

Full Length Research Paper

# Clinical features, epidemiology and outcomes of infective endocarditis at a general hospital in China: A 10-year survey

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This study retrospectively investigated the epidemiology, treatment and outcome of infective endocarditis (IE) in People's Liberation Army (PLA) General Hospital from 1997-2007. Totally, 65 cases were included. The results showed that bacteria were isolated from 63.08% of the IE cases. *Staphylococcus* was the main pathogen causing IE (43.9%), followed by *Streptococcus* (41.5%). Surgical treatment was performed for 81.5% (53/65) of the IE patients. The most common surgery was aortic valve replacement conducted for 58.18% of the IE patients. Six patients (9.23%) died during hospitalization. Antimicrobial agents including penicillin, vancomycin and quinolones were most frequently utilized. We concluded that early diagnosis, timely surgery and appropriate utilization of antibiotics can improve the prognosis of IE patients.

**Key words:** Infective endocarditis (IE), clinical features, epidemiology.

## INTRODUCTION

Infective endocarditis (IE) is an infectious disease caused by invasion of pathogens including bacteria, fungi and rickettsia into the heart valves, endocardium or intima of the surrounding of the aorta via blood (Fitzsimmons et al., 2010). With the development of invasive cardiovascular therapy, the morbidity of IE has been increasing recently (Hill et al., 2007). Antibiotic resistance caused by wide application of antibiotics brought additional difficulties for medical treatment. Moreover, the clinical signs and the pathogens showed some difference because of region and time (Heiro et al., 2006). Therefore, IE remains to be a common severe clinical condition associated with high hospital mortality (Baddour et al., 2005).

We retrospectively analyzed clinical and microbiology features, epidemiology, therapeutic method, antibiotic use and prognosis of IE patients admitted to the People's Liberation Army (PLA) General Hospital, which is a large hospital with 4400-beds. Compared our findings with

those of other countries and regions published, this study provides precise data of IE in east Asia developing countries.

## MATERIALS AND METHODS

Data were collected on all patients with definite IE according to the Duke clinical criteria (Li et al., 2000), who were hospitalized in PLA General Hospital. All patients who were diagnosed with IE from January 1997 to March 2007 were analyzed retrospectively by extracting data from their medical records, including age, sex, underlying heart disease, complications, microbiological findings, treatment (including antibiotic use and surgery) and outcome.

All bacterial cultures used to evaluate IE were obtained by the Microbiology Laboratory of PLA General Hospital and processed by standard methods to identify bacterial and fungal species and antimicrobial susceptibility profiles.

## RESULTS

### General characteristics of included infective endocarditis (IE) cases

A total of 65 IE cases (male, 44; female, 21) admitted to

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**Table 1.** Cardiac disease in IE patients.

<b>Cardiac disease</b>	<b>n</b>	<b>Constituent ratio (%)</b>
Congenital cardiopathy	10	15.38
Rheumatic heart	9	13.85
Mitral incompetence	32	49.23
Aortic incompetence	21	32.31
Mitral and aortic incompetence	16	24.62
Tricuspid incompetence	2	3.08
Interventricular septal defect	3	4.62
Atrial septal defect	2	3.08
Aortic valve ephyma formation	15	23.08

**Table 2.** Functional grading of cardiac disease in f IE patients.

<b>Cardiac functional grading (NYHA)</b>	<b>n</b>	<b>Constituent ratio (%)</b>
Heart function IV	5	7.69
Heart function III	24	36.9
Heart function II	8	12.3
Heart function I	28	43.1

PLA General Hospital from January 1997 to March 2007 were included in this study. The age of these patients ranged from 12-72 years old, with an average of  $41.5 \pm 13.4$  years old. The hospitalized time ranged from 3-79 days with an average of  $30.8 \pm 15.9$  days. Among these cases, 9 patients had a history of allergy to sulfonamides, penicillin or streptomycin.

#### **The basic cardiac disease and heart function in infective endocarditis (IE) patients**

Among the 65 IE cases, only 3 patients (4.62%) had no basic cardiac disease. Four (4) cases (6.15%) had prosthetic valve (PVE). Mitral and aortic valve incompetence accounted for the highest percentage of basic cardiac disease. The detailed distribution of cardiac disease and heart function are shown in Tables 1 and 2.

#### **Biochemical analysis of the blood samples from infective endocarditis (IE) patients**

Among 65 IE cases, 23 patients (35.38%) had abnormal biochemical test results. Ten (10) cases (15.38%) had high level of alanine, 13 patients (20%) had high level of aspartate, 1 patient (1.54%) had high level of inosine, 2 cases (3.08%) had low level of inosine, 5 cases (7.69%) had high level of urea, 2 cases (3.08%) had low level of urea and 5 cases (7.69%) had high level of uric acid in the blood samples.

#### **Bacterial culture test**

Bacterial culture was performed for these 65 IE cases, of which 41 cases were positive (38 cases had blood bacterial culture test, 2 cases had valve tissue culture test and 1 case had drainage of fluid culture test). The positive rate of bacterial culture test was 63.08% (41/68). The major pathogen of IE patients was *Staphylococci* species followed by *Streptococcus*. Detailed results on the bacterial culture were shown in Table 3.

#### **Antimicrobial susceptibility**

Antimicrobial susceptibility test was performed for the bacteria isolated from 29 IE patients. The results of antimicrobial susceptibility of *Staphylococcus* and *Streptococcus* were shown in Table 4. Most *Staphylococcus* strains showed penicillins and cephalosporins resistance, while susceptible to quinolones and glycopeptides. *Streptococcus* showed highly resistant to macrolides and sensitivity to cephalosporins and glycopeptides.

#### **Surgery therapy for infective endocarditis (IE) patients**

Surgeries were conducted for 81.5% (53/65) of the IE patients. The most common surgery was aortic valve replacement accounting for 58.18% (32/65), followed by

**Table 3.** Results of bacterial culture tests for 41 IE patients.

<b>Microorganism</b>	<b>n</b>	<b>Constituent ratio (%)</b>
Staphylococci species	19	46.3
Coagulase negative staphylococcus	7	17.1
<i>Staphylococcus aureus</i>	6	14.6
<i>Staphylococcus epidermidis</i>	4	9.76
Other Staphylococci	2	4.88
<i>Streptococcus</i> species	17	41.5
<i>Streptococcus viridans</i>	12	29.3
<i>Streptococcus sanguis</i>	2	4.88
Microaerophilic	1	2.44
A streptococcus	1	2.44
D streptococcus	1	2.44
<i>Bacillus</i> species	13	31.72
<i>Pseudomonas</i>	3	7.32
G <sup>+</sup> bacillus	3	7.32
<i>Chryseobacterium indologenes</i>	1	2.44
<i>Bacillus coli</i>	1	2.44
<i>Bacterium burgeri</i>	1	2.44
<i>Citrobacter freundii</i>	1	2.44
<i>Bacillus subtilis</i>	1	2.44
<i>Chryseobacterium meningosepticum</i>	1	2.44
Acinetobacter	1	2.44
<i>Micrococcus</i>	6	14.6
<i>Enterococcus faecalis</i>	3	7.32
<i>Klebsiella</i>	2	4.88
<i>Neisseriaceac</i>	1	2.44
<i>Pantoea</i> spp	1	2.44
<i>Blastomyces albicans</i>	2	4.88
<i>Aspergillus</i>	1	2.44

**Table 4.** *In vitro* activity of antimicrobials against top 4 kinds of pathogens.

<b>Antibiotic</b>	<b><i>Staphylococcus aureus</i> (n=4)</b>	<b><i>Staphylococcus epidermidis</i> (n=3)</b>	<b>Coagulase negative <i>Staphylococcus</i> (n=6)</b>	<b><i>Streptococcus viridans</i> (n=5)</b>
Penicilin	2	3	5	1
Oxacillin	1	3	5	1
Piperacillin- tazobactam	-	-	-	-
Piperacillin	-	-	-	-
Amoxicillin-clavulanate	-	0	-	-
Ampicillin-sulbactam	1	1	4	0
Ampicillin	1	1	5	0
Cefazolin	1	-	5	1
Cefuroxime	-	-	-	-
Cefoxitin	1	-	5	0
Ceftazidime	-	-	-	-
Ceftriaxone	-	-	-	0
Cefoperazone	-	-	-	-
Cefoperazone-sulbactam	-	0	-	-
Cefotaxime	-	-	-	-
Cefditoren	0	-	4	-

**Table 4.** Contd

Cefepime	-	0	-	0
Imipenem	-	-	-	-
Meropenem	-	-	-	-
Aztreonam	-	-	-	-
Gentamicin	0	2	0	1
Amikacin	0	0	0	1
Chloromycetin	0	0	-	0
Minocycline	0	2	0	0
Tetracycline	1	1	3	2
Erythrocin	2	3	5	4
Azithromycin	-	1	-	2
Vancomycin	0	0	0	0
Teicoplanin	0	0	0	0
Clindamycin	1	1	4	2
Ciprofloxacin	0	0	1	0
Lomefloxacin	0	0	2	1
Levofloxacin	0	0	1	0
Gatifloxacin	0	0	0	0
Furantoin	0	-	-	-
Bactrim	1	1	3	-
Trimethoprim	-	2	-	-

**Table 5.** Surgeries conducted in 53 IE patients.

<b>Surgery name</b>	<b>n</b>	<b>Constituent ratio (%)</b>
Replacement of mitral valve and aortic valve	12	21.82
Aortic valve replacement	32	58.18
Replacement of mitral valve	29	52.73
Mitral valve shaping	2	3.64
Tricuspid valvuloplasty	3	5.45
Repair of ventricular septal defect	2	3.64
Repair of aortic root	2	3.64
Repair of aortic sinus aneurysm	2	3.64
Ecphyoma cleaning	4	7.27
Take out of ventricular lead	1	1.82

replacement of mitral valve accounting for 52.73% (29/65). Detailed information for the surgeries conducted for the IE patients was shown in Table 5.

#### **Antimicrobial therapy for infective endocarditis (IE) patients**

The antimicrobial agents with top 10 frequency of use were listed in Table 6. Benzylpenicillin sodium was the most applied antibiotics, which used in 51 of 65 included IE patients. Vancomycin was also used frequently, totally 18 patients used. Fluconazol was the only antifungal

agents listed in top 10.

#### **Outcome of infective endocarditis (IE) patients**

A total of 58 (89.23%) IE patients were cured or improved after active treatment. One (1) patient (1.5%) was transferred to other hospitals due to drug eruption with unknown reasons. Six (6) patients (9.23%) died. Causes of death included multiple organ failure in 1 case, respiratory and circulatory failure in 2 cases, circulatory failure in 1 case, heart failure in 1 case and hemorrhagic shock complicated with corpus luteum rupture in 1 case.

**Table 6.** Top 10 antimicrobial agents in terms of use frequency sequence.

Sequence	Antimicrobial agent	n	Constituent ratio (%)
1	Benzylpenicillin sodium	51	76.12
2	Cefazolin sodium	23	34.33
3	Vancomycin	18	26.87
4	Fluconazol	11	16.42
5	Ciprofloxacin	10	14.93
6	Cefuroxime	9	13.43
7	Piperacillin	7	10.45
8	Etimicin sulphuric acid	7	10.45
9	Cefoperazone-tazobactam	6	8.955
10	Oxacillin	5	7.463

## DISCUSSION

The average age of patients with IE in this study was 41.5 years, which is lower than the average age of IE patients in 25 European countries (Tornos et al., 2005). The ratio between male and female IE patients in this study was 2.1:1, which was similar to previous report in Spain (Lopez-Dupla et al., 2006).

The majority of IE occurred due to organic heart disease. In this study, 95.38% of IE patients had basic cardiac diseases including mitral valve and (or) aortic valve insufficiency and age-related degenerative valvular disease. In addition, infection after cardiac surgery or interventional diagnostic and therapeutic procedures has become an important cause of IE. Our results showed that IE caused by non-organic heart disease accounted for 4.62%, which is consistent with other reports showing that IE occurred in patients without organic heart disease accounted for 2-10% (Mylonakis and Calderwood, 2001). Previous epidemiological studies indicate that PVE IE accounted for 10-20% of IE in developed countries (Alexiou et al., 2000). In this study, we showed that PVE only accounted for 6.15% (4/65) of IE cases, which is lower than that in other countries.

Positive bacterial culture is an important basis for diagnosis of IE. Improving the positive rate of blood culture and selection of effective antibiotics can increase the cure rate of IE. Before the results of blood culture are obtained, antibiotics are normally selected according to the clinical prediction of the pathogen that may exist. Once the blood culture results are available, antibiotics are adjusted according to the drug susceptibility tests. In this study, the positive culture was observed in 63.08% of the IE patients, which was lower than that in other countries (Chu et al., 2004; Nashmi and Memish, 2007). This may be associated with two main reasons. Firstly, in China, blood samples were collected normally after antibiotics were used. Secondly, the amount of blood samples is not sufficient and there is lack of continuous sample collection or insufficient times of sample collection, because discharge of bacteria is intermittent in

IE patients. So collection of blood samples during the non-bacterial period causes false negatives. Our results also showed that *Staphylococcus* is the main pathogen of IE accounting for 43.9%, followed by *Streptococcus* (41.5%), which is consistent with previous report (Morris et al., 2005).

Penicillin was the most use antibiotics in our study. It seems contradictory to the result of antibiotic sensitive test, which showed most pathogens tested resisted to penicillin. This is because antibiotics were usually used before blood cultures results were got. So penicillin, with less adverse drug reaction as long as the patient is not allergic, was a safe choice. All 65 included patients received at least two intravenous antibiotics. The change of antimicrobial agents was made on basis on culture and antibiotic sensitive test. For culture-negative endocarditis, choice of antibiotics was based on experience.

In this study, 53 IE patients received surgical treatment and 6 patients died with a mortality rate of 9.23%. This mortality rate is lower than that reported in European countries with a 12.6% mortality rate (Tornos et al., 2005). This may due to the high rate of surgery in our hospital, which reached 81.5% in this study. The recent International Endocarditis-Pro prospective Cohort Study reported that surgery was associated with a 39% decrease in the risk of death in comparison to medical treatment (Murdoch et al., 2009).

## Conclusion

Our study confirms that pathogens of IEs in our hospital is similar with previous reports in other countries and region, staphylococcal species have exceeded streptococcal organisms in causing endocarditis. Early diagnosis, timely surgery and appropriate medical treatment can improve the prognosis of IE patients. To increase the positive rate of bacterial culture, we recom-mended those patients who had already used antibiotics; test should be performed 1 week after termination of antibiotics utilization. If blood culture test must be

conducted immediately after antibiotics are used, the blood samples should be diluted for 20 times, which can reduce the concentration of antibiotics and minimize the antimicrobial effect.

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