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Types of Bacteria associated with Neonatal Sepsis in Al-Thawra University Hospital, Sana'a, Yemen, and their Antimicrobial Profile

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أنواع البكتيريا المرتبطة بالإنتان الوليدي في مستشفى جامعة الثورة، صنعاء ، اليمن وشاكلة مضادات الميكروبات

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الملخص: **الهدف**: تحديد البكتيريا المسببة للإنتانات بين حديثي الولادة في مستشفى الثورة بمدينة صنعاء، بالإضافة إلى تحديد مقاومة البكتيريا للمضادات الحيوية، ووضع توصية للعلاج التجريبي بناء على ذلك. **الطريقة**: تضمنت هذه الدراسة 158 طفلا حديثي الولادة (تتراوح أعمارهم بين 0 و28 يوما)عانوا من واحد أو أكثر من أعراض الإنتانات. تم أخذ عينة من الدم الوريدي من كل الحالات، وثم تم زرعها وتحديد اختبارات الحساسية للجراثيم المعزولة. النتائج: كان فحص الزرع الجرثومي إيجابيا في 09 طفلا (75%)، وأظهرت إصابات الإنتان المبكرة أعلى النتائج الإيجابية للزرع الجرثومي (61.7%) منه في الإصابات المتأخرة (32%). وجدت نتائج الزرع الايجابي المهمة عند مجموعة الأطفال الذين يتراوح وزنهم عند الولادة بين 0.9 إلى 2 كيلو جرام (78.6%). شكلت البكتيريا سالبة الجرام نسبة (97.8%) من إجمالي الزرع الجرثومي، حيث كانت بكتيريا الكلبسيلة الرئوية هي السائدة فيها بنسبة (36.7%)، تليها البكتيريا الزَّائفَة بنسبة (30.0%). أما أكثر الأعراض شيوعا بين المصابين فكان ضيق التنفس بنسبة (72.2%) من الحالات، تلاها اليرقان (62.2%) والزُراق (51.1%) والنُوام (47.8%). أما معدل الوفيات فبلغ (27.8%). كانت نتائج الزرع لكل البكتريا سالبة الجرام حساسة للدواء اميبينيم، وبعضها كان حساسا للجيل الرابع من السيفالوسبورين، لكن معظم نتائج الزرع كانت مُقاومة لأكثر المضادات الحيوية المستخدمة. **الخلاصة**: البكتيريا سالبة الجرام هي المسببة الرئيسية للإنتانات البكتيرية لحديثي الولادة في مدينة صنعاء، وكانت سببا رئيسيا في الوفاة والمرض لحديثي الولادة، خاصة بين المواليد ذوي الوزن المنخفض جدا. يمكن الاستنتاج بأن المضاد الحيوي اميبينيم والجيل الرابع من السيفالوسبورينات يمكن أن تكون الخيار الأول للعلاج التجريبي للحالات المرضية بالإنتان البكتيري .

مفتاح الكلمات: أنتان، وليدي، مبكر، متأخر، مقاومة دواء، علاج، علاج تجريبي، صنعاء، اليمن.

ABSTRACT: ***Objectives:*** This study was undertaken to investigate the organisms causing sepsis in the Neonatal Unit at Al-Thawra Hospital, Sana'a, Yemen, determine their resistance to antibiotics, and recommend policy for empirical treatment. ***Methods:*** A total of 158 neonates having one or more signs of sepsis, and aged from 0 to 28 days, were enrolled in this study. A blood sample was taken from each subject, cultured, and then antibacterial susceptibility tests were performed for isolates. ***Results:*** 90 (57%) cases yielded positive cultures. Early-onset sepsis showed higher positive culture results (61.7%) than late-onset sepsis (32%). Significant positive culture results were found among the group with birth weight 0.9–2 Kg (78.6%). Gram negative bacteria constituted 97.8% of the total isolates, of which *Klebsiella pneumoniae* was the predominant pathogen (36.7%), followed by *Pseudomonas* species (30.0%). The commonest symptoms among the cases were respiratory distress (72.2%), jaundice (62.2%), cyanosis (51.1%), and lethargy (47.8%); the mortality rate was 27.8%. All Gram negative bacterial isolates were sensitive to imipenem and some isolates were sensitive to fourth-generation cephalosporins, but most isolates were highly resistant to the majority of other antibiotics tested. ***Conclusion:*** Gram negative organisms were the most frequent causative agents of bacterial sepsis, which is a significant cause of mortality and morbidity in the newborn, and particularly in those of very low birth weight. It can also be concluded that imipenem and fourth-generation cephalosporins can be used for empirical treatment of bacterial sepsis.

Keywords: Sepsis; Neonatal; Early-onset; Late-onset; Drug resistance; Treatment, empirical; Sanaa; Yemen.

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Advances in knowledge

1. *This study provides current data on the organisms causing sepsis in neonatal units and the resistance of the sepsis-causing organisms to the relevant antibacterial drugs. It was found that Gram negative organisms were the most frequent causative agents of bacterial sepsis (97.8%).*
2. *This information is important in order to recommend policy for empirical treatment.*
3. *This is one of only a few studies from Arabic countries focused on neonatal sepsis.*

Application to patient care

1. *The research reported here could aid in the prevention of neonatal sepsis and build a treatment policy for neonatal bacterial sepsis.*
2. *This study alerts physicians to the defective hygiene in neonatal units and the high rate of resistance to antibiotics.*

Sepsis is a significant cause of mortality and morbidity in the newborn, particularly among those of very low birth weight and premature infants.[1,2] The World Health Organization (WHO) estimates that worldwide 1.6 million newborn babies die every year from neonatal infections. Individual units have reported case fatality rates as low as 2–3% and as high as 50%,[3] but the average overall mortality from neonatal sepsis reported from many neonatal intensive care units in developed countries is around 20%.[4] Despite recent advances in neonatal intensive care and current strategies to treat neonatal sepsis, mortality rates have not fallen for over three decades[4] except in babies born to mothers who have received intrapartum prophylaxis (IAP) for Group B *Streptococcus* (GBS).[5] Whilst IAP has been successful in significantly reducing the incidence of early onset GBS disease in the newborn it has led to an increase in Gram negative infections in institutions where antibiotics other than penicillin are used for IAP.[6] Worryingly, both short and long term neurodevelopmental morbidity in survivors of neonatal sepsis is also significant.[7] The study by Stoll *et al.* in 2002 showed that neonatal infection is associated with a 30–80% increase in neurodevelopmental impairment and a 30–100% increase in odds for poor head growth which is a very good predictor of long-term morbidity.[6]

This study aimed to determine the types of bacteria associated with neonatal sepsis in neonatal unit of Al-Thawra University Hospital in Sana'a, Yemen, and their antibiotic profile.

Methods

This prospective study was carried out during a 12 month period from April 2008 to March 2009. The study proposal was approved by the Department of Medical Microbiology, in the Faculty of Medicine & Health Sciences at Sana'a University, Yemen. A total of 158 hospital-born neonates with a clinical diagnosis of septicaemia, and admitted to the neonatal unit of Al-Thawra University Hospital in Sana'a city, were included in this study. A consent form was completed by the parents for each subject.

Early-onset sepsis (EOS) was defined as sepsis occurring within the first week of life. Late-onset sepsis (LOS) was defined as sepsis that occurred any time after the first week of life until the end of the neonatal period (28 days of age). A full history was taken from doctors and files, and the findings were recorded in a predesigned questionnaire. The data collected included: any complications during delivery, characteristics of the infant, sex, birth weight, temperature, other medical conditions in the infant, major signs and symptoms and other necessary data for the research. Blood culture was preformed for all neonates suspected of having septicaemia. Septicaemia was suspected in the following settings: 1) *At birth:* All neonates born to mothers with maternal fever, prolonged rupture of membranes for more than 24 hours, or foul-smelling or meconium-stained liquor, and those having severe prematurity or birth asphyxia necessitating active resuscitation; 2) *After birth:* All newborns with lethargy, poor feeding, abdominal distension, respiratory distress, instability in temperature, pathological jaundice, and convulsions.

The collected data and the results of this study were statistically analysed for means of significance by the Epi Info computer programme, Version 6 (Epi Info, Centers for Disease Control (CDC), Atlanta, Georgia, USA). The specimens were collected as follows: one blood culture at least was obtained for each neonate with signs of sepsis, by the method described by Buttery.[8] Blood from peripheral venous or arterial punctures was collected under sterile conditions as described by Hall and Lyman.[9] The blood specimen was then inoculated into a BACTEC vial (BACTEC, Rochester, UK) and the

Table 1: The rate of positive bacterial culture among male and female neonates.

Sex:	Total cases		Cases with Positive Culture		χ^2	*P*
	No.	%	No.	%		
Male	96	60.8	51	53.1	1.47	0.22
Female	62	39.2	39	62.9		
Crude rate	158	100.0	90	57		

Legend: $\chi 2$ = chi square; P = probability value.
Note: $\chi 2 > 3.7$ and $P < 0.05$ are significant.

inoculated culture bottles were incubated as soon as possible in the BACTEC brand fluorescent series instrument (BACTEC 9120) for up to 5 days, as recommended by Becton Dickinson Microbiological Systems.[10] Positive blood culture vials were sub-cultured into blood agar, chocolate agar, MacConkey agar, and Sabouraud agar (for yeast), then the media were inspected for the presence of bacterial growth. The isolated bacteria were defined by colonial morphology, Gram stain reaction, biochemical reactions and confirmed by API-20E biotyping (API 20E system, Analytab Products, Plainview, New York, USA). Finally, the sensitivity of isolated bacteria to various antibiotics was assessed according to the modified Kirby and Bauer method on Mueller-Hinton agar. The concentrations of the antibiotics used (µg/disc) were as follows: ampicillin (AMP) - 10; gentamycin (CN) - 10; amikacin (AK) - 30; ceftazidime (CAZ) - 30; ceftriaxone (CRO) - 30; cefepime (FEP) - 30; piperacillin (P) - 100; imipenem (IPM) -10; and aztreonam (ATM) - 30. The Clinical and Laboratory Standards Institute (CLSI) guidelines were used to determine antimicrobial resistance.

Table 2: The rate of positive bacterial culture in early-onset (EOS) and late-onset of sepsis (LOS) and their relative risks for contracting bacteria, confidence interval and test of significance

Type of sepsis	Positive Bacterial Culture		RR	CI	χ^2	*P*
	No.	%				
EOS ≥ 7 days n =133	82	61.7	2.2	(0.77–6.3)	2.7	0.10
LOS < 7 days n = 25	8	32	0.7	(0.4–1.2)	2.7	0.10
Total	90	57				

Legend: RR = Relative risk; CI = Confidence Interval; $\chi 2$ = chi square, P = probability value
Note: $\chi 2 > 3.7$ and $P < 0.05$ are significant

Table 3: The rate of positive bacterial culture and its relationship to birth weight

Birth weight (Kg)	Total cases		Cases with Positive culture		χ^2	*P*
	No.	%	No.	%		
0.9–2	73	46.2	50	68.5	5.7	0.01
2.1–3	63	39.9	31	49.2	3.7	0.05
3.1–4	19	12	08	42.1	0.2	0.68
<4	3	1.9	1	33.3	0.7	0.4

Legend: χ^2 = chi square; P = probability value.
Note: $\chi^2 > 3.7$ and $P < 0.05$ are significant

Results

This study included 158 neonates, their ages ranging from 0 to 28 days with a mean age of 5.2 days.

The standard deviation (SD) was equal to 6.1 days, mode equal to 1 day and median equal to 3 days. There were 96 (60.8%) males and 62 (39.2%) females. The detailed results of this study are presented in Tables 1 to 6. Table 1 shows the distribution of positive bacterial culture according to sex. A total of 90 (57%) of patients had a positive culture for bacterial growth. The rate of positive culture among females (62.9%) was higher compared to males (53.1%), but the variation was not statistically significant in which $\chi^2 = 1.47$ and $P = 0.22$. The EOS showed higher positive culture results (61.7%) than LOS (32%), with the relative risk of contracting EOS bacterial infection 2.2 times that of LOS, but the difference was not statistically significant in which $\chi^2 = 2.7$ and $P = 0.1$ [Table 2]. Table 3 shows that highly significant positive cultures results were found among the group with birth weight 0.9–2 Kg (78.6%, $\chi^2 = 5.7$, $P = 0.01$). The commonest symptoms among the cases studied were respiratory distress (72.2%), jaundice (62.2%), cyanosis (51.1%) and lethargy (47.8%). On the other hand, lethargy, apnoea, poor feeding and unconsciousness occurred significantly less frequently among positive bacterial culture cases in which $\chi^2 > 3.7$ and $P < 0.05$. However, the mortality rate was higher among positive culture cases (27.8%), than negative ones (2.9%) and the variation was statistically significant in which $\chi^2 = 16.86$ and $P = 0.0004$ [Table 4].

Table 4: Presenting clinical symptoms and mortality rate among total patients compared with positive bacterial culture.

Symptoms	Negative culture n = 68		Positive culture n = 90		χ^2	*P*
	No.	%	No.	%		
Fever, n = 20	8	11.8	12	13.3	0.09	0.76
Lethargy, n = 64	21	31	43	47.8	4.6	0.03
Jaundice, n = 98	36	53	56	62.2	0.00	0.95
Apnoea, n = 15	3	4.4	12	13.3	3.6	0.05
Respiratory distress, n = 116	51	75	65	72.2	0.15	0.7
Poor feeding, n = 19	2	2.9	17	18.9	9.3	0.002
Cyanosis, n = 76	30	44.1	46	51.1	0.76	0.38
Abdominal distention, n = 7	4	5.8	3	3.3	0.6	0.4
Pallor, n = 20	5	7.3	15	16.7	3.04	0.08
Convulsion, n = 5	1	1.5	4	4.4	1.12	0.29
Birth asphyxia, n = 8	4	5.9	4	4.4	0.17	0.68
Unconscious, n = 21	5	7.3	16	17.8	3.65	0.05
Mortality rate, n = 27	2	2.9	25	27.8	16.86	0.0004

Legend: χ^2 = chi square; P = probability value.
Note: $\chi^2 > 3.7$ and $P < 0.05$ are significant

Gram negative bacteria constituted 97.8% of the total isolates, of which *Klebsiella pneumoniae* was the predominant pathogen with 36.7%, followed by *Pseudomonas* species with 30.0%. *Citrobacter* species was the least common isolate of Gram negative bacteria with a percentage of 4.4%, while Gram positive bacteria rates were very low (1.1%) [Table 5]. All Gram negative bacterial isolates were sensitive to imipenem and some isolates were sensitive to fourth-generation cephalosporins (cefepime), but most isolates were highly resistant to the majority of other antibiotics tested [Table 6].

Table 5: The frequency and percentage of bacterial species that isolated from neonate sepsis cases

Organism	No.	%
Gram negative bacteria	88	97.8
Klebsiella pneumoniae	33	36.7
***Pseudomonas* species**	27	30
***Enterobacter* species**	14	15.6
***Acinetobacter* species**	10	11.1
***Citrobacter* species**	4	4.4
Gram positive bacteria	1	1.1
Staphylococcus aureus	1	1.1
Fungi	1	1.1
***Candida* species**	1	1.1
Total positive bacteria	90	100.0

Discussion

In this study, blood culture obtained from 158 neonates yielded positive results in 57% of cases, while the remaining 43% gave negative results. A similar result was reported by Ako-Nai and others in Nigeria in 1999 with a positive percentage of 55%.[11] Slightly higher positive results were reported by Rohsiswatmo (65.3%) in Indonesia,[12] Rahman *et al.*[13] in Pakistan (62.8%) and by Macharashvili *et al.*[14] in Georgia (63%). In contrast, much lower positive results were reported from Iran (5.6%),[15] Kuwait (8.7%)[16] and Saudi Arabia (5%).[17] These variations can be attributed to many different factors of which antibiotic therapy prior to the laboratory diagnosis may have had the most important influence on the low culture results.

The EOS rates (61%) were higher than the LOS rates (32%) in this study. This result is compatible

Table 6: Resistant pattern of the isolates to some antibiotics

Antibiotic	*Klebsiella* spp (n = 33)	*Pseudomonas* spp (n = 27)	*Enterobacter* spp (n = 13)	*Citrobacter* spp (n = 4)	*Acinetobacter* spp (n = 10)
AMP	29 (87.8)	23 (85.2)	12(92.3)	3 (75.0)	5 (50)
AML	31 (93.9)	19 (70.3)	13 (100)	4 (100)	9 (90)
ATM	30 (90.9)	20 (74.0)	10(76.9)	4 (100)	7 (70)
PRL	29 (87.8)	3 (11.1)	8 (61.5)	1 (25.0)	1 (10)
CAZ	30 (90.9)	10 (37.0)	12(92.3)	4 (100)	5 (50)
FEP	12 (36.4)	4 (14.8)	0	1 (25.0)	0
CRO	32 (96.9)	19 (70.3)	13 (100)	4 (100)	9 (90)
IPM	0	0	0	0	0
AK	13 (39.3)	12 (44.4)	8 (61.5)	0	5 (50)
CN	9 (27.2)	17 (62.9)	5 (38.4)	0	5 (50)

Legend: AMP = ampicillin; AML = amoxicillin; ATM = azteronam; PRL = pipracillin; AK = amikacin; CN = gentamicin; CAZ = ceftazidim; CRO = ceftriaxon; FEP = cefipime = c; IPM = imipenem.

with the reports from Iran and Pakistan,[18,19] but it contrasts with a report from Bangladesh, where LOS was more common than EOS.[20] However, the most common organism in EOS was *K. pneumoniae*; the same finding was recorded in many developing countries.[21–23] In the present study, females showed slightly higher positive results than males, which is similar to findings reported from Iran.[24]

The commonest symptoms among the cases studied were respiratory distress (72.2%), jaundice (62.2%), cyanosis (51.1%, and lethargy (47.8%). On the other hand, lethargy, apnoea, poor feeding and unconsciousness showed significantly low rates of occurrence among positive bacterial culture cases. In general, the presenting clinical symptoms and signs in our study agreed with the WHO clinical criteria for neonatal sepsis.[25]

There was a significant correlation between low birth weight and the incidence of neonatal sepsis with, statistically significant values of χ^2 = 5.7 and a *P* value equal to 0.01. The same finding was observed in the studies of Al-Umran and Twum-Danso in Saudi Arabia and Jeong in Korea.[17,26] Mortality rate among positive culture cases in this study was 27.8%, which was similar to that found in Zimbabwe,[27] Pakistan[28] and Georgia.[14]

The most common organisms which caused EOS and LOS in the present study were Gram negative bacteria, with a percentage of 97.8%. This result agreed with other related studies in many developing countries,[13,14,23,29] but differed from those reported by Huda *et al.*[16] in Kuwait, Haque *et al.*[4] in the UK and Hyde *et al.*[30] in the USA where Gram positive bacteria were more predominant. *K. pneumoniae* was the predominant isolate in the present study, representing 36.7% of the total isolates. Similar findings were reported by Macharashvili in Georgia,[14], Mehdinejad *et al.* in Iran (33.5%)[15] and by Kumhar *et al.* in India (33.8%),[21] but lower results were reported from Nepal (18.3%) and Pakistan (7.6%).[31,13] Moreover, it was found in this study that *Pseudomonas* species were the second most common isolate; similar findings were reported in Pakistan.[13,32] The overwhelming majority of Gram negative organisms isolated in this study and among the other studies reviewed suggests that these infections may in fact be acquired from the hospital or community environment, due to poor hygienic practices during delivery and postnatal care, rather than reflecting vertical transmission to the infant from exposure to vaginal tract flora.[33,34] Another possible explanation of the predominance of Gram negative bacteria in our study is that asymptomatic colonised patients, the contaminated environment, or both can serve as reservoirs for these pathogens, which are then spread by the hands of health care workers.[35,36] Furthermore, a limitation of our study was that there is insufficient sterility testing or wipe testing of the neonatal wards to confirm if the conditions are unhygienic which could mean that contaminating bacteria might also be recovered from the environment.

Multi-drug resistance of the causative organisms of sepsis is a rapidly emerging and potentially disastrous problem. Infection with resistant organisms has been associated with treatment failure, higher morbidity and mortality and increased costs. The present study shows a very high degree of resistance of Gram negative organisms to commonly used antibiotics (AMP and CN) as well as third-generation cephalosporins. These results agree with many other studies.[12,18,37,,38] The high burden of infection and the degree of antibiotic resistance seen in this study population may signify an emerging trend among sepsis isolates recovered from neonates in developing countries. In a review of data from developing countries, Zaidi *et al.* found rates of neonatal infection in hospitalised infants to be 3–20 times higher than those in developed countries, and approximately 70% of these infections would not be susceptible to conventional empirical antibiotic regimens, such as AMP with CN.[39]

All Gram negative organisms in this study were sensitive to IMP; the same results were reported by Shaw *et al.*, Al-Tawfiq and Antony, Rohsiswatmo, and Waseem *et al.*[31,40,12,23] In contrast, a study in the Philippines reported 20% resistance to IMP.[36] In the present study, there was increasing resistance to third-generation cephalosporins, probably attributable to extended spectrum beta-lactamase (ESBL) production by Gram negative bacteria, especially *Klebsiella*, as also observed in another studies on neonates. [31,39,41] The lack of culture-driven antimicrobial therapy and limited, consistent infection control practices is likely to be responsible for the resistance of Gram negative organisms in this study.

Conclusion

Gram negative organisms were the most common causative agents of bacterial sepsis in this study. In turn, they are a significant cause of mortality and morbidity in the newborn, particularly in very low birth weight infants. IPM and fourth-generation cephalosporins such as FEP can be used for the empirical treatment of bacterial sepsis in Sana'a city, Yemen.

CONFLICT OF INTEREST

The authors reported no conflict of interest.

References

1. Stoll BJ, Hansen N. Infections in VLBW infants: Studies from NICHD Neonatal Network. Semin Perinatol 2003; 27:293–301.
2. Stoll BJ, Hansen N, Chapman AI. Neuro-development and growth impairment among extremely low birth weight infant with neonatal infections. JAMA 2004; 292:2357–65.
3. Bizzarro MJ, Raskind C, Baltimore RD, Gallagher PC. Seventy-five years of neonatal sepsis at Yale: 1928-2003. Pediatrics 2005; 116:595–602.
4. Haque KN, Khan MA, Kerry S, Stephenson J, Woods G. Pattern of culture-proven neonatal sepsis. A district general hospital in the United Kingdom. Infect Control Hosp Epidemiol 2004; 25:759–64.
5. Isaacs D, Doyle JA. Intrapartum antibiotics and early onset sepsis caused by group B streptococcus and other organisms in Australia. Pediatr Inf Dis J 1999; 8:524–8.
6. Stoll BJ, Hansen N, Fanaroff AA. Changes in pathogens causing early onset sepsis in very low birth weight infants. N Engl J Med 2002; 347:240–7.
7. Nelson KB, Willoughby RE. Infection, inflammation and the risk of cerebral palsy. Curr Opinion Neurol 2000; 13:133–9.
8. Buttery JP. Blood cultures in newborns and children: Optimizing an everyday test. Arch Dis Child Fetal Neonatal Ed 2002; 87: F25–8.
9. Hall KK, Lyman JA. Updated review of blood culture contamination. Clin Microbiol Rev 2006; 788–802.
10. Becton Dickinson Microbiological Systems. BECTEC PEDS PLUS/F culture vials: Instruction leaflet. Sparks, Maryland: Becton Dickinson Company, 2000.
11. Ako-Nai Ak, Adejuyigbe EA, Ajayi FM, Onipede AO. The bacteriology of neonatal septicaemia in I1e-Ife, Nigeria. J Trop Pediatr 1999; 45:146–51.
12. Rohsiswatmo R. Multi-drug resistance in the neonatal unit and its therapeutic implications. Paediatr Indones 2006; 46:25–31.
13. Rahman S, Hameed A, Roghani M T, Ullah Z. Multi-drug resistant neonatal sepsis in Peshawar, Pakistan. Arch Dis Child Fetal Neonatal 2002; 87: F52–4.
14. Macharashvili N, Kourbatova E, Butsashvili M, Tsertsvadze T, McNutt LA, Leonard MK. Etiology of neonatal blood stream infections in Tbilisi, Republic of Georgia. Int J Infect Dis 2009; 13:499–505.
15. Mehdinejad M, Khosravi AD, Morvaridi A. Study of prevalence and antimicrobial susceptibility pattern of bacteria isolated from blood cultures. J Biol Sci 2009; 9:249–53.
16. Huda HA, Edet GE, Rajaram UU. Neonatal septicemia in Al-Jahra Hospital, Kuwait: Etiologic agents and antibiotic sensitivity patterns. Med Principles Pract 2001; 10:145–50.

17. AlUmran DK, Twum-Danso K. A case control study of neonatal sepsis: Experience from Saudi Arabia. J Trop Pediatr 1997; 43:84–8.

18. Movahedian AH, Moniri R, Mosayebi Z. Bacterial culture of neonatal sepsis. Iran J Publ Health 2006; 35:84–9.

19. Rasu CH, Hassan MA, Habibullah M. Neonatal sepsis and use of antibiotic in a tertiary care hospital. Pak J Med Sci 2007; 23:78–81.

20. Ahmed AS, Chowdhury MA, Hoque M, Darmstadt GL. Clinical and bacteriological profile of neonatal septicemia in tertiary level pediatric hospital in Bangladesh. Indian Pediatr 2002; 39:34–9.

21. Kumhar GD, Ramachandran VG, Gupta P. Bacteriological analysis of blood culture isolates from neonates in a tertiary care hospital in India. J Health Popul Nutr 2002; 20:343–7.

22. World Health Organization. Explore Simplified Antimicrobial Regimens for the Treatment of Neonatal Sepsis. Geneva: WHO. WHO/FCH/CAH/04.1. 30 Sep–1 Oct 2002.

23. Waseem R, Khan M, Izhar TS, Qureshi AW. Neonatal sepsis. Professional Med J 2005; 12:451–6.

24. Salamati P, Rahbarimanesh AA, Yunesian M, Naseri M. Neonatal nosocomial infections in Bahrami children hospital. Indian J Pediatr 2006; 73:25–31.

25. World Health Organization. Management of the Young Child with an Acute Respiratory Infection. Geneva: World Health Organization: Program for Control of Acute Respiratory Infections, 1990.

26. Jeong IS, Jeong JS, Choi EO. Nosocomial infection in a newborn intensive care unit (NICU), South Korea. BMC Infectious Diseases, 2006; 6:103.

27. Nanthoo K, Mason P, Gwanzura L. Severe Klebsiella infection as a cause of mortality in neonates in Harare, Zimbabwe: Evidence from postmortem blood cultures. Pediatr Inf Dis J 1993; 12:840–4.

28. Bhutta ZA, Yusuf K. Neonatal sepsis in Karachi, factors determining outcome and mortality. J Trop Pediatr 1997; 43:65–70.

29. Sundaram V, Kumar P, Dutta S. Blood culture confirmed bacterial sepsis in neonates in a North Indian tertiary care center: Changes over the last decade. Jpn J Infect Dis 2009; 62:46–50.

30. Hyde TB, Hilger TM, Reingold A, Farley MM, O'Brien KL, Schuchat A. Trends in incidence and antimicrobial resistance of early-onset sepsis: Population-based surveillance in San Francisco and Atlanta. Pediatrics 2002; 110:690–5.

31. Shaw CK, Shaw P, Thapalial A. Neonatal sepsis bacterial isolates and antibiotic susceptibility patterns at a NICU in a tertiary care hospital in western Nepal: A retrospective analysis. Kathmandu Uni Med J 2007; 5:153–60.

32. Pawa AK, Ramji S, Prakash K, Thirupuram S. Neonatal nosocomial infection: Profile and risk factors. Indian Pediatr 1997; 34:297–02.

33. Zaidi AKM, Thaver SMD, Ali SA, Khan TA. Pathogens associated with sepsis in newborns and young infants in developing countries. Pediatr Infect Dis J 2009; 28:S10–18.

34. Litzow JM, Gill CJ, Mantaring JBV. High frequency of multi-drug-resistant gram-negative rods in 2 neonatal intensive care units in the Philippines. Infect Control Hosp Epidemiol 2009; 30:543–9.

35. Gupta A, Della-Latta PD, Todd B. Outbreak of extended-spectrum beta-lactamase–producing Klebsiella pneumonia in a neonatal intensive care unit linked to artificial nails. Infect Control Hosp Epidemiol 2004; 25:210–15.

36. Artemio GV, Dolores AC, Cuauhtli M. Multiresistant extended-spectrum B-lactamase producing Klebsiella pneumoniae causing An outbreak of nosocomial bloodstream infection. Infect Control Hosp Epidemiol 2001; 22:723–5.

37. Vergnano S, Sharland M, Kazembe P, Mwansambo C, Heath PT. Neonatal sepsis: An international perspective. Arch Dis Child Fetal Neonatal Ed 2005; 90:220–4.

38. Thaver D, Ali SA, Zaidi AKM. Antimicrobial resistance among neonatal pathogens in developing countries. Pediatr Infect Dis J 2009; 28:S19–21.

39. Zaidi AKM, Huskins WC, Thaver D, Bhutta ZA, Abbas Z, Goldmann DA. Hospital-acquired neonatal infections in developing countries. Lancet 2005; 365:1175–88.

40. AlTawfiq JA, Antony A. Antimicrobial resistance of Klebsiella pneumoniae in a Saudi Arabian hospital: Results of a 6-year surveillance study 1998–2003. J Infect Chemother 2007; 13:230–4.

41. Bindayna KM, Jamsheer A, Farid E, Botta GA. Neonatal Sepsis 1991–2001: Prevalent bacterial agents and antimicrobial susceptibilities in Bahrain. Med Princ Pract 2006; 15:131–6.