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Retrospective Evaluation of Vancomycin-resistant Enterococci Outbreak in Neonatal Intensive Care Unit

Yenidoğan Yoğun Bakım Ünitesinde Vankomisine Dirençli Enterokok Salgınının Retrospektif Olarak İrdelenmesi

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Abstract

Introduction: Vancomycin-resistance in enterococci (VRE) poses a major threat in hospitals. It is well known that patients in the neonatal intensive care unit (NICU) is especially at risk of nosocomial VRE acquisition. In this study, it was aimed to present the VRE outbreak analysis identified in NICU.
Materials and Methods: Patients with VRE colonization and infection were included in the study between 17.10.2016-30.03.2017 in NICU.
Results: There are a total of 30 beds in the NICU, including five beds in the level 1 ICU, eight beds in the level 2 ICU and 17 beds in the level 3 ICU. Newborns in the NICU are hospitalised in the same ICU (room) in a mixed form. Enterococci were detected in blood culture samples of four patients in the NICU. Three of these cases were VRE and the other was VSE (vancomycin-sensitive enterococci). The most important problem identified in the NICU was the inability to use the interior architecture effectively. In addition, inadequate nurse both in number and level of education and lack of night observations were identified as other problems.
Conclusion: As a result, the outbreak in NICU was controlled thanks to educated nurse support, frequent visits and change in interior architecture.
Keywords: Nurse, outbreak, infrastructure, investigation, education

Öz

Giriş: Vankomisin dirençli enterokok (VRE), hastanelerde büyük bir tehdit oluşturmaktadır. Yenidoğan yoğun bakım (YB) ünitesindeki (YYBÜ) hastaların özellikle nozokomiyal VRE için risk altında olduğu iyi bilinmektedir. Bu çalışmada YYBÜ'de tespit edilen VRE salgınının analizinin sunulması amaçlandı.
Gereç ve Yöntem: Çalışmaya 17.10.2016-30.03.2017 tarihleri arasında YYBÜ'de yatan, VRE kolonizasyonu ve enfeksiyonu olan hastalar dahil edildi.
Bulgular: YYBÜ'de birinci basamak YB'de beş yatak, ikinci basamak YB'de sekiz yatak ve üçüncü basamak YB'de 17 yatak olmak üzere toplamda 30 yatak mevcuttur. Yoğun bakımdaki hastalar karışık şekilde aynı fiziki ortamda yatmaktaydı Yoğun bakımda yatan dört hastanın kan kültürü örneğinde enterokok üremesi oldu. Bu olguların üçü VRE biri ise VSE (vankomisin duyarlı enterokok) idi. YYBÜ'de tespit edilen en önemli sorun iç mimari yapının etkin kullanılamaması idi. Ayrıca hemşirelerin hem sayıca hem de eğitim seviyesindeki yetersizliği ve gece gözleminin olmaması diğer sorunlar olarak tespit edildi.
Sonuç: Sonuç olarak YYBÜ'deki salgın; eğitimli hemşire desteği, sık ziyaret ve iç mimarideki değişiklik ile kontrol altına alındı.
Anahtar Kelimler: Hemşire, salgın, altyapı, araştırma, eğitim

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Introduction

Enterococci are microorganisms with low virulence. They are resistant to heat, desiccation, and some antiseptics, which allows them to survive for long periods on dry surfaces. They are resistant to various antibiotics and are capable of developing new resistance[1]. To date, approximately 35 different species of enterococci have been identified. The most significant of these are *Enterococcus faecalis* and *Enterococcus faecium*, which are responsible for >80% of all enterococci infections[2]. Vancomycin resistance in enterococci (VRE) is an important issue. VRE was first reported in 1986 in England and France and subsequently became one of the major global nosocomial pathogens[3].

Prolonged hospital stays result in intestinal colonization by VRE, thereby making the patient a VRE reservoir. Patient-to-patient transmission of VRE occurs via the hands of healthcare personnel, contaminated surfaces, and contaminated medical instruments. VRE colonization increases the rate of infection 5 to 10 fold[4,5].

According to 2016 data from the Turkish National Hospital Infections Surveillance Network, the overall VRE weighted general average in Turkey was 13.33% (50^{th}-75^{th} percentile) and the VRE weighted general average in the ICUs of university hospitals was 13.76% (50^{th}-75^{th} percentile)[6].

Due to their immature immunity, neonates are a defenseless population. In newborns, infectious diseases usually occur as a result of contact with healthcare personnel, parents, other patients, medical devices, and the hospital environment. This contact may lead to nosocomial outbreaks as well as colonization or infection with severe morbidity and mortality[7]. The aim of this study was to present an analysis of a VRE outbreak detected in a neonatal intensive care unit (NICU) and the precautions taken.

Materials and Methods

The study included patients with VRE colonization and infection who were admitted to the NICU between October 17, 2016 and March 30, 2017 due to preterm birth, neonatal respiratory distress, low birth weight, neonatal jaundice, and neonatal sepsis. Preterm birth was defined as birth before reaching a gestational age of 38 weeks (<37 weeks + 6 days)[8]. Neonatal respiratory distress was defined as acute respiratory failure caused by alveolar epithelial cell injury, acute inflammation, and protein-rich pulmonary edema due to pulmonary or non-pulmonary inflammatory causes[9]. Low birth weight was live birth weight less than 2500 g[10]. Neonatal jaundice was defined as a bilirubin value over 6 mg/dl in the neonatal period[11]. Neonatal sepsis was defined as bacteremia and associated systemic findings occurring in the first month of life[12].

The study design was descriptive and retrospective. Approval for the study was obtained from an Local Ethics Committee (date: 02.28.2018, case number: 03).

Perirectal swab samples obtained for surveillance culture were sent to the Medical Microbiology Laboratory. As recommended by EUCAST the samples were inoculated in 5% sheep blood agar and incubated at 35±1 °C for 24 hours[5]. Colonies with morphologic and Gram-staining characteristics consistent with enterococci were passaged onto Mueller-Hinton agar and a vancomycin disc (5 µg) was applied to the inoculated agar. Isolates with zones of inhibition having sharp borders and a diameter >=12 mm were considered susceptible; for isolates showing indistinct zone borders, colonies growing within the zone of inhibition, and zone diameter <12 mm, vancomycin resistance was confirmed using BD Phoenix 100 (Becton Dickinson Diagnostic Systems, Sparks) automated identification and antibiotic sensitivity system.

By decision of the hospital Infection Control Committee (ICC), rectal swab cultures for VRE were obtained weekly in the NICU, and rectal swab cultures were obtained routinely from all patients upon NICU admission.

Statistical Analysis

The age and gender of the patients included in the study, type of sample showing growth or colonization (blood, rectal swab, etc.), date of NICU admission, diagnosis, date of positive culture, and the antibiotic therapy administered were recorded from the patients' medical records. In addition, physical conditions and operations were analyzed based on the NICU floor plan. The NICU was closely and frequently monitored. The obtained data were recorded. Statistical analysis of the study data was done using SPSS v.17.0 software package (SPSS Inc, Chicago, Illinois, USA). Categorical data were summarized as numbers and percentages.

Results

Our hospital was founded in 1997 and has been providing service in its new premises since 2013. Bed capacity is 595, including the 160 beds in the ICU. The NICU is equipped with five beds in level 1 care, eight beds in level 2 care, and 17 beds in level 3 care, for a total of 30 NICU beds. After assessing general condition and establishing an indication for level 1, 2, or 3 inpatient care, patients were admitted wherever there was a vacant bed. The NICU was staffed by a neonatologist, 4-5 resident physicians during the day (rotating every three months), and two resident physicians on night duty. There were 28 nurses, one acting as the head nurse, and an equal number of nurses were on duty

day and night. Nurse-to-patient ratios were 1:3-4 at level 3, 1:4 at level 2, and 1:5-6 at level 1 ICU. Housekeeping staff included three healthcare workers between the hours of 8 am and 4 pm, two between 4 pm and midnight, and one between midnight and 8 am.

VRE was identified in the blood culture and rectal swab of one patient on November 3, 2016; this patient was considered to be an index case and was isolated. The following day, VRE was identified in the blood culture and rectal swab of another patient (case 2), and an emergency meeting was held on November 4, 2016 with the ICC and the NICU head physician and nurse. The patients with VRE-positive rectal swab (two infected, six colonized patients), staff, and medical tools and equipment were cohorted. The physical environment was thoroughly cleaned twice using chlorine tablets diluted 1/100 (1000 ppm). However, on November 15, 2016, VRE was identified in venous blood and catheter cultures of a third patient (three infected, 15 colonized patients). The characteristics of the patients are presented in Table 1. The diagnosis of catheter-related bloodstream infection prompted an emergency meeting of the ICC. It was decided to stop new NICU admissions until the outbreak was controlled. During that period, a point-prevalence study was conducted in the NICU to evaluate antibiotic use. The rate of antibiotic use was calculated as 61%. Blood culture antibiogram results of the patients are listed in Table 2.

One of the important findings was educational disparities among the nurses. An analysis of the nurses' education levels showed that 67.9% (n=19) were high school graduates and 32.1% (n=9) were university graduates. By ICC recommendation, this ratio was adjusted by increasing the total number of nurses to 34 [17 high school graduates (50%) and 17 university graduates (50%)].

Furthermore, ICC frequently visited and performed observations in the NICU in order to inform all personnel about VRE infection control and protection measures. Neonatal intensive care unit staff compliance with hand hygiene was also investigated and determined to be 60.2% in 2015, 85.6% in 2016, and 89.8% in 2017. Changes implemented in the NICU in line with the decisions are summarized in Table 3.

Risk factors identified in patients with VRE included use of multiple antibiotics (cephalosporin, penicillin, etc.), urinary or venous catheterization, and admission to the ICU (Table 1).

After implementing these changes and precautions, no new infections were detected but the number of colonized patients increased. In the second outbreak, *E. faecalis* was isolated in a blood culture from a patient identified as the index case. During this period, we increased the frequency of training and inspections, which resulted in a decline in the number of colonized patients. For the following six months, no new cases were identified. The four cases identified during the outbreak were not patients transferred from other centers. The first case was initially colonized and later infected. Findings of the colonized patients and index cases between January 2016 and April 2017 are presented in Figure 1. One of the main problems identified was the ineffective layout of the NICU. Therefore, some changes were made in the organization of the NICU.

Table 1. Characteristics of the patients

	Gender	Diagnosis	Admitting diagnosis	Culture isolate	Final outcome
Patient 1*, †, ‡	Male	Bloodstream infection	Fever	*E. faecium*	Death
Patient 2*, †, ‡	Male	Bloodstream infection	Neonatal respiratory failure	*E. faecium*	Survived
Patient 3*, †, ‡, §	Male	Bloodstream infection	Preterm birth Neonatal sepsis	*E. faecium*	Survived
Patient 4*, †, ‡	Female	Bloodstream infection	Neonatal respiratory failure	*E. faecalis*	Survived

Patient risk factors: *: Central venous catheterization, †: Admission to intensive care unit, ‡: Multiple antibiotic use, §: Urinary catheterization

Table 2. Blood culture antibiotic susceptibility results

	Patient 1 *E. faecium*	Patient 2 *E. faecium*	Patient 3 *E. faecium*	Patient 4 *E. faecalis*
Ampicillin	Resistant	Resistant	Resistant	-
Gentamicin	Resistant	Resistant	Resistant	-
Linezolid	**Sensitive**	**Sensitive**	**Sensitive**	**Sensitive**
Nitrofurantoin	Resistant	Resistant	Resistant	Resistant
Quinupristin-dalfopristin	**Sensitive**	**Sensitive**	**Sensitive**	**-**
Streptomycin	Resistant	Resistant	Resistant	-
Teicoplanin	Resistant	Resistant	Resistant	Resistant
Vancomycin	**Resistant**	**Resistant**	**Resistant**	**Sensitive**

Table 3. Changes made in the neonatal intensive care unit

Separate admissions for patients requiring level 1, 2, and 3 care in the NICU
Increased number of educated nurses
Shelf system installed in small store rooms
Recording of routine cleaning
All cleaned and disinfected supplies, equipment, and devices were cleaned again and moved to patient care and treatment areas before use
A washing machine and dryer were installed in the unit
Provision of single-use disposable medical supplies
Use of sterile distilled water in incubator humidifiers and infant care
Passage to pediatric intensive care was closed

NICU: Neonatal intensive care unit

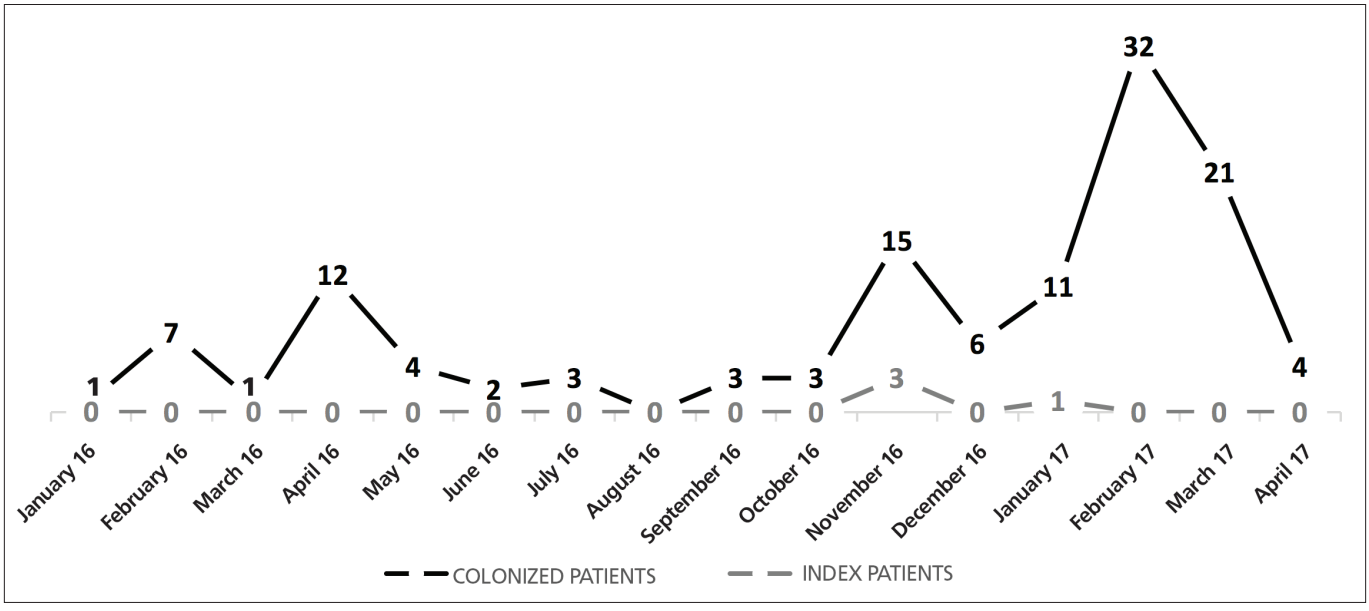


Figure 1. The distribution of vancomycin-resistance in enterococci cases by month

Diagrams showing the old and new NICU floor plans are shown in Figures 2A and 2B. The pre-outbreak VRE infection rate was calculated to be 0 per 1000 patient days in July-September 2016, 1.23 in October-December 2016, 0.44 in January-March 2017, and 0 in April-June 2017.

Discussion

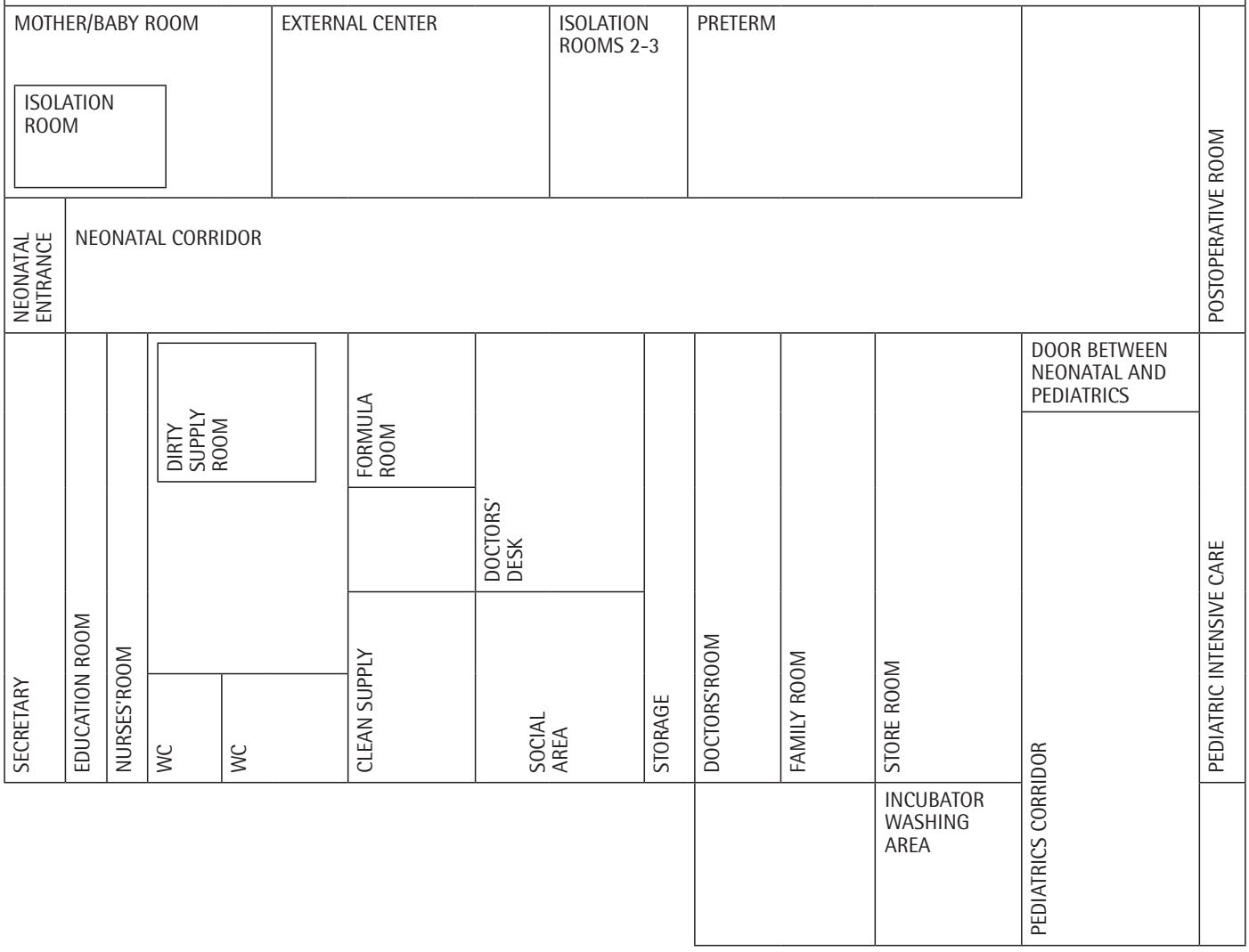
Gram-positive microorganisms such as methicillin-resistant *Staphylococcus aureus* and VRE cause severe nosocomial infections in the NICU and are being isolated with increasing frequency[13]. Enterococci may colonize the mouth, bile ducts, or genital and urinary systems, and is a component of the normal gastrointestinal flora. Although enterococci normally have low capacity to develop resistance, prolonged hospitalization, antibiotic use, and immunosuppression may lead to resistance[1,14,15].

Antibiotic resistance in enterococci is an important problem. Resistance to glycopeptide in particular has made the treatment of enterococcus infections difficult[16]. In this analysis of a NICU outbreak, VRE was found in the blood cultures of three patients and VSE was found in one; rectal swab samples also revealed cases of VRE colonization.

Penicillin and aminoglycoside antibiotic groups are also used against enterococci. However, high-level gentamicin resistance (HLGR) and high-level streptomycin resistance (HLSR) must also be considered. In a study by El-Kersh et al.[17], HLGR and HLSR were detected in enterococci at rates of 25% and 11%, respectively. In a study by Ertürk et al.[18], these rates were found to be 25% and 50%, respectively. In yet another study, 67.9% of enterococci showed HLGR and 67.9% showed HLSR[19]. In the present study, three patients exhibited both gentamicin and streptomycin resistance, but one was not analyzed for aminoglycoside sensitivity.

Risk factors for enterococcus-related bacteremia in newborns include extended hospital stays and the associated prolonged use of the 3rd generation cephalosporin and/or vancomycin,

Figure 2A. Former floor plan of the neonatal intensive care unit

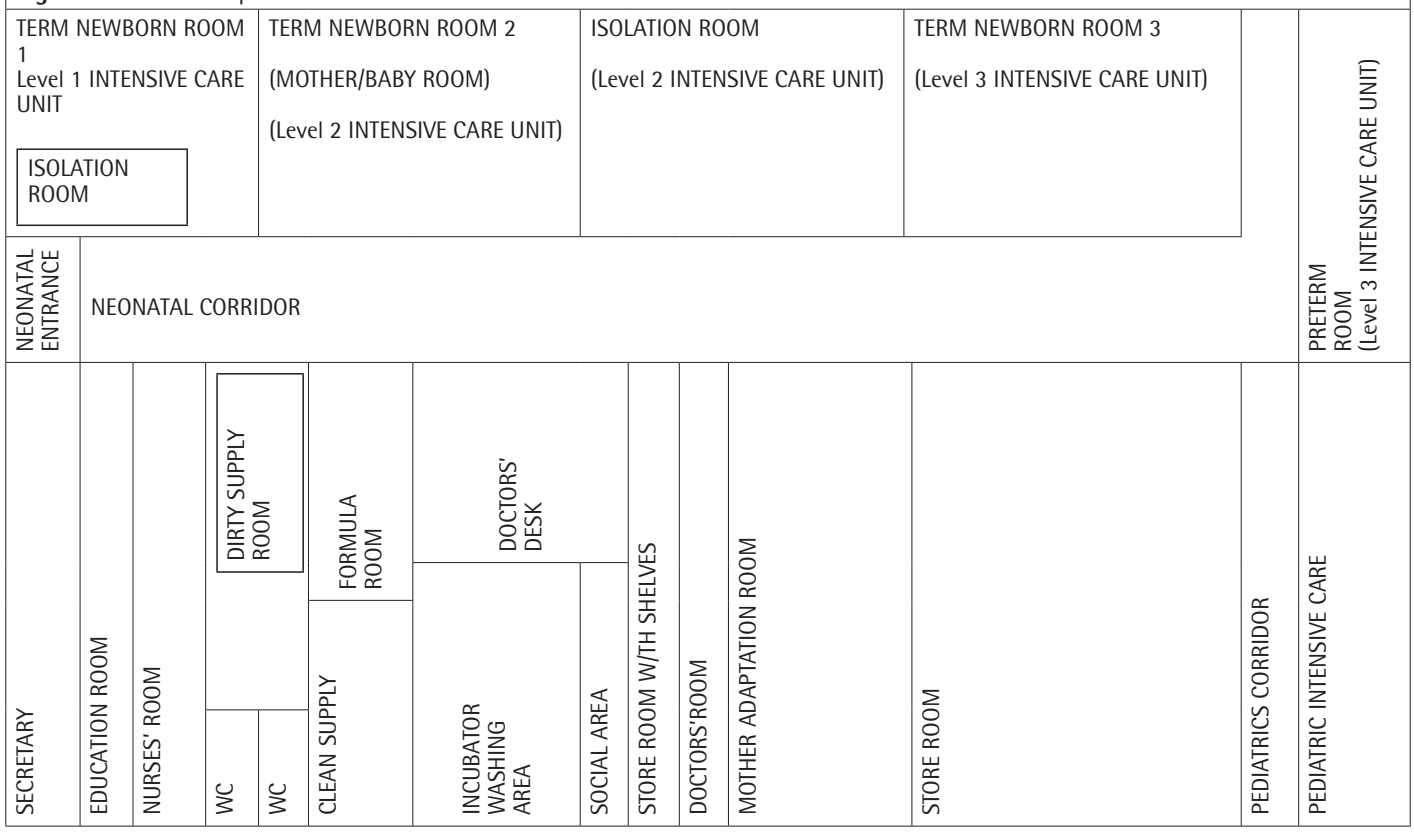


surgical interventions, intrahospital or interhospital transfers, enteral nutrition, urinary and central venous catheterization, and necrotizing enterocolitis[20,21]. Hospital outbreaks occur more frequently in the NICU, pediatric ICU, and hematology/oncology wards[22]. The present study analysed a VRE outbreak in the NICU.

Enterococci are responsible for approximately 10% of neonatal sepsis and bacteremia, and this figure is steadily increasing. This is thought to result from increased survival in preterm neonates and dissemination within the hospital. For this reason, all patients are screened for VRE at the time of admission. Cases of VRE are reported by the microbiology department to the ICC. The ICC takes measures such as patient monitoring, isolation, cohorting, environmental monitoring, disinfection, sterilization, personal protective equipment, hand hygiene, healthcare personnel training and monitoring, antibiotic changes, inspection of equipment and protective- and care-related materials, surveillance, and reducing workloads[23,24]. Similar actions were used in our hospital to control the outbreak and minimize the number of colonized patients.

The hands of hospital workers are important in the dissemination of nosocomial infections, and attention to hand hygiene is therefore crucial in preventing hospital outbreaks[25]. Studies have shown that increased hand hygiene compliance may decrease hospital infections by about 30-50%. Koşucu et al.[26] reported 58% adherence to hand hygiene among health care personnel in their study. In another study conducted in Switzerland, a 3-year monitoring of adherence to hand hygiene resulted in an increase in adherence from 48% to 66% ($p<0.001$) [27]. The rate of adherence to hand hygiene in our hospital increased between assessments conducted before and after the NICU outbreak (from 60.2% in 2015 to 85.6% in 2016 and 89.8% in 2017). These hand hygiene compliance rates are much higher than the figures reported in the literature. This may be attributed to increased training frequency, conducting bedside practice, and a 100% participation in educational activities.

Figure 2B. New floor plan of the neonatal intensive care unit



The recurrence of VRE cases an outbreak despite the high rate of hand hygiene adherence may be related to the temporary lack of hand hygiene monitoring for night shift workers and reduced adherence to hand hygiene and isolation in the absence of observers.

It is important to employ qualified nurses in ICUs to ensure higher quality healthcare service[28]. Needleman et al.[29] determined that better educated and qualified nurses caring for the same number of patients resulted in reduced hospital stays, preventable deaths, adverse events, and costs. In other studies, higher nurse education level was associated with greater job satisfaction and higher morale[30]. Fesci et al.[31] reported that a low nurse-patient ratio resulted in nurses having difficulty fulfilling their duties, even if they are knowledgeable and experienced. Infection rates in our NICU were reduced after improving the nurses' education level and reducing their workload.

Limitations of our study are that the similarity of the four VRE cases was not investigated via molecular methods, colonized patients were not evaluated by antibiotic susceptibility tests, and environmental cultures and personnel colonization were not assessed during the outbreak.

Conclusion

In conclusion, proper isolation measures should be taken for colonized patients, and patients at-risk should be discharged when their treatment is complete. Unnecessary antibiotic use and unnecessarily prolonged hospital stays should be avoided. Surveillance and regular training provided by the ICC will help reduce rates of nosocomial infection and minimize the likelihood of outbreaks.

Ethics

Ethics Committee Approval: Approval for the study was obtained from Local Ethics Committee (date: 02.28.2018, case number: 03).

Informed Consent: Since this was a retrospective outbreak analysis informed consent was not received from patients.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.Y., S.A.,Concept: S.N., S.A., Design: S.N., Ş.İ., Data Collection or Processing: S.N., Ş.İ., S.Y., Analysis or Interpretation: S.N., Literature Search: S.N., A.R.Ş., Writing: S.N., Ş.İ.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. McGeer AJ, Low DE. Vancomycin-resistant enterococci. Semin Respir Infect. 2000;15:314-26.
2. Çelik Ü, Alhan E. A Difficult Pathogen in Pediatric Infections: Enterococcus. J Pediatr Inf. 2008;2:58-66.
3. Lee WG, Ahn SH, Jung MK, Jin HY, Park IJ. Characterization of a vancomycin-resistant *Enterococcus faecium* outbreak caused by 2 genetically different clones at a neonatal Intensive Care Unit. Ann Lab Med. 2012;32:82-6.
4. Huskins WC, Huckabee CM, O'Grady NP, Murray P, Kopetskie H, Zimmer L, Walker ME, Sinkowitz-Cochran RL, Jernigan JA, Samore M, Wallace D, Goldmann DA; STAR*ICU Trial Investigators. Intervention to reduce transmission of resistant bacteria in intensive care. N Engl J Med. 2011;364:1407-18.
5. Kara A, Devrim İ, Bayram N, Katipoğlu N, Kıran E, Oruç Y, Demiray N, Apa H, Gülfidan G. Risk of vancomycin-resistant enterococci bloodstream infection among patients colonized with vancomycin-resistant enterococci. Braz J Infect Dis. 2015;19:58-61.
6. T.C. Sağlık Bakanlığı Türkiye Halk Sağlığı Kurumu Mikrobiyoloji Referans Laboratuvarları Daire Başkanlığı. Last accessed date: 26.07.2018. Available from: https://www.researchgate.net/publication/322854736_ULUSAL_HASTANE_ENFEKSIYONLARI_SURVEYANS_AGI_OZET_RAPORU_2016
7. Stone SP, Cooper BS, Kibbler CC, Cookson BD, Roberts JA, Medley GF, Duckworth G, Lai R, Ebrahim S, Brown EM, Wiffen PJ, Davey PG. The ORION statement: guidelines for transparent reporting of outbreak reports and intervention studies of nosocomial infection. J Antimicrob Chemother. 2007;59:833-40.
8. Neyzi O. Pediatri. 3. Baskı. Nobel Tıp Yayıncılık. 2002;326-40.
9. Bozkurt G. Care of Newborn with Acute Respiratory Distress Syndrome. Journal of the Turkish Society of Critical Care Nurse. 2009;13:19-23.
10. Singh G, Chouhan C, Sidhu MK. Maternal Factors for Low Birth Weight Babies. Med J Armed Forces India. 2009;65:10-2.
11. Hannam S, McDonnell M, Rennie JM. Investigation of prolonged neonatal jaundice. Acta Paediatr. 2000;89:694-7.
12. Stoll BJ. Infections of The Neonatal Infant, Nelson Textbook of Pediatrics. In: Behrman RE, Kleigman RM, Jenson H. WB Saunders Company. 17th ed. Philadelphia, 2004:623-40.
13. Stryjewski ME, Corey GR. New treatments for methicillin- resistant *Staphylococcus aureus*. Curr Opin Crit Care. 2009;15:403-12.
14. Çelik C, Uysal EB, Gözel MG, Bakıcı MZ, Elaldı N. Antimicrobial Resistance Patterns of *Enterococcus faecalis* and *Enterococcus faecium* Bacteria Isolated from Bloodstream Infections. Flora. 2013;18:83-9.
15. Yüce A, Karaman M, Gülay Z, Yulug N. Fecal carriage of vancomycin resistant enterococci in newborn. ANKEM Derg. 1999;13:7-11.
16. Cilo BD, Ağca H, Efe K, Sınırtaş M, Çelebi S, Özkan H, Köksal N, Hacımustafaoğlu M, Özakın C. Investigation of vancomycin resistant *Enterococcus faecium* outbreak in neonatal intensive care unit. Int J Clin Exp Med. 2014;7:5342-7.
17. El-Kersh TA, Marie MA, Al-Sheikh YA, Al-Agamy MH, Al Bloushy AA. Prevalence and risk factors of early fecal carriage of *Enterococcus faecalis* and *Staphylococcus* spp. and their antimicrobial resistant patterns among healthy neonates born in a hospital setting in central Saudi Arabia. Saudi Med J. 2016;37:280-7.
18. Ertürk A, Çopur C, Koksal E, Koksal Z, Ozyurt S. Microorganisms Isolated from Various Clinical Samples and their Antibiotic Susceptibilities in Intensive Care Unit Patients. ANKEM Derg. 2012;26:1-9.
19. Ergül AB, Işık H, Altıntop YA, Torun YA. A retrospective evaluation of blood cultures in a pediatric intensive care unit: A three year evaluation. Turk Pediatri Ars. 2017;52:154-61.
20. Gordts B, Van Landuyt H, Ieven M, Vandamme P, Goossens H. Vancomycin-resistant enterococci colonizing the intestinal tracts of hospitalized patients. J Clin Microbiol. 1995;33:2842-6.
21. Kaufman D, Fairchild KD. Clinical microbiology of bacterial and fungal sepsis in very low birth weight infants. Clin Microbiol Rev. 2004;17:638-80.
22. Nolan SM, Gerber JS, Zaoutis T, Prasad P, Rettig S, Gross K, McGowan KL, Reilly AF, Coffin SE. Outbreak of vancomycin-resistant enterococcus colonization among pediatric oncology patients. Infect Control Hosp Epidemiol. 2009;30:338-45.
23. Murray BE. Vancomycin-resistant enterococcal infections. N Engl J Med. 2000;342:710-21.
24. Ulrich N, Vonberg RP, Gastmeier P. Outbreaks caused by vancomycin-resistant *Enterococcus faecium* in hematology and oncology departments: A systematic review. Heliyon. 2017;3:e00473.
25. World Health Organization (WHO). Last accessed date: 29.05.2018. Available from: http://apps.who.int/medicinedocs/documents/s16320e/s16320e.pdf
26. Koşucu SN, Göktaş SB, Yıldız T. Hand hygiene compliance rate of health professionals. MÜSBED. 2015;5:105-8.
27. Pittet D, Hugonnet S, Harbarth S, Mourouga P, Sauvan V, Touveneau S, Perneger TV. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. Infection Control Programme. Lancet. 2000;356:1307-12.
28. Ulusoy H. The Importance of Safe Staffing. Atatürk Üniversitesi Hemşirelik Yüksekokulu Dergisi. 2008;11:106-12.
29. Needleman J, Buerhaus PI, Stewart M, Zelevinsky K, Mattke S. Nurse staffing in hospitals: is there a business case for quality? Health Aff (Millwood) 2006;25:204-11.
30. Palaz N, Gündüz VC, Solmaz ÜŞ, Doğanay G. Time Divided Into Intensive Care Unit Nursing Services. Journal of the Turkish Society of Critical Care Nurse. 2011;15:9-15.
31. Fesci H, Doğan N, Pınar G. Nurses Working in Medical Clinics in Patients Care were Faced Difficulties and Their Suggestions for Solution. Journal of Anatolia Nursing and Health Sciences. 2008;11:40-50.