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The intertwining of healthcare-associated infections and COVID-19 in Italian intensive care units: an analysis of the SPIN-UTI project from 2006 to 2021

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SUMMARY

Background: Although healthcare-associated infections (HAIs) pose an extraordinary burden on public health, the impact of coronavirus disease 2019 (COVID-19) is still a matter of debate.
Aim: To describe trends of HAIs in Italian intensive care units (ICUs) from 2006 to 2021, and to compare characteristics and outcomes of patients with or without COVID-19.
Methods: We evaluated patients participating in the 'Italian Nosocomial Infections Surveillance in Intensive Care Units' (SPIN-UTI) project, who were admitted to ICUs for more than 48 h. Data regarding diagnosis, clinical conditions, therapies, treatments and outcomes of COVID-19 patients were also collected.
Findings: From a total of 21,523 patients from 2006 to 2021, 3485 (16.2%) presented at least one HAI. We observed an increasing trend for both the incidence of patients with HAI and the incidence density of HAIs (*P*-trend <0.001). Compared with the pre-pandemic period, the incidence density of HAIs increased by about 15% in 2020–2021, with pneumoniae being the greatest contributors to this increase (*P*-trend <0.001). Moreover, incidence of HAIs was higher in ICUs dedicated to COVID-19 patients (*P*<0.001), who showed a greater risk of HAIs and death than patients without COVID-19 (*P*-values <0.001). Accordingly, the mortality in ICUs increased over the years and doubled during the pandemic (*P*-trend <0.001). Notably, co-infected patients had higher mortality (75.2%) than those with COVID-19 (66.2%) or HAI (39.9%) alone, and those without any infection (23.2%).
Conclusions: Our analysis provides useful insight into whether and how the COVID-19 pandemic influenced HAI incidence and death in Italian ICUs, highlighting the need for evaluation of the long-term effects of the pandemic.

Introduction

Healthcare-associated infections (HAIs) impose a significant burden on public health, which may have been exacerbated by

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the coronavirus disease 2019 (COVID-19) pandemic [1–9]. In fact, the priority given to COVID-19 placed extraordinary demands on healthcare systems, probably shifting the attention away from infection prevention and control (IPC) measures [6,8,10–12]. It is undeniable that the pandemic provoked challenges in routine clinical practices and surveillance, especially in intensive care units (ICUs) [1,10,13]. In spite of these considerations, the impact of COVID-19 pandemic on healthcare settings remains controversial and contested [11]. There was evidence, although not clear from a quantitative perspective, that the COVID-19 pandemic caused a significant increase in HAI incidence [1,6,11,13–18]. To some extent, this can be explained by the higher risk of HAIs observed in COVID-19 patients than in the other critical patients admitted to ICUs [6,19,20]. However, IPC strategies adopted to contain the pandemic might actually facilitate the prevention of HAIs in an indirect but positive manner [10,21]. From an individual point of view, some characteristics of patients admitted to ICUs – such as the underlying medical conditions, the exposure to invasive devices, prolonged length of stay, etc. – always placed them at higher risk of HAI [15,18,22]. This is even more true during the current pandemic, which has certainly influenced the clinical status of patients admitted to ICUs, especially older individuals and those with previous comorbidities [23–26]. Consequently, the demand for monitoring trends of HAI in all healthcare settings and in all geographical regions has become even more important following the pandemic caused by SARS-CoV-2 [6,27]. Our study focused on Italy, which is one of the countries most affected by HAIs and COVID-19 in Europe [28–37]. The primary aim was to describe the national trends of HAIs in ICUs from 2006 to 2021, paying particular attention to the potential impact of the pandemic on the incidence of HAIs. For doing so, we also compared clinical features and outcomes of patients with or without COVID-19 admitted to ICUs during the pandemic.

Methods

Study design and population

In the present study, we analysed data from the 'Italian Nosocomial Infections Surveillance in Intensive Care Units' network, the SPIN-UTI project, a prospective surveillance system of HAIs in Italian ICUs launched in 2006 by the Italian Study Group of Hospital Hygiene (GISIO) of the Italian Society of Hygiene, Preventive Medicine and Public Health (SItI), and carried out in accordance with the European Centre for Disease Prevention and Control (ECDC) Healthcare-Associated Infections in Intensive Care Units (HAIICU) protocol [38–40]. Each edition of the SPIN-UTI project consists of a biennial prospective patient-based surveillance of patients admitted to Italian ICUs (i.e., from 1st October of a given year to 31st March of the following year) [41–46]. The protocol for the analysis of these data was approved by the Ethics Committee 'Catania 1' (Catania, Italy) with the following Protocol numbers no. 111/2018/PO and no. 295/2019/EMPO. Further details on protocol and study design have been described elsewhere [41–48]. In the current study, we used data from patients who were admitted to Italian ICUs participating in the eight editions of the SPIN-UTI project, from 2006–2007 to 2020–2021. The study population consisted of all patients admitted to Italian ICUs for more than 48 h.

Data collection

Data collection involves a web-based procedure with an online platform, which was designed to record data regarding the characteristics of patients, infections, and associated micro-organisms. In particular, data about personal and clinical characteristics at ICU admission (e.g., age, sex, Simplified Acute Physiology Score (SAPS II), origin of the patient, admission type), exposure to invasive procedures (e.g., intubation, central venous catheter, urinary catheter), infection status (i.e., infection date, infection site and clinical outcomes) and micro-organisms (e.g., antimicrobial resistance data) were collected for each patient surveyed. Moreover, in the last 2020–2021 edition, a specific form was implemented for the collection of data regarding diagnosis, clinical conditions, therapy, treatments and outcomes of patients with COVID-19 [38,41–46].

Statistical analysis

Descriptive statistics were used to characterize the patients' participants by reporting results as mean, standard deviation (SD) or median (interquartile range, IQR) for continuous variables, or frequency and percentage values for categorical variables. The Mann–Whitney *U*-test/the Kruskal–Wallis *t*-test and the two-tailed Chi-squared tests were applied for the comparisons between continuous or categorical variables, respectively. Simple linear regression was used to test the temporal trend of HAIs and mortality. All the analyses were conducted using the SPSS software (version 26.0, SPSS, Chicago, IL, USA), and considering a statistical significance level of 0.05.

Results

Trends of HAIs from 2006 to 2021

This analysis was conducted using data provided by 108 ICUs during the eight editions of the SPIN-UTI project (from 2006–2007 to 2020–2021). Specifically, 56 ICUs participated in only one edition, while the remaining participated in multiple editions. The participating ICUs in the 2020–2021 edition were primarily of mixed type (79.3%), followed by cardiac ICUs (17.2%) and medical ICUs (3.5%). The average number of beds was 6.7 (median: 7.0; range: 2–12 beds).

Of 21,523 patients staying in ICU for more than two days from 2006 to 2021, 3485 (16.2%) patients presented with at least one HAI (Figure 1a). The incidence of patients with at least one HAI increased from 15.4% in 2006–2007 to 24.5% in 2020–2021 (P-trend <0.001; Figure 1b). A similar trend was observed for the incidence density of HAIs (P-trend<0.001), which increased from 17.1 per 1000 patient-days in 2006–2007 to 24.2 per 1000 patient-days in 2014–2015. After a slight decline in 2016–2017, the incidence density of HAIs increased again up to 24.1 per 1000 patient-days in 2020–2021 (Figure 1c). Part of this increase can be attributed to the increasing incidence density of pneumoniae (PN): from 9.1 per 1000 patient-days in 2006–2007 to 13.2 per 1000 patient-days

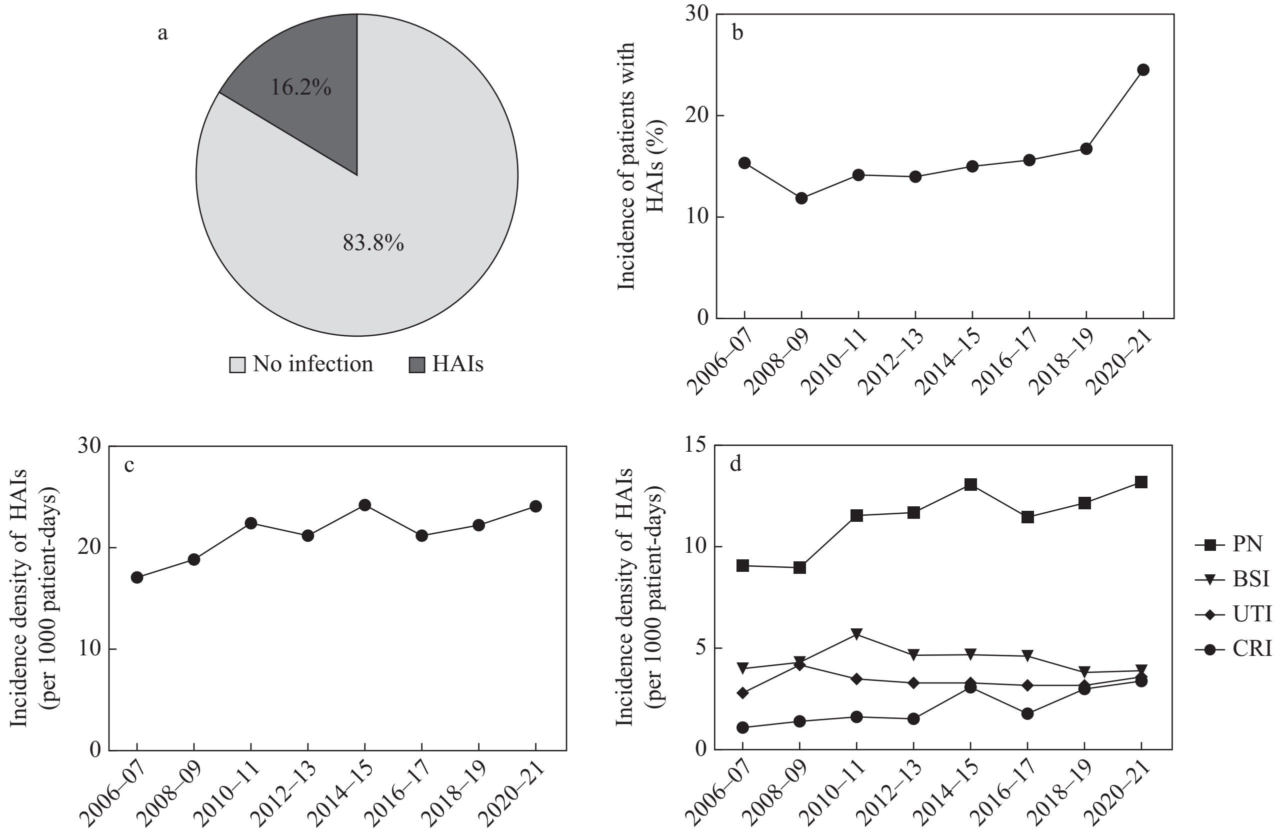

Figure 1. Trend of healthcare-associated infections (HAIs) in Italian intensive care units from 2006 to 2021. (a) Proportion of patients with or without HAIs; (b) incidence of patients with HAIs; (c) incidence density of HAIs; (d) incidence density of pneumoniae (PN), bloodstream infection (BSI), urinary tract infection (UTI), and catheter-related infection (CRI).

in 2020–2021 (P-trend<0.001). Instead, no statistically significant trends were evident for bloodstream infections (BSIs), urinary tract infections (UTIs), and catheter-related infections (CRIs) (Figure 1d).

Table I presents patient characteristics for the study population and the comparison between patients with or without HAIs. Patients with HAI were more likely to come from another ward/hospital, to be traumatized and immunodeficient, to present with urinary catheter and intubation at ICU admission, and to have higher SAPS II score than patients without HAI. Probably due to these conditions, patients with HAI showed longer ICU stay than others.

The impact of COVID-19 pandemic

Compared with 2018–2019, the incidence density of HAIs recorded in 2020–2021 increased by 8.6%. In particular, the incidence density of CRI and PN increased by 13.3% and 8.2%,

Table I

Characteristics of the study population and the comparison of patients with or without healthcare-associated infections (HAIs)

Characteristics	Overall (*N*=21,523)	HAIs (*N*=3485)	Non-HAIs (*N*=18,038)	*P*-value
Age, years[a]	69 (21)	69 (21)	69 (21)	0.064
Male gender	60.5%	62.8%	60.1%	0.084
Transferred from another ward/hospital	73.9%	67.7%	75.1%	<0.001
SAPS II score[a]	40 (27)	47 (27)	38 (27)	<0.001
Surgical admission	52.4%	46.4%	53.5%	<0.001
Trauma	3.5%	5.0%	3.2%	0.001
Immunodeficiency	8.6%	10.4%	8.2%	0.015
Urinary catheter at ICU admission	72.6%	78.0%	71.6%	0.002
Intubation at ICU admission	59.9%	63.8%	59.1%	0.002
Central venous catheter at ICU admission	41.0%	39.7%	41.3%	0.295
Length of stay in ICU[a], days	7 (8)	20 (20)	4 (6)	<0.001

ICU, intensive care unit.

[a] Expressed as median (interquartile range).

Table II
Comparison of characteristics between patients with or without coronavirus disease 2019 (COVID-19)

Characteristics	COVID-19 (N=914)	Non-COVID-19 (N=1563)	P-value
Age, years[a]	70 (14)	70 (17)	0.054
Male gender	67.9%	63.5%	0.061
Transferred from another ward/hospital	90.2%	70.6%	<0.001
SAPS II score[a]	45 (35)	38 (30)	<0.001
Surgical admission	2.8%	49.9%	<0.001
Trauma	0.1%	2.9%	<0.001
Immunodeficiency	2.5%	4.7%	<0.001
Urinary catheter at ICU admission	74.5%	72.6%	0.312
Intubation at ICU admission	20.8%	50.4%	<0.001
Central venous catheter at ICU admission	20.1%	44.5%	<0.001
Length of stay in ICU[a], days	12 (8)	7 (6)	<0.001

ICU, intensive care unit.
[a] Expressed as median (interquartile range).

respectively. These increases were even more pronounced when compared with the entire pre-pandemic period (2006–2019): 14.8% for all HAIs, 18.2% for PN, and 76.3% for CRI.

Among 2477 people admitted to ICUs in 2020–2021, 914 (36.9%) were with PCR-confirmed SARS-CoV-2 infection. The incidence of patients with at least one HAI was higher in ICUs specifically dedicated to COVID-19 patients than in other ICUs (27.0% vs 18.0%; $P<0.001$). Regardless of the type of ward, COVID-19 patients had a higher incidence of HAI than others (35.1% vs 22.2%; $P<0.001$). However, there were no significant differences observed in the distribution of HAIs between COVID-19 patients and those without the infection ($P=0.278$). The percentages for PN were 58.8% in COVID-19 patients and 51.1% in non-COVID-19 patients, for UTI it was 14.3% vs 15.4%, for CRI it was 12.8% vs 16.0%, and for BSI it was 15.0% vs 17.4%.

Table II presents further comparisons between patients with or without COVID-19 in 2020–2021. COVID-19 patients were more likely to come from another ward/hospital and to have higher SAPS II score, and less likely to be traumatized and immunodeficient, to have undergone surgical intervention before ICU admission, and to present intubation and central venous catheter at ICU admission than non-COVID-19 patients. COVID-19 patients also exhibited longer stay in ICU than non-COVID-19 patients.

Mortality in ICUs before and during the pandemic

Of all patients staying in ICU for more than two days from 2006 to 2021, 4476 (20.8%) died in the ward. Overall, mortality increased from 17.7% in 2006–2007 to 42.3% in 2020–2021 (P-trend <0.001; Figure 2a). The mortality in ICU increased by 80.0% compared with 2018–2019 and by 235.0% compared with the entire pre-pandemic period (2006–2019). Looking solely at 2020–2021, there was a higher proportion of deaths among patients with COVID-19 than in those without it (68.9% vs 26.8%; $P<0.001$; Figure 2b). When stratifying for COVID-19 and HAI status (Figure 2c), mortality was higher in patients with the co-infection (75.2%), than in those with SARS-CoV-2 infection or HAI alone (66.2% and 39.9%, respectively), and in those with no infections (23.2%). Among COVID-19 patients, those who died in ICU were more likely to receive respiratory care before ICU admission ($P<0.001$), to be diagnosed with interstitial pneumonia ($P<0.001$), to be subjected to prone position ventilation in ICU ($P=0.008$), to be treated with corticosteroid ($P=0.012$) and heparin

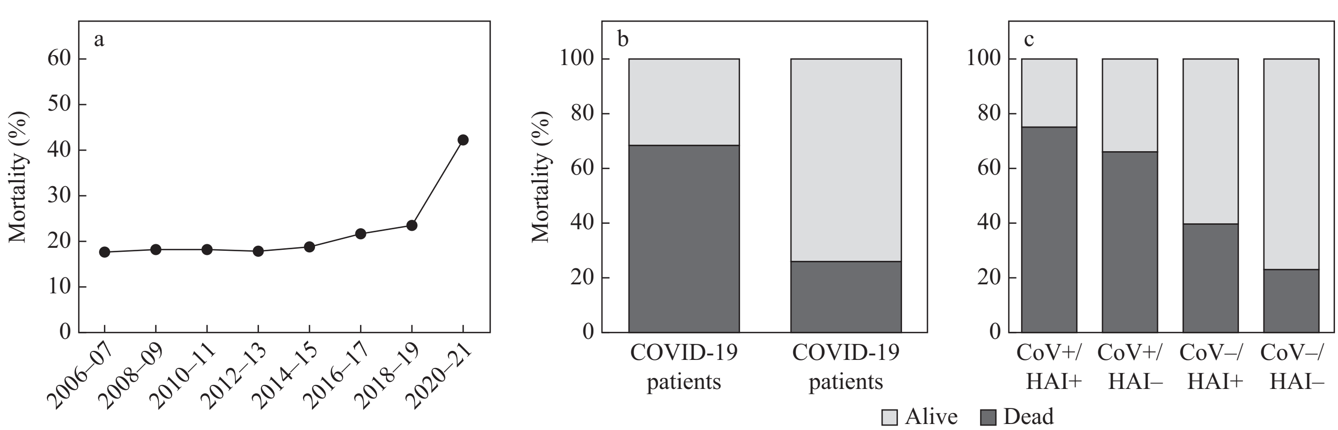

Figure 2. Mortality of patients in Italian intensive care units from 2006 to 2021. (a) Trend in mortality; (b) mortality of patients by coronavirus disease 2019 (COVID-19) status; (c) mortality of patients by COVID-19 status and healthcare-associated infection (HAI) status.

(P=0.004), and less likely to be treated with antiviral drugs (P<0.001) than alive patients.

Discussion

In the present study, we used data from the 'SPIN-UTI' project to explore whether and how the COVID-19 pandemic has influenced national trends of HAIs in Italian ICUs. It is worth mentioning that the project has surveyed more than 21,000 patients and 4000 infections from 2006 to 2021. In our study an increasing trend was observed, both in terms of incidence of patients with HAI and in terms of incidence density of HAI. When compared with the pre-pandemic period, the incidence density of HAIs increased by nearly 15% during the pandemic. The widespread transmission of SARS-CoV-2 infections, in fact, posed pressing conditions for healthcare facilities (e.g., altered staffing and practices, changed usage of personal protective equipment, higher number of admissions, etc.) which impacted the effectiveness of routine HAI surveillance and prevention practices [15,49–56]. Because of this scenario, other studies reported an increase in the incidence of HAIs after the beginning of the pandemic [57]. In an Italian hospital, for example, Baccolini and colleagues reported a greater proportion of patients with HAIs in the first wave of the pandemic than in the pre-pandemic period [13]. A similar increase was observed by Ghali and colleagues in a Tunisian hospital [58]. Baker and colleagues added to this evidence showing a temporal association between the rates of HAIs and the number of hospitalizations for COVID-19 in US hospitals [1]. There was also evidence that the pandemic had a detrimental effect in seven low-middle income countries, with all types of HAI rising sharply, especially central-line-associated BSI [15]. In our study, a significant portion of the general increase in HAIs may be attributed to the increasing incidence density of PN (from approximately 9 to 13 infections per 1000 patient days). Only in the pandemic period, the incidence density of PN has actually increased by 76%. This finding was in line with a Centers for Disease Control and Prevention (CDC) analysis revealing continued increases in HAIs in US hospitals during 2021. In particular, ventilator-associated events had the largest increase across all infection types [18]. Despite the strengthening of IPC measures, these rises were probably due to the overwhelming situation in all hospital settings and to the more critical conditions of patients admitted to ICUs [21,49,58,59]. Accordingly, in our study we found a higher incidence of HAIs in those ICUs specifically dedicated to COVID-19 patients. The latter, in fact, had an approximately 1.6 times greater risk of HAI than patients without COVID-19. In this regard, there is agreement that COVID-19 patients admitted to ICUs are more prone to develop bacterial co-infections [60]. For instance, Buetti and colleagues reported a higher risk of BSI in critically ill patients with COVID-19 than in those without it [61]. Similar findings were obtained by Grasselli and colleagues, but especially for the risk of BSI and PN [62]. Besides the risk of HAI, other studies investigated the undeniable impact of COVID-19 on clinical outcomes of patients admitted to hospitals, especially for older individuals and those with previous comorbidities [23–26]. In our study, COVID-19 patients were already more severe at the time of ICU admission, as shown by their higher SAPSII score. Moreover, they also had an approximately 2.6 times greater risk of death than patients without COVID-19. This explains the intense increase in mortality in the ICU during the pandemic, which has doubled and reached 42%. Even if this data confirms the alarming impact of COVID-19 on ICU patients, the possibility of co-infection must be explored separately and in depth. In fact, there was compelling evidence from systematic reviews and meta-analyses that the presence of co-infection was associated with poor outcomes, including increased mortality [20,63,64]. In our study, patients with co-infection (i.e., SARS-CoV-2 and at least one HAI together) were approximately 35% of COVID-19 patients and 13% of all patients admitted to ICUs. Notably, co-infected patients had a 3.2-fold greater risk of death than those without any infection. The mortality in patients with co-infection was also higher than in patients with COVID-19 infection or HAI alone.

To provide a comprehensive perspective, it is worth noting that reinforcing IPC measures, including rigorous hand-hygiene practices and the consistent use of alcohol rubs, may play a pivotal role in preventing the transmission of COVID-19 and in mitigating the occurrence of specific types of HAIs [57,65]. However, this was one the most controversial and debated issues during the pandemic [13,15,49,50,55,56,66]. As reported by Wee and colleagues, for example, the incidence of HAIs decreased with the improvement of IPC practices [10]. Other studies, instead, did not show any change in the incidence of HAIs after the beginning of the COVID-19 pandemic [17,67]. In particular, in German ICUs a lack of an increase in device-associated HAI was shown probably due to the lower overall incidence of COVID-19 cases in Germany, to a high availability of ICU beds compared with many other countries, including Italy, and a change in the ICU patient mix due to numerous elective procedures that were postponed during the pandemic [17,67]. The fact that the analyses were carried out in different periods is probably the reason for the controversial results. It is reasonable to think that HAIs were negatively affected by COVID-19 during the early stages of the pandemic, but this impact has changed since improvements in IPC practices were implemented. This issue probably represented one of the main limitations of our study. In fact, the last edition of the SPIN-UTI project occurred between October 2020 and March 2021, at a time when the COVID-19 epidemic curve was accelerating, and hospitalizations were more common. It is therefore possible to attribute the increase in HAI incidence to the particular period in which surveillance was conducted [27]. Moreover, our study did not consider additional information other than patients' characteristics, which might affect the incidence of HAIs during the COVID-19 pandemic. For instance, we did not consider information on the workload, the availability of personal protective equipment, the adherence to guidelines and recommendations, the organization of IPC practices, as well as antibody titre of COVID-19 patients. The third limitation is that we used the data of a 16-year surveillance-period from Italian ICUs. This represents a potential historical bias, because characteristics of patients included and their associated risks probably changed over the different editions of the SPIN-UTI project. It is also worth mentioning that the study had some methodological aspects representing its main strengths. The surveillance was conducted in accordance with the structured and standardized protocols provided by ECDC. This should allow comparison and validation of these results with those obtained by other European countries, and better evaluation of the effects of the pandemic worldwide. Moreover, one other strength relies on the fact that the study is multi-centred, allowing the comparison of our findings with different settings and the establishment of a national benchmark.

In conclusion, this study found that COVID-19 pandemic had a significant impact on HAI incidence and death in Italian ICUs. This occurred not only because of the crushing pressure placed on ICUs and their staff, but also because COVID-19 patients were at an elevated risk of HAIs and death. It is, however important to encourage further studies to examine how the pandemic has affected HAI trends in the long run. In fact, there is a possibility that IPC measures implemented against the pandemic could contribute to prevent HAIs across all hospital settings.

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Conflict of interest statement

The authors declare that they have no competing interests.

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