

APPEARANCE OF *CLOSTRIDIUM DIFFICILE* INFECTIONS IN HEALTH CARE INSTITUTIONS IN SLOVAKIA AND IN THE DISTRICT OF MARTIN

NOVAK M^{1,3}, MAZAKOVA I,³ SADLONOVA V², CERVENOVA T³, HUDECKOVA H.^{1,3}

¹Department of Public Health, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava

²Department of Microbiology and Immunology, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava

³Regional Public Health Authority with the seat in Martin

Abstract

Introduction: Decrease of nonspecific immunity in patients and the treatment with broad spectrum antibiotics form appropriate conditions for the appearance of medically severe *Clostridium difficile* infection (CDI) - enterocolitis that can have the characteristics of community or hospital acquired infection (HAI). The aim of our work is to identify the trend of their incidence in Slovakia and to define the risk groups according to age and department of hospitalisation.

Material and Methods: Retrospective analysis and comparison of the appearance of CDI was performed within the groups of patients hospitalised in health care institutions in the SR and those in the district of Martin during the period of years 2010 to 2017. The data of reported cases were taken from the Epidemiological information system of the Slovak Republic (EPIS SR), the source of demographic data was the National Center of Health Information.

Results: Analysis shows an important increase of incidence of CDI during years 2010 to 2017. Diseases had predominantly health care associated – nosocomial – character targeting mostly older patients (65+ - 24/10 000 in the Slovak Republic and 62/10,000 in the county of Martin) and less infants (7/10,000 and 11/10,000 respectively).

Conclusion: The results of our analyses are consistent with literature data about CDI enterocolitis and show their serious health and social impact in our society.

Key words: *Clostridium difficile*, hospital acquired infections, age groups, hospital departments

INTRODUCTION

Clostridium difficile infections (CDI) are becoming one of the leading topics of medical interest because of their increasing appearance. They are closely connected with previous antibiotic therapy. The increasing appearance of CDI is a global problem present in the Slovak Republic, too. CDI represent an important challenge of actual healthcare and are the risk for all hospitalised patients treated with antibiotics. Mostly affected are geriatric, polymorbid, and repeatedly hospitalised patients treated with broad spectrum antibiotics for long time (1, 2).

Existence of correct and exact information about the CDI is required for preparation of correct and effective regulations leading to the decrease of incidence of CDI and their impact. Standardised periodical or continual surveillance enables determination of epidemiological changes. That is why it is an indispensable tool for prevention and CDI infection control. ECDC prepared the project European *Clostridium difficile* Surveillance Network (ECDIS-Net) with the aim to solve this increasing problem. One of the tasks is to estimate the incidence of CDI in European hospitals and to evaluate the burden of the CDI (1).

Address for correspondence:

Mgr. Martin Novák, Department of Public Health, Jessenius Faculty of Medicine in Martin, Malá Hora 4B, 036 01 Martin, Slovak Republic;

E-mail: martin4novak@gmail.com; Phone number: +421 911886256

The aim of our research was to analyse the appearance of reported enterocolitis caused by *Clostridium difficile* in the health care institutions in the department of Martin and in the Slovak Republic and to determine how the appearance changed and developed during the years of interest.

METHODS

The group consisted of hospitalised patients with enterocolitis caused by *Clostridium difficile* in the district of Martin and in the Slovak Republic in years 2010 and 2017 who were reported to the EPIS. We retrospectively analysed data collected during the period from the 1st of January 2010 to the 31st of December 2017. The data from the Statistical Authority of the Slovak Republic and from the National Centre of Statistical Information of the Slovak Republic were used to calculate the overall and age-specific incidence – the Health Statistics Yearbook of the Slovak Republic from years 2010 to 2016.

RESULTS

The incidence of CDI in Slovakia was growing up ever year. From 2010 to 2017 it increased from 0.9 to 20.6/10,000 of hospitalised patients. The increase in the year 2017 in comparison with the year 2016 was 8.7%. Similarly increased the incidence of hospital acquired CDI (HAI-CDI) from 0.6 to 15.3/10,000. The increase in comparison with the year 2016 was 9.4%. Index of the mean incidence in the Slovak Republic in the years 2010 to 2016 was compared with the one for year 2017 being 2.7 for CDI and 2.4 for HAI-CDI.

The incidence of reported CDI and HAI-CDI was increasing in the health care institutions in the district of Martin during the observed period. In the years 2010 to 2017 the incidence of CDI increased from 3.7 to 45.1/10,000 of hospitalised patients. The rise of incidence of HAI-CDI was from 1.3/10,000 of hospitalised patients in the 2010 to 38.3/10,000 in the 2017. Index of the mean incidence in the district of Martin in the period of 2010 to 2016 distracted to the year 2017 was 2.3 for CDI and 2.8 for HAI-CDI. In 2017 the increase in number of cases in comparison with year 2016 was only mild. In 2016 we registered 20 community cases of CDI and 123 HAI-CDI cases, which represented the incidence of 44.7 reps. 37.7/10,000 patients. In 2017 the number of community CDI cases was 22 (incidence of 45.1/10,000) resp. 124 HAI-CDI cases (the incidence was 38.3/10,000) (Fig. 1).

The majority of the reported cases of CDI in 2017 was from Bratislava district (22.8%, 589 cases) and from Žilina district (21.0%, 542 cases). The minority of reported cases was from the county of Banská Bystrica (6.9%, 179 cases). In the period between the years 2010 and 2016 the majority of cases was reported from Bratislava and Žilina counties (25.7%, 219 cases and 17.7%, 151 cases respectively), the minority being in this case again from Banská Bystrica county (5.0%, 43 cases) (Fig 2).

Hospital associated *Clostridium difficile* infections in the Martin district formed 79.5% (419 cases) of the whole amount of reported diseases. During the period of interest their amount increased as well as their proportion to community infections. Before the year 2012 the community infections were predominant ones while from the year 2013 hospital associated infection of CDI were more common (Fig.3).

88.5% (1715 cases) of hospital associated cases of CDI in the Slovak Republic and 83.1% (103 cases) in Martin district were reported from internal departments in 2017. 7.4% (144 cases) of HAI-CDI cases were from surgical departments in the Slovak Republic and 10.5% (13 cases) of them in Martin district. 1.1% (22 cases) resp. 3.2% (4 cases) were reported from pediatric departments and 2.8% (54 cases) resp. 1.6% (2 cases) from anesthesiology-resuscitation departments (Fig.4).

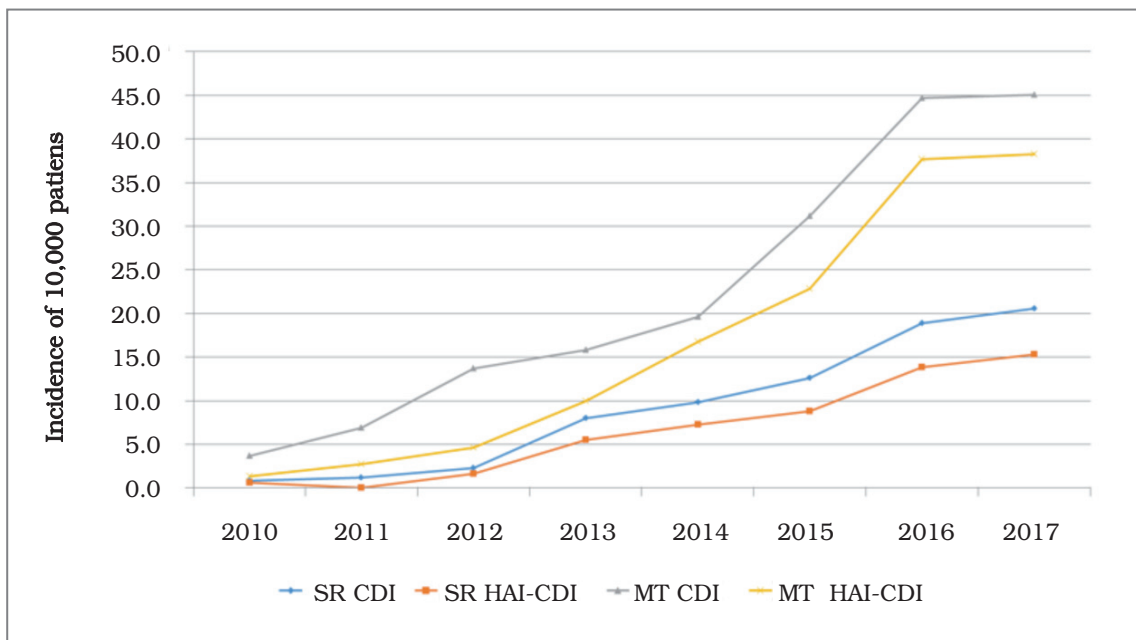


Fig. 1 Incidence of CDI and HAI-CDI (incidence in 10,000 patients *vertical axis*) in the health care institutions in the Slovak Republic (n=8500) and in the district of Martin (n=556) in the period from the 1st of Jan. 2010 to the 31st. of Dec.2017(*horizontal axis*)

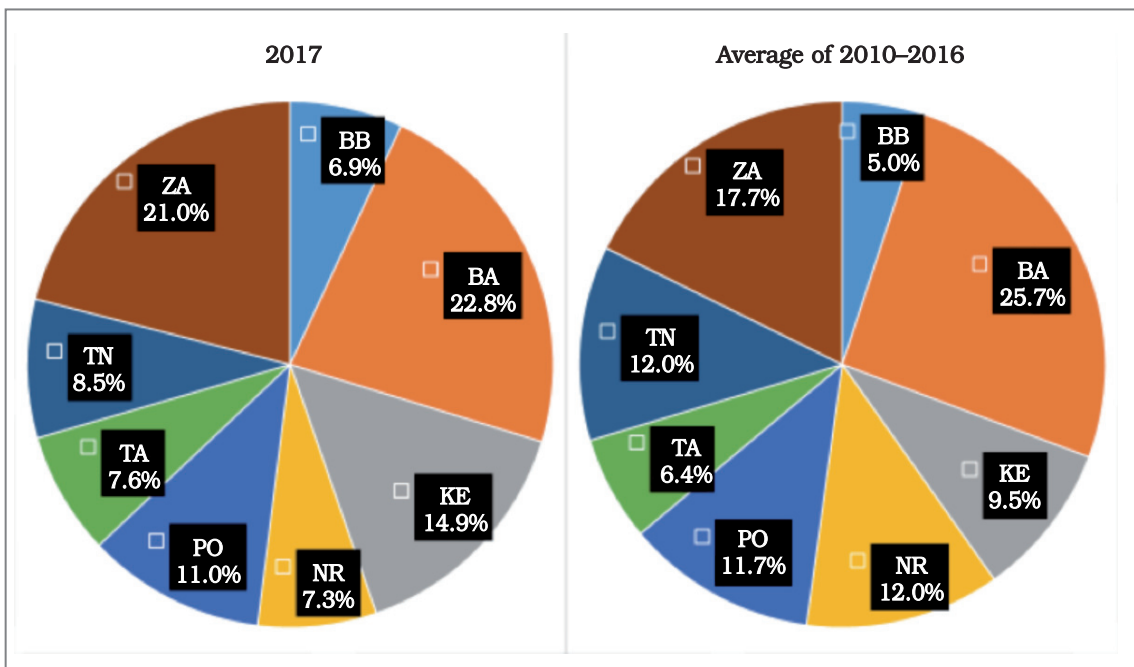


Fig. 2 Ratio of CDI cases in the health care institutions in Slovakia according to the counties in the year 2017 (n=2532) and in the period of years 2010-2016 mean value (n=5968).

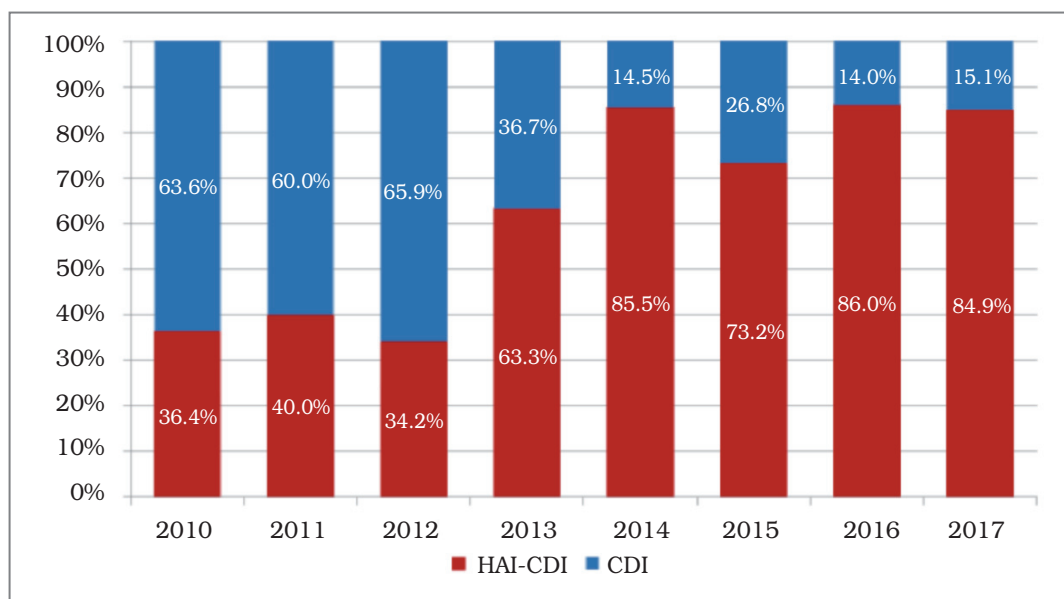


Fig. 3 Ratio of cases (*horizontal axis*) of community CDI and HAI-CDI in health care institutions in the district of Martin in the years of the period 2010–2017 (*vertical axis*) (n=556).

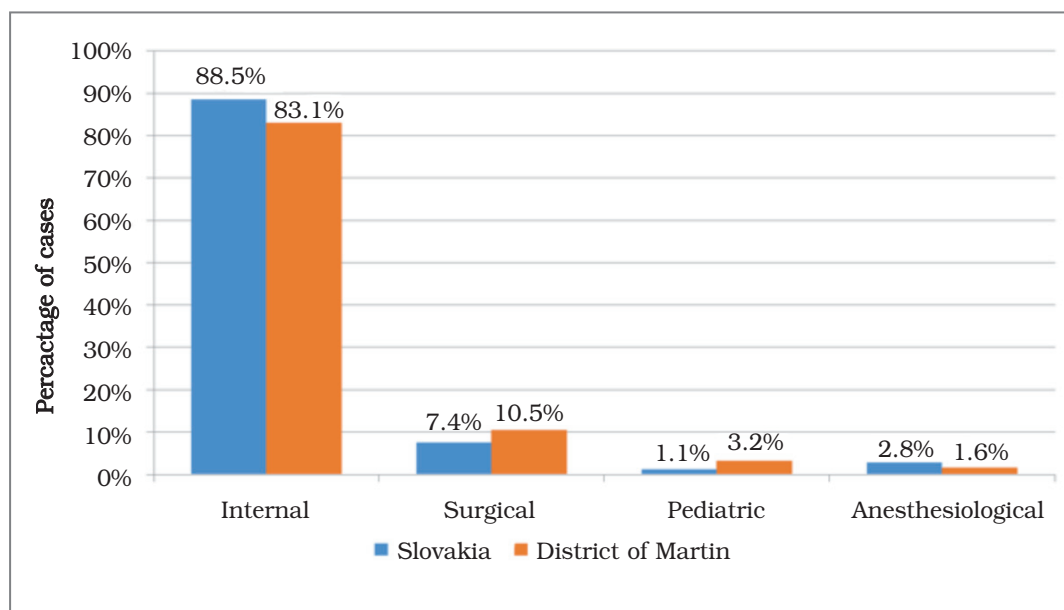


Fig. 4 Number of reported HAI-CDI in health care institutions in the Slovak Republic (n=1935) and in the district of Martin (n=124) to the characteristic of hospital department: internal, surgical, pediatric, anesthesiological, in the period from the 1st of Jan.2017 to the 31st of Dec.2017.

The incidence of patients in the age group of 65 year and more was 24/10,000 inhabitants of the Slovak Republic and 62/10,000 in the district of Martin. The incidence of infants (age group less than 1 year) in the Slovak Republic was 7/10,000 inhabitants(Fig 5).

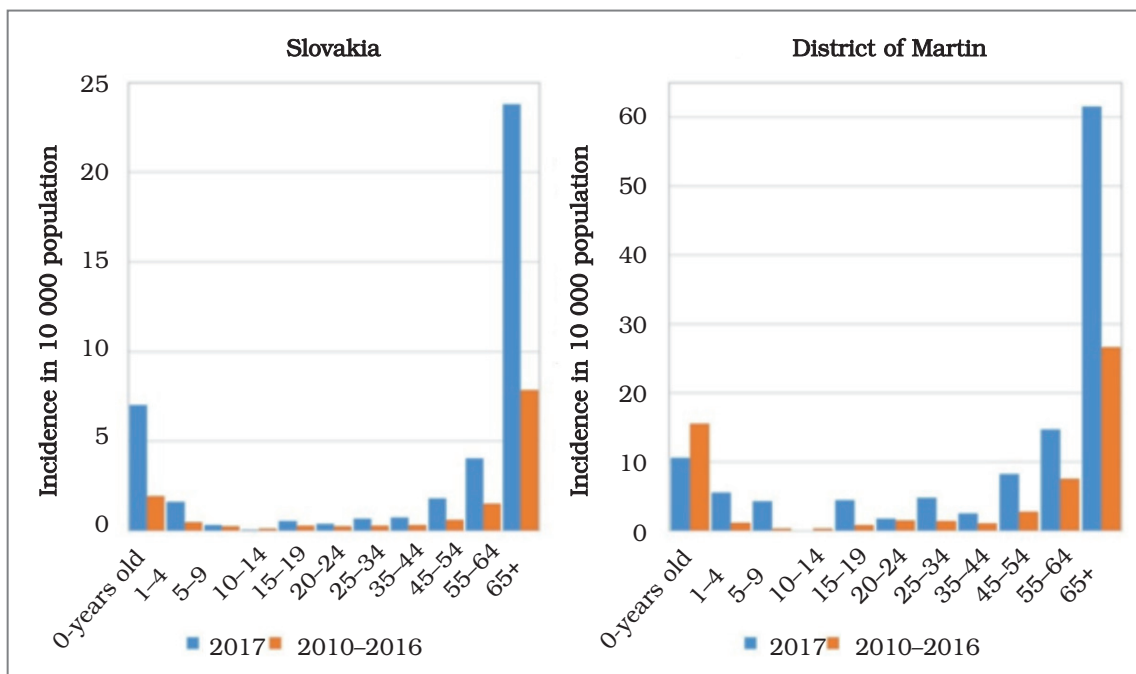


Fig. 5 Age specific incidence of CDI in the health care institutions in Slovakia (*left*) (n=8500) and in the district of Martin (*right*) (n=556) in the year 2017 (blue) and the mean of age distribution in the period from 2010 to 2016 (orange).

DISCUSSION

Etiology of CDI is *Clostridium difficile* anaerobic gram positive sporulating noninvasive and toxigenic bacterium that is usually transmitted via fecal oral transmission. It produces toxin A and B or binary toxin A/B. The CDI is typically presented by frequent diarrhoea (10–15 in a day) connected with abdominal pain and colitis. The course of the disease can vary from mild to a clinically serious one-pseudomembranous colitis (1, 2). Antibiotics are able to eliminate physiological microbial flora (microbiom) and this situation enables overgrowth of *Clostridium difficile* that is present in the colon in minor quantities and is resistant to broad spectrum antibiotics eliminating gram negative rods - facultatively anaerobic coliforms and gram-positive cocci. This is mostly a problem in the health care institutions where use or overuse of antibiotics (together with the neglected decontamination and hygiene) can lead to the outbreak of hospital associated *Clostridium difficile* infection HAI-CDI.

Enterocolitis caused by *Clostridium difficile* represents an important continuously increasing health problem. It touches community and hospital associated cases the incidence of which rises up every year. The incidence of CDI in 10,000 of hospitalised represented 0.9 in 2010 and 20.6 in 2017. The incidence of HAI-CDI increased as well. In 2010 the incidence of reported HAI-CDI was 0.6 and in 2016 it reached the level of 15.3 in 10,000 hospitalised patients. Besides the fact that the number of CDI is rising in the Slovak Republic the increasing incidence is mostly due to the better and more exact surveillance that is able to identify more infections. Anyway, the numbers do not probably reflect the exact situation in the country and the disease is underreported.

The number of cases of CDI is increasing every year also in the district of Martin, without regard if it is community infection or hospital acquired infection. The HAI-CDI started to be more frequently reported in the district of Martin in 2013.

The problem of the increasing number of CDI cases is well known in many countries in Europe as well as other continents of the world. The incidence of CDI in Europe and North America has been constantly increasing in the last 20 years (3). *Clostridium difficile* is overcoming other pathogens in number of caused HAI cases. It is becoming one of the most important microbes from the point of view of complications of therapy. The American Center for Disease Control (CDC) marked CDI as an urgent threat for emergent ATB resistance in the USA (4).

The incidence of CDI and HAI-CDI is increasing in Australia as well and in the years 2011 to 2013 74% of all cases of HAI infections were CDI cases (5). The global increase of community cases is registered while one third of them occurs in North America (6) and Europe (5,7). Fernanda C. Lessa et al. write that from 15,000 cases of CDI in USA in 2011, 65% were HAI-CDI and only 24.2% emerged during hospitalisation (8). Another study from the USA resulted in a statement that between the years 2001 and 2012 the number of CDI cases increased by 42% and in recurrent cases the increase of 118% was registered (9).

The hypervirulent strain 027 characterised by an extremely high and not controlled production of toxins is gradually more frequently reported from many countries (10). In Germany in Heese there was reported an increased incidence of CDI caused by this ribotype in 2011 – 2013 (11). In other study in the USA it is reported that the incidence of CDI correlated with the incidence of mentioned ribotype (027) that produces more toxins A and B and is resistant to fluorochinolons. In Slovakia there is one confirmed case of CDI 027 identified in connection with surveillance that was isolated in Nitra (027). In the district of Martin there has not been identified the ribotype 027 yet (12).

The increasing number of CDI and HAI-CDI cases is connected with the hospitalisation in health care institutions and the therapy there. 124 cases of all 146 reported CDI cases from healthcare institutions in the district of Martin in 2017 had characteristics of hospital acquired infection. Most of the cases (83.1%) were reported from internal medicine departments. The high number of CDI cases connected with hospitalisation is characteristic for all health care institutions. McDonald et al. published information that 94% of CDI cases were connected with previous health care and many of them presented outside the health care institution (after the treatment in medical outpatient office or after being released from hospitalisation) (4).

Use of antibiotics is another important risk factor. Longlasting ATB therapy and high doses of antibiotics are connected with a higher risk of CDI (13). Some antibiotics such as clindamycin, cephalosporins, and fluorochinolons represented higher risk than others. Rational indication of antibiotic therapy is a crucial tool of prevention of CDI (14,15).

Higher age is another risk factor for appearance of HAI-CDI. Patient of high age is usually polymorbid, he requires more frequent hospitalisation and use of more drugs, including ATB. All these favourises the appearance of HAI-CDI (16). Loo et al. qualified this risk and stated that the risk of *Clostridium difficile* infection connected with health care is increasing by 2% every year after the age of 18 (17). The reasons are multifactorial and can partially be connected with more frequent visits of the older people to the hospitals and also with the physiological changes during getting old. Majority of CDI reported in Slovakia as well as in Martin district were in the patient group of 65+. Children less than 1 year old were the second most common group with reported CDI in the Slovak Republic. In the district of Martin there is a local hospital that provides the most specialised health care, which can be the cause of some differences in age distribution of CDI infection when compared with the data from whole Slovakia.

The real number of patients colonised with *Clostridium difficile* is about 7-11% of hospitalised patient, 5-7% of residents in social care institutions, and 2% of outpatient medical offices according to the information of Public Health Authority of the Slovak Republic. It is probable that these numbers are not exact as some cases are not correctly reported or are not reported at all. That is why it is important to do the surveillance in such a way that it would identify the majority of new cases. At the same time it is important that the surveillance is performed universally – in the same way in all (or more) countries of the world to get comparable results

CONCLUSION

Our analysis shows that the global problem of increasing incidence of CDI is present in Slovakia and in the district of Martin. While cases with characteristics of hospital associated infections are increasing the ratio of HAI-CDI and CDI is also increasing. It is important to continue to watch the evolution of the trend on national and local levels and strictly follow the regulations for prevention of spread and outbreak of the CDI. Rational antibiotic therapy and isolation of infected patients can positively influence the situation. Correctly realised CDI surveillance can prevent the disease mostly in the risk groups.

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