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Infection *Clostridium difficile* as increasing epidemiological issue

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Abstract

Introduction: *Clostridium difficile* as an infectious agent of pseudomembranous enterocolitis,
becomes more and more frequent problem among health facilities. Dread disease and its complications can be fatal, especially in elderly and infant group. Epidemiological analysis enables to highlight validity and importance of this issue in, and submit it to National Health Service.
The aim of the study is to show current epidemiological status concerning *Clostridium difficile* frequency in Poland for recent years.
Materials and methods: Data used for the epidemiological analysis was taken from reports of National Hygiene Institute such as „Choroby zakaźne i zatrucia w Polsce" and „Zakażenia *Clostridium difficile*" prepared by NPOA (Narodowy Program Ochrony Antybiotyków).
Results and conclusion: The level of *Clostridium difficile* infections is alarmingly high. Health
facilities should remain alert regarding the rate of carrier state among infant and hospitalized group especially because of complications risk.
Therefore, hygiene and aseptic conditions in medical institutions should be emphasised as well as appropriate antibiotic therapy.

Keywords: *Clostridium difficile***,** pseudomembranous enterocolitis, epidemiology

*Z*akażenia *Clostridium difficile* jako narastający problem epidemiologiczny

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Streszczenie

Wstęp: Rzekomobłoniaste zapalenie jelit, którego czynnikiem etiologicznym jest *Clostridium difficile* staje się częstym problemem placówek medycznych. Bakteria jest szczególnie niebezpieczna dla osób starszych i małych dzieci. Powikłania choroby mogą doprowadzić nawet do zgonu. Analiza epidemiologiczna pozwoli zwrócić uwagę, jak jest to ważny i aktualny problem w polskiej służbie zdrowia.

Celem pracy jest ukazanie aktualnej sytuacji epidemiologicznej dotyczącej występowania *Clostridium difficile* w Polsce w ostatnich latach.

Materiał i metoda: Materiałem wykorzystanym do analizy epidemiologicznej są dane z raportów „Choroby zakaźne i zatrucia w Polsce" Państwowego Zakładu Higieny oraz program „Zakażenia *Clostridium difficile*" Narodowego Programu Ochrony Antybiotyków.

Wyniki i wnioski: Niepokojąca jest duża liczba zachorowań oraz ciągły wzrost odnotowanych przypadków zakażeń *Clostridium difficile*. Niebezpieczny jest wysoki odsetek nosicieli u dzieci i osób hospitalizowanych, u których ryzyko powikłań jest bardzo duże.

W placówkach medycznych należy zwiększyć nacisk na higienę oraz stosowanie środków ochrony osobistej, stosować racjonalną antybiotykoterapię według zaleceń, a w przypadku podejrzenia wystąpienia ogniska postępować zgodnie z zaleceniami służb sanitarno-eoidemilogicznych.

Słowa kluczowe: *Clostridium difficile*, rzekomobłoniaste zapalenie jelit, epidemiologia

Introduction

Gastrointestinal infections are common epidemiological and social problem in Poland. In 2016, 23770 people became infected with bacterial ethology [1]. In 2015, more than 57,000 people were hospitalized with all intestinal infections [2]. The average duration of hospital stays of this patient in this category of ICD-10 [A00-A08] was 4.9 days and for persons over 65 years of age was up to 10.5 days. One of the ethological factors of bacterial intestinal infections, which epidemiological significance increased in last years is Clostridium difficile [2].

Clostridium difficile is a Gram-positive, absolutely anaerobic populating rod that produces toxins. It is commonly found in water, air, human and animal excrements, as well as surfaces in medical facilities and in soil. The optimum temperature of growth and toxins production is a temperature close to the temperature of the human body, i.e. 37°C. The most important way of transferring infections is the fecal-oral route. Moreover, bacteria produce two types of toxins: toxin A and toxin B, which are the most important virulence factor. While most pathogenic strains associated with Clostridium difficile infection produce both types of toxins, the importance of strains that only produce type B toxins has increased recently [3].

In recent years, a new strain of NAP1 (PCR 027 or B1 / NAP1 / 027) has emerged causing both hospital outbreaks and regional outbreaks. Viral virulent strain B1 / NAP1 is characterized by increased production of toxins A and B (16-23x more), binary toxin production, greater spore formation, resistance to fluoroquinolone, and more severe infections [3,4,5,6].

Materials and method

The aim of the study is to show current epidemiological status concerning *Clostridium difficile* frequency in Poland for recent years. Data used for the epidemiological analysis was taken from reports of National Hygiene Institute such as „Choroby zakaźne i zatrucia w Polsce" and „Zakażenia *Clostridium difficile*" prepared by NPOA (Narodowy Program Ochrony Antybiotyków).

Results

In 2013, 4716 cases (incidence rate 12.24/ 100 000) were registered, 6426 (incidence rate 16.69/ 100 000) in 2014, 8970 (incidence rate 23.31/ 100 000) in 2015, and 8736 (incidence rate 22.73/ 100 000) in 2016. By June 15, 2017, 6130 cases were registered with a maturity factor of 15.95/ 100 000. In the comparable period of 2016 there were 4480 cases and the maturity factor was 11.66/ 100 000.
The current epidemiological situation in Poland is presented in Fig. 1.

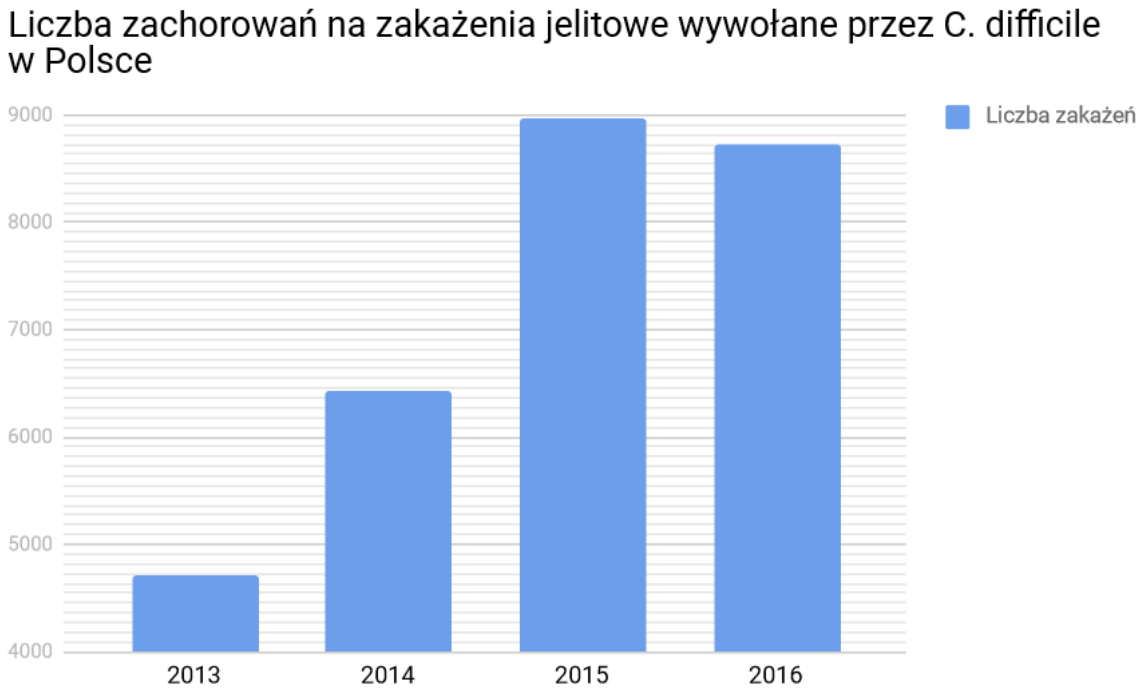

Fig. 1. The number of intestinal infections caused by *C. difficile* in Poland in the years 2013-2016

The overall epidemiological situation is as follows:

- 3% of the population is *C. difficile* carrier,
- 20-40% of hospitalized patients hospitalized are *C. difficile* carriers,
- 50-60% new-borns are *C. difficile* carriers.

Clostridium. difficile infection is responsible for 15-25% of the bacterial diarrhea.

Discussion

Clostridium difficile colonizes the large intestine of man. In most cases, in immunocompetent adults, the infection is asymptomatic. Similarly, asymptomatic progress occurs in newborns who do not yet have intestinal receptors for *C. difficile.* The use of antibiotics, especially broad-spectrum, causes physiological intestinal flora disturbances, which is responsible for the overgrowth of *C. difficile* in the intestine and the symptomatic course of the disease. Its typical image is diarrhea and other symptoms typical for colitis are caused by enterotoxic toxin A and cytotoxic toxin B. Some pathogenic strains also produce binary toxins, whose role in the pathogenesis of the disease is not yet well understood. A toxin-binding receptor is responsible for both the transport of toxin A and the toxin B. After entering the toxin cell, the pathways mediated by Rho-mediated proteins cause direct bowel injury, intracellular disorders, and colitis. Direct activation of neutrophils that aggravate the symptoms of death is caused by toxin A and toxin B by chemotaxis.

The most important risk factor for *C. difficile* infection is the use of broad-spectrum antibiotics that interfere with the natural bacterial flora of the gastrointestinal tract. The drugs with the highest risk of developing diarrhea or pseudomembranous colitis include penicillins, cephalosporins, fluoroquinolones and clindamycin [7,8,9]. Other risk factors include advanced age [10], immunosuppressant use, cytostatics, proton pump inhibitors [11], chronic renal failure, and chronic liver disease.

About 90% of cases of *C. difficile* disease are preceded by antibiotics 1-8 weeks earlier [112]. The course of infection is very diverse, from completely asymptomatic to severe symptoms of colitis resulting in acute bowel irritation due to strong interaction between the virulence factors of the pathogens and the host organism. Watery diarrhea with mucus or blood, lack of appetite, nausea, vomiting, slight raised body temperature and severe abdominal pain are the most common symptoms of *C. difficile* infection. In some cases, there is a fulminant course of illness in which, apart from diarrhea, there is diffuse, severe pain in the entire abdomen, flatulence and hypovolemia. This condition can lead to sepsis, colitis, and perforation of the intestines with diffuse peritonitis. Rarely occurring complications of the disease are protein-deficient enteropathy and symptoms beyond the colon such as appendicitis, reactive arthritis, and cellulitis [13,14,15,16]. *C. difficile* also causes recurrent infections, that is, conditions in which the symptoms of intestinal obstruction are re-established after the symptoms have completely resolved and the medication has stopped. They occur in about 20% of the patients [17].

Mortality is 6.1% for patients in whom intensive therapy is needed and 16.7% for patients infected with the virulent NAP1 strain [18, 19].

To prevent *Clostridium difficile* infections, we include general rules for early detection of all illnesses and strict isolation of all infected patients, as well as taking care of personal hygiene through frequent and thorough hand washing and cleaning and disinfection of the surface, especially the hospital area and people after contact with infected patients. The most important principle, however, is the avoidance of the use of wide-angle antibiotics, and the general limitation of the use of antibacterial drugs.

In case of *C. difficile* infection in hospital we should [20,21, 22,23,24]:

- implement patient contact isolation,
- staff and visitors should wear aprons and disposable gloves before entering the hall
- after contact with the patient and his surroundings, wash hands with soap and water, alcohol does not work well,
- the patient should be insulated to 48 hours after the diarrhea,
- surface disinfectants should be spore-effective agents in appropriate dilutions,
- medical equipment should be dedicated exclusively to patients infected with *C.*

difficile,

- the patient's room should undergo decontamination after the end of the stay.

Conclusions

In last five years, since Polish Institute of Hygiene separated *C. difficile* infection from other intestinal infection we observe continuous increase in the number of cases. This causes an increase in complications, including an increase in the number of surgical interventions, increases the cost of treatment, and increases mortality due to this. In addition, more and more often these infections occur in people outside of the standard risk groups. Combining these facts, as well as infectiousness and the ability to relapse, we have one of the most important challenges for modern medicine. It is also a challenge for the inadequate budget for health care in Poland and for finance in general as the overall cost of treatment and the costs of absenteeism are enormous. For the prevention and treatment of C. difficile-related intestinal infections, it is particularly important to be aware of the current guidelines published by the dedicated working groups, which are briefly cited in this article. It is also important to get acquainted with current research results on new strains, ways of spreading infection, and methods of treatment and prophylaxis. Improved surveillance methods are needed to monitor morbidity, identify endangered populations, and characterize the molecular epidemiology of *C. difficile* strains.

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