Research Article

2348-8069

"Perinatal Risk Factors for Neonatal Sepsis in Diyala Province / Iraq"

Douaa Mohammed Jameel: M.B.Ch.B,
Ministry of Health
Aseel Jasim Mohammed, M.B.Ch.B, F.I.C.M.S, P.,
College of Medicine, Diyala University
Shafaa Mansour Hamsa, M,B,Ch.B, F.I.C.M.S,P.,
Al-Batool Teaching Hospital
Sura Qais Almaaroff, M.B.Ch.B, F.I.C.M.S. C.A.B.P,
Al-Batool Teaching Hospital
Email of **Dr. Douaa:** *Douaa6600@gmail.com*

Abstract

Background: Mortality from neonatal sepsis may be as high as 50% for infants who are not treated. Its incidence increased during the recent years, it may be due to the more common use of invasive procedures and the development of resistant organisms.

Aim of study: To identify factors (Ante – perinatal) that lead to develop sepsis (early or late) in neonatal period and apply early treatment to reduce incidence of sepsis.

Subjects and Methods: A case-control study conducted in the Department of Pediatric in Al-Batool Teaching Hospital, Diyala, Iraq during a period of six months from Sept 2017 to Mar 2018. It included 200 patients aged　28 days. 100 of them were presented to the hospital due to neonatal sepsis (case group) and the other 100 included patients presented to the hospital due to other causes (control group). A questionnaire was used to gather the necessary information including demographic and clinical information for the patients and their mothers.

Results: The mean age of study patients was 8.59 ± 7.28 days. Four factors were found to be significant independent risk factors for neonatal sepsis. These factors were PROM (OR= 12.241), presence of foul smell discharge (OR= 4.705), intrapartum fever (OR= 3.452), and the need for resuscitation (OR= 2.607).

Conclusion: Both maternal and neonatal factors had contributed to the risk of neonatal sepsis. PROM, present of foul smell does not change interpatient fever and the need for resuscitation were identified as possible independent risk factors of neonatal sepsis and the onset of neonatal sepsis was higher in the first week of neonate's life.

Keywords: Neonatal, sepsis, Iraq, risk factor

عوامل الخطورة ما حول الولادة المؤدية الى تسمم

دعاء محمد جميل،

اسيل جاسم محمد، كلية الطب / جامعة ديالى

سرى قيس المعروف، كلية الطب / جامعة ديالى

لخلفية:معدل الوفيات الناتج عن تسمم حديثي الولادة قد يصل إلى 50 ٪ للرضع الذين لا تتم معالجتهم. قد زاد حدوثه خلال السنوات الأخيرة، وقد يكون بسبب الاستخدام الأكثر شيوعًا للإجراءات والتداخلات وتطور الكائنات المقاومة.

الهدف من الدراسة:لتحديد العوامل (   ) (   ) (   ) في الفترة الوليدية وتطبيق المعالجة

بحث:كانت هذه دراسة حالة مصابة مقابل حالة غير مصابة أجريت في قسم طب الأطفال في مستشفى البتول التعليمي، ديالى، العراق خلال فترة ستة أشهر من سبتمبر 2017 .2018. 200 مريض أعمارهم 28 يومًا. 100 منهم إلى المستشفى بسبب الوليدي (   ) 100 الآخرين الذين تم دخولهم إلى المستشفى لأسباب أخرى (مجموعة المراقبة). تم استخدام استبيان لجمع المعلومات الضرورية بما في ذلك المعلومات الديموغرافية والسريرية للمرضى وأمهاتهم.

: 8.59 ± 7.28 يومًا. تم العثور على أربعة عوامل لتكون عوامل خطر مستقلة كبيرة لتسمم حديثي الولادة. هذه العوامل كانت (12.241 = OR) PROM، وجود إفرازات كريهة الرائحة ((4.705 = OR، حمى أثناء الوضع ((3.452 = OR، والحاجة إلى OR = 2.607)).

: امل المتعلقة بالأم وكذلك الوليد قد ساهمت في خطر التسمم لدى حديثي الولادة. تم تحديد عامل تمزق الغشاء السابق لأوانه، وجود رائحة كريهة لا تغير حمى المرضى الداخليين والحاجة إلى الإنعاش على أنها عوامل خطر مستقلة محتملة لتسمم حديثي الولادة وظهور التسمم كان أعلى الأسبوع الأول من عمر الوليد.

Introduction

Neonatal sepsis (NS) is a clinical syndrome of an infant 28 days of life or younger, manifested by systemic signs of infection and isolation of a bacterial pathogen from the bloodstream [1]. More than 40% of under-five deaths occur in the neonatal period, resulting in 3.1 million deaths per year [2]. On the other hand, the survivors of NS are vulnerable to short and long term neurodevelopmental morbidity [3]. Its incidence increased during the recent years, it may be due to the more common use of invasive procedures and the development of resistant organisms [4].Suggestive criteria of NS were: Fever (rectal >38°C), hypothermia (rectal <36°C), metabolic acidosis, WBC count 30,000/mm or <5,000/ mm, or >25% of immature cells, hypotension and respiratory symptoms such as tachypnea (>60 breaths/min), oxygen requirement, or need for mechanical ventilation [5]. According to the time and mode of infection, two types of NS can be distinguished: early onset sepsis, occurred during the first seven days of life or during the first 72 hours of life in very low birth weight infants [6] and Late-onset sepsis occurring after the first week of life [7].The commonest source of pathogens is vaginal bacterial flora ascended before or during labor or direct contact during the delivery, hematogenous transmission and chorioamnionitis, aspiration and digestion of infected amniotic fluid in utero can considered as a source of infection [8]. Group B streptococcus and E. coli together account for about 70% of cases of early onset NS [9], while 70% of first episode of late-onset infections were caused by gram-positive organisms, with coagulase-negative staphylococci accounting for about 48% of the infections, in addition to *Listeria monocytogenes* and Salmonella[10]. Sepsis disturbs the balance exists in healthy state between pro and anti-inflammatory cytokines, coagulant and anti-coagulant elements, and between endothelial integrity and circulating cells and during the inflammatory process, cells of the haemopoetic system and immune modulating mediators are activated to move towards the affected site for destroying the pathogen [11]. Both maternal and neonatal factors had contributed to the risk of NS, as maternal UTI, place of delivery, PROM, intrapartum fever, low APGAR score at 5th minute and not crying immediately at birth. On the other hand; Residence,

parity, ANC service, mode of delivery, foul smelling liquor, prematurity and low birth weight are identified as possible independent risk factors of NS[12].No single laboratory test has been found to be specific and sensitive, so they must be used in conjunction with risk factors and clinical signs [13]. Tests include blood, urine culture and CSF culture, leukocyte profile, platelet count, ESR, C-reactive protein, latex agglutination tests, or counter immune electrophoresis, and polymerase chain reaction (PCR) [14]. Treatment is most often begun before a definite causative agent is identified. It consists of a penicillin (usually ampicillin) plus an aminoglycoside such as gentamycin and therapy for most of blood stream infections should be continued for a total of 7 -10 days or for at least 5-7 days after a clinical response had occurred [15]. With early diagnosis and treatment, term infants are less likely to have long-term health problems, Residual neurologic damage occurs in 15-30% of neonates with septic meningitis [16].

Patients and Methods

Study Design and Setting: A case control study was conducted in the Department of Pediatric in Al-Batool Teaching Hospital, Diyala Governorate, Iraq for the period from 1st September 2017 to 30th March 2018.

Study Population and sample size: This study included 200 neonate patients (28 days) who were admitted to Al-Batool Teaching Hospital. 100 of them were presented to the hospital due to NS (case group) and the other 100 included patients presented to the hospital due to other causes (control group). The hematological criteria along with the established IMNCI (Integrated Management of Neonatal and Childhood Illness) clinical features of NS were used to diagnose NS in this study. Neonates who were not fulfilled the criteria of sepsis and who were admitted to pediatric ward or NICU of Al-Batool hospital were also included with their index mothers as controls. Any neonate with congenital anomaly was excluded from this study. All patients were subjected to detailed history from the mother, complete physical examination, and laboratory investigation including: (Complete Blood Count, CRP and blood culture). A well-structured questionnaire was formed to gather the necessary information through interviewing the mothers and reviewing neonates' medical records throughout the data collection period. This questionnaire gathered the following information: Neonatal information included: (age in days, gender,

and weight in grams, GA, crying immediately or not and need resuscitation or not), and maternal information included: (Age, Residence whether it was rural areas or urban, educational level of mother: divided into Illiterate, primary school, secondary school and higher education), occupation (Housewife or employer), parity, illness during pregnancy (Hypertension, bleeding disorder, PROM, and foul smell discharge), mode of delivery (NVD, C/S), site of delivery (Hospital, Home or health center), ANC attendance, intrapartum fever, and Per-vaginal examination (< 3 cm or 3 cm).

Statistical Analysis: The data analyzed using Statistical Package for Social Sciences (SPSS) version 25. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Pearson's Chi–square test was used to assess statistical association between sepsis and different variables. Logistic regression analysis was applied using NS as the dependent variable and the variables that showed significant association in the binary analysis as the independent variables. A level of P – value less than 0.05 was considered significant.

Results

The total number of neonates who included in this study was 200, half of them were diagnosed as sepsis (case group) and the other half were healthy neonates (control group). The mean age of the neonates was 8.59 ± 7.28 days. The highest proportion of patients with sepsis were aged < seven days (57.1%) with a significant association (P= 0.014) between age of neonate and sepsis. 61.2% of study neonates with birth weight > 2500 gms complained from NS with a statistically significant association between neonatal birth weight and increased prevalence of sepsis (P= 0.025). Also we found that highest proportion of neonates who needed resuscitation complained from sepsis (63.3%) with significant association between resuscitation need of neonates and sepsis (P= 0.001) and it was obvious that there was no significant association between sepsis and each of neonate's gender and immediate crying (P 0.05) as shown in table (1).

Table 1: Association between NS and certain neonatal characteristics

Neonatal Characteristics	Study Group		Total (%) n= 200	P - Value
	Case Group (%) (n= 100)	Control Group (%) (n= 100)		
Age (Days)				
< 7	68 (57.1)	51 (42.9)	119 (59.5)	0.014
7 - 28	32 (39.5)	49 (60.5)	81 (40.5)	
Gender				
Male	63 (53.4)	55 (46.6)	118 (59.0)	0.25
Female	37 (45.1)	45 (54.9)	82 (41.0)	
Birth Weight (gms)				
< 2500	41 (61.2)	26 (38.8)	67 (33.5)	0.025
2500	59 (44.4)	74 (55.6)	133 (66.5)	
Immediate Crying				
Yes	84 (48.6)	89 (51.4)	173 (86.5)	0.301
No	16 (59.3)	11 (40.7)	27 (13.5)	
Need Resuscitation				
Yes	62 (63.3)	36 (36.7)	98 (49.0)	0.001
No	38 (37.3)	64 (62.7)	102 (51.0)	

There was no significant association between prevalence of sepsis in neonates and all of the general characteristics of their mothers (P 0.05) as shown in table (2).

Table 2: Association between NS and general characteristics of study group's mothers

Maternal Characteristics	Study group		Total (%) n=200	P - value
	Case group (%) n= 100	Control group (%) n= 100		
Maternal age (years)				
< 21	15 (45.5)	18 (54.5)	33 (16.5)	
21 - 34	66 (48.2)	71 (51.8)	137 (68.5)	0.274
35	19 (63.3)	11 (36.7)	30 (15.0)	
Residence				
Urban	42 (46.2)	49 (53.8)	91 (45.5)	0.32
Rural	58 (53.2)	51 (46.8)	109 (54.5)	
Education				
Illiteracy	17 (48.6)	18 (51.4)	35 (17.5)	
Primary school	55 (53.9)	47 (46.1)	102 (51.0)	0.504
Secondary school	11 (37.9)	18 (62.1)	29 (14.5)	
Higher education	17 (50.0)	17 (50.0)	34 (17.0)	
Occupation				
Housewife	92 (49.2)	95 (50.8)	187 (93.5)	
Employer	7 (63.6)	4 (36.4)	11 (5.5)	0.449
Student	1 (50.0)	1 (50.0)	2 (1.0)	

The association between NS and certain illnesses during pregnancy is shown in table (3). We noticed that the highest proportion of mothers who complained from (UTI/STD, PROM, and foul smelling discharge during pregnancy had neonates complaining from sepsis (56.3%, 90.3%, and 77.8% respectively) with a statistically significant association between these three illness and increased prevalence of NS (P=0.005, P=0.001, and P=0.001 respectively). While we found that there was no significant association between NS and both of hypertension and bleeding disorders (P 0.05).

Table 3: Association between NS and certain illness during pregnancy

Variable	Study group		Total (%) n=200	P - value
	Case group (%) n= 100	Control group (%) n= 100		
Hypertension				
Yes	17 (60.7)	11 (39.3)	28 (14.0)	0.221
No	83 (48.3)	89 (51.7)	172 (86.0)	
Bleeding disorders				
Yes	11 (73.3)	4 (26.7)	15 (7.5)	0.06
No	89 (48.1)	96 (51.9)	185 (92.5)	
UTI or STD				
Yes	81 (56.3)	63 (43.8)	144 (72.0)	0.005
No	19 (33.9)	37 (66.1)	56 (18.0)	
PROM > 18				
Yes	28 (90.3)	3 (9.7)	31 (15.5)	0.001
No	72 (42.6)	97 (57.4)	169 (84.5)	
Foul smelling discharge				
Yes	49 (77.8)	14 (22.2)	63 (31.5)	0.001
No	51 (37.2)	86 (62.8)	137 (68.5)	

Table 4 shows the association between NS and certain obstetrical information. We noticed that 72.1% of mothers with GA < 37 weeks had neonates complained from sepsis with a statistically significant association between increased prevalence of sepsis and GA (P=0.003). About parity, 62.5% of multiparous mothers (more than five), their neonates were complaining from sepsis with a significant association between NS and parity (P= 0.046). More than three quarters of mothers who suffered from intrapartum fever during pregnancy, were mothers of neonates with sepsis (78.3%) with a significant association between intrapartum fever and NS (P= 0.001).It was obvious that there was no significant association between NS and all other obstetrical information (P 0.05).

Table 4: Association between NS and certain obstetrical information

| Variable | Study group | | Total (%) n=200 | P - value |
	Case group (%) n= 100	Control group (%) n= 100		
Gestational age				
< 37 week	31 (72.1)	12 (27.9)	43 (21.5)	
37 - 42 week	68 (43.6)	88 (56.4)	156 (78.0)	0.003
> 42 week	1 (100.0)	0 (0)	1 (0.5)	
Mode of delivery				
NVD	48 (51.1)	46 (48.9)	94 (47.0)	0.777
C/S	52 (49.1)	54 (50.9)	106 (53.0)	
Place of delivery				
Home	12 (42.9)	16 (57.1)	28 (14.0)	0.415
Hospital	88 (51.2)	84 (48.8)	172 (86.0)	
Parity				
1	31 (56.4)	24 (43.6)	55 (27.5)	
2 - 4	44 (41.9)	61 (58.1)	105 (52.5)	0.046
5	25 (62.5)	15 (37.5)	40 (20.0)	
ANC				
Yes	93 (50.0)	93 (50.0)	186 (93.0)	1.0
No	7 (50.0)	7 (50.0)	14 (7.0)	
Intrapartum fever				
Yes	47 (78.3)	13 (21.7)	60 (30.0)	0.001
No	53 (37.9)	87 (62.1)	140 (70.0)	
Per vaginal examination				
Yes	57 (54.3)	48 (45.7)	105 (52.5)	0.131
No	41 (44.1)	52 (55.9)	93 (46.5)	

Logistic regression analysis was applied (table 5) using NS as the dependent variable and the variables that showed significant association in the binary analysis as the independent variables. Four factors were found to be significant independent risk factors. These factors were PROM (OR=12.241), presence of foul smell discharge (OR=4.705), intrapartum fever (OR=3.452), and the need for resuscitation (OR=2.607).

Table 5: Logistic regression analysis for association of various risk factors with NS

| Factors | Odds ratio | 95% C.I. | | P- value |
		lower	upper	
PROM	12.241	3.160	47.418	0.001
Foul smelling discharge	4.705	2.037	10.868	0.001
Intrapartum fever	3.452	1.476	8.073	0.004
Need Resuscitation	2.607	1.183	5.745	0.017

Discussion

Epidemiological data from developing countries shows important difference in the incidence and risk factors [17]. Despite major advances in researches in developed countries, 40% of infants with sepsis die or had a neurodevelopmental impairment [18]. In this study, four significant independent risk factors for NS and these factors were PROM, presence of foul smell discharge, intrapartum fever, and the need for resuscitation which is in consistent to an Ethiopian study (2015) [12]. Different risk factors observed in Mexico (2014), when only low birth weight, prematurity, abnormal amniotic fluid and any respiratory complication were identified as independent risk factors for sepsis [19]. Egyptian study

in 2016 noticed the highest effect on sepsis was PROM, twin deliveries, multipara mothers and normal vaginal delivery [20]. Finally, postnatal age and parity are independent risk factors for NS in Chinese study in 2017 [21]. These differences are multifactorial, as the gaps in public facilities in terms of skilled health workforce, supply of essential drugs, equipment, regional differences in bacterial strains and logistics analysis of factors affecting sepsis [22].Neonatal birth weight falls as a significant risk factor for sepsis 2.75 times higher than normal babies in an Indonesian study in 2010, [23], and in Nepal (2006) [24]. Additionally, American study in 2002 found that late-onset sepsis was an important risk factor for death among very low birth weight infants [25]. This may have explained by fact that relatively immunodeficiency condition in the premature and low birth weight infant predisposed to the sepsis condition, as a results of invasive procedures for diagnostic and therapeutic purposes [24]. Urinary tract infection or sexually transmitted disease had a significant association with sepsis in an Ethiopian study in 2015 [12] and in India (2005) [26], Ghana (2014) [27] and Ethiopia (2014) [28].These might be explained by sepsis following the colonization of the birth canal by the infectious agent. In this study, PROM was significantly related to sepsis, in line to another studies in USA (2014)[29], in India (2011) [30], in Nepal (2006)[24], in Pakistan (2014)[31]and a Romania (2010)[32]. But in contrary to that in Saudi Arabia (2002), where no significant role was reported[33]. Early PROM increases the chance of ascending microorganisms from the birth canal into the amniotic sac and fetal compromise as well as asphyxia which leads to sepsis [26]. Finally, Intrapartum fever in this study was significantly related to sepsis, in consistent to that in Ethiopia (2015)[25], in Pakistan (2014)[34]and Bangladesh (2011)[31]. This explained by the fact that intrapartum fever is indicative of maternal infections that are frequently transmitted to the baby in utero or during passage through the canal which usually causes early onset sepsis [35]. In conclusion, this study found that both maternal and neonatal factors had contributed to the risk of NS, and the onset of NS was higher in the first week of neonate's life. In conclusion, this study found that both maternal and neonatal factors had contributed to the risk of NS and the onset of neonatal sepsis was higher in the first week of neonate's life.

References

1. Edwards M. S., Baker C. J. Sepsis in the newborn. In: Gershon A. A., Hotez P. J., Katz S. L., editors. Krugman's Infectious Diseases of Children. Philadelphia, Pa, USA: Mosby; 2004. p. p. 545

2. UNICEF. Levels and Trends in Child Mortality. New York, NY, USA: UNICEF; 2011.

3. Ferreira R. C., Mello R. R., Silva K. S. Neonatal sepsis as a risk factor for neurodevelopmental changes in preterm infants with very low birth weight. Jornal de Pediatria. 2014;90(3):293–299.

4. Glodstein B, Giroir B, Randolph A. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. Pediatric Critical Care Medicine. 2005 Jan 1;6(1):99.

5. Khassawneh M, Khader Y, Abuqtaish N. Clinical features of neonatal sepsis caused by resistant Gram-negative bacteria. Pediatrics International. 2009 Jun;51(3):332-6.

6. Mukhopadhyay S, Puopolo KM. Risk assessment in neonatal early onset sepsis. In Seminars in perinatology 2012 Dec 1 (Vol. 36, No. 6, pp. 408-415). WB Saunders.

7. Camacho-Gonzalez, P.W. Spearman, B.J. Stoll Neonatal infectious diseases: evaluation of neonatal sepsis PediatrClin North Am, 60 (2013), pp. 367-389.

8. Chan GJ, Lee AC, Baqui AH, Tan J, Black RE. Risk of early-onset neonatal infection with maternal infection or colonization: a global systematic review and meta-analysis. PLoS medicine. 2013 Aug 20;10(8): e1001502.

9. Bizzarro MJ, Raskind C, Baltimore RS, Gallagher PG. Seventy-five years of neonatal sepsis at Yale: 1928-2003. Pediatrics 2005; 116:595-602.

10. Hansen N, Stoll BJ, Fanaroff AA, Wright LL, Carlo WA, Ehrenkranz RA, et al. Late-onset sepsis in very low birth weight neonates: the experience of the NICHD Neonatal Research Network. Pediatrics 2002; 110:285-91.

11. Rawat S, Neeraj K, Preeti K, Prashant M. A review on type, etiological factors, definition, clinical features, diagnosis management and prevention of neonatal sepsis. Journal of scientific and innovative research. 2013;2(4):802-13.

12. Gebremedhin D, Berhe H, Gebrekirstos K. Risk factors for neonatal sepsis in public hospitals of Mekelle City, North Ethiopia, 2015: unmatched case control study. PloS one. 2016 May 10;11(5): e0154798.

13. Mclntosh N, Stenson B. Neonatal infection. In: McIntosh N, Helms P, SmythR (eds). Forfar and Arneil textbook of pediatrics. 7th ed. Philadelphia. Churchill Livingstone CO 2008: 274-275.

14. Ahmed Z, Ghafoor T, Waqar T, et al. Diagnostics value of C-reactive protein and hematological parameters in neonatal sepsis. J Coll Physician Surgpak 2005; 15(3): 152-156.

15. Zaidi AK, Huskins WC, Thaver D,. Hospital-acquired neonatal infections in developing countries. Lancet. 2005; 365:1175-1188.

16. Anderson-Berry AL., Rosenkrantz T. Cardiac Disease and Critical Care Medicine, Neonatal Sepsis, Updated: Dec 31, 2015. https://emedicine.medscape.com/article/978352-overview#a7

17. Hornik CP, Fort P, Clark RH, Watt K, Benjamin DK, Smith PB, et al. Early and late onset sepsis in very-low-birth-weight infants from a large group of neonatal intensive care units. Early Hum Dev. 2012;88(Suppl 2): S69–74.

18. Brocklehurst P, Farrell B, King A, Juszczak E, Darlow B, Haque K, et al. Treatment of neonatal sepsis with intravenous immune globulin. The New England journal of medicine. 2011;365(13):1201–11.

19. Leal YA, Álvarez-Nemegyei J, Velázquez JR, Rosado-Quiab U, Diego-Rodríguez N, Paz-Baeza E, et al. Risk factors and prognosis for neonatal sepsis in southeastern Mexico: analysis of a four-year historic cohort follow-up. BMC pregnancy and childbirth. 2012 Dec;12(1):48.

20. Medhat H, Khashana A, El Kalioby M. Multivariate Logistic Regression Analysis for the Significant Neonatal and Maternal Risk Factors Related to Neonatal Sepsis, Int J Infect. 2016 ;3(4):e38290.

21. Xiao T, Chen LP, Liu H, Xie S, Luo Y, Wu DC. The analysis of etiology and risk factors for 192 cases of neonatal sepsis. BioMed research international. 2017;2017.

22. Chowdhury S, Hossain SA, Halim A. Assessment of quality of care in maternal and newborn health services available in public health care facilities in Bangladesh. Bangladesh Medical Research Council Bulletin. 2009;35(2):53–6.

23. Utomo MT. Risk factors of neonatal sepsis: a preliminary study in Dr. Soetomo hospital. Indonesian journal of tropical and infectious disease. 2010 Apr 1;1(1):23-6.

24. Shah GS, Budhathoki S, Das BK, Mandal RN. Risk factors in early neonatal sepsis. Kathmandu University medical journal (KUMJ). 2006;4(2):187-91.

25. Stoll BJ, Hansen N, Fanaroff AA, Wright LL, Carlo WA, Ehrenkranz RA, et al. Late-onset sepsis in very low birth weight neonates: the experience of the NICHD Neonatal Research Network. Pediatrics. 2002 Aug 1;110(2):285-91.

26. Siakwa M, Kpikpitse, Mupepi D, Mohamed SS. Neonatal sepsis in rural Ghana: A case control study of risk factors in a birth cohort. IJRMHS & K.A.J.2014 Sept; 4(5) 77–88.

27. Woldu MA, Guta MB, Lenjisa JL, Tegegne GT, Tesafye G, Dinsa H. Assessment of the incidence of neonatal sepsis, its risk factors, antimicrobial use and clinical outcomes in Bishoftu General Hospital, Neonatal Intensive Care Unit, Debrezeit-Ethiopia. Pediat Therapeut.2014 Aug; 4: 214.

28. Chacko B, Sohi I. Early onset neonatal sepsis. Indian J Pediatr. 2005; 72(1):23–26.

29. Gyamfi-Bannerman C, Son M. Preterm premature rupture of membranes and the rate of neonatal sepsis after two courses of antenatal corticosteroids. Obstetrics & Gynecology. 2014 Nov 1;124(5):999-1003.

30. Bhat R, Lewis LE, Vandana KE. Bacterial isolates of early-onset neonatal sepsis and their antibiotic susceptibility pattern between 1998 and 2004: an audit from a center in India. Italian journal of pediatrics. 2011 Dec;37(1):32.

31. Alam MM, Saleem AF, Shaikh AS, Munir O, Qadir M. Neonatal sepsis following prolonged rupture of membranes in a tertiary care hospital in Karachi, Pakistan. The Journal of Infection in Developing Countries. 2014 Jan 15;8(01):067-73.

32. Boia M, Ilie C, Ioanas L, Manea A, Iacob D, Cioboata D. Neonatal septicemia retrospective study on premature newborn. JurnalulPediatrului. 2010; 8:49-50.

33. Asindi AA, Archibong EI, Mannan NB. Mother-infant colonization and neonatal sepsis in prelabor rupture of membranes. Saudi Med J. 2002; 23(10): 1270-4.

34. Hasan MS, Mahmood CB. Predictive values of risk factors in neonatal sepsis. J Bangladesh CollPhysSurg 2011; 29: 187–195.

35. Soman M, Green B, Daling J. Risk factors for early onset neonatal sepsis. Am.J. Epidemiol (1985) 121 (5): 712–719.