

## INFECTIVE ENDOCARDITIS IN CHILDREN OF SOUTHERN IRAN

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### ABSTRACT

Infective endocarditis is an uncommon heart disease with a variable incidence, mostly related to the ever-increasing development of cardiac surgery and the longer survival of patients with congenital heart disease (CHD). Thirty-seven episodes of infective endocarditis (IE) were evaluated in 36 children (under 15 years of age) admitted to hospitals affiliated to Shiraz University of Medical Sciences during a 10 year period. The mean age was 9.2 years, only one boy was under one year of age and 6 of the children were under 5. Overall, the male to female ratio was 1.46/1, but the ratio was equal in children under 5 years. The frequency of IE was 3 per 1000 pediatric admissions. CHD was the most common underlying disease (27 patients, 73.0%), followed by rheumatic heart disease (RHD) (7 patients, 18.9%). Ventricular septal defect was the most common acyanotic CHD and tetralogy of Fallot was the most common cyanotic CHD. Blood cultures were positive in 54% and vegetations were present in 57.5% by 2-dimensional echocardiography. Streptococcus species (mostly *viridans*) was the most common infecting micro-organism. The most common site of vegetation was the pulmonary valve, followed by the aortic valve. There were 6 deaths (16.2%) due to different causes. Mortality occurred mostly in culture negatives or in those infected by Gram-negative micro-organisms ( $p < 0.01$ ). All mortalities had left-sided vegetations ( $p < 0.001$ ). In conclusion, despite medical and surgical advances, this fatal complication of heart disease remains a significant medical problem. An effective chemoprophylaxis strategy for rheumatic fever and IE will decrease the incidence and outcome of this potentially serious illness.

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**Keywords:** Bacterial endocarditis, Congenital heart disease, Rheumatic heart disease, Children, Developing countries.

### INTRODUCTION

Although congenital heart disease (CHD) is the most common underlying cause of IE in children throughout the world, rheumatic heart disease (RHD) is a prevalent

underlying cause of IE in developing countries. However, RHD is either not a cause of IE in industrialized countries<sup>1</sup> or is very rare.<sup>2</sup> The reason for this difference depends on a longer survival of patients with CHD and application of an effective chemoprophylaxis strategy against RHD and IE.

There are only 2 reports of infective endocarditis (IE) in the pediatric age group from developing countries between 1966 to 1998.<sup>3,4</sup> We decided to review the epidemiologic aspects of IE during a ten year admission period in pediatric wards.

### PATIENTS AND METHODS

The hospital records of children with the diagnosis of IE admitted to the pediatric units of Shiraz University Hospitals in a 10 year period (1986 to 1995) were reviewed. We used new diagnostic criteria (Duke) for our patients because of greater accuracy and particularly for diagnosing IE in children.<sup>5</sup> Positive blood culture and vegetation on echocardiography are two major criteria. We also defined two diagnostic categories as definite and possible after

rejected patients. We used chi-square values for statistical analysis.

### RESULTS

Thirty-seven episodes of IE had occurred in 36 children, 31 definite and 6 possible. One patient with RHD had a second episode of IE 2 years after the first one.

The periodic variation in incidence is shown in Fig. 1. The mean occurrence rate was 3 per 1000 of pediatric admissions overall, with a slight increase near the end of the period. Twenty-two patients were male and 15 female with a male to female ratio of 1.46/1. Only one boy was under one year of age. The age and sex distribution are summarized in Table I.

Congenital heart disease was the most common

Table I. Age and sex distribution of 37 episodes of IE.

Sex \ Age	< 1 year	1-5 years	5-15 years	Total (%)
Male	1	3	18	22 (59.5)
Female	0	4	11	15 (40.5)
Total (%)	1 (2.1)	7 (18.9)	29 (78.3)	37 (100)

Table II. Specific type of heart lesion in 37 episodes of IE.

Heart disease	No.
A. CHD:	
1. Isolated ventricular septal defect (VSD)	6
2. Tetralogy of Fallot	6
3. Ventricular septal defect associated with:	8
a. Aortic insufficiency	2
b. Mitral regurgitation	1
c. Aortic stenosis (one valvular, one subvalvar)	2
d. Mitral valve prolapse	1
e. Atrioventricular septal defect	1
f. Pulmonary atresia	1
4. Tricuspid atresia	3
5. Aortic stenosis associated with:	2
a. Bicuspid aortic valve	1
b. Aortic insufficiency	1
6. Patent ductus arteriosus	1
7. Pulmonary valve stenosis associated with cardiomyopathy	1
B. RHD:	
1. Mitral disease (stenosis associated with regurgitation)	3
2. Mitral and associated aortic involvement	4
C: Others:	
1. Marfan syndrome, mitral valve prolapse.	1
2. Mitral valve prolapse	1
3. Normal heart	1

**Table III.** Micro-organisms isolated from 37 episodes of IE.

Micro-organism	No.
a. Streptococcus	9
1. <i>viridans</i>	8
2. Beta-hemolytic	1
b. Staphylococcus	7
1. coagulase-positive	5
2. coagulase-negative	2
c. Gram-negative bacteria	3
1. <i>E. coli</i>	1
2. Klebsiella	1
3. Brucellosis	1
d. Aspergillus	1

underlying cause, observed in 27 patients (73.0%), followed by RHD in 7 patients (18.9%). Ventricular septal defect was the most common CHD (overall), and tetralogy of Fallot was the most common cyanotic CHD (Table II).

Blood cultures were positive in 54%, and the predominant micro-organism was streptococcus (45%), followed by staphylococcus (35%).

Trans-thoracic two-dimensional echocardiography revealed vegetations in 57.5% (transesophageal echocardiography was not available at that time). The most

**Table IV.** Site of vegetations in 19 patients from 33 IE episodes who underwent echocardiography (one had 2 vegetations).

Site	No.
Pulmonary valve	6
Aortic valve	5
Mitral valve	4
Tricuspid valve	1
Common atrioventricular valve	1
Left atrium	2
Right ventricular cavity	1

common site of vegetation was the pulmonary valve, seen in 6 patients. Vegetations on the aortic valve were found in 5 and on the mitral valve in 4 patients (Table IV). Only 4 patients had definitive predisposing factors, including dental abscess, nose bleeding, BCG vaccination and early post-cardiac surgery. The mortality rate was 16.2% (6 patients). The complications, causes of death and other characteristics of these patients are summarized in Table V. Mortality occurred in culture-negative cases or in those infected by Gram-negative micro-organisms ( $p < 0.01$ ). Also, all of these patients had left-sided vegetations, whereas the pulmonary valve was the most common site of vegetation in total and in survivors ( $p < 0.001$ ).

**Table V.** Cause of mortality, micro-organisms, vegetations and heart lesions in 6 patients from among 37 episodes of IE.

No.	Heart disease	Cause of mortality	Site of vegetation	Micro-organism
1	Normal heart	Septic shock and atrioventricular block	Aortic valve	Brucella
2	Tricuspid atresia, ventricular septal defect	Congestive heart failure	Left atrium	Neg. culture
3	Post-operation, ventricular septal defect	Sepsis and disseminated intravascular coagulopathy	--	<i>E. coli</i>
4	Rheumatic heart disease	Pulmonary emboli and ventricular tachycardia	Mitral valve	Neg. culture
5	Marfan syndrome, mitral valve prolapse	Cardiorespiratory arrest, acute renal failure	Mitral valve	Neg. culture
6	Ventricular septal defect	Unknown	Left atrium	Neg. culture

Table VI. Comparison of findings in the present study and a report from India.<sup>4</sup>

Findings	Present study	Indian report	P-value
Age	1-15	2-16	
Sex			
male	22	26	
female	15	11	
Underlying heart disease:			
CHD	70.3%	48.6%	<0.01
RHD	21.6%	35.1%	<0.05
Positive blood culture	60%	43.2%	<0.05
Predominant micro-organism			
Streptococcus	9	6	
Staphylococcus	7	9	
Mortality rate	16.2%	43.2%	<0.01

## DISCUSSION

Decline in the incidence of RHD and favorable prognosis in the treatment of CHD in industrialized countries in recent decades have resulted in an increased rate of CHD being the underlying cause of IE in these countries.<sup>1,2,6</sup> But in developing countries, RHD is still a common underlying cause of IE<sup>4,7,8</sup> as reported in India<sup>7</sup> and Africa,<sup>8</sup> with a lower incidence in our study compared to the report from India ( $p < 0.05$ ). RHD is rare in economically developed countries,<sup>2,9</sup> or altogether absent.<sup>1</sup> Increasing use of transvascular devices in neonates and young infants are another cause of IE, the main risk factor being the use of central venous catheters.<sup>10</sup> In the present series of patients there was no IE in neonates, perhaps because intravascular devices and interventional procedures were not used extensively.

Most recent studies have revealed staphylococcus species as the most common micro-organism grown in blood cultures.<sup>7, 8, 10-18</sup> However, streptococcus species (mostly *viridans*) were predominant in our patients as well as in a few recent studies.<sup>9,19</sup> *Corynebacterium diphtheriae*, which was detected in a significant number of patients in Europe,<sup>19,20</sup> was not detected in our study.

The mortality rate in this study (16.2%) was lower than some other reports,<sup>3,7,13,18</sup> especially the report from India ( $p < 0.01$ ). Mortality occurred mostly in culture negative cases or in those infected by Gram-negative micro-organisms. Left sided involvement was significant in the mortality group. Comparison of these findings with a report from India are summarized in Table VI.

Finally, an effective chemoprophylaxis strategy against rheumatic fever and IE can decrease this fatal complication. Echocardiography, especially transesophageal, is now the technique of choice in diagnosis of IE and vegetation,<sup>6,7</sup> since earlier diagnosis is possible. The availability of this instrument will decrease the complications and mortality of IE.

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