Epidemiology of infective endocarditis in Tunisia: a 10-year multicenter retrospective study

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Summary
Background: Since the first description of infective endocarditis, the profile of the disease has evolved continuously with stable incidence. However, epidemiological features are different in developing countries compared with western countries.
Objective: To describe epidemiological, microbiological and outcome characteristics of infective endocarditis in Tunisia.
Patients and methods: This was a descriptive multicenter retrospective study of inpatients treated for infective endocarditis from 1991 to 2000. Charts of patients with possible or definite infective endocarditis according to the Duke criteria were included in the study.
Results: Four hundred and forty episodes of infective endocarditis among 435 patients (242 males, 193 females; mean (SD) age = 32.4 (16.8) years, range 1–78 years) were reviewed. The most common predisposing heart disease was rheumatic valvular disease (45.2%). Infective endocarditis occurred on prosthetic valves in 17.3% of cases. Causative microorganisms were identified in 50.2% of cases: streptococci (17.3%), enterococci (3.9%), staphylococci (17.9%), and...
Introduction

Despite great medical progress, infective endocarditis (IE) remains a serious infection with stable incidence. However, profound changes have occurred in the epidemiological profile of the disease, especially in developed countries where IE more frequently affects older patients or IV addicts with a decline in underlying rheumatic valvular disease and a larger spectrum of causative microorganisms.1—6 These changes have not been noted in developing countries.7,8

In Tunisia, epidemiological data are fragmentary and show that IE is frequently associated with rheumatic valvular disease resulting in high morbidity and mortality.9,10 The aim of this multicenter study was to describe the epidemiological characteristics of IE in Tunisia.

Patients and methods

This descriptive study was conducted retrospectively for a 10-year period, from 1991 to 2000, in almost all regions of Tunisia. We analyzed the charts of all patients hospitalized, in 13 (from 18) cardiology or infectious diseases units, with a diagnosis of IE. Inclusion criteria were definite or possible IE, according to modified Duke criteria.11 The following data were collected from those cases included: age, sex, underlying heart disease, predisposing conditions for bacteremia, complications, echocardiographic and microbiological data, surgical treatment, and outcome. For blood cultures, conventional manual systems were used with at least three aerobic and anaerobic bottles inoculated with blood, for at least 14 days. Serological tests for brucella and coxiella infections were performed in 17% and 12%, respectively, of IE patients with negative blood cultures. However, antibodies anti-bartonella, legionella and mycoplasma were not performed.

Early surgery was undertaken, if indicated, up to two months following the IE diagnosis. Since it was a retrospective study, only intra-hospital mortality was considered.

Statistical interpretation of data was performed using the computerized software program SPSS version 13 (SPSS, Inc., Chicago, IL, USA).

Results

Among 510 notifications during the study period, 440 episodes of IE among 435 patients were retained (242 males, 193 females; mean (SD) age 32.4 (16.8) years) (Figure 1). Tunisia has a population of 8 million; assuming that all cases are reported, there would be 55 cases/1 000 000 inhabitants. The incidence of IE was also stable during the 10-year period of the study with at least 46 new cases per year.

The mean (SD) duration of hospital stay was 37.6 (21.2) days (range 0—99, median 39 days). Predisposing heart diseases are listed in Table 1. Rheumatic valve disease was noted in 45.2% of native valve IE, with a stable rate in the last two years of 41.6%. No case of IE was associated with IV drug use. IE locations were: mitral valve in 45.7%, aortic in 33.2%, mitral and aortic in 13.4%, and tricuspid in 4.5%. A total of 218 cases (49.5%) had a confirmed or probable portal of entry. Dental procedures/poor dental condition was the most frequent cause of the bacteremia (n = 110), followed by cutaneous route (n = 43), percutaneous iatrogenic procedures and cardiac surgery (n = 23), and miscellaneous other conditions (n = 42).

The median number of blood cultures drawn was three. The causative microorganisms were identified by blood cultures in 204 cases (46.4%) and by other methods in 17 (3.9%) additional cases (six cultures of valve, six serological tests and five in a metastatic location). Blood cultures remained negative in 53.6% of cases and no microorganism was identified in 49.8%. Overall, streptococci, enterococci and staphylococci were the most commonly isolated — 78% of the identified causative microorganisms (Table 2). Congestive heart failure and neurological complications were observed in 45.2% and 20.2%, respectively (Table 3).

Conclusion: Infective endocarditis is still frequently associated with rheumatic disease among young adults in Tunisia, with a high frequency of negative blood cultures and high in-hospital mortality, given that the population affected is relatively young.

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During this period, 223 patients underwent valve surgery after a median (interquartile range) 27 (14–50) days following admission. Sixteen patients (4%) presented with a further episode of IE on the prosthetic valve during the period of study. The in-hospital mortality rate was 20.6% (90 patients).

**Discussion**

The real incidence of IE in our country could not be derived from this study; however, it has demonstrated that this disease remains frequent and serious with more than 46 cases per year and a mortality rate of 20.6%. Although not all Tunisian centers participated, a major strength of our study is the low influence of referral bias compared with most previous studies, which have mainly been based on series in a single tertiary center.

The low age of our patients (mean age = 32.4 years) is comparable to that found in developing countries. In contrast, in western studies an important shift has been observed over the last decades with the mean age of affected patients being 55 to 60 years. This has mainly been attributed to a dramatic decrease in the incidence of acute rheumatic disease, increasing patient longevity that has given rise to degenerative valvar lesions, placement of prosthetic valves, and increased exposure to nosocomial bacteremia. Although rheumatic disease was the most frequent underlying condition in our study (45%), its incidence had decreased when compared to the results of a study conducted in the seventies (67%). On the other hand, we noted an increasing proportion of IE in patients with no previously known heart disease (27.5% versus 1%). This last pattern change should be considered in the diagnosis of IE and the role of degenerative valve lesions.

As described in other series in developing countries, the most characteristic finding in our study was the high frequency of IE negative blood cultures (50%); in contrast, in series from industrialized countries, blood cultures were found to be negative in 5–15% of IE cases. The etiologic factors most incriminated in the high frequency of IE negative blood cultures are previous antibiotic therapy, lack of optimal conventional culture techniques, and lack of systematic investigation for rare and fastidious microorganisms. In a Tunisian study, when sera of IE were tested systematically for fastidious microorganisms, a high prevalence of bartonella endocarditis, associated with blood negative endocarditis, was observed.

In this study, as in previous reports, when blood cultures were positive, staphylococci and streptococci were the most commonly isolated causative agents of IE (35.7% and 34.5%, respectively). These two microorganisms have been reported as etiological agents in 13–49% and 20–63% of cases of native valve endocarditis, respectively. Only 1.1% of all IE were caused by *Brucella* spp; this low rate in spite of the endemicity of brucellosis in our country is probably due to the difficulty in isolating *Brucella* spp from blood cultures, in addition to brucellosis serology not having been performed systematically.

As in other reports, the major complications observed in our population were congestive heart failure and cerebral vascular accidents, noted in 45.2% and 16.4%, respectively. These major complications have the greatest influence on the prognosis of IE. The usual cause of congestive heart failure in patients with IE is infection-induced valvular damage, especially aortic valve infection. In this situation, surgical therapy is usually the only choice, although timing of surgery continues to be a matter for debate.

The overall mortality in the present series was 20.6% compared with 9–35% in others series. The mortality of IE is largely dependent on the underlying conditions of the population and timing of surgery in cases with congestive heart failure.

In conclusion, in our multicenter retrospective study, the incidence of IE has continued to rise and the clinical presentation, site of valvular infection, and types of etiologic microorganisms were typical of IE reported from the west. Nevertheless, compared to patients with IE in developed countries, notable differences in our study population included a greater proportion of rheumatic heart disease and a higher frequency of negative blood cultures. More
effort is needed in the areas of rheumatic heart prophylaxis and negative blood culture IE explorations.

Conflict of interest: No conflict of interest to declare.

References