Turkish Journal of Pediatric Disease

Original Article

Clinical characteristics and outcomes of invasive pneumococcal disease in neonates: A retrospective study

Büşra Demirci[1], Gülsüm İclal Bayhan[2], Tuğba Erat[2], Aysun Yahşi[2], Seval Özen[2], Ahmet Yağmur Baş[3], Dilek Çetin[3], Bedia Dinç[4], Şerife Suna Oğuz[3]

[1]Department of Pediatrics, Ankara Bilkent City Hospital, Ankara, Türkiye
[2]Department of Pediatric Infectious Diseases, Ankara Bilkent City Hospital, Ankara, Türkiye
[3]Department of Neonatology, Ankara Bilkent City Hospital, Ankara, Türkiye
[4]Department of Medical Microbiology, Ankara Bilkent City Hospital, Ankara, Türkiye

ABSTRACT

Objective: Invasive pneumococcal disease (IPD) is a rare but serious cause of neonatal sepsis associated with significant morbidity and mortality. Despite widespread pneumococcal conjugate vaccine (PCV) use in infants, neonates remain vulnerable due to lack of direct vaccination and potential vertical or horizontal transmission. This study aimed to characterize the clinical, laboratory, and microbiological features of neonatal IPD and to evaluate associated outcomes in this high-risk population.

Material and Methods: We conducted a retrospective cross-sectional study of neonates (0–30 days old) diagnosed with IPD between September 2019 and April 2025. Diagnosis was confirmed by isolation of *Streptococcus pneumoniae* from sterile body fluids or PCR detection. Demographic, clinical, microbiological, and outcome data were analyzed.

Results: Among 68 IPD cases, 12 neonates with pneumococcal bacteremia were identified; no meningitis or focal infections were observed. The cohort had equal sex distribution, mean gestational age of 35±3.8 weeks, and 33.3% had comorbidities. Early-onset sepsis (≤72 hours) accounted for 25% of cases, with the remainder presenting as late-onset sepsis (>72 hours). One neonate had concurrent SARS-CoV-2 infection. All patients survived; one preterm infant developed neurological sequelae attributable to pre-existing conditions. Antibiotic susceptibility testing showed reduced sensitivity to penicillin (20%) and ceftriaxone (16.7%), while vancomycin and linezolid remained highly effective.

Conclusion: Neonatal invasive pneumococcal bacteremia, although uncommon, continues to pose clinical challenges, particularly due to evolving antimicrobial resistance. Our findings emphasize the importance of vigilant clinical monitoring and tailored antimicrobial therapy in this vulnerable population. Continued surveillance and prospective studies are warranted to assess the impact of maternal and early infant vaccination strategies on neonatal IPD prevention.

Keywords: Antibiotic resistance, bacteremia, pneumococcal infections, sepsis, *Streptococcus pneumoniae*

INTRODUCTION

Streptococcus pneumoniae is a Gram-positive diplococcus and the etiologic agent of invasive pneumococcal diseases (IPD), which include bacteremia, sepsis, and meningitis. Globally, IPD continues to pose a substantial health burden, particularly in children under five years of age, and remains associated with considerable morbidity and mortality despite the availability of effective vaccines. In 2015, pneumococcal infections were estimated to cause approximately 335.000 deaths in this age group, a decrease from 541.000 deaths in 2008 prior to the widespread implementation of conjugate vaccines in low-income countries (1). Although pneumococcal conjugate vaccines (PCVs) have reduced the incidence of severe infections and antibiotic resistance, the emergence of non-vaccine serotypes continues to pose challenges (2). In Türkiye, PCV13 was introduced into the national immunization program in April 2011 and has been administered in a 2+1 schedule (at 2, 4, and 12 months) since 2019 (3). The indirect protection conferred by pneumococcal conjugate vaccine

Correspondence Address:
Büşra Demirci
e-mail: bozuyukbusra@gmail.com

Received : 20.08.2025
Accepted : 01.12.2025
DOI: 10.12956/TJPD.2025.1217

(PCV) to neonates and infants too young to receive PCV—mediated through herd immunity— has been well documented in the literature. Studies report a 40% to 83% reduction in IPD incidence in this age group, along with an overall declining trend in IPD rates (4,5).

While *S. pneumoniae* infections are rare in neonates, they are associated with considerable mortality and morbidity (6). Transmission may occur via the birth canal, intrauterine spread, or horizontal contact with caregivers (7). Despite herd immunity achieved through childhood vaccination, neonates remain vulnerable to IPD via vertical or horizontal transmission. Pneumococcus accounts for 1–11.5% of neonatal sepsis cases, with reported mortality rates ranging from 14.3% to 60%, often manifesting as sepsis or early-onset pneumonia (8-10). Although neonatal cases are often described as early-onset sepsis, findings from the largest published series indicate that only 6.8% of cases developed symptoms within the first 48 hours, while the majority presented after the first week of life (6-8). These data highlight the variable timing of disease onset and underscore the importance of clinical vigilance throughout the neonatal period.

Given the limited recent data on neonatal pneumococcal infections, this study aimed to characterize the clinical and microbiological features of invasive pneumococcal disease in this unvaccinated population.

MATERIALS and METHODS

This retrospective cross-sectional study evaluated a total of 68 invasive pneumococcal disease (IPD) cases identified in children aged 0–18 years between September 1, 2019, and April 1, 2025. Among these, 12 neonates (postnatal age 0–30 days) with culture-confirmed Streptococcus pneumoniae bacteremia were included as the study sample. Data were obtained from the hospital information system. For each case, demographic characteristics (gender, age, date and type of specimen), risk factors, clinical and laboratory findings, antibiotic susceptibility, and outcomes were recorded.

IPD was confirmed by isolating *Streptococcus pneumoniae* from sterile body fluids (blood, cerebrospinal fluid, synovial/bone, pleural, or middle ear fluid) or by detecting pneumococcal DNA via polymerase chain reaction (PCR) in blood or cerebrospinal fluid samples. All microbiological procedures followed standardized protocols.

Neonatal sepsis was classified according to the timing of symptom onset. Early-onset neonatal sepsis (EONS) was defined as the occurrence of clinical manifestations within the first 72 hours after birth, most frequently resulting from vertical transmission of pathogens from the maternal genital tract during labor or delivery (11). Late-onset neonatal sepsis (LONS) was defined as symptom onset beyond 72 hours of life, generally associated with horizontal acquisition of pathogens from the postnatal environment, including community or healthcare-associated sources (12).

Gram-stained preparations were assessed under 100× magnification for polymorphonuclear leukocytes and Gram-positive diplococci using a BioMérieux device (France). Clinical samples were inoculated onto appropriate culture media and incubated using the WASPLab® system (Copan, Italy), with conditions tailored to the sample type. Blood samples were processed in BACT/ALERT bottles (bioMérieux, France) and incubated for 120 hours in the BACT/ALERT 3D system. Positive signals prompted Gram staining and subcultures, which were incubated for 24–48 hours. Suspicious colonies—alpha-hemolytic, small, gray, mucoid, or button-like with central depression—were identified using MALDI-TOF MS (VITEK® MS, bioMérieux, France). Colonies were transferred to metal slides, overlaid with 1 µL of α-cyano-4-hydroxycinnamic acid matrix solution, air-dried for ~15 minutes, and analyzed.

Antibiotic susceptibility testing was performed using the VITEK® 2 Compact system (bioMérieux, France), and results were interpreted according to EUCAST guidelines. Bacterial inocula were adjusted to 0.5 McFarland standard. A 280 µL aliquot was added to sterile saline (0.45%) in transparent tubes, vortexed, and loaded with AST-ST03 cards into the system. Minimum inhibitory concentrations (MICs) were determined automatically for each antimicrobial agent. As all cases in our cohort represented bacteremia without meningitis, EUCAST non-meningitis breakpoints were applied. Results are presented as susceptible (S), intermediate (I), or resistant (R), expressed as n/N (%), to enhance clarity and minimize misinterpretation in the context of a small sample size.

Statistical analysis

Descriptive statistical analyses were conducted using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables, including sex, prematurity, comorbidities, clinical presentation, and antimicrobial susceptibility patterns, were summarized as frequencies and percentages. Continuous variables, such as gestational age and postnatal age at diagnosis, were assessed for normality and presented as means with standard deviations. Owing to the small sample size and the rarity of neonatal IPD, no inferential statistical analyses or group comparisons were performed. Antibiotic susceptibility rates were calculated based on the proportion of isolates meeting EUCAST-defined sensitivity thresholds. This approach ensured an accurate and transparent representation of clinical and microbiological characteristics within the neonatal IPD cohort.

RESULTS

Among the 68 patients aged 0–18 years who were diagnosed and followed with IPD during the study period, 12 were identified in the neonatal period. In these 12 neonates, Streptococcus

Table I: Clinical characteristics of neonates with invasive pneumococcal disease (n = 12)*	
Prematurity	5 (41.7)
Comorbid conditions	4 (33.3)
Nutrition	
Exclusive breastfeeding	6 (50.0)
Breast milk + formula	6 (50.0)
Respiratory and circulatory support	
Mechanical ventilation	3 (25.0)
Non-invasive ventilation	4 (33.3)
Inotropic support	1 (8.3)

**: n(%), Prematurity is defined as gestational age <37 weeks. Comorbid conditions include congenital anomalies and other significant underlying diseases*

Table II: Laboratory characteristics of neonates with invasive pneumococcal disease (n = 12)	
White Blood Cell count*	11.717±2.446
Absolute Neutrophil Count*	4.996±1.861
Absolute Lymphocyte Count*	4.434±1.822
Hemoglobin *	12.3±1.9
Platelet count*	373.333±143.281
C-reactive Protein†	6.5 (0–46)
Sodium*	138.8±3.6
Potassium*	5.4±1.0
Aspartate Aminotransferase*	36±30
Alanine Aminotransferase*	19±11.5

**: mean ± SD, †: Median (range)*

pneumoniae was isolated exclusively from blood cultures; no growth was detected in cerebrospinal fluid or other sterile body sites, and multiplex PCR panels for sepsis or meningitis/encephalitis were negative in all cases. A detailed overview of demographic features, clinical presentations, comorbidities, and timing of sepsis onset for all neonates is provided in Table I.

Of the 12 included patients, 6 were female and 6 were male. The mean gestational age was 35±3.8 weeks; 5 were born preterm (gestational ages: 36+6, 32+6, 28+5, 32, 30+1, 33+4 weeks). All infants were delivered via cesarean section.

Four patients (33.3%) had underlying comorbidities, including meningomyelocele, tracheoesophageal fistula, gastroschisis, and liver abscess; one of these patients was also small for gestational age (SGA) due to intrauterine growth restriction.

Admission diagnoses were early-onset sepsis in 4 cases (33.3%), late-onset sepsis in 4 (33.3%), and respiratory distress in 4 (33.3%). Based on timing of blood culture positivity, 4 patients had early-onset bacteremia (≤3 days of life), while 8 had late-onset bacteremia (>3 days). Laboratory parameters, including complete blood count and inflammatory markers at admission, are summarized in Table II.

One patient was born to a COVID-19 positive mother. The infant, delivered at 39+1 weeks via cesarean section, presented with fever on postnatal day 4. The infant's nasopharyngeal PCR was also positive for SARS-CoV-2. *S. pneumoniae* was isolated from the initial blood culture, and empiric ampicillin-gentamicin was escalated to vancomycin. The infant completed 10 days of antibiotics and was discharged without sequelae. No other patients had viral coinfections or positive PCR panel results.

One neonate, born at 30 weeks of gestation following preterm premature rupture of membranes (PPROM) and fetal distress, developed IPD manifesting as isolated bacteremia on postnatal day 30. The patient had pre-existing comorbidities, including respiratory distress syndrome, grade 4 intraventricular hemorrhage, posthemorrhagic hydrocephalus, and hepatic hematoma, and subsequently required ventriculoperitoneal (VP) shunt placement. The long-term neurological sequelae observed in this case were attributable to the underlying conditions rather than pneumococcal infection; all other patients recovered without complications.

Antibiotic susceptibility rates for *S. pneumoniae* isolates were as follows: penicillin 20%, ampicillin 16.7%, clindamycin 18.2%, erythromycin 16.7%, ceftriaxone 16.7%, levofloxacin 75%, moxifloxacin 80%, linezolid 100%, tetracycline 9.1%, vancomycin 91.7%, and trimethoprim-sulfamethoxazole 100%.

DISCUSSION

In this 5.5-year retrospective analysis, 12 neonates with invasive pneumococcal disease were identified, all presenting with Streptococcus pneumoniae bacteremia. No cases of meningitis or other focal infections were detected, as cerebrospinal fluid cultures and multiplex PCR panels were uniformly negative. The cohort had equal sex distribution and a mean gestational age of 35 ± 3.8 weeks, with nearly half born preterm; all infants were delivered by cesarean section. One-third had notable comorbidities, including congenital anomalies or intrauterine growth restriction. Clinical presentations were evenly divided among early-onset sepsis, late-onset sepsis, and respiratory distress. Only one infant experienced long-term neurological sequelae, attributed to severe pre-existing conditions rather than pneumococcal infection. All remaining neonates recovered without complications. Overall, IPD in this cohort manifested exclusively as isolated bacteremia, with favorable outcomes following timely management.

Streptococcus pneumoniae is a rare but well-recognized cause of neonatal sepsis, associated with considerable morbidity and mortality (7). Most published data consist of case reports or small series. The largest to date, by Hoffmann et al. (8), included 29 neonatal IPD cases and reported a mortality rate of 14.3%, with most cases presenting as late-onset sepsis. In contrast, Malhotra et al.(7), and Gomez et al.(13) found earlier presentations in 69% and 100% of their small case series, respectively, though sample sizes were limited to five and four cases. Gomez et al. (13), also reported a mortality rate of 50%, while a more recent study reported 39%, with the highest rates

in meningitis cases (14). In our series of 12 neonates with confirmed pneumococcal bacteremia, 25% presented with early-onset sepsis, whereas the majority (75%) were diagnosed with late-onset sepsis. No deaths occurred. The favorable outcomes observed in our cohort could be attributed to advanced supportive care practices, such as early recognition of sepsis, optimized antimicrobial use, and intensive neonatal monitoring. Furthermore, our study represents a post-vaccine era cohort, which may explain lower mortality compared to earlier reports. Notably, no cases of pneumococcal meningitis were observed, a condition historically linked with higher fatality (13,15).

Infants can become colonized with *S. pneumoniae* soon after birth, and the prevalence of colonization tends to rise as they get older. Colonization rates of approximately 0.3%, 7%, 4%, and 10% have been observed at 0, 4, 8, and 12 months of age, respectively (16). Although *S. pneumoniae* is an uncommon cause of neonatal sepsis, infections due to this pathogen have been described as having a more severe clinical course. Interestingly, some studies have reported that *S. pneumoniae* was identified more frequently than Group B Streptococcus (15%) in cases of early-onset sepsis. This suggests that *S. pneumoniae* may represent a more significant pathogen in early neonatal sepsis than previously appreciated (17). In our study, four patients presented with early-onset and four with late-onset neonatal sepsis. Although national data on the incidence of neonatal IPD in Türkiye are limited, the rate appears to be markedly reduced following widespread implementation of pneumococcal conjugate vaccines. Consistent with this, only a small number of neonatal IPD cases were identified over a 5.5-year period at our institution, one of the largest pediatric centers in the country, underscoring the rarity of this condition in the current post-vaccination era.

Maternal factors are thought to play a critical role in the pathogenesis of neonatal IPD, particularly in early-onset disease. Several reports have suggested that vertical transmission during labor or colonization of the maternal genital tract may contribute to infection in neonates (18,19). Other potential risk factors include maternal chorioamnionitis, premature rupture of membranes, and preterm delivery, all of which may facilitate perinatal acquisition of *S. pneumoniae* (20). Despite the biological plausibility of these associations, robust data remain limited, as maternal screening for pneumococcal carriage is not routinely performed in most settings. In our study, detailed obstetric histories and maternal colonization status could not be retrieved due to the retrospective design and incomplete clinical documentation. This gap highlights the importance of prospective surveillance incorporating maternal data to better delineate risk factors for neonatal IPD and inform preventive strategies.

Increasing antimicrobial non-susceptibility among *Streptococcus pneumoniae* isolates has been documented in recent regional reports and mirrors the low penicillin and ceftriaxone susceptibilities observed in our cohort. A recent Turkish surveillance analysis reported a significant rise in penicillin non-susceptibility from 1.9% (2017–2019) to 20.3% (2020–2022), with appreciable ceftriaxone non-susceptibility noted in some periods, underscoring an emerging local trend toward reduced β-lactam susceptibility (21). A two-decade analysis of invasive pneumococcal isolates from Türkiye similarly documented increasing non-susceptibility to penicillin and macrolides over time, suggesting that these trends are not isolated to a single center. More recent multicenter surveillance in neighboring regions and broader analyses report variable but notable rates of reduced susceptibility to penicillins and third-generation cephalosporins, reinforcing the need for ongoing regional monitoring to guide empiric therapy (22). Compared with these regional data, our finding of low penicillin (20%) and ceftriaxone (16.7%) sensitivity likely reflects local epidemiology and the impact of serotype replacement and antimicrobial selection pressure in the post-PCV era. These observations support empiric coverage that includes agents active against resistant pneumococci (e.g., vancomycin), particularly in severe neonatal infections or where initial therapy fails, while underlining the imperative for routine, up-to-date susceptibility surveillance and incorporation of serotype data in future studies to better correlate resistance patterns with vaccine-driven serotype shifts.

Over the years, the introduction of PCVs with broader serotype coverage has led to a marked decline in the incidence of IPD in children. Studies have consistently demonstrated this reduction across vaccine-included serotypes (23,24). Following the implementation of PCV7, a significant decrease was observed in the covered serotypes, which subsequently created the need for vaccines with expanded serotype coverage. In our country, PCV13 is currently in use as the latest formulation. However, due to the retrospective design of our study, we were unable to capture temporal trends in serotype distribution. Nevertheless, we believe that the low number of positive cases observed in our cohort likely reflects the impact of widespread vaccination. Furthermore, the low case count, absence of mortality, and the presence of sequelae only in an infant with significant pre-existing comorbidities suggest that the favorable outcomes observed in our cohort may, in part, reflect the impact of high pneumococcal vaccine coverage on reducing disease severity in the neonatal population.

Historically, neonatal IPD case series have contributed significantly to understanding disease progression. However, older reports may not reflect current trends due to improvements in healthcare and neonatal outcomes. To our knowledge, recent large-scale analyses focusing on post-vaccine era neonatal IPD remain scarce. We believe our study offers updated insights into this rare but serious condition.

Infant immunization at two months contributes to herd immunity, indirectly protecting neonates (25). Maternal vaccination could offer additional protection via transplacental antibodies, though

it is not currently recommended in pregnancy (26). To strengthen prevention strategies, prospective studies should evaluate the safety and efficacy of maternal pneumococcal vaccination, particularly in high-risk populations such as preterm infants or those with underlying comorbidities. Enhanced perinatal screening and surveillance programs, including monitoring of maternal colonization, may further guide targeted interventions. In addition, integration of pneumococcal vaccination into broader maternal immunization platforms—such as those for pertussis and influenza—could improve uptake and provide dual maternal–infant benefits. From a health systems perspective, reinforcing vaccine outreach, ensuring equitable access, and maintaining robust antimicrobial stewardship are essential complementary measures to reduce the burden of neonatal IPD.

Limitations:

This study has several limitations. The small sample size and the absence of a non-pneumococcal control group restrict the generalizability of the findings. The retrospective design also limited access to complete obstetric histories, which may have provided additional insights. Furthermore, incidence rates and pneumococcal serotype data were not analyzed, precluding a broader epidemiological interpretation of the results. Although our study provides valuable clinical insights, the lack of pneumococcal serotype data limits the ability to assess serotype-specific epidemiology and clinical outcomes. This is particularly relevant in the post-vaccine era, as shifts in circulating serotypes may influence both disease severity and antimicrobial susceptibility patterns. Future studies incorporating serotyping are warranted to better characterize the evolving epidemiology of neonatal invasive pneumococcal disease and to guide targeted prevention strategies.

CONCLUSION

Despite widespread infant immunization, pneumococcal infections continue to pose a clinically significant risk in neonates. The presence of unvaccinated and vulnerable populations underscores the importance of strengthening vaccine outreach and ensuring equitable access to neonatal intensive care. Although current vaccines have reduced the overall disease burden, the emergence of non-vaccine serotypes highlights the need for continued epidemiological surveillance and microbiological monitoring. From a clinical perspective, neonates presenting with sepsis should be considered at risk for *Streptococcus pneumoniae*, particularly when unresponsive to standard first-line regimens. In such scenarios, empiric coverage with agents active against resistant strains, including a glycopeptide when meningitis is suspected or devices such as ventricular shunts are present, should be considered until susceptibility results are available. De-escalation to the narrowest effective antibiotic and adherence to evidence-based treatment durations (10–14 days for bacteremia, up to 21 days for meningitis or focal infection) are recommended. Future research should adopt a multicenter design incorporating systematic serotyping and comprehensive incidence estimation to better define the epidemiology of neonatal IPD. Such studies would allow correlation of circulating serotypes with antimicrobial resistance patterns, evaluate vaccine impact across diverse populations, and inform evidence-based strategies for prevention, empiric therapy, and maternal-infant vaccination programs.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Ankara Bilkent City Hospital (12.03.2025, reference number: TABED 1-25-1112).

Contribution of the authors

Conceived and designed the study, collected and analyzed the data, and drafted the manuscript;BD, is contributed to data acquisition, the statistical analysis and interpretation of data, laboratory analysis, and interpretation of microbiological findings; GİB, provided critical revisions of the manuscript and contributed to the study design. All authors reviewed and approved the final version of the manuscript; AY,SÖ,TE,AYB,DÇ,BD,ŞSO.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

1. von Mollendorf C, Tempia S, von Gottberg A, Meiring S, Quan V, Feldman C, et al. Estimated severe pneumococcal disease cases and deaths before and after pneumococcal conjugate vaccine introduction in children younger than 5 years of age in South Africa. PLoS One. 2017;12(7):e0179905. https://doi.org/10.1371/journal.pone.0179905
2. Olarte L, AK. *Streptococcus pneumoniae*. In: In S. S. Long CGP& MF (Eds.), editor. Principles and practice of pediatric infectious diseases. 6th ed. 2023. https://doi.org/10.1016/B978-0-323-75608-2.00123-3
3. Şimşek Orhon F. Genişletilmiş Bağışıklama Programına Her Yönüyle Bakış. Osmangazi Journal Of Medicine. 2020;6-14. https://doi.org/10.20515/otd.681563
4. Poehling KA, Talbot TR, Griffin MR, Craig AS, Whitney CG, Zell E, et al. Invasive Pneumococcal Disease Among Infants Before and After Introduction of Pneumococcal Conjugate Vaccine. JAMA. 2006;295(14):1668. https://doi.org/10.1001/jama.295.14.1668
5. Ladhani SN, Andrews NJ, Waight P, Borrow R, Slack MPE, Miller E. Impact of the 7-Valent Pneumococcal Conjugate Vaccine on Invasive Pneumococcal Disease in Infants Younger Than 90 Days in England and Wales. Clinical Infectious Diseases. 2013;56(5):633-40. https://doi.org/10.1093/cid/cis934
6. Alan S, Yıldız D, Erdeve Ö, Atasay B, Nar Otgun S, İnc E, et al. An Early Neonatal Sepsis Case Due to *Streptococcus pneumoniae* Serotype 7F. Mikrobiyol Bul. 2013;158-63. https://doi.org/10.5578/mb.4237

7. Malhotra A, Hunt RW, Doherty RR. *Streptococcus pneumoniae* sepsis in the newborn. J Paediatr Child Health. 2012;48(2). https://doi.org/10.1111/j.1440-1754.2010.01929.x
8. Hoffman JA, Mason EO, Schutze GE, Tan TQ, Barson WJ, Givner LB, et al. *Streptococcus pneumoniae* Infections in the Neonate. Pediatrics. 2003;112 (5):1095-102. https://doi.org/10.1542/peds.112.5.1095
9. Kaplan M, Rudensky B, Beck A. Perinatal Infections with *Streptococcus Pneumoniae*. Am J Perinatol. 1993;10 (01):1-4. https://doi.org/10.1055/s-2007-994687
10. Sallam A, Paes B. *Streptococcus pneumoniae*: An Old Bug with Significant Maternal-Newborn Implications. Am J Perinatol. 2004;21 (08):491-5. https://doi.org/10.1055/s-2004-835967
11. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. The Lancet. 2017; 390 (10104):1770-80. https://doi.org/10.1016/S0140-6736(17)31002-4
12. Puopolo KM, Benitz WE, Zaoutis TE, Cummings J, Juul S, Hand I, et al. Management of Neonates Born at ≤34 6/7 Weeks' Gestation With Suspected or Proven Early-Onset Bacterial Sepsis. Pediatrics. 2018;142 (6). https://doi.org/10.1542/peds.2018-2896
13. Gomez M, Alter S, Kumar M Lou, Murphy S, Rathore MH. Neonatal Streptococcus pneumoniae infection: case reports and review of the literature. Pediatr Infect Dis J. 1999;18 (11):1014-8. https://doi.org/10.1097/00006454-199911000-00016
14. Moodley K, Coovadia YM, Cohen C, Meiring S, Lengana S, De Gouveia L, et al. Invasive Pneumococcal Disease in Neonates Prior to Pneumococcal Conjugate Vaccine Use in South Africa: 2003-2008. Pediatric Infectious Disease Journal. 2019;38 (4):424-30. https://doi.org/10.1097/INF.0000000000002096
15. Bortolussi R, Thompson TR, Ferrieri P. Early-onset pneumococcal sepsis in newborn infants. Pediatrics. 1977;60(3):352-5. https://doi.org/10.1542/peds.60.3.352
16. Meropol SB, Jacobs MR, Stange KC, Bajaksouzian S, Bonomo RA. Longitudinal Colonization With *Streptococcus pneumoniae* During the First Year of Life in a Healthy Newborn Cohort. J Pediatric Infect Dis Soc. 2020;9(4):442-8. https://doi.org/10.1093/jpids/piz068
17. Oeser C, Pond M, Butcher P, Bedford Russell A, Henneke P, Laing K, et al. PCR for the detection of pathogens in neonatal early onset sepsis. PLoS One. 2020;15(1):e0226817. https://doi.org/10.1371/journal.pone.0226817
18. Coelho I, Baptista S, Ramalho AR, Calado C, Gaspar L, Virtuoso MJ, et al. Early-Onset Neonatal Pneumococcal Sepsis: An Old but Sometimes Forgotten Pathogen. Cureus. 2022 Sep 21; https://doi.org/10.7759/cureus.29403
19. Hermoso Torregrosa C, Carrasco Zalvide M, Ferrer Castillo MT. Streptococcus pneumoniae: un patógeno poco habitual en la sepsis neonatal de transmisión vertical. Arch Bronconeumol. 2012;48(11):425-6. https://doi.org/10.1016/j.arbres.2012.03.010
20. Amin-Chowdhury Z, Bertran M, Abdullahi F, Sheppard CL, Eletu SD, Litt DJ, et al. Risk of invasive pneumococcal disease during pregnancy and postpartum and association with adverse maternal and foetal outcomes: A prospective cohort study, England, 2014-19. Journal of Infection. 2025;90 (1):106363. https://doi.org/10.1016/j.jinf.2024.106363
21. Hascelik G, Sancak B, Kasikci M. A twenty years' results of the antimicrobial resistance profile and multidrug resistance trend of invasive *Streptococcus pneumoniae* isolates recovered from adult patients in Türkiye: A literature review. Indian J Med Microbiol. 2022 ;40(3):342-6. https://doi.org/10.1016/j.ijmmb.2022.06.004
22. Maraki S, Mavromanolaki VE, Stafylaki D, Iliaki-Giannakoudaki E, Kasimati A, Hamilos G. Antimicrobial Resistance of Streptococcus pneumoniae Clinical Serotypes between 2017 and 2022 in Crete, Greece. Infect Chemother. 2024;56 (1):73. https://doi.org/10.3947/ic.2023.0098
23. Kozakova J, Krizova P, Maly M. Impact of pneumococcal conjugate vaccine on invasive pneumococcal disease in children under 5 years of age in the Czech Republic. PLoS One. 2021;16 (2): e0247862. https://doi.org/10.1371/journal.pone.0247862
24. Yen TA, Wu JL, Wang CC, Huang LY, Yeo SH, Patel D, et al. A population-based study on the burden of hospitalized pediatric pneumococcal disease in Taiwan before and after the introduction of 13-valent pneumococcal conjugate vaccine into the childhood immunization program in 2015. BMC Infect Dis. 2025;25 (1) :176. https://doi.org/10.1186/s12879-024-10379-z
25. O'Brien KL, Wolfson LJ, Watt JP, Henkle E, Deloria-Knoll M, McCall N, et al. Burden of disease caused by *Streptococcus pneumoniae* in children younger than 5 years: global estimates. The Lancet. 2009; 374 (9693): 893-902. https://doi.org/10.1016/S0140-6736(09)61204-6
26. Chaithongwongwatthana S, Yamasmit W, Limpongsanurak S, Lumbiganon P, Tolosa JE. Pneumococcal vaccination during pregnancy for preventing infant infection. Cochrane Database of Systematic Reviews. 2015; 2015 (1). https://doi.org/10.1002/14651858.CD004903.pub4