Infective Endocarditis : Prevalence, Characteristics and Mortality in Khon Kaen, 1990-1999

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Abstract

Objective: To update the prevalence, characteristics and mortality of infective endocarditis in a tertiary care hospital in Khon Kaen, Thailand.

Background: Numerous studies have shown that the prevalence and course of infective endocarditis remain unchanged inspite of the advance in treatment, diagnosis and of prophylactic recommendations.

Method: The authors identified 160 patients from 1990-1999 with 86 per cent definite and 14 per cent possible endocarditis based on the Duke criteria. Data were collected from two tertiary care hospitals.

Results: The prevalence was 4 patients per 1,000 hospital admissions. The mean age of the 106 male and 54 female patients was 39±16 years. Twenty-four percent of the patients had no previously known heart disease. Native valve endocarditis was present in 95 per cent and prosthetic valve endocarditis was diagnosed in 5 per cent. Infective endocarditis was located on the aortic valve in 42 per cent, the mitral valve in 43 per cent, both mitral and aortic valves in 9 per cent and the tricuspid valve in 8 per cent. The infective organism was identified in only 62 per cent of cases. *Streptococci* was the most common in 43 per cent, followed by *Staphylococci* in 16 per cent. During the first month after admission, 45 per cent of the patients underwent surgery. In-hospital mortality was 25 per cent.

Conclusion: Despite improved diagnostic techniques and aggressive surgical therapy, infective endocarditis remains a serious problem associated with a high mortality in Khon Kaen.

Key word : Infective Endocarditis, Epidemiology, Microbiology, Mortality

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Infective endocarditis (IE) is uncommon but potentially fatal. In 1885 Sir William Osler[1] described the clinical and pathological features, since then, many studies have reported its mains characteristics[2-7]. The diagnosis of IE is straight forward in those patients with classic oslerian manifestations. However, the variability in the clinical presentation of IE demands a diagnostic strategy that accurately detects the disease and correctly excludes non-IE conditions. In 1981, von Reyn[8] published their clinico-pathological criteria (the Beth Israel criteria) for classifying patients suspected of having IE. In 1994, Durack et al[9] modified the Beth Israel criteria and published a new diagnostic schema (the Duke criteria) for the clinical diagnosis of IE, incorporating echocardiographic findings and intravenous drug use into the clinical parameters. The Duke criteria have been substantially more sensitive than the Beth Israel criteria[10].

The authors set out to document the features of IE presented in Khon Kaen Thailand – prevalence, morbidity and mortality – to determine the demographic, clinical, microbiological and evolutionary characteristics of the disease.

METHOD

Data collection: Data was collected from patients hospitalized with IE, combined retrospective and prospective studies between January 1, 1990 and December 31, 1999 at Srinagarind Hospital, a tertiary referral center and Khon Kaen provincial hospital. The Duke criteria (Table 1) were used as the diagnostic standard.

For each patient the following information was recorded:

- Gender and age.
- History of heart disease, prosthetic valve, infective endocarditis.

Table 1. Duke criteria: definite IE clinical criteria (using special definitions). Patients must meet two major criteria, or one major and three minor criteria, or five minor criteria.

(1) Positive blood culture for infective endocarditis

A. *Typical microorganism consistent with IE from 2 separate blood cultures*
   (i) *Viridans streptococci, S. bovis*, HACEK group, or
   (ii) community-acquired *S. aureus* or *enterococci*, in the absence of a primary focus, or

B. *Microorganisms consistent with IE from persistently positive blood culture, defined as*
   (i) ≥ 2 positive cultures of blood samples drawn> 12hours apart or
   (ii) all of 3, or majority of ≥4 separate blood cultures (with first and last drawn ≥1 hour apart

(2) Evidence of endocardial involvement

A. *Positive echocardiogram for infective endocarditis*
   (i) oscillating intracardiac mass on valve or supporting structures in the path of regurgitant jets, or on implanted material in the absence of an alternating explanation, or
   (ii) abscess, or new partial dehiscence of prosthetic valve, or

B. *New valvular regurgitation* (worsening or changing of preexisting murmur not sufficient)

Minor Criteria	Predisposition :	Predisposing heart condition or IVDA
	Fever:	≥ 38°C
	Vascular phenomenon:	Arterial embolism, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, Janeway lesions
	Immunologic phenomenon:	Glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor
	Echocardiogram:	Consistent with infective endocarditis but not meeting major criteria
	Microbiologic evidence:	Positive blood culture but not meeting major criterion above, or serologic evidence of active infection with organism consistent with infective endocarditis

IVDA = intravenous drug abusers. HACEK group, *Haemphilus aphrophilus, Actinobacillus actinomycetemcomitans* species, *Cardiobacterium hominis, Eikenella corrodens,* and *Kingella kingae.*

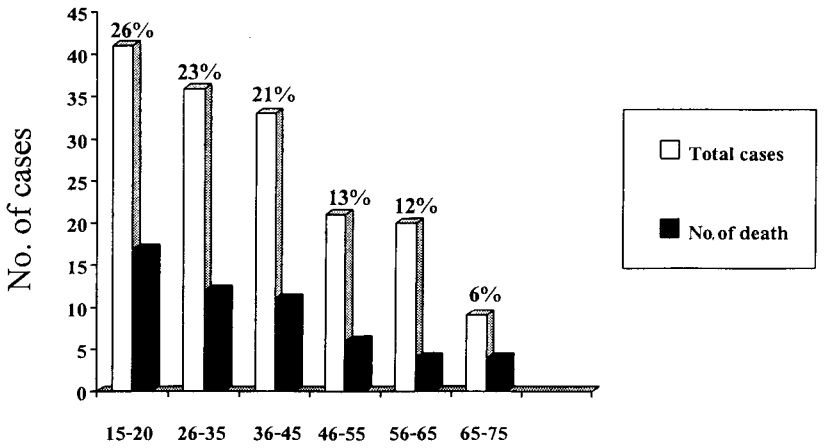

Fig. 1. Prevalence of infective endocarditis by age and mortality.

• Echocardiographic findings: vegetation, abscess, degree of valve regurgitation or obstruction, and prosthetic valve dehiscence.

• Current IE: location, symptoms and physical signs, number of positive blood cultures, causative microorganisms, presumed portal of entry, medical and surgical management.

All medical charts were reviewed by one of our team and data were extracted using a specific form.

Definitions: Renal impairment was defined as: a serum creatinine concentration of 2 mg/dL or more. Heart failure was determined by the presence of pulmonary congestion or pulmonary edema on a chest roentgenogram. Surgery for active endocarditis was defined as : blood culture or a valve or tissue culture positive at the time of surgical procedure and operative macroscropic evidence of endocarditis. Operative mortality was any death that occurred within 30 days of the operation or death during that same hospitalization.

End points: The primary end points of the study were in-hospital and all causes of mortality.

Statistical analysis:

The distribution for all relevant variables is reported either as percentages or as means ± SD. Group comparisons were performed with Student's *t*-test or the χ^2 test, where appropriate. A p-value of less than 0.05 indicated statistical significance.

RESULTS

Of the 203 patients thought to have IE and who were treated in the hospital, 160 patients met the inclusion criteria, 138 (86%) of the patients had IE and were described as 'definite' and 22 (14%) of them only as 'possible'.

Prevalence and demographic data

The prevalence of IE was 4 patients per 1,000 hospital admissions. 106 (66%) of the patients were male.The age distribution was 15 to 75 years, and prevalence decreased dramatically in patients over 65 years of age (Fig. 1). The mean age was 39 ± 16 years. The disease was rare in elderly patients and its prevalence increased dramatically in young patients reaching a peak at 15-35 years.

Underlying heart disease

Among the native valve endocarditis, rheumatic heart disease was the most frequently recognized vulvular abnormality in 60 per cent, while 28 per cent of them had no underlying cardiac abnormality and 12 per cent had other cardiac abnormalities. Prosthetic valve endocarditis was diagnosed in 5 per cent, early prosthetic endocarditis in 2 cases and late prosthetic endocarditis in 6 cases. A previous history of IE was noted in 4 patients. Mortality associated with infection of the

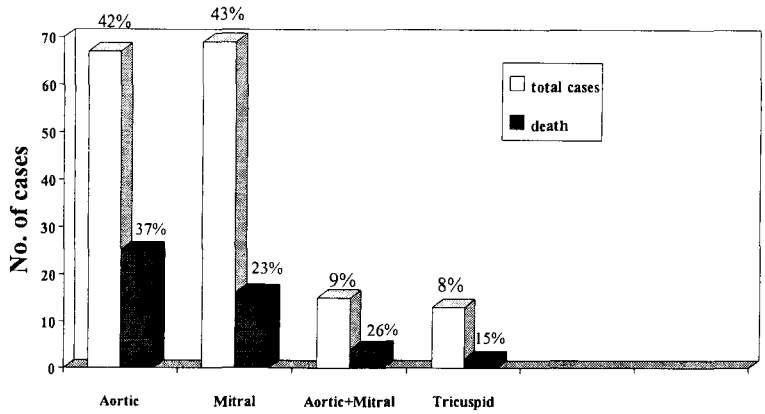

Fig. 2. Site of vegetations and relation to mortality.

Table 2. Clinical symptoms of infective endocarditis.

Sign or symptom	%
Fever	85
Malaise	85
Weight loss	30
Dyspnea	75
Pallor	55
Petechial hemorrage	19
Splenomegaly	12
Clubbing of fingers	5

mitral valve was higher (33%) than infection of the aortic valve (24%) (Fig. 2).

Characteristics of infective endocarditis

Location of infective endocarditis:

Infective endocarditis occurred more frequently in the mitral valve (43%) and aortic valve (42%), while 9 per cent occurred in both aortic and mitral valves and 8 per cent of cases occurred in tricuspid valve (Fig. 2).

Clinical manifestations:

Signs and symptoms at presentation (Table 2) reflected the recognized features of IE. The mean duration of symptoms prior to diagnosis was 5.7 weeks. The duration prior to diagnosis was shorter in the surgically treated patients than in those who were medically treated (5.2 *vs* 6.1 weeks). Central nervous system emboli were present in 12 per cent of cases. The incidence of embolic complications was seen in left-sided infective endocarditis only; and present in 23 per cent of the mitral valve infective endocarditis cases and in 7 per cent of aortic valve infective endocarditis cases. Emboli occurred more frequently before diagnosis and during therapy than after therapy was completed.

Distinction between survival and death is shown in Table 3, the clinical comparison between survivors and nonsurvivors. There was no significant difference in age, gender, congestive heart failure NYHA class, and site of involvement. In univariate analysis, duration of symptoms prior to diagnosis was found to be a predictor of death.

Echocardiographic examination

Echocardiography (transthoracic and/or transesophageal echocardiography) showed evidence of infective endocarditis (vegetation, abscesses, leaflets perforation and prosthetic valve dehiscence) were detected in 157 of the 160 patients (98%). Vegetation was observed in the aortic valve in 67 patients (42%), mitral valve in 66 patients (41%), and tricuspid valve in 13 patients (8%).

Blood cultures and microorganisms

Streptococci were the most frequent microorganisms (43%). *Staphylococci* (both *coagulase positive and coagulase negative*) were responsible for 16 per cent. Negative blood culture, but never-

Table. 3. Clinical characteritics in survivors and nonsurvivors with infective endocarditis.

Variables	Nonsurvivor n=75	Survivor n=85	P
Sex (% male)	46	54	NS
Age (mean)	39±16	38±15	NS
Duration of symptoms prior to diagnosis (mean)	32±31	49±55	0.01
Congestive heart failure			
NYHA class I-II (%)	52	48	NS
NYHA class III- IV (%)	40	60	NS
Site of involvement			
AV endocarditis (%)	41	59	NS
MV endocarditis (%)	40	60	NS
AV ring abscesses (%)	56	44	NS

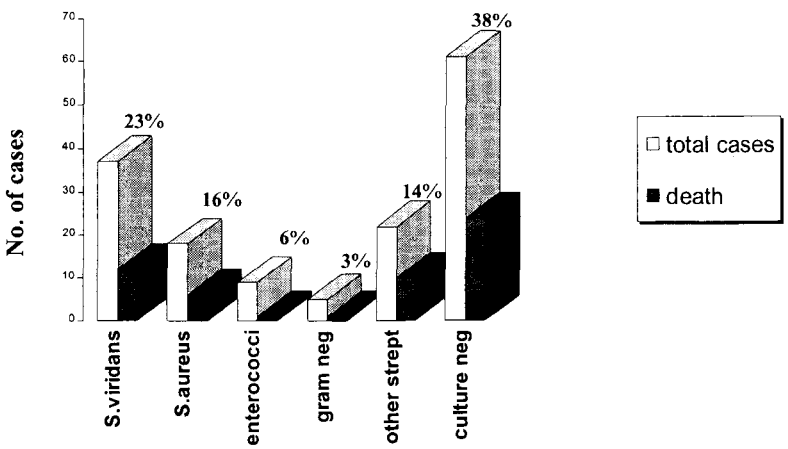

Fig. 3. Infective endocarditis pathogens and relation to mortality.

theless, had clinical, surgical, or pathological findings supporting the diagnosis of IE in 38 per cent. (Fig. 3)

Portals of entry

A presumed portal of entry was recorded in 54 of 160 patients (34%). Dental disease or procedure accounted for half of these. Among the other 27 patients (17%), the non-dental portals were: cystoscope or urethral surgery, septic arthritis, hemodialysis and skin abscesses. Twelve patients (8%) were drug users.

Clinical course

Of 160 patients, 72 patients (45%) were operated on in the active stage of IE. The indications for surgical treatment were congestive heart failure, persistent sepsis, virulence of infective organism, repeated embolism, perivalvular abscesses and large mobile vegetation.The percentage of men who underwent surgery was significantly higher than women (51% *vs* 31% P = 0.02) and patients who underwent surgery were younger than those who did not (34 ± 14 *vs* 42 ± 16 years, P = 0.002). The underlying heart disease and type of causative microorganism did not vary significantly among patients (Table 4). The results of surgical treatment was good: 51 (71%) patients survived, 13 (18%) patients died and 8 (11%) patients were lost to follow-up. The in-hospital mortality of patients with native valve infection treated surgically was considerably less than those treated medically (8% *vs*

Table 4. Surgery and in-hospital mortality.

		Surgery			In hospital mortality		
		N	%	P	N	%	P
Gender	Male	55/106	51	0.022	29/106	27	NS
	Female	17/54	31		11/54	20	
Location	Mitral valve	28/69	40		16/69	23	
	Aortic valve	37/67	54	0.27	25/67	37	0.12
	Tricuspid valve	7/13	53		1/13	8	
Microorganisms	Staphylococci	11/26	42		4/26	36	
	Streptococci	27/68	40	0.54	14/68	51	0.77
	Culture negative	30/61	49		11/61	37	
Previous heart disease	Native valve	71/159	45	0.27	40/159	25	0.03
	Prosthetic valve	2/8	25		5/8	63	

Table 5. Infective endocarditis and congestive heart failure.

Heart failure	No of patients	Medical treatment Hospital death		No of patients	Surgical treatment Hospital death	
		No	%		No	%
NYHA class I¶	3	0	0	1	1	100
NYHA class II¶	12	4	33	8	1	13
NYHAclassIII¶	9	3	33	13	2	15
NYHA class IV¶	27	16	59*	22	12	55*
Total	51	23	45	44	16	36

* P = 0.74

¶ New York Heart Association, functional classification [27]

17%). However, surgical or medical treatment of moderate or severe heart failure showed no significant difference in mortality (Table 5).

Congestive heart failure

Among the complications of infective endocarditis, congestive heart failure (CHF) had the greatest impact on prognosis and mortality whether treated surgically or medically (Table 5). Acute CHF occurred more frequently (16%) in infections of the aortic valve than of the mitral (10%) or tricuspid (0.6%) valves.

Periannular extension of infection

Extension of infective endocarditis beyond the valve annulus caused higher mortality, more frequent CHF and the need for cardiac surgery. Aortic valve infective endocarditis with aortic root abscesses were present in 10 (15%) patients. In the 67 patients with aortic infective endocarditis: heart block developed in 7 (10%) and 5 (7%) of them died.

Overall in-hospital outcome

Overall mortality was 25 per cent. The causes of death were: sepsis (8%), CHF (21%), systemic embolization (4%), sudden cardiac death (8%), non cardiac causes (3%), intraoperative (3%) and undetermined causes (42%).

DISCUSSION

The present study was conducted in order to provide recent and up-to-date data on the prevalence, characteristics and mortality of infective endocarditis in a tertiary care hospital in Khon Kaen, Thailand. Numerous reviews have been published elsewhere describing experiences with infective endocarditis at various institutions[3-8] but the methodologies and use of diagnostic criteria were different. The prevalence of IE in the present study

was 4 cases per 1,000 hospital admissions, which was higher than in other studies[6,7,12] perhaps because of recent improvements in transthoracic and transesophageal echocardiography which is now recognized as an effective tool for the diagnosis of IE which was not used in the past. The twice as high prevalence in males compared with females is common[13,14]. Contrary to other studies, the authors observed a higher frequency in the young and middle-aged compared to the elderly[12,14]. The distribution of underlying heart disease has not changed from previous Thai studies,[4,5,8] or other published data,[11,12] where there was a high rate of prosthetic valve IE. Infective endocarditis complicated by rheumatic heart disease is still a major problem in this region.

The frequency of *Streptococcus viridans* was higher than other microorganisms identified in the present study, and similar to other studies,[3,4,7] which could be related to dental prophylaxis.

Publications on infective endocarditis rarely state that the source of infection may be due to medical or surgical procedures. However, the authors found that patients who underwent such procedures accounted for 34 per cent of the cases. Dental disease or procedures could have been responsible for as many as 27 out of 160 patients (17%). Among the 27 (17%) non-dental patients the portals were: cystoscope or urethral dilatation, septic arthritis, skin abscesses, hemodialysis, and intravenous drug use.

Our study confirmed reports[19-21] of the utility of transthoracic and transesophageal echocardiography in the precise delineation of valvular pathology in patients with IE, and recognized as an effective tool for the diagnosis of infective endocarditis. Including echocardiographic findings among the diagnostic criteria is the main reason why the diagnosis of IE was probably more common in our study. However, we relied on the surgeons' macroscropic findings for classifying infective endocarditis as the definite diagnosis. The overall sensitivity of transthoracic echocardiography for vegetation in our study was 80 per cent but had a relatively low capability to visualize such complications of IE such as periannular abscess, leaflet perforation, and fistula including infection of the prosthetic valve (19-21). Transesophageal echocardiography greatly improved sensitivity and specificity in detection of vegetation and complications of IE.

Regarding the operation rate among younger patients and in-hospital mortality: the higher rate of surgery observed in men compared to women may be due to a higher incidence of intravenous drug users among men in whom *Staphylococcus aureus* infection required surgical management. The reported mortality rate varied in different studies,[12,13,15-18] from 12 per cent to 45 per cent but in the present study, many patients with severe hemodynamic deterioration because of valvular regurgitation or obstruction from bulgy vegetation underwent surgery and had favourable outcomes. Congestive heart failure (CHF) in IE, irrespective of the cause or mechanism, portends a grave prognosis with medical therapy alone and is also the strongest predictor of a poor outcome with surgical therapy. If operation is to be performed, it is best to proceed early,[22,23] espectially if aortic regurgitation is present. The left ventricle is less compliant than the left atrium, and left ventricular end-diastolic pressure and wall stress are substantially higher in patients with aortic regurgitation compared with those with mitral regurgitation. Acute aortic regurgitation will often progress rapidly to severe CHF despite an initial favorable response to medical therapy. Therefore, urgent or even emergency operation should be considered for patients with severe acute aortic valvular regurgitation. Delaying surgery to the point of frank ventricular decompensation dramatically increases operative mortality from 6 per cent to 11 per cent for patients without CHF and from 17 per cent to 33 per cent for patients with CHF[22,23]. Prosthetic infective endocarditis has a different pathological presentation depending on type of valve and infection occurs early after valve replacement (within 2 months) or in the late operative period (greater than 2 months). Overall, the mortality rate with medical therapy alone was higher than that with combined medical and surgical therapy in patients with PV infective endocarditis. After reviewing the records of the study patients who died, mainly because of co-morbidity (*i.e.* renal failure), prevention of the infection, early diagnosis and an effective treatment are the best means of reducing overall mortality.

Prediction of mortality was duration of symptoms prior to diagnosis, this may be related to severity of the disease and complications which developed in the early stage.

The authors concluded that infective endocarditis remains a frequent and serious condition in Khon Kaen. This reinforces the need to improve early and rapid diagnosis, effective treatment, prompt recognition of complications and efficiency of prevention of the disease.

Study limitations: The retrospective analysis and the relatively small number of patients limited the present study. A referral bias resulted in the inclusion of a high proportion of severely compromised patients who might benefit from urgent surgery.

Implications: All patients who have moderate or severe heart failure should undergo immediate valve replacement early in their course, since surgery offers a distinct advantage over medical treatment alone. The authors expect that the overall mortality and survival of patients in this group will improve.

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ลิ้นหัวใจอักเสบติดเชื้อ : ความชุก ลักษณะของโรคและการเสียชีวิตในจังหวัดขอนแก่น 2533–2542

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วัตถุประสงค์ เพื่อหาความชุก, ลักษณะของโรคและการเสียชีวิต ในผู้ป่วยลิ้นหัวใจอักเสบติดเชื้อ ที่รับไว้รักษาในโรงพยาบาลศรีนครินทร์ และโรงพยาบาลศูนย์ขอนแก่น ซึ่งเป็น โรงพยาบาล tertiary care ของ จังหวัด ขอนแก่น

วิธีการรักษา ได้ทำการรักษาย้อนหลังในระหว่างมกราคม พ.ศ.2533 ถึง ธันวาคม พ.ศ.2542 มีผู้ป่วยทั้งสิ้น 160 ราย

ผลการรักษา ความชุกของโรค คิดเป็นอัตราส่วน 4 รายต่อผู้ป่วยที่รับไว้รักษาในโรงพยาบาลศรีนครินทร์ 1,000 ราย, พบว่า 28% ของผู้ป่วยไม่มีโรคหัวใจอยู่ก่อน, 60% ของผู้ป่วยมีโรคหัวใจรูมาติกมาก่อนการติดเชื้อ, 95% เป็นการติดเชื้อของ native valve และ 5% เป็นการติดเชื้อของ prosthetic valve, ตำแหน่งที่มีการติดเชื้อ mitral valve พบ 43%, aortic valve พบ 42 %, mitral และ aortic valve พบ 9%, tricuspid valve พบ 8%, สามารถเพาะเชื้อขึ้นในเลือด 62% ของผู้ป่วยทั้งหมด, เชื้อที่พบได้บ่อยที่สุดคือกลุ่ม Streptococci 37%, ส่วน Staphylococci พบ 16%, ผู้ป่วยได้รับการรักษาด้วยวิธีผ่าตัดในขณะอยู่โรงพยาบาล 45%, อัตราตายของผู้ป่วยในโรงพยาบาล 25%

สรุป ถึงแม้จะมีวิธีการวินิจฉัยใหม่และการรักษาด้วยวิธีการผ่าตัดที่รวดเร็ว ลิ้นหัวใจอักเสบติดเชื้อยังคงเป็นโรคที่พบอยู่เสมอ, เป็นปัญหาสำคัญ และมีอัตราการตายสูง

คำสำคัญ : ลิ้นหัวใจอักเสบติดเชื้อ, ความชุก, ลักษณะของโรค, อัตราการเสียชีวิต

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