Fiji SCHOOL of MEDICINE

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Fiji School of Medicine

"A Descriptive Study of 58 Cases of Infective Endocarditis Admitted to Medical Unit, Colonial War Memorial Hospital, 1993-2003"

sione talanoa latu

MMEDIM IV

2003

Infective endocarditis is an inflammation of the endocardium caused by microorganisms including bacteria, fungi, viruses, and parasites. Infective endocarditis involves infection of the endothelial surfaces of the valves and chambers of the heart. The spectrum of clinical presentation ranges from rapidly progressive and destructive disease to more indolent or chronic infections. Infective endocarditis has catastrophic complications in some patients with severe infection.

The epidemiology of endocarditis is remarkable for its constancy. Up to the 1950s it was linked to the occurrence of rheumatic heart disease. Native valve disease could affect the damaged mitral or sometimes the aortic valve. Despite the significant diagnostic and therapeutic advances over the years in terms of antimicrobial therapy, echocardiography, and valvular heart surgery, the case fatality rate of infective endocarditis still remains at approximately 20% to 40%[1]. It is therefore vital that rapid diagnosis and the institution of appropriate treatment are realised early to ensure good patient outcome.

The incidence of infective endocarditis is difficult to determine because the criteria for diagnosis and the methods for reporting vary with different series. The incidence of infective endocarditis in a general population has been estimated between 2-6 cases per 100,000 patient years[2], but it is clearly higher in patients with underlying valvular heart disease, and those with intravenous drug abuse (IVDA). Furthermore, invasive procedures performed in our technically robust health care system may cause bloodstream infections and result in endocarditis. Men are more often affected than women (mean male-to-female ratio, 1.7 to 1) as increasing longevity has given rise to degenerative valvular disease, placement of prosthetic valves, and increased exposure to nosocomial bacteraemia, the median age of patients has gradually increased; it was 30 to 40 during the preantibiotic era and 47 to 69 more recently[3,4].

Proper use of the diagnostic microbiology laboratory is critical in the diagnosis and management of patients with infective endocarditis. Moreover, newer diagnostic guidelines have improved sensitivity for making the diagnosis of clinically definite infective endocarditis. Advances in non-invasive techniques, such as 2-dimensional echocardiography, have enhanced our ability to diagnose infective endocarditis. Newer antibiotics that can be used in patients with infective endocarditis have become available. In addition, approaches to the prevention of endocarditis recently have been modified and reviewed.

Positive blood culture results remain the mainstay of the laboratory diagnosis of infective endocarditis; expert clinicians often confirming the diagnosis of endocarditis on the basis of blood culture information alone. Culture data are important for confirming the diagnosis and choosing proper antibiotics. Documentable bacteraemia, defined as one or more positive culture results,

occurs in 77% to 90% of patients with infective endocarditis. In a study of 206 cases of culture-positive endocarditis, the first blood culture results were positive in 95% of patients, and one of the first two cultures drawn yielded positive results in 98% of cases. All cultures yielded positive results in 91% of cases. Hence, three sets of blood cultures are adequate in patients in whom infective endocarditis is suspected and who are at low risk for culture-negative disease[5].

New diagnostic approaches including culture and microbiological assessment of vegetations have yielded a better understanding of blood culture-negative infective endocarditis. Only 5 to 7% of patients who have been given a diagnosis of infective endocarditis according to strict criteria and who have not recently received antibiotics will have sterile blood cultures. For example, blood cultures were negative in 88 of 620 cases (14%) of infective endocarditis documented in France during a one-year nation wide survey. In 42 of 88 cases, negative blood cultures were associated with the administration of antibiotics before blood was drawn for culture[6]. Suppression of bacteraemia often persists longer than the antibiotic is present in the blood. Such suppression can be countered in patients with subacute endocarditis by delaying empirical therapy and by obtaining additional blood cultures.

Risk factors for endocarditis have been well studied7. Degenerative valvular lesions, cyanotic congenital heart disease, rheumatic heart disease, prosthetic heart valve, and mitral valve prolapse are well-documented pre-existing cardiac risk factors for endocarditis. Although many community hospitals still report viridans streptococci as the most common isolates among patients with infective endocarditis[8], staphylococci have assumed increasing importance among isolates in community hospitals in recent years[4]. A recent study demonstrated a high frequency of *Staphylococcus aureus* endocarditis secondary to preventable sources[9]. Of fifty-nine cases reported from Duke University, 23 were caused by infected intravascular catheters and 14 from surgical wounds. Approximately 25% of vascular catheter-associated bacteraemia caused by *Staphylococcus aureus* may result in endocarditis.

Infective endocarditis carries with it high risk of morbidity and mortality. It remains a diagnostic problem in a large number of patients with congenital or acquired heart disease. This is due to both the inaccessibility of intracardiac vegetations and the highly variable and sometimes non-specific nature of the clinical manifestations.
In 1994, a group at Duke University proposed standardised criteria for assessing patients with suspected infective endocarditis. These criteria integrated factors predisposing patients to the development of infective endocarditis, the blood culture isolate and persistence bacteraemia, and echocardiographic findings with other laboratory and clinical information. The usefulness of these Duke criteria in assessing patients with potential infective endocarditis has been validated in several subsequent studies. The specificity of the initially proposed criteria was high (0.99, with a 95% confidence interval of 0.97 to 1.0) and the negative

predictive value was greater than 92%. Also, a retrospective study of 410 patients with diagnosed endocarditis found that the Duke criteria have good (72 to 90 percent) agreement with clinical assessment of infectious-disease experts[10].

Infective endocarditis has been recognized as a distinct clinical entity for at least a century. A myriad of complications can result from this infection and occur in the majority of patients with infective endocarditis. As an example, in one review of 223 episodes of infective endocarditis, 57% of patients had one complication, 26% two, 8% three or more, and 6% six or more complications[11]. Complications such as congestive heart failure and stroke are relatively common and feared outcomes of infective endocarditis, while other complications such as blindness and septic arthritis are fortunately rare in modern practice.

Complications of infective endocarditis can be broadly categorized as:

- Cardiac
- Septic
- Embolic
- Neurologic
- Musculoskeletal
- Renal
- Associated with medical treatment.

Mortality varies according to the infecting organism (viridans streptococci 4-16%, Staphylococcus aureus 25-47%, and fungal infections over 50%) and is higher when infection affects a prosthetic valve or is complicated by congestive heart failure, abscess formation, or a neurological event[12].

Infective endocarditis seems to be a rare infectious disease in Fiji although there is no known literature in Fiji to substantiate this. Infective endocarditis is difficult to diagnose in a surprisingly high proportion of cases. This is particularly so in a developing country like Fiji, where patients are referred late, there is low yield of blood cultures, and incidence of rheumatic heart disease is still high.

The overall aim of this study is to describe the clinical manifestations and characteristics of infective endocarditis in Fiji.

OBJECTIVES:

- to determine the common complications including those causing deaths in cases with infective endocarditis.
- to determine the rate of positive blood culture in cases with infective endocarditis and identify factors responsible for culture-negative endocarditis.
- to identify the spectrum of common pathogens isolated as causing infective endocarditis.

This is a retrospective and descriptive study that analysed and evaluated data on consecutive patients admitted to the Medical Unit of the Colonial War Memorial Hospital and had a final discharge diagnosis of infective endocarditis for the period 1 July, 1993 to 30 June, 2003.

The Medical Unit of the Colonial War Memorial Hospital, Suva which is the main tertiary referral hospital for Fiji. The Medical Unit covers the following wards:

- **Acute Coronary Care Unit (ACCU);**
- **Post-Coronary Care Unit(PCCU)/Acute Medical Ward (AMW);**
- **Men's Medical Ward (MMW);**
- **Women's Medical Ward (WMW);**
- **Paying Ward (PW); and**
- **Intensive Care Unit (ICU).**

1. SELECTION OF CASES

The medical records of patients with a primary or secondary final discharge diagnosis of **infective endocarditis** that were admitted and treated at the Medical Unit of the Colonial War Memorial Hospital from 1 July, 1993 to 30 June, 2003 were obtained by searching the 'Admission

Books' of each ward of the Medical Unit. Since the introduction of the computerised PATIS system last year, this database was also accessed to retrieve medical records.

The Admission Books for each Medical Ward are filled in by nurses (usually the Sister In Charge) based on the final and discharge diagnoses classified by the medical officer (usually Team registrar or consultant) associated with the case. The ICU, ACCU, and PCCU are often 'holding areas' for acute cases until their stabilisation and subsequent transfer to other wards of the Medical Unit. Therefore their entries on the 'Final Diagnosis' column are based on the 'Admission Diagnoses' for each case together with a 'transfer out to (T/O)' order. The respective Admission Books of each Medical Ward to which these cases were transferred with an Admission Diagnosis of infective endocarditis were then searched to obtain the true discharge diagnosis.

To be included in the study, subjects had to meet the Dukes criteria proposed by Durack et al in 1994[13] for the diagnosis of infective endocarditis. They proposed two major and six minor criteria. One major criterion was positive blood cultures (two separate blood cultures) where typical organism was isolated or bacteraemia persistent. The second major criteria were evidence of endocardial involvement in the form of a new regurgitant murmur (change in existing murmur is not sufficient) or typical echocardiogram. Three findings considered as typical were vegetations, abscesses or a new partial dehiscence of prosthetic valve. The minor criteria were predisposing cardiac lesions, prolonged fever greater than 38°C with no extra-cardiac focus, vascular phenomenon (major arterial emboli including septic pulmonary emboli, peripheral necrotic skin lesions, mycotic aneurysms, cental nervous system haemorrhages, conjunctival haemorrhages and Janeway lesions), immunological phenomenon (elevated levels of Rheumatoid factor, evidence of immune complex glomerulonephritis, Osler's nodes and Roth spots), suggestive echocardiography (non-oscillating targets, new valvular fenestrations and nodular thickening and suggestive microbiology (positive blood culture which is neither typical nor persistent or serological evidence of Brucella, Legionella, *Coxiella burnetii*, Chlamydia and Rocholimaea species).

Combining these criteria three diagnostic categories were defined by them. The diagnostic criteria was considered 'definite' if there was direct evidence of infection and histopathological or bacteriological examination of the involved tissue, or in patients who had two major or one major and three minor criteria or five minor criteria. It was considered 'possible' in patients who had one major and less than three minor criteria or no major and four minor criteria. The 'rejected' category was one which did not fulfil

the above criteria and another diagnosis was considered. The 'definite' Dukes criteria were used as the inclusion criteria for this study.
In addition to the criteria proposed by Durack, the echocardiographic minor criterion was extended to include echocardiographic findings that were unable to conclusively exclude or rule out infective endocarditis.

2. MICROBIOLOGICAL INVESTIGATION

Blood culture was performed for every patient who was suspected to have infective endocarditis. The BacT/Alert 120 system was used for detecting pathogens. Gram positive, catalase positive pathogens were identified by conventional test including coagulase tubing test (Coagulase plasma EDTA, Difco, USA) and novobiocin disk (BBL, Sensi-Disc; Becton Dickinson, Cockeysville, MD). Gram positive, catalase negative pathogens were identified by conventional biochemical tests, including a sensitised latex agglutination kit for grouping beta-maemolytic streptococci (Streptex), the API-20 Strep kit (bio Merieux Vitek, Hazelwood, MO) and the optochin test (BBL, Sensi-Disc; Becton Dickson, Cockeysville, MD). Gram negative pathogens were identified by conventional biochemical tests, including the API-20E kit (bio Merieux Vitek, Hazelwood, MO), Microbact 12A & B, and API-20NE kit (bio Merieux Vitek, Hazelwood, MO). Routine antibiotic sensitivity testing was done by the disk diffusion method (BBL, Sensi-Disc; Becton Dickinson, Cockeysville, MD) according to guideline of the National Committee for Clinical Laboratory Standards (NCCLS)[14].

The blood culture results were obtained directly from patients' records and in rare instances where this was not available the Log Books of the Microbiology Department were accessed to obtain the appropriate results.

3. ECHOCARDIOGRAPHY

The findings of transthoracic 2-D echocardiography were recorded including cardiac performance, appearance of cardiac valves, chordae tendinae, and presence of perivalvular lesions. The involved cardiac valve was recorded as the valve exhibiting the most damage if more than one valve was involved.

4. COMPLICATIONS

Any complications associated with infective endocarditis were recorded, including neurological complications (such as cerebral embolism, mycotic aneurysm, intracranial haemorrhage, subarachnoid haemorrhage, brain abscess, optic nerve atrophy, and meningitis) and cardiovascular complications (such as congestive heart failure, rupture of chordae

tendinae, coronary artery embolism, perivalvular abscess, and cardiac arrhythmia).

5. STATISTICAL ANALYSIS

The Chi-square test was used to analyse categorical data. A p value < 0.05 was considered statistically significant. Odds ratios of potential risk factors were calculated. All data were analysed on a personal computer using EpiInfo Version 6 software.

A total of 114 episodes of clinically diagnosed infective endocarditis among 112 patients treated during the study period (1 absconded & 1 discharged himself against medical advice). Fifty-six of those patients were excluded due to either incomplete (3/56), untraceable/missing medical records (42/56) or failure to meet Duke's criteria (11/56). The remaining 58 patients, including 32 males (55.2%) and 26 females (44.8%) (M/F ratio 1.25:1), fulfilled the definitive Duke's criteria and were included in the study (see Table 1). The age of these patients ranged from 16 to 68 with a mean of 29 years. 42 (72.4%) of these patients were Fijians, 10 (17.2%) Others, and 6 (10.4%) Indians. Predisposing heart diseases were found in 26 (44.8%) of these 58 patients. Risk factors are shown in Table 2. Fifty of the 58 (86.2%) patients had fever. Nineteen (32.8%) patients had a new cardiac murmur. Peripheral vascular phenomenon was observed in 6 patients, including splinter haemorrhage of nail bed in 4, Roth spot in 1, and petechiae in1. Leukocytosis was found in 47 (81.0%) of the 58 patients, and 45 patients had anaemia. At initial examination, ESR was elevated in 56 (96.7%) of patients. Of the 36 who underwent urinalysis, 6 (16.7%) had haematuria (refer Table 3). All patients had blood cultures taken and transthoracic echocardiograms. Echocardiographic findings are listed in Table 4.

Prior antibiotic usage was known in 19 (32.8%) patients although this status was not ascertained in 23/58 (39.7%) patients. All of these 19 patients who had taken antibiotics had negative blood cultures.

The following pathogens of infective endocarditis were isolated by blood culture in 29 (50%) of the 58 patients (Table 5): *Staphylococcus aureus* 12, viridans streptococci 6, *Staphylococcus epidermidis* 4, *Bacillus subtilis* 3, Acinetobacter 2, Enterococcus sp. in 2. The most common pathogens were *Staphylococcus aureus* (41.4%) and viridans streptococci (20.7%).

All patients received antimicrobial therapy for 3 to 55 days (mean 27.7 days). Initially, all patients were treated with one beta-lactam and an aminoglycoside and 91% (53/58) also had an antistphylococcal agent right from the initiation of antimicrobial therapy. Overall, 10 (17.2%) of the 58 patients died. The in-hospital mortality rate was 10/58 (17.2%). The major causes of mortality included cardiovascular complications in 7 (70%) and neurological complications in 3 (30%). The cardiovascular complications included congestive heart failure (n=29) and cardiac arrhythmia (n=3). The neurological complications included cerebral embolism (n=3) and mycotic aneurysm (n=1). Cardiovascular complications (55.2%) were the most common complications associated with infective endocarditis. Neurological complications (6.9%) were the most serious complications associated with infective endocarditis resulting in 75% (3/4)

mortality. Neurological complications (OR=5.75, 95% CI=1.651-49.428, p=0.01) and heart complications (0R=4.0, 95% CI-1.487-42.177, p=0.02) were the most likely causes of mortality.

Table-1 Selection of Patients based on Dukes Criteria

		N	%
2 Major Criteria		5	8.6
1 Major + 3 minor criteria		38	84.5
	BC Major + 3 Minor (incl. ECHO)	10	
	ECHO Major + 3 Minor (incl. BC)	3	
	BC Major + 3 Other Minor	11	
	ECHO Major + 3 Other Minor	14	
5 Minor Criteria		15	6.9
TOTAL		58	100

Table-2 Demography and Risk Factors in 58 Infective Endocarditis Patients

	N	%
Sex		
Male	32	55.2
Female	26	44.8
Ethnicity		
Fijian	42	72.4
Other	10	17.2
Indian	6	10.4
TOTAL	58	100
Risk Factor		
Prior Endocarditis	4	6.9
Rheumatic Heart Disease	18	31.0
Congenital Heart Disease	2	3.4
Degenerative Heart Disease	2	3.4
No identifiable lesion	32	55.2

Table-3 **Clinical Findings in 58 Patients with Infective Endocarditis**

SIGN/SYMPTOM	NVE (%) (N=60)
Elevated ESR	
Fever	
Leukocytosis	
Anaemia	
New murmur	
Splenomegaly	
Skin lesions	
Haematuria	

Table-4 **Echocardiographic Findings in 58 Infective Endocarditis Patients**

ECHO POSITIVE		**32**	**55.2**
Mitral Valve	**22**	**37.9**	
Aortic Valve	**10**	**17.2**	
ECHO NEGATIVE		**26**	**44.8**

Table-5 **Native Valve Endocarditis Microbiology**

Staphylococcus aureus	**12 (41.4)**
Streptococcus viridans	**6 (20.7)**
Staphylococcus epidermidis	**4 (13.8)**
Bacillus subtilis	**3 (10.3)**
Acinetobacter species	**2 (3.4)**
Enterococcus species	**2 (3.4)**

Estimates of the relative risks for infective endocarditis associated with various cardiac lesions showed that rheumatic heart disease (31.0%) and patients who had prior endocarditis (6.9%) were the most common underlying diseases in this series. In this study, 55.2% (32/58) of patients had no identifiable cardiac lesions. The result is different from previous studies[15,16]. In Moulsdale's study, degenerative heart disease 24% (22/93) was the most common underlying cardiac status in endocarditis. Mckinsey[17] described that the spectrum of recognised cardiac lesions underlying infective endocarditis has been changing as a result of the decline in incidence of rheumatic heart disease, the recognition of the entity of mitral valve prolapse, and the improvement in cardiac diagnostic technique. In their study, only 31.0% of patients had either rheumatic heart disease or congenital heart disease. In contrast, 32.7% of patients in their study had no evidence of underlying cardiac lesions. Although techniques for the diagnosis of heart disease has improved, the high ratio (55.2%) of no identified cardiac lesion in my study may have resulted from that some cardiac lesions may been difficult to recognize in the early stages while other may have been overlooked due to degenerative change or lack of serial detailed clinical examinations . I realise that the risk of infective endocarditis has increased both in patients with degenerative changes of the cardiac valve and in patients with normal cardiac valves. There were no cases of intravenous drug use, right-sided or prosthetic-valve endocarditis.

Fever was present initially in 50 (86.2%) patients. Change in the status or emergent of new cardiac murmur was noted initially in 19 patients (32.8%), and peripheral embolism phenomena were noted initially found in 3 patients (5.2%). It is very likely that the ratio of patients with both changing cardiac murmur and peripheral embolism phenomena were underestimated in this study due to lack of detailed physical examination data for every new patient. Such detailed exams need to be performed to improve diagnostic rates. 32/58 (55.2%) cases had echocardiographic findings consistent with infective endocarditis and 26 (44.8%) showed no vegetation or findings to suggest endocarditis. With improvement in the resolution of echocardiography, its use has become increasingly important for early diagnosis. The diagnostic yield of echocardiography would have increased significantly if trans-oesophageal echocardiography was performed.

In the present study, pathogens of infective endocarditis were identified by blood cultured in 29 of 58 patients. Overall, the two leading pathogens were *Staphylococcus aureus* and viridans streptococci and this reflects the study done by Perman[18] in 2001 where Staphylococcus aureus was the commonest blood culture isolate overall for all cases. The ratio of culture-negative infective endocarditis was 50%. The possible reasons for culture negative findings include previous antibiotic usage seen in 32.8% (19/58) of patients or 66% (19/29) of CNE cases although this status was not known in a further 23 (39.7%) patients, incorrect specimen collection, and failure to identify organisms from the HACEK

(H. parainfluenza, H. aphrophilius, Actinobacillus sp., Cardiobacterium sp., Eikenells sp., Kingella sp.) group. S. aureus has now overtaken viridans streptococci as the most important pathogen responsible for infective endocarditis. It is interesting to note though that the mortality rate associated with *Staphylococcus aureus* infective endocarditis is around 25-47%[12] and one would have expected a higher mortality rate than that quoted worldwide (20-40%[1]) as Staphylococcus aureus was the commonest blood culture isolate for our cases with infective endocarditis however it was only 17% in this study. This would suggest that we are probably managing our cases with infective endocarditis better than overseas centres, or that the high empirical use (91%) of an antistaphylococcal agent is paying dividend here. The other possibility is whether we are seeing a less virulent strain of *Staphylococcus aureus* here in Fiji or that our complication rate is lower however this is not the case as the complication rate is comparable to other studies (62% vs 57%[11]).

The Karchmer's study[19] found that *Staphylococcus aureus* infective endocarditis had a high mortality rate than streptococcus infective endocarditis. However, no significant difference in mortality between S. aureus infective endocarditis and streptococcus infective endocarditis was found in the present study.

Culture negative endocarditis was found in 29 (50%) of 58 patients, which is significantly higher that the Pelletier's[16] series. The rate of microbiological diagnosis obtained might have decreased in this study due to antimicrobial treatment before blood culture, incorrect specimen collection, and HACEK group organisms.

The complications associated with infective endocarditis have catastrophic complications in some patients with severe infection and was seen in 62% of our cases which is similar to the 57% seen in previous studies[11]. The overall in-hospital mortality rate in this study was 17.2% (10/58). This is slightly lower than in a previous study (25-47%)[20]. Neurological complications (OR=5.75, 95% CI=1.651-49.428, p=0.01) and heart complications (OR=4.0, 95% CI=1.487-42.177, p=0.02) were the leading two complications causing deaths in patients with infective endocarditis. In Chao's study, in-hospital mortality was associated with noncardiac shock, neurological complications, cardiac complication, and older age[21].

Overall, even though this study showed that *Staphylococcus aureus* was the commonest blood culture isolate associated with infective endocarditis and that the rate of complications was similar to other studies, the in-hospital mortality rate was still lower (17% vs 20-40%[1]) and the reasons previously discussed together with a host of other related factors needs to be fully evaluated in a separate study.

The limitations of this study are because it is a retrospective study the issue of recall bias and completeness or lack thereof of medical records cannot be

completely ignored. Moreover I was not able to locate the medical records for more than a third of the cases (42/112) identified. A review of the clinical particulars related to the 'untraceable records' reveals no significant difference or any thing peculiar and it is quite possible that these records may have been randomly 'lost' or 'misplaced' and this is, perhaps, a reflection of the inadequacies of the filing system of our Records Department rather than any thing specific to the 'missing' case records. Echocardiography at the Colonial War Memorial Hospital is a self-taught procedure and findings are largely operator-dependent. It is often difficult to exclude the presence of vegetations with transthoracic echocardiography (TTE) since it only has a sensitivity of around 70%[22] hence I had to modify the original minor Dukes criteria of echocardiography due the number of cases (10/58) where the sonographer was unable to confidently exclude infective endocarditis based on TTE findings.

- The leading two causes of death in cases with infective endocarditis were neurological complications (30%) and cardiovascular complications (70%).

- The positive blood culture rate was 50% although 66% of CNE cases had a history of prior antibiotics usage indicating this as a major factor for culture negative endocarditis.

- *Staphylococcus aureus* (41%) and viridans streptococci (21%) were the most common blood culture isolates in cases with infective endocarditis.

- To reduce the associated complications as far as possible is the most critical point in improving survival in cases of infective endocarditis. This involves early recognition of the disease often based on a high index of clinical suspicion together with the prompt institution of the appropriate antimicrobial therapy targeted at covering the most likely pathogens. This also involves prolonged combination antimicrobial therapy (intravenously initially then oral) to minimise relapses and the risks of complications.

- The antibiotic policies regarding empirical antimicrobial treatment of infective endocarditis should cover for the most common pathogens – *Staphylococcus aureus* & *Streptococcus viridans*. In this respect, the current antibiotic recommendations for empirical treatment of infective endocarditis (ß-lactam, antistaphylococcal agent, & aminoglycoside) are appropriate and should remain unaltered.

- Negative blood cultures should not act as a deterrent to treating infective endocarditis if clinical suspicion is high considering the prevalent use of antibiotics prior to patients being assessed in a referral hospital.

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APPENDIX

"A Descriptive Study of 58 Cases of Infective Endocarditis Admitted to the Medical Unit, Colonial Memorial Hospital, 1993-2003"

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INTRODUCTION/LITERATURE REVIEW

- Infective endocarditis (IE) – inflammation of the endocardium caused by micro-organisms including bacteria, fungi, viruses, and parasites
- Despite significant diagnostic and therapeutic advances, case fatality rate remains ~20-40%
- Incidence – 2-6 cases/100,000 patient years[1] Difficult to determine because criteria diagnosis and methods for reporting vary
- Higher in patients with underlying:
  - VHD
  - IVDA

- ♂>♀ - 1.7:1
- Increasing longevity
  - ↑ degenerative valve dis
  - ↑ prosthetic valves
  - ↑ nosocomial exp.
  - ↑ median age
    - pre-antibiotic: 30-40 yrs
    - now: 47-69 yrs[2]
- ADVANCES
  - diagnostic micro lab
  - newer diagnostic guidelines
  - non-invasive diagnostic techniques
  - newer antibiotics
  - better preventive measures

- POSITIVE BLOOD CULTURES (BC) – mainstay of lab. diagnosis
- In one study (206 patients with IE)[11], BC positive in 77-90%
- In another study of 620 IE cases[12]:
  - BC negative in 14%(88) – Culture-Negative Endocarditis (CNE)
  - 42 of 88 IE cases (48%) - prior antibiotic usage

- Risk factors:
  - degenerative valvular lesions
  - cyanotic CHD
  - RHD
  - prosthetic heart valves
  - MVP
- BC isolates:
  - viridans streptococci (30-40%) commonest
  - Staph. aureus increasing (10-27%)

- 1994, Dukes University proposed criteria integrating factors predisposing patients to IE:
  - BC isolate and persistent bacteraemia
  - echocardiographic findings
  - other lab and clinical information
- Validity of Dukes criteria[13]:
  - specificity of 99% with negative predictive value of 92% study of 410 cases diagnosed with IE based on Dukes criteria . Correlation with infectious disease experts – 72-90%

- Mortality*
  - viridans streptococci – 4-16%
  - staph. aureus – 25-47%
  - fungal – >50%
- Fiji – no previous formal studies on IE

AIM & OBJECTIVES

- To describe the clinical manifestations and characteristics of infective endocarditis in Fiji
  - to determine the common complications, including those causing deaths in infective endocarditis
  - to determine the rate of positive blood culture in cases with infective endocarditis and identify factors responsible for culture-negative endocarditis
  - to identify the spectrum of common pathogens isolated as causing infective endocarditis

STUDY DESIGN

- Retrospective/Descriptive study
- Consecutive cases with final diagnosis of infective endocarditis that had been admitted to Medical Unit, CWM between 1 July, 1993 to 30 June, 2003 identified with collation of appropriate data

MATERIALS & METHODS

(Selection of Cases)

- Admission Books for each ward were reviewed for the period – 1 July, 1993 to 30 June, 2003
- All entries with final diagnosis (1° or 2°) of infective endocarditis were identified and medical records retrieved

INCLUSION CRITERIA - Dukes

- Definitive infective endocarditis
  - Clinical criteria
    - two major criteria, or
    - one major and three minor criteria, or
    - five minor criteria

DUKES CRITERIA

- Major criteria
  - positive blood culture for IE
  - evidence of endocardial involvement
- Minor criteria
  - predisposition (heart condition or IV drug use)
  - fever of ≥38°C
  - vascular or immunologic phenomena
  - microbiologic or echocardiographic evidence not meeting major criteria

APPENDIX

Microbiological Investigation

- Blood cultures were performed in all patients suspected with IE
- Pathogens identified through conventional laboratory techniques

Echocardiography

- Criteria:
  - cardiac performance
  - appearance of cardiac valves, chordae tendinae
  - presence of perivalvular lesions
- Recorded as valve exhibiting most damage if more than one valve involved

Complications

- Any associated with IE:
  including neurological & cardiovascular complications

Statistical Analysis

- Chi-square test for categorical data
- P value < 0.05 considered statistically significant
- OR of potential risk factors obtained
- Data analysed on PC using EpiInfo Version 6 software

RESULTS

- 114 clinically diagnosed IE cases; 112 treated
- 56 excluded:
  - incomplete (3) or traceable records (42)
  - failure to meet Dukes criteria (11)
- 58 fulfilled Dukes criteria:
  - 32 ♂
  - 26 ♀
  - ♂:♀ ratio – 1.25:1

- Age range – 16-68 yrs
  Mean – 29 yrs

Table-1 Selection of Patients Based on Dukes Criteria

2 Major Criteria	[illegible]	[illegible]
1 Major + 3 Minor Criteria	[illegible]	[illegible]
[illegible]	[illegible]	
[illegible]	[illegible]	
[illegible]	[illegible]	
[illegible]	[illegible]	
5 Minor Criteria	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]

APPENDIX

Table-2 Demography and Risk Factors in 58 IE Cases

		n	%
Sex	Male	32	55.2
	Female	26	44.8
Ethnicity	Fijian	42	72.4
	Other	10	17.2
	Indian	6	10.4
TOTAL		58	100
Risk Factor	Prior Endocarditis	4	6.9
	RHD	18	31.1
	CHD	2	3.4
	IVDU	2	3.4
	No identifiable factor	32	55.2

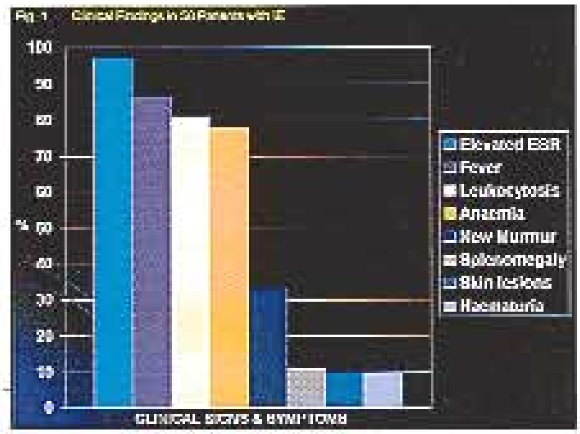

Table-3 Echocardiographic Findings in 58 Patients with IE

		n		%
Echo Positive			32	55.2
	Mitral Valve	22		37.9
	Aortic Valve	10		17.2
Echo negative			26	44.8
TOTAL			58	100

Table-4 Native Valve Endocarditis Microbiology

Organism	Cases (%)
Staphylococcus aureus	10 (34.5)
Streptococcus viridans	6 (20.7)
Staphylococcus epidermidis	[illegible]
Bacillus subtilis	3 (10.3)
Acinetobacter species	[illegible]
Enterococcus species	2 (6.9)
TOTAL	29 (100)

- BLOOD CULTURES
  - positive in 29 (50%) cases
  - negative in 29 (50%) cases
- ANTIBIOTIC USAGE:
  - 19/58 (32.8%) cases (all had negative BC i.e. 19/29 (65.5%))
  - 23/58 (39.7%) cases – prior use of antibiotics not known
- DURATION OF ANTIMICROBIAL THERAPY:
  - 3-55 days (mean – 27.7days)
  - 53/58 (91%) received a B-lactam, antistaphylococcal agent, & aminoglycoside empirically until the BC results are available
- IN-HOSPITAL MORTALITY RATE: 10/58 = 17.2%
  - [illegible]
  - [illegible]

- COMPLICATIONS:
  - Overall (36)
    - Neurological (4)
      - cerebral embolism 3
      - mycotic aneurysm 1
    - Cardiovascular (32)
      - CCF 29
      - arrhythmia 3
  - Causing deaths (10)
    - Neurologic 3
    - Cardiovascular 7

APPENDIX

DISCUSSION

- **STUDY LIMITATIONS:**
  - small numbers (but >30% (58/114) of total cases)
  - large proportion of cases with missing medical records – 42/114 (37%). Judging from the personal particulars in the Admission Books, it is highly unlikely that there were anything peculiar regarding those 'missing' cases. It is quite likely that these medical records have been 'randomly' misplaced or lost and is more a reflection of the inadequacy of our filing system rather than anything specific to the 'missing' medical records

- RHD (31%) is the commonest underlying disease
  - MV commonest valve involved – 22/32 (69%)
- No case of right-sided or prosthetic valve endocarditis
- No case of IV drug use
- 55% had no identifiable cardiac lesion
  - difficulty in early recognition of some cardiac lesions
  - overlooked/lack of detailed examination
- Mckinsey' study:
  - 31% RHD or CHD
  - 33% no identifiable lesion
- 26/58 (45%) ECHO negative
  - no vegetation or echocardiographic findings consistent with IE seen on TTE

- Positive blood culture seen in 29/58 (50%) of cases. Lower than quoted figures worldwide (>90%).
- 33% (19/58) had taken antibiotics (66% of CNE cases) prior to having blood cultures although in a further 23/58 (40%), the drug history was not known. All 19 who had taken antibiotic had negative blood cultures.
- *Staphylococcus aureus* (41%) and viridans streptococci (21%) were the commonest blood culture isolates
- In-hospital mortality rate (17%) is lower than in previous studies (25-47%)
- The incidence of Staph. aureus endocarditis is much higher in this study however the overall mortality is much lower (17% vs 20-49%)
  - are we managing our IE cases better?
  - use of an antistaphylococcal agent empirically in 31% of cases?

- Neurological complications (OR=5.75, 95% CI=1.651-49.428, p=0.01) and
- Cardiovascular complications (OR=4.0, 95% CI=1.487-42.177, p=0.02) were the leading two complications causing deaths in patients with infective endocarditis

CONCLUSION

- The leading two causes of death were neurological complications (30%) and cardiovascular complications (70%)
- The positive blood culture rate was 50% although 66% of CNE cases had a history of prior antibiotics usage indicating this as a major factor for culture negative endocarditis
- *Staphylococcus aureus* (41%) and viridans streptococci (21%) were the most common blood culture isolates in cases with infective endocarditis

RECOMMENDATIONS

- To reduce the associated complications (especially cardiovascular & neurologic) as far as possible is the most critical point in improving survival
- The antibiotic policies regarding empirical antimicrobial treatment of infective endocarditis should cover for the most common pathogens – *Staphylococcus aureus* and *Streptococcus viridans*. In this respect, the current antibiotic recommendations (β-lactam, antistaphylococcal agent, & aminoglycoside) for empirical treatment of IE are appropriate and should remain unaltered
- Negative blood cultures should not act as a deterrent to treating infective endocarditis if clinical suspicion is high considering the prevalent use of antibiotics prior to patients being assessed in a referral hospital