Infective Endocarditis in Pediatric Patients: An Eighteen-Year Experience from King Chulalongkorn Memorial Hospital

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Objectives: *To review the clinical features and outcome of the pediatric patients diagnosed with infective endocarditis (IE) at King Chulalongkorn Memorial Hospital over an 18-year period.*
Material and Method: *From January 1987 to December 2004, 57 pediatric patients; 28 females and 29males, age ranged from 2 months to 15 years, mean of 8.64 ± 3.82 years, classified as "definite" IE according to the Duke criteria were reviewed.*
Results: *Of the 57 patients, 42 patients (74%) had underlying congenital heart diseases, 7 patients (12%) had underlying rheumatic heart disease, 8 patients (14%) had previously normal heart. Nine patients had history of previously palliative or corrective surgery. Blood cultures were positive in 26 patients (46%). Streptococci and staphylococci were the most commonly isolated organisms. Two-dimensional echocardiography demonstrated vegetations in 56 patients (98%). The location of the vegetations was in the right heart in30 patients (54%) and in the left heart in 26 patients (46%). Complications occurred in 28 patients (49%). Common complications included congestive heart failure, cerebral emboli, septic shock, and mycotic aneurysm. The overall mortality was 11% (6 patients). By statistical analysis, vegetations in the left heart had a higher incidence of complication than that in the right heart. The vegetation size of ≥ 10 mm had a significant higher incidence of embolic events.*
Conclusion: *The clinical features and outcomes of the present study have a similar pattern as the earlier studies. The rates of complications and mortality are still high.*

Keywords: *Infective endocarditis, Pediatric, Complication*

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Infective endocarditis (IE) is one of the most dreadful infectious diseases. Its importance lies in the significant morbidity and mortality associated with the disease, the need for prolonged parenteral antibiotic treatment and the potential complications from embolic and immunological phenomenon. An advance in non-invasive techniques such as 2-dimensional echocardiography has enhanced the ability to diagnose the disease. The authors' previous study revealed life-threatening complications which are still common even with highly effective antibiotics and early diagnosis by 2-dimensional echocardiography[1]. In the present study the authors reviewed the clinical features and outcomes of the presented patients over an 18-year period.

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Material and Method

The authors retrospectively reviewed the medical records of the patients who were admitted to the Department of Pediatrics, King Chulalongkorn Memorial Hospital, with the diagnosis of IE, over an 18-year period from January 1987 to December 2004. The cases of IE were identified by conducting a search of data recorded in the Medical Record and Statistic Department using International Classification of Diseases 9th and 10th revision (ICD-9 and ICD-10) labeled as "421.0 and I33.0" for "acute and subacute

infective endocarditis" before and after the year 1993, respectively. In addition, the echocardiography log book maintained by the Pediatric Echocardiography Laboratory was cross-checked for cases. All the reviewed cases were verified the diagnosis of IE by using Duke criteria and were classified as "definite" IE by clinical criteria –the presence of two major criteria or one major and three minor criteria or five minor criteria[2]. There were 72 cases identified. After a final review, 57 cases were included in the present study. Twenty six cases satisfied both major criteria while 31 cases had one major and two minor criteria.

Data were expressed as mean (SD) with range or the number and percentage. Discrete variables were analyzed by chi square test or Fisher's exact test, depending on cell size. Differences were considered statistically significant when $p < 0.05$.

Results

Of the 57 patients, 29 were male and 28 were female. The mean age was 8.64 ± 3.82 years, ranged from 2 months to 15 years. Three patients were under 2 years old, and two third of the patients were over 5 years old.

Congenital heart disease was the most common underlying cardiac condition in the present study (42 patients, 73.7%), with more frequent in non-cyanotic than cyanotic condition. Ventricular septal defect and tetralogy of Fallot were the most frequent underlying congenital anomalies in non-cyanotic and cyanotic condition, respectively. Seven patients (12.3%) had underlying rheumatic heart diseases (all were mitral regurgitation). Eight patients (14.0%) had no previous heart diseases; - one (15 years old) was intravenous drug abuse and had HIV positive. Table 1 summarized the underlying heart diseases in the present study. Nine patients (15.8%) had previous history of cardiac surgery; five had palliative shunt surgery while four had corrective surgery with residual lesions (Table 2).

Blood cultures were positive in 26 patients (45.6%). Streptococci were the most commonly isolated organisms in the patients with underlying heart lesions while *Staphylococcus aureus* was the most common in the previously normal heart patients. The distribution of the organisms is shown in Table 3.

Two-dimensional echocardiography was studied in all patients and revealed vegetations in 56 patients. The sites of the vegetations were summarized in Table 4. Thirty patients had vegetation in the right heart while the other 26 in the left heart. The 2-dimensional echocardiography demonstrated 1 vegetation

Table 1. Underlying heart disease in 57 patients with IE

Heart disease	Number of patients (%)
1. Congenital heart disease	42 (73.7)
Non-cyanotic	
- Ventricular septal defect	18
- Atrioventricular canal defect	5
- Patent ductus arteriosus	2
- Aortic stenosis	2
- Mitral valve cleft	2
Cyanotic	
- Tetralogy of Fallot	8
- Transposition of great arteries[a]	2
- Double outlet right ventricle[b]	2
- Truncus arteriosus[c]	1
2. Rheumatic heart disease	7 (12.3)
3. No previous heart disease	8 (14.0)

[a] with ventricular septal defect and pulmonary stenosis
[b] with pulmonary stenosis
[c] post Rastelli operation

Table 2. Previous history of cardiac surgery in 9 patients

Cardiac surgery	Number of patients
Blalock-Taussig shunt	
- Tetralogy of Fallot	3
- Transposition of great arteries[a]	1
Central shunt	
- Double outlet right ventricle[b]	1
VSD closure	2
Mitral valvular annuloplasty	1
Rastelli operation for truncus arteriosus	1

[a] with ventricular septal defect and pulmonary stenosis
[b] with pulmonary stenosis

Table 3. Organisms isolated from blood cultures

Organism	Number of patients (%)
Streptococci	13 (50.0)
Viridans group streptococci	5
Alpha hemolytic streptococci	5
Streptococci group D	2
Non-hemolytic streptococci	1
Staphylococcus aureus	10 (38.5)
Gram-negative organisms	3 (11.5)
Enterobacter	1
Gram-negative bacilli	1
Pseudomonas species	1
Subtotal	26 (45.6)
No growth on culture	31 (54.4)
Total	57 (100)

in 45 patients, 2 vegetations in 8 patients and more than 2 vegetations in 3 patients. The sizes of the vegetation were able to figure in 43 patients and varied from 5 to 38 mm.

Twenty eight patients had major complications (Table 5). Congestive heart failure was the most common complication. The others included cerebral emboli, septic shock, septic emboli, leg emboli, and mycotic aneurysm.

The overall mortality in the present study was 10.5% (6 patients). Three patients had vegetations in the left heart; - one had cerebral emboli and severe aortic regurgitation and died from intractable heart failure and cardiogenic shock, the other 2 (one had ruptured chordae tendinae) died from intractable heart failure and septic shock. Another two patients had vegetations in the right heart and both died from septic shock. The remaining 1 patient had vegetation in the right subclavian artery and Blalock-Taussig shunt and had a large pseudoaneurysm secondary to ruptured mycotic aneurysm of the right subclavian artery. He underwent resection of pseudoaneurysm and died from massive intra-operative bleeding.

Table 4. Sites of vegetation detected by transthoracic 2-D echocardiography

Site	Number of patients
Mitral valve	20
Right ventricular outflow tract	19
Pulmonary artery	7
Tricuspid valve	7
Aortic valve	6
Subclavian artery and Blalock-Taussig shunt	1

Table 5. Complications of IE in 28 patients

Complications	Number of patients
Congestive heart failure	15
Cerebral emboli	5
Septic shock	4
Glomerulonephritis	3
Brain abscess	2
Osteomyelitis	2
Leg emboli	2
Pericardial effusion	2
Ruptured chordae tendinae	1
Mycotic aneurysm	(4)
Abdominal aorta	1
Pulmonary artery	1
Cerebral artery	1
Subclavian artery	1

The characters of vegetations and complications were statistically analyzed. Vegetation in the left heart had a statistically significant higher rate of complication than that in the right heart (20/26 vs. 15/30, $p = 0.04$). Vegetation size of ≥ 10 mm had a statistically significant incidence of vegetation emboli (1/10 vs. 18/33, $p = 0.01$). There was no statistically significant difference in the number of vegetations as compared to the incidence of complication ($p = 0.14$).

Discussion

In the earlier studies[3-6], congenital heart diseases remain the leading risk factor for IE in the pediatric patients, (about 58-88%). While rheumatic heart disease was found less (0-5%) in the studies from United States and France[3-6], it became more (up to 53%) in the countries in Asia such as Lebanon and Pakistan[7,8]. In the present series, the majority (74%) had congenital heart diseases and 12% had rheumatic heart disease. Rheumatic heart disease is still our problem in acquired heart disease, but its prevalence declined during the past decade. Ventricular septal defect and tetralogy of Fallot were the most common non-cyanotic and cyanotic congenital heart diseases in the present study, which is similar to some other series[8-10].

In the present study only 46% of the patients had a positive blood culture. With the clinical data, 2-dimensional echocardiographic finding and using the Duke criteria[2], the present study included only the patient classified as "definite" IE. Streptococci and staphylococci were the common isolated organisms in the present study, which is similar to the previous reports[6-11].

In children with congenital heart disease, IE was reported to be more frequent in the right heart than left heart[12]. But in children with normal heart, the site of vegetation was usually at the mitral and aortic valve, mostly associated with Staphylococcal aureus bacteremia[13-14]. In the present series, most of the patients with left to right shunt had vegetations in the right heart. All the patients with normal heart and associated with Staphylococcal aureus bacteremia had vegetation at mitral valve; except one with history of intravenous drug abuse and positive HIV who had vegetation at the tricuspid valve.

Factors that predispose children with IE to the development of complications include type of organism, location and size of vegetation, important comorbid cardiac conditions, and occurrence of

endocarditis in an otherwise normal heart, particularly in children under 2 years of age[13]. Among the more frequent complications is congestive heart failure, which may be caused by abrupt structural change and valvular regurgitation. Embolic complications may arise in any patient with IE but particularly in those with larger vegetations. Even in the absence of prior embolization, vegetations > 10 mm seem to have high predictive validity for embolic events[15]. In the present series, congestive heart failure (26%) and embolization (12%) were the common complications. All of the presented 5 cases, who had cerebral emboli, had neurological sequels and one case died from neurological and cardiac complications. Statistical analysis in our series showed that the predisposing factors to development of embolization were the vegetation size of $\geq$ 10 mm and the vegetation in the left heart. Mycotic aneurysms are another complication of endocarditis and can occur in any systemic artery. In the present study these were 4 patients with mycotic aneurysm which involved in different sites and developed serious complications. The patient with abdominal aortic aneurysm also had leg emboli which required amputation, and underwent aneurysmal resection later. The one with pulmonary artery aneurysm also had associated patent ductus arteriosus, developed 2 episodes of massive hemoptysis[16]. The one with cerebral artery aneurysm had right hemiparesis from ruptured aneurysm. The one who had a large intrathoracic pseudoaneurysm from ruptured right subclavian artery aneurysm, died from intraoperative bleeding. The overall rate of complication and mortality in the present study were still high but comparable to the previous studies[1,3,5,6].

Conclusion

The clinical features and outcomes of the present study have a similar pattern as the earlier studies. Despite recent advances in diagnosis and treatment, the mortality and the rate of complications, such as congestive heart failure and systemic embolization, are still high. Early diagnosis for early treatment of IE remains challenging and often depends on a high index of clinical suspicion. Bacterial endocarditis prophylaxis should be emphasized, particularly in patients with underlying congenital heart disease and rheumatic heart diseases.

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เยื่อบุหัวใจอักเสบจากการติดเชื้อในเด็ก: ประสบการณ์ 18 ปีในโรงพยาบาลจุฬาลงกรณ์

พรเทพ เลิศทรัพย์เจริญ, อภิชัย คงพัฒนะโยธิน , ไพโรจน์ โชติวิทยธารากร, จุล ทิสยากร, โชติมา ปัทมานันท์, วิโรจน์ สืบหลินวงศ์

วัตถุประสงค์: *เพื่อศึกษาลักษณะทางคลินิกและผลการรักษาในเด็กที่ป่วยเป็นโรคเยื่อหุ้มหัวใจอักเสบจากการติดเชื้อในโรงพยาบาลจุฬาลงกรณ์*

ระเบียบวิธีการวิจัย: *ได้ทำการศึกษาย้อนหลังโดยรวบรวมข้อมูลในผู้ป่วยเด็กที่เป็นโรคเยื่อหุ้มหัวใจอักเสบจากการติดเชื้อ ระหว่างเดือนมกราคม พ.ศ. 2530 ถึง เดือนธันวาคม พ.ศ. 2547 จำนวน 57 ราย เป็นหญิง 28 ราย และชาย 29 ราย อายุตั้งแต่ 2 เดือน ถึง 15 ปี อายุเฉลี่ย 8.64 + 3.82 ปี*

ผลการวิจัย: *ผู้ป่วยที่ทำการศึกษาจำนวน 57 ราย เป็นโรคหัวใจแต่กำเนิด 42 ราย (74%) โรคหัวใจรูห์มาติก 7 ราย (12%) และไม่มีโรคหัวใจมาก่อน 8 ราย (14%) ผู้ป่วยจำนวน 9 รายมีประวัติได้รับการผ่าตัดหัวใจมาก่อน ผลการเพาะเชื้อในเลือดพบเชื้อจำนวน 26 ราย (46%) เชื้อส่วนใหญ่ที่พบคือเชื้อสเตร็ปโตคอคคัส และสแตฟฟิลโลคอคคัส ผลการตรวจคลื่นเสียงสะท้อนหัวใจพบก้อน vegetation ในผู้ป่วยจำนวน 56 ราย (98%) โดยพบในหัวใจห้องขวา 30 ราย (54%) และในหัวใจห้องซ้าย 26 ราย (46%) พบภาวะแทรกซ้อนในผู้ป่วยจำนวน 28 ราย (49%) ได้แก่ภาวะหัวใจล้มเหลว, cerebral emboli, septic shock และ mycotic aneurysm มีผู้ป่วยเสียชีวิตจำนวน 6 ราย (11%) จากการวิเคราะห์ทางสถิติพบว่าผู้ป่วยที่มีก้อน vegetation ในหัวใจห้องซ้ายมีโอกาสเกิดภาวะแทรกซ้อนได้มากกว่าผู้ป่วยที่มีก้อนในหัวใจห้องขวา และพบอุบัติการณ์ของ embolization เพิ่มขึ้นอย่างมีนัยสำคัญในผู้ป่วยที่มีก้อน vegetation ขนาด $\geq$ 10 มม.*

สรุป: *การศึกษานี้พบลักษณะทางคลินิก และผลการรักษาใกล้เคียงกับการศึกษาที่ผ่านมา อัตราตายและอัตราการเกิดภาวะแทรกซ้อนในโรคนี้ยังสูงอยู่มาก*