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EPIDEMIOLOGICAL CHARACTERISTICS OF HOSPITAL INFECTIONS CAUSED BY *CLOSTRIDIUM DIFFICILE* AT THE UNIVERSITY CLINICAL CENTRE OF NIŠ

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Hospital (nosocomial, hospital-acquired) infections represent the greatest health challenge in more developed countries worldwide. Infections caused by the bacterium *Clostridium difficile* have been a serious medical problem for years. Despite the constant progress and improvement of diagnostic and therapeutic procedures, they still represent one of the most frequent and most severe hospital-acquired infections, and their incidence rate, mortality rate, as well as severity of their clinical picture are all on the rise. This paper aimed to analyse the epidemiological situation surrounding hospital-acquired infections caused by the bacterium *Clostridium difficile* at the University Clinical Centre of Niš between 2015 and 2019. In this study, *Clostridium difficile* was the most frequent cause of hospital-acquired gastrointestinal infections and was identified in as many as 48% of the studied samples. Preventive measures to control the spread of *Clostridium difficile* in a hospital environment are based on identifying transmission routes. In 1995, the first prevention and control guidelines were issued, while the Center for Disease Control and Prevention in Atlanta (CDC) modified the guidelines to control the spread of *Clostridium difficile* in health facilities, which were re-evaluated in 2005, while hygiene guidelines following contact with a patient infected with *Clostridium difficile* were added. The European Centre for Disease Prevention and Control (ECDC) published a new set of guidelines in 2008, while the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA) published the most recent set of guidelines in 2010. A comprehensive examination into the interplay of different aspects of important factors dealing with *C. difficile* would provide a more detailed understanding of the various factors that could inform academics and practitioners and improve theoretical knowledge and actual practices in this really important area of public health. In that sense, the study of potential and significant factors which could have a significant impact on the health of the population, especially illnesses caused by the bacterium *C. difficile* in a hospital environment, should be an imperative in the scientific and professional sphere.

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Introduction

Hospital (nosocomial, hospital-acquired) infections (HIs) represent the greatest health challenge in the developed countries of the world. They include infections contracted by both patients and staff in hospitals or other health facilities. They can manifest as a local or a systemic illness (conditions) which represents the body's response to the presence of an infective agent (one or more) or its toxins, not found in the patient, when the patient was not in an incubation period before admission to the hospital or some other health institution (1–3).

Despite the considerable progress in the development of medicine, as well as the progress made in further developing hospital epidemiology, according to the World Health Organization (WHO), hospital-acquired infections are to this day a global problem which considerably increases overall morbidity and mortality, lengthens treatment time, and increases the overall cost of healthcare. The spread of multidrug-resistant

pathogen bacteria is a particular problem, as is the transmission of infections onto healthcare workers and into the environment (4, 5).

Infections caused by the *Clostridium difficile* (*C. difficile*) bacteria have been a serious medical problem for years. Despite the constant progress and improvement of diagnostic and therapeutic procedures, *C. difficile* infections (CDIs) still represent one of the most frequent and severe hospital-acquired infections, and their incidence rate, mortality rate, and the severity of the clinical picture of a CDI are all on the rise (5, 6). *C. difficile* can normally be found among 3% of the adult population, while the carriage of this bacterium in the digestive tract of hospitalized patients is much higher and reaches up to 21% (8, 9).

This paper aimed to examine the epidemiological situation related to hospital-acquired infections caused by the bacterium *C. difficile* at the University Clinical Centre of Niš from 2015 to 2019. By determining the basic epidemiological characteristics, we obtained the necessary elements to form guidelines for the measures and procedures aimed at preventing and controlling hospital-acquired infections caused by these bacteria at the University Clinical Centre of Niš.

Materials and Methods

This paper includes data from the archives of the Institute of Public Health Niš, the Centre for Disease Control and Prevention, as well as reports of the Department of Sanitary and Epidemiological Supervision of the University Clinical Centre of Niš, including reports on trends in nosocomial infections caused by the bacterium *C. difficile* at the University Clinical Centre of Niš from 2015 to 2019, reports on trends in nosocomial infections caused by the bacterium *C. difficile*, and reports on patients hospitalized at the University Clinical Centre of Niš.

A descriptive method was used to analyse the data. All the data were statistically processed using Microsoft Office and Excel (version 2019).

Results

The University Clinical Centre of Niš consists of 36 organizational units (OUs) of which 14 OUs are clinics of particular surgical branches. In 2018, the General Surgery Clinic was reorganized, and the following clinics were formed: the Abdominal Surgery Clinic, Endocrine Surgery and Breast Surgery Clinic, Vascular Surgery Clinic, Digestive Surgery Clinic, and as a special unit, the Anaesthesiology and Intensive Therapy Clinic.

The data analysis is shown in Table 1, and based on it, we can conclude that in 2015, most HIs caused by the bacterium *C. difficile* were reported in the Physical Medicine and Rehabilitation Clinic (16 infections) and the Gynaecology and Obstetrics Clinic (15), with the highest incidence rate reported in the Physical Medicine and Rehabilitation Clinic (14.16%) and the Urology Clinic (10.68%). The Endocrinology, Haematology, Infectious Disease Clinics, as well as the Vascular, Cardiology, and Paediatric Surgery Clinics, had no instances of infections caused by the bacterium *C. difficile* (Table 1).

In 2016, most hospital-acquired infections caused by *C. difficile* were reported in the Cardiology Clinic (12), while the highest incidence rate was reported in the Physical Medicine and Rehabilitation Clinic (5.38%). The Endocrinology, Haematology, Nephrology, Oncology, Infectious Disease, Paediatric, Gynaecology, as well as the Vascular and Paediatric Surgery Clinics had no instances of hospital-acquired infections caused by the bacterium *C. difficile*.

In 2017, the greatest number of HIs caused by the bacterium *C. difficile* were reported in the Cardiovascular Surgery Clinic (10) and the Nephrology and Neurosurgery Clinics (8). The highest incidence rate for that year was reported in these clinics. The Oncology and Paediatric Clinics, as well as the Vascular and Paediatric Surgery Clinics, had no infections caused by the bacterium *C. difficile*.

Based on the analysis of data from 2018, most of the HIs caused by the bacterium *C. difficile* originated from the Neurosurgery Clinic (10), which had the highest noted incidence rate (6.39%). In the remaining clinics, a significantly lower number of incidences were noted.

Finally, in 2019, most of the HIs caused by the bacterium *C. difficile* were reported in the Nephrology Clinic (7), which also had the highest incidence rate (5.87%). In the Endocrinology, Haematology, Paediatric, Oncology, and Neurology Clinics, as well as the Vascular and Paediatric Surgery Clinics, no hospital-acquired infections caused by the bacterium *C. difficile* were reported.

Epidemics in the University Clinical Centre of Niš

From 2015 to 2019, there were several epidemics at the University Clinical Centre of Niš, two of which were epidemics in the operating theatres, in 2015 and 2016, at the General Surgery Clinic.

Table 1. The number of findings and the incidence rate of HI caused by the bacterium Clostridium difficile from 2015 to 2019

CLINIC	The number of findings/ incidence rate in 2015	The number of findings/ incidence rate in 2016	The number of findings/ incidence rate in 2017	The number of findings/ incidence rate in 2018	The number of findings/ incidence rate in 2019
CARDIOLOGY	*6/1.13*	12/2.31	6/1.13	1/0.18	2/0.35
GASTROENTEROLOGY AND HEPATOLOGY	*6/2.52*	8/3.32	2/0.93	2/1.07	2/1.08
ENDOCRINOLOGY	0.00	0.00	1/0.80	0.00	0.00
HAEMATOLOGY	0.00	0.00	1/0.88	0.00	0.00
NEPHROLOGY	10/9.16	0.00	8/7.92	1/1.00	7/5.87
ONCOLOGY	2/0.69	0.00	0.00	0.00	0.00
INFECTIOUS DISEASE	0.00	0.00	4/3.82	2/2.18	4/5.27
PEDIATRIC	3/0.37	0.00	0.00	0.00	0.00
PULMOLOGY	3/1.13	3/1.16	1/0.41	0.00	2/1.43
NEUROLOGY	10/5.28	0.00	6/3.39	0.00	0.00
REHABILITATION	16/14.16	6/5.38	3/2.91	1/0.94	5/4.94
GENERAL SURGERY	10/3.37	2/0.66	2/0.67	0.00	0.00
NEUROSURGERY	13/8.80	3/2.01	8/	10/6.39	4/2.33
ORTHOPEDIC	3/1.46	2/1.02	4/2.03	0.00	1/0.49
UROLOGY	10/10.68	8/4.20	3/1.74	0.00	3/1.61
VASCULAR SURGERY	0.00	0.00	0.00	0.00	1/2.13
PLASTIC SURGERY	2/2.27	3/3.75	1/1.03	0.00	0.00
CARDIOSURGERY	0.00	5/3.56	10/7.69	1/1.22	1/2.34
GYNAECOLOGY	15/2.28	0.00	6/0.85	0.00	1/0.15
PEDIATRIC SURGERY	0.00	0.00	0.00	0.00	0.00
EMERGENCY AND THORACIC SURGERY	2/1.75	4/2.63	1/0.72	1/1.77	1/1.36

An epidemic caused by the bacterium *Clostridium difficile* in the Neurosurgery

Clinic of the University Clinical Centre of Niš in 2015

A hospital epidemic caused by the bacterium *C. difficile* in the Neurosurgery Clinic of the University Clinical Centre of Niš was declared on April 28, 2015. An epidemiological study determined that the epidemic began on April 22, 2015, when three patients contracted the infection (two females and one male). The number of exposed patients and health workers totalled 95. Following adequate and rapid implementation of measures, the spread of the bacteria in hospital conditions was prevented, and the epidemic was called off on May 6, 2015. There were no casualties.

The source of the contagion was not determined. The patients exhibited the following clinical symptoms: watery stools, weakness, and fatigue. The proposed measures to control the epidemic were: reporting the epidemic, reporting

the infected patients, epidemiological testing, and isolation of the infected; acquiring stool samples from all the exposed patients for laboratory analysis; spatial and personal isolation; heightened measures of general and personal hygiene of the patients and staff; more frequent cleaning of the wards with bleach-based chemical products; the use of gloves and single-use lab coats (PVC aprons); reduced visits; prohibiting outside food intake; as needed, consulting with an infectious disease specialist; health-related and educational work with everyone involved.

An epidemic caused by the bacterium *Clostridium difficile* at the Neurology Clinic of the University Clinical Centre of Niš in 2015

A hospital epidemic caused by the bacterium *C. difficile* in the Neurology Clinic of the University Clinical Centre of Niš was declared on July 14, 2015. Through an epidemiological analysis, it was determined that the epidemic broke out on June 24, 2015, when three patients became infected (one female and two males). The number of exposed patients and healthcare workers amounted to 57. After adequate and rapidly implemented measures, the spread of the bacteria in hospital conditions was stopped, and the epidemic was called off on July 28, 2015. There were no casualties.

The source of the contagion was not determined. The patients had the following clinical symptoms: watery stools, weakness, and fatigue. The proposed measures to control the epidemic covered the following steps: reporting the epidemic; reporting the infected patients; epidemiological testing and isolation of the infected; acquiring stool samples from all the exposed patients for laboratory analysis; spatial and personal isolation; heightened measures of general and personal hygiene of the patients and the staff; more frequent cleaning of the wards with bleach-based chemical products; the use of gloves and single-use lab coats (PVC aprons); reduced visits; prohibiting outside food intake; as needed, consulting with an infectious disease specialist; health-related and educational work with everyone involved.

Discussion

The problem of hospital infections emerged with the introduction of hospital treatment. Little was known about the causes and means of transmission of HIs, and virtually nothing was known about disinfection, sterilization, and aseptic techniques (10–12). The work of Ignaz Philipp Semmelweis provided significant progress in that respect, and remains an example of the importance of epidemiology in the prevention and control of HIs, a full decade before the microbiological discoveries of Pasteur and Koch. Specifically, Semmelweis noted the difference in the maternal mortality rate in two different clinics of the maternity ward of the University Hospital in Vienna. A higher maternal mortality rate was registered in the clinic, which was part of the university hospital, where the doctors and students often, straight from performing autopsies, without previous preparations, took part in deliveries (Figure 1) (13, 14). In the clinic with a lower maternal mortality rate, the midwives were in charge of births. After implementing Semmelweis's guidelines on hand hygiene (hand disinfection using calcium hypochlorite), the maternal mortality rate was reduced significantly in both clinics, in the one that was part of the university hospital by 89%, and the one run by midwives by 52% (15, 16).

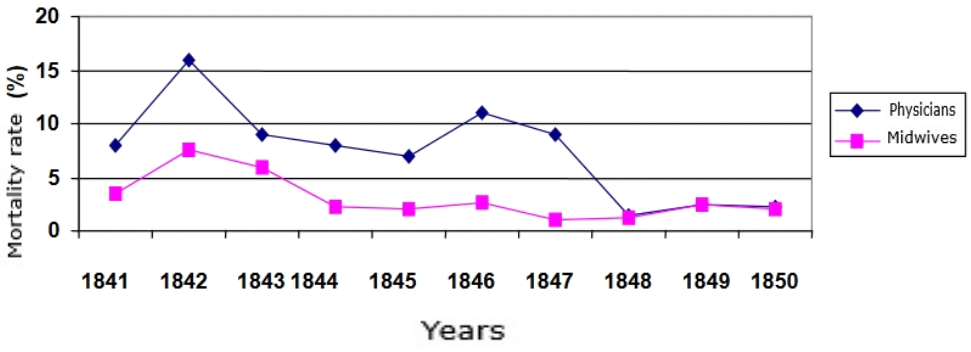

Figure 1. The maternal mortality rate due to infection in the University Hospital in Vienna, Austria, 1841–1850 (7)

All this is an indication that infections caused by the bacterium *C. difficile* have been a serious medical problem for years, especially when it comes to hospital-acquired infections. Considerable efforts have been invested into developing and improving national health strategies, considering that it is known that the quickest means of transmission is through direct contact with the source of the contagion or indirect contact involving the hands of the staff or contaminated medical equipment. It is estimated that at least 20% of HIs can be prevented by implementing specific means of supervision and control. In order to increase the quality of healthcare and the safety of the patients, it is necessary to gain as detailed an insight as possible into the nature and scope of the existing problem. Precisely because of that, epidemiological and microbiological studies of these infections are more than welcome. Their implementation is considerably advocated for and supported by European and American associations (the CDC, ECDC, and ECMID). Thus, this study too was carried out in accordance with their guidelines and with the desire to improve the quality of healthcare at the University Clinical Centre of Niš.

In this study, *C. difficile* was the most frequent cause of hospital-acquired infections of the gastrointestinal system, and it was identified in as many as 48% of the studied samples. Great differences were noted in the prevalence of HA-CDIs among various countries, which is a consequence of the varying frequency of testing, as well as the varying sensitivity and the specific nature of the diagnostic tests. This is probably a result of a lack of funding, but also diagnostic guidelines. Even though numerous European countries have developed regional and/or national networks for reporting CDIs, based on the data provided by the European Commission, monitoring is not standardized or legally binding in all European countries (17–22).

In order for *C. difficile* to cause diarrhoea, at least three conditions need to be met: a change in the normal ratio of bacteria inhabiting the digestive tract, the production of the *C. difficile* toxin, and particular characteristics on the part of the host. Normal intestinal flora among adults usually prevents the onset of colonies of *C. difficile*. *C. difficile* secretes two main toxins: enterotoxin (toxin A) and cytotoxin (toxin B). Previously, it was considered that the strain which only secretes toxin B (A-/B+) cannot cause damage to the mucus tissue of the colon. However, recent studies have shown that toxin B is the main determinant in the virulence and that avirulent strains only secrete toxin A (23, 24). Kuehne et al. (25, 26), based on a genetic analysis, determined that the production of one or both toxins indicates cytotoxin activity both *in vitro* and *in vivo*, so that the current hypothesis regarding the importance of both toxins for the onset of the illness has been adopted. Research done in the relevant laboratories for anaerobic infections of the Institute of Public Health Niš in 2014 resulted in the first isolates of *C. difficile* from 175 samples taken from the environment (23, 24, 27). In soil samples from within the University Clinical Centre of Niš, the parks in the city of Niš, and mud and sand samples from unregulated sewer systems in the municipality of Niška Banja, small numbers of the *C. difficile* bacteria which produce toxins (A+B+) as well as non-toxigenic isolates (A-B-) were registered. The role of the third toxin, known as the binary toxin, has still not been sufficiently studied, even though it caused epidemics associated with a very serious clinical picture (24, 28, 32). The *C. difficile* ribotype 027, which is toxin A-positive and toxin B-positive, also has a gene for a binary toxin, as well as an 18 bp deletion and a mutation on the tcdC gene, leading to a disruption in the expression of toxins A and B. This strain leads to the considerable production of the toxin *in vitro* and is particularly important as it is resistant to fluoroquinolones. A study carried out in 38 hospitals from 14 European countries indicated that the prevalence of the epidemic-inducing 027 strain of *C. difficile* was 6.2%, that all the strains were positive for the binary toxin, resistant to erythromycin and moxifloxacin, but also sensitive to metronidazole and vancomycin. However, the infected patients had a much more severe form of the illness (29). The model of origin of the CDI is as follows: patients are admitted to the hospital, and although intermittently exposed to spores of *C. difficile*, they have a negligible risk of the occurrence of the condition until the application of antibiotics. After they have been included, especially when it comes to broad-spectrum penicillins, cephalosporins, and clindamycins, the normal intestinal flora is disrupted, so that when *C. difficile* enters the digestive tract of such patients, it can proliferate and colonize the mucus tissue without causing any kind of symptoms of the illness (asymptomatic colonization), in the case of a strain which does not secrete toxins or a strain which secretes toxins but where an immunological response has been activated through the secretion of IgG. However, if there is no immunological response, symptomatic conditions will occur (30–32).

A high rate of possible carriage persists over the first 8 months of life, until normal intestinal flora is achieved, and then it decreases to about 2–3% among adults. A study carried out in Sweden indicated a carriage rate of 1.9% in the case of 594 volunteers, while Philips and Rogers (33) determined a rate of 2% after analysing 100 randomly selected stool samples, which were negative for other pathogens of the digestive tract. A special aspect of transmitting *C. difficile* is the carriage of this bacterium in the digestive tract of hospitalized patients. Carriage among hospitalized individuals is considerably higher (up to 21%) (5). In prospective studies in which patients were systematically examined for the presence of the bacteria during admission and one

or possibly two weeks after admission to hospital in Western Europe, the rate of *C. difficile* carriage after a stay in hospital ranged from 5.9 to 11%. This is a much higher rate than the 3% which occurs among the healthy adult population and could be a consequence of using antibiotics or colonisation during previous hospitalizations. A study carried out in Niš also indicated a higher carriage rate of *C. difficile* among hospitalized patients (7%), as well as the presence of toxigenic strains in the intestines of 2% of hospitalized patients with formed stool (34).

The incidence rates of CDIs vary depending on the type of hospital, country, and time of analysis. In all of North America, the incidence rate has been on the rise over the past fifteen years, despite preventive measures, with the highest noted in university hospitals. Over the past decade, the number of the infected has doubled (35, 36). In a prevalence study carried out in 2008 in 648 hospitals in the USA, it was determined that 13 out of 1,000 hospitalized patients (1.3%) were suffering from CDIs or were colonised (37, 38). That is a higher rate than previously predicted. This considerable increase can be ascribed to the occurrence of a very virulent ribotype 027 (NAP1/HI/27), which caused major epidemics in the USA and Canada from 2001 to 2003 (39–42). Even though the increase in the incidence rate can be a reflection of improved diagnostics and the identification of this condition, it is still clear that the incidence rate has actually increased. In Europe, the incidence rates also vary by country and hospital. It was recently estimated that the average incident rate in Europe was 4.1 per 10,000 hospitalized patients. It is important to note that, after many epidemics which were caused by ribotype 027, other ribotypes of *C. difficile* are now also prevalent in Europe. In a large-scale study which included data from 106 laboratories from 34 European countries (the aim was to compile data from at least one hospital in each country with a population of fewer than two million citizens, three hospitals in the case of two to twenty million citizens, and five hospitals in the case of more than twenty million citizens), according to the latest published data for November 2008, the most frequent ribotypes were 014 and 020 (identified in 19 countries), then 001 (in 13 countries), and 078 (in 18 countries). The PCR-ribotype 027 is sixth in terms of frequency of occurrence (41, 42). Few data exist on the frequency of occurrence of CDIs in the countries of South-East Europe. In the cited study for Europe, there are data for Bulgaria, Croatia, Slovenia, and Greece. The average incidence rate of hospital-acquired infections related to *C. difficile* ranges from three per 10,000 hospitalized patients in Bulgaria, six in Croatia, 19 in Slovenia and 29 in Greece (42, 44). In a study carried out during 2008 in Niš, in 12.4% of clinical stool samples obtained from patients experiencing diarrhoea, a cause was isolated. Of the overall number of positive isolates (351), *C. difficile* was isolated in 27.1% (45).

Even though most of the patients with CDIs are hospitalized, this condition should not be linked to medical interventions, since it can also occur in institutions for long-term care, housing for the elderly, and also in day hospitals. A reservoir could also be colonized (asymptomatic) or ill patients, and the hospital environment. Cases of CDAD noted in a health institution, where there are also numerous asymptomatic carriers in the same room, or on the same ward, should also be taken into consideration, as they represent a significant source of hospital diarrhoea. Still, routine screening is not recommended as a preventive measure. All surfaces and objects contaminated by spores of *C. difficile* (the floor, furniture, and medical equipment) are also a significant reservoir. The rate of contamination usually correlates with the epidemic nature of the illness.

According to the results of a study of European countries, serious comorbidities and antibiotic therapy were considered risk factors for older age patients (approximately two-thirds of those infected were over the age of 65). Almost all the patients who took antibiotics for three months before a *C. difficile* infection usually received cephalosporins, quinolones, and beta-lactamase inhibitors (28). Almost all the antibiotics administered either orally or parenterally can be linked to CDIs. The first antibiotic linked to this illness was clindamycin. More recent studies indicate that this illness is linked to therapy involving cephalosporins and fluoroquinolones (45, 46). The more recent occurrence of the resistance of *C. difficile* to fluoroquinolones is linked to their broad application (45, 46). Ceftriaxone is especially marked as an antibiotic that disrupts normal gastrointestinal flora, and has no effect on *C. difficile* itself, which promotes the occurrence of CDIs during its use in the recovery stage of intestinal flora. However, not all patients taking antibiotics will develop a CDI as well. What is also important is the ability of the immune system to produce the serum IgG anti-toxin A. This explains why CDIs are more frequent among the elderly. It should be mentioned that using more antibiotics at the same time is linked to a higher risk of CDI occurrence (42, 45).

The incidence rate of CDADs varies and ranges from 0.1 to 2% (47–51). This incidence rate includes patients who are hospitalized due to a *C. difficile* infection, as well as patients with a hospital-acquired *C. difficile* infection. Most researchers agree that the infections caused by *C. difficile* occur in a hospital environment. Insufficient attention is paid to the role and prevalence of *C. difficile* as the cause of diarrhoea in non-hospital environments.

Measures aimed at preventing the spread of *C. difficile* in hospital environments depend on the identification of transmission routes. Back in 1995, the first guidelines for the prevention and control

of CDIs were provided. The CDC in Atlanta published guidelines for the prevention and control of *C. difficile* in healthcare facilities, which were renewed in 2005, and recommendations for hand hygiene following contact with a patient with a CDI were added (52–54). The European Centre for Disease Prevention and Control (ECDC) published new guidelines in 2008, while SHEA and IDSA published the most recent set of guidelines in 2010 (55–57).

Conclusion

Illnesses caused by the bacteria *C. difficile* in a hospital environment represents a great challenge for modern-day medicine. An increase in the number of more severe cases and the irresponsible use of antibiotics are the main factors which contribute to their spread. Healthcare workers and health service providers are facing the important task of adopting suitable and proven preventive measures and, where necessary, therapeutic measures, so that the spread of the illness caused by *C. difficile* could fully be brought under control. A comprehensive examination into the interplay of different aspects of important factors dealing with *C. difficile* would provide a more detailed understanding of the various factors that could inform academics and practitioners and improve theoretical knowledge and actual practices in this really important area of public health. In that sense, the study of potential and significant factors which could have a significant impact on the health of the population, especially illnesses caused by the bacterium *C. difficile* in a hospital environment, should be an imperative in the scientific and professional sphere.

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EPIDEMIOLOŠKE KARAKTERISTIKE BOLNIČKIH INFEKCIJA IZAZVANIH BAKTERIJOM *CLOSTRIDIUM DIFFICILE* U UNIVERZITETSKOM KLINIČKOM CENTRU NIŠ

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Bolničke (nozokomijalne, intrahospitalne) infekcije predstavljaju najveći izazov u zdravstvu u razvijenim zemljama. Infekcije izazvane bakterijom *Clostridium difficile* ozbiljan su medicinski problem već godinama. I pored konstantnog napredovanja i usavršavanja dijagnostičkih i terapijskih procedura, ova infekcija je i dalje jedna od najčešćih i najtežih infekcija stečenih u bolničkoj sredini. Došlo je i do porasta incidencije, obolevanja, smrtnosti, kao i težine kliničke slike. Cilj ovog rada bio je da se sagleda epidemiološka situacija u vezi sa bolničkim infekcijama izazvanim bakterijom *Clostridium difficile* u Univerzitetskom kliničkom centru u Nišu u periodu od 2015. do 2019. godine. Ovo istraživanje je pokazalo da je bakterija *Clostridium difficile* bila najčešći uzročnik bolničkih infekcija gastrointestinalnog sistema; dokazana je čak kod 48% ispitanih uzoraka. Mere sprečavanja širenja bakterije *Clostridium difficile* u bolničkoj sredini zasnivaju se na poznavanju puteva prenošenja. Godine 1995. date su prve preporuke za prevenciju i kontrolu, a Centri za prevenciju i kontrolu bolesti u Atlanti objavili su preporuke za prevenciju širenja bakterije *Clostridium difficile* u zdravstvenim ustanovama, koje su dopunjene 2005. godine. Dodate su i preporuke za higijenu ruku posle kontakta sa bolesnikom sa bakterijom *Clostridium difficile*. Evropski centar za prevenciju i kontrolu bolesti publikovao je 2008. godine nove preporuke. Godine 2010. SHEA (engl. *Society for Healthcare Epidemiology of America*) i IDSA (engl. *Infectious Diseases Society of America*) izdale su najnovije preporuke. Sveobuhvatna istraživanja i objašnjenja u vezi sa međusobnim odnosima različitih aspekata važnih za borbu sa efektima prouzrokovanim bakterijom *Clostridium difficile* omogućila bi da se bolje i jasnije razumeju razni faktori koji su od značaja za unapređenje znanja ne samo članova akademske zajednice nego i profesionalaca u praksi. Na taj način mogla bi se proširiti teorijska saznanja, ali i poboljšati načini reagovanja u praksi u veoma važnoj oblasti javnog zdravlja. Dakle, studije o potencijalnim i značajnim faktorima koji utiču na zdravlje ljudi, a posebno o oboljenjima prouzrokovanim bakterijom *Clostridium difficile* u bolničkim uslovima, moraju se postaviti kao svojevrstan imperativ, kako u naučnoj sferi, tako i u medicinskoj praksi.

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***Ključne reči**: intrahospitalne infekcije, Clostridium difficile, prevencija i kontrola bolesti*