

RESEARCH PAPER

Implementation of control measures against an outbreak due to *Clostridioides difficile* producing toxin B in a tertiary hospital in Mexico

OSCAR SOSA-HERNÁNDEZ¹, BERNARDINA MATÍAS-TÉLLEZ¹, JUANA GONZÁLEZ-MARTÍNEZ¹, ROCIO JUÁREZ-VARGAS¹, NORMA ELIZABETH GONZÁLEZ-GONZÁLEZ¹, ABRIL ESTRADA-HERNÁNDEZ¹, MONSERRAT RUÍZ-SANTANA², JUAN CARLOS BRAVATA-ALCÁNTARA², JUAN MANUEL BELLO-LÓPEZ³

¹Unidad de Vigilancia Epidemiológica Hospitalaria, Hospital Juárez de México; ²Laboratorio de Genética y Diagnóstico Molecular, Hospital Juárez de México; ³División de Investigación, Hospital Juárez de México

Keywords

Hospital outbreak • Infection control • *Clostridioides difficile* • Toxin B

Summary

Introduction. To describe the outbreak of *Clostridioides difficile* infection (CDI), and the impact of the prevention and control measures that were implemented in the “Hospital Juárez de México” (HJM) for its control.

Methods. A cross-sectional, descriptive, observational, and retrospective study was designed. All information on the hospital outbreak and on health care-associated infections (HCAI) was obtained from the files of the Hospital Epidemiological Surveillance Unit (HESU) of the HJM.

Results. A total of 15 cases of CDI were detected from February 20th to May 22nd, 2018, which represented 55.6% and 44.4% for the male and female gender, respectively, with an average age of

56 years and a range of 24 to 86 years old. It was possible to identify six failures and deficiencies that involved health personnel and hospital logistics through analyses based on the situational diagnosis in the services involved and through the construction of cause-effect diagrams. Additionally, through the detection of the outbreak by means of laboratory tests and timeline, the HESU team implemented measures and prospective surveillance to control and prevent the emergence of new cases.

Conclusions. The implementation of basic quality tools, control measures, and the prospective epidemiological surveillance had a positive impact on the control against the outbreak of *C. difficile* producing toxin B.

Introduction

Clostridioides difficile (*C. difficile*) is a Gram-positive bacillus, spore-forming and toxin producer that in recent years has represented a great challenge in terms of infection control within health institutions in the world, being one of the main etiological agents of the health care-associated infections (HCAI) [1]. *C. difficile* infection (CDI) is the most common cause of diarrhea associated with health care and long-term use of antimicrobials [1]. The transmission of this pathogen mainly occurs in hospital facilities, where exposure to antimicrobials and contamination of the environment by *C. difficile* spores is common [1]. *C. difficile* produces toxins that cause damage to the epithelial cells, these toxins are known as toxin A and toxin B [1]. Toxin A, called enterotoxin, which is more potent, increases secretion, causes more mucosal damage and inflammation, however, in cell cultures, toxin B has been shown to have greater cytotoxic activity, and in subsequent studies it has been shown that it is more toxic in the human colonic epithelium than toxin A [1, 2]. Worldwide, it is estimated that between 20 and 30% of cases of diarrhea associated with antibiotics are caused by *C. difficile*. In Canada, a rate between 3.8 to 9.5 cases per 10,000 patient days is calculated between 1997 and 2005. As of 2002, more severe and recurrent outbreaks

have been observed, the great majority associated with the use of antimicrobials, mainly fluoroquinolones, with an attributable mortality of 6.9 to 7.5% [3, 4].

In some hospitals in Mexico, the presence of *C. difficile* has been detected as one of the main infectious agents, showing a higher prevalence in hospital services such as Internal Medicine, General Surgery, and Intensive Care Units [5].

According to the literature, the main risk factor for *C. difficile* infection is the indiscriminate use of antimicrobials, mainly from the family of carbapenems and cephalosporins [6, 7]. The outbreaks that have occurred in our country have shown difficulties in their control and prevention, even remaining constant with an endemic behavior [8, 9].

The aim of this work was to describe the hospital outbreak of *C. difficile* infection and the impact of the prevention and control measures that were implemented in the “Hospital Juárez de México” (HJM).

Methods

STUDY DESIGN

A cross-sectional, descriptive, observational, and retrospective study was designed. All information was obtained from the hospital outbreak and from the

health care-associated infections (HCAI) from the Hospital Epidemiological Surveillance Unit (HESU) of the HJM.

PERIOD OF ANALYSIS AND CASE DEFINITION OF CDI

The period of the outbreak study was from February 20th to May 22nd, 2018. For the identification of cases, operational definitions were made and inclusion criteria was included such as patient of any age who had been hospitalized for at least 48 hours and who had presented more than three diarrheic stools in 12 hours, accompanied by one or more of the following symptoms: fever, abdominal distension and/or abdominal pain was considered as a suspected case of CDI. For a confirmed case of CDI, we had to meet the operational definition of a suspected case and have a positive result on any of the following tests:

- commercial immunochromatographic qualitative test against glutamate dehydrogenase (GDH) (CERTEST *Clostridium difficile* antigen GDH, Certest Biotec S.L.);
- real-time PCR amplification of a fragment of the gene coding for *C. difficile* toxin B was performed by using the automated BD MAX technology (Becton Dickinson) according to the supplier's instructions.

COLLECTION AND ANALYSIS DATA

The outbreak information was handled in Microsoft Excel package (Microsoft Corporation; Redmond, WA). The variables and risk factors described and analyzed were age, gender, hospital service, use of antimicrobials before CDI diagnosis, use of proton pump inhibitors, and type of diagnosis. Frequencies and percentages are used for data description.

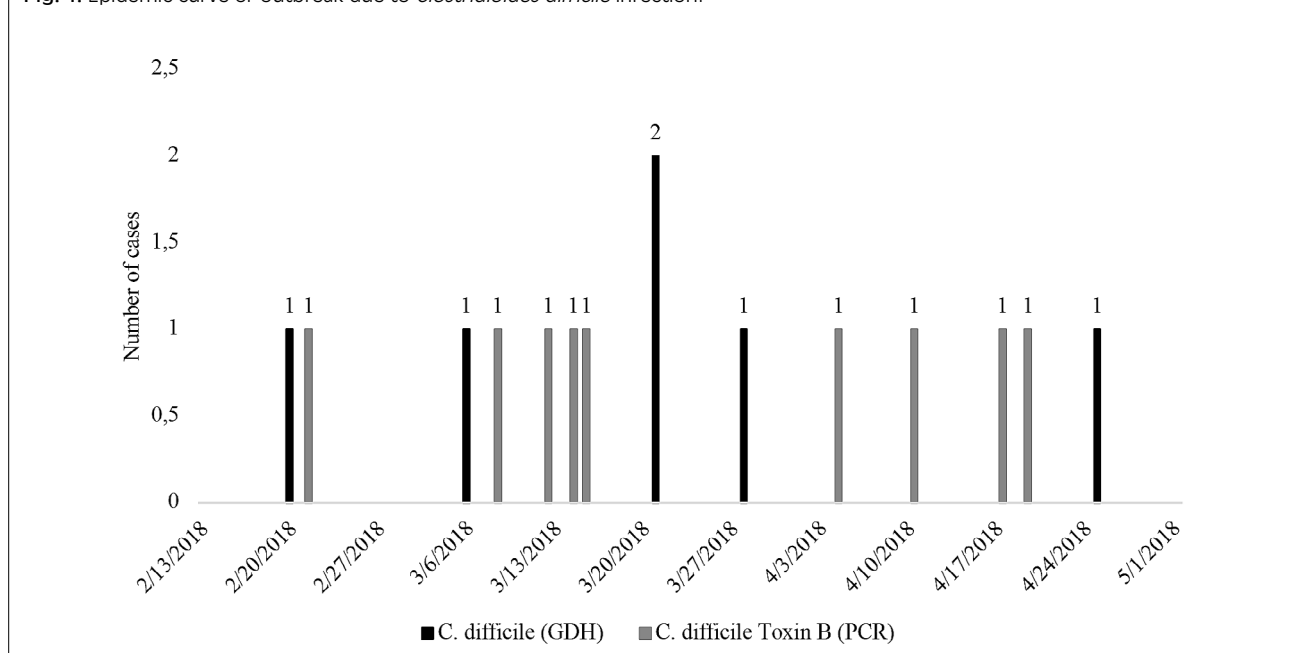
Results

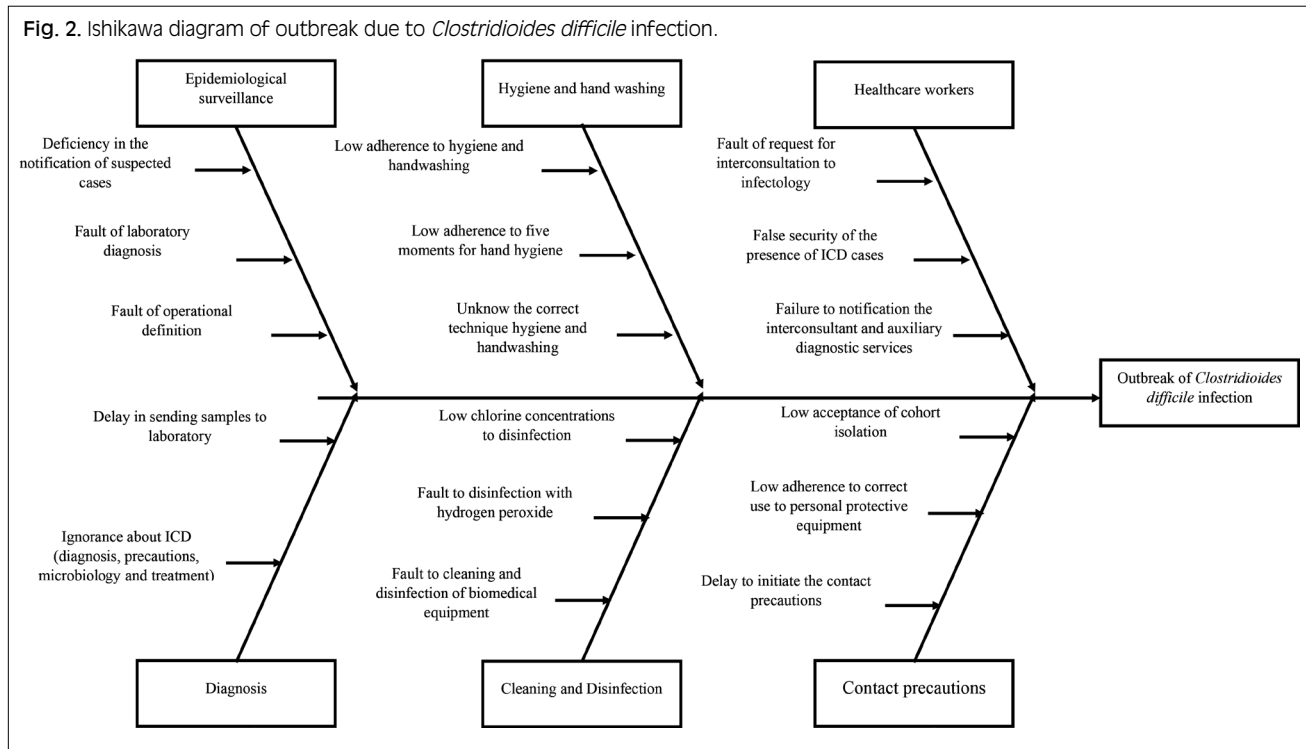
A total of 15 cases of CDI were detected during February 20th to May 22nd, 2018. The index case was a patient who had a history of having been previously hospitalized in the HJM during December 2017 and January 2018 in General Surgery. One week after his hospital discharge, his start with characteristic symptomatology in his home (diarrheic discharge, abdominal pain and fever). Since the clinical picture began at home, the health personnel who valued his readmission did not suspect that the etiologic agent was *C. difficile*. For this reason, there was a delay in the diagnosis and in the implementation of preventive measures, which generated exposure to patients and health personnel.

The epidemiological investigation and case analysis showed that 66.6 and 34.4% of patients corresponded to the male and female gender, respectively, with an average age of 56 years and a range of 24 to 86 years of age. According to the hospital services, where the cases were detected, 40% were in Internal Medicine, 26.7% in General Surgery, 13.3% in Neurosurgery, 13.3% in Hematology, and 6.7% in Thoracic Surgery. According to the timeline, 13.3% was detected in February 40% in March, and 46.7% in April. Figure 1 shows the distribution of cases in the epidemic curve.

Three deaths were recorded, of which only one was related to CDI, therefore, the fatality rate was 5.6%. The index case began with diarrheic discharge in February; however, when reviewing the epidemiological background, he was hospitalized at the HJM in December; despite identifying this data, it could not be determined whether if it was the primary case or the source of the outbreak. Among the risk factors detected, 88.9% of the cases had some antimicrobial scheme, the most commonly used being carbapenems, quinolones,

Fig. 1. Epidemic curve of outbreak due to *Clostridioides difficile* infection.





and cephalosporins. In all cases, the use of proton pump inhibitors was detected. When determining that it was a hospital outbreak due to *C. difficile*, the HESU team began with the prospective epidemiological surveillance, the implementation of control measures for the outbreak, and the prevention of the appearance of new cases, based on the situational diagnosis carried out in the services involved, where faults and deficiencies were identified and outlined in the cause-effect diagram (Fig. 2).

IMPLEMENTATION OF OUTBREAK CONTROL MEASURES

Hygiene and hand washing, and contact precautions

During the outbreak, a low percentage of adherence to hygiene and hand washing was detected in the services involved, the above was determinate by personalized questioning. Therefore, training for the personnel of the involved areas on the correct technique of hygiene and hand washing, as well as, the five moments for hand hygiene was carried out. A total of 118 health workers from the hospital wards involved were trained, of which 75% were nurses, 13% cleaning staff, 9.2% doctors, and 2.7% were support staff. 0.1% corresponded to administrative staff, family members, and patients. These measures were applied to patients who met the operational definition of a suspected case of CDI. In addition, family members, patients, and health personnel were trained in the matter of the correct use of personal protective equipment.

Hospital cleaning and disinfection

A diagnosis of the situation was performed, where it was identified that the hospital cleaning and disinfection

process was not standardized, and it had errors in the sequence of steps. Consequently, it was decided to use two concentrations of sodium hypochlorite, 1,600 ppm for routine cleaning, and 5,000 ppm for final cleaning at patient discharge.

The cleaning of the biomedical equipment and objects that were found inside the patient's room or environment, was carried out daily and at the time of the patient's discharge with towels impregnated with peroxide. This step was complementary to disinfection with the chlorine concentrations mentioned above, before and after, but always together. As a last step in the sequence of disinfection, in the suspected or confirmed cases, the nebulization with hydrogen peroxide with silver particles was used, where it was requested by the services and authorized by the staff of the HESU, and after this step a patient could be allowed to enter the room.

LABORATORY DIAGNOSIS

When a suspect case was detected, the sample of diarrheic stools was collected and submitted for emergency diagnosis to the Genetics and Molecular Diagnostic Laboratory of the HJM for their corresponding study. One of the weaknesses detected during the study process of the outbreak was that the medical and nursing staff did not have sufficient knowledge to perform a differential diagnosis of CDI. Therefore, the necessary training was initiated to identify CDI and the operational definition of the case. The second problem was that even when the personnel that identified a suspected case of CDI, they did not notify it, the case was detected through active epidemiological surveillance. The third and final problem was that samples were occasionally sent to the laboratory for CDI diagnosis.

COHORT ISOLATION

One of the obstacles for the isolation of CDI cases was the structural characteristic of the HJM, since it limited the correct application of precautions contact measures, thus, relocation of beds and/or rooms was carried out in order to be able to shape specific and unique areas for suspected and confirmed cases. These measures were carried out until the discharge of the patient. In the same period of the outbreak, a total of three positive cases of *C. difficile* coming from other hospital units were identified, along with eight cases of gastroenteritis associated with health care with negative results to *C. difficile*.

INTERVENTION WITH HEALTH WORKERS

During training on hygiene and hand washing, the matter of identification, notification, diagnosis and treatment of suspected or confirmed cases of CDI was also addressed. The training covered the following points:

- operational definition of suspected case of CDI to improve detection;
- sample submission to the central or research laboratory for the timely diagnosis of CDI cases;
- application and registration in clinical file and medical indications of contact precautions in suspected and confirmed cases of CDI;
- effective communication of the suspicion or confirmation of the CDI to the interconsultant, surgical, and auxiliary diagnostic services (imaging);
- correct cleaning and disinfection of biomedical equipment in contact with suspected or confirmed CDI patients;
- interconsultation to the infectology service when detecting a suspected case of CDI for the timely initiation of antimicrobial treatment.

Discussion

To our knowledge, this is the first study of a hospital outbreak of diarrhea caused by *C. difficile* producing toxin B in Mexico, although there are previous reports in our country of the presence of this toxin, they only focus on isolates of clinical origin [10].

It is known that the identification of the source of dissemination in a *C. difficile* outbreak is very complex, which is why it is necessary to take into account that the hospital environment is probably the main source of contamination. This is due to poor cleaning and disinfection processes, combined with a low adherence to hygiene and hand washing of health workers [10]. The constant training and supervision of health personnel on hygiene and hand washing, and on cleaning and disinfection is a task of great importance, since it is easy to lose habits in the application of these measures. Previous studies have shown that hygiene and hand washing are the most important measures for the prevention and control of HCAI [11, 12].

One of the points to improve, is the importance of having an effective cleaning and disinfection process, with the appropriate products, of the areas involved in

the circulation of *C. difficile*. Hospital environments should be evaluated, since there are different surfaces and biomedical equipment that can be difficult to disinfect, such as mattress surfaces, beds, and toilets [13]. The disinfectants that are used should be evaluated, as well as the concentrations to achieve a significant reduction of the spores [11]. Wong et al., 2018, concluded that the use of disinfectants with sporicidal activity in the hospital environment after discharge of the patient with CDI helps to reduce the risk of cross-transmission of *C. difficile* [14]. The effectiveness of cleaning and disinfecting with impregnated towels or with nebulization with hydrogen peroxide, complemented with silver particles has been demonstrated [15-17].

To obtain positive results with this type of products, it must be considered that they will always have to be complementary to the use of suitable concentrations of chlorine, either before or after the cleaning and disinfection step [18, 19]. They must be used strategically to optimize this input, and always with good communication with the technical team in charge of the application and with the hospital services involved [20, 21].

Although *C. difficile* is an infectious agent that is difficult to control, and that in a large number of hospitals its presence has an endemic behavior, efforts to make effective prevention and control measures of the outbreak must be constant with the trainings and supervisions in the hospital services involved. It is important to mention that hospital epidemiological surveillance actions work in a similar way to field epidemiology, having the structure based on the surveillance of morbidity, mortality, and by laboratory. It is necessary to establish the operational definition of CDI cases, both of suspected and confirmed cases, the technique in collecting and submitting samples for laboratory diagnosis, and the assessment by endoscopy and pathology services, if required. The establishment of these parameters will allow to carry out a proper epidemiological surveillance of cases of CDI. Furthermore, it is important to integrate indicators such as the incidence rate [22, 23]. One factor to take into account of the CDI cases is the increase in the costs derived from medical care, van Buerden et al, 2017, calculated the costs attributable to the care and control of an outbreak of *C. difficile* ribotype 027, and it was of approximately € 1,222,376, the factor that increased the cost was the increase in hospital stay and the closing of rooms to implement contact precautions [24]. The impact on the economy of the institutions is important, without considering the cost that it generates to the family members of the infected patients. One of the characteristics of the HJM, which represents a barrier for infection control, is the deficient number of rooms for the isolation of cases, these limits and impacts the adherence to precautions based on the transmission of diseases, in this case contact precautions. Ideally when making plans on the construction of new hospitals or the remodeling of existing institutions, the team of the HESU should consider aspects related to the prevention and control of infections. Without a doubt, the effective communication with the

staff of the diagnostic laboratories was the key to contain the outbreak, since there is a coordinated notification with the HESU team, which strengthens the timely detection activities. It is important to permanently assemble a system for the notification and detection of suspected cases of CDI to identify a case in a timely manner, initiate contact precautions and antimicrobial treatment, and effective measures of cleaning and disinfection. The importance of communicating this report is to raise awareness about the importance of prevention and control measures, which must be well executed and supervised, since the success or failure of the risk of infection to patients, family members, and health workers depends on this.

Conclusions

The implementation of effective and adequate measures of prevention and control of *C. difficile* are a constant challenge for hospital epidemiology, for which strategies should be designed for hospital structures, so that the results are as favorable as possible. The use of basic quality tools to carry out the analysis with a risk approach for the study of outbreaks is a methodology that we must explore, since they can give a wider perspective to face the barriers that are detected. Additionally, we must not forget that epidemiological surveillance is based on morbidity, mortality, and the laboratory, the latter was a strength for our HESU group, because having results in a timely manner allowed us to implement prevention and control measures in a short time.

Ethical considerations

There are no ethical implications, since the information used was obtained as part of the routine activities of the HESU. The collection and presentation of the information was carried out under the observation of the principles of confidentiality and discretion according to the Federal Law of Responsibility and Access to Public Information.

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Conflict of interest statement

None

Authors' contributions

O.S.H and J.M.B.L.: Original idea, article writing, critical review and discussion of data and data analysis, B.M.T., J.G.M., R.J.V., N.E.G.G., A.E.H. and M.R.S.: Collection data, critical review, J.C.B.A.: Laboratory tests.

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Correspondence: Oscar Sosa Hernández, Unidad de Vigilancia Epidemiológica Hospitalaria, Hospital Juárez de México, Av. Instituto Politécnico Nacional 5160, Magdalena de las Salinas, 07760 Ciudad de México, México - Tel.: +52 57477560 - E-mail: dr.oscar.sh@gmail.com

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