



Bloodstream Infections in a Neonatal Intensive Care Unit

Yenidoğan Yoğun Bakım Ünitesinde Kan Akımı Enfeksiyonları

Bloodstream Infections in Neonates

Mehmet Şah İpek¹, Erdal Özbeğ²

¹Department of Neonatology, ²Department of Microbiology, Maternity and Children Hospital, Diyarbakir, Turkey

Özet

Amaç: Bir yenidoğan yoğun bakım ünitesindeki kan akımı enfeksiyonlarının dağılımını ve etken organizmaların antimikrobiyal duyarlılığını belirlemek. **Gerçek ve Yöntem:** Türkiye Güneydoğu Anadolu Bölgesindeki Diyarbakir Kadın Doğum ve Çocuk Hastanesi yenidoğan yoğun bakım ünitesinde Mart 2011-Mart 2014 tarihleri arasında kan kültür pozitifliği olan hastane kaynaklı sepsis tanılı yenidoğanlar geriye dönük olarak değerlendirildi. **Bulgular:** 142 yenidoğan bebekte toplam 148 etken izole edildi. En yaygın izole edilen mikroorganizmalar *Klebsiella pneumoniae* (%40.5) ve bir hastane salgını sonucu olarak *Acinetobacter baumannii* (%29.7) idi. İzole edilen *K. pneumoniae* türlerinin %20'si, *A.baumannii* türlerinin ise %93.2'si çoklu-ilaç direnci olan türlerdi. Sepsis-ilişkili mortalite oranı, çoklu-ilaç direnci olan türlerle enfekte olgularda, çoklu-ilaç direnci olmayan türlerle (kandida hariç) enfekte olgulardan daha fazlaydı (%24'e karşı %9.7, p=0.032). **Tartışma:** Ünitimizde, kan akımı enfeksiyonları daha çok gram negatif bakteri kaynaklıydı. Çoklu-ilaç direnci olan türlerin neden olduğu kan akımı enfeksiyonları, daha yüksek sepsis-ilişkili mortalite oranı ile birliktedir.

Anahtar Kelimeler

Hastane Kaynaklı Enfeksiyon; Yenidoğan Yoğun Bakım; Çoklu-İlaç Direnci; Türkiye

Abstract

Aim: To determine the pattern of bloodstream infections (BSIs) and antimicrobial susceptibility of pathogens in a neonatal intensive care unit (NICU). **Material and Method:** Positive hemoculture of neonates diagnosed with nosocomial sepsis from March 2011 to March 2014 in the NICU of Diyarbakir Maternity and Children's Hospital, in the southeastern region of Anatolia, Turkey, were retrospectively reviewed. **Results:** A total of 148 pathogens were isolated in 142 neonates. The most common microorganisms isolated were *Klebsiella pneumoniae* (40.5%) and *Acinetobacter baumannii* (29.7%) which was a result of a hospital outbreak. Multi-drug resistant (MDR) strains accounted for 20.0% of *K. pneumoniae* isolates and 93.2% of *A. baumannii* isolates. The sepsis-attributable mortality rate was higher in cases infected with MDR strains than in cases infected without MDR strains or *Candida* spp (24% vs. 9.7%, p=0.032). **Discussion:** In our unit, BSIs were more often caused by Gram negative bacteria. BSIs caused by MDR strains were associated with a higher rate of sepsis-attributable mortality.

Keywords

Nosocomial Infection; Neonatal Intensive Care; Multi-drug Resistance; Turkey

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Corresponding Author: Mehmet Şah İpek, Maternity and Children Hospital, Urfa Road 7th km, Bağlar, Diyarbakir, Turkey.

T.: +90 4122519125-1215 F.: +90 4123156611 E-Mail: md.msipek@yahoo.com

Introduction

Nosocomial infection is a common complication in hospitalized patients, and is an important cause of morbidity and mortality in neonatal intensive care units (NICUs) [1,2]. The incidence of nosocomial infection varies between 18% and 50% [3-7] and accounts for as much as 40% of neonatal deaths in developing countries [2,5,6]. In a survey of 16 centers, conducted by the Turkish Neonatal Society, it was reported that the incidence of nosocomial sepsis varied from 2.1% to 17%, and sepsis-related mortality was approximately 24% [8].

Bloodstream infections (BSIs) were the single most important type of infection because of their high frequency and potentially life-threatening consequences [3,5,7]. The variety and the antimicrobial sensitivity of the microorganism causing sepsis can vary among NICUs and it can also change over time for the same unit [7-9]. The identification of the microorganisms and their antibiotic susceptibility is essential for determining an empirical antibiotic treatment and the appropriate antibiotic. In this study we have evaluated the distribution rate and antibiotic sensitivity of the pathogenic microorganisms growing in blood cultures in our NICU.

Material and Method

Setting: The NICU at Diyarbakir Maternity and Children's Hospital, at which 20,000 deliveries occur yearly, is one of the largest hospitals in the southeastern region of Anatolia in Turkey. It is supplied with 25 tertiary level, 35 secondary level, and 10 primary level beds. The unit usually receives newborns from the obstetric department. Two neonatologists work during the day (unfortunately there was no sustained neonatologist during the first year of the study period) and one pediatricist works at night. A trained infection control nurse is available on the unit at all times with an average of 1 nurse for 6-7 neonates. Automatic preparation of total parenteral nutrition has also been available as of the year 2012.

Study Design: This retrospective study was performed on data gathered between March 2011 and March 2014. All blood culture positive cases were selected and their records evaluated in terms of sepsis criteria, gestational age, age at onset, gender, birth weight, and microorganism and antimicrobial susceptibilities. Clinical data were analyzed by episodes, which were defined as distinct periods of clinical illness in association with positive blood cultures. Patients who had no infection and/or were not in the incubation period at presentation and who developed blood stream infection 72 hours after hospitalization were eligible for inclusion. Patients who died or were discharged from the NICU within the first 48 hours or who had perinatal or community-acquired infections or recurrent admissions were excluded from the study.

Definitions: BSI was defined as isolation of at least one positive peripheral-blood culture, except for coagulase-negative staphylococcus, for which isolation of two positive blood cultures was required [10]. Sepsis was determined by previous described criteria [9-11]. A C-reactive protein (CRP) value of >1 mg/dl was considered to be significant [10]. Multi-drug resistant (MDR) strains were defined as those resistant to at least 1 agent in ≥ 3 of the following antimicrobial categories: carbapenems (imipenem and meropenem), penicillins (piperacillin, ticarcillin,

and piperacillin/tazobactam), third-generation cephalosporins (ceftazidime and cefotaxime), aminoglycosides (amikacin), and fluorquinolones [12]. Sepsis attributable mortality (SAM) was defined as a patient who expired within 7 days after onset of sepsis, those who died of infectious complications, or clinically progressive deterioration following BSI [12].

Microbiological Methods: Hemoculture is taken under sterile conditions using sterile gloves and cloths. The blood culture system is Bactec 9240 (Becton Dickinson, USA), and the volume of blood taken for each culture is at least 0.5 mL but usually 1.0 mL. When *Bacillus*, *Corynebacterium*, and coagulase negative staphylococcus (CNS) are cultured without clinical findings, contamination is considered to be present [4]. Bacteria identification and antimicrobial susceptibility testing were performed using a BD Phoenix Automated Microbiology System (BD Diagnostic Systems, Sparks, MD) according to the manufacturer's recommendations. The extended-spectrum β -lactamase (ESBL) production was confirmed by the Double-Disc Synergy Test according to Clinical Laboratory Standards Institute (CLSI) 2010 guidelines. Carbapenem resistance was confirmed with a modified Hodge test.

Statistical Analysis: Statistical Package for the Social Sciences (SPSS) for Windows 17.0 program was used for statistical analysis of the results obtained in the study. Demographic properties in the study were assessed by "descriptive" statistical analysis. Chi-square and Fisher's exact chi-square test were used for categorical variables. Mann-Whitney U test was used for continuous variables. $P < 0.05$ was considered statistically significant.

Results

Of 5166 patients admitted to NICU during this study period, 982 were excluded for the reasons described above. Given the overall cohort of 4184 neonates, 246 (5.9%) infants developed clinical signs of sepsis. Sepsis was confirmed by blood culture as BSI in only 142 (67.6%) neonates with a total of 148 episodes. Total length of hospital stay in the NICU was 45,080 days, and the incidence rate of BSI in our NICU was 3.28 case episodes per 1000 hospital days. The distribution of episodes according to year is shown in Figure 1.

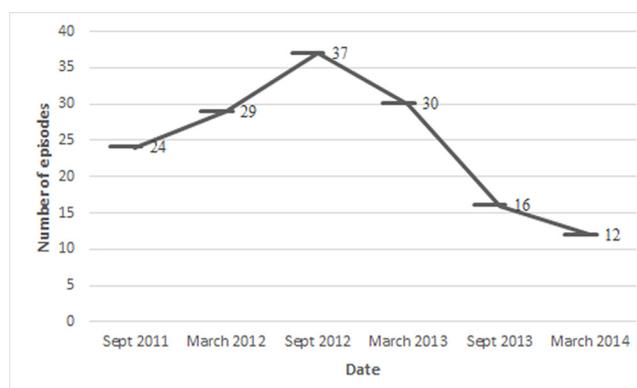


Figure 1. Distribution of episodes in 6-month intervals between March 2011-March 2014

Demographic characteristics of the patients with positive hemoculture are shown in Table 1. BSI rate distribution did not differ among cases with birth weight < 1500 g and higher ($p =$

0.18). According to day of infection onset, there was not a significant difference between the two groups of cases with birth weight < 1500 g or higher ($p = 0.32$). At the beginning of infection, CRP was negative in 51 (34.5%) patients.

Table 1. Baseline and demographic characteristics and outcome of cases (n=148)

Characteristic	No (%)
Birth weight, mean (min-max), g	1693 (520-4400)
Birth weight (<1500 g)	82 (55.4)
Gestational age, mean (min-max), wk	33.0 (24-40)
Age at onset of infection, mean (min-max), d	23 (4-115)
Male	70 (47.3)
Inborn	130 (87.8)
Cesarean delivery	86 (58.1)
Low Apgar score at 5 min (≤ 7)	38 (25.7)
Major congenital anomalies	8 (5.4)
Neurologic disorders (congenital or acquired)	9 (6.1)
Previous cardiopulmonary resuscitation	8 (5.4)
Previous antibiotic exposure (within 1 month)	
Third-generation cephalosporin	28 (18.9)
Carbapenem	13 (8.8)
Invasive mechanical ventilation (within 1 week)	98 (66.2)
Use of total parenteral nutrition	96 (64.9)
Use of central venous catheter (within 1 week)	26 (17.6)
Exchange transfusion	7 (4.7)
Thorax tube	5 (3.4)
Outcome †	
Discharged alive	98 (69.0)
Died in the first week of infection	25 (17.6)

† n=142

Table 2. Pathogens isolated in 148 cases of bloodstream infection

Pathogens	No (%)
Klebsiella pneumoniae	60 (40.5)
Acinetobacter baumannii	44 (29.7)
Candida spp.	18 (12.2)
Escherichia coli	8 (5.4)
Pseudomonas aeruginosa	6 (4.1)
Serratia marcescens	5 (3.4)
Coagulase-negative Staphylococcus	4 (2.7)
Enterobacter spp.	3 (2.0)

Table 3. Antimicrobial susceptibility patterns of Gram negative bacteria

Antimicrobial	Gram negative bacteria (n†/n‡) (%)					
	K. pneumoniae	A. baumannii	E. coli	P. aeruginosa	S. marcescens	Enterobacter
Ampicillin	58/60 (%96.7)	42/43 (%97.8)	6/6 (%100)	4/4 (%100)	1/1 (%100)	3/3 (%100)
Piperacillin	20/31 (%64.5)	4/6 (%66.7)	2/5 (%40.0)	2/5 (%40.0)	0/5 (%0.0)	0/2 (%0.0)
Amikacin	8/36 (%22.2)	39/40 (%97.5)	0/6 (%0.0)	1/2 (%50.0)	0/2 (%0.0)	0/1 (%0.0)
Gentamicin	24/57 (%42.1)	38/44 (%86.4)	4/7 (%57.1)	1/6 (%16.7)	0/3 (%0.0)	0/3 (%0.0)
Ceftriaxone	39/55 (%70.9)	41/42 (%97.6)	6/6 (%100)	1/1 (%100)	1/5 (%20.0)	1/3 (%33.3)
Ceftazidime	36/47 (%76.6)	42/44 (%95.5)	5/7 (%71.4)	3/6 (%50.0)	1/5 (%20.0)	0/2 (%0.0)
Ciprofloxacin	1/26 (%3.8)	37/38 (%97.4)	1/3 (%33.3)	0/2 (%0.0)	0/1 (%0.0)	-
Colistin	5/16 (%31.3)	1/39 (%2.7)	0/2 (%0.0)	1/2 (%50.0)	2/2 (%100)	0/1 (%0.0)
Imipenem	12/40 (%30.0)	40/43 (%93.0)	0/6 (%0.0)	3/5 (%60.0)	0/4 (%0.0)	0/1 (%0.0)

† No of isolates resistant, ‡ No of isolates tested

Of 148 blood cultures, 126 (85%) isolates were Gram negative bacteria (GNB), 18 (12.2%) isolates were Candida, and only 4 (2.7%) isolates were Gram positive bacteria (GPB). The microorganisms that were identified from the blood cultures are shown in Table 2.

Meropenem and amikacin resistance for Klebsiella pneumoniae were found in 30% and 22.2% of the cultures, respectively. K. pneumoniae was found to be highly resistant to ampicillin, piperacillin, and third-generation cephalosporins. ESBL production of K. pneumoniae was found as 37.2%. The majority of Acinetobacter baumannii isolates (93.2%) were MDR. Antibiotic resistance of GNB is shown in Table 3. CNS were found to be sensitive to vancomycin. Because of technical limitations, susceptibility tests were not performed for Candida isolates. An outbreak of A. baumannii was identified in the second half of 2012. Despite all the measures taken, elimination of A. baumannii required six months, probably due to the fact that the unit is large and crowded.

Of 142 neonates, 44 (31%) died. The SAM rate was 17.6%. The SAM rate was marginally nondifferent among cases with birth weight < 1500 g compared to those higher (21.9% vs. 10.6%, $p = 0.052$). But, the SAM rate was higher in cases infected with MDR strains (n=58) than in cases infected without MDR strains or Candida spp (24% vs. 9.7%, $p = 0.032$).

Discussion

As in most previous reports, BSI was the most commonly observed form of nosocomial infection [4-8,13]. In other national studies, the incidence of nosocomial sepsis ranges from 2.1% to 17% [8-10]. In this study, sepsis frequency was 5.9%, and BSI occurred at a rate of 3.28 case episode per 1000 hospital days. However, the frequency of sepsis with positive hemoculture was lower (3.5%). It is reported that at least 25% of clinically diagnosed septic episodes are culture-negative [14]. This may be due to many factors such as concurrent use of antibiotics and suboptimal sample volumes [6]. Our findings did not include overall nosocomial infections. Most cases of BSIs in the NICU are associated with indwelling central vascular catheters [4,6,10,13]. In some studies, nosocomial infection was observed 2-3 fold more frequently when catheterization was used [7,10,15]. In our NICU, catheterization is usually not used except in very low birth weight infants, and this may be a reason for the low incidence observed in sepsis. The median onset of infection from day of admission was 23 days, which is comparable with

other studies [16,17]. It is well known that in addition to gestation age, prolonged hospital stay with a number of therapeutic interventions is associated with nosocomial infection.

In developed countries GPB is the most common cause of nosocomial sepsis in the NICU [18]. However, nosocomial sepsis caused by GNB is more frequent in developing countries [4,6]. Some authors have reported that *K. pneumoniae* account for most infections in developing countries [4,6]. In technologically advanced NICUs, following the adoption of tertiary neonatal care with a high rate of invasive device use, CNS stands out as the main agent of neonatal nosocomial sepsis [7,18]. In national studies, some authors [9-11,15] have reported that the most commonly isolated pathogen from blood cultures of neonates diagnosed with nosocomial sepsis was CNS, followed by *K. pneumoniae*, whereas others [19,20] have reported *K. pneumoniae* as the most common pathogen. In our study, *K. pneumoniae* and *A. Baumannii* were responsible for 40.5% and 29.7% of nosocomial sepsis, respectively. The high rate of *A. Baumannii* was due to an outbreak that occurred during the study period. It is a ubiquitous microorganism implicated in a number of outbreaks in NICUs [21,22].

Gram negative bacteria have a high degree of resistance to commonly used antibiotics [22-24]. This is not just a problem for developing countries [21,22], but also is a growing threat in developed countries [24]. Couto et al. [4] reported a high resistance of *K. pneumoniae* to third-generation cephalosporins (64.1%), whereas Bolat et al. [10] reported lower rates (18.7%-37.5%) from Turkey. Shehab El-Din et al. [23] reported that GNB including *K. pneumoniae*, *Serratia marcescens*, and *A. baumannii* have a higher resistance to third-generation cephalosporins (>85%), amikacin (68.5%), imipenem (29.6%) and ciprofloxacin (38.9%). In a study conducted by Mutlu et al. [11] from Turkey, it was reported that GNB were highly resistant to third-generation cephalosporins (31.5%-37.8%) but had low resistance to amikacin (5.2%) and meropenem (2.9%). In our study, 20% of *K. pneumoniae* isolates was MDR. The majority of *Acinetobacter* isolates were resistant to all antimicrobial agents (>90%) except for colistin (2.7%). Tsai et al. [12] reported that bacteremia caused by MDR GNB accounted for nearly one-fifth of all episodes of GNB bacteremia.

Like distribution of etiological pathogens, their antimicrobial susceptibilities were also different from other studies reported in our country. These differences may be related to heavily contaminated environmental sources, high rates of cross-transmission [2], overcrowding, understaffing, inappropriate or insufficient clinical practices (e.g. absence of permanent intensive care physicians like neonatologists), or the later adoption of appropriate and sophisticated tertiary neonatal care practices [7] in our region, which is the least developed region of Turkey [25]. However, the SAM rate in the present study (17.6%) is in accordance with the national average [8,9,11].

According to the findings outlined above, the empirical antibiotic treatment administered may not always be effective for all microorganisms. Therefore, blood cultures and their results should be obtained at an early time and appropriate antibiotics applied. Because outbreaks are often caused by MDR organisms, complete identification and susceptibilities need to be available as soon as possible. It should be noted that additional

infection control measures and antimicrobial stewardship programs providing instructions urgently need to be developed for our NICU.

There are some limitations of our study. Although our data came from one of the largest NICU centers in the region, the small study size was unable to detect a difference in outcomes and potential risk factors. Molecular epidemiologic analysis of MDR microorganism types could not be performed due to facilities limitations. Given the retrospective nature of this study, data collection may not have included some needed variables, and consequently this may have led to the difficulty in evaluating temporal relationships between events. Finally, the fact that the data was from a single NICU center limits its representativeness for other geographical areas or institutions.

In conclusion, GNB, especially *K. pneumoniae*, were the leading causative agents of nosocomial sepsis in our NICU, and they were resistant to commonly used antibiotics. In view of our findings, it seems mandatory to begin empirical broad-spectrum antibiotics in a neonate suspected with nosocomial sepsis. In response to blood culture results obtained as soon as possible, appropriate and adequate antibiotics should be applied. In the meantime, the strict application of infection control measures, antibiotic stewardship, decreased antibiotic overconsumption, and avoidance of antibiotic under-dosing are valuable in decreasing the resistance rates of MDR GNB.

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Competing interests

The authors declare that they have no competing interests.

References

1. Stoll BJ, Hansen NI, Bell EF, Shankaran S, Laptook AR, Walsh MC, et al. Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. *Pediatrics* 2010;126(3):443-56.
2. Zaidi AK, Huskins WC, Thaver D, Bhutta ZA, Abbas Z, Goldmann DA. Hospital-acquired neonatal infections in developing countries. *Lancet* 2005;365(9465):1175-88.
3. Kawagoe JY, Segre CM, Pereira CR, Cardoso MF, Silva CV, Fukushima JT. Risk factors for nosocomial infections in critically ill newborns: a 5-year prospective cohort study. *Am J Infect Control* 2001;29(2):109-14.
4. Couto RC, Carvalho EA, Pedrosa TM, Pedrosa ER, Neto MC, Biscione FM. A 10-year prospective surveillance of nosocomial infections in neonatal intensive care units. *Am J Infect Control* 2007;35(3):183-9.
5. Dal-Bó K, Silva RM, Sakae TM. Nosocomial infections in a neonatal intensive care unit in South Brazil. *Rev Bras Ter Intensiva* 2012;24(4):381-5.
6. Kishk RM, Mandour MF, Farghaly RM, Ibrahim A, Nemr NA. Pattern of Blood Stream Infections within Neonatal Intensive Care Unit, Suez Canal University Hospital, Ismailia, Egypt. *Int J Microbiol* 2014;2014:276873.
7. Urzedo JE, Levenhagen MM, Pedrosa RS, Abdallah VO, Sabino SS, Brito DV. Nosocomial infections in a neonatal intensive care unit during 16 years: 1997-2012. *Rev Soc Bras Med Trop* 2014;47(3):321-6.
8. Turkish Neonatal Society; Nosocomial Infections Study Group. Nosocomial infections in neonatal units in Turkey: epidemiology, problems, unit policies and opinions of healthcare workers. *Turk J Pediatr* 2010;52(1):50-7.
9. Yalaz M, Cetin H, Akisu M, Aydemir S, Tunger A, Kultursay N. Neonatal nosocomial sepsis in a level-III NICU: evaluation of the causative agents and antimicrobial susceptibilities. *Turk J Pediatr* 2006;48(1):13-8.
10. Bolat F, Uslu S, Bulbul A, Comert S, Can E, Kiray Bas E, et al. Hospital acquired bloodstream infections in neonatal care unit. *Turk Arch Ped* 2011;46:130-6.
11. Mutlu M, Aslan Y, Saygin B, Yilmaz G, Bayramoglu G, Koksali I. Neonatal Sepsis Caused by Gram-negative Bacteria in a Neonatal Intensive Care Unit: A Six Years Analysis. *HK J Paediatr (new series)* 2011;16:253-7.
12. Tsai MH, Chu SM, Hsu JF, Lien R, Huang HR, Chiang MC, et al. Risk factors and outcomes for multidrug-resistant Gram-negative bacteremia in the NICU. *Pediatrics* 2014;133(2):e322-9.
13. Crivaro V, Bogdanović L, Bagattini M, Lula VD, Catania M, Raimondi F, et al. Surveillance of healthcare-associated infections in a neonatal intensive care unit in Italy during 2006-2010. *BMC Infect Dis* 2015;15:152.
14. van der Zwet WC, Kaiser AM, van Elburg RM, Berkhof J, Fetter WP, Parlevliet GA, et al. Nosocomial infections in a Dutch neonatal intensive care unit: surveil-

lance study with definitions for infection specifically adapted for neonates. *J Hosp Infect* 2005;61(4):300-11.

15. Yapicioglu H, Ozcan K, Sertdemir Y, Mutlu B, Satar M, Narli N, et al. Healthcare-associated infections in a neonatal intensive care unit in Turkey in 2008: incidence and risk factors, a prospective study. *J Trop Pediatr* 2011;57(3):157-64.

16. Aziz K, McMillan DD, Andrews W, Pendray M, Qiu Z, Karuri S, et al. Canadian Neonatal Network Variations in rate of nosocomial infection among Canadian neonatal intensive care units may be practice-related. *BMC Pediatr* 2005;5:22.

17. Hacimustafaoğlu M, Çelebi S, Köksal N, Kavurt S, Özkan H, Çetinkaya M. Yenidoğan ve Yenidoğan Yoğun Bakım Servisinde Hastane Enfeksiyonları. *Türk Ped Arş* 2011;46:302-7.

18. 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;110(2 Pt1):285-91.

19. Ünal S, Çelik FC, Tezer H. Bir Yenidoğan Yoğun Bakım Ünitesinde Nozokomiyal Enfeksiyonlar ve Klebsiella Sorunu. *Türkiye Çocuk Hast Derg* 2010;4(3):133-9.

20. Parlak E, Kahveci H, Köksal Alay H. Yenidoğan Yoğun Bakım Ünitesindeki Hastane Enfeksiyonları. *Güncel Pediatri* 2014;1:1-8.

21. Hosoglu S, Hascuhadar M, Yasar E, Uslu S, Aldudak B. Control of an Acinetobacter [corrected] baumannii outbreak in a neonatal ICU without suspension of service: a devastating outbreak in Diyarbakir, Turkey. *Infection* 2012;40(1):11-8.

22. Berezin EN, Solórzano F; Latin America Working Group on Bacterial Resistance. Gram-negative infections in pediatric and neonatal intensive care units of Latin America. *J Infect Dev Ctries* 2014;8(8):942-53.

23. Shehab El-Din EM, El-Sokkary MM, Bassiouny MR, Hassan R. Epidemiology of Neonatal Sepsis and Implicated Pathogens: A Study from Egypt. *Biomed Res Int* 2015;2015:509484.

24. Souli M, Galani I, Giamarellou H. Emergence of extensively drug-resistant and pandrug-resistant Gram-negative bacilli in Europe. *Euro Surveill* 2008;13(47).

25. Ünal C. İnsani Gelişmişlik Endeksine Göre Türkiye'nin Bölgesel Farklılıkları. *Coğrafi Bilimler Dergisi* 2008;6:89-113.

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