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# Prevalence and Antibiotic Susceptibility of *Escherichia coli* Isolated from Early-Onset Sepsis in Shiraz, Iran

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ABSTRACT

**Background:** Neonatal sepsis is a clinical syndrome in neonates, which is an uncommon but significant cause of morbidity and mortality in infants. The aim of this study was to evaluate the incidence of sepsis caused by *Escherichia coli* and its antibiotic resistance pattern as well as to assess the potential risk factors in neonates and maternal characteristics in Shiraz.
**Material & Method:** This retrospective study was performed on infants with sepsis in the first three days of life during February 2019 to March 2021. Patients' information was obtained using their hospital records and a questionnaire. All statistical analyses were conducted using SPSS software Ver. 18.0. A *p*-value <.05 was considered as statistically significant
**Findings:** During this study, a total of 250 positive blood cultures were reported for infants less than 3 days old. Of these, 21(8.4%) *E. coli* strains were isolated from 14 preterm and 7 term neonates. In all patients, the most effective antibiotic was meropenem, and the highest resistance was observed to cefoxitin.
**Conclusion:** Base on the present study results, *E. coli* is the most prevalent Gram-negative bacterium isolated in Shiraz. Premature birth and very low weight are the most important risk factors for developing early-onset sepsis.

**Keywords:** Early-onset sepsis, *E. coli,* Antibiotic susceptibility.

CITATION LINKS

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## Introduction

Neonatal sepsis is a clinical syndrome in neonates, which is an uncommon but significant cause of morbidity and mortality in infants, predominantly in developing countries; it is responsible for 30-50% of infant mortality in these populations [1, 2]. Premature neonates are susceptible to nosocomial infections due to immaturity of the immune system and the need for numerous invasive procedures. Neonatal sepsis is divided into two categories based on the time of onset: early-onset sepsis (EOS) (in the first 72 hours of life) and late-onset sepsis (LOS) (after 72 hours) [3].

Various factors are involved in the development of neonatal sepsis, including type of delivery, preterm birth, premature rupture of the fetal membrane (PROM), and maternal infection [4]. Bacterial infection is one of the prominent causes of neonatal death worldwide. In recent years, the most important cause of EOS has been group B *Streptococcus*. The use of intrapartum antibiotic therapy as prophylaxis has drastically reduced the prevalence of premature neonatal sepsis with this organism. However, the prevalence of infections with other antibiotic-resistant bacteria causing infections in preterm and very low birth weight (VLBW) infants has increased [5]. Among infants, one of the most common causes of EOS is *Escherichia coli*. This organism is responsible for about 24% of all sepsis cases. In the last two decades, *E. coli* has been the most common cause of EOS in premature infants as well as LOS. In hospitalized neonates, EOS caused by *E. coli* has a high mortality rate compared to Gram-positive organisms. [6, 7].

*E. coli* infection is a substantial cause of mortality and morbidity in neonates, particularly preterm ones. It is a major etiological agent of a variety of clinical manifestations, including sepsis, pneumonia, meningitis, skin and soft tissue infections [8]. Since the introduction of intrapartum antibiotic prophylaxis, the prevalence of *E. coli* has remained stable, but its prevalence has increased in VLBW infants [7]. Empirical antibiotic therapy with ampicillin, gentamicin, or cefotaxime is essential for the successful treatment of neonatal sepsis. Therefore, treatment is commonly started before receiving blood culture results [9]. The prevalence and resistance of bacteria have increased over time due to the use of antibiotics in different countries. As a result, continuous epidemiological monitoring along with frequent local adjustment of susceptibility patterns to antimicrobial agents is essential to establish a rational treatment approach [10].

**Objectives:** The aim of this study was to evaluate the incidence of sepsis caused by *E. coli* and its antibiotic resistance pattern as well as to assess the potential risk factors in neonates and maternal characteristics in Shiraz.

## Material and Method

This retrospective study was performed on infants less than 3 days old with sepsis in the teaching hospitals of Shiraz University of Medical Sciences during February 2019 to March 2021. The ethics code of this study (99-7819) was received from the Ethics Committee of Shiraz University of Medical Sciences. EOS is the sign and symptom of clinical sepsis in infants less than 3 days old. If the pathogen is isolated from the blood or CSF of patients, and the result of the first culture is positive, it is considered as the beginning of sepsis. Patients' information was obtained using their hospital records and a questionnaire. This information includes: sepsis type, age, gender, type of cultured pathogen, delivery method, antibiotic susceptibility, abortion, PROM, birth weight, and gestational age. Categorical variables were expressed as frequency and percentage (%), and continuous variables were expressed as mean. Continuous variables were analyzed by employing Student's t-test. Multiple logistic regression analysis was used to determine the most powerful risk factors such as demographic data, including age,

gender, etc. All statistical analyses were conducted using SPSS software, Ver. 18.0 (SPSS Inc., Chicago, IL, USA). A *p*-value <.05 was considered as statistically significant.

## Findings

During this study, a total of 250 positive blood cultures were reported for infants less than 3 days old. After performing specific microbiological tests, Gram-positive bacteria were identified as the most common causes of infections. *Staphylococcus aureus* and coagulase-negative staphylococci with 156 (62.4%) and 53 (21.2%) isolates were the most prevalent Gram-positive bacteria in the studied samples. *E. coli* with 21 (8.4%) isolates was the most prevalent Gram-negative bacteria and the third most common cause of infection. Other isolated Gram-negative organisms included *Klebsiella pneumoniae* with 4 (1.6%) isolates, *Pseudomonas aeruginosa* with 3 (1.2%) isolates, *Acinetobacter baumannii* with 3 (1.2%) isolates, and *Enterobacter* species with 3 (1.2%) isolates, respectively. *E. coli* strains were isolated from 14 preterm and 7 term neonates. Antibiotic susceptibility of *E. coli* isolates was evaluated based on the principles of the CLSI table. In preterm infants, the highest sensitivity was observed to meropenem (86%), and the highest resistance was related to cefoxitin (52%). The highest resistance to cefoxitin (57%) was also reported in term neonates. In general, the most effective antibiotic against this organism was meropenem (80%). The results of antibiotic susceptibility testing are shown in Table 1. In this study, 12 (57%) infants with EOS were male, and 9 (43%) neonates were with VLBW. Also, seven mothers had a history of PROM. Among mothers with preterm infants, there were 7 (33%) cases of abortion and 4 (19%) cases of multiple abortion. Also, 4 (19%) neonates were born by natural delivery, and the other were delivered by caesarian section. Other information on the

**Table 1)** Antibiotic resistance of *E. coli* isolates in blood culture (early onset sepsis)

| Antibiotics | Preterm | | Term | | Total | |
|---|---|---|---|---|---|---|
| | Susceptible N(%) | Resistance N(%) | Susceptible N(%) | Resistance N(%) | Susceptible N(%) | Resistance N(%) |
| Ciprofloxacin | 8(57) | 6(43) | 5(71) | 2(29) | 13(62) | 8(38) |
| Cotrimoxazole | 11(79) | 3(21) | 5(71) | 2(29) | 16(76) | 5(24) |
| Amikacin | 6(43) | 8(57) | 4(57) | 3(43) | 10(48) | 11(52) |
| Gentamicin | 8(57) | 6(43) | 5(71) | 2(29) | 13(62) | 8(38) |
| Cefoxitin | 7(50) | 7(50) | 3(43) | 4(57) | 10(48) | 11(52) |
| Imipenem | 8(57) | 6(43) | 5(71) | 2(29) | 13(62) | 8(38) |
| Meropenem | 12(86) | 2(14) | 5(71) | 2(29) | 17(80) | 4(20) |
| Cefepime | 10(71) | 4(29) | 5(71) | 2(29) | 15(71) | 6(29) |
| Ceftazidime | 8(57) | 6(43) | 5(71) | 2(29) | 13(62) | 8(38) |
| Cefixime | 10(71) | 4(29) | 4(57) | 3(43) | 14(67) | 7(33) |


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risk factors among preterm and term neonates is shown in Table 2.

## Discussion

Sepsis is one of the most important causes of infant mortality, especially in developing countries. It is estimated that about 2% of infants become infected before birth and about 10% in the first month of life [11]. *E. coli* infection in neonatal period is a major health concern. However, information on the prevalence, distribution, and clinical signs of *E. coli* infection in neonates is controversial and limited. In recent years, *E. coli* has surpassed group B *Streptococcus* as the most important etiological agent of bacteremia in neonates in both preterm and term groups. Despite strict infection control programs in various countries, *E. coli* is the most common cause of severe infections such as meningitis with a mortality rate of over 40% [12, 13]. In this study, the most common Gram negative organism isolated was *E. coli*, which is consistent with other literature [14-16], but in contrast to other Iranian studies in which *P. aeruginosa* has been reported as the most prevalent organism [17, 18]. The difference in the results suggests that the microbial agents of newborn sepsis

**Table 2)** Risk factors for neonatal sepsis in teaching hospitals of Shiraz

| Risk Factor | | Preterm N(%) | Term N(%) | P-Value |
|---|---|---|---|---|
| **Gender** | Male | 8(57) | 4(57) | .24 |
| | Female | 6(43) | 3(43) | |
| | Total | 14(100) | 7(100) | |
| **PROM** | Yes | 5(36) | 2(29) | .74 |
| | No | 9(64) | 5(71) | |
| | Total | 14(100) | 7(100) | |
| **VLBW** | Yes | 8(57) | 1(14) | .03 |
| | No | 6(43) | 6(86) | |
| | Total | 14(100) | 7(100) | |
| **NVD** | Yes | 1(7) | 3(43) | .049 |
| | No | 13(93) | 4(57) | |
| | Total | 14(100) | 7(100) | |
| **Abortion** | Yes | 4(28) | 0(0) | .11 |
| | No | 10(72) | 7(100) | |
| | Total | 14(100) | 7(100) | |
| **Mother's age (year)** | | 33.00±7.00 | 28.00±4.00 | .25 |
| **Gestational age (week)** | | 29.07±3.00 | 38.00±2.00 | .04 |
| **Birth weight (gr)** | | 1405±527 | 2410±717 | .01 |

PROM: premature rupture of fetal membrane, VLBW: very low birth weight, NVD: normal vaginal delivery


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may vary in different geographical locations and change over time. Therefore, various studies in different places and times are necessary in this regard. In the present study, the rate of sepsis in male neonates was higher than in female neonates, which is similar to other studies results in Iran, the Persian Gulf countries, and Taiwan [17-20]. Based on antibiotic susceptibility testing results in this study, the highest susceptibility in preterm neonates was to meropenem, cotrimoxazole, and cefepime, respectively, and the highest resistance was observed to amikacin. However, the highest resistance to cefoxitin was observed in term neonates as well as in all isolates. There are many reports about antibiotic resistance of routine EOS-related organisms [16, 21-23]. Aftab and Iqbal (2006) reported that resistance to gentamicin and cephalosporins was higher than to imipenem [24]. Another study by Aurangzeb and Hameed (2003) found that there was a higher resistance to routinely used antibiotics than to less commonly used antibiotics such as imipenem and ciprofloxacin [25]. In the present study, due to the routine use of gentamicin and amikacin, which are prescribed as prophylaxis, a higher rate of resistance to these antibiotics was observed. Unfortunately, despite the widespread use of ampicillin in hospitals, the degree of resistance to this antibiotic was not investigated in the present study.

Preterm birth and VLBW are the most important risk factors for EOS in infants [26]. In this study, 67% of patients with EOS were preterm neonates, and 57% had VLBW, while only 14% of them were term neonates. This suggests that preterm birth could be a double risk factor for VLBW newborns. In this study, only 20% of neonates were born by normal vaginal delivery. Almost one-third of our patients were exposed to PROM, which is consistent with other studies, concluding that the risk of neonatal sepsis increases with premature membrane rupture [27]. PROM and VLBW significantly increase the risk of early-onset sepsis, which is similar to a study by Nikpay et al. (2018) in Ilam. The study of Al Amir et al. (2019) in Egypt is also similar to our study [23] Limitations of this study include the small number of samples and the lack of evaluating antibiotic susceptibility to ampicillin, which is used as prophylaxis.

## Conclusion

Base on the present study results, *E. coli* is the most prevalent Gram-negative bacterium isolated in Shiraz. On the other hand, by examining the risk factors, it is concluded that premature birth and VLBW are the most important risk factors for developing EOS. The results of antibiotic susceptibility testing indicate that antibiotics should be reconsidered, and antibiograms should be performed.

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**Ethical Permission:** approval of conduct study was obtain from Ethics committee of Shiraz university of medical science (IR.SUMS.RESEARCH.REC.1399.7819).

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