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Infectious Diseases / Bulaşıcı Hastalıklar

Risk Factors for Colonization of Vancomycin-Resistant Enterococci in Patients in the Intensive Care Unit: A single-center Retrospective Study

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ABSTRACT

Background: Patients colonised with vancomycin-resistant enterococci (VRE) remain a problem worldwide, especially in intensive care units (ICU), necessitating the identification of associated risk factors. The aim of this single-centre retrospective study was to determine the risk factors for VRE colonisation in patients admitted to medical and surgical ICUs.

Methods: We analyzed data from 190 patients admitted to the ICUs between January 2020 and December 2022. Demographic information, clinical characteristics, laboratory results, antimicrobial usage, and comorbidities were obtained from digital patient records. Rectal swabs were collected weekly within 48 hours of ICU admission to detect VRE colonization.

Results: Out of 190 patients, 54 were colonized with VRE. Significant independent risk factors for VRE colonization included higher APACHE II scores on ICU admission (OR: 1.26, 95% CI: 1.03-1.55, p=0.024), longer hospital stay (OR: 1.25, 95% CI: 1.14-1.36, p<0.001), non-abdominal surgery (OR: 22.85, 95% CI: 6.90-75.72, p<0.001), and use of teicoplanin in the past three months (OR: 14.47, 95% CI: 4.55-46.03, p<0.001). VRE-colonized patients had lower mean C-reactive protein and albumin levels than non-VRE patients.

Conclusion: Higher APACHE II scores, prolonged hospital stays, non-abdominal surgeries, and recent teicoplanin use are significant risk factors for VRE colonization in ICU patients.

Keywords: Vancomycin-resistant enterococci, intensive care unit, colonization, risk factors

ÖZET

Amaç: Vankomisine dirençli enterokoklarla (VRE) kolonize olan hastalar, özellikle yoğun bakım ünitelerinde (YBÜ) olmak üzere dünya çapında bir sorun olmaya devam etmekte ve bu durum da VRE kolonizasyonu ile ilişkili risk faktörlerinin tanımlanması ihtiyacığını gündeme getirmektedir. Retrospektif olarak gerçekleştirdiğimiz bu tek merkezli çalışmanın amacı medikal ve cerrahi YBÜ'lere kabul edilen hastalarda meydana gelen VRE kolonizasyonu için risk faktörlerini tespit etmektir.

Yöntemler: Ocak 2020 ve Aralık 2022 tarihleri arasında YBÜ'lere kabul edilen 190 hastanın verileri analiz edilmiştir. Demografik bilgiler, klinik özellikler, laboratuvar sonuçları, antimikrobiyal kullanımı ve komorbiditeler elektronik tıbbi kayıtlardan elde edilmiştir. VRE kolonizasyonunu tespit etmek için YBÜ'ye kabulden sonraki 48 saat içinde başlanmak kaydıyla haftalık olarak rektal sürüntü örnekleri toplanmıştır.

Bulgular: Çalışma döneminde YBÜ'de takip edilen 190 hastanın 54'ü VRE ile kolonize olmuştur. VRE kolonizasyonu için anlamlı bağımsız risk faktörleri arasında YBÜ'ye kabulde daha yüksek APACHE II skorları (OR: 1.26, %95 GA: 1.03-1.55, p=0.024), uzamış hastanede kalış süresi (OR: 1. 25, %95 GA: 1.14-1.36, p<0.001), non-abdominal cerrahi operasyon geçirmek (OR: 22.85, %95 GA: 6.90-75.72, p<0.001) ve son üç ayda teikoplanin kullanımı (OR: 14.47, %95 GA: 4.55-46.03, p<0.001) bulunmuştur. Ayrıca VRE kolonize hastaların ortalama C-reaktif protein ve albümin düzeyleri VRE kolonize olmayan hastalara göre daha düşüktü.

Sonuç: Yüksek APACHE II skorları, hastanede kalış süresinin uzaması, abdomen dışı cerrahi operasyon geçirmek ve son üç ayda teikoplanin kullanımı, YBÜ hastalarında VRE kolonizasyonu için önemli risk faktörleridir.

Anahtar Kelimeler: Vankomisine dirençli enterokoklar, yoğun bakım ünitesi, kolonizasyon, risk faktörü

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Vancomycin-resistant enterococci (VRE) are increasingly prevalent nosocomial pathogens, especially among severely ill patients in the intensive care unit (ICU) (1). The global increase in VRE presence in hospitals has led to the need for examining the factors linked to VRE colonization (2). The transmission dynamics of VRE in the hospital environment and the factors contributing to its spread remain complex (3). Colonization with VRE is essential for transmitting these multidrug-resistant organisms in healthcare (4). Identification of risk factors for VRE colonization is imperative to guide the implementation of effective infection control measures. Advanced age, comorbid conditions, antimicrobial exposure and healthcare contact have been recognized as contributing factors to VRE colonization in previous studies (5-7). Factors contributing to VRE colonization in ICU patients include extended ICU stays, previous renal replacement therapy, and the use of penicillin and third-generation cephalosporins in medical and surgical wards, use of carbapenems in intensive care units, enteral tube feeding, metabolic diseases, male gender, and a Charlson comorbidity index <3, emphasizing the need for infection control strategies, reduced ICU stay, and prudent antibiotic use (8–10). VRE colonization among critically ill patients in the ICU is a rising worry because of its link to higher rates of illness, death, and healthcare expenses (8). The aim of this single-centre retrospective study was to determine the risk factors for VRE colonisation in patients admitted to medical and surgical ICUs in our institution.

Materials and Methods

This retrospective study, carried out at a single center, examined patients admitted to the medical and surgical ICUs at our hospital from January 2020 to December 2022. Patient data for the study were collected from the digital patient records of those admitted to the ICUs within the specified timeframe. Demographic information, clinical characteristics, laboratory results, antimicrobial usage, comorbidities, and other relevant variables were extracted from the digital patient records. The study included patients who were 18 years or older and had been admitted to the medical and surgical ICUs during the specified period. Patients with incomplete medical records or missing data relevant to the study variables were excluded. During the study, rectal swabs were taken within 48 hours of admission to the ICU to detect existing VRE colonisation. Samples from patients staying in the ICU for over 48 hours were collected weekly until a positive VRE culture was detected, the patient left the ICU, or they passed away. *Enterococci* were considered to have been acquired in the ICU if detected in a patient in the unit for more than 48 hours. If a patient's result is negative for VRE according to the first swap taken within the 24 hours in ICU and on weekly rectal swaps taken three times consecutively, then the patient was accepted as negative for VRE (11). Prior antibiotic use was defined as administering antimicrobials three months before ICU admission. Prior ICU hospitalization was defined as an inpatient admission to the ICU for any reason three months before the current ICU admission. The key outcome evaluated was the colonization of VRE among ICU patients during their hospital stay.

Statistical Analysis

The participants' demographic and clinical details were delineated through descriptive analysis. We verified the normality of the variables with the Shapiro-Wilk assessments. Continuous data were presented as average ± standard variation or as a range from minimum to maximum values. We employed either Mann-Whitney U evaluations or t-examinations to contrast continuous data across groups. Categorical data regarding counts and proportions were detailed; group comparisons were made using either Pearson's chi-square or Fisher's precise chi-square assessments. To determine potential mortality risk factors, we implemented univariate logistic regression methods. Factors with a p-value below 0.10 in the univariate analysis were assessed using multivariate logistic regression to identify significant mortality-associated risks. The SPSS software version 28.0 facilitated all statistical investigations, setting the significance bar at $p < 0.05$

Results

In this retrospective study, we analyzed data from 190 patients admitted to the medical and surgical ICUs to determine the risk factors linked to VRE colonization. Out of these, 54 patients were colonized with VRE, while 136 were not. The mean age of VRE-colonized patients was 53.57 ± 20.37 years, compared to 51.25 ± 20.27 years in non-VRE-colonized patients (p=0.490) (Table 1). The two groups had a similar distribution of sexes., with females comprising 46.3% of the VRE group and 54.4% of the non-VRE group (p=0.396).

The APACHE II score on ICU admission was significantly higher in the VRE group (19.46 ± 2.87) compared to the non-VRE group (17.88 ± 3.53, p=0.007). A similar proportion of patients in both groups had been hospitalized within the three months preceding the study (46.3% vs. 41.9%, p=0.698) (Table 1).

Table 1: Comparison by univariate analysis of the demographic and clinical features of colonisation with VRE in intensive care unit patients

Variables	VRE colonization (n=54)	non-VRE colonization (n=136)	*P* Value
Age, years, mean ± SD	53.57 ± 20.37	51.25 ± 20.27	0.490
Sex, famale, n (%)	25.0 (46.30%)	74.0 (54.41%)	0.396
APACHE II score on ICU admission, mean ± SD	19.46 ± 2.87	17.88 ± 3.53	**0.007**
Previous hospitalization within 3 months, n (%)	25.0 (46.30%)	57.0 (41.91%)	0.698
Non-abdominal surgery, n (%)	29.0 (53.70%)	12.0 (8.82%)	**<0.001**
Abdominal surgery, n (%)	12.0 (22.22%)	14.0 (10.29%)	0.054
Charlson Comorbidity Index, mean ± SD	3.61 ± 1.38	3.33 ± 1.57	0.227
Diabetes mellitus, n (%)	15.0 (27.78%)	28.0 (20.59%)	0.381
Hypertension, n (%)	7.0 (12.96%)	28.0 (20.59%)	0.310
Chronic obstructive lung diaseses, n (%)	16.0 (29.63%)	25.0 (18.38%)	0.132
Coronary artery disease, n (%)	16.0 (29.63%)	24.0 (17.65%)	0.103
Chronic renal disease, n (%)	12.0 (22.22%)	13.0 (9.56%)	**0.037**
Cerebrovascular disease, n (%)	13.0 (24.07%)	18.0 (13.24%)	0.108
Malignancy, n (%)	7.0 (12.96%)	11.0 (8.09%)	0.447
Chronic steroid or immunosuppression therapy, n (%)	7.0 (12.96%)	18.0 (13.24%)	1.000
Pressure ulcers, n (%)	15.0 (27.78%)	45.0 (33.09%)	0.591
Mechanical ventilation, n (%)	26.0 (48.15%)	49.0 (36.03%)	0.169
Total parenteral nutrition, n (%)	16.0 (29.63%)	58.0 (42.65%)	0.135
Blood transfusion, n (%)	11.0 (20.37%)	26.0 (19.12%)	1.000
Urinary catheter, n (%)	52.0 (96.30%)	133.0 (97.79%)	0.624
Central-line catheter, n (%)	20.0 (37.04%)	51.0 (37.50%)	1.000
Nasogastric tube, n (%)	22.0 (40.74%)	54.0 (39.71%)	1.000
Drainage tubes, n (%)	8.0 (14.81%)	13.0 (9.56%)	0.432
White blood cells (G/L), mean ± SD	8.68 ± 1.53	8.79 ± 1.52	0.662
Neutrophil-to-lymphocyte ratio, mean ± SD	1.71 ± 0.45	1.71 ± 0.50	0.831
C-reactive protein (mg/L), mean ± SD	4.49 ± 1.18	4.93 ± 1.26	0.031
Platelets, (mm^3), mean ± SD	144.91 ± 24.66	144.41 ± 25.11	0.926
Albumin, (g/L),mean ± SD	3.85 ± 0.27	3.95 ± 0.29	**0.027**
Use of meropenem in past 3 months, n (%)	20.0 (37.04%)	37.0 (27.21%)	0.247
Use of vancomycin in past 3 months, n (%)	10.0 (18.52%)	32.0 (23.53%)	0.578
Use of teicoplanin in past 3 months, n (%)	25.0 (46.30%)	14.0 (10.29%)	**<0.001**
Use of metronidazol in past 3 months, n (%)	6.0 (11.11%)	21.0 (15.44%)	0.589
Use of tigecycline in past 3 months, n (%)	14.0 (25.93%)	29.0 (21.32%)	0.623
Use of linezolid in past 3 months, n (%)	4.0 (7.41%)	23.0 (16.91%)	0.109
Use of quinolone in past 3 months, n (%)	33.0 (61.11%)	65.0 (47.79%)	0.135
Use of third or fourth generation cephalosporins in past 3 months, n (%)	31.0 (57.41%)	56.0 (41.18%)	0.062
Use of beta-lactam/lactamase inhibitors in past 3 months, n (%)	18.0 (33.33%)	43.0 (31.62%)	0.955
Length of hospital stay, (day) mean ± SD	21.59 ± 5.37	15.12 ± 6.29	**<0.001**
Length of stay in ICU, (day) mean ± SD	15.06 ± 2.15	16.88 ± 6.17	0.092

The groups did not show a significant difference in the Charlson Comorbidity Index (3.61 ± 1.38 vs. 3.33 ± 1.57, p=0.227) (Table 1). Specific comorbidities, including diabetes mellitus, hypertension, chronic obstructive lung disease, coronary artery disease, chronic renal disease, cerebrovascular disease, malignancy, and chronic steroid or immunosuppression therapy, did not show significant differences except for chronic renal disease, which was more prevalent in the VRE group (22.2% vs. 9.6%, p=0.037) (Table 1).

A significantly higher number of VRE-colonized patients underwent non-abdominal surgery (53.7%) compared to non-VRE patients (8.8%, p<0.001). Abdominal surgery was performed in 22.2% of the VRE group and 10.3% of the non-VRE group (p=0.054) (Table 1). Pressure ulcers, mechanical ventilation, total parenteral nutrition, blood transfusion, urinary catheter, central-line catheter, nasogastric tube, and drainage tubes usage did not significantly differ between the groups (Table 1).

Laboratory findings indicated that the mean C-reactive protein level was significantly lower in the VRE group (4.49 ± 1.18 mg/L) compared to the non-VRE group (4.93 ± 1.26 mg/L, p=0.031). The albumin level was also significantly lower in the VRE group (3.85 ± 0.27 g/L) compared to the non-VRE group (3.95 ± 0.29 g/L, p=0.027) (Table 1).

Use of teicoplanin in the past three months was significantly higher in the VRE group (46.3%) compared to the non-VRE group (10.3%, p<0.001) (Table 1). There was no significant difference in the usage of other antibiotics, including meropenem, vancomycin, metronidazole, tigecycline, linezolid, quinolone, third or fourth generation cephalosporins, and beta-lactam/lactamase inhibitors (Table 1).

The mean length of hospital stay was significantly longer in the VRE group (21.59 ± 5.37 days) compared to the non-VRE group (15.12 ± 6.29 days, p<0.001). However, the length of ICU stay did not differ significantly between the groups (15.06 ± 2.15 days vs. 16.88 ± 6.17 days, p=0.092) (Table 1).

Multivariate logistic regression analysis identified four independent risk factors for VRE colonization in ICU patients: APACHE II score on ICU admission (OR: 1.26, 95% CI: 1.03-1.55, p=0.024), length of hospital stay (OR: 1.25, 95% CI: 1.14-1.36, p<0.001), non-abdominal surgery (OR: 22.85, 95% CI: 6.90-75.72, p<0.001), and use of teicoplanin in the past three months (OR: 14.47, 95% CI: 4.55-46.03, p<0.001) (Table 2).

Table 2: Multivariate analysis of risk factors for colonisation with VRE in intensive care unit patients

Variables	OR (Odds Ratio)	95% CI (Confidence Interval)	*P* Value
APACHE II score on ICU admission	1.26	1.03, 1.55	**0.024**
Length of hospital stay, (day)	1.25	1.14, 1.36	**<0.001**
Non-abdominal surgery	22.85	6.90, 75.72	**<0.001**
Use of teicoplanin in past 3 months	14.47	4.55, 46.03	**<0.001**

Discussions

In our study, we identified several significant risk factors for VRE colonization in ICU patients, including higher APACHE II scores on ICU admission, longer hospital stays, non-abdominal surgery, and the use of teicoplanin in the past three months, which provide critical insights for improving infection control strategies in healthcare settings.

We observed that higher APACHE II scores on ICU admission were significantly associated with an increased risk of VRE colonization. This finding aligns with previous studies suggesting that severe illness and higher severity scores are correlated with greater susceptibility to VRE colonization (12). Critically ill patients with higher APACHE II scores are more likely to have underlying comorbidities, require invasive procedures, and receive broader-spectrum antibiotics, all of which contribute to the risk of VRE colonization.

Our analysis highlighted the significant impact of prior antibiotic use on VRE colonization risk. The recent use of teicoplanin, a glycopeptide antibiotic, emerged as a strong independent risk factor for VRE colonization in our study. This finding is consistent with previous reports highlighting the association between glycopeptide antibiotic exposure and VRE colonization (13,14).

Teicoplanin, like vancomycin, exerts selective pressure on the intestinal microbiome, favoring the proliferation and persistence of VRE. The use of antibiotics such as piperacillin/tazobactam, meropenem, and vancomycin was particularly associated with higher risks of VRE colonization (15,16). In a similar study conducted in patients in the neonatal intensive care unit in Turkey, exposure to vancomycin was found to be a risk factor for VRE colonization (17). Our results underscore the importance of judicious use of glycopeptide antibiotics and the implementation of antimicrobial stewardship programs to mitigate the risk of VRE colonization.

We found that the length of hospital stay significantly influenced VRE colonisation. Prolonged hospitalisations provide more opportunities for exposure to hospital-acquired pathogens, including VRE. This is consistent with previous studies reporting higher VRE colonisation rates with prolonged length of hospital stay (5,18). In a similar study conducted in patients in intensive care units in Turkey, it was found that prolonged hospitalization was a risk factor for colonization (19). Longer hospitalization increases the exposure to potential VRE reservoirs, such as contaminated surfaces, healthcare workers, and other colonized patients, thereby enhancing the risk of transmission. Therefore, minimizing hospital stay durations should be a key component of infection control measures.

Our study also revealed a strong association between non-abdominal surgery and VRE colonization. This suggests that invasive procedures can increase the risk due to heightened exposure to antibiotics and healthcare environments. Previous studies have primarily focused on the role of gastrointestinal procedures or abdominal surgeries in VRE colonization (20,21). Our results suggest that non-abdominal surgical interventions may also contribute to the risk of VRE colonization, potentially due to factors such as surgical site infections, disruption of mucosal barriers, or increased antibiotic exposure.

It is noteworthy that chronic renal disease was more prevalent among VRE-colonized patients in our univariate analysis, although in the multivariate model, it did not appear as an independent risk factor. This finding aligns with previous studies reporting an association between chronic kidney disease and VRE colonization, potentially due to frequent healthcare exposures, invasive procedures, and altered immune function (22,23).

Interestingly, in our study, we did not find a significant relationship with VRE colonization and several factors previously reported as risk factors, such as advanced age, specific comorbidities (excluding chronic renal disease), the use of invasive devices, or exposure to specific antibiotics other than teicoplanin (24,25). These discrepancies may be attributed to differences in study populations, local epidemiology, and infection control practices.

We have a number of strengths in our study, such as a sample size that is relatively large and a comprehensive evaluation of potential risk factors. On the other hand, since the study was carried out in a single center, the applicability of the results to other healthcare environments may be limited.

In conclusion, this retrospective study identified higher APACHE II scores on ICU admission, longer hospital stays, non-abdominal surgeries, and recent use of teicoplanin as independent risk factors for VRE colonization among ICU patients. These findings highlight the importance of implementing targeted infection control measures, promoting antimicrobial stewardship, and minimizing modifiable risk factors to prevent the spread of VRE in the ICU setting. Future prospective, multicenter studies are warranted to validate and expand upon these findings.

Declarations

Ethical Approval

The study was granted ethical approval by the University of Health Sciences Bursa Yuksek İhtisas Training and Research Hospital Ethics Committee (Approval No. 2011-KAEK-25, Dated: 2023/08/14)

Author Contributions

Concept: C.S, Literature Review: C.S, Design : C.S, Data acquisition: C.S, Analysis and interpretation: C.S, Writing manuscript: C.S, Critical revision of manuscript: C.S

Conflict of Interest

The authors have no conflicts of interest to declare.

Financial Disclosure

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