Clinical and pathogen features of infective endocarditis: A retrospective study of 111 episodes in a teaching hospital in southwest China

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Abstract

Background Infective endocarditis (IE) is a health-threaten infectious disease. Diverse and complicated etiology and causative microorganisms make IE difficult to diagnose and treat. As we know, current investigations of clinical and pathogen features of IE in West china are scarce. In this study, we aimed to investigate the epidemiology and pathogen characteristic of IE in our region. Methods A retrospective analysis of clinical and laboratory data was performed from all blood culture positive IE patients between 2012 to 2017 in Westchina Hospital of Sichuan University. The diagnosis is traditionally based on the modified Duke criteria. Results The mean age of the patient cohort was 40.7±21.5 years (ranging from 2-78); 73 cases (65.2%) were males and 39 cases (34.8%) were females. Of the 111 cases, 100 were native valve endocarditis (NVE) while 11 were prosthetic valve endocarditis (PVE), 87 cases (78.4%) were left-heart infection. Congenital heart disease (28.6%) and rheumatic heart disease (11.6%) were most common history of heart disease. Primary clinical manifestations were fever (87.5%) and heart murmur (78.6%). Streptococci spp (20.7%) was the most common organism, followed by Staphylococcus spp (17.9%). Streptococcus viridians showed no resistance to penicillin, erythromycin and clindamycin resistance rate were 47.4% and 40%. Benzocillin resistance rate of staphylococcus aureus to was 26.3%. Vancomycin or linezolid resistance staphylococcus aureus were not found. 75 patients died while 36 patients survived at last. With respect to risk factors, history of heart disease was the only prognostic risk factor (OR: 0.239, 95%CI 0.08-0.68) Conclusions Epidemiological and clinical characteristics of infective endocarditis are various and complex, distribution of pathogen is regional difference. Our research of infective endocarditis with bloodstream infection verified regional characteristics of infective endocarditis. The variations we observed in the study will be of important value to clinical preventive medication in our region.

Methods

Study sample
A retrospective analysis was performed of clinical data collected from 111 cases clinically diagnosed IE with positive blood culture at Westchina Hospital of Sichuan University from Jan 2012 to Dec 2017. The data of retrospective analysis included general information, history of heart disease, clinical manifestations and laboratory findings (taken at the time of first presentation at the hospital), pathogen and outcome.

**Pathogen identification and antibiotic sensitivity test (AST)**

Identification and AST of pathogens were conducted by VITEK-2, ATB FUNGUS 3, and API 20C (BioMerieux, France).

**Statistical method**

All data were analyzed using the SPSS version 21.0 software (SPSS, Chicago, IL, USA). P-values less than 0.05 were considered statistically significant.

**Results**

**General characteristics.** A total of 100 patients with NVE and 11 patients with PVE were included in our study. 73 patients were male (65.2%) and 38 patients were female (34.8%). The mean age was 40.7±21.5 years, with a range from 12-78 years. 1 patient had a history of intravenous drug use (IDU). 51 patients (46.4%) had history of heart disease, include 32 congenital heart disease (CHD), 13 rheumatic heart disease (RHD) 2 coronary artery disease (CAD) and 4 valvulopathy. 4 cases were hospital acquire infection (3 cases were infection after flap replacement, 1 case was infection caused by streptococcus sepsis), the remaining 107 cases were community acquire infection. The most common symptom of IE patients was fever (87.5%), followed by cardiac murmurs (78.6%). (Table 1)

**Laboratory Findings.**

66 cases (58.9%) had leukocytosis; 95 cases (84.8%) had exhibited N% (neutrophil percentage) increased, 89 cases (79.5%), 61 cases (54.5%) and 82 cases (73.2%) had PCT, ESR and CRP increased respectively. (Table 1)

**Echocardiographic Findings.**

All the 111 patients underwent transthoracic heart color doppler ultrasound (TTE). 87 patients were left heart vegetations, including 36 cases of mitral valve vegetations, 46 cases of aortic valve vegetations, 5 cases of mixed mitral and aortic valve vegetations, and 1 case of left atrial wall vegetations. 18 patients were right heart vegetations, including 12 cases of tricuspid valve vegetations 6 cases of pulmonary valve vegetations and 2 cases of mesh vegetation. Descending aortic vegetations were found in 1 patient and no vegetations were found in 4 patients. (Table 1)

Among the 46 patients with aortic valve vegetation, 82.6% were associated with mild, moderate and severe aortic valve regurgitation (10 cases, 7 cases and 21 cases, respectively). Among the 36 cases of
mitral valve vegetations, 75.0% were associated with mild, moderate and severe mitral regurgitation (4 cases, 11 cases and 12 cases, respectively). In the 12 cases with tricuspid valve vegetations, 75% of them were associated with moderate and severe tricuspid regurgitation, which were 3 cases and 6 cases respectively. Among the 5 cases of pulmonary valve vegetations, 1 was severe, 1 was moderate and 1 was mild reflux. Among the 5 patients with multiple valve excrescences, 1 patient had severe mitral regurgitation and 4 patients had multiple valve regurgitation. The other 8 cases were 2 cases of ventricular septal mesh vegetation, 1 case of descending aorta vegetation and 1 case of left atrial wall vegetation, 4 cases of no vegetation and 5 cases of no reflux. (figure 1) it can be seen that although the damaged valves are different, they are all dominated by severe reflux, which has a great impact on heart function.

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**Microbiological findings.**

Streptococci spp (59.5%) and Staphylococcus spp (25.2%) were the most common pathogen found in bloodstream of IE patients (Table 2). Isolation rate of Streptococci spp is higher than Staphylococcus spp in 100 NVE patients, and Staphylococcus spp is higher than Streptococci spp in 11 prosthetic valve endocarditis patients (P<0.05).

Staphylococcus aureus has no sensitive to penicillin, resistance rate of erythromycin and clindamycin were 52.5% and 33.3%, resistance rate of other antibiotics were not more than 30%, methicillin-resistant Staphylococcus aureus (MRSA) was 26.3%. Coagulase negative staphylococcus (CNS) had no sensitive to penicillin and methicillin-resistant coagulase negative staphylococcus (MRCNS) was 75%, and resistance rate of other antibiotics was not exceeding 30% (table 3). Resistance rate of Streptococcus viridans and streptococcus angina to erythromycin, azithromycin, clindamycin and tetracycline were over 30%. (table 4). Gram-Negative strains were only 7 cases and no statistical significance could be found.

**Prognosis**

At last, 75 patients survived and 36 patients died In 111 patients of our study. Using a logistic regression analysis, we determined that history of heart disease was the only prognostic risk factors (OR: 0.239, 95% CI 0.08-0.68) (table 5)

**Discussion**

The incidence rate of IE is between 2-7.9 per 100,000 people²,³, and has remained stable⁴. Although relatively rare, IE continues to be characterized by increased morbidity and mortality and is now the third or fourth most common life-threatening infection syndrome.⁵ In 2010, IE was associated with 1.58 million disability-adjusted life-years or years of healthy life lost, as a result of death and nonfatal illness or impairment worldwide⁶. The demographics of patients affected by IE have shifted in recent years, with an increase in mean patient age, an increase in the proportion of patients with prosthetic valves and other cardiac devices, and a decrease in the proportion of patients with rheumatic heart disease⁶,⁷. The average age of the patients in this study was 40.7 years old, 49.1% of the patients were over 40 years old, and 65.2% of the patients were male⁸ and congenital heart disease (CHD) is the most common cardiac
disease history that showed in IE patients, a same idea we could find in the research of Fefer P, which considered no-rheumatic valvular heart disease of the elderly was the most common underlying factor.

In this study, lung infection is the leading clinical features in IE patients without heart disease history. It was similar to the studies of Aylin Tugcu. Electrocardiogram showed that valvular vegetations were mainly generated in the left heart, and most of them were accompanied with varying degrees of regurgitation. Some infectious markers, such as CRP, erythrocyte sedimentation rate, and neutrophil, may contribute to early detection of the disease. In this study, more than 50% patients accompany with WBC, N, ESR, PCT and CRP increased, infectious indicators may be used as an auxiliary basis for the diagnosis of infective endocarditis. However, due to the poor specificity of various infectious indicators, pathogen culture and electrocardiogram are required as the final basis for the diagnosis of IE.

Staphylococcus spp is the most common cause of IE, followed by Streptococci spp. Staphylococcus spp associate IE has became increasingly common in most industrialized countries because of increased medical intervention; meanwhile Streptococci spp has became less common. The presence of S. aureus bacteremia should be considered a major criterion, regardless of whether the infection is nosocomially acquired or whether a removable source of infection is present. In the studies from Spain, more than one third of IE cases were related to medical treatment, and the main pathogen of these patients was staphylococcus, however, pathogens may vary in different areas. In our study, the most common pathogen was Streptococcus viridans (20.7%), followed by staphylococcus aureus 18.0%. This prevalence pattern differs significantly from studies before. This may be related to economic development. Patients of our research selected crowd in the southwest China where economic level and medical conditions is weak, few patients had medical treatment. Study from Jerusalem shows that staphylococcus often exists in medical care IE patients while more streptococci is found from community infection. Study from Lauren Hartman et al. showed that staphylococcus aureus is the most common in patients with IDU-IE, while streptococcus is more common in patients without IDU-IE, only 1 patient had IDU history in our study. Above may be the reasons for the difference in distribution of pathogens. It is also reported that this difference may be due to adhesion molecules from Streptococcus viridans and staphylococcus aureus, which are related to the presence of surface adhesion factors on valve surfaces or in favor of bacterial colonization.

Indicate in European endocarditis management guidance, only for part of patients with congenital heart disease or valvular surgery, preventive use of antibiotics was necessary. Empirical treatment may include vancomycin or ampicillin/ Sulbactam and aminoglycosides, but ultimately antibiotic treatment options need to be based on antibiotic sensitive test. In this study, neither staphylococcus nor streptococcus showed resistance to vancomycin, vancomycin could be used as a preventive treatment antibiotic. The resistance rate of staphylococcus and streptococcus to erythromycin, azithromycin, clindamycin and tetracycline are all over 30%, and it is not recommended to use in the experience of treatment.
To further explore the impact of the major death factors, the following information is included in the analysis model: gender, age $\geq 60$ years, history of heart disease, PVE, Vegetative site and some lab data. Our results indicate that only history of heart disease is a major risk factor for the prognosis of IE patients ($\text{OR} = 0.01, 95\% \text{CI}: 0.08-0.68$), while some studies indicated that age $\geq 60$ years ($\text{OR} = 6.861, 0.94-50.1$), congestive heart failure ($\text{OR} = 8.854, 1.34-54.7$), diabetes ($\text{OR} = 7.224, 1.17-44.7$), and Staphylococcus aureus or negative tuberculosis infection ($\text{OR} = 18.81, 2.39-148.2$) were major risk factors for the prognosis of IE patients. This may be related to regional differences in studies.

**Conclusions**

Our study summarized the clinical and pathogenic characteristics of endocarditis patients in southwest China, and found that history of cardiac disease has an impact on the prognosis of patients.

**Abbreviations**

IE = Infective endocarditis  
NVE = Native valve endocarditis  
PVE = Prosthetic valve endocarditis  
ESC = The European Society of Cardiology  
CHD = Congenital heart disease  
RHD = Rheumatic heart disease  
CAD = Coronary artery disease  
TTE = Transthoracic heart color doppler ultrasound  
MRSA = Methicillin-resistant Staphylococcus aureus  
CNS = Coagulase negative staphylococcus  
MRCNS = Methicillin-resistant coagulase negative staphylococcus

**Declarations**

*Ethics approval and consent to participate* Ethical approval was given by Westchina Hospital of Sichuan University Biomedical Ethics Committee with the following approval number: 203(2015).

*Consent for publication* Not applicable
Availability of data and materials Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Competing interests the authors declare that they have no competing interests

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**Authors’ contributions**

Conception MK

design of the work MK YFW ZXC

the acquisition, analysis YLS YWW LZ

interpretation of data YFW JD YLY X

drafted the work or substantively revised it MK CH YM

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**Tables**
|                         | All IE patients | NVE patients | PVE patients | P value |
|-------------------------|-----------------|--------------|--------------|---------|
| age (year)              | 38.9            | 38.8         | 39.5         | NS      |
| male                    | 73/65.2         | 70/70.7      | 3/25         | <0.05   |
| Basic heart disease     |                 |              |              |         |
| CHD (%)                 | 32/28.6         | 29/29.3      | 3/25         | NS      |
| RHD (%)                 | 13/11.6         | 9/8.1        | 5/41.6       | <0.05   |
| CAD (%)                 | 2/1.8           | 2/2.2        | 0/0          | NS      |
| valvulopathy (%)        | 4/3.6           | 3/3.3        | 1/8.3        | NS      |
| other (%)               | 7/6.2           | 4/4.4        | 3/25         | NS      |
| No basic heart disease  | 60/48.2         | 54/54.4      | 61/54.5      | NS      |
| symptom                 |                 |              |              |         |
| fever (%)               | 98/87.5         | 87/87.9      | 11/91.7      | NS      |
| cardiac murmurs (%)     | 88/78.6         | 81/81.8      | 7/58.3       | NS      |
| algor (%)               | 46/41.1         | 40/40.4      | 6/50         | NS      |
| dyspnea (%)             | 44/39.3         | 40/40.4      | 4/33.3       | NS      |
| palpitation (%)         | 40/35.7         | 36/36.4      | 4/33.3       | NS      |
| Chest pain (%)          | 11/9.8          | 10/10.1      | 1/8.3        | NS      |
| Vegetation place        |                 |              |              |         |
| Left heart (%)          | 88/78.6         | 79/79.8      | 9/75         | NS      |
| mitral valve (%)        | 36/32.1         | 32/32.3      | 4/33.3       | NS      |
| aortic valve (%)        | 46/41.1         | 41/41.4      | 5/41.6       | NS      |
| mitral valve and aortic valve (%) | 5/4.5 | 5/5.5 | 0/0 | NS |
| Left atrial wall (%)    | 1/0.9           | 1/1          | 0/0          | NS      |
| Right heart (%)         | 18/16.1         | 18/18.2      | 0/0          | NS      |
| tricuspid valve (%)     | 12/10.7         | 12/12.1      | 0/0          | NS      |
| pulmonic valve (%)      | 6/5.4           | 6/6          | 0/0          | NS      |
| Other position (%)      | 3/2.7           |             |              |         |
| mesh vegetation (%)     | 2/1.8           | 0/0          | 2/16.6       | NS      |
| Descending aortic vegetations (%) | 1/0.9 | 1/1 | 0/0 | NS |
| no vegetations (%)      | 3/2.7           | 2/2.2        | 1/8.3        | NS      |
| Valve replacement before admission (%) | 10/8.9 | 0/0 | 10/83.3 | <0.05 |
| Laboratory findings     |                 |              |              |         |
| WBC increase (%)        | 66/58.9         | 58/58.6      | 8/66.7       | NS      |
| N% increase (%)         | 95/84.8         | 85/85.6      | 10/83.3      | NS      |
| PCT increase (%)        | 89/79.5         | 79/79.8      | 10/83.3      | NS      |
| ESR increase (%)        | 61/54.5         | 56/56.6      | 5/41.6       | NS      |
| CRP increase (%)        | 82/73.2         | 74/74.7      | 8/66.7       | NS      |
| Death                   | 36/32.4         | 30/30.3      | 6/50.0       | 0.331   |
Table 1 baseline data and laboratory findings of patients with IE

| Pathogen                        | All IE patients | NVE patients | PVE patients | P value |
|---------------------------------|----------------|--------------|--------------|---------|
| Gram-Positive Cocci%            | 96%86.5%       | 87%87.9%     | 9%75%        | NS      |
| streptococcus%                  | 66%59.5%       | 63%63.6%     | 3%25%        | <0.05   |
| streptococcus viridans%         | 23%20.7%       | 23%23.2%     | 0%0%         | NS      |
| Streptococcus anginosus%        | 13%11.7%       | 11%11.1%     | 2%16.6%      | NS      |
| Other Streptococcus %           | 30%27.0%       | 29%29.3%     | 1%8.3%       | <0.05   |
| staphylococcus%                 | 26%25.2%       | 22%22.2%     | 6%50%        | <0.05   |
| staphylococcus aureus%          | 20%18.0%       | 17%17.2%     | 3%25%        | NS      |
| CNS%                            | 8%7.2%         | 5%5.1%       | 3%25%        | <0.05   |
| enterococcus%                   | 2%1.8%         | 2%2.0%       | 0%0%         | NS      |
| Gram Negative Bacilli%          | 9%8.1%         | 8%8.1%       | 1%8.3%       | NS      |
| Escherichia coli%               | 5%4.5%         | 4%4.0%       | 1%8.3%       | NS      |
| other Gram Negative Bacilli%    | 4%3.6%         | 4%4.0%       | 0%0%         | NS      |
| Gram Positive Bacilli%          | 1%0.9%         | 1%1.0%       | 0%0%         | NS      |
| fungus%                         | 5%4.5%         | 3%3.0%       | 2%16.6%      | <0.05   |
| Total                           | 111            | 99           | 12           |         |

Table 2 distribution of pathogen in patients with IE
| Antibiotic         | staphylococcus aureus | CNS                  |
|-------------------|-----------------------|----------------------|
|                   | number | resistance rate [%] | number | resistance rate [%] |
| Penicillin G      | 19     | 100                | 8      | 100                |
| Oxacillin         | 19     | 26.3               | 8      | 75                 |
| Erythrocin        | 19     | 52.6               | 8      | 25                 |
| Clindamycin       | 18     | 33.3               | 8      | 12.5               |
| Ciprofloxacin     | 19     | 10.5               | 8      | 0                  |
| Levofloxacin      | 19     | 0                  | 8      | 0                  |
| Vancomycin        | 19     | 0                  | 9      | 0                  |
| Linezolid         | 19     | 0                  | 9      | 0                  |
| Tetracycline      | 19     | 15.8               | 9      | 22.2               |

Table 3  sensitivity of staphylococcus in patients with IE

| Antibiotic         | streptococcus viridans | streptococcus anginosus |
|-------------------|------------------------|-------------------------|
|                   | number | resistance rate [%] | number | resistance rate [%] |
| Penicillin G      | 10     | 0                    | 8      | 12.5               |
| Cefotaxime        | 11     | 0                    | 4      | 25                 |
| Cefepime          | 11     | 0                    | 3      | 0                  |
| Erythrocin        | 19     | 47.4                 | 12     | 83.3               |
| Azithromycin      | 21     | 40                   | 11     | 63.6               |
| Levofloxacin      | 10     | 0                    | 6      | 16.7               |
| Clindamycin       | 10     | 40                   | 5      | 100                |
| Tetracycline      | 18     | 38.9                 | 9      | 66.7               |
| Chloramphenicol   | 17     | 0                    | 10     | 0                  |
| Vancomycin        | 23     | 0                    | 13     | 0                  |

Table 4 sensitivity of staphylococcal in patients with IE
|                          | P   | OR  | 95% CI of OR |
|--------------------------|-----|-----|--------------|
| gender                   | 0.85| 1.107| 0.39-3.18    |
| Age ≥ 60(years)          | 0.46| 0.569| 0.13-2.54    |
| Basic heart disease      | 0.01| 0.239| 0.08-0.68    |
| PVE                      | 0.84| 1.163| 0.28-4.86    |
| Vegetation place         | 0.68|--|--            |
| WBC increase             | 0.19| 2.375| 0.65-8.71    |
| N% increase              | 0.39| 0.498| 0.10-2.48    |
| PCT increase             | 0.35| 1.771| 0.54-5.85    |
| CRP increase             | 0.42| 0.662| 0.24-1.79    |
| Staphylococcus aureus or negative bacilli | 0.87| 1.090| 0.38-3.14 |

Table 5 Death risk factor analysis in IE patients

**Figures**

![Bar chart showing case distribution by valve and regurgitation severity](chart.png)

**Figure 1**

Blood reflux of Infective endocarditis patients.