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Epidemiology of Infective Endocarditis

Fabian Andres Giraldo Vallejo

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Abstract

Infective endocarditis is a rare disease, with an incidence of two to six episodes per 100,000 habitants/year. Incidence is higher in elderly people; besides, this group is often affected by many comorbidities. There is a clear and observable change in the spectrum of heart diseases predisposing to infective endocarditis in the last decades. Up to one-third of the patients acquire the disease on a health-care-associated environment. Despite advances in health-care logistics, infective endocarditis remains a big concern especially in low-income countries, where the main cause of infection is rheumatic fever. In-hospital mortality persists relatively high despite development in medical and surgical treatment. Patients with infective endocarditis need rapid response and prompt diagnosis from a multidisciplinary group including cardiologists, surgeons, infectologists, and radiologists.

Keywords: endocarditis, epidemiology, microbiology, outcome, incidence, mortality

1. Introduction

The term *infective endocarditis* (IE) denotes infection of the endocardial surface of the heart. Infection involves heart valves most commonly but may occur within a septal defect, chordae tendinae, or in the mural endocardium. Infections of arteriovenous shunts, arterioarterial shunts (patent ductus arteriosus), or coarctation of the aorta are clinically and pathologically similar to IE. The characteristic lesion of the IE, the vegetation, is a variably sized mass with inflammatory cells, platelets, fibrin, and abundant immerse microorganisms. The term *infective endocarditis,* first used by Thayer and later popularized by Lerner and Weinstein,is preferable to the former term bacterial endocarditis, because chlamydiae, rickettsiae, mycoplasmas, fungi, and perhaps even viruses may be responsible for the syndrome [1].

Diagnostic criteria for IE were published in 1982 by von Reyn and colleagues (The Beth Israel criteria), but these criteria did not use echocardiographic findings in the case definitions [2]. Including the central role of echocardiography in the evaluation of suspected IE, new case definitions and diagnostic criteria (The Duke criteria) were proposed in 1994 [3], modified in 2000, and widely used since then (**Table 1**) [4]. Echocardiography utility in the diagnosis of IE is clearly recognized [5], transesophageal imaging has superior sensitivity and specificity, is cost-effective, and is recommended when transthoracic approach is negative and a high clinical suspicion is present. The utility of both modalities is diminished when used indiscriminately [6, 7]. Advances in imaging technology have had minimal impact at the day-to-day clinical level; the role of three-dimensional (3D) echocardiography and other modes of clinical imaging (magnetic resonance imaging, computed tomography, and technetium scintigraphy) are yet to be formally evaluated [8].

Definition of infective endocarditis (IE) according to modified Duke criteria

Definite infective endocarditis

Pathologic criteria

- **Microorganisms demonstrated by culture or histologic examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen;** *or*

- **Pathologic lesions; vegetation or intracardiac abscess confirmed by histologic examination showing active endocarditis**

Clinical criteria

- **Two major criteria;** *or*

- **One major criterion and three minor criteria;** *or*

- **Five minor criteria**

Possible infective endocarditis

- **One major criterion and one minor criterion;** *or*

- **Three minor criteria**

Rejected

- **Firm alternate diagnosis explaining evidence of IE;** *or*

- **Resolution of IE syndrome with antibiotic therapy for ≤4 days;** *or*

- **No pathologic evidence of IE at surgery or autopsy, with antibiotic therapy for ≤4 days;** *or*

- **Does not meet criteria for possible IE, as above**

Major criteria

Blood culture positive for IE

- **Typical microorganisms consistent with IE from two separate blood cultures: viridans *Streptococci*, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus*;** *or*

- **Community-acquired *Enterococci*, in the absence of a primary focus; *or***

- **Microorganisms consistent with IE from persistently positive blood cultures, defined as follows:**

- **At least two positive cultures of blood samples drawn >12 h apart; *or***

- **All of three or a majority of ≥ four separate cultures of blood (with first and last sample drawn at least 1 h apart)**

- **Single positive blood culture for *Coxiella burnetii* or antiphase I IgG antibody titer >1:800**

Evidence of endocardial involvement

- **Echocardiogram positive for IE (TEE recommended in patients with prosthetic valves, rated at least "possible IE" by clinical criteria, or complicated IE (paravalvular abscess); TTE as first test in other patients), defined as follows:**

  ◦ **Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; *or***

  ◦ **Abscess; *or***

  ◦ **New partial dehiscence of prosthetic valve New valvular regurgitation (worsening or changing of preexisting murmur not sufficient)**

Minor criteria

- **Predisposition, predisposing heart condition or injection drug use**

- **Fever, temperature >38·C (100.4·F)**

- **Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway lesions**

- **Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor**

- **Microbiologic evidence: positive blood culture but does not meet a major criterion as noted above[*] or serologic evidence of active infection with organism consistent with IE**

- **Echocardiographic minor criteria eliminated**

TEE, transesophageal echocardiography; TTE, transthoracic echocardiography. Modified from [4].

Table 1. HACEK, *Hemophilus* spp., *Aggregatibacter* spp., *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* spp.

The challenges associated with IE are of increasing importance. The patients affected are older and sicker than those in the past, often with many comorbidities [9]. *Staphylococcus aureus* has surpassed penicillin-sensitive *Streptococci* as the most common cause in many high-income countries [10]. The population at risk is growing and health-care-associated *Staphylococcal bacteremia*, a conditioning of IE, is a major problem around the world [11].

In the last 30 years, the overall incidence of IE has remained between two and six per 100,000 individuals per year in the general population [12–14], whereas associated mortality has remained between 10 and 30% depending on the type of pathogen [15], the site of infection (native or prosthetic valve), and the underlying condition [16]. This quiescent trends in

mortality and incidence are due to a continuing evolution of epidemiological features and risk factors rather to a lack of medical progress. The variability of disease presentation and course represents a challenge for the physician [8]. Even though clinical practices are clearly explained by international guides, they are derived mainly from observational cohort studies rather than randomized trials [17, 18]. Chronic rheumatic heart disease was considered a primary risk factor for IE until the widespread introduction of antibiotics; nevertheless, this finding prevails for low-income countries [14]. Current behavior in industrialized countries portraits different risk groups including prosthetic valve recipients, intravenous (IV) drug users, individuals with intravenous catheters, patients undergoing hemodialysis, and elderly people with degenerative valve lesions. Oral *Streptococci* are the main cause of IE in the general population [14, 19, 20], whereas *S. aureus* and coagulase-negative *Staphylococci* (e.g., *S. epidermidis*) are more frequently found in intravenous drug users, individuals with prosthetic-valve IE and in those with health-care-related IE [12, 21–23] and group *D Streptococci* (e.g. *S. gallolyticus*) are increasingly prevalent in elderly patients [12, 14, 19, 24, 25]. Patients with IE require opportune diagnosis and prompt response from a multidisciplinary group including cardiologists, cardiac surgeons, infectious disease specialists, and radiologists. The logistics of high-level patient care remains difficult even in developed countries and is frequently unobtainable in low-income countries.

2. Epidemiology

The incidence of IE is difficult to determine, because the diagnosis criteria and reporting methods vary with different series [2, 26]. The annual incidence of IE reported in Olmsted County, MN, was five to seven cases per 100,000 person-years, from 1970 to 2000, with practically no change in this period interval [27]. Parallel results of 1.7 per 100,000 person-years were reported from a survey in Louisiana [28], similar to reports from France (2.4/100,000 person-year) [19, 29] and United Kingdom [30]. But these results are less than incidence reports from the Delaware river Valley region (11.6/100,000 population) [31]. Several series have reported considerable increments in hospitalizations for IE, with most of the increase ascribable to *S. aureus* [32]. The proportion of acute cases of IE has increased from approximately 20% in the pre-antibiotic era, to more than 75% in the majority of high-income countries today [9].

When investigating at IE history, it can be seen that it affected children and young adults as a result of chronic rheumatic heart disease [33]; nevertheless, this remains the first key factor for IE in developing countries representing up to two-thirds of cases [34, 35] and infection is caused predominantly by community-acquired, penicillin-sensitive *Streptococci* entering via the oral cavity. The mean age of patients with IE has increased gradually in the antibiotic era. In 1926, the median age was younger than 30 years [36]; by 1943, it was 39 years [25], 50 years in the 1980s, and 55–60 years in the 1990s and 2000s [2, 12, 13, 19]. In a recent report including 58 centers in 25 countries, covering more than 2700 patients with definite IE by modified Duke criteria, the median age was 57.9 year [9]. In the period from 1993 to 2003, including 3784 patients with IE, the incidence of infection was <5 per 100,000 patients per year in individuals aged 50 years or less and >15 per 100,000 patients per year in those older

than 65 years [12]. In a recent review comprising 3477 patients, the mean age of individuals with IE in 1980s was 45.3 years versus 57.2 years in 2000s [37]. These increasing rates of IE in the elderly could be the accumulation of factors such as improved living standards, which indirectly increase the population with degenerative valve disease hence leading to increasingly prosthetic valve surgeries in older patients. More men are affected than women; 58.6% in 1970s versus 66.3% in 2000s [37]. In a French study, the incidence of IE increased in patients older than 50 years and peaked at 194 infected per million habitants in men aged 75–79 years (**Figure 1**) [10].
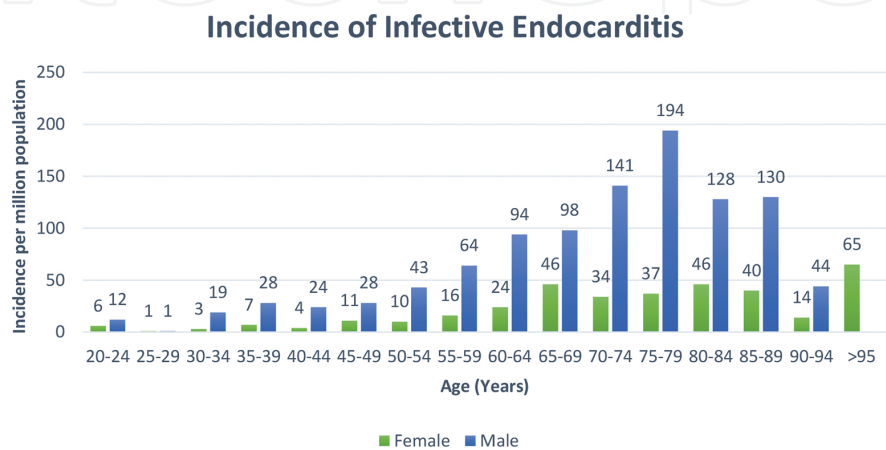

Figure 1. Incidence of infective endocarditis according to age and sex in a French population study of 497 patients. Zenith at 194 cases per million in men aged 75–79 years. Adapted from Selton-Suty et al. [10].

The causative agent has not changed much over time: *Staphylococci* spp., *Streptococci* spp., and *Enterococci* spp. still comprising more than 80% of all cases. Among these, *S. aureus* exceeds *Streptococci* spp. by 12% (**Figure 2**) [9].
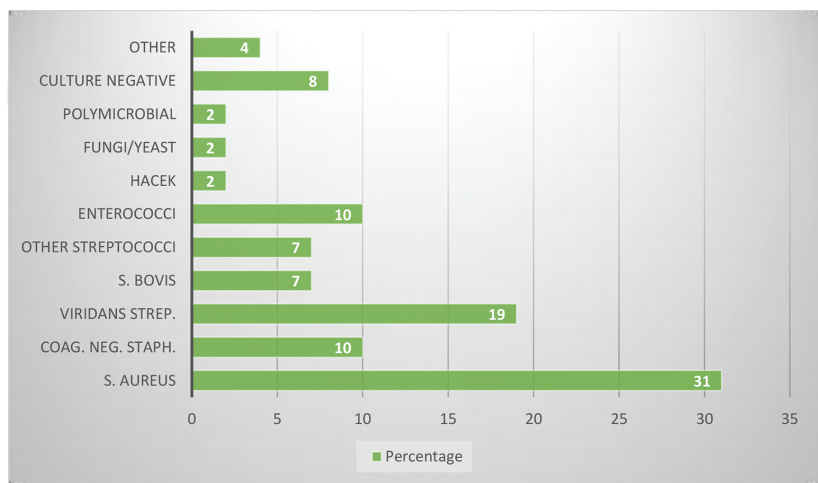

Figure 2. Microbiologic etiology of endocarditis in 1558 patients. Fifty-eight hospitals in 25 countries between June 2000 and September 2005. Data from Murdoch DR, Corey CR, Hoen B., et al. [9]

2.1. Health-care-associated endocarditis

Owing to introduction of new therapeutic modalities (e.g., pacemakers, intravenous catheters, hyperalimentation lines, and dialysis shunts), health-care-associated IE, a relatively new form of the disease, has emerged [2, 9, 22, 23, 38–40]. Health-care-associated endocarditis includes nosocomial IE as well as community IE after a recent hospitalization or as a consequence of long-term indwelling devices. In a recent prospective, multinational cohort study from 61 hospitals in 28 countries comprising 1622 patients with native valve endocarditis (NVE), and no intravenous drug abuse, 34% of patients had health-care-associated endocarditis with nearly half being community acquired [40]. Infection may compromise normal valves, including the tricuspid valve, as well as implanted intracardiac devices and valves [9, 21, 40–43]. The heart valve involved by infection varies considerably according to the different series. For mitral valve alone, the distribution ranges from 28 to 45%, aortic valve alone 5–36%, and aortic and mitral combined 0–35%. The tricuspid valve rarely is involved ranging from 0 to 6% and even less the pulmonary valve (<1%) [9, 44]. Health-care-associated IE accounts for 24 to 34% of cases not related to current cardiac surgery, and it involves an even larger proportion of cases in the United States [9, 23, 40]. Proportion of health-care-associated native valve endocarditis is 54% for nosocomial cases and 46% for community-based cases [40]. Mortality rates among these patients are high, ranging from 27 to 38%; aggravating factors include older patients and complex comorbidities [40, 41]. Among patients with health-care-associated IE, the largest subgroup belongs to individuals undergoing hemodialysis [22, 45]. Chronic hemodialysis has been identified as an independent risk factor for this type of IE [22, 40]. Patients undergoing hemodialysis have a higher risk of *S. aureus* infection causing IE [40, 45, 46]. The two most common pathogens related to health-care-associated IE are *Staphylococci* and *Enterococci*; the infection usually originates in the urinary tract or skin and intravenous lines or invasive procedures are often identified [40]. The risk of IE can be as high as 10% in cases of catheter-induced *S. aureus* bacteremia [39, 47, 48].

2.2. Immunocompromised patient IE

A special group is the immunocompromised patient who has a suboptimally functioning immune system. A number of conditions alter the immune response. The elderly has weak bactericidal response to infection. Impaired B-cell and T-cell function may develop in poor nutrition status or malnutrition. Hematologic and lymphoid malignancies and the medications used to treat them result in significant vulnerability to infection. The immune response is further reduced through the corticoids and cytotoxic drugs used to treat these conditions. Radiation therapy used to treat or palliate solid tumors and lymphoma suppresses antibody formation for weeks after treatment [49]. The degree of immunosuppression plays a major role in the outcome among human immunodeficiency virus (HIV)-infected patients with IE. Poor outcome is associated with a CD4+ cell count lower than 0.200 per 10(9)/L and left-sided or mixed IE [50, 51]. Common organisms associated with IE in HIV-infected patients are *S. aureus* and *Salmonella* [52]. Fungal microorganisms such as *Candida albicans, Aspergillus*, and *Crypto-coccus neoformans* are more common in IV drug abusers with HIV. These patients possess a

greater risk of developing IE on the right-sided heart valves [52]. Infection with HIV should not preclude cardiac surgery.

2.3. Prosthetic valve endocarditis.

Different series suggest that prosthetic valve endocarditis (PVE) accounts for 10–30% of cases of IE in the developed world [23, 41, 53, 54]. In patients undergoing valve surgery between 1965 and 1995, the cumulative incidence of PVE ranged from 1.4 to 3.1% at 12 months and 3 to 5.7% at 5 years [42]. Associated risks for the development of PVE include male sex, previous native valve compromise, and long cardiopulmonary bypass for prosthetic valve placement [55]. Microbial seeding may occur in the early postimplantation period, before endothelialization has established. The incidence is greatest in the first 6 months after valve surgery, then declines to a lower but stable rate (0.2–0.35% per year) [56–58]. The range of age of PVE patients varies from 50 to 74 years [19, 43, 53, 59–62]. The risk of PVE is higher when valve replacement is performed during active IE, especially with unknown pathogen or incomplete antibiotic treatment [58, 63–66]. Mechanical prostheses seem to have a slightly higher risk for PVE in the first 3 months after implantation and bioprosthetic valves have a higher risk after 1 year of replacement [56, 64, 65], maybe as a result of degeneration of bioprosthetic leaflets. Although the cumulative risk comparing mechanical with biological prosthesis is similar [42, 67, 68], the weighted mean incidence for infections of bioprostheses calculated from different series is 0.49% per patient-year for mitral valves and 0.91% per patient-year for aortic valves. For mechanical prostheses, the incidence is 0.18% per patient-year for mitral, 0.27% per patient-year for aortic, and 0.29% per patient-year for multiple implants [63]. PVE has been called *early* when infection occurred within 2 months of valve surgery and *late* when onset was >2 months. These terms were established to help distinguish PVE that instituted early as a complication of valve surgery from tardy infection that was likely to be community acquired [58, 69, 70]. However, in 2007, a study demonstrated a major shift according to the biological profile at 12 months after surgery, indicating that a more appropriate cutoff time to distinguish early from late PVE was 1 year [71]. Moreover, the European guidelines use this limit to classify the condition [17]. The causative pathogens involved in early PVE usually are methicillin-resistant *Staphylococci*, whereas in late PVE the common pathogens found are coagulase-negative *Staphylococci* and *Enterococci* (**Table 2**) [53]. In a large series including 2572 patients who underwent transcatheter aortic valve replacement (TAVR) in 14 centers between January 2008 and April 2013, the incidence of TAVR PVE was 1.13% (29 patients); the incidence of TAVR PVE by transfemoral approach was 1.1%, transapical 1.98%. The incidence of IE was 1.93% for balloon-expandable (23 of 1191) and 0.45% (6 of 1343) for self-expandable transcatheter heart valves. Early-onset IE (within 60 days) was diagnosed in 28% (eight patients), intermediate-onset IE (between 60 and 265 days) was diagnosed in 52% (15 patients), and late-onset IE (>1 year) was diagnosed in 20% (six patients) resulting in 80% of incidence of IE within the first 12 months of implantation (higher rates), contrasting with surgical valve IE. In the early-onset group, *S. aureus* and coagulase-negative *Staphylococci* were the most prevalent (50%), in the intermediate-onset group *Staphylococcal*, *Enterococcal*, and *non-viridans Streptococcal* species were the predominant pathogens (20% each), and in the late-onset group *Staphylococci* and *Enterococci* were identified (33% each), which does not resemble the late-onset surgical PVE [72].

PATHOGEN	EARLY PVE* (%) N = 53	LATE PVE* (%) N = 331
Staphylococcus aureus	36	18
Coagulase-negative Staphylococci	17	20
Enterococcus	8	13
Viridans streptococci	2	10
Streptococcus bovis	2	7
HACEK	0	2
Fungi	9	3
Other	6	14
Culture negative	17	12

Adapted from Wang et al. [53]. *Early refers to IE within 2 months and late after 2 months, according to Wang et al. HACEK: *Hemophilus, Aggregatibacter spp., Cardiobacterium hominis, Eikenella corrodens, Kingella kingae*. PVE: Prosthetic valve endocarditis.

Table 2. Causative organisms for early and late PVE.

2.4. Cardiovascular-implantable electronic devices infection

The most commonly used cardiovascular-implantable electronic device (CIED) are permanent pacemaker, cardiac resynchronization therapy, and implantable cardioverter-defibrillator. Most of these are implanted using transvenous leads. This practice had dramatically reduced the risk of infection associated with the procedure. Nevertheless, complication by infection remains a problem that can lead to significant morbidity, mortality, and elevated costs [73–75]. Reports of CIED infection vary according to different series and range from 0.13 to 19.9% [76–78]. In a 16-year survey of Nationwide Inpatient Sample (NIS) from 1993 to 2008, the rate of CIED implantation increased 4.7% annually. The incidence of CIED infection remained stable until 2004, but increased almost twice in a 4-year period (2004–2008) from 1.53 to 2.41%, respectively [75]. The rate of infection associated with implantable cardioverter-defibrillator surpasses greatly that of the pacemaker [79–81].

2.5. Ventricular-assist devices infection

Patients who receive ventricular-assist devices (VADs) usually have various comorbidities, including a state of immune compromise. The risk of infection varies depending on the duration of VAD support [82]. Higher rates of infection are observed in the destination therapy group compared with the group where VAD is used as a bridge to transplantation [82]. Hravnak reported that registry patients with implant duration longer than 60 days were twice as likely to develop infection than those patients supported for less than 30 days [83]. The reported rates of infection in patients with VAD range from 13 to 80% and depend on multiple factors, including comorbidities, type of device implanted, and duration of VAD support [84]. Infection of VAD can present as three different syndromes: driveline infection (most frequent)

presenting with local inflammatory changes and drainage at exit site, pocket site infection is the second syndrome presenting with local inflammatory changes, and the third (least frequent) is endocarditis comprising valves and/or internal lining of the device [84].

2.6. Infection of closure devices (atrial septal defect, patent ductus arteriosus, and ventricular septal defect)

Minimally invasive procedures are increasingly accepted as an option for cardiovascular congenital diseases [85–87]. Fortunately, complications derived from implantation of such devices are very rare, including infection (<1%) [85, 88–90].

2.7. Infective endocarditis in children

As in adults, trends in children IE are related to the evolution of care in the sick child, particularly children born with congenital heart disease. The incidence of children IE provides limited data, mostly based on inpatient admission which could not represent accurately the general population. In a report between 1933 and 1972, the incidence was 0.22–0.55 cases per 1000 pediatric hospital admissions [91]. A retrospective review between 1972 and 1982 found an incidence of 1/1280 pediatric admissions [92]. Later, in a multicenter study, the incidence of IE slightly decreased, ranging from 0.005 to 0.12 cases per 1000 pediatric admissions [93]. In other report including 47,518 patients, from 1998 to 2010, congenital heart disease was found as the major underlying condition associated to IE in children in high-income countries, with a cumulative incidence of 6.1 per 1000 children [94]. The distribution of IE between boys and girls is balanced in contrast with series in adults in whom men have a higher tendency to suffer the condition [94, 95]. Rheumatic fever is rare in developed countries, nevertheless is commonly found in low-income countries. In the presurgical era, the proportion of IE in children with rheumatic heart disease ranged from 30 to 50% [96]. A single center report covering seven decades found that IE occurred in 31% of rheumatic heart disease patients in presurgical era, compared to era 3 (1992–2004) with only 1.1% of patients having the condition [97]. Approximately 50% of cases of pediatric IE complicating congenital heart disease have had previous cardiac surgery, especially palliative shunts of complex cardiac repair [98]. Risk of postoperative IE in children depends greatly on the type of surgery; for example, a study from Oregon found a relatively low incidence of IE after tetralogy of Fallot repair (1.3%), ventricular septal repair (2.7%), atrial septal repair (2.8%), and aortic coarctation repair (3.5%). Nevertheless, a high incidence of IE was found in aortic stenosis (valve replacement) with a cumulative incidence at 25 years of 13.3% [99]. The rate of IE in structurally normal hearts is lower than those with a predisposing condition (22 vs. 78%), respectively [100]. A major risk factor to develop IE in an anatomically normal heart is an indwelling vascular catheter [101].

2.8. Infective endocarditis in adults

An important condition related to IE in the elderly is the congenital bicuspid aortic valve. In a prospective multicenter study, it was present in 16% of cases of native valve endocarditis [102]. Degenerative cardiac lesions assume an important role in the development of IE without underlying valve disease. In one study, degenerative lesions were present in 50% of patients

with native valve IE older than 60 years [103]. Calcified mitral annulus is a common finding in elderly women but rarely complicate with IE (3.8%) [104]. Even not a classical condition related to IE, idiopathic hypertrophic subaortic stenosis may represent up to 5% of incidence of the infection [105]. And there is a higher mortality rate correlation if a murmur is present (up to 36% of patients with hypertrophic aortic stenosis and IE) [105]. Another condition associated with IE is the mitral prolapse syndrome. In different series, the range of IE in those patients with mitral valve prolapse can go from 11 to 23% [106, 107]. In another study, 8.6% of patients with mitral valve prolapse who were monitored prospectively for 9–22 years developed IE [108]. This syndrome must be suspected in patients with mid-systolic click with or without a late systolic murmur. This condition is not uncommon and has been found in 0.5–20% of otherwise healthy people, especially young women. It has become apparent that a significant proportion of patients with mitral valve prolapse have an anthropometrically distinct habitus, suggesting that this condition is only an element of a generalized developmental syndrome [109]. It may be useful to have in mind these characteristics to help identify patients with a high risk of developing IE. Having valvular redundancy and thickened leaflets may increase the risk of IE [103]. The combination of mitral valve prolapse and men older than 45 years also may increase the risk of IE [110]. In a detailed case-control study, 25% of patients with IE had mitral valve prolapse; the odds ratio (8.2 of 95% confidence interval, 2.4–28.4) indicated a substantially higher risk for IE in patients with mitral valve prolapse than for those without it [111]. Another study found that mitral valve prolapse IE presented with more subtle symptoms, less mortality, and responded better to antimicrobial therapy than other types of left-sided IE, even though recognition of the infection was delayed [112].

2.9. Infective endocarditis in drug abusers

All estimations of IE incidence in drug abusers are hindered because there are no enough data reporting the exact number of victims of illicit drug-abuse epidemic. Reports from the United States present an incidence of IE in intravenous drug abusers that range from 2 to 5% per year [113] or 1.5–2 cases per 1000 years of IV drug abuse with men more commonly affected [114]. Although congenital cardiac disease and right-sided heart instrumentation are associated with IE, IV drug abusers retain the majority of cases. Intravenous drug users and those with HIV primarily consist of relatively young adults [115]. Acute infection accounts for approximately 60% of hospital admissions among drug abusers and IE is responsible of 5–15% of these episodes [116]. The presence of IE in a drug addict is difficult to predict, especially from history and physical examination findings alone [117, 118]. More than 60% of IV drug abusers with IE do not have an underlying preexisting valvular disease [119]. Although cocaine use by an intravenous drug abuser should raise the suspicion of IE infection [120], the most credible predictors of IE in febrile intravenous drug users are visualization of vegetations by echocardiography and the presence of embolic phenomena [118]. Up to 13% of cases of IV drug abusers with febrile episodes have an echocardiographically demonstrated IE [118]. Although left-sided native valve endocarditis may be present in this group of patients, the tricuspid valve is more commonly affected in intravenous drug users [121, 122]. Only two-third of patients with proven IE diagnostic presented with heart murmurs on admission [116]. The frequency of valvular involvement is tricuspid alone or in combination with other valves, 52.2%; aortic

alone, 18.5%; mitral alone 10.8%; and mitral and aortic combined, 12.5% [123]. Most of these patients are young (20–40 years old), and men are more commonly affected than women with a ratio of 4:1–6:1. Approximately 66% of the patients have extravalvular compromise which may help in the diagnosis [124–126]. Although there are studies reporting infection rate reductions (such as HIV, hepatitis, or abscess) with the implementation of a needle-exchange program [127, 128], to date, there are no conclusive evidence showing reduction in IE among this special group.

3. Conclusions

Much work remains to be completed. IE is a complex and challenging pathology with a high mortality rate despite current advancements in health care. Even though diagnostic and therapeutic modalities have progressed since the "rheumatic fever" era, there is still a concern in developing countries where rheumatic fever represents a major cause of IE and access to appropriate health care is not possible in large areas. Curiously, the changing epidemiology of IE depict us a disease that used to affect young patients, native valves, and had *Streptococci* as the main pathogen, to a disease that affect mainly older people with prosthetic valves implanted and *S. aureus* as the main pathogen. These changes occur alongside a better survival in older people but also with several comorbidities accompanying these patients. Imaging modalities such as echocardiography had greatly helped in the diagnosis of IE; the role of advanced imaging had yet to be clinically evaluated in a day-to-day basis. Chronic and immunosuppressive diseases play a major role as predisposing factors to develop IE. IV drug users comprise other group of patients severely affected by the disease. Adequate clinical analysis and high suspicion are necessary to help these "risk" patients and provide the right tools (multidisciplinary team) to detect and treat this limiting and deadly condition.

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