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Multidrug resistant microorganisms in the ıntensive care unit without COVID-19 during pandemic

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Abstract

There are very few reports on the prevalence of multidrug-resistant microorganisms during the COVID-19 pandemic. In addition, these publications usually cover covid-19 patients.Our study aimed to compare the prevalence of multidrug-resistant microorganisms in patients without COVID-19 undergoing treatment in an intensive care unit (ICU) during the COVID-19 pandemic with those in the pre-pandemic period. The study was planned retrospectively. In our country, the prevalence of multi-drug-resistant microorganisms was evaluated in the intensive care unit where internal and surgical patients were hospitalized in a single center in 6-month periods before and after the occurrence of covid-19 cases. The prevalence of multidrug-resistant microorganisms increased in patients being followed up in our ICU during the pandemic period ($p<0.05$). Statistically significant relationships were found between the incidence rate of microorganisms with multi-drug resistance and sex ($p=0.028$), presence of malignancy ($p=0.011$), and nurse's duration of work in the ICU ($p=0.04$). The increased prevalence of multidrug-resistant microorganisms and the infections caused by these microorganisms are other challenges that must be tackled during the pandemic period.

Keywords: coronavirus pandemic, multidrug-resistant microorganisms, intensive care, COVID-19

1. Introduction

At present, there is a global endeavor to manage the third and most severe corona virus-related disease in the last two decades (1). By June 03, 2021, there have been 170. 812. 850 confirmed cases and 3.557.586 deaths worldwide due to coronavirus disease (COVID-19) (2). Although various antiviral, antibiotic, and antimalarial drugs have been used in treatment, no treatment with proven efficacy specific to COVID-19 infection has been found in randomized controlled studies (3). Therefore, preventive strategies and breaking the transmission chain of the disease have been major targets. Hand hygiene and the use of personal protective equipment are recommended by health authorities since the early days of the pandemic (4).

Along with primary infection with severe acute respiratory syndrome-coronavirus-2, infection with other microorganisms (as coinfection or superinfection), complicates diagnosis and treatment and adversely affects the prognosis (5). In order to prevent this, World Health Organization (WHO) recommended the use of empirical antibiotic treatment during COVID-19 pandemi (6). It was reported that, despite coinfection was 3.5% and secondary infection was 14.3% of patients hospitalized due to COVID-19, 70% of the patients used broad-spectrum antibiotics (7). With increasing knowledge on and experience with COVID-19, the use of empirical or prophylactic antibiotic treatment is no longer recommended in patient management in both WHO guidelines andthe local guideline that we take as basis (8, 9). In addition, COVID-19 outbreak has had an impact on healthcare services. A significant number of healthcare workers have contracted COVID-19, and in many cases, the disease was fatal. The resulting healthcare personnel shortage has been mitigated by employing less experienced healthcare professionals. Moreover, healthcare workers have had to face many issues such as psychological stress, extreme workload, extra working hours, and insufficient personal protective equipments (10).

Uncontrolled use of unproven treatment regimens (therapy with steroids, immunosuppressives, cytokine binders), reserve hospital staff being channeled to COVID-19 clinics, and in particular, inexperienced and exhausted healthcare workers, as well as intensive use of empirical antibiotics in intensive care units (ICUs), added a serious problem for medical professionals; multidrug-resistant (MDR) microorganisms. In our study, we aimed to analyze whether the incidence rate of MDR (resistance against at least three categories of antibiotics) microorganism-related infections increased during the COVID-19 pandemic compared to the pre-pandemic period in patients in ICU.

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2. Materials and Methods

The study was planned retrospectively after obtaining ethics committee approval (OMUKAEK: 2020/618). Patients in the 20-bed ICU in which patients who have undergone internal surgery during 10.01.2019–10.01.2020 (two 6-month periods before and after COVID-19 notification in our country) are monitored were included in the study. The included patients wereover the age of 18 years, and their cultures were positive for MDR microorganisms. The factors analyzed included the following: patients' demographic data (age, sex, chronic diseases); Acute Physiology and Chronic Health Evaluation II (APACHE II) score (a mortality prediction score based on acute health problems and chronic health conditions of patients in ICUs); indications for intensive care admission;the location from where the patients were admitted to the intensive care unit (hospital, emergency service, home, operating room); culture results before intensive care admission and date of sample collection before intensive care admission, culture results during intensive care (on which day of intensive care admission reproduction happened and the microorganism that reproduced); need for mechanical ventilation; whether tracheotomy was performed; invasive procedures performed (central catheter, urinary catheter, nasogastric catheter); presence of open wound; presence and degree of decubitus ulcer;and need for renal replacement therapy.

Simultaneously, the number of intensive care physicians, nurses, auxiliary healthcare personnel, number of new healthcare personnel starting work in the COVID-19 pandemic period, amount of hand disinfectant used in the ICU in the 6-month time periods before and after the beginning of COVID-19 pandemic, and number of personal protective equipment were evaluated to determinethe incidence rate of microorganismsin patient samples in our ICU before and after the pandemic.

The data were analyzed using IBM SPSS Statistics 21.0 software. Friedman and Wilcoxon tests were used for intragroup comparisons. Mann–Whitney U test was used for numerical variables, and chi-square test was used for categorical variables for intergroup comparisons. Logistic regression models were used to determine the risk factors in the culture results with MDR (+) microorganisms, and $p < 0.05$ was considered significant.

3. Results

Over a period of 1 year, 1731 patients were admitted to our ICU. Monitoring and treatment of 857 patients were conducted in the 6-month period before March 2020 when COVID-19 cases started to occur in our country and that of 874 patients were conducted in the 6-month period after this date. MDR microorganism growth was detected in the cultures of 118 out of 857 patients admitted in the first six months before March 2020 and in those of 157 out of 874 patients admitted in the first six months after March 2020 (Fig. 1). When MDR microorganism cultures grown in both periods were compared, it was found that the rate increased significantly during the COVID-19 pandemic period ($p < 0.05$).

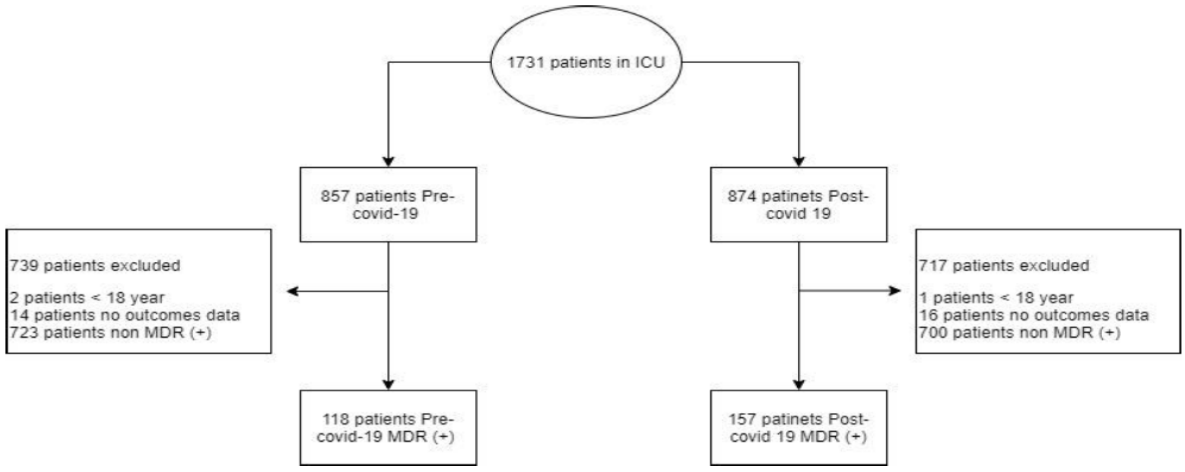

Fig 1. Flow chart of the patients included in the study; ICU: Intensive Care Unit, MDR: Multidrug Resistance

Demographic data, additional systemic diseases, and clinical characteristics of patients with MDR microorganisms grown in their cultures in the ICU during the two different time periods are summarized in Table 1. It was observed that the average intensive care stay of the patients was 24 days (range 1–233 days) in the 6-month period before the COVID-19 pandemic and 18 days (range 1–149 days) in the 6-month period after the pandemic, whereas intensive care stay durations of the patients in both periods was found to be statistically similar ($p = 0.108$). The average day on which microorganism growth was observed was found to be the 10th day (range 1st – 213th days) after admission among the patients who were monitored in the 6-month period before the pandemic, whereas this was the 9th day (range 1st – 326th days) in the patients admitted in the 6-month period after the pandemic ($p = 0.86$). MDR microorganisms and the site of their growth in the body in both periods evaluated in the study are shown in Table 2 and 3. *Acinetobacter baumannii* was found as the dominant MDR ICU pathogen in the first samples collected after the patients were admitted to the ICU, according to the surveillance data during ICU stay.

Table 1. Relationship between patients with multi-drug resistant microorganisms in their cultures before and after the Covid-19 pandemic and demographic, additional systemic diseases and their clinical characteristics

	Pre Covid-19 MDR (+) n=118	Post Covid-19 MDR (+) n=157	P value
Age, year mean ± SD	61.9 ± 18.2	60.2 ± 18.9	0.337
Gender (F / M) %	47.4 / 52.6	60.4 / 39.6	0.028
Systemic Disease			
Diabetes Mellitus %	18.1	21.4	0.231
Hypertension %	32.4	29.9	0.342
Malignancy %	17.2	28.9	0.011
COPD %	8.6	4.4	0.144
APACHE II Score mean ± SD	21.2 ± 8.5	22.5 ± 10	0.342
Intensive Care Admission			
Postoperative %	76.7	60.4	0.037
Sepsis %	10.3	18.9	0.054
Trauma %	9.5	12.6	0.611
Post Resüscitation %	3.4	8.2	0.413
Blood-Blood Product Transplantation			
Erythrocyte Suspension %	18.1	21.4	0.691
Fresh Frozen Plasma %	5.2	6.9	0.614
Platelet Suspension %	3.4	6.3	0.446
Mechanical Ventilation %	87.1	81.1	0.184
Tracheotomy%	24.1	22.6	0.993
Central Catheter%	57.8	54.1	0.583

MDR: Multi Drug Resistance, COPD: Chronic Obstructive Pulmonary Disease, APACHE II = Acute Physiology and Chronic Health Evaluation

The intensive care work experience of our intensive care nurses was an average of 124 months before the pandemic. Instead of our 12 nurses who had positive Covid-19 swab culture, intensive care service was tried to be provided with our nurses with no or less intensive care experience. After the pandemic, our nurses' intensive care experience decreased to an average of 108 months, due to our newly recruited inexperienced nurses. The rate of MDR that increased during the pandemic period was found to be statistically significant with decreased nurse experience (p = 0.04)

Table 2. Resistant microorganisms that grow in 6-month time periods before and after the Covid-19 pandemic

	Pre Covid-19 MDR (+) n=118	Post Covid-19 MDR (+) n=157	P
Acinetobacter Baumannii %	14.7	20.1	0.814
Staphylococcus Epidermidis %	19.0	15.1	1,000
Staphylococus Hominis %	10.3	12.6	0.406
Klebsiella Pneumoniae %	9.5	11.9	0.810
Escherichia Coli %	9.5	10.1	0.976
Enterococcus Faecalis %	7.8	8.2	0.414
Staphylococcus Haemolyticus %	2.6	5	0.536
Staphylococcus Aureus %	2.6	4.4	0.273
Pseudomonas Aeruginosa %	9.5	2.5	0.346
Candida Albicans %	1.7	1.4	0.721
Corynebacterium Striatum %	1.7	1,3	0.661
Enterobacter Cloacae %	0.9	1,3	0.423
Enterococcus Avium %	1.7	1.3	0.589
Staphylococcus Capitis %	2.6	1.9	0.638
Haemophilus İnfluenzae %	2.6	0.6	0.999
Providencia Rettgeri %	0.9	1.2	0.488
Streptococcus Pneumoniae %	1.7	0.6	0.885
Staphylococcus Caprae %	0.9	-	-

Table 3. Resistant microorganism breeding sites for 6 months before and after Covid-19 pandemic

	Pre Covid-19 MDR (+) n=118	Post Covid-19 MDR (+) n=157	P value
Peripheral Blood Culture %	36.2	30.2	0.428
Tracheal Aspirate Sample %	23.3	26.5	0.896
CSF %	11.2	14.5	0.899
Catheter Blood Culture %	12.1	13.8	1,000
Urine Sample %	11.2	8.2	0.310
Surgical Material %	3.4	3.1	0.620
Wound Culture %	2.6	3.1	0.955

CSF: Cerebrospinal Fluid

The mortality rates of patients with MDR microorganisms detected in culture follow-ups in the ICU of our hospital was 36.4% in the first 6 months period (before the COVID-19 pandemic) and 51.6% in the second 6-month period (COVID-19 pandemic period) and this increase was statistically significant (Fig. 2) ($p < 0.05$).

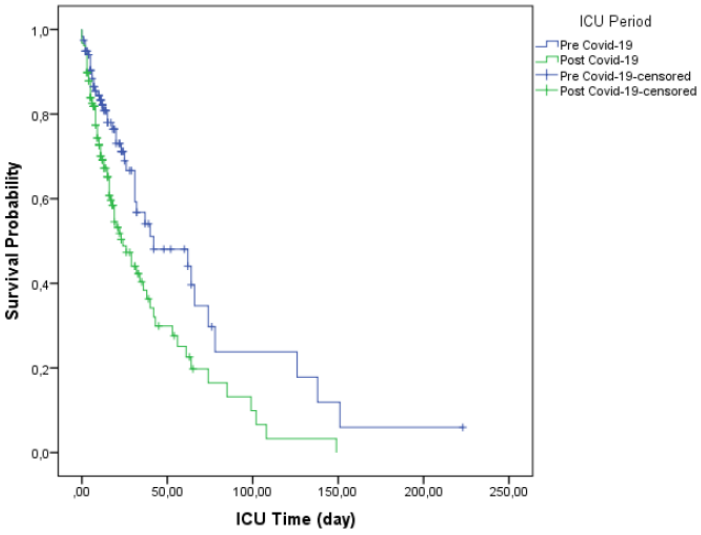

Fig 2. Mortality rates with Kaplan Meier curve in patients with resistant microorganism culture (+) in Intensive Care Unit during Pre Covid-19 (6 months before Covid-19) and Post Covid-19 (6 months after Covid-19) periods, ICU: Intensive Care Unit ($p < 0.05$)

4. Discussion

MDR microorganism culture-positive rates increased statistically significantly during the pandemic period compared to the prepandemic period in the patients included in the present study. MDR microorganism species and growth sites during the pandemic period were found to be similar to those of prepandemic period. During the COVID-19 pandemic period, it was observed that among important MDR microorganisms; incidence of *Acinetobacter baumannii* (14.7% / 20.1%) and *Klebsiella pneumoniae* (9.5% / 11.9%) increased, whereas that of *Pseudomonas aeruginosa* (9.5% / 2.5%) decreased.

MDR infections are a growing public health problem.(11) Risk factors for the development of resistant infections observed in ICUs are mainly stated as sex, surgical history, central venous catheterization, mechanical ventilation, previous antibiotic therapy, and duration of stay in the ICU (12-14).

Sex is a controversial risk factor for MDR microorganism growth (15). In a meta-analysis evaluating 17 studies, male sex was specified as a risk factor for MDR growth, and it was explained withpossible related physiopathology, physiological differences, and lifestyle (12). In our study, MDR microorganisms were observed in 151 male and 124 female patients in the total study period, and a significant relationship was found between the presence of MDR microorganism culture, which increased during the pandemic period compared to the prepandemic period, and female sex. In previousstudies, urinary tract infections in particular are stated as a risk factor for MDR microorganism growth in patients of the female sex (16). In our data, no relationship could be demonstrated between female/malesexand MDR microorganism growth sites.

Surgical procedures, stress response, medical treatments during the process, and surgery-related immunosuppression increase the possibility of the occurrence of MDR microorganisms (17). In our center, based on the guidelines of our country's Ministry of Health, elective surgeries were postponed within the framework of the fight against the pandemic, while emergency and malignancy surgeries continued to be performed. Therefore, the number of postoperative patients admitted to our ICU decreased during the pandemic period (76.7% / 60.4%). Despite decreased number of surgical procedures being performed in our center during the pandemic period, the incidence rate of MDR microorganisms observed in the ICU increased compared to that of the pre-pandemic period.

Immunodeficiency occurring in patients with malignancy increases the likelihood of MDR microbial growth (18). When our data are examined, it is observed that admission of patients with malignancy to the ICU increased significantly between the periods before and after the pandemic. The presence of malignancy and the likelihood of detection of MDR microorganisms were directly correlated in our study. Most of the patients with malignancy admitted to the ICU during the pandemic period were admitted for postoperative follow-up rather than due to terminal malignancy and possible complications. It was observed that the ratio of patients with malignancy and those with MDR samples detected to non-operative patients admitted to postoperative intensive care before pandemic was 86.4%, whereas the corresponding ratio during the pandemic was 71.3%. Since most palliative care units in our country were transformed into “COVID-19 ICUs” during the pandemic period, treatment of the patient population for whom the follow-up and treatment processes should be carried out mainly in palliative care centers was arranged in “Non-COVID-19 Internal Surgery ICUs” As a result, the rate of patients with malignancy accepted for medical treatment, which was 13.6% before the pandemic in our ICU where internal surgery patients were admitted, increased to 28.7% during the pandemic period. Despite the generally reduced number of surgical procedures, the increased rate of patients with malignancy being admitted to the ICU during the postoperative period might have contributed to the increased incidence of MDR microorganisms.

It is known that invasive procedures in ICUs increase the rate of MDR microbial reproduction (19, 20). Pathogenic microorganisms colonize and multiply in the invasive material (such as a central venous catheter, endotracheal tube, and urinary catheter) inserted for prolonged periods and

consequently increase the possibility of infection. MDR infections can be reduced with proper nursing care and catheter management (21, 22). During the pandemic period, 18 healthcare professionals (3 doctors, 3 assistant healthcare personnel, 12 nurses) in our ICU were infected with SARS-CoV-2. The staff shortage that occurred during the treatment and quarantine process of infected healthcare professionals was filled with healthcare professionals who did not have sufficient intensive care experience. As a result, the average level of intensive care experience of the nurses in our center, who were the most affected group, decreased during the pandemic period. In our study, it was found that decreased intensive care experience level correlated with the prevalence of MDR microorganisms.

When the mortality rates before and during the pandemic period were compared, it was observed that the mortality rate was significantly higher during the pandemic period. Admission of the increased number of patients with malignancy to our ICU during the pandemic period could have led to an increased mortality rate. However, an increase in mortality during the pandemic period was also observed in patients without malignancy according to the results of the subgroup analyses performed on these patients.

At present, the world is facing a test of large magnitude in the form of COVID-19. However, it is likely that we will also encounter problems triggered by the pandemic in addition to the pandemic itself. Although a solution for antibiotic resistance does not exist at the moment, it is important to identify the factors that cause its increased prevalence. We believe that our study, by revealing the increased prevalence of MDR microorganism growth in the ICU of our center during the pandemic period, will enable healthcare personnel worldwide to take adequate measures to avoid this public health issue.

Conflict of interest

None to declare.

Acknowledgments

None to declare.

References

1. Morens DM, Daszak P, Taubenberger JK. Escaping Pandora's Box - Another Novel Coronavirus. N Engl J Med. 2020;382(14):1293-5. doi: 10.1056/NEJMp2002106. PubMed PMID: 32101660.
2. WHO. Coronavirus Disease (COVID-19) Dashboard. Data last updated: 2021/6/03.
3. Song Y, Zhang M, Yin L, Wang K, Zhou Y, Zhou M, et al. COVID-19 treatment: close to a cure? A rapid review of pharmacotherapies for the novel coronavirus (SARS-CoV-2). International Journal of Antimicrobial Agents. 2020;56(2):106080. doi: https://doi.org/10.1016/j.ijantimicag.2020.106080.
4. Alzyood M, Jackson D, Aveyard H, Brooke J. COVID-19 reinforces the importance of handwashing. J Clin Nurs. 2020;29(15-16):2760-1. Epub 2020/05/15. doi: 10.1111/jocn.15313. PubMed PMID: 32406958; PubMed Central PMCID: PMCPMC7267118.
5. Ruuskanen O, Lahti E, Jennings LC, Murdoch DR. Viral pneumonia. Lancet. 2011;377(9773):1264-75. doi: 10.1016/S0140-6736(10)61459-6. PubMed PMID: 21435708; PubMed Central PMCID: PMCPMC7138033.
6. Organization WH. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance, 13 March 2020. World Health Organization, 2020.
7. Langford BJ, So M, Raybardhan S, Leung V, Westwood D, MacFadden DR, et al. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2020;26(12):1622-9. Epub 07/22. doi: 10.1016/j.cmi.2020.07.016. PubMed PMID: 32711058.
8. WHO. Clinical management of COVID-19. WHO-2019-nCoV-clinical-20205-eng.
9. saglik.gov.tr. covid-19 rehberi eriskin hasta tedavisi. covid19saglikgovtr/Eklenti/39061/0/. 2020.
10. Cai H, Tu B, Ma J, Chen L, Fu L, Jiang Y, et al. Psychological Impact and Coping Strategies of Frontline Medical Staff in Hunan Between January and March 2020 During the Outbreak of Coronavirus Disease 2019 (COVID19) in Hubei, China. Med Sci Monit. 2020;26:e924171. doi: 10.12659/MSM.924171. PubMed PMID: 32291383; PubMed Central PMCID: PMCPMC7177038.
11. Jolivet S, Lolom I, Bailly S, Bouadma L, Lortat-Jacob B, Montravers P, et al. Impact of colonization pressure on acquisition of extended-spectrum β-lactamase-producing Enterobacterales and meticillin-resistant Staphylococcus aureus in two intensive care units: a 19-year retrospective surveillance. J Hosp Infect. 2020;105(1):10-6. Epub 2020/02/25. doi: 10.1016/j.jhin.2020.02.012. PubMed PMID: 32092367.
12. Ang H, Sun X. Risk factors for multidrug-resistant Gram-negative bacteria infection in intensive care units: A meta-analysis. International Journal of Nursing Practice. 2018;24(4):e12644. doi: https://doi.org/10.1111/ijn.12644.
13. Kaye KS, Patel DA, Stephens JM, Khachatryan A, Patel A, Johnson K. Rising United States Hospital Admissions for Acute Bacterial Skin and Skin Structure Infections: Recent Trends and Economic Impact. PLoS One. 2015;10(11):e0143276. doi: 10.1371/journal.pone.0143276. PubMed PMID: 26599005; PubMed Central PMCID: PMCPMC4657980.
14. Chelazzi C, Pettini E, Villa G, De Gaudio AR. Epidemiology, associated factors and outcomes of ICU-acquired infections caused by Gram-negative bacteria in critically ill patients: an observational, retrospective study. BMC Anesthesiol. 2015;15:125. doi: 10.1186/s12871-015-0106-9. PubMed PMID: 26392077; PubMed Central PMCID: PMCPMC4578757.
15. Liu Q, Li W, Du X, Li W, Zhong T, Tang Y, et al. Risk and Prognostic Factors for Multidrug-Resistant Acinetobacter Baumannii Complex Bacteremia: A Retrospective Study in a Tertiary Hospital of West China. PLOS ONE. 2015;10(6):e0130701. doi: 10.1371/journal.pone.0130701.
16. Tenney J, Hudson N, Alnifaidy H, Li JTC, Fung KH. Risk factors for aquiring multidrug-resistant organisms in urinary tract infections: A systematic literature review. Saudi Pharmaceutical Journal. 2018;26(5):678-84. doi: https://doi.org/10.1016/j.jsps.2018.02.023.
17. Hogan BV, Peter MB, Shenoy HG, Horgan K, Hughes TA. Surgery induced immunosuppression. The Surgeon. 2011;9(1):38-43. doi: https://doi.org/10.1016/j.surge.2010.07.011.

18. Patolia S, Abate G, Patel N, Patolia S, Frey S. Risk factors and outcomes for multidrug-resistant Gram-negative bacilli bacteremia. Therapeutic advances in infectious disease. 2018;5(1):11-8. Epub 09/12. doi: 10.1177/2049936117727497. PubMed PMID: 29344356.

19. Timsit JF, Schwebel C, Bouadma L, Geffroy A, Garrouste-Orgeas M, Pease S, et al. Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: a randomized controlled trial. Jama. 2009;301(12):1231-41. Epub 2009/03/26. doi: 10.1001/jama.2009.376. PubMed PMID: 19318651.

20. Jung JY, Park MS, Kim SE, Park BH, Son JY, Kim EY, et al. Risk factors for multi-drug resistant Acinetobacter baumanniibacteremia in patients with colonization in the intensive care unit. BMC Infectious Diseases. 2010;10(1):228. doi: 10.1186/1471-2334-10-228.

21. Lebeaux D, Fernández-Hidalgo N, Chauhan A, Lee S, Ghigo JM, Almirante B, et al. Management of infections related to totally implantable venous-access ports: challenges and perspectives. Lancet Infect Dis. 2014;14(2):146-59. Epub 2013/12/10. doi: 10.1016/s1473-3099(13)70266-4. PubMed PMID: 24314751.

22. Osti C, Wosti D, Pandey B, Zhao Q. Ventilator-Associated Pneumonia and Role of Nurses in Its Prevention. Journal of the Nepal Medical Association. 2017;56(208).