Infective Endocarditis Pattern Among Pediatric Patients

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Abstract

Background: The second half of the 20th century has witnessed major changes in the epidemiology, bacteriology and clinical presentation of infective endocarditis (IE).

Aim of Work: To evaluate local patient characteristics, risk factors, clinical sequelae, microbiology, morbidity and mortality in pediatric patients with IE and to explore the use of trans-thoracic echocardiography (TTE) in the diagnosis of this illness.

Methods: Thirty patients with probable or definite diagnosis of IE were prospectively enrolled in this study. Infective endocarditis was diagnosed according to the Duke criteria. Patients with rejected diagnosis of IE were excluded. Underlying risk factors were sought. Initial evaluation and in-hospital follow-up included the documentation of vascular or immunological phenomena, morbidity and mortality.

Results: Of the 30 patients included, 24 cases (80%) had definite IE and 6 cases (20%) had possible IE. The studied patients had a mean age of 7.2 ± 3.9 years with a male predominance (1.5:1). Rheumatic heart disease was present in 14 (46.7%), two of them had prosthetic valves (PVE). Fifteen had congenital heart disease (50%), one patient (3.3%) with no underlying cardiac lesion. Congestive heart failure and fever were detected in 100%, Glomerulonephritis without renal failure was observed in 2 patients (6.7%), embolic events in 8 cases (26.7%). Blood culture was positive in 27 cases (90%), with staph. aureus the most common isolates. TTE was definitive for vegetation in 25 cases (83.3%), possible in 4 cases including the two cases of PV and negative in one case. TEE required for the 2 PVE cases. The in-hospital mortality rate (medical and surgical) was 13.3%.

Conclusion: The clinical features of the present study almost have a similar pattern as the earlier studies. Increasing staph. aureus IE. The in-hospital morbidity and mortality are high. TTE remains the most appropriate first-line imaging investigation in the paediatric age group. TEE is indicated when the clinical suspicion of endocarditis is high and the TTE study is inconclusive.

Key Words: Infective endocarditis – RHD – Prosthetic valve endocarditis.

Introduction

INFECTIVE endocarditis (IE), as defined by the European Society of Cardiology [1] is an endovascular microbial infection of cardiovascular structures. Its incidence is estimated at between 1.9 and 6.2 infections per 100 000 general population [2,3]. The second half of the 20th century has witnessed major changes in the epidemiology, bacteriology and clinical presentation of infective endocarditis [2] as well as major. Advances in the diagnosis and management of this classical disease [4].

The changes observed in the patient profile and clinical presentation of infective endocarditis in affluent societies [5,4] as well as a definite decline in 'culture-negative' endocarditis [2,4,6] have been highlighted extensively. Despite knowledge of these changes, and considerable improvements in diagnostic and therapeutic strategies, IE is still a severe disease. The high morbidity and mortality rate of IE is the consequences of both the destructive valvular lesions causing valve regurgitation and heart failure, and the valvular vegetation with their high embolic potential [7]. Echocardiography is often requested in patients with fever who have a low probability of endocarditis, and is also requested in patients in whom the diagnosis is virtually certain, however, echocardiography has some limitations [8].

Aim of work:

This study aimed first at evaluation of paediatric patients with IE as regards the clinical characteristics, causative organisms, outcome of management in terms of mortality or symptomatic improvement in patients treated medically and/or surgically, secondly at exploration of the use of trans-thoracic (TTE) echocardiography in the diagnosis of this illness.

Patients and Methods

Among the paediatric patients who were referred to the Echo-laboratory of the New Children Hospital of Cairo university because of presumptive diagnosis of IE, during the period from September
2006 to September 2008, thirty patients with probable or definite diagnosis of IE were included in this study. Infective endocarditis was diagnosed according to the Duke criteria [9]. Patients with rejected diagnosis of IE were excluded.

Patients evaluation:

All patients were examined on the day of referral and followed up thereafter throughout their hospital stay period. Specific attention was paid to the potential risk factors e.g. history of previous rheumatic fever (RF) or rheumatic heart disease (RHD), Congenital heart disease (CHD), cardiac surgery or catheterization. The presence or absence of any vascular or immunological phenomena (as defined by the Duke criteria) [9] were sought and documented. Results of the laboratory investigations that are routinely performed for such cases in our hospital were also documented namely complete blood picture (CBC), Sedimentation rate (ESR), C-reactive protein (CRP), urine analysis and blood culture. Two separate blood cultures taken from different sites 12-24 hours apart were performed for all patients. Any exposure to oral or intravenous antibiotics during the three days prior to culture sampling was documented.

All patients were subjected to TTE using 5500 Sonos Hb machine (assessment was performed using 4 and 8 MHz transducers). Parasternal long and short-axis and suprasternal windows, as well as apical four- and two-chamber views, were used to obtain two-dimensional evaluations, M–mode dimensions and Doppler studies. Vegetation was defined according to the Duke criteria [9]. Transoesophageal echo cardiography (TEE) was performed in two cases (with prosthetic valves) where TTE was suboptimal.

Primary evaluation was followed by secondary evaluation within 72 hours if the diagnosis of IE was not confirmed or rejected. Echocardiographic examination was repeated 3-8 weeks after starting antibiotic treatment and at the end of the in-hospital follow-up period.

Patients management:

All patients were managed according to published guidelines [1]. Cultures and antimicrobial susceptibility testing guided the choice of antibiotics, whereas empirical therapy was given to culture-negative cases. Paediatric doses of antimicrobials were calculated. Antibiotics were administered intravenously for the appropriate duration with a minimum of four weeks. Patients were discharged on high doses of an appropriate oral antibiotic, usually amoxicillin.

In-hospital follow-up:

All patients were followed up regularly while hospitalized. Embolic and immunological sequelae were actively sought and further diagnostic evaluations, for example computerized tomography (CT) of the brain, were performed when indicated. The following clinical outcomes were specifically documented: death, duration of hospital admission, worsening left ventricular function, surgical management, and vascular/embolic and immunological phenomena as defined by the Duke Criteria [9].

Statistical analysis:

Demographic data, symptoms and signs, laboratory tests, and outcome of the patients were reported as the percentage, mean, and standard deviation (SD) as appropriate. A comparison between the different groups, i.e. group I and II, was done by Student’s t test, p-value of less than 0.05 was considered significant. Group III could not be compared as it included one patient.

Results

Thirty paediatric patients with definite or probable IE were included in this study. There were 18 males (60%) and 12 females (40%) with a male-to-female ratio of 1.5:1. The mean age was 7.2 ± 3.9 years. Fourteen (46.7%) patients had RHD, group I, (two of them were newly diagnosed). Among cases of group I, two were having prosthetic valves. Fifteen (50%) patients had CHD, group II. Both group I and II are community-acquired IE. One patient (3.3%), group III, was complaining of chronic renal failure (CRF) with no under-lying heart lesion, however a history of indwelling central venous catheter was detected in this case (i.e. nosocomial IE). A history of tooth extraction without IE prophylaxis (one group I), cardiothoracic surgery (total correction of TOF) and cardiac catheterization (valvular PS) was recorded (Table 1). According to the Duke criteria, 24 cases (80%) { 10 cases of group I and 14 cases of group II} were categorized as definite IE, however, 6 cases (20%) { 4 cases of group I, one case of group II and group III} were categorized as possible IE. Of those with definite IE, 19 patients satisfied two major criteria and the remaining 5 patients satisfied one major and three minor criteria (Table 2).

Physical examination revealed an audible cardiac murmur and heart failure in every patient evaluated. Fever was detected in all patients with no significant statistical difference regarding the degree of fever between group I & II. The time elapsed between the onset of symptoms till hospital
referral was relatively long with no statistical significant difference between group I & II. Embolic events were the most common observed vascular phenomena in the whole patients being detected in eight cases (26.7%) where stroke accounted for 75% (6 cases) and other major artery emboli accounted for 25% (2 cases). No other vascular phenomena were detected. Glomerulonephritis without renal failure was observed in 6.7% of the studied population (2 cases of group II). Microscopic haematuria with urinary sediment with or without proteinuria was used to establish a diagnosis of renal involvement in these patients. No other immunological phenomena were detected. Unfortunately the circulating C3 and C4 complement and rheumatoid factor assays were unavailable to our laboratory for a period, which limited the collection of study data in this regard (9/30 of the studied patients were tested with no abnormal results). There was no statistical significant difference regarding the duration of hospital admission between both groups (Table 2).

**Laboratory data:** Gathered showed the presence of raised ESR, leucocytosis with shift to left, positive CRP (only qualitative assessment was available) and anaemia (normocytic normochromic in 80% and microcytic hypochromic in 20%) in all cases (Table 3).

Table (1): Characteristics of thirty patients with infective endocarditis.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: Female</td>
<td>18:12</td>
</tr>
<tr>
<td>Age (mean±SD) (years)</td>
<td>7.2±3.9</td>
</tr>
</tbody>
</table>

Table (2): Clinical manifestations of the studied patients.

<table>
<thead>
<tr>
<th>Item</th>
<th>Group II RHD (n=14, 46.7%)</th>
<th>Group I CHD (n=15, 50%)</th>
<th>p-value (GI &amp; GII)</th>
<th>Group III no-underlying heart lesion (n=1,3.3%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite IE</td>
<td>9 (2 major criteria)</td>
<td>10 (2 major criteria)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Possible IE</td>
<td>4 (1 major+3minor)</td>
<td>4 (1 major+3minor)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Grade of fever (°C mean±SD)</td>
<td>39.07±0.65</td>
<td>39.2±0.53</td>
<td>0.44</td>
<td>40</td>
</tr>
<tr>
<td>Time from onset of symptoms to hospital referral (days mean±SD)</td>
<td>8.5±3.8</td>
<td>9±3.9</td>
<td>0.7</td>
<td>–</td>
</tr>
<tr>
<td>Heart failure</td>
<td>100%</td>
<td>100%</td>
<td>–</td>
<td>HF (new murmur)</td>
</tr>
<tr>
<td>Vascular phenomena (n=8, 26.7%)</td>
<td>2 (25%)→ unilateral brain infarction</td>
<td>2 (25%)→ unilateral brain infarction</td>
<td>–</td>
<td>Unilateral central retinal artery occlusion (12.5%)</td>
</tr>
<tr>
<td>Imnunologic phenomena</td>
<td>–</td>
<td>2 cases (6.7%)→ GN without renal failure</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Duration of hospital stay (Ds)</td>
<td>43.5±17.5</td>
<td>46.7±13.6</td>
<td>0.6</td>
<td>55</td>
</tr>
</tbody>
</table>

NG = glomerule nephritis
Infective Endocarditis Pattern Among

Table (3): Laboratory results of the studied population.

<table>
<thead>
<tr>
<th>Item</th>
<th>Group I (n=14)</th>
<th>Group II (n=15)</th>
<th>Group III (n=1)</th>
<th>Total number (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (Hb gm%)</td>
<td>8.5±0.54</td>
<td>8.85±1.08</td>
<td>0.26</td>
<td>8.0</td>
</tr>
<tr>
<td>Total leucocytic count x1000/mm²</td>
<td>13±±2.1</td>
<td>13.46±2.75</td>
<td>0.94</td>
<td>13.5</td>
</tr>
<tr>
<td>(shift to left in 100%)</td>
<td></td>
<td>(shift to left in 100%)</td>
<td></td>
<td>(shift to left)</td>
</tr>
<tr>
<td>ESR at 60 minutes (mm/hr)</td>
<td>58±16.6</td>
<td>55.3±13.5</td>
<td>0.63</td>
<td>40</td>
</tr>
</tbody>
</table>

An aetiological organism: Was reached in 27 of the 30 patients. Positive blood cultures demonstrated the following organisms: Staph. aureus (n=13/30, 43.3%), viridans streptococci (n=9/30, 30%), enterococci (n=2/30, 6.7%), staph epidermidis (n=1/30, 3.3%), pseudomonas (n=2/30, 6.7%). The 2 cases with prosthetic valve endocarditis, one demonstrated staph. aureus and the other showed strept. Veridans. Among the 8 patients with vascular phenomena, staph. aureus was yielded in 4 cases (50%), pseudomonas in 2 (25%), enterobacter in one (12.5%) and the last one (12.5%) demonstrated negative blood culture (Table 4).

All patients were subjected to TTE examination: TEE was additionally required for the 2 cases with PVE. According to Duke criteria, oscillating mass (vegetation) consistent with positive echocardiographic result for IE was detected in all group I patients (100%) including those with prosthetic valves and in 80% of group II (12 cases) and in group III case. The remaining 3 cases of group II, mass detected in 2 of them was suggestive of IE but not positive for major criteria for IE, however no vegetation was detected in the third case. Left sided vegetation was detected in 20 cases (66.7%). On the other hand, right sided vegetation occurred in 9 cases (30%) of the studied population. All cases of group I demonstrated Left sided vegetation, however, group II showed more prevalence of right sided vegetation than left one. The patient of group III showed right sided vegetation. Vegetation was mobile in most of the studied patients (80%) with no statistical significant difference regarding its size between those with and those without vascular phenomena (Tables 5,6).

Table (4): Blood culture results in the studied patients.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Group I (n=14)</th>
<th>Group II (n=15)</th>
<th>Group III (n=1)</th>
<th>Total number (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staph. aureus</td>
<td>6 (brain infarction in 3 cases)</td>
<td>7 (Pul.embolism in one)</td>
<td>–</td>
<td>13 cases (43.3%)</td>
</tr>
<tr>
<td>Strept viridans</td>
<td>5</td>
<td>4</td>
<td>–</td>
<td>9 cases (30%)</td>
</tr>
<tr>
<td>Enterococci</td>
<td>1</td>
<td>1 (brain infarction)</td>
<td>–</td>
<td>2 cases (6.7%)</td>
</tr>
<tr>
<td>Staph.epidermidis</td>
<td>–</td>
<td>1</td>
<td>–</td>
<td>One case (3.3%)</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>–</td>
<td>1 (brain abscess)</td>
<td>1 (central retinal a.occlusion)</td>
<td>2 cases (6.7%)</td>
</tr>
<tr>
<td>No growth</td>
<td>2</td>
<td>1 (brain infarction)</td>
<td>–</td>
<td>3 case (10%)</td>
</tr>
</tbody>
</table>

Table (5): Echocardiographic detection of vegetation in the studied patients.

<table>
<thead>
<tr>
<th>Item</th>
<th>Group I (n=14)</th>
<th>Group II (n=15)</th>
<th>Group III (n=1)</th>
<th>Total number (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lt-Sided vegetation (n=20, 66.7%)</td>
<td>MV: 10</td>
<td>MV: 3</td>
<td>–</td>
<td>MV: 13 (43.3%)</td>
</tr>
<tr>
<td></td>
<td>AV: 4</td>
<td>AV: 3</td>
<td></td>
<td>AV: 7 (23.3%)</td>
</tr>
<tr>
<td>Rt-Sided vegetation (n=9, 30%)</td>
<td>–</td>
<td>TV: 4</td>
<td>TV: 1</td>
<td>TV: 5 (16.7%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PV/P.Inf.: 2</td>
<td>PV/P.inf.: 2</td>
<td>PV/P.inf.: 2 (6.7%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RV wall: 2</td>
<td>RV wall: 2</td>
<td>RV wall: 2 (6.7%)</td>
</tr>
<tr>
<td>Vegetation mobility</td>
<td>Mobile: 12 (brain infarction in 3)</td>
<td>Mobile: 11 (brain infarction in 2 &amp; brain abscess in 1)</td>
<td>Mobile (central retinal a. occlusion)</td>
<td>Mobile: 24 (80%)</td>
</tr>
<tr>
<td></td>
<td>Immobile: 2</td>
<td>Immobile: 3</td>
<td></td>
<td>Immobile: 5 (16.7%)</td>
</tr>
<tr>
<td>No vegetation</td>
<td>–</td>
<td>1 (Pulm.embolism)</td>
<td>–</td>
<td>1 (3.3%)</td>
</tr>
</tbody>
</table>

MV = mitral valve, AV = aortic valve, TV = tricuspid valve, PV = pulmonary valve, P. inf = pulmonary infundii, RV = right ventricle
Table (6): Comparison between vegetation size and mobility (as detected by Echo) in patients with and those without vascular phenomena.

<table>
<thead>
<tr>
<th>Item</th>
<th>Patients with vascular phenomena [7]</th>
<th>Patients without vascular phenomena [22]</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetation surface area (mm$^2$)</td>
<td>13.7±5.17</td>
<td>11.34.04</td>
<td>0.23</td>
</tr>
<tr>
<td>Vegetation mobility</td>
<td>Mobile in 100%</td>
<td>Mobile in 18(81.8%)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immobile in 4 (18.2%)</td>
<td></td>
</tr>
</tbody>
</table>

At the end of the in-hospital follow-up period for the whole studied patients (45.16 ± 15.15 Ds), 21 cases (87.5%) of the medically treated survived patients (n=24) did not show change regarding the vegetation size, however 3 cases (12.5%) demonstrated reduction of the vegetation size. The significance of this reduction could not be statistically assessed due to small sample size.

Valvular destruction with regurgitation that consistent with positive echo results for IE was detected in 15 cases (2 with prosthetic valves, one with RHD, 11 cases with CHD and the last one was that of group III). In the remaining 15 cases valvular disruption could not be considered positive for IE either due to absence of pervious echo reports or it was just worsening of previously existing valvular affection.

Table (7) shows the outcome of medical and surgical management during hospital admission period. The mortality rate of medically treated patients was 11% with the identified causes of death as follows: intracerebral stroke (1-Group I), intractable heart failure (1-Group II) and sepsis (1-Group II), all showed staph. aureus endocarditis. Eleven (40.8%) cases were discharged with worsening of LV function. Seven (26%) were discharged with other various complications such as embolic stroke (5), pulmonary embolism (1), peripheral arterial occlusive disease (1). Two patients (group I) were survived without complications. Four cases (14.8%) opted discharge against medical advice because of social and/or financial constraint for further hospital stay. One patient of group I and 2 of group II underwent reconstructive and valve replacement surgery because of progressive heart failure and/or persistent bacteraemia despite appropriate antibiotic therapy. The operative mortality was noted in one case (group II) (33.3%) and the cause of operative death was intractable arrhythmia. One surgical case had uncomplicated postoperative course and the last one demonstrated persistent CHF despite clearance of infection.

Table (7): Outcome of management.

<table>
<thead>
<tr>
<th>Management</th>
<th>N</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>3</td>
<td>11%</td>
</tr>
<tr>
<td>Survived without complica</td>
<td>2</td>
<td>7.4%</td>
</tr>
<tr>
<td>Survived with worsening of LV function</td>
<td>11</td>
<td>40.8%</td>
</tr>
<tr>
<td>Survived with complications</td>
<td>7</td>
<td>26%</td>
</tr>
<tr>
<td>Embolic stroke</td>
<td>5</td>
<td>14.3%</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1</td>
<td>14.3%</td>
</tr>
<tr>
<td>PAOD</td>
<td>1</td>
<td>14.3%</td>
</tr>
<tr>
<td>DAMA*</td>
<td>4</td>
<td>14.8%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>27</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Surgical:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>1</td>
<td>33.3%</td>
</tr>
<tr>
<td>Survived with persistence of CHF**</td>
<td>1</td>
<td>33.3%</td>
</tr>
<tr>
<td>Survived without complication</td>
<td>1</td>
<td>33.3%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>3</td>
<td>100%</td>
</tr>
</tbody>
</table>

*discharged against medical advice. **CHF = Congestive heart failure.

Discussion

In the present study, 50% of cases had CHD and 46.7% had RHD. Previous reviews of CHD demonstrated that the majority of children with IE had CHD [10].

A study from Pakistan showed that rheumatic heart disease predominated [11]. Left sided endocarditis was detected in all patients with RHD, however in those with CHD, right sided endocarditis was predominating and the case of group III showed right sided IE. Hemodynamic factors, induced by CHD or rheumatic valvular disease, that predispose to turbulent blood flow are important factors in the pathophysiology of IE [12]. Only one case (3.3%) with right sided endocarditis, that of group III, did not demonstrate underlying cardiac lesion but an indwelling central venous catheter was encountered in that case (nosocomial IE). It
was found that patients whose endocarditis was associated with venous catheters generally developed infections of the right side of the heart–valvular or mural-at sites of endocardial trauma induced by catheter itself. These patients commonly lacked underlying valvular disorder. Infection of the catheter with subsequent colonization of the foci of platelets and fibrin at sites of endocardial trauma seems the most probable mechanism for the development of endocarditis in these cases [13].

Previously corrective cardiac surgery (TOF) was detected in one patient (3 months before IE), and cardiac catheterization (balloon dilatation of valvular pulmonary stenosis) was found in another case (one month before IE). It is possible that the risk of IE following cardiac catheterization is higher in children (especially infants) than in adults because the procedure is technically more difficult [11].

Tooth extraction 3 weeks prior to development of IE was demonstrated in one patient (group I). It is widely accepted that dental procedures are associated with a risk of developing IE in patients with a variety of structural cardiac diseases [14].

Late hospital referral was noted in the studied population with no difference between both groups. One of the main problems is that the majority of these patients are initially not seen by a cardiologist or an infectious disease specialist but by a general physician. Furthermore, under real-life conditions, physicians often prescribe antibiotics to febrile patients before a definite diagnosis is made and especially before blood cultures are obtained [1].

Clinical presentation:

Fever and heart murmur associated with heart failure were the most common clinical presentation being present in the whole patients group. Fever is the most frequent symptom of IE [7]. Koegelenberg et al. [15] demonstrated cardiac murmur in all their studied patients with IE. The murmurs associated with endocarditis are almost always regurgitant. These murmurs must be distinguished from murmurs associated with fever and anaemia, which frequently accompany this clinical entity [16].

Heart failure in the studied population can be generally a consequence of valvular lesions whether newly occurred or was previously present and get worsened by the disease process. CHF may also develop more insidiously, despite appropriate antibiotics, as a result of a progressive worsening of valvular insufficiency and ventricular dysfunction, two thirds of those patients will do so within the first month of therapy [17].

Vascular phenomena were reported in 26.7% of the whole patients, 6 patient with CNS affection giving rise to hemiplegia, focal neurological deficits and seizures, one case with pulmonary embolism giving rise to cough and chest pain and the last one with unilateral central retinal artery occlusion giving rise to blindness. Staph. aureus was isolated from 50% of these patients. This is concordant with Di Salvo et al. [18] who mentioned that Staph aureus infection was associated with a high incidence of embolic events. Perhaps distinct bacterial characteristics and virulent mechanisms (e.g binding of the organism to the component constituents of the vegetations or exo-toxin production) might impact the frequency of embolic events.

Immune phenomenon was elicited in two patients of group II in the form of glomerulo nephritis but this didn’t end with renal failure. Lames and Eykyn [19] found that 1/3 of IE cases had renal affection which ends with renal failure. In the current work, no case presented with skin manifestations of IE. The specific skin lesions associated with IE are more common in adults than in children [20].

Causative organisms:

Regarding the organisms isolated by blood culture from the studied population, the most common was staph aureus (43.3%), followed by strept. viridans (30%). Other studies found that strept viridans was the most common causative organism and staph. suis was the 2nd common organism [4,21]. Ferrieri et al. [22] stated that most organisms that cause IE in children are Gram positive cocci, including viridans group streptococci, staphylococci, and enterococci. Enterococcal endocarditis occurs much less frequently in children than in adults. This latter organism was detected in only 6.7% of the studied patients. The predominance of staph. aureus in the current work and in several studies [23-26] suggests that the etiological agents of paediatric IE may be changing. The 2000 modification of the Duke criteria added community-acquired staph. aureus bacteraemia as a major criteria [27] (the original version accepted only nosocomial staph. aureus bacteraemia as a major criteria) recognizing that many cases of staph. aureus IE are now community acquired.

Blood culture of the 2 cases with prosthetic valve endocarditis demonstrated staph. aureus in one and Strept viridans in the other that showed no peculiarity.
Blood culture was positive in almost all cases (90%), versus rates as low as 37% in previous paediatric studies [28]. However, these differences may be accounted for by variation in definition chosen for positive culture (i.e., 2 separate samples drawn >12 hours apart versus all of three or a minority of four or more separate blood cultures, with first and last drawn at least one hour apart), and it is possible that cases of culture negative IE were missed by our definition.

Culture negative endocarditis was encountered in 3 cases (10%). This close to the results of another study [10] where 3/40 (7%) of their cases were culture negative. Jose et al. [29] reported that culture negative cases accounted for 13% of IE case. The administration of antimicrobial agents to patient with IE before blood cultures are obtained, which was the case in the culture negative patients of this study, reduces the recovery rate of bacteria by 35% to 40% [30]. Culture negative cases can be also related to low volume of blood sampled, inadequate laboratory techniques and infection secondary to fastidious organisms, very chronic subacute endocarditis and uraemia [31].

Other laboratory results:
Leucocytosis with shift to the left, anaemia, elevated ESR and positive CRP were present in the whole patient group with no significant differences regarding these parameters between group I and group II. These laboratory tests are not specific for confirming the diagnosis of endocarditis, but may be helpful in the management and follow-up of patients with this infection [32]. The anaemia of IE may be haemolytic or may represent the anaemia of chronic disease. It should be noted that chronic low-grade haemolysis also may be caused by a prosthetic valve in the absence of IE [22].

Echocardiography:
Vegetation, the hallmark of IE was detected in almost all of the studied patients. Among the 7 cases with systemic embolization, mitral valve vegetation was detected in 5 cases (3 in group I and two in group II) and aortic valve vegetation was found in 2 cases (one in group I and the second in group II).

One case with pulmonary embolism was found among group II patients, but no vegetation could be detected. From that we found that most cases with systemic embolization used to have mitral valve vegetation. This is in agreement with Rohmann et al. [33] who found that mitral valve endocarditis, particularly in the presence of large vegetations, might be associated with an increased risk for arterial embolism.

In the whole patients’ group no significant difference was found regarding vegetation size between cases with embolization and those without. Vegetation was mobile in all cases with systemic embolization. Di Salvo et al. [18] reported a significant relationship between vegetation mobility and embolic events. But they thought that vegetation size is a better clinical predictor of embolic events because of its lower inter-observer variability.

Studies using TTE have demonstrated a trend toward higher embolic rates with left-sided vegetations that are 1 cm in diameter [34]. Overall, these data are compatible with previous observations that in general, mitral vegetations, regardless of size, are associated with higher rates of embolization (25%) than aortic vegetations (10%). Of interest, the highest embolic rate (37%) has been seen in the subset of patients with mitral vegetation attached to the anterior rather than the posterior mitral leaflet [33,35]. This implies that the mechanical effects of broad and abrupt leaflet excursion, occurring twice per heartbeat, may contribute to the propensity of a vegetation to fragment and embolize. In contrast, staphylococcal or fungal IE appears to carry a high risk of embolization that is independent of vegetation size. The number of vegetation, the number of valves involved, and vegetation characteristics (e.g., lack of calcification) predicted embolic complications in one study [36]. Vegetation mobility has not been shown to be an independent risk factor for embolic events, probably because it is strongly correlated with vegetation size [37].

An echo-cardiographic evidence of vegetation could not be found in the patient who developed pulmonary embolism. This may be due to embolization of a previously present vegetation. Shapiro and Kupfer [38] found in their study that embolic events occurred in 20% of the patients in whom vegetation couldn’t be detected by echocardiography. These occurrences might be a result of embolization of the macroscopic portion of the vegetation or due to vegetation adherent to non valvular cardiac structures.

Valvular destruction (with valvular regurgitation) that consistent with positive echo result for IE was detect in 50% of the whole patients. Other studies demonstrated valvular regurgitation in almost all examined patient with IE [39,40]. The presence of regurgitation doesn’t prove the diagnosis, however the absence of regurgitation makes
the diagnosis of IE unlikely [40]. Insufficiency of an infected valve may result from different mechanisms: vegetation preventing proper leaflet or cusp coaptation, valvular destruction (from small perforation to flail leaflet), [41] or rupture of chordae tendineae [42,43].

TTE demonstrated the presence of vegetation consistent with positive echo result for IE in all of our cases except 4 cases (including the 2 cases with PV) where the presence vegetation was questionable and one case where vegetation could not be detected. The high positivity of TTE, in this work, for IE was likely related to young age of the studied population. TTE is more sensitive in the paediatric population than in the adult population for detection of vegetation. Although standard TTE is sufficient in most clinical circumstances, especially in younger infants or children, it may not be adequate when imaging is inhibited by poor ultrasound penetration, e.g. in post–cardiac surgery patients. In these circumstances, TEE may be an important adjunct to TTE [22].

The absence of vegetation on echocardiography does not in itself rule out IE. Conversely, an echogenic mass can represent a sterile thrombus, sterile prosthetic material, or normal anatomic variation rather than an infected vegetation [37].

At the end of in-hospital follow-up period, the vegetation size did not change in the majority of medically treated survived patients.

Vegetation require a fair amount of time to regress and the persistence of vegetation doesn’t necessarily imply a therapeutic failure. In a previous study, [44] an overall reduction in the vegetation size was found during transition from the active to the chronic stage. However, in some patients the vegetation didn’t change in size and in some patients, actually showed a small increase. It was mentioned that no apparent correlation between clinical cure of IE and change in vegetation size [44].

Complications:

Factors in children with IE that predispose to the development of complications include type of organism, location and size of vegetation, important co-morbid cardiac conditions, and occurrence of endocarditis in an otherwise normal heart, particularly in children <2 years of age [45].

Mortality in medically treated infective endocarditis patients was 11 %, which is much less than recorded in other studies where the rate was around 35% [31,46]. This can be related to the relative short follow-up duration of this study which was confined to the in-hospital period, however that studies either conducted retrospectively or prospectively with longer follow up duration (> 6 months after hospital discharge). Not necessarily due to poor medical management or inadequate antimicrobial coverage, mortality may be secondary to a severely compromised physical or hemodynamic condition before the onset of infective endocarditis aggravated by a sudden hemodynamic deterioration [31]. Many factors complicate the comparison of mortality data, including variables such as stage of presentation, degree of underlying cardiac decompensation, number of affected valves in patients with chronic rheumatic heart disease, age of the patient, prosthethic or native valve involvement, and many other factors [15].

Staph aureus was detected in these three cases. Staph aureus and fungal endocarditis are at more risk of mortality [47].

Further surgical management was performed in 3 cases with mortality rate of 33.3% (one case). Surgery is mandatory in at least 30% of cases with active IE and in another 20-40% after healing [47, 48]. Prognosis is better if surgery is performed before cardiac pathology develops and the general condition of the patient severely deteriorates, regardless of the duration of prior antibiotic therapy. Age per se is no contraindication for surgery [1].

Conclusion & recommendations:

1. The clinical features of the present study have a similar pattern as the earlier studies. The rates of in-hospital complications and mortality are high especially with staph aureus endocarditis that seems to show increasing incidence.

2. The relatively high in-hospital complications encountered can be partly related to the late referral of the patients that could point to the inefficiencies in the local primary and secondary health care centres.

3. The use of Duke’s criteria in clinical practice was found to be useful by putting guidelines for IE diagnosis.

4. Echocardiography is useful in children with known endocarditis, and in children in whom there is a high level of clinical suspicion for endocarditis. However its value as a screening tool for patients without clinical or bacteriologic evidence for endocarditis was not evaluated in this study. TTE remains the most appropriate first-line imaging investigation in the paediatric
age group. If the clinical suspicion of endocarditis is high and the TTE study is negative or inconclusive, a TEE should be obtained.

5- General practitioners and parents of predisposed children should be informed that the course of any fever should be investigated before antibiotics are given to these patients stressing on the importance of prior blood culture performance.

6- In a developing country like ours, it will be of great benefit to give written information and a certificate to predisposed patients demonstrating the potential threats and risk which might occur in particular with dental procedures.

**Study limitation:**

1- Collection of patients was through the echo laboratory of the hospital which serves in- and out patients, however ICUs patients are served within these units and this accounted for small sample size with small size of different subgroups (nosocomial IE and community acquired IE, Medical and surgical, NVE and PVE) which consequently precluded adequate statistical comparison and could explain the lack of statistical power to account for some negative findings.

2- Four cases were discharged against medical advice because of social and/or financial constraint for further hospital stay, which to some extent might affect the statistical assessment of the study.

However, this study; first, indicates that it is vital to continue to fund research on endocarditis secondly it highlighted several points (the increased incidence of staph. aureus in community-acquired IE, high in-hospital mortality and morbidity, late referral of the patients and the prolonged hospital admission with its social and financial implications for the patient as well as for the community) that would have to be specially addressed in further analyses.

**References**


Infective Endocarditis Pattern Among


