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## Clinical Case Study

## Carbapenemase-producing Enterobacterales outbreak: Another dark side of COVID-19



Eric Farfour MD, PhD<sup>a,\*</sup>, Marion Lecuru PharmD<sup>a</sup>, Laurent Dortet PharmD, PhD<sup>b</sup>, Morgan Le Guen MD, PhD<sup>c</sup>, Charles Cerf MD<sup>d</sup>, Françoise Karnycheff PharmD<sup>a</sup>, Rémy A. Bonnin PharmD, PhD<sup>b</sup>, Marc Vasse PharmD, PhD<sup>a</sup>, Philippe Lesprit MD<sup>a</sup>, on behalf of the SARS-CoV-2 Hospital Foch study group<sup>1</sup>

<sup>a</sup> Service de Biologie Clinique, Hôpital Foch, Suresnes, France<sup>b</sup> Service des Microbiologie, Centre National de Référence de la Résistance aux Antibiotiques, Hôpital Bicêtre, Le Kremlin-Bicêtre, France<sup>c</sup> Service d'Anesthésie-réanimation, Hôpital Foch, Suresnes, France<sup>d</sup> Service de Réanimation Polyvalente, Hôpital Foch, Suresnes, France

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In the hospital department dedicated to COVID-19-patient, infection prevention and control measures were upgraded. Therefore, the cross-transmission of other micro-organisms was thought unlikely to occur. However, we report an outbreak of NDM-5-producing *Escherichia coli* in a 12-beds ICU dedicated to COVID-19 patients. This outbreak involved 6 patients of which 5 were asymptomatic carriers and 1 was infected. Several findings might have contributed to cross-transmission including the multiple-bedroom configuration of the department, uncomplete compliance for standard and contact precautions, overwork due to the burden of the disease, lack of training of staff for the care of ICU-patients, and misuse of gloves. Furthermore, as infection prevention and control measures were thought to be applied, contact patients were not screened for eXDR carriage. Applying rigorously standard and contact precautions and performing screening in contact patients when indicated must be the rules in COVID-19 wards.

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## INTRODUCTION

Due to its high morbidity and mortality, coronavirus disease (COVID-19) has led to a dramatic increase in the number of hospitalized patients in intensive care units (ICU).<sup>1</sup> In order to limit the spread of SARS-CoV-2 to other patients and health care workers, infection prevention and control (IPC) measures (ie, contact and respiratory precautions) should be rigorously applied.<sup>2,3</sup> Furthermore, the hospitals

were organized with specific departments dedicated to SARS-CoV-2-infected patients (COVID-19-departments). As this context implies upgraded IPC measures, the risk of hospital-transmission of other micro-organisms such as extremely drug-resistant micro-organisms (eXDR), that is, carbapenemase-producing Enterobacterales (CPE) and vancomycin-resistant *Enterococcus* might be reduced in COVID-19-departments. However, these units also experienced overwork due to the rapid increase of patients' admissions and shortages in personal protective equipment (PPE) which could play a role in hospital-transmissions.<sup>4,5</sup> In this particular context, we describe an outbreak of an NDM-5-producing *Escherichia coli* occurring in an ICU dedicated to COVID-19-patients.

## METHODS

## CPE screening

As recommended by French guidelines, CPE carriage was screened in all contact patients, and those with a previous history of hospitalization outside of France within the past year.<sup>6</sup> CPE screenings were performed on rectal swabs and processed using both a multiplex PCR

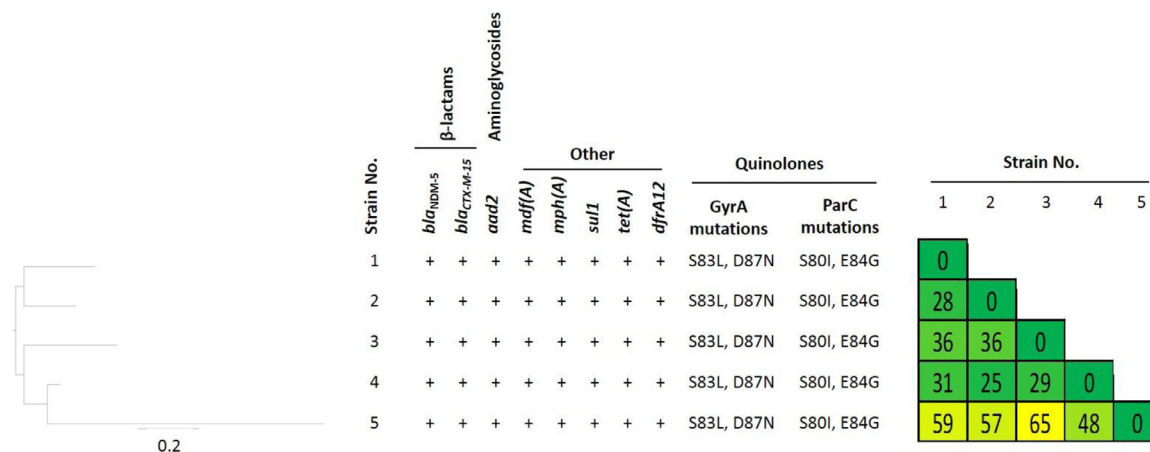
\* Address correspondence to Eric Farfour, Service de Biologie Clinique, Hôpital Foch, Suresnes, France.

E-mail addresses: [efarfour@hopital-foch.org](mailto:efarfour@hopital-foch.org), [ericf6598@yahoo.fr](mailto:ericf6598@yahoo.fr) (E. Farfour).

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<sup>1</sup> Members of the Sars-Cov-2 Foch Hospital study group: Emilie Catherinot, Colas Tcherakian, Louis-Jean Couderc, Antoine Roux, Hélène Salvatore, Sylvie Colin de Verdière and Charlotte Roy (service de pneumologie et transplantation pulmonaire), Richard Galliot, Benjamin Zuber, Mathilde Neuville, Anthony Lancelleur and David Cortier (service de réanimation), Camille Cornet (service d'anesthésie), Gustavo Bazzouni-Barreiro, Marie de Fondaumière, Floriane Grade, Sandrine Grandin and Annabelle Marache (Service de biologie clinique), Mathilde Roumier, Mathieu Groh, Yoland Schoindre, David Khau, Felix Ackermann and David Zucman (Service de médecine interne), Philippe Grenier, Anne-Laure Brun and François Mellot (service d'imagerie médicale), Anne Verrat, Marie-Christine Ballester, Charlotte Rachline and Etienne Imhaus (service des urgences).





**Fig 2.** Phylogenetic tree and SNP matrix of phylogenetic analysis of NDM-5-producing *E. coli* ST-361. Scale bar on tree indicates the number of single-nucleotide polymorphisms per position of common sequences. SNPs matrix was obtained from CSI phylogeny (<https://cge.cbs.dtu.dk/services/CSIPhylogeny/>).

carriers. But, an additional carrier was identified on the admission screening performed in another hospital on April 26, 2020. Unfortunately, due to overwork, the strain isolated from this patient was not recovered for whole-genome sequencing. Overall, the NDM-5-producing *E. coli* outbreak involved 6 patients. The index case (patient No. 1), was a known carrier when admitted in the PACU. Four patients (No. 2 to 5), all close contact of the index patient, were identified within the PACU. The remaining one (patient No. 6), also a close contact of patient No. 1, was screened positive for the first time after his transfer in another hospital. Whole-genome sequencing analysis revealed that all analyzed NDM-5-producing *E. coli* isolates (n=5) belonged to the same sequence type (ST), ST-361. In addition, the phylogenetic analysis demonstrated that all strains were clonally related with an average of 41.4 ± 12.7NPs along their whole genome (Fig 2). On April 30, 2020, all but 2 patients were discharged from hospital. All patients were colonized except one that presented ventilator-associated pneumonia related to the eXDR strain. He recovered with a combination of aztreonam plus ceftazidime-avibactam and colimycin.

**DISCUSSION**

The prevention of micro-organisms transmission required a rigorous application of IPC measures,<sup>6</sup> which should be implemented according to a case-by-case analysis risk. In the atypical context of the COVID-19 pandemic, we considered the risk of cross-transmission was low, as contact precautions were upgraded and applied to all patients of the COVID-department. Consequently, we decided not to screen contact patients. This strategy was not effective, as an outbreak involving 6 cases occurs but resolved when screening of contact patients was applied.

Several findings might have contributed to the spread of the NDM-5-producing *E. coli* strain. First, the geographical configuration of the PACU transformed in a multiple bedroom COVID-ICU might have favored the transmission of micro-organisms by inoculation of the environment. However, cleaning was performed at least twice a day and it was previously demonstrated that applying contact precautions in a multiple bedroom was noninferior to a strategy of contact precautions in a single bedroom.<sup>10</sup> But, in the present outbreak, patient's beds were closely located. This latter finding suggests that incomplete compliance of standard and contact precautions was probably a cause of the present outbreak. The overwork due to the burden in care could have led to less vigilance of medical and paramedical staff and punctual low compliance for contact precaution.

Understaffing which can be assessed by the health care worker: patient ratio was previously associated with a higher risk of eXDR cross-transmission.<sup>4</sup> Despite sufficient staff, the burden of care for these patients in prone positions was high. Then, the implementation of COVID-19 IPC measures that are more restrictive than those for eXDR could have falsely reassured medical and paramedical staff. The lack of training has also been associated with lower adherence to IPC measures.<sup>11</sup> In the present context, medical and paramedical staff was mainly those of the PACU which were not usually in charge of ICU patients. We introduced the practice of wearing gloves and gowns anytime in order to protect staff. However, misuse of PPE has been previously associated with an increased risk of cross-transmission.<sup>12,13</sup> Specifically, an outbreak of Imipenem-resistant *Acinetobacter baumannii* related to the misuse of gloves was previously described.<sup>14</sup> Moreover, the shortages in medical PPE has led to the use of probably unsuitable alternative PPE. Unfortunately, due to the overwork of the ITC team, we were unable to audit the compliance for specific IPC measures despite the misuse of gloves were reported.

Last, antimicrobial exposure was previously associated with hospital acquisition of CPE strains and with an outbreak of MRSA.<sup>4,15,16</sup> However, as the outbreak occurs in an additional COVID department which was opened for 20 days, we were not able to compare antibiotic consumption to baseline use. Finally, as eXDR cross-transmission occurred, we could hypothesize cross-transmission of other micro-organisms, such as MRSA, ESBL-producing Enterobacterales or *C difficile* occurred in this department. In a previous report, Yap et al described an outbreak of MRSA in an ICU in the context of SARS-infected patients in 2003 in Hong Kong.<sup>16</sup>

In conclusion, despite the implementation of upgraded ICP measures in the context of the COVID-19 pandemic, CPE outbreak may occur in COVID-19 departments. Several changes could have contributed to this outbreak such as overwork, misuse of PPE, and low compliance for standard and contact precaution. We believe the absence of screening in contact-patient has probably led to a delay in the identification of the outbreak. Therefore, we emphasize the need for applying rigorously standard precaution at all time. Applying contact precaution for eXDR carriers and performing screening in contact patients must be the rule.

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