การศึกษาความชุกของเชื้อที่ก่อโรคและอัตราการเสียชีวิตของโรคเยื่อบุหัวใจติดเชื้อในโรงพยาบาลอุตรดิตถ์

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บทคัดย่อ

บทนำ: โรคเยื่อบุหัวใจติดเชื้อเป็นโรคที่ส่งผลให้เกิดความผิดปกติรุนแรงต่อลิ้นหัวใจ ในประเทศไทยพบว่ามีอัตราการเสียชีวิตของโรคนี้สูง ประชากรในจังหวัดอุตรดิตถ์มีปัจจัยเสี่ยงต่อการติดเชื้อโรค Streptococcus suis มากกว่าพื้นที่อื่นเนื่องจากพฤติกรรมการบริโภคหมูดิบและอาชีพที่สัมผัสหมู อย่างไรก็ตามข้อมูลความชุกของเชื้อนี้และเชื้อก่อโรคอื่นๆ อัตราการเสียชีวิตของโรงพยาบาลอุตรดิตถ์ยังไม่มีการรวบรวมข้อมูลมาก่อน

วิธีการศึกษา: การศึกษานี้เป็นการศึกษาย้อนหลัง รวบรวมข้อมูลผู้ป่วยโรคเยื่อบุหัวใจติดเชื้อเฉพาะฝั่งซ้าย และลิ้นที่เกิดโรคไม่ใช่ลิ้นหัวใจเทียมระหว่างเดือนมกราคม ปี 2560 ถึงเดือนธันวาคม ปี 2565 ข้อมูลของผู้ป่วยจะวิเคราะห์โดยแบ่งจากชนิดของเชื้อก่อโรค และดูผลลัพธ์หลักเป็นอัตราการเสียชีวิตในโรงพยาบาล ผลลัพธ์รองเป็นอัตราการเสียชีวิตที่ 6 เดือน

ผลการศึกษา: มีผู้ป่วยทั้งหมด 69 คนที่รวบรวมได้ Streptococcus suis เป็นเชื้อก่อโรคที่พบมากที่สุดถึง 17 ราย (ร้อยละ 24.6) อัตราการเสียชีวิตในโรงพยาบาลสูง ร้อยละ 24.6 และอัตราการเสียชีวิตที่ 6 เดือนคือ ร้อยละ 33.3 เมื่อแบ่งจากชนิดเชื้อก่อโรคอัตราการเสียชีวิตจากเชื้อ Streptococcus suis สูงกว่าเชื้ออื่นๆแต่ไม่มีนัยสำคัญทางสถิติ ร้อยละ 29.4 และร้อยละ 23.1 ตามลำดับ อัตราส่วนความเสี่ยงอันตราย 1.35 (95% CI 0.48-3.84, p=0.569) อัตราการเสียชีวิตที่ 6 เดือนจากการติดเชื้อ Streptococcus suis สูงกว่าเชื้ออื่นๆแต่ไม่มีนัยสำคัญทางสถิติเช่นกัน ร้อยละ 47.1 และร้อยละ 28.8 ตามลำดับ อัตราส่วนความเสี่ยงอันตราย 1.64 (95% CI 0.74-4.10, p=0.207) การวิเคราะห์ข้อมูลแบบตัวแปรเดียวพบว่าโรคเบาหวาน Euroscore II และการเปลี่ยนแปลงของระดับความรู้สึกตัวสัมพันธ์กับอัตราการเสียชีวิตที่ 6 เดือน แต่เมื่อวิเคราะห์ข้อมูลแบบหลายตัวแปรนั้นพบว่ามีเพียงการเปลี่ยนแปลงของระดับความรู้สึกตัวที่ยังคงสัมพันธ์กับอัตราการเสียชีวิตอย่างมีนัยสำคัญทางสถิติ อัตราส่วนความเสี่ยงอันตราย 4.96 (95% CI 1.88-13.08, p=0.001)

สรุป: โรคเยื่อบุหัวใจติดเชื้อที่โรงพยาบาลอุตรดิตถ์มีอัตราการเสียชีวิตในโรงพยาบาลและอัตราการเสียชีวิตที่ 6 เดือนสูง มีความชุกของเชื้อ Streptococcus suis สูงและมีอัตราการตายสูงกว่าเชื้อก่อโรคอื่นๆ แต่ไม่มีนัยสำคัญทางสถิติ

คำสำคัญ: โรคเยื่อบุหัวใจติดเชื้อ, อุตรดิตถ์, อัตราการเสียชีวิต, สเตร็พโตค็อกคัส ซูอิส

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The Prevalence of Pathogen and Clinical Outcomes of Infective Endocarditis in Uttaradit Hospital

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ABSTRACT

Background: Infective endocarditis (IE) is a severe cardiac infection that affects individuals with multiple cardiac valve conditions. In Thailand, the overall in-hospital mortality rate is high, and people in Uttaradit province are at risk of exposure to Streptococcus Suis due to certain behaviors and occupations. However, data on the prevalence of pathogens and clinical outcomes, especially Streptococcus Suis, at Uttaradit hospital are limited.

Methods: This retrospective cohort study collected data from left-sided, native-valve endocarditis patients who underwent echocardiography at Uttaradit Hospital between January 2017 and December 2022. Patients were stratified by the organism, and the primary outcome was in-hospital death. The secondary outcome was death at 6 months of follow-up.

Results: Of the 69 patients with IE included in the study, Streptococcus Suis was the most prevalent pathogen 17 patients (24.6%). In-hospital mortality and any death at 6 months were 24.6% and 33.3%, respectively. The Streptococcus Suis group had a numerically higher in-hospital mortality than the non-Streptococcus Suis group (29.4% vs. 23.1%), but the difference was not significant (HR=1.35, CI 0.48-3.84, p=0.569). At 6 months, all-cause mortality in both groups was 47.1% and 28.8%, respectively (HR=1.64, CI 0.74-4.10, p=0.207). The study found that in univariate analysis, T2DM, Euroscore II, and alteration of consciousness were all associated with 6-month mortality in IE patients. However, in multivariate analysis, only alteration of consciousness remained a significant predictor of mortality, with a hazard ratio of 4.96, 95% CI 1.88-13.08, and p=0.001.

Conclusions: The overall in-hospital mortality and 6-month mortality rate of IE at Uttaradit hospital were high. Streptococcus Suis was prevalent, but not significantly associated with higher mortality compared to other organisms.

Keywords: Infective endocarditis, Uttaradit, mortality, Streptococcus suis

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Introduction

Infective endocarditis (IE) is a life-threatening cardiac infection and is predisposed to occur in some individuals with multiple cardiac valve conditions, with an annual incidence of ~3–10 per 100,000 people. Globally, IE remains a highly lethal disease, with the overall mortality remaining at ~25%[1]. In Thailand, the overall in-hospital mortality rate is 17.7-25%[2,3,4,5]. The clinical history of IE is highly variable according to the causative microorganism, the presence or absence of pre-existing cardiac disease, the presence or absence of prosthetic valves or cardiac devices and the mode of presentation. Hence, IE should be suspected in a variety of different clinical situations. It may present as an acute, rapidly progressive infection, but also as a subacute or chronic disease with low-grade fever and non-specific symptoms that may mislead or confuse initial assessment. The modified Duke criteria 2015 is the standard diagnostic criteria, that depending on pathologic, blood culture and imaging criteria. Imaging, particularly echocardiography, plays a key role in both the diagnosis and management of IE. Recent advances in imaging techniques have resulted in an improvement in identification of endocardial involvements and extracardiac complications of IE[6]. The most common pathogens are Viridans streptococci, Streptococcus gallolyticus, HACEK group, Staphylococcus aureus, and community Enterococci. But in Southeast Asia, especially Thailand, Streptococcus suis, a gram-positive diplococci alpha-hemolytic bacteria mainly found in pigs. The pathogen has been classified into 29 serotypes of which serotype 2 is the most prominent cause of infection in humans contributing to meningitis, septicemia, infective endocarditis and other serious complications such as hearing loss[7,8].

In Thailand, infective endocarditis is discovered in 6.4% of reported cases[8], which is quite intriguing. Chiang Mai, the largest province in northern Thailand and its provincial capital, had the most investigations of S. suis infections. A two-year study of 41 S. suis patients at Chiang Mai University Hospital in 2000 showed a mortality rate of up to 19.5%[9].

In Uttaradit province, people in this area have many risk factors to expose to Streptococcus Suis, such as behavior of raw or undercooked pork consumption, pig related occupation[10]. The Cardio-Thoracic-Vascular surgery unit at Uttaradit hospital has been providing services since 2016, and there is no available previous observational data on infective endocarditis at this hospital.

Our study aimed to determine the prevalence of pathogen and clinical outcomes of infective endocarditis, especially Streptococcus Suis in Uttaradit hospital.

Methods

This retrospective cohort study collected data from all left-sided, native-valve endocarditis patients who underwent echocardiography at Uttaradit Hospital, Thailand, between January 2017 and December 2022. Inform consent was waived as the data collection is retrospective and without patient identifiers.

Study population

The study population were patients who 18 years of age or older, presented with left sided, native-valve endocarditis and underwent echocardiography at Uttaradit hospital. Baseline characteristics, clinical-presentation, laboratory investigations, echocardiography, and antibiotic regimens were retrospectively collected in the Uttaradit hospital database. Patients were eligible for enrollment if they had received a diagnosis of definite infective endocarditis according to the modified Duke criteria[6]. The patients were stratified by the organism, especially Streptococcus Suis and non-Streptococcus

Suis, and received surgery or not. Patients were excluded if they had infective endocarditis involving a prosthetic valve, right-sided vegetations.

Outcome

The primary outcome was in-hospital death including cardiovascular and cardiovascular death. Secondary outcome was death at 6 months of follow-up

Statistical analysis

Data analysis and statistical methods were analysed by SPSS version 23 (IBM Corp). Categorical variables were reported with frequencies and percentages. The continuous variables were summarized as mean ~ standard deviation (SD) or median and interquartile ranges (IQR) or maximum-minimum as appropriate. Categorical data were compared with chi-squared or Fisher's exact test, as appropriate. Continuous data were analysed by independent t-test in normal distribution data or Mann-Whitney U test in non-normal distribution data.

At 6 months follow up, event rates of the two groups were estimated using the Kaplan-Meier method. The hazard ratio (HR) and two-sided 95% confidence intervals were calculated using the Cox proportional-hazards model. The Kaplan-Meier curve was done to determine the relationship between the organisms and the death at 6 months. Adjustments were made for the following potential confounders: age, gender, diabetes mellitus (DM), left ventricular ejection fraction (LVEF), Euroscore II. A two-sided p-value < 0.05 was considered statistically significant.

Results

Baseline characteristics

Between January 2017 and December 2022, a total of 69 patients with infective endocarditis (IE) were enrolled in our study and had sufficient clinical data for analysis.

Table 1 shows the different organisms identified in the blood cultures of the IE patients. Streptococcus suis was the most prevalent pathogen, identified in 17 patients (24.6%), followed by Streptococcus viridans (12 patients, 17.6%), Staphylococcus aureus (11 patients, 15.9%), Enterococci (2 patients, 2.9%), and 18 patients (26.1%) had culture-negative IE.

Table 1. Organisms of infective endocarditis identified in the blood cultures of the IE patients at Uttaradit hospital

Total	69 patients
Streptococcus viridans	12(17.4%)
Streptococcus suis	17(24.6%)
Other Streptococci	9(13.0%)
Staphylococcus aureus	11(15.9%)
Enterococci	2(2.9%)
Negative culture	18(26.1%)

The baseline characteristics of the patients are presented in Table 2 which categorizes the patients into three groups: Streptococcus suis, non-Streptococcus suis, and total. The patients had a mean age of 54 years, with two-thirds of them being male. Among them, 15 patients (21.7%) had a medical history of diabetes, 29 patients (42%) had hypertension, and 8 patients (11.6%) had CAD. The mean duration of fever was 3 days, and 8 (11.6%)

of patients had altered consciousness at presentation. At admission, 40 (58%) of patients had heart failure, and 46.4% had mitral valve involvement, 36.2% had aortic valve involvement, and 17.4% had both mitral and aortic valve involvement. Most patients 57 (82.6%) had severe valvular regurgitation, and 37 patients (53.6%) underwent valve surgery.

When the patients were divided into two groups according to their pathogen, namely the Streptococcus suis group and non-Streptococcus suis group, there was no significant difference in their mean age (58.7 vs. 52.6 years, p = 0.130), or male to female ratio (64.7% vs. 65.4%, p = 1.000). However, the presentation of heart failure on admission was significantly higher in the Streptococcus suis group (88.2%) than in the non-Streptococcus suis group (48.1%, p = 0.004). The mean LVEF was 69.7% in the Streptococcus suis group and 67.0% in the non-Streptococcus suis group (p = 0.248).

Valve involvement was non-significantly higher in the aortic valve in the Streptococcus suis group (52.9%) than in the non-Streptococcus suis group (30.8%, p = 0.092). The mean vegetation diameter was 1.0 cm in the Streptococcus suis group and 0.8 cm in the non-Streptococcus suis group (p = 0.859). The infection process causing severe valve regurgitation was observed in 82.4% of patients in the Streptococcus suis group and 82.7% in the non-Streptococcus suis group (p = 0.847). Valve surgery was performed in 47.1% of patients in the Streptococcus suis group and 55.8% in the non-Streptococcus suis group (p = 0.196). The most common antibiotic regimen used was beta-lactam alone, with 76.5% in the Streptococcus suis group and 88.5% in the non-Streptococcus suis group

Table 2 Baseline Characteristics

	Streptococcus suis (n=17)	Non-Streptococcus suis (n=52)	Total (n=69)	*p*-value
Age (years)	58.7±13.7	52.6±14.9	54.1±14.7	0.130
Male sex	11 (64.7)	34 (65.4)	45(65.2)	1.000
Diabetes	3 (17.6)	12 (23.1)	15(21.7)	0.746
Hypertension	7 (41.2)	22 (42.3)	29(42)	1.000
Atrial fibrillation	0 (0.0)	1 (1.9)	1(1.4)	1.000
CAD	2 (11.8)	6 (11.5)	8(11.6)	1.000
Immunocompromised hostE	1 (5.9)	2 (3.8)	3 (4.3)	1.000
Underlying valve disease	0 (0.0)	5 (9.6)	5 (7.2)	0.323
Prior valve surgery	0 (0.0)	2 (3.8)	2 (2.9)	1.000
Fever (days)*	3 (0-7)	2 (0-8)	3 (0-7)	0.755
Alteration of consciousness	1 (5.9)	7 (13.5)	8 (11.6)	0.669
Embolism on admission	1 (5.9)	9 (17.3)	10 (14.5)	0.431
HF on admission	15 (88.2)	25 (48.1)	40 (58%)	0.004
Conduction abnormality	2 (11.8)	5 (9.6)	7 (10.1)	1.000
Euroscore value*	3.3 (2.1-6.3)	2.2 (1.4-4.5)	2.4 (1.6-5.4)	0.223
LVEF	69.7±8.9	67.0±8.1	67.6±8.3	0.248
Cr*	0.9 (0.8-1.1)	0.9 (0.7-1.3)	0.9 (0.8-1.3)	0.636

Table 2 Baseline Characteristics (ต่อ)

	Streptococcus suis (n=17)	Non-Streptococcus suis (n=52)	Total (n=69)	*p*-value
Valve involved				0.092
Mitral	4 (23.5)	28 (53.9)	32(46.4)	
Aortic	9 (52.9)	16 (30.8)	25(36.2)	
Mitral and aortic	4 (23.5)	8 (15.4)	12(17.4)	
Vegetation diameters*	1.0 (0.6-1.4)	0.8 (0.5-1.3)	0.9 (0.5-1.4)	0.859
Valvular disease				0.847
Severe stenosis	0 (0.0)	1 (1.9)	1 (1.4)	
Severe regurgitation	14 (82.4)	43 (82.7)	57(82.6)	
Non severe regurgitation	3 (17.6)	7 (13.5)	10 (14.4)	
Treatment				
Valve surgery	8 (47.1)	29 (55.8)	37 (53.6)	0.196
Mechanical valve	6	21	27	
CABG	1 (5.9)	3 (5.8)	4 (5.8)	0.211
Antibiotic regimen				0.007
- Beta-lactam antibiotic alone	13 (76.5)	46 (88.5)	59 (85.5)	
- Beta-lactam antibiotic with aminoglycoside	1 (5.9)	6 (11.5)	7 (10.1)	
- Fluoroquinolone	3 (17.6)	0 (0.0)	3 (4.3)	
Duration of ATB	32.8±12.7	29.1±11.2	29.6±11.8	0.236
Defervescence days*	5.5 (0.5-7.5)	6 (0-8)	6 (0-8)	0.756

Abbreviations:

CAD coronary artery disease; HF heart failure; LVEF left ventricular ejection fraction; Cr creatinine; CABG coronary bypass surgery; ATB antibiotics

Primary outcomes:

At Uttaradit hospital, the overall in-hospital mortality and any death at 6 months for infective endocarditis were 24.6% and 33.3%, respectively (table 3).

Table 3 Primary endpoint and secondary endpoint

	Overall (n=69)	Streptococcus Suis (n=17)	Non-Streptococcus Suis (n=52)	Unadjusted HR (95%CI)	p-value	Adjusted HR*	p-value
Primary Endpoint							
- In hospital death	17 (24.6%)	5 (29.4%)	12 (23.1%)	1.35 (0.48-3.84)	0.569	1.73 (0.59-5.05)	0.317
Secondary Endpoint							
Any death at 6 months	23 (33.3%)	8 (47.1%)	15 (28.8%)	1.64 (0.74-4.10)	0.207	2.2 (0.88 -5.54)	0.094

Abbreviations:

* Adjusted for DM, Euroscore II, AOC

Although in-hospital mortality was numerically higher in the Streptococcus suis group (29.4%) than in the non-Streptococcus suis group (23.1%), with an HR of 1.35 (0.48-3.84) and p=0.569. At 6 months, the all-cause mortality in both groups was 47.1% and 28.8%, with an HR of 1.64 (0.74-4.10) and p=0.207, respectively. The Kaplan-Meier survival analysis showed that there was difference in survival between the two groups, with the separation of the survival curves occurring after 2 months from the time of diagnosis (figure 1).

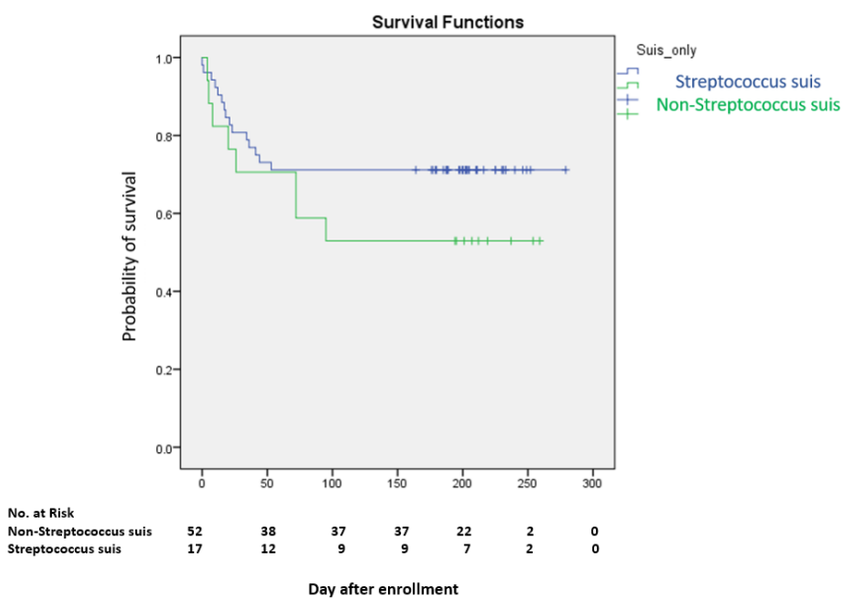

Figure 1 Probability of survival between Streptococcus suis and non-Streptococcus suis

Univariate analysis revealed that T2DM (HR 0.40, 95% CI 0.17-0.94, p=0.035), Euroscore II (HR 1.06, 95% CI 1.03-1.10, p=0.001), and alteration of consciousness (HR 6.54, 95% CI 2.63-16.26, p=0.001) were associated with 6-month mortality in IE patients (table 4). However, multivariate analysis indicated that only alteration of consciousness remained a significant predictor of mortality (HR 4.96, 95% CI 1.88-13.08, p=0.001).

Table 4 Factors that associated with 6 months mortality in IE patients.

Factors	Univariate analysis			Multivariate analysis		
	HR	95%CI	P-value	HR	95%CI	P-value
Age (year)	1.02	1.00-1.05	0.097			
Male sex	1.11	0.71-1.73	0.645			
DM	0.40	0.17-0.94	0.035	0.69	0.43-1.09	0.114
HT	0.65	0.29-1.46	0.294			
CAD	1.43	0.34-6.09	0.630			
Cr	1.14	0.89-1.47	0.310			
Euroscore II	1.06	1.03-1.10	0.001	1.04	1.00-1.09	0.060
Fever(day)	0.99	0.96-1.03	0.754			
AOC	6.54	2.63-16.26	0.001	4.96	1.88-13.08	0.001
Embolism on admission	0.70	0.49-1.16	0.165			
HF on admission	0.69	0.29-1.63	0.395			
LVEF	0.98	0.93-1.03	0.360			
Vegetation diameter	1.56	0.97-2.51	0.070			
Multiple valves involved	1.04	0.35-3.06	0.940			
Valve surgery	0.50	0.21-1.17	0.111			

Abbreviations: DM diabetes; HT hypertension; CAD coronary artery disease; Cr creatinine; AOC alteration of consciousnes

Discussion:

The retrospective study conducted at Uttaradit hospital aimed to investigate the mortality rates in left-sided infective endocarditis (IE) patients. The study found that the incidence of mortality was higher than previous studies (1), with 24.6% of patients dying in the hospital and 33.3% dying within 6 months. Interestingly, the most prevalent pathogen was Streptococcus suis, and although mortality rates were not significantly higher than other pathogens, there was a higher proportion of heart failure in these cases which contributed to the increased mortality. The study also found that alteration of consciousness was the only independent predictor of 6 months mortality in IE patients. Although previous studies have identified several independent predictors,

such as heart failure, systemic embolism, Staphylococcus aureus etiology (11), septic shock, drug abuse (12), and NT-proBNP (13), they did not show significance in this study.

Moreover, previous studies have shown that early surgery in patients with IE and large vegetation significantly reduced the composite endpoint of death and embolic events (14). This study found that although the vegetation diameter was small, early surgery may still be beneficial in reducing mortality in IE patients. Despite a low EUROscore risk, the rate of valve surgery remained low, indicating the need for further development in the surgical team's potential.

Limitations:

Some limitations of this study are deserved discussion. First, we cannot exclude selection bias and residual confounding that were the nature of the retrospective study. Second, the small sample size and single-center analysis may limit the generalizability of the study findings

Conclusion:

The overall in-hospital mortality and 6-month mortality rate of IE at Uttaradit hospital were high. Streptococcus Suis was prevalent, but not significantly associated with higher mortality compared to other organisms.

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