Newborns and Sepsis: An Overview of the Condition of Neonates Hospitalized with a Diagnosis of Sepsis in Iran in 2014-2015

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Abstract

Background: Sepsis is a serious neonatal infection and is one of the causes of mortality and complications during infanthood. Studies conducted to identify neonatal and maternal risk factors can indicate methods for prevention, better and faster diagnosis, and the selection of the most appropriate antibiotics.

Objective: The Aim of this study was to determine the clinical symptoms, the results of laboratory tests, and maternal risk factors among neonates hospitalized with a diagnosis of sepsis.

Material and Methods: In this descriptive and cross-sectional study, 78 infants who had been diagnosed with sepsis in the Madani Hospital of Khorrmabad in 2014-2015 were included in the study using tconvenience sampling method. Data were collected using a questionnaire, by studying the medical records of the infants, and by interviewing the mothers. Data were analyzed using the SPSS software and descriptive and interferential statistics.

Results: Blood cultures were positive in 16 cases (21.9%). The most prevalent isolated pathogens included Acinetobacter (37.5%) and Staphylococcus epidermidis (37.5%). Urine cultures were positive in 20.3%, the most prevalent pathogens found being various species of E. coli (23%) and Enterobacter (23%). Significant relationships were found between a positive blood culture with mother's urinary tract infections during pregnancy (p = 0.05), the presence of maternal risk factors (p = 0.008), presentation with respiratory distress (p = 0.02), and a WBC higher than 11,000 (P = 0.036).

Conclusion: The results of this study suggested the need for raising the level of hygiene of the maternity and neonatal wards and the training of mothers and the nursing staff in order to prevent its occurrence.

Key words: Bacterial sepsis, newborn, risk factors, laboratory tests, Iran

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Background

Sepsis is a serious neonatal infection and is one of the causes of mortality and complications during infanthood, which afflicts around 30 million neonates each year and leads to the death of 1 to 2 million [1]. Individuals who live in less developed environments with limited resources are at higher risk, [2]. A study in the UK showed that gram-positive bacteria caused 75 percent of the infections [3]. In another study by Fesharakinia and Miri (2003), 6 out of 67 blood cultures were positive, in which the most prevalent germ was coagulase-negative Staphylococcus [4]. As is apparent, the range of infection-causing organisms is very different in the developed countries as compared with the developing countries [5]. In the developing countries too, regional variation can be observed in the range and varieties of these organisms [6]. This has been attributed to differences in the prescription patterns of antibiotics and differences in lifestyle [7]. Early warning signs and symptoms and clinical manifestations of this disease are few, deceptive, and non-specific [8]. Therefore, the treatment decisions are often based on neonatal, delivery room, prenatal, and maternal risk factors [9]. In their encounters with this uncommon disease, which at the same time has serious complications, most providers of health care services to neonates seek to find ways to identify neonates who are at risk, to quickly identify infected neonates, and start the antibiotic treatment to stop the progression of the disease. Neonates who show symptoms of serious disease at birth receive empiric antibiotic treatment, all over the world, until the presence of sepsis is rejected by negative culture results. Moreover, due to the problem of the presence of infections despite negative cultures, most specialists prefer to empirically treat these neonates with antibiotics for longer periods of time [10]. Due to changes in the pathogenic patterns causing septicemia in neonates over time, the application of various antibiotics, the development of antibiotic resistant species, and variations in the prevalence and causes of septicemia from hospital to hospital and from one community to another, the epidemiological monitoring of sepsis in hospitals, especially in neonatal units, is essential [8]. Currently, neonates suffering from sepsis comprise a large part of the patients admitted to neonatal units and involve great expenditure. Therefore, studies conducted to identify neonatal and maternal risk factors can indicate methods for prevention, better and faster diagnosis, and the selection of the most appropriate antibiotics.

Objectives: The present study aimed to determine individual and familial characteristics of the neonates suffering from sepsis, the bacterial agents causing sepsis in infants, antibiotic resistance among neonates suffering from sepsis, and the relationship between confirmed cases of sepsis with the demographic and familial characteristics, and the clinical and laboratory symptoms and signs that the neonates suffering from sepsis display.

Material and Method

This descriptive cross-sectional study was based on the information obtained from patient records present in the hospital. The statistical population consisted of all the neonates hospitalized in the neonatal units and the NICU of the Shahid Madani Hospital of Khorramabad, Iran, from October 22, 2014 to October 21, 2015. The study sample consisted of 78 neonates who were diagnosed with sepsis by a neonatologist and were hospitalized and treated in the said units during the aforementioned period. The sequential sampling method was used. The data collection instrument was a researcher-designed questionnaire including items related to the demographic and familial information of the neonates and the history of pregnancies and childbirth of the mothers, which was completed via structured interviews with the mothers. The second part of the instrument included the patient information form regarding clinical symptoms, the results of tests, treatments, and the course of the disease. Part of the information recorded in this form was the results of the neonate's blood culture, which is carried out routinely for all neonates diagnosed with sepsis and which determined the type of bacteria causing the sepsis. Moreover, the results of other culture tests such as urine culture, cerebrospinal fluid culture, ocular secretions, and umbilical secretions, which were tested if needed, were recorded in this form. In case blood cultures or other cultures sent to the laboratory were positive (after 24, 48, and 96 hours), antibiotic sensitivity tests were performed on the samples too, and the sensitivity and resistance of the pathogen to commonly used antibiotics was investigated and reported. Based on the results of blood cultures, if gram-negative bacteria were in the blood, resistance to ciprofloxacin, amikacin, gentamycin, and ampicillin would be examined and if gram-positive bacteria were found in the blood, resistance to vancomycin, oxacillin, erythromycin, and ciprofloxacin would be investigated. Additionally, another part of the data recording form included blood index tests, such as CRP, Na, K, BS, CREA, BUN, ESR, Ca, CBC, etc, which were routinely carried out on the neonates and reported. The validity of the questionnaire and the data recording form was investigated and confirmed using the content validity method and by collecting the views of faculty members and neonatologists. After the hospitalization of a neonate and the confirmation of the diagnosis of sepsis by a neonatologist, the objectives of the study were explained to the mother and her consent was obtained. Next, the questionnaire was completed using interviews. The data recording form was gradually completed by studying the patient records during the period of hospitalization of the neonate. The collected data were analyzed using descriptive statistical tests, including frequency, mean, and percentage, and the chi-squared test. If needed, Fisher's exact test, and the independent t-test were also used.

Results

The studied neonates were mostly hospitalized in the neonatal ward (75.6%) and were mostly hospitalized during Autumn (37.1%). The other individual characteristics of the neonates are mentioned in Table 1. The mean and standard deviation of the ages of the mothers of the studied neonates were 27.38 ± 6.28 and their age range was 17-46. The mean and standard deviation of the ages of the fathers were 31.81 ± 5.88 with an age range of 21-48. No significant relationship was found between any of the familial characteristics and the positivity of the blood culture (Table 2).

Table 1: The frequency of the neonates suffering from sepsis based on the individual characteristics of the neonates

Individual characteristics		Number (Percentage)	BC+	Statistic and significance
Hospitalization ward	Neonatal unit	59 (75.6)	15 (93.75)	$X^2 = 3.74$
	NICU	19 (24.4)	1 (6.25)	P = 0.046
Time of hospitalization (in seasons)	Spring	13 (16.7)	3 (18.75)	$X^2 = 1.62$
	Summer	18 (23.1)	4 (25)	P = 0.65
	Autumn	29 (37.1)	4 (25)	
	Winter	18 (23.1)	5 (31.25)	
Sex	Male	44 (56.4)	9 (56.25)	$X^2 = 0.06$
	Female	34 (43.6)	7 (43.75)	P = 0.5
Birth order	1	45 (56.4)	7 (43.75)	$X^2 = 1.28$
	2	23 (29.5)	9 (56.52)	P = 0.19
	3	10 (12.8)		
Embryonic age (in weeks)	Pre-term (less than 38 weeks)	26 (33.3)	3 (18.75)	$X^2 = 2.54$
	Term (38-40)	45 (57.7)	13 (81.25)	P = 0.09
	41-42	7 (9)		
Birth weight	Less than 2800 g	31 (39.7)	5 (31.25)	$X^2 = 0.44$
	2800 – 4000 g	45 (57.7)	11 (68.75)	P = 0.36
	More than 4000 g	2 (2.6)		
Weight at admission	Less than 2800 g	17 (21.8)	1 (6.25)	$X^2 = 2.56$
	2800 – 4000 g	48 (61.5)	15 (93.75)	P = 0.1
	More than 4000 g	13 (16.7)		
Postnatal age (in days)	3 days or less	15 (20.5)	4 (25)	$X^2 = 0.25$
	More than 3 days	58 (79.5)	12 (75)	P = 0.62
Exposure to second-hand smoke after birth	Yes	26 (33.3)	8 (50)	$X^2 = 2.26$
	No	52 (66.7)	8 (50)	P = 0.12
The use of antibiotics before admission	Yes	9 (11.5)	2 (12.5)	$X^2 = 0.7$
	No	69 (88.5)	15 (87.5)	P = 0.65

51.3% of the mothers had a history of antibiotic use during pregnancy. The other characteristics of the pregnant mothers are mentioned in Table 3. In 60.3 percent of the cases, the type of delivery was cesarean section and 13.9% of the mothers underwent prolonged labor. Fisher's exact test did not show any significant relationships between any of the characteristics of childbirth with the positivity of the blood cultures (Table 4). Table 5 shows the most common clinical symptoms with which the neonates presented. Fisher's exact test showed a significant relationship only between respiratory distress and the positivity of the blood culture (X2 = 5.29, P = 0.02). No significant relationship was found between icterus (X2 = 1.93, P = 0.15) and restlessness (X2 = 0.45, P = 0.36) with the positivity of the blood culture. The range of the time needed for the improvement and resolution of symptoms was 1-12 days and the mean and standard deviation for this resolution were 7.35 ± 2.93.

Table 2: The frequency of the studied neonates based on familial characteristics

Familial characteristics		Number (Percentage)	BC+
Mother's age (in years)	Less than 20	10 (12.8)	2 (12.5)
	21-35	56 (71.8)	11 (58.75)
	More than 35	12 (15.4)	3 (18.75)
Father's age (in years)	21-30	38 (48.7)	9 (66/3)
	31-40	34 (43/6)	6 (37.5)
	≥ 41	6 (7.7)	1 (6.2)
Mother's education	Illiterate	5 (6.4)	0
	Primary school – junior high school	14 (17.9)	4 (25)
	High school – High school diploma	43 (55.1)	10 (62.5)
	University	16 (20.6)	2 (12.5)
Father's education	Illiterate	7 (9)	3 (18.8)
	Primary school – junior high school	11 (14.11)	4 (25)
	High school – High school diploma	36 (46.2)	8 (56.2)
	University	24 (30.7)	0
Mother's job	Housewife	69 (88.4)	15 (93.8)
	Employee	7 (9)	0
	Self-employed	2 (2.6)	1 (6.2)
Father's job	Employee	21 (27)	2 (12.5)
	Self-employed	48 (61.5)	11 (68.8)
	Farmer	3 (3.8)	2 (12.5)
	Unemployed	6 (7.7)	1 (6.2)
Place of residence	Urban areas	56 (71.8)	12 (75)
	Rural areas	22 (28.2)	4 (25)

Table 3: The frequency of the participants based on the characteristics of the pregnancy

Characteristics of the pregnancy		Number (Percentage)	BC+	Statistics and significance level
Problems during pregnancy	Amniotic sac rupture	12 (15.2)	3 (27.3)	$X^2 = 0.22$ P = 0.45
	Urinary tract infections	22 (30.1)	8 (36.4)	$X^2 = 3.84$ P = 0.05
	Hypertension	7 (8.8)	2 (12.5)	$X^2 = 1.03$ P = 0.3
	Vaginal secretions	15 (19)	4 (28.6)	$X^2 = 0.45$ P = 0.36
	Edema	2 (2.5)	-	-
	Spotting	2 (2.5)	-	-
	Diabetes	5 (6.4)	-	-
	No problems	26 (32.9)	1 (4.2)	$X^2 = 6.6$ P = 0.008
The place where pregnancy care was received	Clinics and health centers	36 (46.2)	11 (68.75)	$X^2 = 9.68$ P = 0.08
	Midwife's office	4 (5.1)	2 (12.5)	
	Specialist's office	10 (12.8)	-	
	More than one of the above-mentioned places	28 (35.9)	3 (18.75)	
Having a history of antibiotic use during pregnancy	No	38 (48.7)	5 (31.2)	$X^2 = 2.30$ P = 0.11
	Yes	40 (51.3)	11 (68.8)	

Table 4: The frequency of the subjects based on the characteristics of the delivery

The characteristics of the delivery		Number (Percentage)	BC+	Statistic and significant level
Type of delivery	Natural	31 (39.7)	9 (56.2)	$X^2 = 1.28$ P = 0.2
	Cesarean section	47 (60.3)	7 (43.8)	
Person in charge of delivery	Obstetrician-gynecologist	51 (65.4)	8 (50)	$X^2 = 1.50$ P = 0.18
	Midwife	27 (34.6)	8 (50)	
Place of delivery	Hospital	77 (98.7)	16 (100)	-
	Home	1 (1.3)	-	-
Problems during childbirth	No problems	59 (74.7)	11 (19.6)	$X^2 = 0.73$ P = 0.29
	Hypoxia	8 (10.1)	3 (37.5)	$X^2 = 1.30$ P = 0.24
	Prolonged labor	11 (13.9)	2 (22.2)	$X^2 = 0.001$ P = 0.64
	Placenta previa	1 (1.3)	-	-

Table 5: The frequency of the participants based on clinical symptoms at presentation

Clinical symptoms	Number (Percentage)	BC+ Number (Percentage)
Poor feeding	13 (17.7)	2 (13.5)
Icterus	12 (16.4)	5 (31.25)
Fever	13 (17.7)	2 (13.5)
Respiratory distress	13 (17.7)	6 (37.5)
Lethargy	12 (15.2)	-
Restlessness	13 (17.7)	4 (25)
Diminished reflexes	1 (1.13)	-
Seizure	3 (3.8)	-
Vomiting	2 (2.5)	2 (13.5)
Distension	2 (2.5)	-
Purulent pustule	2 (2.5)	-
Petechiae and purpura	1 (1.3)	1 (6.25)
Hepatomegaly	3 (3.8)	-
Splenomegaly	1 (1.3)	-
Oral thrush	1 (1.3)	-
Smelly urine	1 (1.3)	-
Ocular secretions	3 (3.8)	1 (6.25)
Umbilical secretions	2 (2.5)	1 (6.25)
Perianal abscess	1 (1.3)	1 (6.25)
Knee joint swelling	1 (1.3)	-
Thigh ulcers and burns	1 (1.3)	1 (6.25)
Ichthyosis	1 (1.3)	1 (6.25)

In the studied neonates, the result of the ESR test was higher than 10 in 55.4% of the cases. The frequency of the participants based on blood test results are presented in Table 6. The time range for the improvement and normalization of laboratory values was 1-13 days and the mean and standard deviation for this time were 7.17 ± 2.94 days. The range for hospital stay was 4-34 days and the mean and standard deviation for hospital stay were 12.19 ± 6.89 days.

Table 6: The frequency of the participants based on blood test results

Test results			BC+	Statistic and Significance
ESR	< 10	29 (44.6)	7 (50)	$X^2 = 0.005$
	≥ 10	36 (55.4)	7 (50)	P = 0.94
WBC	4000 – 11000	53 (67.9)	7 (43.8)	$X^2 = 4.43$
	> 11000	25 (32.1)	9 (56.2)	P = 0.036
Platelet count	< 150000	11 (14.9)	1	$X^2 = 3.06$
	150000-450000	45 (60.8)	9 (56.2)	P = 0.08
	> 450000	18 (24.3)	7 (43.8)	
HB	< 10	22 (29.7)	5 (31.25)	$X^2 = 4.92$
	10-14	28 (37.8)	3 (18.75)	P = 0.17
	14-16	13 (17.6)	5 (31.25)	
	> 16	11 (14.9)	3 (18.75)	
BS	≤ 45	1 (1.3)	-	-
	> 45	77 (88.7)	16 (100)	
Cα	< 8	0(0)	-	-
	8-11	78 (100)	16 (100)	
CRP	Negative	47 (60.3)	14 (87.5)	$X^2 = 6.34$
	1+	12 (15.4)	2 (12.5)	P = 0.02
	2+	15 (19.2)		
	3+	4 (5.1)		

Results of blood and urine cultures in the studied neonates are shown in Table 7. CSF cultures were performed in 3 cases, the results of all being negative. Umbilical discharge cultures were performed in 2 cases. The result of one of them was negative, and the pathogen found in the other culture was Pseudomonas. In one case, wound discharge culture was positive, and the discovered pathogen was Staphylococcus aureus. Ocular discharge cultures were performed in 6 cases. In 2 cases, the results were negative; in one case, the pathogen was gram-positive cocci; and in 3 cases, the discovered pathogen was Staphylococcus epidermidis. In one case, Candida albicans was found in both blood culture and urine culture. Therefore, this neonate was removed from the samples and all calculations and statistical tests were performed on 78 neonates.

Table 7: The frequency of the subjects based on the results of blood and urine cultures

Culture type		Number (Percentage)
Blood	Not performed	5 (6.5)
	Negative	56 (72.7)
	Acinetobacter	6 (37.5)
	Staphylococcus epidermidis	6 (37.5)
	Staphylococcus aureus	2 (13.5)
	Citrobacter	1 (6.25)
	Moraxella catarrhalis	1 (6.25)
Urine	E. coli	3 (23)
	Enterobacter	3 (23)
	Klebsiella	1 (7.7)
	Citrobacter	1 (7.75)
	Pseudomonas	2 (15.4)
	Acinetobacter	1 (7.75)
	Staphylococcus aureus	2 (15.4)

The most frequently administered antibiotics to the studied neonates are listed in Table 8.

Table 9 (page 102) presents the comparisons of the means of some quantitative variables related to the neonates suffering from sepsis based on the results of the blood cultures. From among these variables, only the length of hospital stay showed a significant difference between the two groups.

Table 8: The frequency of the participants based on the administered medicines

Administered medicine	Number (Percentage)
Ampicillin	56 (71.8)
Cefotaxime	63 (79.7)
Vancomycin	50 (63.3)
Amikacin	22 (27.8)
Meropenem	21 (26.6)
Erythromycin	9 (11.4)
Gentamycin	3 (3.8)
Mupirocin	8 (10.3)
Ciprofloxacin ophthalmic solution	8 (10.1)
Cefepime	2 (2.5)
Glucosaciline	2 (2.5)
Acyclovir	2 (2.5)
Ceftazidime	1 (1.3)
Tozacin	4 (5.2)
Metronidazole	1 (1.3)
Fluconazole	1 (1.3)
IVIG	2 (2.5)
Ranitidine	3 (3.8)
Levothyroxine	1 (1.3)
Phenobarbital	6 (7.6)
Hydrocortisone	4 (5.2)

Discussion

The results showed that blood cultures were positive only in one fifth of the hospitalized neonates. Gram-negative bacteria, especially Acinetobacter, Citrobacter, and Moraxella catarrhalis, and gram-positive bacteria, particularly Staphylococcus epidermidis and Staphylococcus aureus, in equal proportions, were the pathogens causing sepsis in the neonates. Infections caused by these pathogens are mostly common opportunistic and hospital-acquired infections, which are transmitted by hospital staff, family members, and contaminated instruments, like venous catheters, etc. Additionally, in the present study, late-onset sepsis was more common. In late-onset sepsis, frequently organisms acquired from the hospital and the community are involved [11]. The results of the study by Movahedian also showed that only 11 percent of neonatal blood cultures were positive [12], However, in another study, the prevalence of neonatal sepsis was 7 percent and the most common bacterial pathogen causing sepsis was group B Streptococcus[13]. Additionally, in a study by Mojtabaei and et al., the most common pathogens causing gram-negative sepsis among neonates and infants were E. coli (46%), and Klebsiella (27%) [13], and the findings of Fallahi et al. showed that among neonates with suspected sepsis, 8 cases (10.5%) had positive blood cultures. In 5 cases (62.5%), coagulase-negative Staphylococcus was responsible for the infection. Escherichia coli, Moraxella, and Pseudomonas aeruginosa were identified in the remaining blood cultures, each bacteria accounting for one positive blood culture (12.5%) [14]. Therefore, our study is largely consistent with the results reported in previous studies regarding the percentage of the positivity of the blood cultures. The high percentage of negative blood cultures in neonates having the symptoms of systemic infection and hospitalized with a diagnosis of sepsis can be due to two factors. First, to improve the processing of microorganisms, taking 3 blood samples with adequate volume is recommended to avoid the dilution of the blood in the culture media [15]. However, due to the condition of the neonates and their blood volume, usually only one sample is taken, and this makes the isolation of the pathogen less likely. Secondly, the use of antibiotics before hospitalization and before the performance of culture tests affects the results of the cultures. However, the results of our study is different from most studies in terms of the types of pathogenic agents. One of the differences is the lower prevalence of Staphylococcus aureus in our study, while in other studies, it was one of the most prevalent. A notable point is the relatively high prevalence of Staphylococcus epidermidis in our study, which is only observed in hospital-acquired infections. Additionally, in the present study, no records were found of group B Streptococcus causing neonatal sepsis. In the developed countries, group B streptococcus is generally the most prevalent pathogen [16], and early-onset sepsis is more common [17]. Lack of reports regarding GBS infections in the neonates investigated by the present study could be due to lower levels of streptococcal infections in our society. Given the fact that most neonates were older than 3 days and late-onset sepsis was more common than early onset sepsis, this finding can be confirmed. Additionally, the lower prevalence rates of early-onset sepsis can be explained by the fact that almost half of the mothers took antibiotics during pregnancy. Studies have also shown that implementing prophylactic antibiotic treatment in the delivery room can considerably reduce the prevalence of

Table 9: The comparison of the mean of some variables related to the neonates suffering from sepsis based on the results of the blood cultures

Characteristics	BC-	BC+	
The age of the neonates (in days)	13.10 ± 48	13.17 ± 10.96	T = -0.42 P = 0.68 df = 71
Birth weight (Kg)	3.46 ± 851.54	3.58 ± 560.47	T= -0.64 P = 0.52 df = 71
Mother's age (in years)	27.53 ± 6.47	26.64 ± 6.04	T = -0.64 P = 0.52 df = 71
Gestational age (in weeks)	37.37 ± 2.24	38.52 ± 2.53	T = 1.12 P = 0.27 df = 71
Birth weight (Kg)	2.93 ± 706.582	3.09 ± 507.54	T = -0.63 P = 0.53 df = 71
ESR (ml/h)	25.56 ± 27.86	21.21 ± 22.92	T = -0.49 P = 0.62 df = 59
WBC (1000/mm³)	10.23 ± 4.18	10.27 ± 3.14	T = -0.73 P = 0.46 df = 71
Neutrophil (1000/mm³)	47.17 ± 18.16	50.15 ± 16.63	T = -0.23 P = 0.82 df = 60
Lymphocyte (1000/mm³)	50.85 ± 17.18	49.75 ± 16.63	T = -0.05 P = 0.96 df = 60
Platelet (1000/mm³)	336 ± 8.535	432 ± 10.996	T = -0.37 P = 0.71 df = 67
BS (mg/dl)	85.24 ± 28.64	73.25 ± 21.11	T = -0.371 P = 0.17 df =64
Ca (mg/dl)	9.61 ± 0.65	9.28 ± 0.69	T = -0.691 P = 0.09 df = 64
Urea	29.66 ± 17.23	26.13 ± 8.28	T = -0.64 P = 0.52 df = 71
The period of time during which clinical symptoms resolved (in days)	6.98 ± 2.78	7.8 ± 3.34	T = 1.10 P = 0.28 df = 65
The period of time during which laboratory markers resolved (in days)	7.07 ± 2.91	6.66 ± 3.77	T = -0.36 P = 0.72 df = 65
Hospital stay (in days)	11.53 ± 6.84	15.65 ± 6.64	T = 2.11 P = 0.04 df = 70

early-onset sepsis caused by GBS [18]. The absence of GBS infection cases could also be attributed to technical and laboratory faults. A study by Maamouri (2013) found that group B Streptococcus grew in none of the ordinary and enhanced culture media and 64 percent of the mothers of the neonates suffering from sepsis had received antibiotics before childbirth [18]. Since in the conventional culture method, the chances of isolating microorganisms decreases, and since the administration of antibiotics before the culture test reduces the opportunity to grow bacteria in the conventional method, the use of newer and faster systems for blood culture like the BACTEC method and the use of more sensitive methods like enhanced blood culture and molecular studies with the PCR test alongside the conventional method have been recommended to achieve faster and more accurate diagnoses, so that treatment starts in time and antibiotics are not administered without adequate evidence [19]. The main causes of neonatal sepsis vary in different geographical regions. The bacterial etiology varies from community to community and from hospital to hospital. The reason for the differences in the reported prevalence rates can be due to differences in the studied environments, differences in the research methods, different criteria used for the diagnosis of sepsis, different culture methods, different sampling methods, and the administration of antibiotics to the mothers and the neonates. Given the fact that sepsis pathogens were mostly opportunistic and hospital-acquired in the present study, being acquired from the hospital or the community, improving the hygiene of maternity and neonatal wards and training mothers and the nursing staff can help prevent the spread of this disease. To prevent late-onset hospital acquired infections, strategies like improvements in hand hygiene, early breastfeeding, meticulous skin care, limited use of invasive procedures, minimizing manipulations when the use of such procedures is required, and the standardization of methods of venipuncture and management of intravenous catheters can be helpful. Additionally, designing the environment so that personal care instrument hygiene is optimized and increasing the number of staff can reduce the chances of transmission of hospital-acquired infections [20]. Moreover, due to the higher prevalence rates of late-onset sepsis in the present study, many microorganisms, such as viruses, fungi, and anaerobic bacteria, which play a role in the development of late-onset sepsis gain importance, because these pathogens can produce clinical symptoms similar to bacterial sepsis [21]. These pathogens were not investigated in the present study, and therefore it is likely that they played a role in the development of sepsis in the studied population.

In the present study, the clinical symptoms of respiratory distress, jaundice, fever, and poor feeding were more common. However, among the clinical symptoms, only respiratory distress showed a significant relationship with the positivity of the blood culture. In the majority of the studies, clinical symptoms of the respiratory tract in the form of respiratory distress were more common [22]. The occurrence of respiratory distress, including tachypnea, nasal flaring, grunting, and intercostal retraction, could be the only clinical symptom of sepsis with or without pneumonia [23].

In the present study, in the majority of the cases where blood culture was positive, the CRP test was negative. This could be attributed to quick referral after the beginning of the symptoms and the performance of the blood culture in the early stages of the disease, and because the CRP index is a delayed index in inflammatory diseases, its values were reported to be negative in most neonates. In the present study, no significant relationship was found between the values of ESR and the positivity of the blood cultures. Studies have shown that even though ESR, WBC, and CRP are used to diagnose bacterial infections and sepsis, they lack diagnostic accuracy, especially CRP, which is less accurate during the early stages of the disease [24].
In the present study, about one third of the studied neonates had a gestational age of less than 38 weeks, and the majority of them had been born by caesarian section. In the study by Shah Ali et al., the most common underlying factor was preterm birth with a prevalence of 10.2% [25]. In the study by Rafati too, out of the 100 studied neonates, 86 were born by caesarian section and 14 had undergone vaginal birth [26]. The findings of a study by Bailit et al. (2010) showed that as the pregnancy age increases week by week and approaches 39 weeks, when the pregnancy is ended by caesarian section, the prevalence of sepsis is reduced and this should be kept in mind in cases of elective caesarian section [27]. In the present study, from among maternal risk factors, only a history of maternal urinary tract infections during pregnancy showed a significant relationship with the positivity of the blood culture. Neonates, whose mothers did not have any of the risk factors of the pregnancy period, were much less likely to have positive blood cultures. Perinatal and prenatal data can be used to assess risks and as guidelines for action in the delivery room during childbirth and during infancy to make the most appropriate decisions [10].

In the present study, 14.30% of the cases had positive urine cultures, E. coli and other intestinal bacteria being the most common pathogens. However, in no cases, both blood culture and urine culture became positive simultaneously. In the study by Mojtabaei, it was reported that urinary tract infections accompany sepsis in 10.5% of the cases. Additionally, some of the neonates showed symptoms of skin and epithelial infections, such as omphalitis, conjunctivitis, and purulent wounds. In the study by Mojtabaei, too, in 40% of the cases there were symptoms of localized infections, urinary tract infections being the most common [28]. Therefore, given the fact that the clinical symptoms of various neonatal infections appear to be similar, and given that sometimes advanced laboratory equipment is not available, in case sepsis is suspected, it is necessary to investigate the origins of the infection and start treatment measures for the patient. Despite repeated follow-ups, in the majority of the cases, one of the limitations of this study was that, in cases where the blood cultures were positive, antibiotic sensitivity test results (antibiograms) were not included in the patient medical records and the resistance of the

sepsis-causing bacterial pathogens to antibiotics could not be investigated. Moreover, it is obvious that the results of the present study are limited to the studied population and cannot be generalized to the whole city and further studies are needed with larger numbers of participants.

Conclusion

In this study, gram-positive and gram-negative bacteria were responsible for the positivity of the blood cultures in equal proportions. However, in the case of urine culture, enteric gram-negative bacteria, especially the Enterobacteriaceae family were the most commonly found pathogens. Confirmed sepsis was more common among neonates with respiratory distress, white blood cell counts of higher than 11,000, and a maternal history of urinary tract infections. This disease was much less common among neonates who had none of the risk factors of the pregnancy period. These points provide appropriate strategies for fighting the microorganisms causing neonatal sepsis by proper and on-time prescription and administration of antibiotics to prevent antibiotic resistance. Furthermore, it seems that the laboratory tests that are currently used to diagnose sepsis are not fast and accurate enough and require a review.

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