Hospital-acquired infective endocarditis during Covid-19 pandemic

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ABSTRACT

Background: The COVID pandemic has had a major impact on healthcare in hospitals, including the diagnosis and treatment of infections. Hospital-acquired infective endocarditis (HAIE) is a severe complication of medical procedures that has shown a progressive increase in recent years.

Objectives: To determine whether the incidence of HAIE during the first two months of the epidemic (March–April 2020) was higher than previously observed and to describe the clinical characteristics of these cases. The probability of the studied event (HAIE) during the study period was calculated by Poisson distribution.

Results: Four cases of HAIE were diagnosed in our institution during the study period. The incidence of HAIE during the study period was 2/patient-month and 0.3/patient-month during the same calendar months in the previous 5 years (p=0.033). Two cases presented during admission for COVID-19 with pulmonary involvement treated with methylprednisolone and tocilizumab. The other two cases were admitted to the hospital during the epidemic. All cases underwent central venous and urinary catheterization during admission. The etiology of HAIE was Enterococcus faecalis (2 cases), Staphylococcus aureus and Candida albicans (one case each). A source of infection was identified in three cases (central venous catheter, peripheral venous catheter, sternal wound infection, respectively). One patient was operated on. Two patients died during hospital admission.

Conclusions: The incidence of HAIE during COVID-19 pandemic in our institution was higher than usual. In order to reduce the risk of this serious infection, optimal catheter
Methods

Introduction

The COVID pandemic has had a major impact on healthcare in hospitals, including the diagnosis and treatment of infections [1–3]. In order to reduce the spread of SARS-CoV-2 to patients and hospital staff, priority has been given to the care of life-threatening diseases over non-urgent conditions. In addition, restrictions to the performance of various diagnostic procedures and invasive treatments have been recommended [4,5]. Experience with prior epidemics has been useful to point out some infection-related issues such as the difficulties to comply both with the use of personal protective equipment (PPE) and the preventive measures for nosocomial infections, as well as the delay in the collection of microbiological cultures and misinterpretation of symptoms and results of diagnostic tests [6–8].

Hospital-acquired infective endocarditis (HAIE) is a severe complication of medical procedures that has shown a progressive increase in recent years [9–11]. This progression has been linked to the aging of patients, increased use of venous catheters, parenteral nutrition, hemodialysis, implantation of cardiac devices or cardiac surgery [10–12]. To date, no studies have been reported that examine the relationship between the COVID-19 outbreak and the risk of HAIE.

The aim of the study was to determine whether the incidence of HAIE during the first two months of the epidemic was higher than previously observed and to describe the clinical characteristics of these cases.

Results

Four cases of HAIE were diagnosed in our institution during the study period. During the months of March and April of the previous five years (2015–2019), 23 cases of infectious endocarditis were treated in our hospital, of which 3 cases were acquired in our hospital. The 4 cases detected during the months of March and April 2020 represent an increase compared to the same months during the previous 5 years. The incidence of HAIE during the study period was 2/patient-month and 0.3/patient-month during the previous 5 years (p=0.033). The incidence of HAIE per 1000 days of stay during the study period was 0.119 and during the months of March and April of the previous 5 years it was 0.0194 (p<0.001).

According to Duke’s criteria, the first 3 cases were classified as definite IE whereas the 4th was classified as possible IE (Table 1). Case 1 was diagnosed after the patient had been hospitalized twice in the previous month, for surgical resection of urothelial carcinoma, followed by repair of iatrogenic arteriovenous fistula. Eight days later she was readmitted to a ward specifically dedicated to COVID-19 due to suspicion of having this infection. Five days after admission, IE was diagnosed in the context of moderate heart failure. Case 2 suffered
| Case | Decade | Time from admission (days) | Comorbidity | Risk factors<sup>a</sup> | Type of IE | Infection source | Clinical presentation | COVID-19 (treatment) | ETE findings | Blood cultures | Treatment | Surgery indicated | Surgery performed |
|------|--------|---------------------------|-------------|--------------------------|------------|-----------------|---------------------|---------------------|--------------|---------------|-----------|-----------------|-------------------|
| 1    | 7th    | 1                         | Carcinoma (surgery two w before) | Mitral and aortic rheumatic valvulopathy, mitral insufficiency, UC, CVC | Native | Forearm phlebitis | Fever, dyspnea, leg edema | No | Vegetation 7 mm on mitral valve | Enterococcus faecalis + ceftriaxone (4w) | No | No |
| 2    | 7th    | 48                        | HTA. DMID. HCOL. | Aortic and mitral prosthetic valve, sacral pressure ulcers, ICU admission, UC, CVC | Prosthetic | Sternal wound infection | Fever, thoracic pain, wound erythema and serosanguinous exudate (Serratia marcescens, Candida albicans) | No | Hypoecogenic aortic perivalvular thickening (1.3 cm). Extension to mitroaortic junction and aortic root (abscess) | C. albicans | Anidulafungin (8w) Fluconazole (indefinitely) | Yes | No<sup>b</sup> |
| 3    | 6th    | 15                        | Atrial fibrillation, obesity, rheumatic fever without valve functional impact | UC, CVC | Native | Unknown | Fever, dyspnea, productive cough | Yes (Tocilizumab, methylprednisolone) | Vegetation 22 mm on mitral valve. Moderate mitral insufficiency | E. faecalis<sup>c</sup> | ampicillin + ceftriaxone (6w) | Yes | Yes |

<sup>a</sup> Risk factors include variables that may increase the risk of IE.

<sup>b</sup> The patient was not operated on due to the severity of the disease.

<sup>c</sup> The type of IE is unspecified for Case 3.
from an aortic prosthetic IE due to Candida albicans acquired during admission for aortic valve surgical replacement. During the study period, surgical activity was reduced due to the SARS-CoV-2 pandemic, and the capacity of the surgical ICU was restricted to prioritize COVID-19 cases needing critical care. The surgical treatment was rejected because of the high risk of technical complications and frailty of the patient who died during hospital admission. Cases 3 and 4 presented IE after being diagnosed with COVID and treated with methylprednisolone (more than 1000 mg, each) and two doses of tocilizumab (600 mg, intravenously). Case 3 underwent surgery due to severe mitral insufficiency and evolved favorably. Case 4 presented a progressive sepsis that proved fatal despite antibiotic treatment. The patient presented several secondary foci: right costoclavicular arthritis, left wrist, several psoas abscesses, L2-L3 spondylodiscitis, lumbar anterior epidural collection and meningitis. The intervention was not considered because the TEE only showed mild mitral insufficiency without vegetations. However, it was considered that the patient most likely suffered from infectious endocarditis.

All included patients underwent central venous and urinary catheterization and had received systemic antibiotic treatment during the month prior to the diagnosis of HAIE. Comorbidity, risk factors, infection source, clinical presentation, TEE findings, microbiology and treatment of the patients are shown in Table 1. There were no more fatalities during the first 60 days of follow-up.

**Discussion**

There is a growing concern about the potentially negative impact of the COVID-19 pandemic on the prevention, diagnosis and treatment of other infectious diseases [1–3]. Our study suggests that the risk of developing HAIE may increase during an outbreak of coronavirus infection. To reduce the risk of HAIE, efforts to improve the prevention and treatment of bacteremia and other hospital-acquired infections potentially related to HAIE should be undertaken during outbreaks of viral respiratory infections.

HAIE cases usually comprise approximately 10% of the IE cases in the literature. The characteristics of the patients included in this small series are similar to those of series published before the COVID-19 pandemic [9–12]. Advanced age, prolonged contact with the hospital, the presence of previous heart disease or invasive devices often characterize these patients. With respect to etiology, it should be noted that half of the cases were caused by E. faecalis. This result is in accordance with the increase in enterococcal HAIE frequency that typically affects elderly patients with prior valvular damage or invasive diapositives [16].

Our results represent a remarkable finding because, to our knowledge, no link has been reported between outbreaks of coronavirus and the increase in IE cases so far. In contrast, co-infection with bacteria and fungi is a proven fact in severe cases of COVID-19 and has been estimated at about 8–10%, with a bacteremia rate of about 6% [17–21]. Lymphopenia and immunosuppressive treatments such as corticosteroids and interleukin-6 antagonists such as tocilizumab could potentially favor this complication [18,22].

Viral pneumonia itself could be considered a risk factor for the development of IE although the occurrence of
pneumococcal endocarditis in the context of a respiratory virus pandemic is considered a rare event [23]. As has been observed in previous outbreaks, some of our patients may have suffered a delay in the diagnosis of IE due to postponement of blood culture collection, the difficulties in obtaining a TEE for fear of contagion of the viral infection and to the misinterpretation of clinical and microbiological results [7,8]. Because of the similarity in clinical presentation between COVID-19 and other infections, appropriate diagnostic tests (including blood cultures) should be promoted when patients show signs suggestive of bacteremia or endocarditis [19]. Although TEE is a high-risk procedure for transmission of CoV-SARS-2 to health-care workers, because it can generate aerosols, its use should not be restricted only to life-threatening cases, even in the context of the COVID-19 pandemic, as has been proposed [5,13]. Providing healthcare workers with the appropriate PPE and facilitating TEE in appropriate cases, a proper diagnosis of IE during outbreaks of coronavirus infection can be done.

With regard to extrinsic risk factors, our patients frequently had invasive devices that increase the risk of developing HAIE such as venous or urinary catheters [14,17]. In fact, the use of PPE could constitute an additional difficulty in the correct maintenance of these devices due to a decrease of the time dedicated to patient care [6]. In our experience, the number of newly recruited nurses, the possible reduction in the number of patient visits attributed to the need to put on and take off PPE each time, and the impact of PPE on the tactile and visual performance of healthcare workers may have affected the quality of care. The WHO has insisted on the convenience of verifying sterile insertion in these patients and the need for removal when no longer needed [24]. Of note, cases 1, 2, and 4 presented a distinct original source of infection (peripheral catheter infection, sternal wound infection and central venous catheter infection, respectively).

The fact that the study was done in a single center and the small number of cases makes it advisable to await beforehand acknowledging the increased risk of HAIE during coronavirus outbreaks. We recognize that several potential biases that could have influenced our results such as changes in the number and characteristics of patients at risk, ICU admissions, surgical procedures or transfer of patients from other hospitals. Larger and multicenter epidemiological studies based on designs such as time-series or healthcare evaluation studies are needed to more definitively affirm this potential increase in the incidence of HAIE during coronavirus epidemics.

In summary, we have detected an incidence of HAIE higher than usual during the first two months of the COVID-19 pandemic. In order to reduce the risk of this serious infection, it could be recommended to strengthen basic preventive measures such as optimal catheter care, early treatment of any local infection and appropriate use of diagnostic techniques (TEE) in patients with suspected IE during the peak or second waves of COVID-19.

Credit author statement

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Ethical statement

This study was approval the local Clinical Research Ethics Committee (CEIC). All patients gave their consent to participate in the study.

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Declaration of Competing Interest

None declared.

References

[1] Zhou P1, Liu Z, Chen Y, Xiao Y, Huang X, Fan XG. Bacterial and fungal infections in COVID-19 patients: A matter of concern. Infect Control Hosp Epidemiol 2020 [Epub ahead of print].

[2] Ong CWM, Goletti D. Impact of the global COVID-19 outbreak on the management of other communicable diseases. Int J Tuberc Lung Dis 2020. https://doi.org/10.5588/ijtld.20.0140 [Epub ahead of print].

[3] Wahidi MM, Shojaee S, Lamb CR, Ost D, Maldonado F, Eapen G, et al. The use of bronchoscopy during the COVID-19 pandemic: CHEST/AABIP guideline and expert panel report. Chest 2020 [Epub ahead of print].

[4] Peloso A, Moekili B, Oldani G, Triponez F, Toso C. Response of a European surgical department to the COVID-19 crisis. Swiss Med Wkly 2020 [Epub ahead of print].

[5] Gackowski A, Lipczyńska M, Lipiec P, Szymański P. Echocardiography during the coronavirus disease 2019 (COVID-19) pandemic: expert opinion of the Working Group on Echocardiography of the Polish Cardiac Society. Kardiol Pol 2020 Apr 24;78(4):357–63.

[6] Houghton C, Meskell P, Delaney H, Smallle M, Grinton C, Booth A, et al. Barriers and facilitators to healthcare workers’ adherence with infection prevention and control (IPC) guidelines for respiratory infectious diseases: a rapid qualitative evidence synthesis. Cochrane Database Syst Rev 2020 Apr 21;4:CD013582. https://doi.org/10.1002/14651858.CD013582.

[7] Loudon MA, Prendergast BD, Moody W, Steeds R. Infective endocarditis mislabelled as ‘swine influenza. J Infect 2011 Apr;62(4):317–8 [21 se podría quitar son muy similares].

[8] Bleibtreu A, Arias P, Vallois D, Debat A, Lermuzeaux M, Rioux C, et al. Delayed management of Staphylococcus aureus infective endocarditis in a Middle East respiratory syndrome coronavirus possible case hospitalized in 2015 in Paris, France. Clin Microbiol Infect 2017;23:416–7.

[9] Hill EE, Vanderschueren S, Verhaegen J, Herijgers P, Claus P, Herregods MC, et al. Risk factors for infective endocarditis and outcome of patients with Staphylococcus aureus bacteraemia. Mayo Clin Proc 2007;82:1165–9.

[10] Martin-Dávila P, Fortun J, Navas E, Cobo J, Jiménez-Mena M, Moya JL, et al. Nosocomial endocarditis in a tertiary hospital: an increasing trend in native valve cases. Chest 2005;128:772–9.

[11] Lomas JM, Martinez-Marcos FJ, Plata A, Ivanova R, Gálvez J, Ruiz J, et al. Healthcare-associated infective endocarditis: an
undesirable effect of healthcare universalization. Clin Microbiol Infect 2010;16:1683–90.

[12] Murdoch DR, Corey GR, Hoen B, Miró JM, Fowler Jr VG, Bayer AS, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. Arch Intern Med 2009;169:463–73.

[13] Li JS, Sexton DJ, Mick N, Fowler Jr VG, Ryan T, Bashore T, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30:633–8.

[14] Fernández-Hidalgo N, Almirante B, Tornos P, Pigrau C, Sambola A, Igual A, et al. Contemporary epidemiology and prognosis of health care-associated infective endocarditis. Clin Infect Dis 2008;47:1287–97.

[15] Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J 2015;36:3075–128.

[16] Slipczuk L, Codolosa JN, Davila CD, Romero-Coral A, Yun J, Pressman GS, et al. Infective endocarditis epidemiology over five decades: a systematic review. PLoS One 2013;8:e82665.

[17] Zhang G, Hu C, Luo L, Fang F, Chen Y, Li J, et al. Clinical features and short-term outcomes of 221 patients with COVID-19 in Wuhan, China. J Clin Virol 2020 [Epub ahead of print].

[18] Jang TN, Yeh DY, Shen SH, Huang CH, Jiang JS, Kao SJ. Severe acute respiratory syndrome in Taiwan: analysis of epidemiological characteristics in 29 cases. J Infect 2004;48:23–31.

[19] Dong X, Cao YY, Lu XX, Zhang JJ, Du H, Yan YQ, et al. Eleven faces of coronavirus disease 2019. Allergy 2020 [Epub ahead of print].

[20] Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, et al. Clinical Characteristics of Covid-19 in New York City. N Engl J Med 2020 [Epub ahead of print].

[21] Kozak R, Prost K, Yip L, Williams V, Leis JA, Mubareka S. Severity of Coronavirus Respiratory Tract Infections in Adults Admitted to Acute Care in Toronto, Ontario. J Clin Virol 2020;126:104338.

[22] Pawar A, Desai RJ, Solomon DH, Santiago Ortiz AJ, Gale S, Bao M, et al. Risk of serious infections in tocilizumab versus other biologic drugs in patients with rheumatoid arthritis: a multidatabase cohort study. Ann Rheum Dis 2019;78:456–64.

[23] Alhushki W, Rongkavilitt C. Austrian syndrome associated with pandemic (H1N1) 2009 in child. Emerg Infect Dis 2010;16:1493–5.

[24] World Health Organization. Clinical management of severe acute respiratory infection when COVID-19 disease is suspected. 2020. WHO/2019-nCoV/clinical/2020.4.