

Incidence of Infective Endocarditis during the Coronavirus Disease 2019: Study of 41 Cases

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Abstract

Original Research Article

Introduction: The COVID-19 pandemic had a remarkable impact on the profile of patients suffering from acute cardiovascular syndromes. Among them, acute infective endocarditis. With an increasing incidence during the past two decades which clinical manifestations are challenging. **Objective:** To enlighten the impact of the COVID-19 pandemic on the incidence of infective endocarditis. **Methods:** We have performed a descriptive retrospective study of 41 cases conducted over a 2 years period from March 2020 to January 2022 from the department folders. Weekly incidence rates of IE admissions were computed and incidence rate ratios. **Results:** In total 41 patients were admitted with IE. The incidence of IE during the study period was 2/patient-month. The cases detected represent an increase compared to previous 5 years with a slight though non-significant decline after lockdown in 2020 when compared with the average in the previous years. **Conclusion:** A notable difference in the incidence of IE admissions during the COVID-19 pandemic was found with a significant increase compared to the previous years.

Keywords: Infective endocarditis, covid.

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INTRODUCTION

COVID-19 may cause variable symptoms from mild upper respiratory disease to severe lower respiratory disease potentially complicated by acute respiratory distress syndrome, sepsis, and multi-organ failure.

The COVID-19 pandemic had a remarkable impact on the profile of patients suffering from acute cardiovascular syndromes. Among them, acute infective endocarditis (AIE) represented a frequent part of these urgent procedures during first and second waves of the outbreak, often requiring challenging operations.

Infective endocarditis (IE) is associated with high morbidity and mortality. Recent studies have reported an increasing incidence of IE during the past two decades.

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. To date, no studies have been

reported that examine the relationship between the COVID-19 outbreak and the risk of AIE

Cardiovascular disease is the most common comorbidity found in COVID-19 patients. The clinical manifestation of Infective endocarditis and COVID-19 are challenging, both diseases could develop fever, chills, dyspnea, fatigue, cough and myalgia. However, COVID-19 concomitant infective endocarditis will be found in developing countries and initial screening will be vague.

In order to enlighten the impact of the COVID-19 pandemic on IE, we conducted a study to determine the incidence of AIE during the first two years of the epidemic and to describe the clinical characteristics of these cases.

PATIENTS AND METHODS

This is a descriptive retrospective study, conducted over a 2 years period from March 2020 to January 2022.

We collected 41 hospitalized patients for acute infective endocarditis at the Cardiology Department at the University Hospital in Marrakech.

Patients admitted with IE prior to the abovementioned study periods were excluded. The retrospective analysis was done by collecting data from the department folders.

The parameters studied were epidemiological (age, sex, and cardiovascular risk factors), the following comorbidities were assessed: stroke, atrial fibrillation, peripheral vascular disease, heart failure, chronic renal failure, dialysis, acute renal failure, diabetes, chronic obstructive pulmonary disease, liver disease, rheumatologic disease, presence of a cardiac implantable electronic device.

Microbiological diagnosis was based on blood or valve culture. Transthoracic and transesophageal echocardiography (TEE) were performed in patients with clinical or microbiological suspicion of IE according to European guidelines, in order to confirm or rule out valve dysfunction and intracardiac complications such as abscesses, vegetations, pseudoaneurysms or fistulae. Antibiotic therapy and surgical indications followed as well the European Guidelines.

RESULTS

The incidence

41 cases of AIE were diagnosed in our institution during the study period. The mean number of cases of endocarditis per year treated at our center during the last 5 years was 62.

The cases detected represent an increase compared to previous 5 years with a slight though non significant decline after lockdown in 2020 when compared with the average in the previous years.

The incidence of AIE during the study period was 2/patient-month.

Comorbidities

There were 22 men (53.65%) and 19 women (46.35%) with a sex ratio of 1.15.

The average age was 52 years, with extremes of 33 and 76 years. Sixty-seven percent of our patients were 50 years of age or older.

Many comorbidities were reported, as shown on the following table.

	Nbr	Rate
Age (years)		
>60	27	65.85%
<60	14	34.15%
Sex		
Male	22	53.65%
Female		
Comorbidities	19	46.35%
Stroke	9	21.95%
Atrial flutter/fibrillation	14	34.14%
Peripheral vascular disease	7	17.07%
Chronic heart Failure	18	43.90%
Chronic renal failure	13	31.70%
Dialysis	6	14.63%
Diabetes	21	51.21%
Liver disease	11	26.82%
Rheumatologic disease	8	19.51%
Prosthetic heart valve	27	65.85%
Hypertension	19	46.34%

Overall, no differences in sex, age, or comorbidities were found. Hence, no significant differences pre- versus post-lockdown was found.

Pharmacotherapy

	Number	Rate
Beta blockers	12	29.26%
Calcium channel blockers	16	39.02%
RASi	11	26.82%
Loop-diuretics	17	41.46%
Statins	9	21.95%
ASA	7	17.07%
OAC	13	31.70%

RASi: renin angiotensin system inhibitor, ASA: aspirin, OAC: oral anticoagulant therapy

Microbiology

	Rate
Staphylococcus aureus	25.8%
Coagulase-negative staphylococci	8.7%
Oral streptococci	18.2%
Non-oral streptococci	17.6%
Enterococci	10.4%
Other: haemophilus, aggregatibacter, cardiobacterium, Eikenella corrodens, kingella	1.3%
Candida species	1.6%
Polymicrobial (≥ 2 microorganisms)	1.2%
No microorganism identified	15.2%

ECHOCARDIOGRAPHY

Echocardiography showed that the diameter of the vegetation was 2 to 27 mm and that it was in the form of flocculent, cordlike, lumps with an irregular morphology.

The fresh vegetation exhibited low echoes and good activity. Increases in the disease duration were associated with a gradual increase in the extended echo and a reduced vegetation activity. The vegetation was either single or multiple in number.

The echocardiography results for the patients revealed 14 cases involving the aortic valve, 11 cases involving the mitral valve, 7 cases involving the tricuspid valve, 6 cases involving the pulmonary valve, and 3 cases involving an artificial valve.

Twenty-four of these cases had multiple valve involvement. Fourteen of the patients in this study experienced severe complications, including chordae tendineae rupture (4 cases), valve prolapse (5 cases), valve perforation (3 cases), and paravalvular abscess (2 cases).

	Nbr	Rate
Congenital heart disease	2	4.8%
Bicuspid aortic valve	3	7.3%
Aortic valve disease	14	12.7%
Mitral valve disease	11	26.8%
Tricuspid valve disease	7	17.1%
Pulmonary valve disease	6	14.63%
Multiple valve disease	4	9.7%
Postoperation heart valve surgery	7	17.1%
Prosthetic valve replacement Valvoplasty	9	21.9%
Rheumatic heart disease	5	12.1%
No obvious heart disease	3	7.3%

TREATMENT

Among the 41 patients, 13 underwent surgical treatment, 11 had significantly decreased vegetation numbers after undergoing anti-infective therapy using intensive antibiotic therapy, and 5 patients died due to cardiogenic shock, multiple organ failure (1 patient), and cardiac arrest (1 patient).

DISCUSSION

In recent studies, the annual incidence of IE have been found to range from 3 to 7 per 100,000 person-years [9, 6]. Patients with prior IE, prosthetic heart valve, or a cyanotic congenital heart disease are considered in high risk of IE, whereas patients with heart valve disorder, cardiac implantable electronic devices, or hypertrophic cardiomyopathy are considered in moderate risk of IE [5, 25, 26].

Correspondingly, a number of diseases and conditions has been associated with increased susceptibility to and severe course of COVID-19; in Denmark, it concerns elderly (>65 years), persons with chronic diseases including cardiovascular disease, immune-compromised patients, and children with sequelae of pre-maturity [27].

Thus, there is an overlap of risk factors among patients in risk of IE and COVID-19.

Cutaneous hygiene is the general advice for those in moderate- and high- risk of IE[5], consequently, increased awareness in the general population and among vulnerable persons may potentially ameliorate the effort of precautions and one may have expected a decline in the admission rate of IE.

Further studies are needed in order to enlighten the course of concomitant IE and COVID-19 infection. Lockdown has proven to be an effective strategy in slowing down the COVID-19 pandemic with significant reduction in infection and death rates [29]. Our study provides evidence of a significant effect of lockdown on the incidence of IE.

About 10% of patients with infective endocarditis show no growth from blood cultures resulting in thwarted diagnosis.

Several causes can account for this: antibiotics given before blood cultures, infection with fastidious bacteria or fungi, or alternative diagnoses such as nonbacterial thrombotic endocarditis, which occurs in advanced cancer.

The staphylococcus, streptococcus, and enterococcus species account for 84% of infective endocarditis. *S aureus* is the most frequently isolated microorganism and is reported in up to 30% of cases such as patients on haemodialysis and intravenous drug users, and can affect both native and prosthetic valves. Moreover, it has notorious propensity to acquire antibiotic resistance.

Coagulase-negative staphylococci (eg, *Staphylococcus epidermidis*, *Staphylococcus lugdunensis*, and *Staphylococcus capitis*) are ubiquitous skin commensals. They colonise indwelling lines and devices and are the most common isolate in early prosthetic valve endocarditis.

Coagulase-negative staphylococci also frequently cause hospital-acquired native valve endocarditis and multi-antibiotic resistance are characteristic features of these commensals.

Streptococcal infective endocarditis caused by the oral viridans group remains most common in low-income countries, this group includes *Streptococcus mutans*, *Streptococcus salivarius*, *Streptococcus anginosus*, *Streptococcus mitis*, and *Streptococcus sanguinis*.

These organisms are notable for causing infective endocarditis associated with an underlying colonic tumour, which provides the portal of entry. Enterococci account for 10% of cases overall.

Most isolates are *Enterococcus faecalis*, causing both native valve endocarditis and prosthetic valve endocarditis in elderly or chronically ill patients. *Enterococcus faecium* carries increasing resistance to vancomycin, aminoglycosides, and ampicillin.

The remaining microbes that can cause infective endocarditis are a mixture of fastidious bacteria, zoonotic bacteria, and fungi. The HACEK bacteria (*Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella corrodens*, *Kingella*), which cause about 3% of cases, are slow-growing organisms that colonise the oropharynx.

Zoonotic endocarditis is caused by *Coxiella burnetii* and *Brucella* (from livestock), *Bartonella henselae* (from cats), and *Chlamydia psittaci* (from parrots, pigeons). Other rare causes include Gram-negative bacteria (eg, *Acinetobacter* spp, *Pseudomonas aeruginosa*), and *Legionella* spp, *Mycoplasma* spp, and *Tropheryma whippelii*. Fungal endocarditis, usually *Candida* or *Aspergillus*, is rare but often fatal, arising in patients who are immunosuppressed or after cardiac surgery, mostly on prosthetic valves.

Previous studies have shown that 50% to 80% of IE cases occur primarily due to rheumatic heart disease. In contrast, recent data show that the proportion of IE cases with rheumatic heart disease as the underlying etiology is significantly decreased, and as a result, congenital heart disease has become the most common etiology of IE.

This result might be related to improvements in living standards, the widespread application of antibiotics, the significantly reduced incidence and recurrence of acute rheumatic fever, and the decreased incidence of rheumatic heart disease [12].

According to statistical analyses, the sensitivity of vegetation detection by transthoracic echocardiography is 60% to 75%, and the sensitivity of vegetation detection by transesophageal echocardiography is >95%.

Transthoracic echocardiography can rapidly and accurately detect vegetation and accurately determine the vegetation size, number, and location.

Left ventricular vegetation was more common in the 41 patients diagnosed with IE by transthoracic echocardiography in this study.

Published studies have shown that the frequency of valve infection is positively proportional to the risk of valve injury. Valves under high-pressure blood flow are subjected to the highest shear stress, and thus, left heart valve involvement has been observed in most IE patients [14].

The mitral and aortic valves receive the greatest blood pressure and are thus the most susceptible to infection, which is consistent with the findings obtained in this study.

In addition to the formation of valvular vegetation, the disease course of IE is accompanied by other complications, such as chordae tendineae rupture, valve prolapse, valve perforation, and paravalvular abscess [15].

It has been reported that the vegetation echoes, size, and activity can be used as independent factors in the prediction of embolism, particularly for a vegetation size >10mm, which is associated with the highest incidence of embolism [16].

The surgical rate in this study was 31.7% lower than the reported rate of 50%, and the overall mortality rate was 2.4%, which was lower than the rate of 17.7% reported in the literature [17].

The prognosis associated with active surgical treatment is significantly better than that associated with simple medical therapy, which shows the importance of timely surgical treatment at an early stage for the successful treatment of IE.

Therefore, the pros and cons of the 2 aspects must be weighed when determining the timing of surgery; specifically, if the patient's condition is progressively aggravated and heart failure cannot be controlled after medical treatment, the efficacy of surgery will be better than that of conservative treatment.

However, antibiotic treatment for IE should still be applied throughout the entire course of treatment. Once diagnosed, a sufficient dose of antibiotics should be administered, and a patient should continue to undergo antibiotic treatment for 4 to 6 weeks after surgery until sufficient treatment is achieved.

IE vegetation should be differentiated from calcified lesions in the valve, primary small tumors of cardiac valve leaflets, and thrombosis. Cardiac valve calcification is common in elderly patients with atherosclerosis or long-term rheumatic heart disease. Calcifications primarily appear as dense echoes visible as spots and lumps, whereas the vegetation mostly moves with valve opening and closing.

The echo associated with vegetation is relatively weak, and the vegetation structure is relatively loose. Calcification develops in the vegetation over time, and the vegetation echo might thus be enhanced [18].

CONCLUSION

In this study, remarkable significant difference in the incidence of IE admissions during the COVID-19 pandemic was found as compared to similar periods in the preceding years and to the pre-lockdown period of 2020.

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