To cite this article: Dogan A, Gezer Y, Kalaycı HO. Bloodstream Infections in COVID-19 Positive and COVID-19 Negative Patient Groups Followed Up in the Intensive Care Unit: Case-Control Study. Turk J Clin Lab 2022; 2: 182-187.

Original Article

Bloodstream Infections in COVID-19 Positive and COVID-19 Negative Patient Groups Followed Up in the Intensive Care Unit: Case-Control Study

Yoğun Bakımda Takip Edilen COVID-19 Pozitif ve COVID-19 Negatif Hasta Gruplarında Kan Dolaşımı Enfeksiyonları: Vaka Kontrol Çalışması

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ABSTRACT

Aim: Bloodstream infections are one of the most important problems we encounter in patients followed up in intensive care units. In our study, we aimed to comparatively examine the demographic characteristics and bacteremia epidemiology of patients who were followed up for SARS-CoV-2 (COVID-19) positivity or other reasons in the intensive care units.

Material and Methods: 192 cases (>18 age) whose blood cultures were studied were included in the study. The blood culture results of a total of 60 cases, 30 of which were positive for COVID-19 in the study group and 30 were negative for COVID-19 in the control group, were examined.

Results: Thirteen (43.3%) of the patients in the case group were female, 17 (56.7%) were male, and the mean age of the group was 63.8±19 (22-88). In the control group, 15 (50%) were female, 15 (50%) were male, and the mean age of the group was 76.1±17.6 (48-92). There was no statistically significant difference between the two groups in terms of sex (p=0.605), comorbid conditions (excluding sepsis (p=0.005)), the number of isolates produced (p=0.260), the amount of blood culture set (p=0.118), bacteremia risk factors and mortality rates (p=0.612). However, there were differences in mean age (p=0.000), skin contamination (p=0.028) and prednisolone treatment (p=0.000).

Conclusion: The risk of bloodstream infection in patients hospitalized in the intensive care units due to COVID-19 is not different from the group of patients hospitalized for non-COVID-19 reasons.

Keywords: Covıd-19; intensive care unit; blood culture; bacteremia

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Recevied: 23.11.2021 accepted: 08.05.2022
Doi: 10.18663/tjcl.1027448

TJCL Volume 13 Number 2 p: 182-187

ÖZ

Amaç: Kan dolaşımı enfeksiyonları, yoğun bakım ünitelerinde takip edilen hastalarda karşılaştığımız en önemli sorunlardan biridir. Çalışmamızda yoğun bakım ünitesinde SARS-CoV-2 (COVID-19) pozitifliği veya diğer nedenlerle izlenen hastaların demografik özellikleri ve bakteriyemi epidemiyolojilerini karşılaştırmalı olarak incelemeyi amaçladık.

Gereç ve Yöntemler: Çalışmaya kan kültürü çalışılan 192 olgu (>18 yaş) dahil edildi. Olgu grubunda 30'u COVID-19 pozitif, kontrol grubunda 30'u COVID-19 negatif olmak üzere toplam 60 vakanın kan kültürü sonuçları incelendi.

Bulgular: Olgu grubundaki hastaların 13'ü (%43.3) kadın, 17'si (%56.7) erkekti ve grubun yaş ortalaması 63.8±19 (22-88) idi. Kontrol grubunun 15'i (%50) kadın, 15'i (%50) erkek ve grubun yaş ortalaması 76.1±17.6 (48-92) idi. Cinsiyet (p=0.605), sepsis dışı komorbid durum (p=0.005), üretilen izolat sayısı (p=0.260), kan kültür seti miktarı (p=0.118), bakteriyemi risk faktörleri ve ölüm oranları (p=0.612) açısından iki grup arasında istatistiksel olarak anlamlı fark yoktu. Ancak yaş ortalaması (p=0.000), cilt kontaminasyonu (p=0.028) ve prednizolon tedavisi (p=0.000) açısından farklılıklar vardı.

Sonuç: COVID-19 nedeniyle yoğun bakım ünitelerinde yatan hastalarda kan dolaşımı enfeksiyonu riski, COVID-19 dışı nedenlerle yatırılan hasta grubundan farklı değildir.

Anahtar Kelimeler: Covıd-19; yoğun bakım ünitesi; kan kültürü; bakteriyemi

Introduction

TThe COVID-19 pandemic continues to be a global problem with the number of cases exceeding 220 million and a death rate of over 4.5 million as of September 2021.[1. In our country, as of September 10, 2021, approximately 6.5 million cases and 57.500 mortal cases have been reached.[2] About 5% of cases are critical and need intensive care.[3] Intensive Care Unit (ICU) related bloodstream infections often progress with high morbidity and mortality in COVID positive and negative cases.[4-5] In addition, the length of hospital stay and cost increase significantly due to these infections.[6] Many reasons are known for the high hospital infection rates in the ICU. Age of the patient, immune status, comorbid diseases, nutrition, number of patients in the unit, number of staff serving, rate of compliance with infection control measures, foley catheter, central or peripheral catheter, intubation, surgical procedure, open wound, antibiotic use rate and duration are some of these.[7]

The aim of this retrospective case-control study is to determine the epidemiology of bloodstream infections in COVID-19 positive and negative patients followed in the tertiary Anaesthesiology and Reanimation ICU of our hospital. It is also to evaluate the relationship between risk factors for the development of these infections and mortality.

Material and Methods

Study population

192 patients who were hospitalized in the ICU due to COVID-19 positivity or other reasons between 23 April and 31 July 2021 were included in the study. All patients were over 18 years of age. The data were obtained by scanning our hospital's automation system "Fonet Web HBYS". Sixty patients whose blood cultures were studied with the suspicion of bacteremia were included in the study. 30 COVID-19 positive patients in the study group and 30 COVID-19 negative patients in the control group were examined. Demographic characteristics of the patients, reproductive factors, contamination rates, antibiotic sensitivities, bacteremia development time, inappropriate antibiotic use, and bacteremia predisposing factors were recorded. Typing and antimicrobial susceptibility testing of the isolates were performed by the BD Phoenix Automated Microbiology System (USD).

Data analysis

The data in the study were recorded in the IBM SPSS ver.26.0 (SPPS Inc. Chicago, IL, USA) package program. $p<0.05$ value was considered statistically significant. For the variables, mean (± standard deviation), median value (Min-Max), and number (percent) values were calculated. Variables that did not show normal distribution were analyzed using the "Mann-Whitney U" test. Categorical variables were compared with "Pearson Chi Square" or "Fisher's exact test".

Ethics Committee Approval

For the permission of the study, a clinical study was planned with the decision of the Ordu University Clinical Research Ethics Committee dated 18.10.2021 and numbered 2021/234.

Results

Thirteen (43.3%) of the patients in the case group were female, 17 (56.7%) were male, and the mean age of the group was 63.8±19 (22-88). In the control group, 15 (50%) were female, 15 (50%) were male, and the mean age of the group was 76.1±17.6 (18-92). While there was no statistically significant difference between the two groups in terms of sex and comorbid conditions (except for sepsis (p=0.605)), the mean age of the case group was significantly lower (p=0.000). While 80% of the case group received prednol treatment, there was no patient in the control group who received prednol treatment (p=0.000). Among the comorbid conditions, sepsis was found significantly more in the control group than in the case group. (p=0.005). When the bacteremia risk factors were examined, no significant difference was observed between the 2 groups (Table 1).

Table 1. Demographics and bacteremia risk factors in the case-control group

Demographic data and bacteremia risk factors		Case Group N=30 (%)	Control Group N=30 (%)	p value
Seks	Female	13(43.3)	15(50)	0.605
	Male	17(56.7)	15(50)	
Age		63.8±19(22-88)	76.1±17.6(48-92)	0.000
Hypertension (HT)		13(43.3)	8(26.6)	0.176
Diabetes mellitus (DM)		10(33.3)	8(26.6)	0.573
Heart failure (HF)		5(16.6)	7(23.3)	0.519
Acute kidney failure (AKF)		4(13.3)	7(23.3)	0.317
Cerebrovascular event (CVE)		4(13.3)	7(23.3)	0.317
COPD*		4(13.3)	5(16.6)	1
Sepsis		0(0)	8(26.6)	0.005
Pneumonia		1(3.3)	6(20.0)	0.176
Length of stay in ICU		13.9±9.8(2-39)	17±17.8(1-80)	0.994
Duration of bacteremia		3.2±5.2(0-20)	3.5±9.1(0-37)	0.230
İntubation time		9.7±7.9(0-25)	14±18.5(0-80)	0.935
Nasogastric catheter		19(63.3)	23(76.7)	0.260
Foley catheter		30(100)	30(100)	-
Hemodialysis		3(10)	8(26.7)	0.095
Open wound		3(10)	4(13.4)	1
Surgical procedure		0	3(10)	0.237
Antacid		30(100)	30(100)	-
Endoscopy		0	1(3.3)	1
Total Parenteral Nutrition		26(86.7)	22(73.3)	0.197
Central Catheter		10(30)	17(56.7)	0.069
İntubation rate		29(96.7)	29(96.7)	-
Inappropriate antibiotics		6(20)	1(3.3)	0.103
Prednisolone		24(80)	0	0.000

*Chronic obstructive pulmonary disease

When the causative pathogens grown in the blood culture were examined, the most common isolated agent in both groups was Klebsiella pneumoniae (22.3%). Enterococcus and Staphylococcus from Gram-positive (GP) agents were isolated less frequently. Gram-negative (GN) isolate and fungus were detected in one case, and GP and GN isolates were found together in another case. The isolated causative pathogens are listed in Table 2.

When the amount of blood culture studied was examined, it was seen that one set of blood cultures was taken in 60% of the case group and 2 sets of blood cultures were taken in 43.3% of the control group. No statistically significant difference was observed between the 2 groups in terms of set amounts (p=0.118). When the number of isolates produced (p=0.260) and mortality rates (p=0.612) were examined, no statistically significant difference was observed again. It was observed that skin contamination in blood cultures was higher in the case group (p=0.028) (Table 3).

Table 2. Causative pathogens isolated in blood culture

Causative pathogen	Case Group n (%)	Control Group n (%)	Total n (%)
Klebsiella pneumoniae	4(22.30)*	0	4(22.30)*
Staphylococcus epidermidis	1(5.55)	2(11.10)	3(16.65)
Enterococcus faecalis	1 (5.55)	1(5.55)	2(11.10)
Acinetobacter baumannii+ Candida spp	0	1(5.55)	1(5.55)
Acinetobacter lwoffii/haemolyticus	1(5.55)	0	1(5.55)
Candida parapsilosis	1(5.55)	0	1(5.55)
Enterobacter aerogenes	0	1(5.55)	1(5.55)
Enterococcus faecalis+ Enterobacter gergoviae	1(5.55)	0	1(5.55)
Enterococcus faecium	1(5.55)	0	1(5.55)
Pseudomonas putida	0	1(5.55)	1(5.55)
Staphylococcus aureus	0	1(5.55)	1(5.55)
Staphylococcus hominis	1(5.55)	0	1(5.55)
Toptal, n (%)	11 (61.15)	7 (38.85)	18 (100)

*The fraction is complete.

Table 3. Blood culture data and mortality in the case-control group

Data	Case Group N=30 (%)	Control Group N=30 (%)	p value
Blood culture set			
one set	18(60)	11(36.6)	0.118
two set	6(20)	13(43.3)	
three set	6(20)	6(20)	
Reproduction in culture			
yes	11(36.6)	7(23.3)	0.260
no	19(63.4)	23(76.7)	
Contamination			
yes	14(46.6)	6(20)	0.028
no	16(63.7)	24(80)	
Mortality			
yes	29(96.6)	27(90)	0.612
no	1(3.4)	3(10)	

When the factors isolated in blood culture are examined; Two of K. pneumoniae and one of Acinetobacter were found to be multidrug resistant. While two of the staphylococci were found resistant to oxacillin, no GP strains resistant to vancomycin were isolated. P. putida was found to be resistant to meropenem. E. gergoviae not included in the table. E. gergoviae not included in the table were resistant to ceftriaxone, ceftazidime, gentamicin, ciprofloxacin, levofloxacin and trimethoprim sulfamethoxazole. It was determined that susceptibility testing was not performed on E. Aerogenes, C. parapsilosis and Candida spp strains. The amount of causative pathogens isolated from blood culture and resistant to antibiotics are given in Table 4.

Discussion

In the ICUs, the patient group who has a severe clinic and needs many medical interventions is treated. For this reason, ICUs have a higher mortality rate than wards.[8] And it is reported as half a million cases per year (8). In a study reported from our country, the mortality rate in ICU is in the range of 20.5-40.2%.[9] In a study conducted in an ICU where Covid patients were followed and 101 patients were included, the in-hospital mortality rate due to all causes was 61.4%.[10] In some studies conducted abroad, the mortality rate in COVID ICUs has been reported as 60-85%. [11-13] In our study, the mortality rate was 96% in COVID 19 patients and 90% in the other patient group. Our mortality rate was found to be higher than the expected general mortality rate in intensive care units. We think that this is because only patients with suspected bacteremia or sepsis were included in the study.

Comorbid conditions such as acute renal failure, infectious diseases, cardiovascular diseases, neurological diseases and DM are important parameters that affect the ICU mortality rate. [14,15] In studies that included patients older than 18 years of age who were admitted to the ICU without a history of COVID-19; neurological system diseases, infectious diseases, postoperative causes and cardiovascular system diseases were determined as the most common sub-diseases in patients who died.[15,16] Similarly, in the non-COVID patient group in our study, HT 26.6%, DM 26.6%, sepsis 26.6%, CVE 23.3% and pneumonia were the

Table 4. Amount of isolates resistant to antibiotics

Antibiyotik	K.pneumoniae (n=4)	Acinetobacter spp (n=2)	Enterococcus spp (n=4)	Staphylococcus spp (n=5)	P. putida (n=1)
Ampicillin	4	-*	1	-	-
Oxacillin	-	-	-	2	-
Clindamycin	-	-	-	0	-
Erythromycin	-	-	-	2	-
Streptomycin	-	-	3	-	-
Amoxicillin-Clavunic acid	2	-	-	-	-
Amikacin	2	1	-	0	0
Tobramycin	-	1	-	0	-
Gentamicin	2	1	2	0	0
Ciprofloxacin	2	1	-	1	0
Levofloxacin	2	1	-	0	0
Fosfomycin	0**	-	-	0	-
Cotrimaxazole	2	1	-	1	-
Ceftazidime	2	-	-	-	0
Ceftriaxone	2	-	-	-	-
Piperacillin-Tazobactam	2	-	-	-	0
Meropenem	2	1	-	-	1
Imipenem-Cilastatin	2	1	-	-	0
Ertapenem	2	-	-	-	-
Teicoplanin	-	-	0	0	-
Linezolid	-	-	0	0	-
Vancomycin	-	-	0	0	-

*Antibiotics not studied in the antibiogram
**Only in one isolate.

most common comorbid conditions with 20%. No significant difference was observed between the two groups in terms of comorbid conditions (except the presence of covid).

Patients followed up in the intensive care unit receive infusion therapy at a high rate. Catheters are responsible for 40% of bacteremia in ICU.[14] In our study, the factors considered as exogenous risk factors for bacteremia were examined and it was observed that the risk factors (except prednol use) were at a similar frequency in both groups.

In a study that included 750 patients followed up in the COVID ICU, it was observed that bloodstream infection developed in 8.5% of the cases. When the frequency of isolated strains was examined, GN pathogens were detected at a rate of 82.8%. It was observed that 32.8% of them were Acinetobacter and 21.9% were K. pneumoniae. Less frequently, Enterococcus spp., E. coli and P. aeuroginosa have been reported. When all isolates were examined, 57.8% of them were found to be MDR.[5] In our study, 2 of 4 isolated K. pneumoniae and 1 of 2 Acinetobacteria were found to be MDR. In another study conducted in our country, 208 blood cultures thought to be causative agents of bacteremia and sepsis were included in the study. Of the causative pathogens, 105 (50.5%) were found to be GP, 97 (46.6%) GN bacteria, and 6 (2.9%) Candida spp. isolated. Unlike our study, the most common GN bacteria was E.coli (20.19%), and the most common GP bacteria was S.epidermidis (17.7%).[17] Service patients were also included in this study. For this reason, we think that the rate of E.coli is different from our study and other studies. Although the number of cases included in our study was limited, similar results were observed in both groups.

Contamination is one of the important problems in blood culture taking in patients followed up in the COVID ICU. Unfamiliarity with personal protective equipment or compliance problems can increase the rate of contamination. [18] In addition, anxiety, fear and anxiety related to covid are not missing in healthcare workers.[19-21] We think that this also affects the possibility of contamination. In an intensive care study in which 267 cases were included, 38 blood cultures were taken during hospitalization, and 31 of them had no growth, while 7 (18.4%) were contaminated. Of the 15 blood cultures taken after the 5th day of hospitalization, 10 had no growth, 3 were contaminated, and only 2 had significant growth (20). In our study, there was a significant increase in blood culture in 11 (36.6%) patients in the case group and in 7 (23.3%) patients in

the control group. Similarly, contamination in the COVID patient group was significantly higher in the other group (p=0.028).

Conclusion

According to the results of our study, COVID 19 reduces the average age of patients in ICU admissions. Comorbid conditions appear to be similar between COVID 19 and the other patient group. The risk of bacteremia or sepsis in COVID 19 patients is not higher than in non-COVID 19 patient groups. However, high-dose prednol intake of COVID 19 patients is an important factor that increases the risk of bacteremia. The factors causing bacteremia or sepsis in patients with and without COVID 19 are not very different from each other in terms of type or frequency. It is necessary to be more careful to reduce the frequency of contamination, especially in COVID 19 patients, during blood culture collection. The overall mortality of COVID 19 patients in severe clinical and tertiary intensive care groups is not much different from the non-COVID 19 patient group. There is a need for multicenter, comprehensive studies on this subject in which more cases will be examined.

Financial support and conflict of interest: There is no person/organization that financially supports the work and the authors have no conflict of interest.

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