Neonatal sepsis in southwest of Iran; prevalence of microbial pathogens, risk factors, clinical manifestations and laboratory findings

Marjan Salahi
Yasuj University of Medical Sciences
Abdolkarim Ghadimi Moghadam
Yasuj University of Medical Sciences
Ali Mousavizadeh
Yasuj University of Medical Sciences
Masoud Marashifard
Yasuj University of Medical Sciences
Seyed Jabar Taghavi
Yasuj University of Medical Sciences
Mohamadtaher Rezanejad
Yasuj University of Medical Sciences
Sedighe Moradi
Yasuj University of Medical Sciences
Seyed Sajjad Khoramrooz (Khoramrooz@gmail.com)
Yasuj University of Medical Sciences

Research Article

Keywords: Neonatal sepsis, Bacterial profile, Risk factors, Laboratory findings

Posted Date: December 17th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-122635/v1

Neonatal sepsis in southwest of Iran; prevalence of microbial pathogens, risk factors, clinical manifestations and laboratory findings

Marjan Salahi[1], Abdolkarim Ghadimi Moghadam[2], Ali Mousavizadeh[3], Masoud Marashifard [1], Seyed Jabar Taghavi[1], Mohamadtaher Rezanejad[1], Sedighe Moradi[1], Seyed Sajjad Khoramrooz[2*]

[1]Student Research Committee, Yasuj University of Medical Sciences, Yasuj, Iran
[2]Cellular and Molecular Research Center, Yasuj University of Medical Sciences, Yasuj, Iran
[3]Social Determinants of Health Research Center, Yasuj University of Medical Sciences, Yasuj, Iran

[*]**Corresponding author**. Cellular and Molecular Research Center, Yasuj University of Medical Sciences, Next to Imam Sajjad Hospital, Shahid Ghorbanali Jalil Blvd, Yasuj, Iran.

Tel/Fax: +98 7433235153. *E-mail address*: Khoramrooz@gmail.com (SS Khoramrooz)

Abstract

Background: Neonatal sepsis is a serious worldwide problem causing significant rates of mortality and morbidity in newborns, especially in cases with delayed infection diagnosis and management. The present study aimed to evaluate the bacteriological profiles, antibiotic susceptibility patterns, risk factors, clinical manifestations, and laboratory findings in neonatal sepsis in southwest of Iran.

Methods: In this descriptive-analytic study, 342 neonates with suspected sepsis admitted to the neonatal ward and NICU were included. Using standard protocols, blood samples were transported to the BACTEC blood culture system. Then, conventional biochemical tests were used for the identification of bacterial genera and species. The bacterial antimicrobial susceptibility patterns were determined using agar disk diffusion method according to the CLSI guidelines. Demographic data, clinical findings, risk factors, mortality rates, and laboratory parameters were collected for each patient.

Results: Forty-three (12.6%) cases were culture-positive, among which CoNS, *Staphylococcus aureus*, *Escherichia coli*, *Acinetobacter* and *Beta hemolytic streptococcus* were the most prevalent. The prevalence of early-onset sepsis and late-onset sepsis were 53.5% and 46.5%, respectively. Significant differences between prematurity, very low birth weight, and invasive procedures were observed between neonates with and without sepsis. Teicoplanin and vancomycin were the most efficient antibiotics against Gram-positive bacteria, while amikacin was more efficient against Gram-negative bacteria.

Conclusion: Risk factors such as prematurity, abnormal birth weight, anemia, leukopenia, prolonged hospitalization, and invasive processes and cesarean section, can increase the incidence of neonatal sepsis.

Keywords: Neonatal sepsis, Bacterial profile, Risk factors, Laboratory findings

Introduction

Neonatal sepsis is a clinical syndrome referring to the systemic presence of microorganisms within the first 28 days of life. The undesirable effects of this clinical syndrome are due to the uncontrolled systemic inflammatory responses against infection, leading to organ dysfunction through several pathophysiological mechanisms.[1]

The neonatal period is considered as the most vulnerable period of life owing to high susceptibility to infectious agents, immaturity of immune system, low levelor short term exposure to infectious agents, and low immunoglobulin production.[2]

Neonatal sepsis is a serious complication leading to mortality and morbidity, especially among very low birth weight (VLBW, <1500 g) and preterm infants in Neonatal Intensive Care Units (NICUs).[3, 4]

Late complications of neonatal sepsis include impaired bone marrow function (neutropenia, thrombocytopenia, and anemia), renal failure, heart failure, neurological disorders, disseminated intravascular coagulation (DIC), and shock.[5, 6]

Depending on the neonatal age and timing of the presentation, sepsis has been classified into early-onset-sepsis (EOS) and late-onset-sepsis (LOS). Early-onset infections are usually acquired through mother-to-infant vertical transmission during the first week after birth and late-onset infections appear after first week of life due to interactions with the hospital environment or the community with nonspecific clinical symptoms, such as respiratory distress, temperature instability, seizure, cyanosis, tachypnea, apnea, lethargy, irritability, poor feeding, and tachycardia.[7]

Maternal, neonatal, and environmental risk factors as well as the virulence of infectious organisms can lead to neonatal sepsis.[8]Various etiologic agents, including Gram-positive and Gram-negative bacteria, cause this syndrome. Organisms responsible for neonatal sepsis can vary depending on geographical region and the age of onset.[2, 9]

In addition, bacteriological profile of neonatal sepsis has changed over time in various areas due to lifestyle differences and antibiotic overuse, and subsequent alterations in antibiotic susceptibility patterns.[10, 11]

The most common organisms isolated from blood culture are Gram-positive bacteria, including *coagulase-negative Staphylococcus* (CoNS), *Group B Streptococcus* (GBS), *Enterococus, Listeria monocytogenes*, and Gram-negative bacteria, such as *Escherichia coli*, *Enterobacter*, *Klebsiella*, *Citrobacter*, *Serratia*, *Acinetobacter*,*Pseudomonas*.[11, 12]

Pro-inflammatorymediatorsare recruited following bacterial entry tothe bloodstream. Bacterial virulence factors, such as lipopolysaccharide, lipoteichoic acid, peptidoglycan, enzymes, super-antigens, and toxins not only over-stimulate the immune system, but also lead to bacterial tolerance to the destructive and deadly effects of the immune system.

Non-specific symptoms of neonatal sepsis can challenge the diagnosis and treatment of this syndrome, especially in preterm very low birth weight neonates.[2]

Prolonged and inappropriate antibiotic administrations can adversely affect the intestinal microbiota, especially in early days of life. Therefore, broad-spectrum antibiotics may easily replace a pathogen with a more dangerous one.[13-15]

Given the alterations in microbial profile and antibiotic susceptibility patterns, identification of the most common bacteria isolated from neonatal sepsis as well as the appropriate antibiotic administration are highly important.

Little information is present regarding the epidemiology of bacterial profile and risk factors associated with neonatal sepsis in Iran. Hence, the present study aimed to evaluate the bacteriological profile, antibiotic susceptibility patterns, risk factors, clinical manifestations and laboratory findings in neonatal sepsis in southwest of Iran.

MATERIALS AND METHODS

Sample collection

This descriptive-analytic study was conducted from June 2017 to April 2018 in neonatal ward and NICU of Imam Sajjad hospital in Yasuj, southwest of Iran. The study was conducted in accordance with the Declaration of Helsinki. This study has been approved by Yasuj University of Medical Sciences, Research Ethics Committee (IR.YUMS.REC.1395.190). Prior to sample collection, written informed consents were obtained from parents / guardians of each individual.

Infants with clinical symptoms, including temperature instability (temperatures >38 °C and <35/5 °C), lethargy, irritability, poor feeding, respiratory distress, tachypnea, apnea, cyanosis, seizure, grunting, diarrhea, vomiting , skin rash as well as neonates with sepsis risk factors, such as prematurity (age in weeks<37), low birth weight (birth weight 2500-1500 gr), very low birth weight (birth weight ≤ 1500 gr),premature rupture of membranes (PROM), and low Apgar score in neonatal and NICU wards were included in the study.

Under aseptic conditions, one ml blood was taken from each neonate before antibiotic administration and transferred to BACTEC pediatric bottles (BACTEC 9050; Becton Dickinson, MD, United States of America).

Demographic information, clinical manifestations, risk factors, and laboratory findings of each neonate were extracted from their medical records.

For bacterial identification, after alerting by BD system, bottle contents were sub-cultured on blood agar, chocolate agar, and McConkey agar media and incubated in both CO2 and non-CO2 conditions at 37ºC for 24 -48h. After Gram staining, biochemical tests, such as catalase, coagulase, Novobiocin sensitivity, bile solubility, optochin sensitivity, hippurate hydrolysis, CAMP, and PYR tests were performed for the identification of Gram-positive cocci. Enterobacteriacae members were identified at the species levels using conventional

biochemical tests, including indole production, methyl red, Voges-Proskauer, citrate utilization, hydrogen sulfide production, amino acids utilization, and urea hydrolysis[16]. In cases of CONS isolation, samples entered the study according to the National Institute of Child Health and Human Development (NICHD).[17]

Neonates with culture-positive blood samples were categorized into two groups: early-onset sepsis (age < 7 days) and late-onset sepsis (age > 7 days).[18]

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing was performed using agar disc diffusion method according to the Clinical and Laboratory Standards Institute(CLSI)guidelinesfor the following antibiotics: teicoplanin (30µg), oxacillin (1µg), vancomycin (30µg), gentamicin (120µg), penicillin (10µg), amikacin (30 µg), cefepime ((30µg), ceftazidime (30 µg), cefoxitin (30µg), imipenem (10 µg), sulfamethoxazole (23/75µg), ciprofloxacin (5µg) and tazobactam (10µg) + piperacillin (100µg) (BD-BBL, USA).[24]*E. coli* ATCC 25922 was used as quality control.

Statistical analysis

Data were analyzed by Chi-square and odds ratio (OR) tests using SPSS software version 18. A *P* value of < 0.05 was considered statistically significant.

RESULTS

The demographic characteristics

A total of 342 neonates suspected with sepsis were admitted to Imam Sajjad hospital in Yasuj, Iran, of which 207 were in the NICU and 135 were in the neonatal ward. Among 342 cases suspected with sepsis,43 neonates (12.6%) had positive blood cultures, of which 32 were in the NICU and 11 in the neonatal ward. The mean and median hospitalization duration were 13.4 ± 0.8 and 9 days, respectively. Among neonates with culture-positive samples, 28 (65.2%) were preterm and 24 (55.8%) had abnormal birth weight. Twenty-eight (65.2%) of

these neonates were female and15 (34.8%) were male among which25 (58.2%)were born by cesarean section. Demographic characteristics and risk factors based on the wards and sepsis type are illustrated in Table 1.

The prevalence of EOS was 53.3 % (23:43) of which 60.8% were preterm and 43.5% had abnormal birth weight (Table 1). The mean and median age of neonates with EOS were2.1 ± 0.3 and one day. In this group, 11 and 12neonates were born by cesarean section and vaginal delivery, respectively. The mean and median hospitalization duration in neonates with EOS was 14.5±3and 10.5 days, respectively. LOS accounted for 46.5 % (20:43)of sepsis episodes and was observed in 70% of preterm neonates and 70% of neonates with abnormal birth weight. The mean and median age of neonates with LOS were 27.5± 4.5and 20 days, respectively. In the LOS group, 14 neonates were born by cesarean section and sixneonates were born by vaginal delivery. The mean and median hospitalization duration in neonates with LOS were 26.7± 4.6and 17 days, respectively.

Prevalence of pathogens

Gram-positive bacteria were major etiological agents of sepsis in this study (36:47, 76.5%), among which CoNS was identified as the most common pathogen (21:47, 44.6%), followed by *S. aureus* (21.2%). Gram-negative organisms accounted for 23.4% cases of sepsis, with *A. baumanni* and *E.coli* being the most common Gram-negative pathogens (3:47; 6.3%).

Among 43 neonates with positive blood cultures, four cases (9.3%) had poly-microbial infection with *S. aureus* + GBS (25%), *S. aureus* + CoNS(25%), and CoNS + GBS(50%).

Among the newborns with EOS, 27 pathogens were isolated includingCoNS (59.2%), followed by *S. aureus* (14.8%), and beta-hemolytic *Streptococcus* (7.4%). Also, among the newborns with LOS, 20 pathogens were isolated as follows: CoNS (35%), *S. aureus* (30%),

and Gram-negative pathogens, such as *E. coli*, *E.aerogenes*, *A.baumanni*, *S.marcescens* , and *K. pneumoniae* (Table 2).

Mortality

Out of 342 cases suspected with sepsis, 33 (9.6%) died, of which seven cases (21.2%)had positive bacterial culture. The most common bacteria isolated from fatal sepsis was CoNS.

Mortality in neonates with EOS was higher than those with LOS (72% vs. 28%)(Table 3). The highest mortality rate in EOS was associated with CoNS(3:5; 60%),while *E. aerogenes* (1:2; 50%) and *A.baumanni* (1:2; 50%) contributed to mortality in LOS(Table 3).

Antimicrobial susceptibility pattern

According to antibiotic susceptibility patterns, most Gram-positive isolates were sensitive to vancomycin (34:36; 94.4%)and teicoplanin(28:36; 77.7%) followed by amikacin (63.8%; 23:36) and ciprofloxacin (60.53%; 21:36).

The highest rate of resistance was observed against penicillin (91.6%), cefepime (72.2%) sulfamethoxazole (58.3%) and gentamycin (50%), respectively.

The most common and effective antibiotics for Gram-negative bacteria included: tazobactam/piperacillin (81.81%; 9:11), ciprofloxacin, and amikacin (63.63%; 7:11), respectively (Tables 4 and 5).

Risk Factors and Clinical Symptoms

The common risk factors for sepsis included prematurity (65.2% ;$P = 0.02$), cesarean section (58.2% ; $P = 0.8$), very low birth weight (27.9% ; $P = 0.03$), and abnormal Apgar score (27.9% ; $P = 0.2$).

Invasive procedures (OR= 2.14, CI= 1.03 - 4.4), very low birth weight (OR= 1.8, CI= 1.05 - 3.18), prematurity (OR=1.47 CI= 1.09 - 1.83), and abnormal Apgar score (OR=1.4, CI= 0.826 - 2.4) increased the risk for sepsis in neonates (Table 6).

The most common symptoms were cyanosis (62.7%; 27:43, P= 0.06),respiratory distress (55.8%; 24:43, P= 0.7), tachypnea (46.5%; 20:43, P= 0.3), hypothermia (41.8%; 19:43, P= 0.07), poor feeding (37.2%; 16:43, P= 0.01), and lethargy (34.8%; 15:43, P= 0.05) (table 5). Clinical findings, such as skin rashes (OR=4.47, CI= 1.3 -15.2), convulsion (OR=2.09, CI= 0.808 – 5.4),poor feeding (OR=1.8, CI= 1.1 - 3.03), apnea (OR=1.74, CI= 0.754 - 4.05), malaise (OR=1.7, CI= 0.941 - 3.1) and fever (OR=1.4, CI= 0.562 - 3.5) were the most common risk factors for neonatal sepsis(Table 7).

Laboratory parameters

The laboratory parameters studied in neonates with sepsis included CRP, white blood cells, hemoglobin, and platelets. CRP increased in 16.27% of newborns. Leukopenia, anemia, and polycythemia were observed in 32.5%,39.5.3%, and 30.2% of neonates, respectively.

The laboratory parameters such as leukocytosis (P=0.01), CRP([OR],2.2;P=0.04), and anemia ([OR],2.3; P=0.001) were significantly associated with sepsis and were indicated as risk factors of sepsis(Table 8).

DISCUSSION

Today, infectious diseases, especially sepsis, are one of the main causes of death in neonates. Sepsis is a clinical syndrome due to an inflammatory systemic inflammatory response to infection which can lead to organ dysfunction through several pathophysiologic mechanisms.[19] The greatest challenge in combating high mortality due to sepsis is the lack of rapid, accurate, and effective detection as well as inappropriate treatment and improper discontinuation of treatment.[5, 20]

The present study was carried out for the first time in Yasuj, southwest of Iran. The prevalence of neonatal sepsis in the present study was 12.6% which is higher than similar previous studies by Mohammadi et al. (2014), Afjeh et al. (2009) and Behmadi et al. (2016)

who reported the prevalence of 6.7, 9.11 and 2.9% for their study population. However, this prevalent is lower than the prevalence reported in studies by Rafati et al. (2014) in Iran (20%) and West et al. (2012) in Nigeria (33.1%).[10, 21-24] These differences can be due to the type of study, antibiotic resistance in bacteria, changes in economic and social status, variations in maternal and neonatal risk factors, differences in health control and infection management in medical centers, as well as inappropriate antibiotic treatment due to deficiency in epidemiological studies.

Contrary to the current study, in studies by Gebremedhin et al. (2015), Aku et al. (2018), and Hosseini et al. (2014), the prevalence of male neonates among sepsis cases was higher than female neonates, however, similar to the current study, the studies by Nikkhoo et al. (2015) and Atefi et al. (2016)showed a higher prevalence of sepsis in females compared to the males.[9, 25-28]

In the present study, high prevalence of immature and very low birth weight neonates, which is one of the most important risk factors for sepsis, was attributed to the female sex, so they were more have chance for sepsis than males.

In this study, similar to the studies by Gebremedhin et al. (2015) and Atefi et al. (2016), neonates aged 0 to 10 days and 30 days old showed the highest incidence of sepsis due to premature or immature immune responses.[25, 28]

In our study, similar to the studies by Mohammed and El Seifi (2014) and Aku et al. (2018), and contrary to the study by Mohsen et al. (2017)the duration of admission for two weeks or more than four weeks was associated with sepsis.[26, 29, 30]By examining the severity of luck, it was found that neonates admitted for four weeks were more likely to develop sepsis due to prolonged exposure to hospital pathogens. Also, these neonates underwent invasive procedures, which facilitate the entry of various microorganisms.

In our study, similar to the studies by Khalili Matinzadeh et al. (2007), Shah Farhat et al. (2014) and Hosseini et al. (2014), and contrary to the studies of G/eyesus et al. (2017), Gebremedhin et al. (2015) and Signore et al. (2008), neonates born by cesarean section were more likely to develop sepsis.[8, 25, 27, 31-33]

In the cesarean section, the neonate is exposed to environmental microbes, while in vaginal delivery, the neonate is exposed to normal vaginal flora. Moreover, neonates born by cesarean section have a higher risk of immune response disorders.[34]

Similar to the studies by Pokhrel et al. (2018), Tsai et al. (2015), Rafati et al. (2014) and Asghari Sana et al. (2011), and contrary to the studies by Khosravi et al. (2017) Karambin et al. (2011), in the present study, Gram-positive organisms were the most common isolated organisms among which CoNS was the most prevalent and the most common isolated Gram-negative organisms were *E.coli* and *A. baumanni*.[24, 35-39]

The variations in bacterial number and type in neonatal sepsis depend on several factors, such as geographic regions, economic and social conditions, changes in the course of antibiotic injections, and different lifestyles.[26]

In the present study, unlike the studies carried out in Egypt and Taiwan, and similar to the studies by Sheth et al (2012), Behmadi et al. (2016), and Tehrani et al. (2017), EOS was more prevalent compared to the LOS.[23, 30, 40-42]

In our study, similar to most previous studies, staphylococcal pathogens were the most common organisms in both EOS and LOS. The most common and effective antibiotics for the treatment of Gram-positive organisms were teicoplanin followed by amikacin and ciprofloxacin. These results were similar to the studies by Shahian et al. (2015), Hosseini et al. (2014) Asghari Sana et al. (2011), and opposite to the study by G/eyeus et al. (2017).[8, 27, 35, 43]

Most studies conducted in Iran showed a lower resistance rate of CoNS isolated from neonate with sepsis compared to the present study. The most effective antibiotic for the treatment of CoNS was teicoplaninandamikacin.Similar to the studies by Asghari Sana et al. (2011) in Orumiyeh and Hosseini et al (2014) in northwestern of Iran, and contrary to the studies by Aletayeb (2011), Nikkho et al. (2015) and Mohsen et al. (2017), the most common and effective antibiotics for the treatment of Gram-negative organisms isolated from the blood of neonates with sepsis were tazobactam/piperacillin, ciprofloxacin, and amikacin .[9, 27, 30, 35, 44]

Similar to the studies by Movahedian et al. (2006), Masaybi et al. (2013), Afsharpaiman et al. (2012), G/eyeus et al. (2017) and Hosseini et al (2014), in the current study, preterm neonates, neonates with abnormal birth weight and neonates who underwent invasive procedures were more likely to contract sepsis.[8, 27, 45-47]

In the studies by Tsai et al. (2015) and Hematyar et al. (2014),similar to the present study, an increased incidence of sepsis was observed in anemia neonates.[37, 48] In the present study, neonates with anemia, polycythemia, and leukopenia were more likely to develop sepsis in comparison with those who had abnormal hemoglobin. Increased recruitment of leukocytes and neutrophils caused by bacterial antigens in the first 96 hours of the life in neonates is associated with hypoxia-ischemia, leading to abnormal neurodevelopment, as well as neutropenia, leukopenia, and anemia.[49] In this regard, oxygenation to the neonatal organs is impaired, leading to a suitable condition for bacterial growth and pathogenicity.[50]

In this study, platelet and white blood cell counts were not associated with sepsis and the incidence of sepsis in neonates with leukopenia increased similarly to the study by Shah Farhat et al. (2014).[31]

In this study, contrary to the studies by Asghari Sana et al. (2011), MatinzadehKhalili et al. (2007), Wu et al (2009), and similar to the studies by Tsaiet al. (2015) and Hematyar et al. (2014), positive CRP was associated with bacterial presence in blood.[32, 35, 37, 41, 48]

CRP depends on the type of delivery, age, type of microorganism causing sepsis, leukopenia, and type of sepsis.[34, 51]

In the present study, CRP in neonates with LOS was twice morethanneonates with EOS, indicatingthat the higher the age of the neonate, the more advanced and specific the immune system works. In the present study, there was a correlation between positive CRP and bacterial species, and this marker is greater in Gram-negative bacteria than in Gram-positive bacteria and fungi. Lipid A is a partial endotoxin of the cell wall in Gram-negative bacteria. Its presence in blood leads to the release of inflammatory mediators such as CRP and TNF-α. On the other hand, CoNS can reduce interaction with the host immune system by biofilm formation, and plays a significant role in reducing the host inflammatory responses.[52-54]

Sepsis is the third most common cause of death among neonatesworldwide.[23]Similar to the studies by Tsai et al. (2015) and Pokhrel et al. (2018), in this study, mortality rate among neonates suspected with sepsis was 10%, of which 23.5% were due to sepsis. The highest mortality rates were related to the Gram-negative bacteria similar to the studies byWu et al. (2017), Tsai et al. (2015), and Bentlin and de Souza Rugolo (2010).[34, 36, 37, 55]

Gram-negative bacteria, with immunogenic cell wall components, can cause severe sepsis and a subsequent septic shock. In our study, all neonates who died following sepsis had respiratory distress due to the production of pro-inflammatory cytokines, excessive activation of the immune system, and severe damage to body organs caused by endotoxins and cell wall elements, especially in Gram-negative bacteria. Systemic inflammation and leukocyte recruitment due to LPS is associated with cerebral and myocardial infarction.[49]

Conclusion

More than half of the studied neonates were infected with skin normal microflora and hospital-residing bacteria. Most of these neonates were subjected to invasive procedures and

were born via cesarean section. Risk factors such as prematurity, abnormal birth weight, anemia, leukopenia, prolonged hospitalization, and invasive procedures increase the chance of sepsis in newborns. Clinical symptoms are nonspecific and therefore are not considered as appropriate indicators of sepsis. In this study, all neonates with sepsis developed a different pattern of clinical symptoms. Increased antibiotic administration and increased reservoir of antibiotic resistance genes in bacteria can alleviate the immunity against microbial pathogens in newborns. In the present study, the most effective antibiotics for the experimental treatment of Gram-positive bacteria were teicoplanin, aminoglycosides, and fluoroquinolones. The most common and effective antibiotics for the treatment of Gram-negative organisms were beta-lactam antibiotics, such as piperacillin, beta-lactamase inhibitor, aminoglycosides, and ciprofloxacin.

Acknowledgements: This study has been supported by Deputy of Research and Technology, Yasuj University of Medical Sciences

Authors' contributions: S S Kh Ph.D., MS MSc and A GM M.D. design of the work, M S, SM MSc, SJ T MSc and MR MSC acquisition data and performed research, AM M.D. / Ph.D and S S Kh analysis data, SS Kh , MS,MM BSc Drafting the work and wrote the paper

Funding: This study has been supported by Deputy of Research and Technology, Yasuj University of Medical Sciences

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate:

The study was conducted in accordance with the Declaration of Helsinki. This study has been approved by Yasuj University of Medical Sciences, Research Ethics Committee (IR.YUMS.REC.1395.190). Prior to sample collection, written informed consents were obtained from parents/ guardians of each individual.

Competing interests: The authors declare that they have no competing interests. The authors have no conflicts of interest to disclose.

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Table 1. Demographic characteristics and risk factors based on the wards and the type of sepsis in infants

Demographic characteristics and risk factors	Wards			sepsis type		
	neonatal (135)	NICU (207)	total number (342)	early sepsis (23)	late sepsis (20)	total number (43)
Female	55 (40.7 %)	87 (42 %)	142 (41.5 %)	15(60.86%)	13 (60 %)	28 (65.2%)
Male	80 (59.3 %)	120 (58 %)	200 (58.5 %)	8 (39.13 %)	7 (40%)	15 (34.8 %)
vaginal delivery	61 (45.2 %)	74 (35.7 %)	135 (39.5 %)	12 (47.8 %)	6 (25 %)	18 (41.9 %)
cesarean section	74 (54.8 %)	133 (64.3 %)	207 (60.5 %)	11(52.17%)	14(75 %)	25 (58.1 %)
Normal birth weight	114(84.4 %)	87 (42%)	201 (58.8 %)	13 (47.8 %)	6 (30 %)	19 (44.1%)
low birth weight	14 (10.4 %)	69 (33.3 %)	83 (24.2 %)	4 (21.7 %)	8 (45 %)	12 (27.9 %)
very low birth weight	7 (5.2 %)	51 (24.7%)	58 (17 %)	6 (30.4 %)	6 (25 %)	12 (27.9%)
abnormal Apgar	13 (9.6 %)	58 (72 %)	71 (20.8 %)	6 (26.08 %)	6 (30%)	12 (27.9 %)
normal Apgar	122(90.4 %)	149 (33.6 %)	271 (79.2 %)	17 (73.9 %)	14 (70 %)	31 (72.09 %)
Preterm	27 (18 %)	136 (65.7 %)	163 (47.8%)	14(60.86%)	14 (75 %)	28 (65.2%)
Term	107 (80 %)	71 (34.3 %)	178 (52.2 %)	9 (39.13 %)	6(25 %)	15 (34.8 %)

Table 2. Frequency of pathogens in neonates with sepsis

Pathogens	Total (N:47) n (%)	EOS (N:27) n (%)	LOS (N:20) n (%)
Gram-positive bacteria	36 (76.6)	24 (88.8)	12 (60)
CONS	21 (44.64)	16(59.2)	7 (35)
Staphylococcus aureus	10 (21.2)	4 (14.8)	6 (30)
GBS	3 (6.35)	2 (7.4)	1 (5)
Enterococcus fecalis	2 (4.25)	2 (7.4)	0
Gram-negative bacteria	11 (19.61 %)	3 (11.1)	8 (40)
Escherichia coli	3 (5.35)	1 (3.7)	2 (10)
Acinetobacter baumanni	3 (5.35)	1 (3.7)	2 (10)
Serratia marscesens	1 (1.78)	0	1 (5)
Enterobacter aerogenes	2 (3.57)	0	2 (10)
Klebsiella pneumoniae	1 (1.78)	0	1 (5)
Klebsiella oxitoca	1 (1.78)	1 (3.7)	0

Table 3. Mortality in neonates with sepsis and related pathogens

Pathogens	total mortality (N:7) n (%)	mortality in EOS (N:5) n (%)	mortality in LOS (N:2) n (%)
Gram-positive bacteria	4 (50 %)	4 (66.66)	0
CONS	3 (37.5)	3 (50)	0
Staphylococcus aureus	1 (12.5)	1 (16.66)	0
Enterococcus fecalis	0	0	0
GBS	0	0	0
Gram-negative bacteria	3 (37.5 %)	1 (16.66)	2 (100)
Escherichia coli	1 (12.5)	1 (16.6)	0
Acinetobacter baumanni	1 (12.5)	0	1 (50)
Serratia marsecens	0	0	0
Enterobacter aerogenes	1 (12.5)	0	1 (50)
Klebsiella pneumoniae	0	0	0
Klebsiella oxitoca	0	0	0

Table 4. Number and percentage of antibiotic resistance in Gram-negative bacteria isolated from blood of infants with sepsis

Bacteria	*S. marsecens* (n=1)		*E. coli* (n=3)		*E. aerogenes* (n=2)		*K.pneumoniae* (n=1)		*K.oxitoca* (n=1)		*A. baumanni* (n=3)	
Antibiotics	**Sensitivity n(%)**	**Resistance n (%)**	**Sensitivity n(%)**	**Resistance n (%)**	**Sensitivity n(%)**	**Resistance n (%)**	**Sensitivity n(%)**	**Resistance n (%)**	**Sensitivity n(%)**	**Resistance n (%)**	**Sensitivity n(%)**	**Resistance n (%)**
Amikacin	0	1 (100)	3 (100)	0	1 (50)	1 (50)	1 (100)	0	1 (100)	0	1 (33.3)	2 (66.6)
Ceftazidime	0	1 (100)	0	3 (100)	0	2 (100)	0	1 (100)	0	1 (100)	2 (66.6)	1 (33.3)
tazobactam+ piperacillin	0	1 (100)	2 (66.6)	1 (33.3)	2 (100)	0	1 (100)	0	1 (100)	0	3 (100)	0
Ciprofloxacin	0	1 (100)	3 (100)	0	2 (100)	0	1 (100)	0	1 (100)	0	0	3 (100)
Gentamicin	0	1 (100)	1 (33.3)	2 (66.6)	1 (50)	1 (50)	1 (100)	0	1 (100)	0	1 (33.3)	2 (66.6)
Imipenem	0	1 (100)	0	3 (100)	2 (100)	0	1 (100)	0	1 (100)	0	1 (33.3)	2 (66.6)
Sulfamethoxazole	0	1 (100)	0	3 (100)	1 (50)	1 (50)	1 (100)	0	1 (100)	0	1 (33.3)	2 (66.6)
Cefoxitin	0	1 (100)	1 (33.3)	2 (66.6)	1 (50)	1 (50)	1 (100)	0	1 (100)	0	1 (33.3)	2 (66.6)
Cefepime	0	1 (100)	1 (33.3)	2 (66.6)	1 (50)	1 (50)	0	1 (100)	1 (100)	0	1 (33.3)	2 (66.6)

Table 5. Number and percentage of antibiotic resistance in Gram-posetive bacteria isolated from blood of infants with sepsis

Bacteria	*CONS* (n=21)		*S. aureus* (n=10)		*GBS* (n=3)		*E. fecalis* (n=2)	
Antibiotics	**Sensitivity n(%)**	**Resistance n (%)**	**Sensitivity n(%)**	**Resistance n (%)**	**Sensitivity n(%)**	**Resistance n (%)**	**Sensitivity n(%)**	**Resistance n (%)**
Teicoplanin	16 (76.1)	5 (23.8)	9(90)	1 (10)	2 (66.6)	1 (33.3)	1 (50)	1 (50)
Amikacin	13 (61.9)	8 (38.09)	9 (90)	1 (10)	1 (33.3)	2 (66.6)	0	2 (100)
Vancomycin	21(100)	0	9(90)	1 (10)	3 (100)	0	1 (50)	1 (50)
Oxacillin	8 (38.09)	13 (61.9)	6 (60)	4 (40)	1 (33.3)	2 (66.6)	1 (50)	1 (50)
Ciprofloxacin	12 (57.14)	9 (42.85)	8 (80)	2 (20)	1 (33.3)	2 (66.6)	0	2 (100)
Gentamicin	11 (52.38)	10 (47.6)	5(50)	5 (50)	2 (66.6)	1 (33.3)	0	2 (100)
Penicillin	2 (9.5)	19 (90.5)	0	10 (100)	0	3 (100)	1 (50)	1 (50)
Sulfamethoxazole	9 (42.85)	12 (57.14)	4 (40)	6 (60)	1 (33.3)	2 (66.6)	1 (50)	1 (50)
Cefepime	6 (28.5)	15 (71.5)	2(20)	8 (80)	1 (33.3)	2 (66.6)	1 (50)	1 (50)

Table 6.Comparison of risk factors between blood infection and nonblood infection in infants with suspected sepsis

Risk factors	Categories	Blood infection n(%) (N=43)	No Blood infection n(%) (N=299)	*P*-value	OR (95% CI)
Gestational age (weeks)	< 37	28 (65.2)	137 (45.8)	0.02	1.47 (1.09 - 1.83)
	≥ 37	15 (34.8)	162 (54.18)		
PROM	Yes	9(21)	52(17.3)	0.6	1.16(0.616 - 2.18)
	No	34(79)	247(82.6)		
Apgar 5th minute	< 7	12(27.9)	240(80.2)	0.2	1.4(0.826 - 2.4)
	≥7	31(72.09)	59(19.7)		
Delivery type	C/S	25(58.2)	185(61.8)	0.8	1.04(0.711-1.53)
	NVD	18(41.8)	114(38.12)		
Sex	Female	28(65.2)	181(61.5)	0.002	1.61(1.2 - 2.1)
	Male	15(34.8)	118(39.4)		
VLBW (≤ 1500 gm)	Yes	12(27.9)	46(15.3)	0.03	1.8(1.05 - 3.18)
	No	31(72.09)	253(84.6)		
LBW (1500 – 2500 gm)	Yes	12(27.9)	75(25.08)	0.6	1.1(0.663 - 1.88)
	No	31(72.09)	224(74.92)		
Aggressive (trachal tube)	Yes	8(18.7)	27(9.03)	0.04	2.14(1.03 - 4.4)
	No	35(81.3)	272(90.9)		

Table 7. Comparison of clinical symptoms between blood infection and nonblood infection in infants with suspected sepsis

Clinical symptoms		Blood infection n(%) (N=43)	No Blood infection n(%) (N=299)	*P*-value	OR (95% CI)
Respiratory distress	Yes	24(55.8)	154(51.5)	0.7	1.05 (0.791–1.4)
	No	19(45.2)	144(48.5)		
Apnea	Yes	6(13.96)	25(8.4)	0.1	1.74 (0.754- 4.05)
	No	37(86.04)	274 (91.6)		
Tachypnea	Yes	20(46.5)	111(37.2)	0.3	1.09 (0.758 - 1.5)
	No	23(53.5)	188(62.8)		
Lethargy	Yes	15(34.8)	60(20.06)	0.05	1.58 (0.978 - 2.56)
	No	28(65.2)	239(79.94)		
Irritability	Yes	11(25.5)	42(14.04)	0.07	1.7 (0.941 - 3.1)
	No	32(74.5)	257(85.96)		
Poorfeeding	Yes	16(37.2)	53(17.7)	0.01	1.8 (1.1 - 3.03)
	No	27(62.8)	246(82.3)		
Cyanosis	Yes	27(62.8)	125(41.8)	0.06	1.3 (0.983 - 1.74)
	No	16(37.2)	174(58.2)		
Rash	Yes	4 (9.3)	8(2.7)	0.01	4.47 (1.3 - 15.2)
	No	39 (90.7)	291(97.3)		
Hypothermia	Yes	19(44.2)	89(29.8)	0.07	1.4 (0.984 - 2.15)
	No	24(55.8)	210(70.2)		
Granting	Yes	12 (27.9)	115(38.5)	0.1	0.712 (0.43 - 1.17)
	No	31 (72.09)	184(61.5)		
Seizure	Yes	5(11.62)	18(6.02)	0.1	2.09 (0.808 - 5.4)
	No	38(88.37)	281(93.98)		
Fever	Yes	5(11.62)	28(9.4)	0.4	1.4 (0.562 - 3.5)
	No	38(88.37)	271(90.6)		

Table 8.Comparison of laboratory data between blood infection and nonblood infection in infants with suspected sepsis

Laboratory data	Categories	Blood infection n(%) (N=43)	No Blood infection n(%) (N=299)	*P*-value	OR (95% CI)
CRP	positive	7 (16.27)	22 (7.35)	0.04	2.2 (1.01 - 4.94)
	negative	36 (83.7)	277 (92.65)		
Anemia	Hb < 12 g/dl	17 (39.5)	51 (17.05)	0.001	2.3 (1.4 - 3.6)
	Hb >12 g/dl	26 (60.5)	248 (82.95)		
Polycitemia	Hb > 24 g/dl	13 (30.23)	145 (48.5)	0.01	0.61 (0.38 – 0.976)
	Hb < 24 g/dl	30 (69.77)	154 (51.5)		
leukopenia	WBC< 9000mm^3	14 (32.5)	63 (21.07)	0.09	1.5(0.946 - 2.5)
	WBC>30000mm^3	29 (67.5)	236 (78.93)		
leukocytosis	WBC> 30000mm^3	1 (2.3)	0 (0)	0.01	–
	WBC> 30000mm^3	42 (97.7)	299 (100)		
thrombocytopenia	Yes	4 (9.3)	18 (6.02)	0.3	1.6 (0.587 - 4.7)
	No	39 (90.7)	281 (93.98)		
thrombocytosis	Yes	14 (32.5)	82 (27.4)	0.5	1.17 (0.732 - 1.8)
	No	29 (67.5)	217 (72.6)		