

# Infective Endocarditis at Maharaj Nakorn Chiang Mai Hospital, 2002-2003

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## ABSTRACT

Infective endocarditis remains a significant health problem despite the improvement in a health care system. Our study aimed to determine the epidemiology, clinical features, and treatment outcome of patients with infective endocarditis at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, northern Thailand.

A retrospective chart review was done at Maharaj Nakorn Chiang Mai Hospital from January 2002 to December 2003 to assess the clinical features, laboratory data, and clinical outcome of 96 patients with infective endocarditis. There were 69 men and 27 women with a mean age of 45 years (range 14-85 years). Thirty-nine patients (40.6%) had identified risk factors for infective endocarditis. Sixty patients (62.5%) had an infection of the aortic valve. Twenty-eight (29.2%) and 68 patients (70.8%) were categorized as acute and subacute infective endocarditis, respectively. The most common pathogen was viridans group of streptococci (12 patients), followed by *Streptococcus suis* (nine patients). The most commonly used antibiotic regimen is the combination of penicillin G sodium or ampicillin plus gentamicin (30 patients, 31.3%), followed by ampicillin plus ceftriaxone (15 patients, 15.6%). Forty-seven patients (49.0%) underwent a surgical intervention. The overall mortality rate was 17.7 percent. (*J Infect Dis Antimicrob Agents* 2006;23:75-81.)

## INTRODUCTION

Despite the improvement in a health care, the incidence of infective endocarditis has not decreased over the past decades. A delay in diagnosis and treatment is still responsible for high morbidity and mortality. The incidence of community-acquired native-valve endocarditis in the United States and western Europe

is about 1.7-6.2 cases per 100,000 person-years.<sup>1,2</sup> Men are more often affected than women with a mean male-to-female ratio of 1.7:1. A development of Duke criteria for diagnosis, an availability of echocardiogram, an increased longevity that has given rise to degenerative valvular disease, an increasing number of intravenous drug users and nosocomial cases,

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and a development of cardiac surgery for valve replacement have resulted in the marked change of the epidemiology and clinical manifestations of infective endocarditis over the past decades. For instance, the mean age of patients increased from 30-40 years during the preantibiotic era to 47-69 years in recent years.<sup>3</sup>

Our study aimed to determine the prevalence, clinical manifestations, and outcome of patients with infective endocarditis at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand.

### PATIENTS AND METHODS

We conducted a retrospective study of patients aged of > 15 years with the diagnosis of infective endocarditis who were hospitalized at Maharaj Nakorn Chiang Mai Hospital, a referral center in northern Thailand, between January 2002 and December 2003. The diagnosis was made using the modified Duke criteria.<sup>4</sup> Acute infective endocarditis was defined as infective endocarditis with the duration of onset <1 week. Subacute infective endocarditis was defined as that with the duration of onset >1 week.<sup>5,6</sup> Acute renal failure was defined as a rise of the creatinine level to >2 times of the baseline level or a creatinine level of >2 mg/dL if the baseline was <1.2 mg/dL. Acute liver failure was defined as altered mental status (hepatic encephalopathy) and coagulopathy (INR > 1.5) within 8 weeks after the onset of illness concurrent with hyperbilirubinemia in the patients who had no preexisting liver disease.<sup>7,8</sup> Hospital-acquired pneumonia was defined as pneumonia that occurs after hospitalization for at least 48-72 hours.<sup>9</sup>

The following data including age, sex, risk factors for infective endocarditis, underlying diseases, symptoms and signs, results of laboratory tests, treatment regimens, and outcome were collected.

### Statistic analysis

Demographic data, symptoms and signs, laboratory tests, and outcome of the patients were reported as the percentage, mean, range, and standard deviation (SD) as appropriate. A comparison between the patients who survived and died was done by Student's t test, Mann Whitney U test, Chi-square test, or Fisher's exact test as appropriate. A two-tailed p-value of less than 0.05 was considered significant. The analysis was performed using the SPSS program (the SPSS for windows, Rel. 13.0.1997. Chicago: SPSS Inc.).

### RESULTS

There were 30,658 patients hospitalized at Maharaj Nakorn Chiang Mai Hospital during the study period. Of these, 100 patients were diagnosed with infective endocarditis, accounting for 1.63 cases per 1,000 inpatient-years. The medical records of four patients were not available, thus there were 96 patients in our study. There were 69 men (71.9%) and 27 women (28.1%) with a male-to-female ratio of 2.6:1. A mean age of the patients was 45.1±13.9 years (range 14-85 years). Twenty-one patients (21.9%) had prior medical illnesses before the diagnosis of infective endocarditis was made (Table 1).

Thirty-nine patients (40.6%) had the risk factors for infective endocarditis, including rheumatic heart diseases (23 patients, 23.9%), congenital heart diseases (seven patients, 7.3%), prosthetic valve replacement (seven patients, 7.3%), and intravenous drug user (two patients, 2.1%). A history of medical or dental procedure such as urinary catheterization and tooth extraction was not recorded. Forty-six patients (47.9%) were referred from other hospitals.

According to the modified Duke criteria, 47 (49.0%) and 49 (51.0%) were categorized as the definite and possible infective endocarditis, respectively.

**Table 1. Characteristics of ninety-six patients with infective endocarditis.**

Characteristics	Number of patients (%)
Male: female	69 : 27
Age (mean + SD) (years)	45.1+ 13.8
<b>Risk factors for infective endocarditis</b>	
Rheumatic heart disease	23 (24.0)
Congenital heart disease	
Mitral valve prolapse	3 (3.1)
Bicuspid aortic valve	2 (2.1)
Atrial septal defect (secundum type)	1 (1.0)
Ventricular septal defect	1 (1.0)
Prosthetic valve	
Onset within two months after the operation	0
Onset after two months of the operation	7 (7.3)
No underlying heart disease	57 (59.4)
Intravenous drug use	2 (2.1)
<b>Other underlying diseases</b>	
Diabetes	4 (4.2)
Cirrhosis and chronic alcohol drinking	10 (10.4)
Chronic kidney disease	2 (2.1)
Cancer	1 (1.0)
Human immunodeficiency virus (HIV) infection	4 (4.2)

SD: standard deviation

Of those with definite infective endocarditis, 44 patients satisfied two major criteria and the remaining three patients satisfied one major and three minor criteria. The site of infection was the aortic valve in 60 patients (62.5%), the mitral valve in 44 patients (45.8%), the tricuspid valve in four patients (4.2%), and the pulmonic valve in two patients (2.1%). Fourteen patients (14.6%) had more than one site of infection: 10 patients with infections of the aortic and mitral valves, three patients with the infections of the mitral and tricuspid valves, and one patient with the infections of the pulmonic and tricuspid valves. Of the patients with rheumatic heart diseases, 14 (12.7%) had an infection of the aortic valve and 12 (10.9%) at the mitral valve. Of the two intravenous drug users, one had an infection at the mitral valve and the other at the mitral and tricuspid

valves (Table 2).

Of 96 patients, one refused to have his blood drawn for the cultures and the cultures from another 48 patients did not reveal any bacterial growth. The results of the blood cultures from the remaining 47 patients are shown in Table 3. The most common pathogens were streptococci (25 patients), followed by staphylococci (10 patients). The determination of the minimal inhibitory concentration (MIC) was performed in nine patients with streptococci (five cases of *Streptococcus suis* and four cases of viridans group of streptococci). Of these nine patients, the MIC to penicillin was <0.5  $\mu$ g/ml.

Twenty-eight patients (29.2%) were diagnosed with acute infective endocarditis, and 68 patients (70.8%) had subacute infective endocarditis. The most

**Table 2. The site of infection and the risk factors for infective endocarditis.**

Risk factors	Site of infection (number of patients, %)			
	Mitral valve	Aortic valve	Tricuspid valve	Pulmonic valve
Rheumatic heart disease	12 (10.9)	14 (12.7)	1 (0.9)	-
Congenital heart disease	4 (3.6)	3 (2.7)	-	1 (0.9)
Prosthetic valve	6 (5.5)	2 (1.8)	-	-
Intravenous drug use	2 (1.8)	-	-	-
No underlying diseases	20 (18.2)	41 (37.6)	2 (1.8)	1 (0.9)

**Table 3. The causative organisms causing infective endocarditis.**

Microorganisms	Number of patients (%)
No growth	48 (50.0)
<b>Streptococci</b>	
Viridans group of streptococci	12 (12.5)
Group D streptococci	2 (2.1)
<i>Streptococcus</i> spp.	2 (2.1)
<i>S. suis</i>	9 (9.4)
<i>Lactococcus</i> spp.	2 (2.1)
<b>Staphylococci</b>	
Methicillin-susceptible <i>S. aureus</i>	7 (7.3)
Methicillin-resistant <i>S. aureus</i>	1 (1.0)
Coagulase-negative staphylococci	2 (2.1)
Other pathogens	
<i>Enterococcus faecalis</i>	4 (4.2)
<i>Alcaligenes xylosoxidans</i>	2 (2.1)
<i>Salmonella</i> spp.	2 (2.1)
<i>Lactobacillus</i> spp.	2 (2.1)
<b>No available culture</b>	1 (1.0)

common presenting symptoms were congestive heart failure (70 patients, 72.9%) and fever (69 patients, 71.9%) (Table 4).

The most commonly used antibiotic regimen is the combination of penicillin G sodium or ampicillin plus gentamicin (30 patients, 31.3%), followed by ampicillin plus ceftriaxone (15 patients, 15.6%) (Table 5). Forty-seven patients (49.0%) underwent a surgical intervention. The indication for surgery was congestive heart failure in 30 patients (63.8%), embolism in six patients (12.8%), perivalvular abscess in four patients (8.5%), and chordae rupture in four patients. The

reason was not reported in the other three patients. The mortality rate was 17.7 percent (17 patients).

## DISCUSSION

Infective endocarditis remains a significant health problem. Despite the advance in medical sciences, several studies both from Thailand and other countries showed the incidence of infective endocarditis had not decreased. In our study, the incidence was 48 cases per year, in accordance with those reported during the last decade.<sup>5,10-13</sup> The incidence was higher than that reported two decades ago when Von Reyn criteria were

**Table 4. Clinical manifestations and laboratory data of ninety-six patients with infective endocarditis.**

Variable	Number of patients (%)
<b>Duration of onset</b>	
Acute onset	28 (29.2)
Subacute onset	68 (70.8)
<b>Symptoms</b>	
Dyspnea	70 (72.9)
Fever	69 (71.9)
Myalgia, fatigue, arthralgia	13 (13.5)
Weakness	13 (13.5)
Headache	6 (6.3)
Convulsion	5 (5.2)
Chest pain	4 (4.2)
<b>Signs</b>	
Fever (temperature > 37.8°C)	54 (56.3)
Cardiac murmur	67 (69.8)
Osler's nodes, splinter hemorrhage	4 (4.2)
Janeway lesions	1 (1.0)
Clubbing of fingers	2 (2.1)
Roth's spots	1 (1.0)
Congestive heart failure	70 (72.9)
<b>Laboratory data (mean + SD)</b>	
Hematocrit (%)	32.2 ± 6.9
White blood cell count (cells/mm <sup>3</sup> )	12,091.8 ± 5,536.7
Serum creatinine (mg/dl)	1.6 ± 1.0
Serum albumin (g/dl)	3.4 ± 0.5
Erythrocyte sedimentation rate at 60 minutes (mm/hr)	77.7 ± 47.3
C-reactive protein (mg/dl)	70.5 ± 53.6

**Table 5. Medical treatment of ninety-six patients with infective endocarditis.**

Antibiotics	Number of patients (%)
<b>Combination regimen</b>	
Penicillin G sodium or ampicillin plus gentamicin	30 (31.3)
Ampicillin plus ceftriaxone	15 (15.6)
Cloxacillin plus ampicillin and ceftriaxone	4 (4.2)
Cloxacillin plus ampicillin plus gentamicin	3 (3.1)
Penicillin G sodium plus ceftriaxone	3 (3.1)
Penicillin G sodium plus ceftriaxone and gentamicin	1 (1.0)
Cloxacillin plus gentamicin	3 (3.1)
Cloxacillin plus ceftriaxone	2 (2.1)
Cloxacillin plus ampicillin	1 (1.0)
Cloxacillin plus ceftazidime	1 (1.0)
Ceftazidime plus vancomycin	1 (1.0)
Imipenem plus vancomycin	1 (1.0)
<b>Single-drug regimen</b>	
Ceftriaxone	13 (13.5)
Penicillin G sodium	7 (7.3)
Cloxacillin	5 (5.2)
Ampicillin	3 (3.1)
Imipenem	1 (1.0)

used.<sup>14</sup> The modified Duke criteria used in our study has a better sensitivity and specificity than the Von Reyn criteria.<sup>14</sup> The mean age of patients in our study was higher than that in previous studies.<sup>10-12,15,16</sup> This finding may be due to the increased life expectancy in Thai population, which may in turn result in the increased incidence of degenerative valve disease.<sup>14,17,18</sup> However, the most common risk factor for infective endocarditis in our study was rheumatic heart disease. This is in accordance with previous studies of Thailand.<sup>5</sup> In addition, we found that the most common site of infection was the aortic valve. This is similar to a previous study conducted at our hospital between 1997 and 2001.<sup>5</sup> However, other studies had found that the mitral valve was the most common site of infection.<sup>10-18</sup> This difference might be explained by the older population in our study than the previous studies that might result in increasing number of patients with degenerative valvular disease especially aortic sclerosis.

Similar to previous studies, we found that the most common causative organism was viridans group of streptococci.<sup>10-12,16,19</sup> The second most common pathogen in our study was *S. suis*. This organism is not a common cause of infective endocarditis in other studies.<sup>10-12,16,19</sup> However, we have documented six cases of *S. suis* in the 5-year period prior to our study<sup>5</sup> and nine cases during the two-year period of our study. All nine cases had perivalvular abscesses. Although the increased incidence of *S. suis* endocarditis can be explained by the increased awareness and better detection in the microbiological laboratory, we believe that the incidence of *S. suis* endocarditis and other forms of infection caused by this organism in our patient population is really increasing.<sup>20-23</sup> Of 48 patients whose blood cultures did not show any growth, half had been given antibiotics before being referred to our hospital. The rest may be infected with bacteria

that were difficult to grow in the cultures such as those that belong to the HACEK group (*Haemophilus parainfluenzae*, *H. aphrophilus*, *H. paraphrophilus*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*) and *Abiotrophia* species.

In our study, a high rate of patients (48.9%) had to receive a valve replacement. In other studies, this rate was between 0 and 16.7 percent.<sup>10-13,15-16</sup> Our high rate of surgery might be due to the higher number of patients with aortic valve infection and congestive heart failure. Our data were similar to a previous study conducted at our hospital between 1997 and 2001.<sup>5</sup>

There are the limitations in our study. Our study was conducted retrospectively and in a referral center. However, it has documented the changing epidemiology of this infectious diseases in northern Thailand such as the increased prevalence of *S. suis* as the causative organism. The information presented may lead to the early diagnosis and treatment of infective endocarditis which, in turn, results in a better outcome.

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