational, descriptive study was conducted in Prof Ngoerah Hospital, Bali. This study sample was selected by consecutive sampling. The inclusion criteria were neonates, examined for culture and antibiotic sensitivity with blood specimens. If data from medical records were incomplete or could not be read, the samples were excluded. Data were collected retrospectively from the blood culture registry of patients with neonatal sepsis.
Neonatal sepsis is a systemic response to infection in newborns, one of the main causes of mortality and morbidity in neonates worldwide. In this study, 52 (54.17%) subjects were male, and the other 44 (45.83%) were female. Compared to the results of a study in India in 2015, it was found that male neonates had a higher rate than female neonates. It is because the factors that regulate the higher rate than female neonates.

RESULTS
The characteristics of the research subjects
There were 690 with sign and symptom neonatal sepsis, 96 patients (13.91%) with confirmed blood culture and fulfilled inclusion and exclusion criteria. Bacterial patterns and antibiotic susceptibility were collected retrospectively (January 2021 to August 2022) from a blood culture registry from neonatal sepsis. Table 1 summarizes the characteristics of our research subjects (96 patients).

Identification of Microorganisms in the positive culture
The bacterial pattern was categorized into gram-positive and gram-negative microorganisms. As shown in Table 2, we found a higher proportion of gram-negative organisms (66; 68.75%) than gram-positive organisms (30; 31.25%).

Antibiotic sensitivity among isolated microorganisms
This study investigated the antibiotic sensitivity pattern among 96 isolated bacteria. Antibiotic with highest sensitivity rates overall were Gentamicin (50%), Doxycycline (43.33%), Moxifloxacin (43.33%), Erythromycin (30%) as seen in Figure 3.

DISCUSSION
Neonatal sepsis is a systemic response to infection in newborns, one of the main causes of mortality and morbidity in neonates worldwide. In this study, 52 (54.17%) subjects were male, and the other 44 (45.83%) were female. Compared to the results of a study in India in 2015, it was found that male neonates had a higher rate than female neonates. It is because the factors that regulate the
The preterm group (56.25%) had higher results than the term group (43.75%) in this study. According to a study in 2017, preterm neonates are more common than term neonates. Low birth weight (52.08%) was higher than normal. It is caused by immaturity of the immune system, prolonged mechanical ventilation,
long hospital stays, use of catheters and other invasive procedures. In this study, the survival rate was only 40.62%. Similar findings in a study in Tanzania in 2010 found that 28.5% of neonates with positive blood cultures died compared to only 8.6% of those with negative blood cultures (p = 0.0001). Gram-negative sepsis has been associated with severe sepsis and increased mortality. The outcome is usually determined by the duration of the inflammatory response to the offending pathogens, with severe and worse outcomes in gram-negative sepsis. We found mostly (80.20%) neonates had EONS than L.O.N.S. (19.80%), and gram-negative had a higher mortality rate.

This study found a higher proportion of gram-negative organisms (68.75%) than gram-positive organisms (31.25%). The findings are consistent with a study in Pakistan in 2016 that found 78.6% of isolates were gram-negative bacteria, while gram-positive bacteria accounted for 27.2% of cases of neonatal septicemia (P = 0.00). It may also indicate some of these infections are hygiene-related, including poor infection control practices, which can be challenging in limited resource settings. Thus, a key area of focus in trying to reduce the prevalence of neonatal sepsis could be improving infection control policies, including overall hygiene around routine and high-risk newborn care.

In this study, the predominance of gram-negative bacteria is Acinetobacter baumannii, followed by Klebsiella pneumoniae, and gram-positive bacteria is Staphylococcus haemolyticus, followed by Staphylococcus epidermidis. Mishra A et al. found the incidence of acinetobacter accounted for 31.5% of causes of neonatal sepsis, followed by Escherichia coli (26.3%), Klebsiella pneumoniae (10.7%) and Pseudomonas aeruginosa (7.2%). In another study at Adam Malik Hospital (2020), the pattern of bacteria was dominated by Klebsiella pneumonia (34.1%), followed by Acinetobacter baumannii (29.3%). Another study in Germany (2021) contained most of the isolates; 99 (73.9%) were gram-positive bacteria. The most predominant isolates were Staphylococcus epidermidis, 51 (38.1%), followed by Escherichia coli, 23 (17.2%); Staphylococcus haemolyticus, 15 (11.2); and Staphylococcus aureus, 11 (8.2%).

The other study by Kardana IM in Prof Ngoerah Hospital was dominated by gram-negative bacteria (68.3%), mostly Serratia marcescens (23.5%). The proportion of gram-positive bacteria, only 31.7%, such as Staphylococcus coagulase positive (16.4%), Staphylococcus coagulase negative (10.2%), and Streptococcus viridans (4.6%). Acinetobacter baumannii is the most common type of gram-negative bacteria found in this study. Bacterial colonization is commonly found in hospital equipment and the hands of health workers. Meanwhile, Klebsiella pneumonia is commonly found in the respiratory tract and feces in about 5% of normal individuals. Klebsiella pneumonia can cause extensive hemorrhagic necrotizing consolidation of the lungs.

Staphylococcus haemolyticus and Staphylococcus epidermidis are this study's most common type of gram-positive bacteria. Despite multiple studies over the past decade suggesting that Staphylococcus epidermidis and Staphylococcus haemolyticus are important causes of nosocomial and bloodstream infections in neonates in the gram-positive bacteria group.
Indonesia did not have a national registry for the incidence of neonatal sepsis up until this point. The rise of multi-drug-resistant infections in neonatal units has also recently sparked concerns. To determine the most suitable empiric treatment, it is crucial to monitor antibiotic and pathogen sensitivity levels, which vary from one unit to another.

As a first line of therapy for neonatal sepsis, the World Health Organization (WHO) recommends using a combination of the narrow-spectrum medications penicillin and an aminoglycoside. In our center, ampicillin and gentamicin are the first-line empirical antibiotic, and our result showed that their susceptibility rate was 4.17% and 57.29%, which means ampicillin had low sensitivity, but gentamicin still had high sensitivity. It had the same result as previous research by Suarca et al., that ampicillin had no longer sensitive to bacteria that cause sepsis. This study found that Acinetobacter baumannii is the most common type of gram-negative sensitive to Amikacin (75%). It is the same with another study that showed Acinetobacter baumannii is sensitive to Amikacin (78.9%).

Our data was based on single-center experience. Thus, the results are most likely related to the local epidemiological conditions. Differences observed in the bacterial spectrum and antibiotic resistance pattern of the isolates between recent studies and previous studies can be attributed to epidemiological differences, the prevalence of resistant strains in the region, and the type of antibiotic treatments. Our study showed that implementing a local epidemiological survey plays an important role in treating neonatal sepsis. The pattern of antibiotic sensitivity appears to be different in various research reports and, at other times, possibly due to the emergence of resistant strains due to the indiscriminate use of antibiotics.

CONCLUSION
This study found gram-negative bacteria were the most frequent cause of neonatal sepsis. The most sensitive antibiotics were gentamicin, ciprofloxacin, levofloxacin, TMP/SM, Amikacin, Meropenem, ampicillin/sulbactam, cefepime, piperacillin/tazobactam, cefoperazone sulbactam, Tigecycline, ceftriaxone, vancomycin. This study results in gentamicin still being an option as an empirical antibiotic, but ampicillin had low sensitivity; another broad-spectrum antibiotic with better sensitivity is considered another option due to its significantly higher susceptibility. Bacterial surveillance and resistance patterns must be carried out routinely to determine policies for the use of antibiotics in each neonatal care unit.

CONFLICT OF INTEREST
There is no competing interest regarding the manuscript.

ETHICAL CONSIDERATION
Ethics approval was obtained from the Ethics Committee, Faculty of Medicine, Universitas Udayana, Prof. Dr. I.G.N.G. Ngeorah Hospital, Bali, Indonesia, before the study was conducted.

FUNDING
None.

AUTHOR CONTRIBUTIONS
All authors equally contribute to the study from the conceptual framework, data acquisition, and data analysis until reporting the study results through publication.

ACKNOWLEDGMENT
We thank all of the patients who participated in this research and all of the research staff in our hospital for their invaluable support regarding the making of this manuscript.

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