SUMMARY

Neonatal sepsis remains one of the leading causes of morbidity and mortality in the neonatal period, particularly among preterm infants. Two forms are distinguished: early-onset sepsis (EOS), occurring within the first 72 hours of life, and late-onset sepsis (LOS), developing thereafter. These two entities differ in etiology, risk factors, and therapeutic implications. EOS most commonly results from vertical transmission, whereas LOS is usually associated with hospital-acquired infections related to intensive medical care.

The aim of this dissertation was to provide a comprehensive assessment of the epidemiology of neonatal sepsis and the antimicrobial susceptibility of pathogens responsible for EOS, with particular emphasis on their relevance for optimizing empirical therapy. This analysis was based on two publications encompassing a retrospective review of data from patients hospitalized in the tertiary referral Neonatal Intensive Care Unit of University Hospital No. 2 in Bydgoszcz between 2014 and 2023.

In the first study, positive blood cultures in newborns born before 37 weeks of gestation were analyzed to assess the etiology of EOS and LOS as well as their variability over time. The second study examined cases of EOS in both preterm and term infants, taking into account antimicrobial susceptibility profiles, resistance mechanisms, the adequacy of empirical therapy, and mortality. Pathogen identification was performed using MALDI-TOF MS or biochemical tests, and antimicrobial susceptibility was assessed according to EUCAST guidelines.

Significant differences in the etiology of EOS and LOS were demonstrated. Gram-negative bacteria, primarily *Escherichia coli*, predominated in EOS, whereas Gram-positive bacteria, mainly coagulase-negative staphylococci (CoNS), were most common in LOS. No significant trends in pathogen frequency were observed throughout the study period, including during the COVID-19 pandemic. The antimicrobial susceptibility analysis demonstrated high resistance of *E. coli* to ampicillin, while susceptibility to third-generation cephalosporins, aminoglycosides, and carbapenems remained high. In some isolates, ESBL mechanisms were detected, although they did not affect the efficacy of aminoglycosides or carbapenems. No increase in antimicrobial resistance was observed over the study period. *Streptococcus agalactiae* remained fully susceptible to penicillins. Infections caused by *E. coli* were

associated with higher, although not statistically significant, mortality. Ampicillin resistance did not have a significant impact on clinical outcomes. Empirical therapy using ampicillin in combination with an aminoglycoside remains a justified initial strategy until the etiological factor is identified. In selected clinical situations, however, it may be more beneficial to use a third-generation cephalosporin combined with an aminoglycoside or a carbapenem.

Despite limitations related to the retrospective and single-center design, the findings underscore the importance of continuous monitoring of local epidemiology and antimicrobial susceptibility patterns, which forms the basis for rational antibiotic therapy and improved outcomes in neonatal sepsis.