

Infective endocarditis at a tertiary care centre in Saudi Arabia: review of 47 cases over 10 years

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التهاب الشغاف العدوائي في مركز للرعاية الثالثية في المملكة العربية السعودية: مراجعة 47 حالة على مدى 10 سنوات

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الخلاصة: أجرى الباحثان مراجعة استيعادية لكل الحالات التي أدخلت في ما بين عامي 1993 و2003 إلى مستشفى للرعاية الثالثية (التخصصية) في الرياض، بالمملكة العربية السعودية، لتحديد طراز التهاب الشغاف العدوائي فيها. فوجدوا أنه من بين 47 مريضاً، تمّ اكتشاف صمام أصيل في 37 منهم (78.7%) وصمام بديل في 10 منهم (21.3%). وشوهدت حالات قلبية مؤهبة لدى 27 مريضاً، حيث كانت الأمراض القلبية الخلقية والروماتزمية من أكثر الأمراض شيوعاً. وكان زرع الدم إيجابياً لدى 76.4% من المرضى. وكانت أنواع المكورات العنقودية أكثر الجراثيم المستفردة شيوعاً لدى 20 مريضاً (12 منها عنقودية ذهبية، و8 عنقودية سلبية الكواغولان) تليها أنواع المكورة المعوية (6 مرضى). وبلغ معدل المضاعفات 78.7% ومعدل الوفيات في المستشفى 8.5%.

ABSTRACT To describe the pattern of infective endocarditis in a tertiary hospital in Riyadh, Saudi Arabia, a retrospective review was made of all cases admitted between 1993 and 2003. Of 47 patients, a native valve was involved in 37 (78.7%) and a prosthetic valve in 10 (21.3%). Predisposing cardiac conditions were present in 27 patients: rheumatic and congenital heart disease were the most common. Blood cultures were positive in 76.4% of patients: the most commonly isolated organisms were *Staphylococcus* spp. in 20 patients (12 *St. aureus* and 8 coagulase-negative staphylococci) and *Enterococcus* spp. (6 patients). The complication rate was 78.7% and hospital mortality rate was 8.5%.

Endocardite infectieuse dans un centre de soins tertiaires en Arabie saoudite : étude de 47 cas sur 10 ans

RÉSUMÉ Afin de décrire le profil de l'endocardite infectieuse dans un hôpital tertiaire de Riyadh (Arabie saoudite), il a été procédé à une analyse rétrospective de tous les cas admis entre 1993 et 2003. Sur 47 cas, 37 (78,7 %) avaient pour origine une valve native et 10 (21,3 %) une prothèse valvulaire. Vingt-sept patients présentaient une cardiopathie prédisposante, la cardite rhumatismale et la cardiopathie congénitale étant les plus fréquentes. Les hémocultures se sont avérées positives chez 76,4 % des patients : les micro-organismes les plus fréquemment isolés étaient *Staphylococcus* spp. dans 20 cas (12 *St. aureus* et 8 staphylocoques coagulase-négatifs) et *Enterococcus* spp. (6 patients). Le taux de complication s'est élevé à 78,7 % et la mortalité hospitalière à 8,5 %.

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Introduction

Infective endocarditis (IE) remains a relatively rare disease worldwide, with an estimated incidence between 1.8 and 7.0 per 100 000 per year [1,2]. Recent reports from developed countries have focused on the changes in the epidemiology, bacteriology and clinical presentation of IE [3–11] as well as major advances in the diagnosis and management of this clinical disease [1]. Despite considerable advances in medical and surgical treatment, the overall mortality remains high, ranging from 21% to 50% over the past 3 decades [12–14].

However, data from Saudi Arabia and the Gulf region are lacking and the epidemiology of IE in this part of the world remains largely unknown; even current knowledge of the incidence and prevalence of rheumatic carditis and valvular heart disease remains limited due to the lack of nationwide epidemiological studies. All the published studies from Saudi Arabia on rheumatic fever are case series with descriptions of surgical and medical intervention.

The aim of this retrospective case series study was to describe the clinical, microbiological and echocardiographic characteristics and management of patients with IE, over a period of 10 years in a large hospital, as well as the short-term in-hospital mortality rate. The hospital serves a large community of 100 000 people that includes soldiers and their extended families and that could be considered as representative of the rest of the country.

Methods

Data were collected on a retrospective basis from a computer database and handsearch of the medical records of all patients who

were admitted to the King Fahad National Guard Hospital, Riyadh, Saudi Arabia, with the diagnosis of endocarditis or IE from May 1993 to May 2003. The hospital is a tertiary care centre with 700 beds that serves Saudi National Guard soldiers and their extended families. The wide range of services offered include paediatrics, internal medicine, obstetrics and gynecology, neurosurgical sciences, and 6 critical care units, liver and renal transplantation, and a major cardiac science programme.

The modified Duke criteria were used in the diagnosis of IE in our cohort. Only patients who met the Duke “definitive” criteria for IE were included [15]. Prosthetic valve endocarditis cases were considered as early if they occurred during the first 2 months after valve replacement, and late if they appeared thereafter. At this institution, the workup for patients with suspected IE includes 3 to 5 sets of blood cultures, haemogram, urine examination, chest X-ray, electrocardiogram and echocardiogram. Fungal blood cultures are not routinely done, but serology for a typical pathogens (*Chlamydia* spp., *Bartonella* spp., *Coxiella burnetii* and *Brucella* spp.) are done if needed.

The data collected included age, sex, predisposing factors, the causative organism, the presence or absence of vegetations on echocardiogram, the location of the IE lesions, the frequency of surgical treatment, the indication for surgery, and the short-term in-hospital mortality rate.

Statistical analysis

Data were collected and entered into a database using Microsoft *Access 2000*. Statistical analysis was conducted using *SPSS* version 10.0 for Windows and Microsoft *Excel 2000*.

Results

Patient characteristics

Forty-seven (47) patients with a diagnosis of IE at discharge were identified. The male to female ratio was 1.6:1 (29 male:18 female). The mean age was 32 (standard deviation 20) years (range 0.4–78 years). Endocarditis was acquired nosocomially in 2 patients, and another 2 patients had a central line for haemodialysis at onset of IE.

The cases were equally distributed throughout the study period from May 1993 to May 2003. The overall number of admissions to King Fahad National Guard Hospital during the study period was 321 407, therefore IE was responsible for 14.6 cases per 100 000 hospital admissions.

Predisposing factors

Predisposing factors for IE are shown in Table 1. Of the 47 patients, 10 (21.3%) had

Table 1 Predisposing factors among 47 patients with infective endocarditis (IE) in a tertiary hospital in Riyadh, Saudi Arabia

Type of endocarditis/ predisposing factor	No. of patients	%
Native valve IE		
Rheumatic heart disease	12	25.5
Congenital heart disease	10	21.3
Previous IE	3	6.4
Sepsis	3	6.4
Intravenous drug abuse	2	4.3
Degenerative valvular heart disease	2	4.3
Haemodialysis through central line	2	4.3
None	3	6.4
Prosthetic valve IE		
Multiple valve replacement	4	8.5
Aortic valve replacement	4	8.5
Both	2	4.3

prosthetic valve endocarditis, all of them were late onset, and 37 (78.7%) had native valve IE (all of them were late onset). Of the native valve patients, 12 had rheumatic heart disease with valvular lesions and 10 had congenital heart disease (3 ventricular septal defect, 3 transposition of the great vessels, 2 pulmonic valve stenosis, 1 bicuspid aortic valve and 1 complex structural malformations). A further 3 patients had prior history of IE, 2 had degenerative valve disease, 2 patients were intravenous drug users, 2 patients had chronic renal failure on haemodialysis through a central line, 3 patients had sepsis (2 diabetic foot, 1 intensive care unit burn patient) and 3 patients had no identifiable risk factors.

Clinical manifestations

The most frequent symptoms on presentation were fever in 44 cases (93.6%) with mean temperature of 38.6 °C, stroke in 6 cases (12.7%), dyspnoea in 4 patients (8.5%), cough in 3 patients (6.38%). On physical examination, fever was confirmed in 44 patients (93.6%), heart murmur in 34 patients (72.3%), splinter haemorrhage in 13 patients (27.6%), and 6 patients (12.8%) had stroke (Table 2).

Microbiology

Blood cultures were taken in all patients and were positive in 35 patients (76.4%) (Table 3). The most commonly isolated organisms were *Staphylococcus* spp. in 20 patients: 12 were *Sta. aureus* (8 methicillin-sensitive, 4 methicillin-resistant) and 8 were coagulase-negative. The second most commonly isolated organism was *Enterococcus* spp. in 6 patients; other isolates included *Streptococcus viridans*, *Brucella melitensis*, beta-haemolytic *Streptococcus*, *Hemophilus* spp. and diphtheroids (*Corynebacterium jeikeium*).

Table 2 Clinical manifestations among 47 patients with infective endocarditis

Symptom/sign	No. of patients	%
Symptoms		
Fever	44	93.6
Stroke	6	12.8
Dyspnoea	4	8.5
Weakness	3	6.4
Arthralgia	3	6.4
Cough	3	6.4
Headache	2	4.3
Sweats	1	2.1
Weight loss	1	2.1
Oedema	1	2.1
Haemoptysis	1	2.1
Back pain	1	2.1
Vomiting	1	2.1
Signs		
Fever	44	93.6
Heart murmur	34	72.3
Splinter haemorrhage	13	27.6
Splenomegaly	8	17.0
Osler nodes	6	12.8
Stroke	6	12.8

Echocardiography

Echocardiography was performed in all patients; transthoracic echocardiography

Table 3 Blood culture results in 35 patients with infective endocarditis

Causative organism	No.	%
Staphylococcus aureus	12	33.3
Methicillin-sensitive	(8)	
Methicillin-resistant	(4)	
Coagulase-negative staphylococci	8	22.3
Enterococcus spp.	6	16.7
Streptococcus viridans	5	13.9
Brucella melitensis	2	5.6
β -haemolytic streptococci	1	2.8
Diphtheroids	1	2.8

(TTE) in 36 (76.6%) and transoesophageal echocardiography (TEE) in 25 patients (53.2%). Echocardiography findings defined as positive included presence of vegetation, new valvular regurgitation, intracardiac abscess, valve perforation or valve dehiscence. TTE was positive in 24/36 (66.6%) and TEE in 22/25 (88.0%). Overall, echocardiography was positive in 41 patients (87.2%). Vegetations were seen in 37 patients (78.7%), new valvular regurgitations in 2 (4.3%) and perivalvular complications and perforation abscess in 2 (4.3%).

The mitral valve alone was involved in 20 patients (45.6%) and aortic valve in 10 (21.3%) and there was disease on both valves in 5 (10.6%). In addition, the tricuspid valve was affected in 3 patients (6.4%), the pulmonic valve in 2 patients and both pulmonic valve and tricuspid valves in 1 patient (2.1%).

Both investigations (TTE and TEE) were done in 14 patients which showed the sensitivity of TEE to be 63.6% and specificity 66.7% (Table 4).

Treatment

The mean duration of antibiotic therapy was 6 weeks (range 1–12 weeks for native valve IE and 1–8 weeks in prosthetic valve IE) (Table 5). Patients with staphylococcal

Table 4 Findings of transthoracic echocardiography (TTE) and transoesophageal echocardiography (TEE) in the 14 patients with infective endocarditis investigated by both echocardiographic modalities

TTE findings	TEE findings		
	Positive	Negative	Total
Positive	7	1	8
Negative	4	2	6
Total	11	3	14

Table 5 Management of care for 47 patients with infective endocarditis

Item	Native valve	Prosthetic valve
Antibiotic regimen [No. of weeks (range)]	6 (1–12)	6 (1–8)
Surgical treatment (No. of patients)	14/37	7/10
Indications (No. of patients):		
Heart failure	3	1
Uncontrolled infection	3	0
Large mobile vegetation	3	4
Septic emboli	1	1
Severe valvular regurgitation	3	1
Valvular ring abscess	1	1

Table 6 Complications and outcome for 47 patients with infective endocarditis

Complication	No. of patients	
	Native valve (n = 24)	Prosthetic valve (n = 5)
Heart failure	6	1
Renal insufficiency	3	1
Embolic events		
Brain	5	1
Spleen	2	0
Lungs	5	0
Brain haemorrhage	3	2
Death	4	0
Stroke/haemorrhage	(2)	–
Septic shock	(1)	–
Other	(1)	–

n = total number of patients.

endocarditis were treated with combination therapy, vancomycin, gentamicin and rifampicin in 13 patients or cloxacillin, gentamicin and rifampicin in 7 patients. Eight (8) patients without a microbiological diagnosis received an empiric regimen consisting of penicillin and gentamicin and 2 patients received ceftriaxone. Surgery was performed in 21 patients (44.7%). The most commonly encountered indications for surgery were large mobile vegetation in 7 (33.3%), heart failure in 4 (19.0%) and severe valvular regurgitation 4 (19.0%); other indications included uncontrolled infection, valvular ring abscess and systemic embolization. The mean time for surgery was 20 days (range 1–56 days) and the mean duration of stay in hospital was 33 days (range 28–90 days).

Complications and outcome

Complications occurred in 29 patients (61.7%) (Table 6); the most common were congestive heart failure in 7 patients, stroke in 6 patients, intracerebral haemorrhage in 5 patients, systemic embolization to the lung and spleen in 5 patients. The hospital

mortality rate was 8.5% (4 patients); in 3 patients the etiologic organism was *Sta. aureus* and in 1 patient it was *Strep. viridans*.

Discussion

Changes have been reported in the epidemiology and microbiology of IE over the last 30 years [16–18]. IE has been most commonly seen in older age groups with a predominance of male patients and an increased incidence of acute cases caused by virulent organisms such as *Sta. aureus*, Gram-negative bacilli and fungi, with decreasing mortality.

When comparing our results with other reports, the male to female ratio was in agreement with most case series [19–21]. However, our patient population was younger; the mean age was 32 years and 72.3% were aged under 40 years: only 3 patients were aged over 65 years. This contrasts with recent reports from the United States showing that more than 50% of all IE cases were seen in patients over the age

of 60 years, with a steady increase in the median age [22]. This trend in the developed countries is likely due to 2 factors; the increasing proportion of elderly people in the general population and the decline in the incidence of rheumatic heart disease as a risk factor [19,23].

In contrast, our study showed that rheumatic heart disease was the most common underlying cardiac condition. A recent study from Lebanon showed similar trends [24]. The antibiotic therapy used in our patients conforms in most cases to the guidelines of the American Heart Association for treatment of IE [25]. In certain clinical situations, a combined medical and surgical approach is necessary for the successful treatment of IE. During the last 3 decades, valve replacement and repair have become commonplace in the management of selected complications of IE, and the combination of antibiotic therapy and timely surgical intervention has substantially reduced the mortality from IE. Our results demonstrate that 44.7% of the cases of IE have required surgical intervention. Reports in the literature showed a figure between 17% and 64% [26]. Over time, the indications for surgery have been extended and valve replacement surgery has been undertaken progressively earlier in the course of the illness. The indications for surgery in our patients were consistent with the guidelines of the American College of Cardiology/American Heart Association, namely congestive heart failure, systemic embolic events, valve dysfunction, failure of medical therapy and perivalvular complications such as abscess formation [27]. Some authors include large mobile vegetation.

The second most common predisposing factor for IE was congenital heart disease. The incidence of prosthetic valve endocarditis was much higher than reports from developed countries. In this study, the yield of positive blood cultures (76.6%) was

lower than the rate of over 90% reported from a review of 206 cases of IE seen over a 15-year period at a New York hospital [25] but similar to a recent report from Lebanon [24]. Unlike several reports from developing countries of increasing incidence of streptococcal endocarditis [26], our study showed a predominance of staphylococcal endocarditis similar to several reports from developed countries [27–30].

Over the last 20 years, the use of echocardiography has been instrumental in confirming the diagnosis of endocarditis. The sensitivity of TTE in this study was 63.6% and is within the reported range of 50%–75% from other studies. The low negative predictive value confirms that TEE would be essential to the diagnosis of IE when TTE is normal.

A large body of evidence has shown that the aortic valve has replaced the mitral valve as the most commonly infected site in IE. Our study, however, showed a predominance of mitral valve infection [31–33].

Our data indicate that 61.7% of patients had complications. All complications described in our study have been previously reported in the literature [30]. The in-hospital mortality in this study was 8.5%, which is lower than 15%–30% reported in most cases series [31–33]. The low mortality rate of our cases of *St. aureus* endocarditis (15%) is inconsistent with other reports in the literature with a figure of at least 40% [34–37].

In conclusion, the epidemiology of IE in our institution is similar to that in developed countries with the major difference being the age group of our patients. Most of our patients were younger and had rheumatic heart disease or congenital heart diseases as the predisposing factor. In addition, we continue to see unusual pathogens such as *Brucella* spp. as an etiologic agent for IE where the disease is endemic.

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