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A 27-year experience with infective endocarditis in Lebanon

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ABSTRACT

Although rare, infective endocarditis (IE) continues to cause significant morbidity and mortality. Previous data from the American University of Beirut Medical Center (AUBMC) had shown predominance of streptococcal infection. As worldwide studies in developed countries show increasing trends in *Staphylococcus aureus* endocarditis, it becomes vital to continually inspect local data for epidemiological variations. We reviewed all IE cases between 2001 and 2014, and we performed a comparison to a historical cohort of 86 IE cases from 1987 to 2001.

A total of 80 patients were diagnosed with IE between 2001 and 2014. The mean age was 61 years. The most commonly isolated organisms were streptococci (37%), compared to 51% in the previous cohort. *S. aureus* accounted for 11%. Only one *S. aureus* isolate was methicillin-resistant. In the historical cohort, 26% of cases were caused by *S. aureus*. Enterococci ranked behind staphylococci with 22% of total cases, while in the previous cohort, enterococcal IE was only 4%.

Compared to previous data from AUBMC, the rates of streptococcal and staphylococcal endocarditis have decreased while enterococcal endocarditis has increased. This study reconfirms that in Lebanon, a developing country, we continue to have a low predominance of staphylococci as etiologic agents in IE.

Introduction

Infective endocarditis (IE) is a disease which, for reasons not fully elucidated, still has an almost unchanged incidence and mortality over the past three decades despite unparalleled medical advances [1–6]. This, coupled with a dynamic epidemiology, makes IE an area of active research.

Over the past few years, the emerging literature, mostly from the Western hemisphere, has shed light on the various features of IE. A wealth of information is now available through several population-based studies [3,4,7,8], in addition to the International Collaboration on Endocarditis-Prospective Cohort Study (ICE-PCS) [1,9–12]. What the data reveal in essence is that IE is increasingly becoming a hospital-acquired and healthcare-associated infection, and affecting a significantly older population. *Staphylococcus aureus* has become the leading pathogen, at the expense of the more traditional streptococci, primarily owing to a decline in rheumatic heart disease (RHD), an increasing use of intravascular catheters, a rise in hospital and healthcare acquisition, among other reasons.

The only studies available from Lebanon, carried by our group, demonstrate a different pattern, whereby streptococci were still predominant amidst a high incidence of RHD [13]. A similar study published earlier in the pediatric age group at our center corroborates these findings in children [14]. Data from neighboring countries are mixed, some, from Turkey, Israel, Saudi Arabia and Yemen [15–18], agreeing with the Lebanese findings, while others, from Greece, Turkey, Saudi Arabia and Tunisia [19–22], suggesting a changing epidemiology similar to that reported in the Western literature. The present analysis compares two timeframes in terms of epidemiology, microbial etiology, outcome, and treatment of IE at a tertiary care center in Lebanon.

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Methods

AUBMC is a 400-bed, university teaching facility and tertiary referral center for Lebanon and the region located in Beirut, Lebanon. Patients older than 18 years who were hospitalized at the American University of Beirut Medical Center (AUBMC) between September 1987 and June 2014 and had a discharge diagnosis of IE were included in the study. This was a mixed retrospective and prospective analysis, since AUBMC joined the ICE group in 2001. All cases prior to 2001 were reviewed retrospectively, while cases between 2001 and 2014 were identified prospectively.

The revised Duke criteria, characterized by high sensitivity and specificity and validated by several studies, were used for the selection of both retrospectively- and prospectively-identified cases [23,24]. Definite and possible cases of IE were included in the analysis. Demographic, clinical, microbiological, outcome, and treatment data were collected from patients' records and entered into a database using IBM® SPSS® Statistics version 21. Chi square (or Fisher's exact test, when applicable) was used to compare categorical variables and the Student's *t* test was used for continuous variables. Differences were deemed significant at a p-value of <0.05. Univariable analysis was performed to compare patients and disease characteristics, microbial etiologies, and treatment patterns before and after 2001. Predictors of in-hospital mortality and risk factors for paravalvular complications were derived by multivariable analysis using a backward logistic regression model.

Results

Patient characteristics

A total of 166 patients with a discharge diagnosis of IE were identified between September 1987 and June 2014, 86 before 2001 and 80 after 2001. Thirty-four cases fulfilled the definition of possible IE and 132 that of definite IE. There was no difference in the proportion of possible/definite cases between the two time periods. Patients were significantly older in the second time period (mean of 48.0 ± 18.2 years before 2001 vs. 59.0 ± 17.8 years after 2001; p < 0.001). Overall, diabetes mellitus was the most common comorbid condition (10.5% and 16.3% before and after 2001, respectively; p = 0.27), but there was a significant increase in the proportion of patients with underlying malignancies over time (2.3% vs. 13.8%; p = 0.01). Prosthetic valve IE (PVIE) rates increased, albeit not significantly (19.8 vs. 30%; p = 0.13), and RHD remained the most common native valve predisposition with almost unchanged frequency between the two time frames (15.1% vs. 16.3%, p = 0.84). On the other hand, nosocomial acquisition of IE increased from 7.0% to 26.3% (p < 0.001). Population characteristics before and after 2001 and predisposing conditions are shown in Table 1.

Clinical manifestations

Classical signs and symptoms of IE were infrequent with the most common sign on presentation being fever in 90.6% and the most reported physical examination finding being a new murmur in 17.5%. Clinical and laboratory findings on admission are shown in Table 2.

Microbiology

Blood cultures were drawn from all patients and were positive in 83.8% after 2001 (compared to 96.1% cultured blood samples before 2001, of which 74.4% were positive). Streptococci accounted for the majority of isolates throughout, despite a non-significant decrease (39.5% vs. 26.3%, p = 0.07), most of which were identified as viridans group streptococci (22.1% and 17.5% respectively, p = 0.46). Most viridans streptococci (96.5%) were susceptible to penicillin. The proportion of *S. aureus* isolates remained unchanged

Table 1
Characteristics of patients with infective endocarditis before and after 2001.

Characteristics	Before 2001 (n = 86)	After 2001 (n = 80)	p-Value
Age *in years*, mean ± SD	48.0 ± 18.2	59.0 ± 17.8	<0.001
Male gender	53 (61.6)	60 (75.0)	0.06
Transfer from another hospital	15 (17.4)	11 (13.9)	0.54
Co-morbidities			
Diabetes	9 (10.5)	13 (16.3)	0.27
Malignancy	2 (2.3)	11 (13.8)	0.01
Immunosuppression	2 (2.3)	6 (7.5)	0.12
Hemodialysis	1 (1.2)	4 (5.0)	0.15
IVDU	0	1 (1.3)	0.48
HIV-positive	0	1 (1.3)	0.48
Recent dental procedure	13 (15.1)	9 (11.3)	0.70
Other recent invasive procedures	7 (8.1)	11 (13.8)	0.51
Intravascular catheters			
Peripheral intravenous line	4 (4.7)	8 (10.0)	<0.001
Short term central catheter	2 (2.3)	5 (6.3)	0.26
Chronic central catheter	1 (1.2)	2 (2.5)	0.61
Arteriovenous fistula	1 (1.2)	2 (2.5)	0.61
Cardiac devices			0.01
Pacemaker	2 (2.3)	7 (7.8)	0.09
AICD	0	1 (1.3)	0.48
Other	0	2 (2.5)	0.34
History of endocarditis	7 (8.1)	12 (15.0)	0.16
Congenital heart disease	7 (8.1)	7 (8.8)	0.89
PVIE	17 (19.8)	24 (30.0)	0.13
Native valve predisposition			
RHD	13 (15.1)	13 (16.3)	0.84
Rheumatic heart MS	9 (10.6)	7 (8.8)	0.69
Non rheumatic MS	0	1 (1.3)	0.48
MI	15 (17.6)	12 (15.0)	0.65
Rheumatic heart AS	9 (10.6)	7 (8.8)	0.69
Non rheumatic AS	0	3 (3.8)	0.11
AI	10 (11.8)	5 (6.3)	0.22
Other	7 (8.1)	7 (8.8)	0.89
Nosocomial acquisition	**6 (7.0)**	**21 (26.3)**	**<0.001**

All numbers indicate no. (%) unless otherwise specified.
SD = standard deviation; IVDU = intravenous drug use; AICD = automated implantable cardiac defibrillator; PVIE = prosthetic valve infective endocarditis; RHD = rheumatic heart disease; MS = mitral stenosis; MI = mitral insufficiency; AS = aortic stenosis; AI = aortic insufficiency.

Table 2
Clinical and laboratory findings of patients with endocarditis on admission, compared with published data from ICE-PCS.

Findings	n/N (%) of patients	
	Current study	ICE-PCS [1]
Clinical findings		
Fever	145/160 (90.6)	2322/2428 (95.6)
Vascular embolic event	32/160 (20.0)	456/2665 (17.1)
New murmur	29/166 (17.5)	1068/2232 (47.8)
Splenomegaly	19/160 (11.9)	284/2662 (10.7)
Osler's nodes	5/160 (3.1)	77/2648 (2.9)
Worsening murmur	10/166 (6.0)	359/1787 (20.1)
Positive rheumatoid factor	9/152 (5.9)	138/2549 (5.4)
Roth spots	9/160 (5.6)	50/2649 (1.9)
Splinter hemorrhage	9/160 (5.6)	213/2655 (8.0)
Janeway lesions	5/160 (4.4)	123/2650 (4.6)
Conjunctival hemorrhages	5/160 (3.1)	122/2655 (4.6)
Laboratory findings		
Elevated ESR	93/152 (61.2)	1611/2645 (60.9)
Hematuria	49/157 (31.2)	666/2587 (25.7)
Elevated CRP	24/152 (15.8)	**1632/2650 (61.6)**

ICE-PCS = International Collaboration on Endocarditis-Prospective Cohort Study; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.

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