LETTER TO THE EDITOR

Compared lethality rates of Clostridium difficile infections at the local, regional and national levels in France

M. Huart1,2, C. Abat1, M. T. Jimeno4, X. Deparis2, D. Raoult1 and P.-E. Fournier1,3

1) Institut Hospitalo-Universitaire Méditerranée-Infection, Fédération de Bactériologie-Hygiène-Virologie, Hôpital de la Timone, 2) Centre d’Épidémiologie et de Santé Publique des Armées (CESPA), camp militaire de Saint Marthe, 3) Unité de Recherche sur les Maladies Infectieuses et Tropicales Emergentes (URMITE) UMR 63, CNRS 7278, IRD 198, INSERM U1095, Ax-Marseille Université and 4) Service de l'Information Médicale, Hôpital de la Timone, Marseille, France

Original Submission: 22 June 2016; Revised Submission: 12 July 2016; Accepted: 25 July 2016

Article published online: 29 July 2016

Corresponding author: P.-E. Fournier
E-mail: pierre-edouard.fournier@univ-amu.fr

Dear Sir,

In December 2013, we reported a Clostridium difficile (CD) outbreak caused by the hyper-virulent ribotype 027 in the Provence-Alpes-Côte d’Azur (PACA) area, southeastern France [1]. Sixty-one patients were hospitalized from March 2013 to April 2014 in the four university hospitals of Marseille (Timone, Conception, North and Sainte-Marguerite) for CD 027 infection, with a mortality of 43% [2]. Following this outbreak, we developed an automated epidemiological surveillance system for CD cases.

Clostridium difficile is associated with an elevated lethality worldwide [2–4]. This lethality has gradually increased, exceeding that of many other bacterial species. In the present retrospective study, from January 2012 to December 2015, we compared the lethality rates of CD isolated in enterocolitis and the three most common bacterial pathogens isolated from any specimen (Escherichia coli, Staphylococcus aureus and Pseudomonas aeruginosa) in the university hospitals of Marseille, in the PACA area, France. The analysed data include the numbers of patients infected by each of the four above-mentioned bacterial species and the associated lethality for patients over 65 years old. The data at the Marseille and regional levels were obtained using our epidemiological surveillance system whereas national data were obtained by the medical information service in Timone hospital (National Data obtained by Convention de droit d’usage des données PMSI, N°d’agrément 2015-111111-88-46). Duplicates were removed. For a given patient, only the first infection caused by a given microorganism was registered. We calculated the annual lethality rates (for the years 2012 to 2015) by dividing the number of deaths by the number of patients affected by the respective bacterial species by each year. All data collection and descriptive epidemiological analyses were performed in Excel.

Within Marseille university hospitals, we observed a stable lethality rate of E. coli urinary-tract infections between 2012 and 2015 (3.6%–5.6%, Table 1). For E. coli bacteraemia, the lethality increased from 2012 to 2014 (11.8%–18.3%, Table 1) and decreased in 2015 (10.7%). For S. aureus bacteraemia, the lethality decreased constantly from 22.9% in 2012 to 19.1% in 2014 (Table 1) then increased in 2015 (20.3%). For P. aeruginosa bacteraemia the lethality increased from 2012 (28.6%) to 2013 (31.7%), then decreased in 2014 (23.1%) and increased in 2015 (30.4%; Table 1). The CD lethality rate was lower in 2012 (10.6%) than in other years and reached a peak of 18.3% in 2013 (1.7-fold increase) and then decreased in 2014 (17.9%) and 2015 (12.4%).

At the PACA level, in 2012, 2013 and 2014, the lethality rate of CD infections was also lower than those of other pathogens (Table 1). At the country level, the highest lethality rate in 2012 and 2013 was that of P. aeruginosa, which was slightly higher than that of C. difficile.

When considering the evolution of lethality rates over time (Table 1), we observed that CD-related mortality had the greatest variation among bacterial pathogens in Marseille and PACA, which may be explained by the 2013–2014 CD 027 outbreak [2]. We also observed a great reduction in CD-related lethality in 2015, although non-significant (two-sided Pearson’s chi-square test, p 0.09). This reduction followed the implementation of systematic faecal microbiota transplantation for patients hospitalized in Marseille university hospitals with CD 027 infections [2].

Together, these results confirmed that CD is a major life-threatening bacterial pathogen, especially for the elderly, like P. aeruginosa. This confirms what was previously observed in our region [1,5] and also in northern France and other countries [6,7]. The rapid decrease in the lethality of CD infections in Marseille university hospitals (18.3% to 12.4%) and the PACA
region can be explained by the introduction of new treatment for all patients in PACA, the faecal microbiota transplantation [5].

Our study demonstrated that the CD-related lethality was similar in Marseille university hospitals and at the regional and national levels and was lower than those caused by *P. aeruginosa* or *S. aureus*. CD remains a major public health concern. Moreover, our results should encourage hospitals to extensively survey CD infections by the implementation of automatic monitoring systems, and also by developing rapid screening procedures to identify and isolate infected patients and healthy carriers upon hospitalization.

### References

[1] Lagier J-C, Delord M, Million M, Parola P, Stein A, Brouqui P, et al. *Clostridium difficile* 027 emerging outbreak in Marseille, France. *Infect Control Hosp Epidemiol* 2013;34:1339–41.

[2] Lagier J-C, Delord M, Million M, Parola P, Stein A, Brouqui P, et al. Dramatic reduction in *Clostridium difficile* ribotype 027-associated mortality with early fecal transplantation by the nasogastric route: a preliminary report. *Eur J Clin Microbiol Infect Dis* 2015;34:1597–601.

[3] Burke KE, Lamont JT. *Clostridium difficile* infection: a worldwide disease. *Gut Liver* 2014;8:1–6.

[4] Gabriel B. Dynamique des souches de *Clostridium difficile* en Europe [Internet]. Gabriel Birgand—Pharmacien Hygiéniste—Épidémiologiste; 2011. Available from: http://www.gabrielbirgand.fr/2011/09/dynamique-des-souches-de-clostridium-difficile-en-europe/.

[5] Kuijper EJ, Barbut F, Kleinlauf N, Eckmanns T, Lambert ML, et al. Update of *Clostridium difficile* infection due to PCR ribotype 027 in Europe, 2008. *Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull* 2008;13(31).

[6] Mascart G, Delmée M, Van Broeck J, Cytryn E, Karmali R, Cherifi S. Impact of ribotype 027 on *Clostridium difficile* infection in a geriatric department. *Eur J Clin Microbiol Infect Dis Off Publ Eur Soc Clin Microbiol* 2013;32:1177–82.

[7] Lessa FC, Gould CV, McDonald LC. Current status of *Clostridium difficile* infection epidemiology. *Clin Infect Dis Off Publ Infect Dis Soc Am* 2012;55(Suppl. 2):S65–70.

---

**TABLE 1. Number of deaths and lethality rate of infection caused by *Clostridium difficile* and the three most common bacterial pathogens in Marseille university Hospitals, Provence-Alpes-Côte d’Azur region and France from January 2012 to December 2015**

| Bacterial species | Numbera of patients | Number of deaths | Lethality rate | Number of patients | Number of deaths | Lethality rate | Number of patients | Number of deaths | Lethality rate |
|-------------------|---------------------|-----------------|---------------|------------------|-----------------|---------------|------------------|-----------------|---------------|
|                   | 2012                |                 |               | 2013              |                 |               | 2014              |                 |               |
| *Clostridium difficile* | 390                  | 51              | 5.1           | 339              | 37              | 5.6           | 304              | 30              | 5.6           |
| Escherichia coli bacteraemia | 136                | 16              | 11.8          | 114              | 29              | 26.0          | 120              | 33              | 26.6          |
| Escherichia coli UTI | 130                | 21              | 5.5           | 8                | 2               | 19.3          | 104              | 15              | 14.3          |
| *Staphylococcus aureus* bacteraemia | 105              | 24              | 22.9          | 660              | 238             | 36.1          | 813              | 253             | 31.2          |
| *Pseudomonas aeruginosa* bacteraemia | 28                 | 8               | 28.6          | 324              | 131             | 40.4          | 3028             | 1176            | 38.8          |

UTI, urinary tract infection.

*p < 0.09, not significant.

*a*National Data obtained by: Convention de droit d’usage des données PMSI, N°d’agrément 2015-111111-88-46.

*b*Includes all causes of death, infectious or not.