TITLE:

TWO-DIMENSIONAL ECHOCARDIOGRAPHIC OBSERVATIONS IN PATIENTS WITH CLINICAL DIAGNOSIS OF ACTIVE INFECTIVE ENDOCARDITIS AT KENYATTA NATIONAL HOSPITAL.

BY:

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A dissertation submitted in part fulfilment for the degree of Master of Medicine (Internal Medicine) at the University of Nairobi, 1990.

DECLARATION

This dissertation is my original work and has not been presented for a degree in any other University.

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LIST OF ABBREVIATIONS

Abd. - Abdominal

AF - Atrial Fibrillation

AI - Aortic Incompetence

CBA - Chocolate Blood Agar

CVA - Cerebrovascular Accident

CCF - Congestive Cardiac Failure

DST - Drug Sensitivity Test Agar

ECG - Electrocardiogram

ESR - Erythrocyte Sedimentation Rate

EAMJ - East African Medical Journal

Hb - Haemoglobin

IE - Infective Endocarditis

KNH - Kenyatta National Hospital

MCNA - Medical Clinics of North America

MME - M-Mode Echocardiography

2DE - 2-dimensional Echocardiography

MI - Mitral Incompetence

MS - Mitral Stenosis

NS - Not significant

PS - Pulmonary Valve Stenosis

PMN - Polymorphonuclear leucocytosis

SBA - Sheep Blood Agar

SD - Standard Deviation

ToF - Tetralogy of Fallot

TR - Tricuspid Regurgitation

UTI - Urinary Tract Infection

VSD - Ventricular Septal Defect

Echo - Echocardiography

WBC - White Blood Cell Count

LIST OF FIGURES AND TABLES

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to the following people:-

- My supervisors, Dr. A.K. Muita and Dr.(Mrs.) N.B. Mirza for their constant guidance and constructive criticisms and suggestions during the preparation of this document.
- Prof. Wamola - Chairman, Department of Microbiology for permission to do my bacteriological work in the departmental laboratory, and in particular, Mrs. Pamela Kabiru of the same department for her constant guidance and help with the bacteriological work.
- Staff of Media Section - National Public Health Laboratories for kindly assisting in the preparation of culture media.
- Messers Joel Tinga and Baraza Lusasi and Mrs. Anne Waweru of Cardiology Unit for their kind cooperation and excellent echocardiograms.
- Mr. Lambert Nyabola - Lecturer, Department of Community Health for valuable advice on statistical analysis and Miss Florence Ndolo for excellent secretarial work.

Finally, but not least to all the patients or their guardians who gave consent to participate in the study and to all members of my family, in particular my wife, Sylvia and the children Maureen and Beryl for their patience and endurance during the long periods I spent away doing the study.

SUMMARY

The sensitivity and clinical relevance of 2-dimensional echocardiographic presence of vegetations were examined prospectively in patients with clinical diagnosis of active infective endocarditis at Kenyatta National Hospital, Nairobi.

A pattern of echocardiographic vegetations was present in 45% of the 40 patients diagnosed clinically to have active infective endocarditis.

The major criteria for clinical diagnosis in these 40 patients included the presence of fever (manifested by chills, sweating, shivering and rigors) 80%, Toxaemia (manifested by malaise, tiredness, weakness, anorexia with generalised aches and pains) 77.5%, Cardiac murmurs 100%, congestive cardiac failure 80% and Pyrexia (Temp $\geq$ 38^{o}C) 62.5%. 77.5% of the cases had rheumatic valvular heart disease. Blood cultures were positive in 37.1% of the patients, with staphylococci being the commonest isolate. Only 30.8% of patients with bacteriologically proven endocarditis had vegetations on ultrasound whereas 54.5% of patients with negative blood cultures had vegetations at ultrasound. 47.5% of the patients had antibiotic therapy prior to diagnosis, which was significantly correlated to the presence of bacteriologically negative cultures.
The case fatality rate was 37.5% and was significantly related to the presence of severe CCF, and Renal insufficiency.
The presence of vegetations on ultrasound in this series had no prognostic implications in so far as CCF, major emboli or death were concerned.

INTRODUCTION

Infective endocarditis is the appropriate term that has been used to describe vegetative lesions on the surface of heart valves (native or prosthetic) and mural endocardium of a heart chamber that result from colonization by bacterial, ricketsial, fungal and probably viral infections.

Most cases are bacterial in origin, and in most of them the source of bacterial infection is apparent. The clinical manifestations of infective endocarditis are non-specific and a result of the local destructive effects of the vegetative lesions, the peripheral embolic phenomenonthat arise from fragmentation of the vegetations and their propagation in circulation, the diffuse vascular disease of probable immune complex nature, and the constitutional effects of circulating toxins from the infecting agent. The clinical course is either acute or subacute, and a large number of patients have a rapid course of illness and diagnosis only possible at autopsy (1). Diagnosis of infective endocarditis requires a high index of suspicion.

It is difficult to quantify the exact frequency of this condition because hospital figures of incidence relate to index of suspicion, facilities for bacteriological diagnosis and frequency of necropsy studies as well as criteria used to accept diagnosis which are arbitrary and everchanging (2,3,4,5).

Due to widespread use of antibiotics in all types of infections, the application of chemoprophylaxis in susceptible individuals and the ease of treatment in community health institutions, it has been suggested that the frequency of the condition is on the decline in developed countries (3). However, although the condition may not be as frequent as it was in the pre-antibiotic era, it remains a common disorder.

Studies by various workers exemplify the varying magnitude of this condition especially in the tropics. D'Arbella (6) working in Mulago, Kampala found a clinical incidence of 2.2%. Namuli (7) in a five year retrospective study at Kenyatta National Hospital found overall incidence of 8.8% of cardiac admissions per year, whereas Ochieng (8) in a one year prospective study at the same hospital found an incidence of 1.5% of cardiac admissions. At necropsy, Brenton (9), and Steiner (10) working at Mulago Hospital found an incidence of 6%, 3.2% respectively among the cardiac necropsies.

Somers et al (1) in a 2 year prospective study of clinical and autopsy cases in the same hospital found 102 consecutive cases of infective endocarditis.

In majority of cases, the condition is associated with antecedent cardiac disorder of acquired or congenital nature, however, rheumatic valvular heart disease is the major underlying condition in the tropics (1,6,7,8,11).

Post-streptococcal rheumatic fever and rheumatic valvular heart disease are common in developing countries (12-14) and the prevalence of the later influence to a considerable extent the risk of infective endocarditis. Indeed rheumatic heart disease plays a prominent role in the cardiovascular morbidity and mortality in this region and invariably infective endocarditis is involved in majority of the cases (12-18).

Infective endocarditis has been described as a disease in evolution (19,20). Due to its changing nature, it's myriad of presentation, wide range of complications, increasing absence of antecedent cardiac lesion, the traditional diagnostic criteria is infrequently seen, and subsequently the disease poses a major diagnostic and therapeutic challenge to the clinicians (3,12,19-23).

Despite advances in microbiological technique, availability of new drugs and regimen, the disease still carries a high mortality (24-26).

Among the numerous factors that determine the ultimate outcome in infective endocarditis, delay in diagnosis accounts considerably for the high mortality as it is associated with an increased incidence of complications (24-26). A firm diagnosis of the condition can only be made with demonstration of the characteristic vegetative lesions on the valves or endocardium at surgery or autopsy. Nevertheless, the clinical diagnosis is still based on a high index of suspicion and various clinical criteria. Although this clinical expertise is paramount it has to be supported by more objective scientific measurements whenever definite evaluation is required.

Rapid technological advances, in particular the advent of non-invasive investigative methods have contributed enormously to scientific medical progress. Since two Swedish investigators, Edler and Hertz used ultrasound in 1954 to visualise intracardiac structures in vivo, non-invasive diagnostic cardiac techniques have become well developed (27,28). Echocardiography which is the non-invasive method employing ultrasound to visualise and study the movements and dimensions of cardiac structures was developed about early 1969.

Initially, time motion mode (M-mode) technique which provides a unidimensional view of the heart displaying intantenously the depth of cardiac stoactures from chest wall throughout cardiac cycle was used.

Later, in early 1970's this technique was expanded into two-dimensional technique, which has inherent spatial orientation enabling determination of lateral dimensions, lateral motion and shape of cardiac structures (28,29).

This two-dimensional echocardiography has broadened further the diagnostic scope of ultrasonography and with Doppler Echocardiography which has improved on hemodynamic assessment, the technique now stands alone as the most complete anatomic study of the beating heart (27).

The use of echocardiography to detect vegetative lesions in heart valves in patients with infective endocarditis was initially described by Dillon et al in 1973 (29). Subsequently this observation was confirmed by several workers (30-47). This technique can also define the size, mobility and natural history of vegetations (47,48), the degree of valvular destruction (47,49), the hemodynamic derangement caused by the endocarditis process (50) and the assessment of left ventricular function (51).

Published reports (34,35,41,44,47,49,52) on the application of echocardiography in infective endocarditis have demonstrated its diagnostic capability and prognostic value in patients with this condition. The M-mode technique has been shown to have a diagnostic sensitivity range of 14% to 65%, whereas the two-dimensional technique has a sensitivity range of 43% to 100% in infective endocarditis (45).

These reports indicate a general agreement that echocardiography identifies a subset of patients with a high incidence of complications such as severe congestive cardiac failure

and major embolic phenomena, and these subset generally requires, aggressive management including surgical intervention during active disease for succesful treatment. The major indications for surgical intervention are severe hemodynamic deterioration, persistent sepsis and recurrent emboli (53). Bed$$de techniques for assessment of cardiac function lack sensitivity required to make tangible clinical decisions. Invasive techniques like cardiac catheterization and ventricular angiography are impracticable in many situations and are not frequently repeatable. They are also expensive and potentially dangerous (54). Whereas echocardiography is non-invasive, reproducible, safe, and can provide serial studies of the same individual.

Therefore in conjunction with careful clinical assessment, echocardiography may provide useful information about presence of significant hemodynamic compromise and thus circumvent the need for invasive procedures. It may be an important modality in determining need for surgical intervention prior to development of life threatening complications, while at the same time be useful in directing surgical procedures.

Blood cultures are an important investigation in infective endocarditis, so that the inability to confirm presence of endocarditis by this investigation often delays institution of therapy while other diagnosis are being considered.

Although clinical features may strongly suggest infective endocarditis, failure to identify causative organisms makes selection of an effective antimicrobial agent(s) difficult. Consequently, culture negative disease has been considered among the adverse prognostic factors in this condition (55). Rubenson et al (44) confirmed the useful diagnostic role of echo in culture negative endocarditis. The relevance of echocardiography in diagnosis and management of infective endocarditis at Kenyatta National Hospital has not been evaluated hence above issues have not been addressed, and therefore the need for the present study.

Kenyatta National Hospital is both a University teaching and national tertiary care referral facility with a fully fledged cardiac unit in which modern echocardiographic facilities encooperating two-dimensional echo and doppler unit are available and functional.

AIM/OBJECTIVES

AIM:

The aim of the studywas to determine the ability of two-dimensional echocardiography to detect the presence and location of vegetative lesions, and their clinical relevance in patients with clinical diagnosis of active infective endocarditis at Kenyatta National Hospital.

OBJECTIVES

The objectives of the study were to:-

1. Determine the infecting agent(s) in patients with a clinical diagnosis of active infective endocarditis.

2. Determine the two-dimensional echocardiographic findings in patients with clinical diagnosis of active infective endocarditis.

3. Compare the clinical observations, laboratory data and complications in patients with and without vegetative lesions on 2-dimensional echocardiography.

MATERIALS AND METHODS

This was a prospective descriptive study conducted at KNH, Nairobi, between May 1989 and December 1989. All consecutive patients admitted in the hospital with clinical diagnosis of active IE were investigated if they met the following criteria based on most common symptoms and signs found in previous studies of the disease at KNH (7,8).

- Cardiac murmurs with fever and/or toxaemia
- Plus one or more of the following:-

a. Central Pallor
b. Vascular lesions (Petechial) or Splinter haemorrhages)
c. Finger clubbing
d. Splenomegally

Patients in whom an alternative reason for any combination of criteria was clearly established plus those with terminal illness (say malignancy) or connective tissue disease were excluded. Each patient (or guardian) upon entry gave a written consent and investigations and management conformed to a standard routine. All patients included in the study were considered to have active IE by their attending physicians and received appropriate treatment. A thorough clinical evaluation for symptoms and signs was undertaken on each subject by the author on entry and subsequently daily until end of hospital stay. Patients were followed up for a maximum of six weeks.

Specimen samples of blood, urine, were obtained from each patient for laboratory analysis on entry and subsequently when indicated. A chest X-ray, an ECG and Echocardiogram were obtained on each patient. The author recruited the patients, collected specimens for laboratory analysis and participated in preparation and reading of bacteriological cultures and echocardiographic studies.

TECHNIQUES

Within 24 hours of admission, blood was drawn by venepuncture from veins of antecubital fossa or forearm which were distended by tourniquet. The operator's hands were washed with soap and water then thoroughly dried in air. The site of puncture was identified, first the skin was cleaned with cotton swabs soaked in 70% alcohol and second, 1% tincture of iodine was applied in concentric fashion, the site was allowed to dry. A sterile needle was used to withdraw blood into a sterile disposable syringe as follows:-

BLOOD CULTURES

Three sets of blood cultures were taken at 1-6 hourly intervals. The interval was shorter for the very ill patients. Inoculation of broth culture media was done directly at the bedside. Each set of broth cultures consisted of two closed bottles of culture broth media consisting of heartbrain infusion broth and sodium polyanetholesulfonate (Liquoid). One was for aerobic culture and the other for Micro-aerophilic culture.

There were no facilities for anaerobic or fungal cultures at the time of the study. A fresh sterile needle was used to deliver the blood into the broth media bottles after cleaning the top with alcohol swabs. One millilitre of blood was delivered into 10mls of broth media for aerobic Culture and another one millilitre into 10mls of broth media for micro-aerophilic culture (incubated at 37°C in a candle extinction jar) so as to achieve a dilution of 1:11. The second and third sets of broth media were inoculated in a similar fashion. After obtaining blood and urine specimens the patients were immediately commenced on an intravenous course of combined crystalline penicillin and gentamycin. After culture and sensitivity reports were available, antibiotics were substituted appropriately and given for six weeks. The culture broth was incubated appropriately at 37°C within ½ hour of inoculation, Gram stain and subculture on solid media (SBA, CBA, MacConkey) were done after 18-24 hours incubation. The subcultures on solid media were also incubated appropriately at 37°C. The plates were examined daily for growth upto 48 hours, if negative, they were discarded.

Re-incubation of the culture broth media continued for a maximum of 3 weeks and daily macroscopic evaluation of broth cultures for growth were done and any cultures that looked turbid, or hemolysed had immediate gram stain and were subcultured on solid media.

Material for subculture on solid media was obtained by removing the bottle caps, flaming the mouth of the broth media bottle, and using a flamed wire loop to scoop colonies when visible or pick a loopful of gently mixed culture broth.

Routine (blind) cultures of grossly negative broth media were performed at intervals of 24 hours, 72 hours, 1 week, 2 weeks and 3 weeks. Each plate of SBA, CBA and MacConkey inoculated was incubated appropriately. All plates were inspected for bacterial growth after 18-24 hours. All plates with no growth were re-incubated for a total of 48 hours before being discarded.

Bacterial growth was significant if same organism was isolated from both bottles of a set, or appeared in more than one set of culture broth or if a rare skin commensal, and was isolated from a single bottle of a set of blood cultures.

Identification of Bacteria

Bacterial growth were identified by standard methods (65).

Antibiotic Sensitivity Tests

These were performed using the disc diffusion technique. Control organisms used were AICC Staph aureus No. 25923 for gram positive organisms and E. coli 25922 for gram negative organisms. In this study colonies of identified bacteria were sub cultured on DST with application of antibiotic discs and incubated appropriately and read by comparative method.

Antibiotic sensitivity was positive if inhibition zone for the antibiotic was equal or greater than that around control organism for the same antibiotic.

Haemogram

For estimation of haemoglobin level, total white cell count and differential and peripheral blood film, 2mls of blood were collected in sequestrene bottle for analysis by appropriate methods.

Urea and Electrolytes

For serum urea, creatinine and electrolyte levels 5mls of blood were collected in plain bottles for biochemical analysis by appropriate methods.

Midstream Specimen of Urine

Fresh urine was collected into a sterile bottle after patient was instructed on meticulous antisepsis, and taken for culture by standard methods and microscopy for cells and casts. Protenuria was assessed by Combur 9 strips.

X-ray of Chest and Electrocardiogram

These were recorded at entry and subsequently repeated when indicated.

Echocardiography

This was performed on the Aloka Echocardiographic unit SSD-725 incooperating an ultrasonor recorder, a doppler unit and video display that allows the examiner to adjust a hand held scanner (transducer) position until tomographic section to be examined in detail is displayed.

A complete standard echocardiographic study included tomographic sections from parasternal long axis view, 3 parasternal short axis views, at level of left ventricle papillary muscles, at level of mitral valve and at level of great vessels, an apical four chamber and two chamber views and a subcostal 4 chamber view. The scanning was done in a conventional fashion (66). Vegetative lesions were def as the appearance of a non-uniform echogenic mass, shaggy in appearance and attached to a valve leaflet or endocardium and seen in both systole and diastole and without restricting leaflet motion. Cardiac chamber dimensions were obtained by incooperation of MME and left ventricular function parameters were worked out automatically on Doppler and displayed for recording on tape. During the entire study period, appropriate polaroid films for still-frame pictures were unavailable and therefore photographs for display in this document were not obtained.

A-coustic coupling between scanner and chest wall was provided by a layer of ultrasound gel. This examination was performed within one week of entry into study. Repeat examinations were done at 4-6 week intervals The echocardiograms were performed by experienced technologists under a cardiologist's supervision. Relevant information was recorded on video tape. All echocardiographic and other laboratory and clinical data obtained were entered in a proforma (appendix I)

Data Analysis

The following tests of significance were applied. The Z-test (based on the standard normal distribution) was used, to compare proportions between groups. The student t-test was used to compare the group means.

The level of significance was fixed at 5%.

RESULTS

Forty consecutive patients who were clinically diagnosed to have active infective endocarditis were seen over a seven month period. All patients were considered to have infective endocarditis by the attending physicians and received appropriate treatment.

In section A, the characteristics of these 40 patients are described, while in section B, the characteristics of patients with and without vegetations at Echocardiography are compared.

SECTION A: CHARACTERISTICS OF 40 PATIENTS WITH INFECTIVE ENDOCARDITIS

1. Age and Sex distribution

There were 15 males and 25 females, giving a male:female sex ratio of 1:1.7 (Figure 1). The age distribution is shown in figure 2. The overall mean age (± SD) was 15.7 ± 10.3 years with an age range of 4-48 years. Males had a mean age of 18.9 ± 11.9 years, with a range of 5-48 years, whereas females had a mean age of 15.3 ± 7.5 years with a range of 4-32 years. The difference in mean age between the sexes was not statistically significant. The peak age group was 11-20 years, with 47.5% of patients in this group. 75% of the patients were 20 years or younger. Only 3 patients were over 30 years of age.

Figure 1: Sex Distribution of 40 patients with Infective Endocarditis

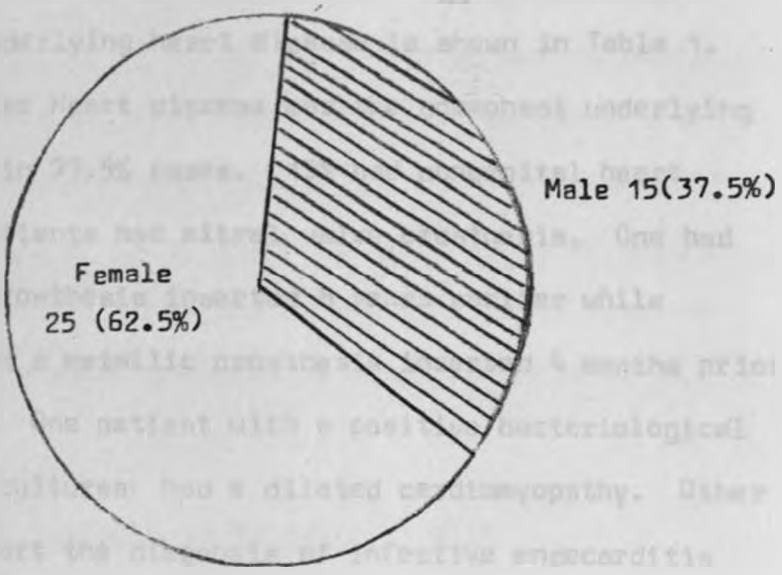
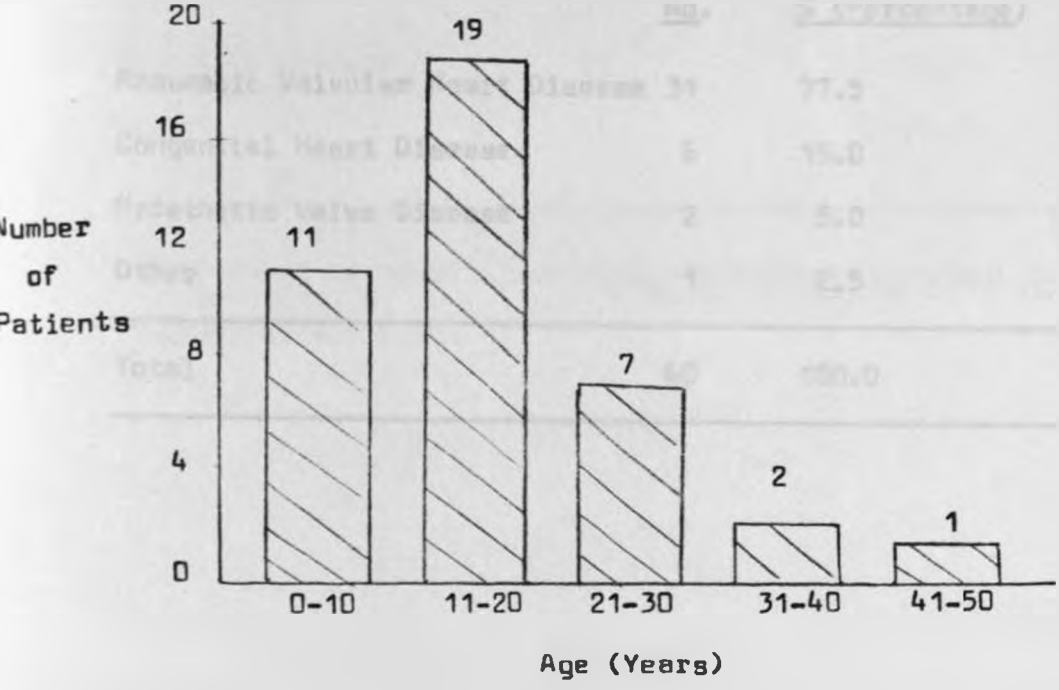


Figure 2: Age Distribution



ii. Underlying Heart Disease

The nature of underlying heart disease is shown in Table 1. Rheumatic Valvular Heart disease was the commonest underlying cardiac disease in 77.5% cases. 15% had congenital heart disease. Two patients had mitral valve prosthesis. One had a biosynthetic prosthesis inserted 8 years earlier while the other one had a metallic prosthesis inserted 4 months prior to presentation. One patient with a positive bacteriological growth on blood cultures had a dilated cardiomyopathy. Other features to support the diagnosis of infective endocarditis in this patient included gross fingerclubbing, splinter haemorrhages and microscopic hematuria.

Table 1: Underlying heart disease in 40 patients with Infective Endocarditis

	No.	% (Percentage)
Rheumatic Valvular Heart Disease	31	77.5
Congenital Heart Disease	6	15.0
Prosthetic Valve Disease	2	5.0
Other	1	2.5
Total	40	100.0

iii. Clinical Symptoms and Physical Signs

Table 2 shows the commonest presenting symptoms. 80% of the patients had fever (manifested by chills, sweating, shivering and rigors). 77.5% of the patients had toxaemia (manifested by malaise, tiredness, weakness, anorexia with generalised aches and pains). Cough and chest pain occured in 80% of patients, 42.5% of patients had history of weight loss. 20% of patients presented with neurological symptoms (manifested by transient confusional state hemiparesis or hemiplegia).

Table 2: Clinical Symptoms in 40 patients with Infective Endocarditis

Symptoms	No. of total	% (Percentage)
Fever	32	80
Toxaemia	31	77.5
Cough and chest pain	32	80.0
Weight loss	17	42.5
Gastro-intestinal *	21	52.5
Neurological	8	20.0

* Manifested by nausea, vomiting, abdominal pains and abdominal swelling.

Table 3 shows the presenting signs, 80% of patients had congestive cardiac failure at presentation. Pyrexia (temperature $\geq 38^{0}C$) was noted in 62.5% of patients. 67.5% of patients had pallor of mucous membranes. Other signs were: fingerclubbing (42.5%), splenomegaly (32.5%) Jaundice (27.5%) and splinter haemorrhages (22.5%). Six patients (15%) had major emboli manifesting as cerebrovacular accident.

Roth spots, Janeways lesions and Osler's nodes were absent in this series.

Table 3: Physical signs in 40 patients with Infective Endocarditis

	No.	% Percentage
Congestive cardiac failure	32	80.0
Pyrexia (temp $\geq 38^{0}C$)	27	62.5
Splenomegally	13	32.5
Fingerclubbing	17	42.5
Splinter haemorrhages	9	22.5
Jaundice	11	27.5
Pallor	27	67.5
CVA (Stroke)	6	15.0

iv. Predisposing Events

Only seven patients had lesions or illnesses that may have predisposed to bacteraemia and subsequent endocarditis. Three patients had urinary tract infection, however all had negative blood cultures. Two of these patients had echocardiographic confirmation of endocarditis. One patient with urinary tract infection had persistent fever, even after urine became sterile. The patient responded to treatment for endocarditis. In 82.5% of the patients the predisposing event was apparent.

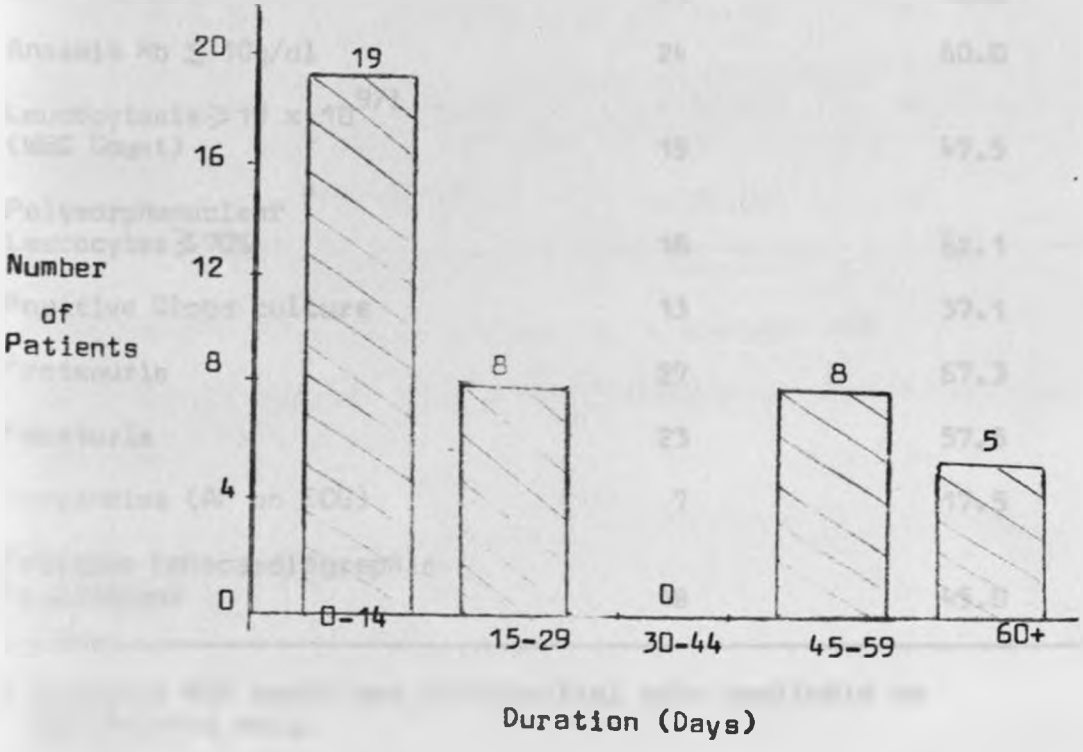
Table 4: Predisposing Events in 7 patients with Infective Endocarditis

Event	No. of Total	% (Percentage of total)
Phlebitis	2	5.0
Cellulitis	1	2.5
Gingivitis	1	2.5
UTI	3	7.5
TOTAL	7	17.5

v. Duration of Illness prior to diagnosis

52.5% of the patients had illness for more than two weeks before presentation, only 12.5% had symptoms for over 8 weeks before presentation (figure 3). The mean duration at presentation was 4.6 weeks. Thirteen patients with positive blood cultures had a mean duration of illness of 3.5 weeks, while patients with echocardiographic vegetative lesions had a mean duration of illness prior to diagnosis of 6 weeks.

Figure 3: Duration of Illness prior to presentation in 40 patients with Infective Endocarditis



vi. Laboratory Findings

Table 5 shows the laboratory findings in these patients. Initial ESR was raised above $30mmhr^{-1}$ in 72.5% of the patients. 67.3% of patients had protenuria, whereas 60% had anaemia. Leucocytosis was seen in 47.5% of cases. 62.1% of patients had polymorphonuclear leucocytosis. Microscopic hematuria and protenuria were noted in 57.1% and 67.5% respectively. 17.5% of the patients had arrythmias predominantly atrial fibrillation. Only 13(37.1%) patients had positive blood cultures. Only 18(45%) patients had vegetative lesions at echocardiography.

Table 5: Laboratory Findings in 40 patients with Infective Endocarditis

Parameter	No. of Total	% Percentage
ESR $\geq 30mmhr^{-1}$	29	72.5
Anaemia Hb $\leq$ 10g/dl	24	60.0
Leucocytosis $\geq 10 \times 10^{9/l}$ (WBC Count)	19	47.5
Polymorphonuclear Leucocytes $\geq$ 70% •	18	62.1
Positive Blood culture	13	37.1
Protenuria	27	67.3
Hematuria	23	57.5
Arrythmias (AF on ECG)	7	17.5
Positive Echocardiographic Vegetations	18	45.0

• Complete WBC count and differential were available on 29 patients only.

Table 6 shows the comparison of culture positive and culture negative disease. 19(42.5%) of all patients had history of prior antibiotic treatment within one week of diagnosis. Antibiotic use prior to diagnosis was significantly associated with culture negative disease. The presence of leucocytosis was comparable in both groups of patients. 54.5% of patients with culture negative disease had detectable vegetation compared to 30.8% with culture positive disease.

Table 6: COMPARISON OF CULTURE POSITIVE AND CULTURE NEGATIVE IE

Feature	+ culture	- Culture	P Value
	n=13	n=22	
Prior antibiotic treatment	4(30.8%)	15(68.2%)	$P < 0.05$
Leucocytosis (WBC $\geq 10 \times 10^{9/l}$)	5(38.5%)	9(40.9%)	NS
Neutrophilic* PMN $\geq$ 70% WBC	8(80.0%)	8(50.0%)	NS
Positive Echo Vegetations	4(30.8%)	12(54.5%)	NS

* 26 patients had blood cultures plus complete WBC differential counts, 10 of these had positive and 16 negative cultures.

Table 7: Causative Micro-organisms in 13 patients with Bacteriologically proven endocarditis

Organism	No.	Percentage
Staph aureus	5	35.8
Staph albus	2	14.3
Listeria Spp.	1	7.1
Moraxella Spp.	2	14.3
Haemophilus Spp.	1	7.1
Acinetobacter Spp.	1	7.1
Salmonella Spp.	2	14.3
TOTAL	14	100.0

Table 7 shows the causative organisms isolated in thirteen patients with positive blood cultures. One patient had a mixed growth of Staph. aureus and acinetobacter spp. Staph aureus was the commonest isolate. Although very few isolates, staphylococcal infection was the commonest isolate in both Echo groups. Constituting of 75% of echo positive group anf 44.4% of echo negative group.

Antibiotic sensitivity showed 80% resistance of Staph aures to penicillin, However, sensitivity to aminoglycoside gentamycin was 100% for the same organism. All gram negative isolates, Salmonella spp., Moraxella spp. and Acinetobacter spp., showed 100% sensitivity to gentamycin.

vii. Echocardiographic findings in 40 patients with clinically diagnosed Infective Endocarditis

Two-dimensional echocardiographic patterns of definite vegetative lesions were seen in 18(45%) of all patients. However, the sensitivity of echocardiography at KNH is 30.8% as only 30.8% of patients with positive blood cultures had echocardiographic vegetations. 54.5% of patients with culture negative endocarditis had vegetative lesions at echo. However, the difference between echo positivity in culture positive and culture negative disease was not statistically significant. The distribution of vegetative lesions in these patients is shown in table 8. One patient had mural thrombi in the left atrial chamber. Majority of vegetative lesions (76.1%) were localised to the mitral valve leaflets. 3 patients had vegetations at two sites, one patient with a VSD repaired 9 years earlier had right sided endocarditis involving the tricuspid valve and right ventricular outflow tract. The patient had no history of intravenous drug use or abuse. Complications associated with the endocarditic process such as ring abscesses, aneurysms and fistulae were not seen. Commonest finding was thickening of multiple valves, features consistent with rheumatic valvular heart disease. Mixed valve disease AI/MI and mixed mitral valve disease MI/MS were the commonest lesions seen, as shown in table 9. Two patients had mitral valve prosthesis. No vegetations were detected in these two patients.

Table 8: Site of Vegetative lesions in 18 patients as seen at two-dimensional Echocardiography

Site	No. of Total (n)	% Percentage
Mitral valve	16	76.1
Aortic valve	2	9.5
Tricuspid valve	1	4.8
Pulmonary valve	1	4.8
Mural Endocardium	1	4.8
Total	21	100.0

Table 9: Echocardiographic Diagnosis of Cardiac lesions in 40 patients with Infective Endocarditis

Lesion	No.	% Percentage
AI/MI	11	27.5
MI/MS	10	25.0
MI	7	17.5
MS	3	7.5
AI/AS	1	2.5
ToF	2	5.0
VSD	2	5.0
Prosthetic Mitral Valve	2	5.0
Dilated Cardiomyopathy	1	2.5
PS/TR	1	2.5
TOTAL	40	100.0

viii. Major complications within six weeks of follow up

Table 10 shows the major short term complications in 40 patients with clinical infective endocarditis. 20% of the patients had refractory CCF, 22.5% had renal insufficiency, 15% of the patients had major cerebrovascular accident and case fatality rate was 37.5%. Mortality was significantly associated with higher incidence of congestive cardiac failure and renal insufficiency (Table 11).

Table 10: Major short term complications in 40 patients with Infective Endocarditis

Complication	No. of Total	% Percentage
Refractory CCF	8	20
Cerebrovascular Accident	6	15
Death	15	37.5
Renal Insufficiency	9	22.5

Table 11: Comparison of Short Term complications among survivors and Deceased in 40 patients with Infective Endocarditis

Features	Survivors n=25	Deceased n=15	P Value
Congestive Cardiac Failure	17(68%)	15(100%)	$P < 0.05$
Renal Insufficiency	3(12%)	6(40%)	$P < 0.05$
Stroke	3(12%)	3(20%)	NS
Arrythmias	4(16%)	4(26.7%)	NS
Anaemia	16(64%)	11(73.3%)	NS

SECTION B: COMPARISON OF CHARACTERISTICS OF PATIENTS WITH AND WITHOUT VEGETATIONS AT ECHOCARDIOGRAPHY

In this study two groups of patients were recognised on the basis of the presence or absence of vegetations at ultrasound. 18 patients (45%) had detectable vegetations, and 22 patients (55%) had no demonstrable vegetations.

i. Clinical/Laboratory Features

The mean duration of illness prior to diagnosis was significantly longer in patients with vegetations. The presence of microscopic hematuria and polymorphonuclear leucocytosis were significantly higher in patients without vegetations compared to those with detectable vegetations (Table 12). There was no significant difference in between the two groups with regard to sex ratio, mean age, presenting symptoms or signs and other laboratory findings.

ii. Shortterm Complications

Patients were followed up over a maximum 6 week duration. Table 12 shows that the incidence of complications was higher in patients without vegetations. These patients had higher incidence of Renal insufficiency (significant $P < 0.05$), cerebrovascular accidents and case fatality rate.

Table 12: Comparison of Characteristics of Patients with and without Vegetations at Echocardiography

Feature	With Vegetations n=18	Without Vegetations n=22	P Value
Mean duration of illness before diagnosis (Weeks ± SD)	5.7 ± 4	3.5 ± 3	P < 0.05
Hematuria	7(38.9%)	16(72.7%)	P < 0.05
PMN leucocytosis*	5(38.5%)	13(81.2%)	P < 0.05
Positive Blood cultures**	4(25%)	9(47.4%)	NS
Renal Insufficiency	1(5.5%)	8(36.4%)	P < 0.05
Cerebrovascular Accidents	2(11.1%)	4(18.2%)	NS
Case fatality rate	5(27.8%)	10(45.4%)	NS

* 29 patients had complete differential WBC cell counts, 13 with positive echos and 16 with negative echos.

** 35 patients had blood cultures done, 16 among patients with positive vegetations and 19 with negative vegetations at echocardiography.

DISCUSSION

Characteristics of Patients with IE

Infective endocarditis in Western countries has undergone considerable change over the past 50 years, in the clinical, bacteriological, and histopathological features (3,5,19,56,57). These changes have resulted mainly from alterations in predisposing causes especially the decline in rheumatic heart disease, also from widespread use of antibiotics, and the development of new techniques in cardiac surgery. There has been a real increase in the incidence of IE in the middle aged and elderly. The incidence of staphylococci as an agent has been increasing whereas Strep. Virid. ans has been declining. Some of these changes have also been noted in this region especially with regard to bacteriology, where strep virid ans has been rarely isolated (1,7,8). As a whole these changes in IE have been accompanied by a significant departure of the disease in presentation from the classical pattern described in the pre-antibiotic and early antibiotic era. This has made the clinical diagnosis of IE relatively difficult. However, in the present series the clinical picture resembled the classical pattern of IE, with the presence of established heart disease or cardiac murmur with fever or toxaemia, fingerclubbing, embolic phenomenon, and splenomegaly making clinical diagnosis of IE less difficult.

The characteristics of patients in this series were quite similar to previous published series (1,7,8) in this region. Majority of the patients were young, with peak incidence in age group 11-20 years. However, females were predominant over males in this series unlike other reported series where male:female sex ratio was 1:1 (7,8). The male-female sex ratio of 1.1:7 in this series may be attributed to the hospital attendance at KNH which shows that more females are seen with male-female sex ratio of attendance of 1:1.4, or it may be due to the fact that rheumatic fever and its sequela chronic rheumatic valvular heart disease are also seen more in females than in males at KNH with a male-female sex ratio of 1:2 (58). Rheumatic valvular heart disease was the predominant underlying cardiac disease, however congenital heart disease and prosthesis endocarditis were also noted. One patient with a dilated cardiomyopathy was considered because of positive blood cultures, fingerclubbing and microscopic hematuria. Echo showed no intra cardiac masses. Since it is unusual in this condition, the other possibility might have been an infected mural thrombus which embolized giving rise to metastatic infection elsewhere. Previous series (1,8) have reported cases without antecedent cardiac disease ranging from 2.2% to 26%. Due to the rigid inclusion criteria in this study these cases might have been excluded. Mitral and aortic valve were main sites of involvement, this was also the finding by Steiner et al (10) in an autopsy series at Mulago, Kampala.

Positive blood cultures were low (37.1%). Except for Ochieng (8) who reported a high rate of 69.1%, other series in this region have reported lower yields (1,7). Negative cultures were significantly associated with history of antibiotic use prior to diagnosis in this study (Table 6). Other factors that may have contributed to high negative cultures may include presence of fastidious organisms or non-bacterial causes like fungi, in view of the limited blood culture techniques. The major complications seen included CCF, CVA and uremia which was also the finding by Steiner et al (10) in Mulago. Mortality of 37.5% was within the previously reported rates of 26.1% (7) and 42.2% (8). Studies in developed countries have also shown that mortality has remained high around 30% (26,59) despite advances in medical and surgical management.

Echocardiography

No study has entailed the use of echo in evaluation of IE in this region. Reports from elsewhere in the use of echocardiograph in IE (36,44,60) have shown that echo detection of vegetations identifies a high risk group of patients with increased incidence of serious complications like embolization, CCF and death. The use of 2DE technique here did not confirm that finding. Similarly the overall sensitivity of 2DE in detection of vegetations in those centres is about 75% (45). In this study the sensitivity was 30.8% for patients with positive blood cultures. Multiple factors may have influenced the sensitivity of these technique and these are discussed.

A limitation to evaluating the echocardiographic features of infective endocarditis in this series and elsewhere is that the definition of the disease and echocardiographic vegetations are both relatively arbitrary. There is no pathological absolute standard with which to compare the accuracy of either the clinical diagnosis or the echocardiographic detection of vegetations in this condition as most patients with clinical diagnosis of the disease do not die or require valve replacement during hospitalization. In the present series, consent for post mortem was not granted for any of the patients who died and surgical intervention in acute disease was not offered to any of the patients. Nevertheless, studies limited to patients with pathological confirmation would also be skewed towards a population with more severe disease and thereby likely to demonstrate a higher prevalence of echocardiographic vegetations. Similarly the sensitivity of echo in detecting vegetations in IE is not uniform as several published reports on the use of echocardiography in infective endocarditis have shown wide variations in sensitivity (34,35,37,39,60) and even these variability has also been observed in same laboratories (34,39). The size of patient population studied and the type of population studied have also influenced the sensitivity of echocardiographic detection of vegetations. Large referral cardiac centres that are likely to receive an increased percentage of critically ill patients with considerable hemodynamic instability, and thus selecting out uncomplicated cases have tended to show higher sensitivities for this technique.

The patients in this study were largely indigenous people from around Nairobi who utilise KNH as a primary health facility, only 30% were referred from other institutions and at time of referral a diagnosis of infectiveendocarditis had not been made. Therefore these patients were more representative of a general patient population, with infective endocarditis. Other factors that may have influenced the relative insensitivity of this technique in the present series may be one of the size of vegetations. Several observers agree that a vegetation must be 2-3mm in size to be reliably visualised by ultrasound (30,32). Many small vegetations may not be visualised as separate from underlying valve tissue especially in the presence of valvular heart disease. Majority (77.5%) of patients in this series had valvular heart disease, hence the presence of vegetations might have been obscured by the valvular thickening associated with chronic rheumatic valvular heart disease. Secondly it requires about two weeks of illness for vegetations to attain a size that will allow visualization by ultrasound (61). Patients who had vegetations in this series had a mean duration of illness of about six weeks. Those without vegetation had mean duration of illness of 3.5 weeks. (Table 12) The overall mean duration of illness for patients in this series was 4.6 weeks which is lower than mean duration of illness for patients with detectable vegetations. Similarly acoustic impendance properties of vegetations may not differ sufficiently from those of valve tissue to allow differentiation from each other and therefore lesions located on endocardial surface other than valve tissue may have failed to be recognised.

In the absence of pathological absolute standard for comparison some of the patients who met arbitrary clinical criteria for endocarditis may infact not have had active disease.

Finally, since attention to echocardiographic technique is the only means of improving recognition of vegetations it follows that for maximum results valves need to be visualised through multiple echo windows which may not be entirely possible especially when dealing with very ill patients. Majority of patients in this study were very ill and the echo examination had to be done under difficult conditions.
In this study the presence of vegetations did not identify a subset of patients with high incidence of clinical embolization or death, instead the incidence of embolization and death was higher in the echo negative group. Interestingly reported incidence of grave complications in patients with detectable vegetations by ultrasound has varied widely. Wann et al (34) in a study of 65 patients found 22 with vegetations and these had poor progress in terms of requiring surgery or dying during hospital stay. Similarly Davis et al (52) in 30 patients noted that those with vegetations on ultrasound had significant increased risk of CCF, major emboli and death. In contrast Stewart et al (38) noted a lower incidence of these events during infective endocarditis in 47 patients with vegetations at echocardiography.

The major difference between these studies was the use of two-dimensional technique by Stewart (38) like in this study, as opposed to motion mode technique by Wann (34)

and Davis (52). It is thought that the sensitivity of 2 dimensional echocardiography is such that it detects a larger array of sizes of vegetations which are inaccessible to M-mode so that prognostic importance are readily seen in series where M-mode was utilised as these will tend to detect larger vegetations which are likely to be associated with extensive local destructive effects and therefore considerable heomdynamic compromise.

However, there is also conflicting evidence with regard to the felative sensitivity of M-mode and 2-dimensional technique in detection of vegetations. Mintz et al (37) and Wann et al (39) found no difference whereas Schapira et al (32) and martin et al (35) found 2-dimensional technique more sensitive than M-mode technique.

In the present study, 2 dimensional echocardiographic evaluation of endocarditis showed that higher incidence of CCF, CVA and case fatality were associated although not significantly (table 12), with absence of vegetations than their presence. Therefore the absence of vegetations does not preclude hemodynamic compromise. These observations although not statistically significant does show that absence of vegetations indicates higher morbidity and poor outcome. Patients in this category exhibited higher toxaemia, leucocytosis and neutrophilia with micro-scopic hematuria and renal insufficiency. The later was significantly associated with mortality (Table 11). The mean duration of symptoms in this category of patients without detectable vegetations was 3.5 weeks, a period that still falls within the presence of vegetative lesions even if they were not

visualised at echo, so that the higher proportion of CVA, hematuria and renal insufficiency may be a result of embolic phenomenon which has been described as very common in IE. Steiner et al (10) found high prevalence (75%) of embolization in IE at an autopsy series in Mulago, Kampala.

Patel (18) in a review of cardiac mural thrombi at KNH, Nairobi found that embolization in rheumatic valvular heart disease complicated by IE occured in 80% cases and that majority were clinically unrecognised. Similarly, whether the higher proportion of polymorphonuclear leucocytosis in this category (table 12) is as a result of metastatic infection from embolic phenomenon is not clear, it is important to note that follow up of patients in these series was for only six weeks, whereas in published series they have had a longer duration of follow up. It is also not known at what stage embolization occurs in IE as in some patients very large vegetations have been visualised on echo (63). The prevalence of culture negative endocarditis was high in this series in agreement with other series in these region (7,9). Rubenson et al (44) confirmed the important role of echocardiography in culture negative disease. In this series echocardiographic detection of vegetations was higher in culture negative disease, than culture positive disease although statistically, the difference was not significant, however these does indicate that the technique is valuable as an adjuvant in the setting of negative cultures, especially after a presumptive clinical diagnosis has been made.

Serial evaluation of echo measurements in valvular heart disease, (with or without IE) may indicate a deterioration in left ventricular dimensions and function indices (62). Such measurements may be of use in predicting surgical intervention say in IE patients during or after medical treatment, however proven criteria by which to make such decisions is lacking. Due to short follow up period in this series, the value of these measurements was not evaluated.

Serial studies have also illustrated that vegetations decrease in size when healing long after bacteriological cure, but may also show no change in size during treatment (36,47,63). This serial evaluation may be difficult because the accuracy of the observation will depend on the ability of the observer(s) to reproduce both transducer position and gain setting so that size and density of lesions are comparable in each study as increased gain setting will tend to cause lesions to appear large whereas low gain setting will reduce the apparent size of the vegetations. Similarly ultrasonography cannot differentiate between active and healed lesions, although some reviews suggest that healed vegetations may be more reflective as an indication of calcification (36).

Patients with vegetations in this study showed persistence of lesions on serial studies except in one patient where the lesion disappeared. This patient had no clinically recognisable embolic phenomenon.

Stewart et al (38) and Roy et al (47) in their series showed that the total disappearance of vegetations on serial evaluation during acute episode or chronic follow up maybe associated with an embolic episode, however, these may also be observed without clinical evidence of embolization (38,63). This phenomenon of embolization may account for some of the false negative studies in the present series, especially in the few patients who presented with neurological deficit without detectable vegetative lesions.

The high prevalence of embolization in IE has already been noted (10,18). Some interesting observations were noted in this study. Renal insufficiency was a rare complication (table 10) but significantly associated with mortality (table 11). Renal disease in infective endocarditis may be a result of direct emboli giving rise to infarcts and/or abscesses, or it may be of immunological nature giving rise to focal or diffuse glomerulonephritis, or a result of toxic effects of antimicrobial therapy (61). Renal evaluation in this study was based only on urine examination and monitoring of serum levels of urea, creatinine and electrolytes, so that the cause or type of renal injury was not established. Penicillin and Gentamycin combination given parenterally for prolonged periods ranging from 4 to 6 weeks was the antimicrobial therapy used in this study. Facilities for serum gentamycin assays were not available so that the serum levels of this drug were not monitored and therefore the toxic effects of gentamycin cannot be ruled out.

The rationale for prolonged parenteral therapy is not clear but it is intended to achieve high antimicrobial concentrations in circulation over a long time to achieve a cure against microbials which are hidden within vegetations, however, due to the high prevalence of culture negative disease in our setting it may also be justified (A. Muita - personal communication Staphylococcal endocarditis is emerging as an important cause of culture positive disease in the place of streptococcal infection, the latter was not found in the present study (table 7). Published series (1,8,9) have shown that staphylococci is the commonest isolate in this region. The antibiotic sensitivity pattern in vitro, for these organism showed high resistance to penicillin, in contrast to high sensitivity to cloxacillin. The isolates in this study were too few to make any tangible conclusions, however, it would be interesting to know the role of cloxacillin as a substitute for penicillin in combination therapy for IE in our setting. This type of regime has been used for staphylococcal IE in some centres with good results (64).

CONCLUSIONS

The diagnosis of IE in KNH is based solely on a high index of suspicion, and is rarely substantiated as blood cultures are rarely available and when present are of limited scope so that culture negative endocarditis is common. From this echocardiographic evaluation of IE a few conclusions can be drawn.

1. Routine Echocardiography has a limited role in the assessment of patients with active IE as the sensitivity for detection of vegetations is low.

2. A higher proportion of culture negative disease had a higher detection rate of vegetations by echocardiography (table 6), therefore in the setting of culture negative disease, echo is a useful adjuvant to the substantiation of the clinical diagnosis.

3. Echocardiographic absence of vegetations was associated with poor prognosis as opposed to findings in most series in developed countries.

RECOMMENDATIONS

1. Patients with clinical diagnosis of IE should be evaluated by Echocardiography as an adjuvant to clinical criteria especially in the absence of positive blood cultures.

2. Patients who die of IE should have post mortem evaluation so as to obtain a clinicopathological standard with which to compare echocardiographic findings. Echo sensitivity and specificity can then be defined more precisely.

3. Due to high proportion of patients with culture negative endocarditis, blood culture techniques need to be expanded to include routine anaerobic and fungal studies in these patients.

REFERENCES

1. Somers, K., Patel, A.K., D'Arbella, P.C., Steiner I., Hutt, M. Infective Endocarditis - an African experience British Heart Journal 34, 1107, 1972

2. Robinvichs, Smith, I.M., January, L.E., Changing patterns of Bacterial endocarditis, Medical Clinics of North America, 52,5,1091, 1968.

3. Leiner, P.I., Weinstein, L., Infective endocarditis in antibiotic era. New England Journal of Medicine 274, 199, 259, 323, 1966

4. Weinstein, Rubin; Infective endocarditis, Progress in Cardiovascular Disease Vol. 16 pg 239-274, 1973.

5. Hayward, G.H. Infective Endocarditis, A changing disease British Med. Journal 35, 706, 1973

6. D'Arbela, Kanyerezi, Tulloch, A study of heart disease in Mulago Hospital, Kampala, Uganda. Transactions of Royal Society of Trop. Med. and Hygiene, 60, 782, 1966.

7. Namuli, E., Pattern of Infective Endocarditis (Retrospective Study) at Kenyatta National Hospital. M.Med thesis - Nairobi University, 1982.

8. Ochieng, C. Pattern of infective endocarditis at Kenyatta National Hospital (Prospective Study). M.Med Thesis Nairobi University, 1984.

9. Brenton, D.P., Fewler, J.M., Philips, I.
Infective endocarditis. East African Medical Journal 45, 750-754, 1968.

10. Steiner, I., Patel, A.K., Hutt., R., Somers, K.
Pathology of Infective Endocarditis - Post mortem evaluation. British Heart Journal 35, 159, 1973.

11. Somers, K.: Infective Endocarditis today - an African comparison in cardiovascular Diseases in Africa, Editor Akinkugbe.

12. Lore, W., Editorial - Priorities in Cardiovascular Disease in Kenya, E.A.M.J. 58, 385-387, 1981.

13. Pobee, J.M.: Cardiovascular Research. A luxury in tropical Africa ? E.A.M.J. 64, 396-410, 1987

14. Lore, W. Prevention of Rheumatic Fever and Rheumatic Heart Disease E.A.M.J. 64, 795-800, 1987.

15. Gichinga, H.W., Rees, P.H., Fulton, W.F.M., Cardiac causes of death in Nairobi (Abstract) E.A.M.J. 51,955, 1974.

16. Parkar, H.T. Cardiac disorders in Nairobi
E.A.M.J. 50, 530-536, 1973

17. Kahare, A.M., Anabwani, G.M., Mugambi, M.
Valvular heart disease as seen at cardiac catheterization in KNH. E.A.M.J. 63, 803, 1986.

18. Patel, K.J., Cardiac Mural Thrombi at K.N.H.
E.A.M.J. 60, 140, 1983.

19. Kaye, D.: Changes in spectrum, diagnosis and Management of Bacterial Endocarditis
MCNA 67, 941-957, 1973.

20. Naggar, C.Z., Forgacs, P.: Infective endocarditis
A challenging disease MCNA 70, 1279-1294, 1986

21. Tompsett, Bacterial Endocarditis, Changing Clinical Spectrum
Arch Int. Med. 119, 329-332, 1967.

22. Cherubin, C.E., Neu, H.C., Infective Endocarditis
in Presbyterian Hospital, New York, 1939-1967
Am. J. Med. 51, 83-96, 1971.

23. Ingenbaum, M.J. Kaplan, M.K.: Infective Endocarditis in elderly Geriatrics 39, 121-127, 1984.

24. Pelletier, C., Petersdoff, R.G.: Review of 125 cases of Infective Endocarditis in Washington, 1963-1972
Medicine 56, 287-313, 1977.

25. Baylis et al: Microbiology and Pathogenesis of infective endocarditis.
British Heart J. 50, 513, 1983

26. Monksdale, Eyka et al: A study of Infective endocarditis 1970-1979.
Quarterly J. Medicine, 49, 315, 1980.

27. Seward, J.B., Jalik, A.: Two dimensional echocardiography
MCNA 64(2), 177, 1980.

28. Feigenbaum, H.: Principles of Echocardiography
Amer. J. Med. 62, 805, 1977

29. Dillon, J.C., Feigenbaum, H., Konecke, L. et al
Echocardiographic Manifestations of valvular vegetations
Amer. Heart J. 86, 698, 1973.

30. Gilbert B., Haney, R., Crawford, D.F., et al
2DE Assessment of vegetative endocarditis circulation
55, 346, 1977

31. Valovia, R., Charazi, V.: 2DE distinguishing between
opening snap of Aortic valve and flop of Myxoma.
Amer. Heart J. 103, 1982.

32. Schapira, J.N., Martin, R.P., Fowles, R. et al:
2DE assessment of patients with Bioprosthetic valves
Amer. J. Cardiology 43, 510, 1979.

33. Melvin, E.T., Berger, M., Lutzker, L.G., et al:
Non-invasive methods for detection of valvular
vegetations, Amer. J. Cardiology 47, 271, 1981.

34. Wann, L.S., Hallam, C.C., Dillon, J.C. et al:
Echocardiography in Bacterial Endocarditis
NEJM 295, 135-139, 1976.

35. Martin, R.P., Metlzer, R.S., Chia, B.L.:
Clinical utility of 2DE in Infective Endocarditis
Amer. J. Cardiology 46, 379, 1980.

36. Stafford, A., Wann, L.S., Dillon, J.C. et al:
Serial Echo appearance of Healing Infective Endocarditis
Amer. J. Card. 44, 754, 1979

37. Mintz, G.S., Kotler, M.N., Segal, B.L. et al.
Comaprison of 2DE and MME in Infective Endocarditis
Amer. J. Card. 43, 738, 1979

38. Stewart J.A., Silmperi, D.,harris, P. et al
2DE in Infective Endocarditis
Circulation 61, 374, 1980

39. Wann, L.S., Hallman, C., Dillon J. et al:
Comparison of 2DE and MME in Infective Endocarditis
Circulation 60, 728, 1979.

40. Thompson, K.R., Nanda, Gramak: Reliability of Echo in diagnosis of infective E., Radiology, 125, 473, 1977.

41. Hickey, A., Wolfers, J. Wicken, D.: Reliabilitya and Clinical relevance of detection of vegetations by Echo in Infective Endocarditis.
British Heart J. 46, 624-8, 1981.

42. Pavidis, I.P., Kotler, Mintz, et al: Right heart Inf. Endocarditis.
Amer. Heart J. 107, 759-64, 1984.

43. Come, P., Isaacs, R., Riley, M.: Diagnostic Accuracy of MME in Active Infective Endocarditis, Amer. Heart J. 103, 839-47, 1982.

44. Rubenson, D., Tucker, C., Stinson, et al:
Echo in culture negative endocarditis Circulation 64, 641, 1981.

45. Obrien, Geiser, Infective Endocarditis and Echocardiography Amer. Heart J. 108: 386-94, 1984.

46. Pietro, D., Parisi, A.: Intracardiac masses in Non-invasive Cardiology, MCNA 64, 239, 1980.

47. Roy, P., Tajik, et al: Spectrum of Echocardiographic findings in Infective Endocarditis. Circulation 53, 474, 1976

48. Gington, L., Giegel, R., Griley, J: Natural history of Tricuspid valve Endocarditis: 2DE study. Amer. J. Cardiology 49, 1853, 1980

49. Come, P., Riley, M.: Echo recognition of perivalvular infection complicating Infective Endocarditis (Abstract) Amer. Heart J. 108, 166, 1984.

50. Mann, T., McLaurin, Grossman, et al: Assessing hemodynamic severity of aortic Regurgitation Due to Infective endocarditis NEJM 293, 108, 1975.

51. Quinones, M., Wagoner, R., Reduto, L. et al. Determination of Ejection fraction with 2DE Circulation 64, 744, 1981.

52. Davies, R., Stom, et al: MME in Infective Endocarditis Amer. J. Medicine 69, 57, 1980.

53, Dinubile, J., Mark, et al: Role of surgery in Infective Endocarditis, Ann. Int. Med. 96, 650, 1982.

54. Bowley et al: Right sided endocarditis, Consequences of Pulmonary artery Catheterization N.E.J.M. 311, 1152, 1984.

55. Pelletier/Petersdoff: Infective endocarditis pg 970-975
Harrisons Principles of Internal Medicine, 11th Edition

56. Goldwin, John, The challenge and Reproach of IE
British Heart J. 54, 115-8, 1985.

57. Gray, Ian R.,: Infective Endocarditis - Editorial
British Heart J. 57, 211-3, 1987.

58. Statistical Returns (Annual), 1988, K.N.H.

59. Varma, M., McHiskey et al, Heart Failure in IE
British Heart J. 55, 191, 1986

60. Andy, J., Sheikh, M., Ali, N. et al, Echo Observation
in Opiate addicts with Active IE.
Amer. J. Cardiology 40, 17, 1977.

61. Weinstein Louis, Infective Endocarditis Pg 1093-1134
in Textbook of Cardiovasc. Medicine 3rd Edition
Editor Braunwald.

62. Lore, W., Use of Echo in diagnosis and follow up of
Aortic Valve Endocarditis
E.A.M.J. 64, 561, 1987

63. Silimperi Harris, P. Kisslo, Lesion Fate in Endocarditis
Circulation (Supp II) 58, 236, 1978.

64. Infective Endocarditis, The Journal of Antimicrobial
Chemotherapy Supp. A., Vol. 20, Sept. 1987

65. Cowan and Steel: Manual for Identification of
Medical bacteria.

66. Henry, W.L., De Maria, A.W. Graunia, K. et al.
Report of American Society of Echocardiography Committee on
nomenclature and Standards in 2DE. Circulation 62, 212-217, 1980.

Appendix I

Proforma.

1. Name ..... Unit ..... Age ..... Sex .....

2. Presenting symptoms 1-YES 2-NO

Fever ..... Headaches ..... Skin rash .....

Chills ..... Cough ..... Haemoptysis .....

Malaise ..... Dyspnoea ..... Neurological Deficit ..

Nausea/Vomiting ..... Night sweats .... Mental status change

Anorexia ..... Myalgia/Arthralgia ..... Abd pains .....

Weight loss ..... Swollen feet ..... Abd Swelling .....

palpitation ..... Chest pain ..... Other(Specify) .....

3. Duration of symptoms prior to diagnosis (... weeks)

1. < 2/52 2. 2/52 - 8/52 3. > 8/52

4. Presenting Clinical signs 1-YES 2-NO

Fever Temp $38^{o}C$ ..... Janeways lesions ..... Splenomegaly

Pallor ..... Fingerclubbing ..... Hepatomegaly .....

Petechial Haemorrhages ..... Arthritis .... Neural deficit .

Splinter Haemorrhages .... Edema .... Mental Status change ...

Osler's nodes ..... Crackles ..... Roth spots .....

5. Cardiovascular System

Pulse/beats/Min) ..... Rhythm ..... Character .....

BP systolic ..... Diastolic ..... Apex beat .....

Murmurs: Location	Systolic	Diastolic	Radiation
Apical	.....	.....	.....
Tricuspid	.....	.....	.....
Aortic	.....	.....	.....
Pulmon	.....	.....	.....

6. Antibiotic therapy within one week prior to diagnosis

1-YES 2-NO ....

Drug ..... Duration .....

7. Precipitating events 1-YES 2-NO

Local foci of infection ..... Genitor Urinary instrumentation

Dental manipulation ..... Surgical Operation .....

Parenteral drug abuse/use ..... No precipitating event .....

I.V. indwelling ..... Other .....

8. Predisposing cardiac disease 1-YES 2-NO

Rheumatic heart dx ..... Cardiac murmur (Unclear cause) ....

Cardiac prosthesis/surgery ..... Other(Specify) .....

Congenital heart dx ..... No cardiac lesion .....

9. Complications 1-YES 2-NO

Congestive cardiac failure (grade) ..... Anaemia .....

Stroke ..... Death.....

Neuropsychiatric ..... Nil .....

Renal dx ..... Other(Specify) .....

10. Laboratory data

Hb level < 6g/dl 2.6-8g/dl 3.8-12g/d 4 > 12g/dl ....

WBC count 1. < $10x10^{9/l}$ 2. ≥ $10x10^{9/l}$ .....

Platelet Count 1.< 50000 2. 50-100000 3. > 100000 ..

ESR 1. 0-10mmhr 2. 11-30mmhr 3. > 30mmhr .....

Blood cultures 1. Positive 2. Negative

Organisms ..... Sensitivity .....

Urine Hematuria 1. YES 2. NO ..... Protenuria .....

Culture 1. Positive 2. Negative

Organism ..... Sensitivity .....

Blood Urea Nitrogen 1 ⩽ 7mmol/l 2. ⩾ 7mmol/l .....

Serum creatinine 1 ⩽ 106Hmol/l 2. > 106Hmol/l .....

Widal test 1. Positive 2. Negative

Brucella test 1. Positive 2. Negative

Throat swab 1. Positive 2. Negative

Organism ..... Sensitivity

11. Chest X-ray 1. Normal 2. Abnormal

Specify 2. .....

12. Electrocardiogram 1. Normal 2. Abnormal

Specify 2. .....

13. PM done (where applicable) Vegetations confirmed 1. YES

2. NO CVS Report .....

14. Disease other than IE 1-YES 2-NO

Specify .....

14. Echocardiographic data

Examination No.	Date of Exam	Duration of Symptoms	Duration of Therapy	Vegetations # 1-YES 2-NO SITE: MV	AV	TV	PV	ME	Echo Measurements. AoR	LA	LVID d	LVIDs	IVS	LVPW	EF	SV	HR	CO	Vcf	Other Echo Abnormalities	Echo Diagno Sys
1ST																					
2ND																					
3RD																					
4TH																					

Key MV - Mitral valve
AV - Aortic "
TV - Tricuspid valve
PV - Pulmonary valve
ME - Mural endocardium
AoR - Aortic root (cm)
LA - Left Atruim (cm)
LVIDs - Left Ventr. Internal Dia meter (cm) "Systole
LVIDd " " " " " (") "
IVS - Intr - Ventricular Septum

LVPW - Left Ventric. Posterior wall (CM)
EF - Ejection fraction
SV - Echo Stroke Vol l/min
HR - Heart rate beats/Min
CO - Cardiac Output
Vcf - Mean circumferential fibre shortening circles/sec.