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AN EVALUATION OF RETROSPECTIVE RESULTS DETECTED IN THE HOSPITAL INFECTION RESEARCH LABORATORY

HASTANE ENFEKSİYONU ARAŞTIRMA LABORATUVARINDA SAPTANAN RETROSPEKTİF SONUÇLARIN DEĞERLENDİRİLMESİ

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ABSTRACT

Objective: Hospitals are a potential source of infection risk during healthcare delivery. Since vancomycin-resistant enterococci (VRE) and carbapenemase producing Gram-negative rods cause persistent colonization and multi-drug resistant bacterial infections, they are important in nosocomial infections. In this study, we aimed to retrospectively evaluate rectal swab samples of patients hospitalized in the clinics in terms of VRE and carbapenem-resistant (CR) Gram-negative rods as nosocomial infection agents between 1st January 2020 and 31st December 2020.

Materials and Methods: Standard clinical laboratory methods were used to isolate and identify CR Gram-negative rods and VRE from rectal swab samples of hospitalized patients sent to our Hospital Infection Research Laboratory.

Results: There was growth in 777 (28.9%) of 2688 samples examined. Of the bacteria that grew, 627 (80.7%) were defined as VRE, and 150 (19.3%) as Gram-negative rods resistant to carbapenem. Seventy-five of these were defined as CR *K. pneumoniae*: 7 as CR K. oxytoca: 26 as CR *Enterobacter* species: 2 as CR *E. coli*: and 40 as CR *Acinetobacter* species. Vancomycin-resistant enterococci were detected most frequently in the internal medicine ward (56.3% - 353/627) and pediatric intensive care-neonatal ward (37.6% - 236/627). In pediatric services, 146 of total 296 bacteria isolated were identified as VRE.

Conclusion: With the surveillance studies carried out in the control of hospital infections, each health institution determines the microorganisms that make up its own hospital flora, their resistance status and their distribution. It is thought that the data we obtain will contribute to the infection control processes of the hospitals.

Keywords: Nosocomial infection, vancomycin-resistant enterococci, carbapenem-resistant bacteria, infection control measures

ÖZET

Amaç: Hastaneler, sağlık hizmeti sunumu sırasında potansiyel enfeksiyon riski kaynağıdırlar. Vankomisine dirençli enterokoklar (VRE) ve karbapenemaz üreten Gram-negatif çomaklar, kalıcı kolonizasyona ve çok ilaca dirençli bakteriyel enfeksiyonlara neden olduğundan hastane enfeksiyonlarında önemlidirler. Bu çalışmada, 1 Ocak 2020 / 31 Aralık 2020 tarihleri arasında kliniklerde yatan hastaların rektal sürüntü örneklerinin hastane enfeksiyonu etkeni olan VRE ve karbapenem-dirençli (KD) Gram-negatif çomaklar açısından retrospektif olarak değerlendirmesi amaçlanmıştır.

Gereç ve Yöntem: Hastanede yatan hastaların Hastane enfeksiyon Araştırma Laboratuvarı'na gönderilen rektal sürüntü örneklerinden KD Gram-negatif çomaklar ve VRE'yi izole etmek ve tanımlamak için standart klinik laboratuvar yöntemleri kullanılmıştır.

Bulgular: İncelenen 2688 örneğin 777'sinde (%28,9) üreme olmuştur. Üreyen bakterilerin 627'si (%80,7) VRE ve 150'si (%19,3) KD Gram-negatif çomaklar olarak tanımlanmıştır. Bunlardan 75'i KD *K. pneumonia*; 7'si KD *K. oxytoca*; 26'sı KD *Enterobacter* türleri; 2'si KD *E. coli*; ve 40 suş KD *Acinetobacter* türü olarak belirlenmiştir. Vankomisine dirençli enterokoklar en sıklıkla dahiliye servisinde (%56,3 - 353/627) ve pediatrik yoğun bakım-yenidoğan servisinde (%37,6 - 236/627) tespit edilmiştir. Pediatri servislerinde toplam 296 bakterinin 146'sı VRE olarak tanımlanmıştır.

Sonuç: Hastane enfeksiyonlarının kontrolünde yapılan sürveyans çalışmaları ile her sağlık kuruluşu kendi hastane florasını oluşturan mikroorganizmaları, direnç durumlarını ve dağılımlarını belirlemektedir. Elde edilen verilerin hastanelerin enfeksiyon kontrol süreçlerinde katkı sağlayacağı düşünülmektedir.

Anahtar Kelimeler: Hastane enfeksiyonu, vankomisine dirençli enterokoklar, karbapeneme dirençli bakteriler, enfeksiyon kontrol önlemleri

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INTRODUCTION

Nosocomial infections (NI) are a significant health problem that is now on our agenda with the developments in medicine, moreover it is a problem that concerns the whole world (1). Surveillance studies were initiated in hospitals in developed countries in the 1960s. In the United States of America (USA) in 1987, a series of definitions were introduced by the Infection Control and Prevention Centers (CDC) which were to be applied in hospitals participating in the National Nosocomial Infection Surveillance (NNIS) to determine the presence of nosocomial infection (NI). The implementation of the detected infection identification has also started. These definitions were used later all over the world (2).

The emergence of this problem in our country occurred in the 1990s. In 2005, it became mandatory to establish infection control committees in inpatient institutions (3). Between 450,000 and 700,000 patients experience at least one NI during their hospital stay. Therefore, monitoring and surveillance of NI are considered a very important activity for prevention and control programs (4). The records of the microbiology laboratory are the main source of surveillance. Therefore, microbiological and immunological reports from the laboratory constitute the starting point of research on endemic and epidemic nosocomial infections.

Nosocomial infections, also called hospital-acquired infections, can occur 48 hours after hospitalization. These infections can sometimes occur after the patient has been discharged. A patient is exposed to various microorganisms during a hospital stay. The probability of these microorganisms causing infection depends in part on the microorganisms' resistance to antimicrobial agents, virulence factors, and characteristics such as bacterial inoculum (5).

Health services are an environment where both infected people and people with a high risk of infection come together. Patients with infections or pathogenic microorganisms admitted to the hospital become a potential source of infection for other patients and staff if this is left uncontrolled.

Enterococci are inherently resistant to a variety of antimicrobials and have been recognized as one of the important nosocomial pathogens, due both to their virulence properties and their ability to acquire multiple antibiotics resistance (MAR) (6). Vancomycin has been the most reliable antibiotic used in the treatment of enterococcal infections with MAR. The emergence of vancomycin resistance in enterococci in the late 1980s made the treatment of these infections is a serious problem. The hospital environment is ideal for the growth of resistant Gram-negative bacteria due to the selective pressure of antibiotics. The seriousness of NI caused by such bacteria increases, and their treatment becomes difficult (7). Carbapenems have long been recognized as the most active and potent agents against MAR Gram-negative pathogens (8). However, due to life-threatening infections caused by MAR microorganisms, the use of carbapenem antibiotics is restricted, and treatment of NI with existing antibiotics becomes difficult (9).

Hospital infections constitute an important health problem in our country as well as all over the world. Surveillance studies are essential in ensuring the control of nosocomial infections. Thus, microorganisms forming the hospital's own flora and resistance patterns are determined. Each hospital determines its specific infection rates in line with the infection factors and rates obtained. It should identify high-risk services, take infection control measures accordingly, and rearrange the training programs of healthcare personnel according to their needs. Knowing each center's own patient profile, microorganisms that make up the hospital flora, their resistance patterns, along with the distribution and frequency of nosocomial infections in each unit enable the development of correct prevention strategies (10-12).

In the study, it was aimed to evaluate the retrospectively rectal swab samples, which were examined in the Hospital Infections Research Laboratory between 1 January 2020 and 31 December 2020 in terms of vancomycin-resistant enterococci (VRE) and carbapenem-resistant (CR) Gram-negative rods, which are important nosocomial infection factors.

MATERIAL AND METHODS

Cultivation of specimens

Rectal swab samples taken from the patients were sent to our laboratory with transport medium (Stuart transport medium, Letsswab, Turkey). Bile Esculin Azide agar (BEA) (Bile Esculin Azide Agar, Biolab Zrt., Hungary) supplemented with 6 mg/L vancomycin (Vancomycin HCL, Multicell) as vancomycin resistance screening medium and MacConkey agar (BBL ™ MacConkey Agar, BD; Becton, Dickinson and Company, USA) media supplemented with 3 mg/L meropenem (Meropenem Trihydrate, Tokyo Chemical Industry Co., LTD. Japan) as the screening medium of carbapenem resistance were used (13-14). Samples from Pediatric Intensive Care-Neonatal units were planted on both BEA agar with vancomycin for VRE and MacConkey agar with meropenem for the screening of bacteria producing carbapenemase, while samples from other clinics were only planted on BEA media with vancomycin for the screening of VRE.

After planting, all media were incubated for 24 hours in a 35 °C incubator, and the results were evaluated according to CLSI criteria (15-16). The control of the antibi-

otic discs used in the experiments was performed with the *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 standard strains. This study was approved by the ethics committee of Istanbul University, Istanbul Faculty of Medicine (Date: 13.11.2020, No: 196733).

Enterococcus identification

A Gram-stained and catalase test was performed to determine if there was a growth that hydrolyzed esculin in the BEA agar medium. Colonies with Gram-positive cocci and catalase-negative results were evaluated as enterococci. The PYR test was used for enterococcal confirmation. A disc diffusion sensitivity test was performed on these growths with vancomycin and teicoplanin antibiotics (13).

Identification of Gram-negative rods

To identify Gram-negative rods grown on MacConkey agar media supplemented with meropenem, triple sugar iron agar (TSI) (Triple Sugar Iron agar, BD; Becton, Dickinson and Company, USA), Motility-Indole-Ornithine (MIO) (Biolab Zrt., Hungary), Clark-Lubs (CM0043, MRVP Medium, OXOID LTD., England) and DNase agar (DNase Agar, Biolab Zrt., Hungary), the bacteria were identified by investigating various biochemical and enzyme properties of the strains (17-18). *Stenotrophomonas maltophilia* bacteria were not reported because they are naturally resistant to carbapenems (14).

Determination of sensitivity to antibiotics

Antimicrobial susceptibilities were determined by the disk diffusion method, and the results were evaluated according to CLSI criteria (14-16, 19). For the susceptibility test, 5-10 colonies were taken from each petri dish and inoculated into Mueller-Hinton broth (Mueller Hinton Broth, BD; Becton, Dickinson and Company, USA) medium, and the bacterial suspension was brought to the standard turbidity of McFarland and its pure culture was prepared. The pure culture of each strain was then homogeneously spread on the surface of the Mueller-Hinton agar (Mueller-Hinton II Agar, Biolab Zrt., Hungary) medium. Vancomycin (30 µg) (Oxoid Ltd., UK) and teicoplanin (30 µg) (Oxoid Ltd., UK) for *Enterococcus* strains, imipenem (10 µg) (Oxoid Ltd., UK), meropenem (10 µg) (Oxoid Ltd., UK) and ertapenem (10 µg) (Oxoid Ltd., UK) for Gram-negative rods were used. Antibiogram plates were incubated for 24 hours in a 35 °C incubator. The control of the antibiotic discs used in the experiments was performed with the *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 standard strains.

RESULTS

In total, 2688 rectal swab samples from various services of the university hospital in a one-year period between the first of January 2020 and December 31, 2020 were evaluated. In total, 1068 were female, and 1620 were male. It was determined that 895 of these samples belonged to pediatric patients and 1793 to adult patients. Of the adult patients, 713 were female, and 1080 were male (table 1).

The distribution of VRE growths detected in all rectal swab samples according to the clinics and the distribution of the isolated CR Gram-negative bacteria in the genus and species levels are shown in table 2.

Gram-negative rods producing carbapenemase were investigated only in the 741 samples sent from all Pediatrics Intensive Care and Neonatal units (including Intensive Care, Level 1, Level 2, Level 3, and Pediatrics Surgery). Vancomycin-resistant enterococci and/or CR Gram-negative rods growth was detected in 777 of the total samples (29% - 777/2688).

Accordingly, out of a total of 741 (27.5% - 741/2688) samples sent from the Pediatrics Intensive Care-Neonatal wards, growths were detected in 236 (31.8% - 236/741) of these samples as both 86 (11.6% - 86/741) VRE and 150 (20% - 150/741) CR Gram-negative rods (table 1, 2). As well as Pediatrics Intensive Care-Neonatal services, data from other services, including Pediatrics Infection; Pediatrics-Pandemic Intensive Care; Pediatrics-Emergency; Pediatrics-Nutrition; Pediatrics Gastroenterology; Pediatrics-Hematology and Oncology; Pediatrics-Cardiology; Pediatrics-Nephrology; Pediatrics-Neurology; Pediatrics-Special and Pediatrics-Clean were collected under Other Pediatrics services and are shown in table 1 (1). In total, 154 samples from Other Pediatrics services were investigated for VRE, and growth was detected in 60 samples (39% - 60/154). A total of 139 samples from various surgical services grouped under general Surgery

Table 1: Distribution of all examined rectal swab samples by clinics and gender

Sending services	Number of samples	Female	Male
1. Other pediatrics	154	67	87
2. Pediatrics Intensive Care-Neonatal	741	288	453
3. Surgical services	139	54	85
4. Internal medicine	1290	519	771
5. Intensive Care-Emergency Trauma	345	130	215
6. Other services	19	10	9
Total	2688	1068	1620

Table 2. Distribution of the growths of total VRE according to the services and CR rods

Units	VRE (627) (%)	CR Gram-negative rods (150)				
		K. pneumoniae	*K. oxytoca*	*Enterobacter* spp.	*E. coli*	*Acinetobacter* spp.
1. Other pediatrics	60 (9.6)	--	--	--	--	--
2. Pediatrics Intensive Care Neonatal	86 (13.7)	75	7	26	2	40
3. Surgical services	34 (5.4)	--	--	--	--	--
4. Internal Medicine	353 (56.3)	--	--	--	--	--
5. Intensive Car Emergency Trauma	88 (14)	--	--	--	--	--
6. Other services	6 (1)	--	--	--	--	--
Total	627	75	7	26	2	40

VRE: Vancomycin-resistant enterococci; CR: Carbapenem-resistant.

Table 3. Distributions of CR Gram-negative rods growth together with VRE strains in Pediatrics Intensive Care-Neonatal wards

Units	Number of samples	VRE and CR Gram-negative rods				
		K. pneumoniae	*K. oxytoca*	*Enterobacter* spp.	*E. coli*	*Acinetobacter* spp.
2. Pediatrics Intensive Care - Neonatal	19	12	1	3	1	2

VRE: Vancomycin-resistant enterococci; CR: Carbapenem-resistant.

Services (table 1) such as Chest surgery and Brain surgery were studied, and the growth of VRE was detected in 34 (24.5% - 34/139) samples. Vancomycin-resistant enterococci were detected in 353 of a total of 1290 samples (27.4% - 353/1290) sent from various services of Internal Medicine (table 1). A total of 345 samples were sent from various other Intensive Care-Emergency Trauma services were studied and VRE growth was detected in 88 (25.5% - 88/345) samples (table 1). The total number of samples coming from Other Services including Skin and Venereal Diseases, Chest Diseases, Eye Diseases, Clinical Microbiology outpatient clinic, Gynecological Oncology, Ear-Nose-Throat A-service, Neurology Dr. Edip Aktin Stroke service, Urology service was 19 and the growth of VRE was detected in 6 (31.6% - 6/19) samples (table 1).

In total, 627 VRE strains (23.3% - 627/2688) were isolated from all services. The VRE strains were isolated mostly in Internal Medicine Service with 353 (56.3% - 353/627), then 88 (14% - 88/627) in Intensive Care-Emergency Trauma, 86 (13.7% - 86/627) in Pediatrics Intensive Care-Neonatal, then 60 (9.6% - 60/627) in Other Pediatrics services, 34 (5.4%, 34/627) in Surgical Services and 6 VRE strains (1%, 6/627) in Other Services (table 2). Additionally, 150 CD Gram-negative rods were isolated from the samples of Pediatrics Intensive Care-Neonatal Wards. The distributions of these strains were as follows: 75 CR *K. pneumonia*, 7 CR *K. oxytoca*, 26 CR *Enterobacter* species, 2 CR *E. coli* and 40 CR *Acinetobacter* species (table 2).

In 19 rectal swab samples sent from Pediatrics Intensive Care - Neonatal wards, both VRE and CR Gram-negative rod growth were isolated together (table 3). In 12 of these samples, CR *K. pneumoniae* with VRE; In 1 example, VRE and CR *K. oxytoca*; VRE and CR *Enterobacter* species in 3 samples; VRE and *E. coli* in 1 example; In 2 samples, VRE and *Acinetobacter* species were isolated together.

DISCUSSION

Hospitals are a potential source of infection transmission risk during healthcare delivery (20-21). Vancomycin-resistant enterococcal infections are among the leading causes of healthcare-associated infections (22-24). Surfaces and medical devices in the rooms of patients colonized and/or infected with vancomycin-resistant enterococci are fre-

quently contaminated by this microorganism and form an important VRE reservoir within the hospital (2, 22).

In a study conducted in Germany, it was reported that 263 VR-*Enterococcus faecium* colonization were detected among 16350 patients hospitalized in six university hospitals between 2014 and 2018. In addition, it was also reported that VR-*E. faecium* prevalence rates increased from 0.8% to 2.6% in a five-year period (25). Carbapenem-resistant *Enterobacteriaceae* (CRE) poses a serious public health threat worldwide. Carbapenem-resistant *Enterobacteriaceae* infections appear rapidly and cause serious difficulties in treatment (26). One of the most important nosocomial pathogens from the *Enterobacteriaceae* family in the world is *Klebsiella pneumonia* (27-28). In other studies, risk factors for colonization or infection with CR *K. pneumoniae* (CRKP) in long-term intensive care hospitals have been evaluated. It has been reported that solid organ or hematopoietic stem cell transplantation, mechanical ventilation and lack of patient stool control are important risk factors for infection or colonization with CRKP (29). In a CRE prevalence study, 150 stool swabs from 150 patients from intensive care units and hematopoietic stem cell transplant services were examined. Among them, 25 (16.6%) CRE strains were isolated. Of the 25 CRE strains isolated, 17 (65.3%) were *K. pneumoniae*, 6 (23%) *Escherichia coli*, 1 (3.8%) *Citrobacter freundii* and one (3.8%) were defined as *Enterobacter* species (30). In another study conducted at a university hospital in China, CRE was investigated in 704 stool samples. Samples were taken from the Central Intensive Care Unit (CICU), Traditional Chinese Medicine Service (TCMS), pediatric service, and 62 other services. A total of 60 (8.5%) CRE were isolated from 704 stool samples examined. Of these, 42 (5.9%) were identified as *K. pneumoniae*, 7 *E. coli*, 3 *C. freundii*, 3 *K. oxytoca* , 3 (0.4%) *Enterobacter cloacae* and 1 (0.1%) *Enterobacter aerogenes* (12). In a research study conducted in a university hospital in our country to determine nosocomial infections and their causative agents to determine local data, in total 112 nosocomial infection agents had been isolated from 97 of 3254 patients (3.5% - 112/3254) who were hospitalized, followed up and treated in various services between January 2009 and March 2010. The most frequently isolated microorganisms causing the infections were followed by *Acinetobacter baumannii* 23.2%, *Klebsiella* spp. 20.5%, *E. coli* 19.6% and *Pseudomonas* spp. 11.6%. In the same study, it was reported that the rate of resistance to carbapenem antibiotics was quite high. In addition, *E. faecium* was detected at a rate of 9.2% (1). In another research study from Turkiye, meropenem resistance was reported at a rate of 5.7% in 53 *K. pneumoniae* strains isolated from various specimens of patients diagnosed with nosocomial infections in various clinics between 2011 and 2013 (28). Additionally, it was reported that the *Acinetobacter* genus was increasingly identified as a nosocomial infection agent, especially in patients in intensive care units (31-32). Şahin AR et al. investigated the epidemiology of *A. baumannii* and antimicrobial resistance in various clinical samples were taken from patients who were hospitalized and diagnosed with nosocomial infections between 2012 and 2017 (10). The most common isolation of it was from the anesthesia and reanimation intensive care units with 58.9% (284), then 21.7% (105) from internal medicine intensive care units, 9.5% (46) in neurology, 5.3% (26) in general surgery, 3.9% (19) in neurosurgery and in coronary intensive care units with 0.2% (1). It was reported that imipenem, meropenem and ertapenem discs and carbapenem resistance was detected in over 97% of these strains.

In our study, the rate of hospital infection was found to be 28.9% (777/2688) in the retrospective evaluation made between the 1st of January 2020 and December 31st, 2020. The distribution rate of this reproduction (777) according to services was as follows: Internal Diseases 45.43% (353/777), Pediatrics Intensive Care - Neonatal Services 30.37% (236/777) (150 CR bacteria + 86 VRE), Intensive Care Emergency Trauma Services 11.32% (88/777), 7.72% (60/777) in Other Pediatrics Services, 4.37% (34/777) in all Surgery Services, and 0.77% (6/777) in Other Services. Microorganisms causing nosocomial infections in Pediatrics Intensive Care-Neonatal Services were 86 VRE strains isolated from 741 samples of this unit and 150 CR Gram-negative rods as 75 CR *K. pneumoniae*, 7 CR *K. oxytoca*, 26 CR *Enterobacter* spp., 2 CR *E.coli* and 40 CR *Acinetobacter* spp.

Hospital-acquired *K.pneumoniae* is the main source of carbapenemase producing *Enterobacteriaceae* (CPE) infection in Europe. As a result, the emergence and spread of antibiotic resistance to last-line antibiotics, the opportunities to treat successfully CPE-infected patients in countries with a high prevalence of CPE have become less and less. However, it does not seem possible to introduce new and effective antibiotics to healthcare in a short time. Aims should include the prevention of cross-contamination, reduction of healthcare-associated infections by strictly following infection control measures, and infection control training should be planned for this target (33).

CONCLUSION

Nosocomial infections constitute an important health problem in the whole world. Surveillance studies are essential in ensuring the control of these infections. Thus, microorganisms forming the hospital's own flora and resistance patterns have been determined. Nosocomial infection rates differ between regions, countries and even hospitals. In line with the infection factors and rates obtained, each hospital should determine its own specific infection rates, determine high-risk services, take infection control measures accordingly, and rearrange

the training programs of health personnel according to the needs. It is essential for surveillance studies to keep the spread of infections to a minimum in the nosocomial infections control studies reducing the transmission and the spread of multiple antimicrobial resistant microorganisms and thus preventing epidemics. The fact that each center knows its own patient profile, the microorganisms that make up the hospital flora, their resistance patterns, the distribution and frequency of nosocomial infections in each unit, enables the development of correct prevention strategies.

Ethics Committee Approval: This study was approved by Istanbul Faculty of Medicine Clinical Research Ethics Committee (Date: 13.11.2020, No: 28).

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