

Clinical Profile and Short Outcome of Infective Endocarditis as A Single Center Experience

Dr. Sabah Shalal Hussain. ⁽¹⁾ Dr. Ahmed Mohammed Saeed. ⁽²⁾ dr. Ahmed Shams-Aldeen Thanoon. ⁽¹⁾ Dr Fawaz Mahmood Mustafa AlFaqe ⁽³⁾

- (1) Internal physician, cardiology. / MBChB., C.A.B.M. (med). Mosul center for cardiology and cardiac surgery.
- (2) Lecturer in internal medicine/M.B.CH. B, A.B.M.S (Med). College of Medicine, Ninevah University
- (3) Assistant Professor, Consultant Cardiovascular & thoracic surgeon, department of surgery, College of Medicine, Ninevah University.

Abstract

Background: growth of microorganisms on heart valves inner lining eventually cause what is called infective endocarditis. The pathological core lesion of infective endocarditis is termed a vegetation, which is composed of colonies of microorganisms, inflammatory cells, fibrin and platelets.

Aims: to clarify the clinical background, microbiological entity and in hospital course of patients with infective endocarditis in Ibn-AL Betar cardiac Centre.

Methods: all patients with infective endocarditis admitted to Ibn-AL Betar cardiac center between June 2018 and January 2020 were studied. Echocardiography and lab tests done for all patients. Pregnant women and pediatrics less than 14 years old were excluded from the study.

Results: our studied group was 30 patients, 30% female and 70% male with a median age of 34 years. Infective endocarditis affecting native valves in 20 patients (66.6%), prosthetic valves in 5 patients (16.6%), associating congenital heart disease in 4 patients (16.6%) and device related in one patient (3.3%). most common valve to be infected was the aortic valve. Blood culture was positive in 8 patients (26.6%). Staphylococcus aureus were the prevalent microorganism (16.6%). In hospital complications included: heart failure in 22 patients (73.3%), septic shock in 5 patients (16.6%), acute renal failure in 4 patients (13.3%), paravalvular abscess in 2 patients (6.6%), systemic embolization in 2 patients (6.6%) and septic pulmonary embolization in 2 patients (6.6%). Surgery is indicated in 14 patients (46.6%); of them 5 patients (16.6%) undergoing early surgical intervention. In hospital mortality was (16.6%).

Conclusion : Infective endocarditis is a hazardous disease. It comprises an increase in-hospital complications with an enhanced mortality rate (16.6%). Staphylococcus aureus are the prevalent microorganism. Fever and dyspnea are commonest presentations while peripheral stigmata of endocarditis were rarely observed in our study.

Introduction: Infective endocarditis (IE) is a term deals with cardiac valves or endocardium infection happened by microorganisms including mainly bacteria and fungi leading to a plenty of clinical stigmata to the body systems. ⁽¹⁾

Two clinical courses of infective endocarditis is known; the acute form which is mainly caused by staphylococcus aureus microorganism, manifests by rapid evolving symptoms and signs over a days to a little weeks, while the subclinical form is caused by streptococcus viridians, coagulase negative staphylococcus, enterococci and gram negative coccobacilli usually evolves over weeks to many months. ⁽¹⁾

Infective endocarditis has a world annual incidence of 3 to 9 cases per 100,000 persons. ⁽²⁻⁸⁾ The males are more infected than females. Risk factors for the disease are intravenous drug users, rheumatic heart disease, dialysis patients, diabetes and elderly. Infective endocarditis can involve cardiac valves with no known endocardial or valve lesions, while the more toxic course of the disease occur in patients with previous infective endocarditis, intravenous drug users, complex congenital heart diseases and prosthetic heart valves. ⁽²⁻³⁻⁶⁾ patients over 65 years old had a more propensity to suffering the disease may be due to the aging process.

Microbiology: Two most common causes of infective endocarditis are streptococci and staphylococci estimating to be 80% of all the cases, with accounts alternating with age of the patient, infection source, valve type and associated diseases. The incidence of Staphylococci now times are more encountered in different types of infective endocarditis, ⁽³⁻⁸⁻⁹⁾ mainly due to health care attributable cases, while the streptococci incidence becomes less in developed countries. ⁽³⁾ Culture negative endocarditis means a blood culture is negative occurring in one of two conditions; first one the patient had been taking an antibiotic previous to diagnosis of infective endocarditis ,while the second one is the patient exposed to fastidious microorganisms including HACEK group (Hemophilus, Aggregatibacter, Cardiobacterium, Eikenella and kingella), Bartonella, Brucella and Coxiella species in which more serological tests and specific microbiological investigations are needed.

(10-11-12-13)

Presentation And Diagnosis

The most important step in the diagnosis of infective endocarditis is the high clinical suspicion at the first stage of the disease. The precise diagnosis depends on modified Duke criteria which had 80% accuracy for the diagnosis in most cases, as delineated in table (1) and table (2).⁽¹⁴⁾

Table (1) definition of infective endocarditis according to the modified Duke criteria.

Definite IE
<p>Pathological criteria</p> <ul style="list-style-type: none"> • Microorganisms demonstrated by culture or on histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or • Pathological lesions; vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis <p>Clinical criteria</p> <ul style="list-style-type: none"> • 2 major criteria; or • 1 major criterion and 3 minor criteria; or • 5 minor criteria
Possible IE
<ul style="list-style-type: none"> • 1 major criterion and 1 minor criterion; or • 3 minor criteria
Rejected IE
<ul style="list-style-type: none"> • Firm alternate diagnosis; or • Resolution of symptoms suggesting IE with antibiotic therapy for ≤ 4 days; or • No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for ≤ 4 days; or • Does not meet criteria for possible IE, as above

Table (2) definitions of the terms used in the European society of cardiology 2015 modified criteria for the diagnosis of infective endocarditis.

Major criteria
<p>1. Blood cultures positive for IE</p> <p>a. Typical microorganisms consistent with IE from 2 separate blood cultures:</p> <ul style="list-style-type: none"> • <i>Viridans streptococci, Streptococcus gallolyticus (Streptococcus bovis), HACEK group, Staphylococcus aureus</i>; or • Community-acquired enterococci, in the absence of a primary focus; or <p>b. Microorganisms consistent with IE from persistently positive blood cultures:</p> <ul style="list-style-type: none"> • ≥ 2 positive blood cultures of blood samples drawn > 12 h apart; or • All of 3 or a majority of ≥ 4 separate cultures of blood (with first and last samples drawn ≥ 1 h apart); or <p>c. Single positive blood culture for <i>Coxiella burnetii</i> or phase I IgG antibody titre $> 1:800$</p>
<p>2. Imaging positive for IE</p> <p>a. Echocardiogram positive for IE:</p> <ul style="list-style-type: none"> • Vegetation; • Abscess, pseudoaneurysm, intracardiac fistula; • Valvular perforation or aneurysm; • New partial dehiscence of prosthetic valve. <p>b. Abnormal activity around the site of prosthetic valve implantation detected by ^{18}F-FDG PET/CT (only if the prosthesis was implanted for > 3 months) or radiolabelled leukocytes SPECT/CT.</p> <p>c. Definite paravalvular lesions by cardiac CT.</p>
Minor criteria
<p>1. Predisposition such as predisposing heart condition, or injection drug use.</p> <p>2. Fever defined as temperature $> 38^\circ\text{C}$.</p> <p>3. Vascular phenomena (including those detected by imaging only): major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions.</p> <p>4. Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor.</p> <p>5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.</p>

Microbiologic Diagnosis

The microorganism should be specified in microbiological diagnosis of infective endocarditis for clarifying the demanded treatment. Routinely Blood cultures should be done before the treatment. three subsets of blood cultures are crucial to be performed. in 90% of the cases the causative agent can be identified. If infective endocarditis suspected to be caused by fastidious organisms, special serologic tests and immunostaining techniques should be done in patients with negative blood culture tests in whom associated risk factors for the disease is founded. ⁽¹⁰⁻¹⁶⁾

Diagnosis Of Valvular Lesions

A vegetation on a native valve or a localized abscess or a dehiscence of a prosthetic valve is mandatory for the echocardiographic diagnosis of the disease whether done by transthoracic or transesophageal route. Transesophageal echocardiography should be done in patients where the transthoracic views is suggestive but not informative for fully diagnosing the disease and in presence of intracardiac devices or prosthetic heart valves due to higher resolution and well positioning of the prop during the examination. ⁽⁷⁾

Combined transthoracic and transesophageal echocardiography shows vegetation's (Fig. 1). ⁽⁷⁻⁸⁾ if a new complication had been occurred, transthoracic or transesophageal echocardiography must be repeated for the suspicion of finding a new stigma. ⁽⁸⁾

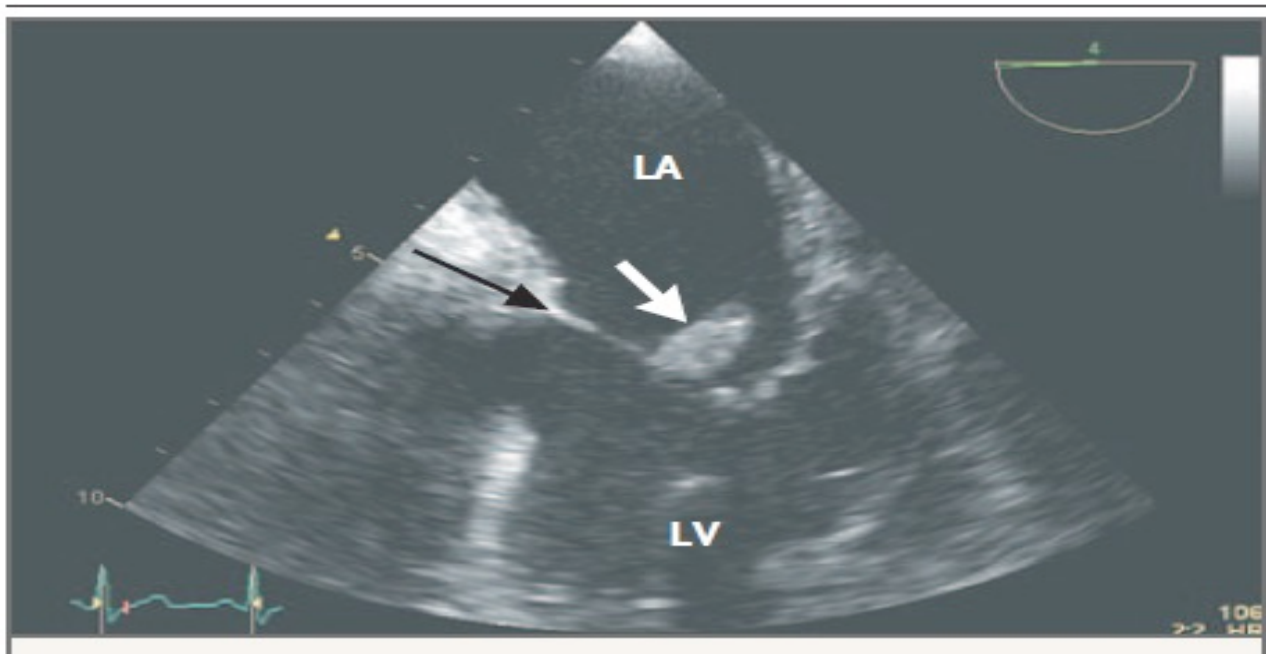


Figure (1) Transesophageal echocardiography showing a large vegetation on a native mitral valve

Treatment

In patients with infective endocarditis, empirical treatment at the first to be accomplished without any delay, and later treatment according to the culture and sensitivity tests had been identified the microorganism. Duration of treatment ranged from 2 weeks for uncomplicated native valve endocarditis to 6 weeks for a prosthetic valve endocarditis including special regimes for each microorganism.⁽¹⁷⁾ surgery should be offered for patients not responded to antimicrobial therapy or intractable heart failure or a large vegetation.⁽¹⁸⁾

The main indications for early valve surgery are heart failure, uncontrolled infection, and prevention of embolic events (Table 2).⁽¹⁹⁾

Aortic or mitral-valve infective endocarditis with large vegetations (>10 mm in length) after one or more embolic episodes, despite appropriate antibiotic therapy, especially during the first 2 weeks of therapy	Urgent
Aortic or mitral-valve infective endocarditis with large vegetations (>10 mm) and other predictors of complicated course (heart failure, persistent infection, or abscess)	Urgent
Isolated, very large vegetations (>15 mm); surgery may be preferred if a procedure preserving the native valve is feasible	Urgent

Table 2. Indications for and Timing of Surgery in Patients with Left-Sided, Native-Valve Infective Endocarditis.*	
Indication	Timing of Surgery†
Heart failure	
Aortic or mitral-valve infective endocarditis with severe acute regurgitation or obstruction causing refractory pulmonary edema or cardiogenic shock	Emergency
Aortic or mitral-valve infective endocarditis with fistula into a cardiac chamber or pericardium causing refractory pulmonary edema or cardiogenic shock	Emergency
Aortic or mitral-valve infective endocarditis with severe acute regurgitation or obstruction and persistent heart failure or signs of poor hemodynamic tolerance (early mitral-valve closure or pulmonary hypertension)	Urgent
Aortic or mitral-valve infective endocarditis with severe regurgitation and heart failure easily controlled with medical treatment	Elective
Uncontrolled infection	
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation, or dehiscence of prosthetic valve)	Urgent
Persistent fever and positive blood cultures for >5–7 days	Urgent
Infection caused by fungi or multidrug-resistant organisms, such as <i>Pseudomonas aeruginosa</i> and other gram-negative bacilli	Elective
Prevention of embolism	

* Adapted from Habib et al.^{19†} Emergency surgery was defined as surgery performed within 24 hours after the condition was identified, urgent surgery as that performed within a few days after the condition was identified, and elective surgery as that performed after at least 1 or 2 weeks of antibiotic therapy.

Aim of study :To determine the clinical characteristics, microbiological profile, and in hospital outcome of patients with infective endocarditis in Ibn-AL Betar cardiac center.

Patient and Methods :our study was a cross-sectional, observational study involving 30 patients had been estimated to be as infective endocarditis in regard to the definition clarified by modified Dukes 'criteria in a period of 19 months from June 2018 to January 2020 who had been admitted to Ibn Al-Betar cardiac Centre whether referred from another hospital or private clinic.

Every patient having symptoms or signs goes with the diagnosis of IE was accepted for clinical estimation and sent for demanded investigations.

A detailed background history with a history of old events of Rheumatic heart disease and infective endocarditis, and any elapsed treatment history was looked for. Detailed clinical examination was applied with specified precordial examination was made, any characteristics of IE, and its metastatic infections was followed. Investigated parameters including a blood count, blood film, erythrocyte sedimentation rate, serum biochemistry profile, general urine analysis, and specific investigations for special patients.

Microbiological analysis including at least three bottles of blood cultures, each done from different puncture site at least one hour apart, for aerobic media (BacT/ALERT).

Transthoracic echocardiography (TTE) on vivid E 9 analyzer with standardized view done for every patient, by one echo cardiographer to reduce bias. Whole study was accomplished with consideration to the heart valves and intra cardiac shunts, size, number and location of vegetations, with careful estimation of systolic left ventricular ejection fraction, abnormal wall motions abnormalities, and local abscesses or perforations sited at the valves and/or sub valvular apparatus. If the presence of vegetation, abscess or valve dehiscence is in doubt then sending the patient for transesophageal echocardiography is the role.

Statistical Analysis :By using Microsoft Excel, data had been entered into a specific sheet, then transferring the file into statistical package for social science (SPSS, Chicago, IL, USA) version 25 formats. With performing the normality test, variables show significant Kolmogorov-Smirnov indicating that variables are normally distributed and dealt with metric statistics. Comparing the variables by students T test, while Chi square test were used for comparing categorical statistics. Paired t test using for dealt with repeated measures. Our study adopted a level of 0.05 to ificant.

Results

A total number of 30 patients had been enrolled in the study. Patients age were encountered between 16 and 68 years with a mean of 34 ± 15 years. Sex distribution shows 21 males (70%) and 9 females (30%).

The duration of symptoms before diagnosis was long ranged between 7 days and 120 days with a mean of 35 ± 29 days. Hospital stay of our patients ranged between 5days and 49days with a mean of 29 ± 12 days as shown in table (1).

Table (1) demographic data for IE patients

Parameters	Mean ±SD
Age	34±15
Sex	21male/9 Females 70% /30%
Clinical Presentation	Acute / Sub-Acute 13 (43%)/ 17(56%)
Duration Of Symptoms Before Diagnosis	35±29
Duration Of Hospitalisation	29±12

Among the comorbid diseases associated with IE patients, hypertension was common followed by diabetes mellitus which present less frequently as clarified in figure (1).

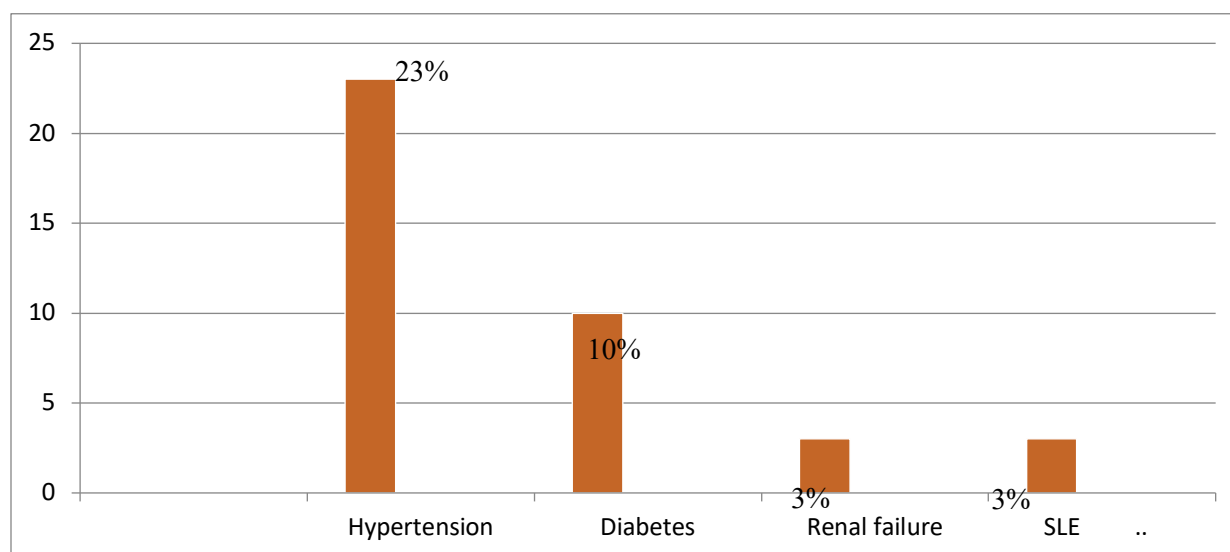


Figure (2) Comorbidity associated with IE patients.

According to modified Dukes criteria, 8 patients (27%) having two major criteria while 22 patients (73%) having one major with three minor criteria. Most patients (93.3%) had fever and temperature was between 38°C and 40°C followed by dyspnea (70%).other manifestations in a decreasing frequency showing malaise (63.3%), anorexia (56.6%), cough (43.3%), weight loss

(23.3%).chest pain presented in (20%) of patients .while arthralgia also documented in (20%) of patients, backache occur in only one case (3.3%) as shown in figure (2).

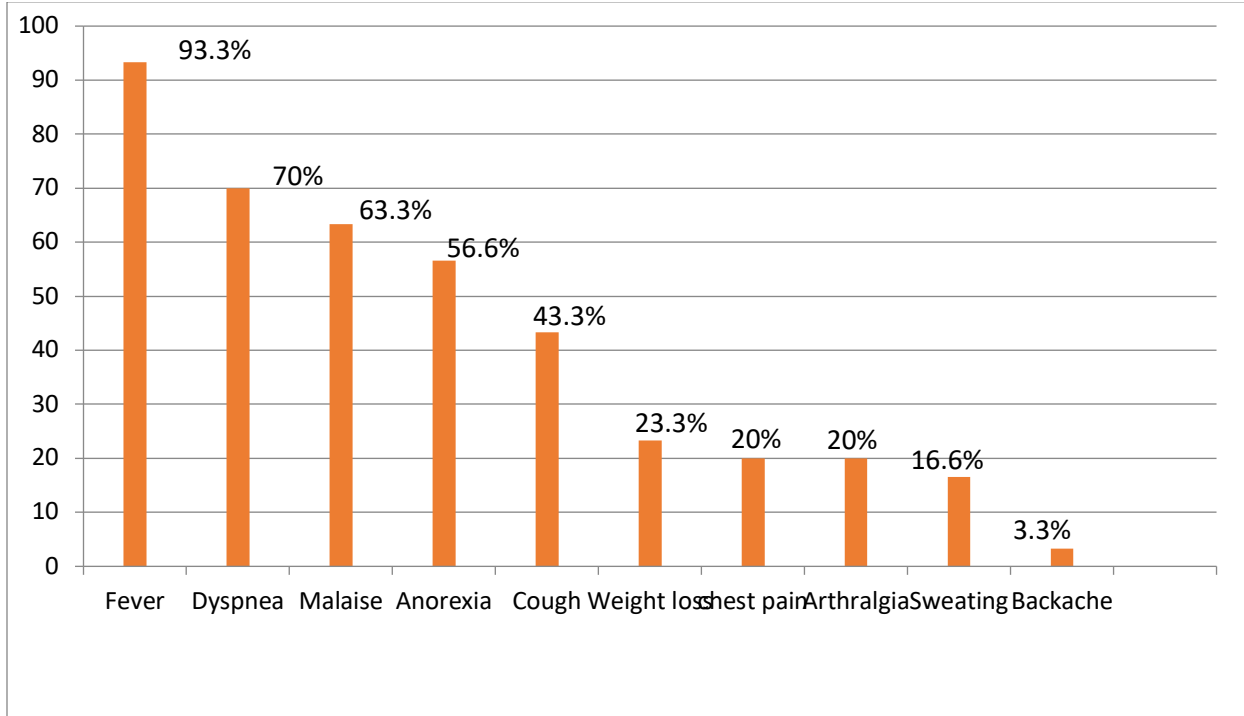


Figure (3) Symptoms associated IE Patients

Physical examination of our patients shows (56.6%) had pallor, 53.3% with auscultated murmur, 36.6% with pedal edema, finger clubbing with 33.3% and raised JVP in 26.6%.splenomegaly was observed in 26.6%.documented splinter hemorrhage and Jane way lesions occur in two patients for each while Osler nodes had been observed in one case.as shown in figure (3).

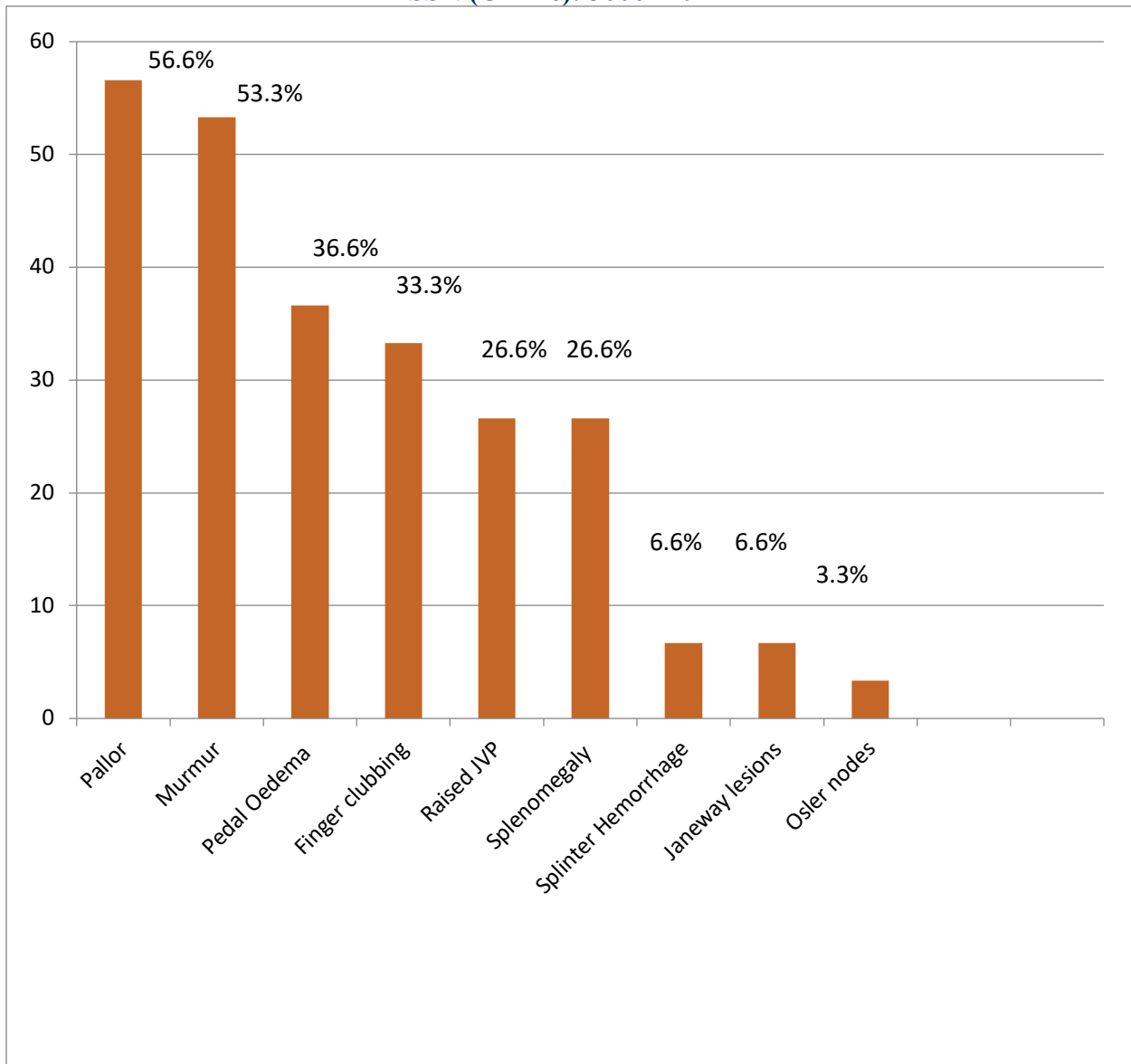


Figure (4) Signs associated IE patients

In our study 19 patients (63.4%) having pre-existing cardiac disease by history while 11 patients (36.6%) were not known to have cardiac disease. There is a one case of tricuspid valve IE with history of previous infective endocarditis had been documented in our patients, also there was no preceding dental intervention before clinical sequel of infective endocarditis had been reported. The spectrum of previous cardiac diseases were demonstrated in figure (4).

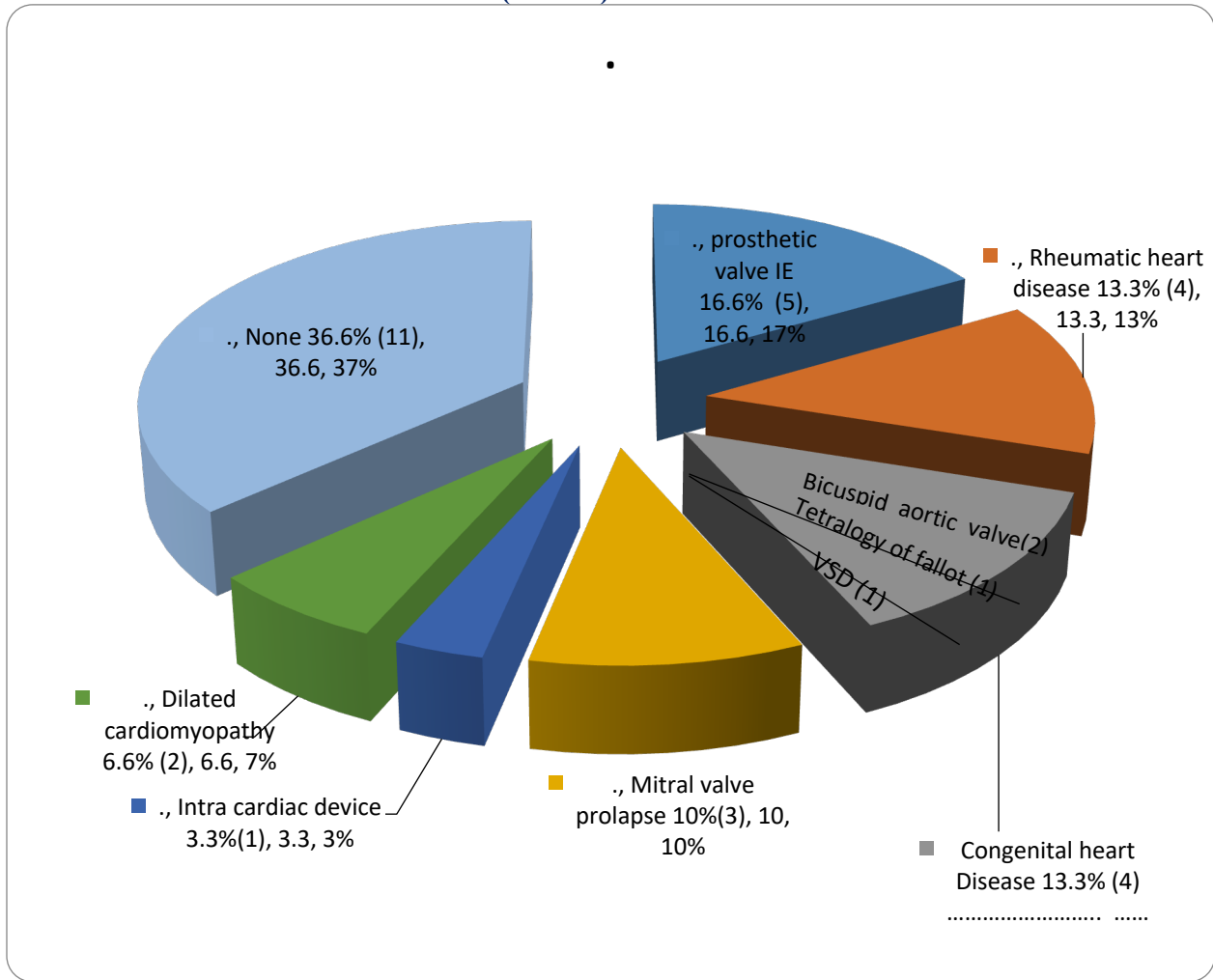


Figure (5) Distribution of the patients according to pre-existing cardiac disease.

Base line investigatory parameters show a mean of white blood cell count of 11.088 ± 6.54 and 10 patients have a leukocytosis. The mean of erythrocyte sedimentation rate and hemoglobin were 64.067 ± 30 and 11.14 ± 2.42 , with other lab findings are shown in table (2).

Table (2) Baseline laboratory investigation values.

Parameters	Mean ±SD	Reference Range
Haemoglobin	11.14±2.427	12-16 G/L
White Blood Cell	11.088±6.54	4-11 *10 ³
Erythrocyte Sedimentation Rate	64.067±30.1	<20
Blood Urea	42.37±32.1	15-45 Mg/Dl
Creatinine	1.08±0.567	0.5- 1.3 Mg/Dl
SGOT	55±58.5	15-40 IU /L
SGPT	40±39.8	15-40 IU /L
Albumin	3.3±0.7	3.5-5.3 Mg/Dl

Blood culture was positive in 8 patients (26.6%) while it was negative in the remaining 22patient (73.3%) in spite of repeating blood sample taking and incubation for 7 days. The main pathogen identified was gram positive microorganism, and of those staph. Aureus was the commonest (71.4%), followed by (14.3%) for each staph.epidermidis and streptococcus viridians. A single culture was positive for gram negative organism and was pseudomonas.spp. Figure (5) pie chart showing a distribution of microbial causative agents of IE on blood culture basis.

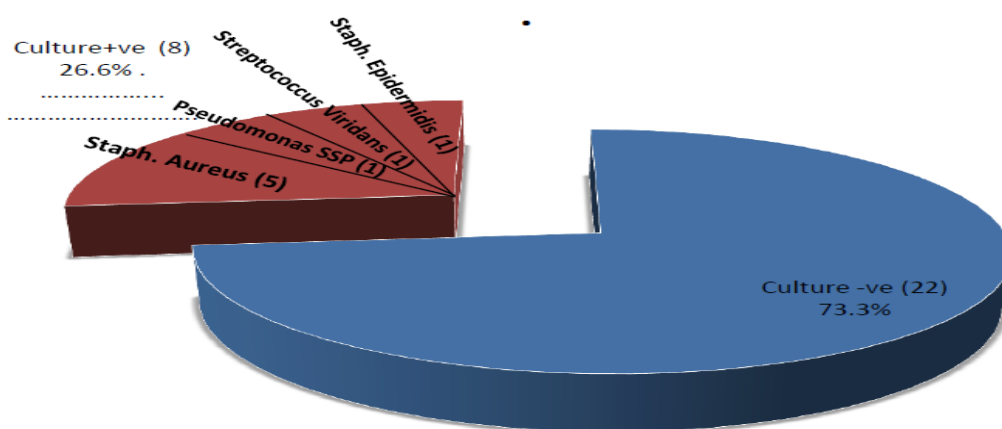


Figure (6) Pie chart showing a distribution of microbial causative agents of IE on blood culture basis.

Transthoracic echocardiography (TTE) has been done in all cases. Aortic valve was the commonest involved site (43.3%) while mitral valve involvement was (26.6%) followed by

tricuspid valve (13.3%) and mixed aortic and mitral valves in (6.6%).regarding the nature of the valves involved, they are native in (76.6%) and prosthetic in (13.3%).lesions identified by echocardiography are a vegetation in (93.3%) and localized aortic root abscess in (6.6%) of which had been proved by TTE were (63.3%) in native valves and (3.3%) in prosthetic ones while transesophageal echocardiography (TEE) has an approval of the remaining suspicious native valves involvement in (13.3%) and the remaining prosthetic valves (10%) and three cases (10%) of none valve structures involvement. Table (3) showing the findings of echocardiography among the enrolled patients.

Table (3) Echocardiographic findings among the studied patients

Site Of Involvement	Number	Percentage
Aortic Valve	13	43.3%
Mitral Valve	8	26.6%
Tricuspid Valve	4	13.3%
Mitral And Aortic Valve	2	6.6%
Non- Valve Structure:	3	10%
-VSD	1	
-TOF	1	
-Pacemaker Lead Related	1	
Nature Of The Valve		
Native	23	76.6%
Prosthesis	4	13.3%
Identified Lesions		
Vegetation	28	93.3%
Abscess	2	6.6%
Lesions Proved By TTE		
Native	19	63.3%
Prosthetic	1	3.3%
Lesions Proved By TTE		
Native	4	13.3%
Prosthetic	3	10%
Non Valve Structure	3	10%

Regarding the outcome of our patients during their stay in the ward ,22 patients (73.3%) developed heart failure of whom; 4 patients (13.3%) had NYHA class I ,8 patients (26.6%) with class II ,7 patients with (23.3%) with class III and 3 patients with class IV .four patients suffered from acute renal failure which needs dialysis, three of them received antibiotic course (vancomycin +gentamycin).

Septic shock were diagnosed in 5 patients (16.6%). thromboembolic sequel ,as a spread of emboli from vegetation of IE were documented in 4 patients (13.3%); two of whom having pulmonary embolism causing infarction or lung collapse and one patient had cerebrovascular accident resulting in left sided hemiparesis and the other develop brain abscess due to transmission of infected embolus.

Treatment was began at empirical evidence in all the patients after the samples of blood for blood culture had been aspirated and later on according to results of sensitivity. While approximately half of the patients were discharged after completing the course of antimicrobial therapy (53.3%), the remaining 14 patients (46.4%) were referred to surgery. 9 patient (36.6%) had been referred lately(after completing the course of antibiotics therapy) while 3 patients (10%) refereed early (during the course of antibiotics therapy) for surgical intervention; one of them with large vegetation, the second with uncontrolled infection and the third with associated brain abscess.

Mortality was high of five patients (16.6%) and death was attributed to sepsis in 10%, refractory heart failure in 3.3% and brain abscess in the last one. Table (4) clarify the clinical outcome of studied patients with infective endocarditis.

Table (4) Clinical outcome of studied patients with infective endocarditis

Outcome	Number	Percentage
Heart failure	22	73.3%
I	4	13.3%
II	8	26.6%
III	7	23.3%
IV	3	10%
Acute renal failure	4	13.3%
Septic shock	5	16.6%
Pulmonary embolism	2	6.6%%
Brain Abscess	1	3.3%
Cerebrovascular Accident	1	3.3%
Management		
Medical therapy only	16	53.3%
Referral to surgery	14	46.6%
Early Referral	5	16.6%
Late Referral	9	30%
Prognosis		
Discharge	25	83.3%
Death	5	16.6%

Discussion

Infective endocarditis remains a less common disease with a catastrophic entity in general medicine, as its diagnostic modalities requires an index of suspicion and its treatment needs a multidisciplinary approach. ⁽²⁰⁾

Mean age of patients was 34 ± 15 years with a preponderance of ratio of male to female patients by 70%:30%. it is a comparable to an Indian study done Kothari et al.2005⁽²¹⁾ and Gar et al.2005⁽²²⁾ where mean age was 34 years and 29 years respectively while Hill et al ⁽²³⁾ found that 50% of IE cases in Europe and united states of America happened in patients more than sixty years old. This propensity could be caused by the reduction of incidence of rheumatic heart disease in the developed world and increasing numbers of elderly people who suffered a long standing degenerative valvular disease and more required valvular replacement.

In the present study, mean duration of symptoms before diagnosis was 35 ± 29 days. Hill et al. ⁽²³⁾ represented the mean among symptoms beginning and diagnosis of IE was 8 days, while Kaser Elini ⁽²⁴⁾ has reported a mean of 65 ± 96 days which is long. The delay of diagnosis may be related to treatment of fever without finding the real cause, the expeditious use of antimicrobial therapy by our patients and pharmacists and the undue delay in referring the patient to the tertiary cardiac Centre.

Fever is an important manifestation of IE. Our study shows (93.3%) of patients had mild to moderate grade fever which was the most common symptom encountered followed by dyspnea (70%). This is comparable to a study done by Murdoch et al.2009 ⁽²⁵⁾ which documented fever to be the predominant symptom (100%) of cases.

Regarding physical examination, pallor was the commonest sign (56.6%) followed by auscultated murmur (53.3%).pallor was attributed to anemia as our study shows high percentage of patients with low hemoglobin (11.14 ± 2.427).this is in accordance with an Indian study done by Chaudhary et al. ⁽²⁶⁾ however anemia in one American series was 34% of cases. ⁽²⁷⁾ Anemia could be pronounced mainly due to long illness duration before diagnosis and loss of appetite encountered the clinical sequel. In present study, enlargement of spleen occurs in 8 patients (33.3%).it had been identified to be in 36-60% of Indian patients. ⁽²⁶⁾

Although we searching vigorously for peripheral stigmata of IE, there is a paucity of these findings (splinter hemorrhage in 2 patients, Jane way lesions in 2 patients and Osler nodes in one patient). many studies have enrolled that these features are less common signs of IE nowadays. ⁽²⁸⁻²⁹⁾

our study showed 36.6% had no preexisting heart disease.it was 47%in a French study done by B.Hoen et al. ⁽³¹⁾ the incidence of rheumatic heart disease (RHD) was 13.3% in current study which is approximately similar to studies of Thailand and Hong Kong that document RHD in 12% and 18% of the cases respectively. ⁽³²⁾ While a study from Singapore, ⁽³³⁾ showed that RHD incidence was just 4% of IE cases. The changing percentages among these studies could be due to a much incidence of RHD in developing countries. Rivas p et al. ⁽³³⁾ found that prosthetic

valve IE accounts for 15-32% which is similar to our study showing prosthetic valve IE to be 16.6% of cases.

Regarding congenital (CHD) as a risk factor IE, current study found an incidence of 13.3%. CHD with IE documented by Tariq M et al. ⁽³⁴⁾ to be 31% and 2.2% by Rathor et al. ⁽³⁵⁾ the differences between researches may be due to improved survival with congenital heart disease. Presenting study showed that mitral valve prolapse associated IE was 10% of cases which is approximate to a study done by Stekelberg J M et al. ⁽³⁶⁾ and was 7%.

IE precipitated by intra cardiac devices in our study was 3.3% which is in agreement with documented rate between 0.13% to 19.9% for permanent pacemakers and 0.7% to 1.2% for implanted intra cardiac defibrillators. ⁽³⁷⁾

According to our blood culture results, 73.3% was represented to have negative result. This entity is concordant with multi studies from developing countries. ⁽³⁴⁻³⁸⁾ while other studies like Chen CH et al. ⁽³⁹⁾ documents 5.2%, Zamorano J et al. ⁽⁴⁰⁾ 8.7% and in united states of America enrolls only 2.5-30% of all IE cases. ⁽⁴¹⁾ the high culture negative IE is explainable due to infection with fastidious microorganisms or nonbacterial organisms or that patient in our country and other developing countries take a lot of antibiotics prior hospital admission by their local area doctors or even pharmacists.

Staphylococcus aureus was the comment organism which cultured accounting for 16.6% followed by 3.3% for streptococcus viridian's, staphylococcus epidermidis and pseudomonas spp. respectively. Rostagno et al. ⁽⁴²⁾ found in his study an increasing incidence of staph. Spp. (40%) than streptococcal spp. (20%) in 2010, also Castillo et al. ⁽⁴³⁾ reported an important increment in staph infection Epidemiology in 2011. These two studies are similar to our results.

TTE sensitivity for vegetation's detection in native valve endocarditis (NVE) is 45% to 65% while in TEE is 85% to 95%. TEE is the optimal technique in whom TTE is non diagnostic and is the preferred one in imaging the prosthetic valve endocarditis and pulmonary valve. ⁽⁴⁴⁾

In current study, vegetation's were present in 93.3% of cases and mostly involved the aortic valve and mitral valve. Aortic valve was infected in 43.3% while mitral valve in 26.6% of cases. Same results had been obtained in various Indian studies. ⁽²⁶⁻²⁹⁾ however mitral valve was more involved in western studies. ⁽⁴⁵⁾ This difference could be due to increasing incidence of mitral prosthetic valve and MVP as a risk factor for IE in Europe.

Regarding non valve structures associated IE we have three cases; two are CHD (VSD and TOF), in both of which vegetation's are appeared on the right aspect of the septal defect forming in the down pressure area and the associated leaflet of tricuspid valve. The remaining third case are a device (PPM) lead related IE; where vegetation's were seen as a thread like along the lead inside the right sided chamber.

In our study, transthoracic echocardiography clarify the presence of the lesions whether a vegetation or localized abscess in native valves (63.3%) and one case of prosthetic valve (3.3%) while transesophageal echocardiography identify the lesions in the remaining suspicious native

valves involvement (13.3%) ,remaining prosthetic valves (10%) and three cases (10%) of non-valve structure involvement.

Most common complication of IE in our study was heart failure, it represents 73.3% of cases, which is more than had been estimated by Tornos et al. ⁽⁴⁵⁾ and Van Le et al.⁽⁴⁶⁾ showing an incidence of 65% and 50% respectively. This is pronounced by the fact that IE causing destruction of valve leading to acute valve incompetence is the cardinal lesion of heart failure in the native valve IE.

Renal function impairment at hospital stay time is important indicator of less favorable outcome. ⁽⁴⁷⁾ Four patients (13.3%) were complicated an acute renal failure. AL-Aghbari et al. ⁽⁴²⁾ reported renal failure in 2.8% of his study, also Miyake et al.⁽⁵¹⁾ documented only one case of acute renal failure that occur during his study. This relative increment in in renal failure cases occurred due to delaying diagnosis of IE and the antibiotic regimen which the patient received during hospital stay.

Septic shock represent 16.6% of our patients, which is approximate to a study done by Habib et al.⁽⁴⁷⁾ which documented 13% of cases. Higher incidence of may be related to infection aggressiveness and improper early antibiotic therapy.

Embolic events are common life threatening complication of IE.² in our study we report 2 cases of systemic embolization, both of them due to aortic valve IE; one causing CVA and the second brain abscess by a seeding of infected embolus while Habib et al. ⁽⁴⁷⁾ report 13% of cases having systemic embolization. Differences between studies may be explained by the divergence in duration of study and number of vegetations and its size. In current study pulmonary embolization occur in two cases; one had tricuspid valve vegetation and the other complicating lead vegetation, both are caused by staph.aureus. Mathew et al.⁽³¹⁾ and Ruotsalainen et al.⁽⁵⁰⁾ observed that pulmonary emboli mostly complicating right sided IE that happened in 40-75% of intravenous drug addicts who have tricuspid valve IE. This decrement in pulmonary embolization in our study was due to the fact that tricuspid valve IE found in only four cases of our patients.

Management of IE patients rely on antimicrobial drugs and surgery for those with large vegetation, refractory heart failure or uncontrolled infection.

Although surgical opinion had been sought in all cases of IE in the present study, approximately half of the cases (46.6%) had been referred to surgery; 16.6% of them had early referral due to aortic root abscess (6.6%), large vegetation (3.3%), uncontrolled infection (3.3%) and brain abscess (3.3%) while 30% of patients referred late to surgery mostly due to heart failure complicating valve regurgitation. Nashmi et al. ⁽⁴⁸⁾ document that common indicators for surgery were heart failure in 7 cases (33.3%), large mobile vegetation in 4 cases (19%).

Patients receiving medical therapy only including the course of antimicrobial drugs constitute 53.3% of cases with favorable outcome and regular follow up.

In our result, mortality was 5 patients (16.6%); of whom blood culture was positive in 4 patients and three of them had staph. Infection. This result is near a Turkish cohort study done by Erbay

et al. ⁽⁴⁹⁾ that reported expired rate to be 20% while AL-Magheer et al. ⁽³⁴⁾ found a mortality of 38.7%. This difference between studies could be due to the small number of our patients.

Conclusion

Infective endocarditis remains a great challenge, with associated morbidity and mortality. age group of a youngsters is found to be more exposed with a mean of thirties. Fever, dyspnea and malaise are the main symptoms and pallor with auscultated murmur were the frequent signs documented. Mild anemia, leukocytosis and high ESR are very common. Vegetation's are considered the core lesions in echocardiographic study with TEE observed the better in detection of lesions. Aortic valve incompetence was the most common lesion. Staphylococci were the prevalent microorganism grown in positive blood culture. Heart failure was the more frequent and aggressive complication. The three commonest indications for early surgery were localized abscess formation, uncontrolled infection and large vegetation. Infective endocarditis is associated with high mortality (16.6%).

Limitations The followings are limitations of our study:

1. A short duration of the study in a single center encountered.
2. no long-term study of saved IE patients.
3. High incidence of culture negative IE may be due to improper lab technique in isolation of the causative microorganism or improper antibiotics giving previous to admission.
4. Estimation of fastidious organisms was not enrolled due to a lack of special serologic investigations.

Recommendations

1. Further larger multi-center study with large duration is recommended.
2. Improve lab facilities for more microbiological diagnosis.
3. Doing PCR (polymerase chain reaction) test for culture negative infective endocarditis who referred to surgery.

References

1. D. T. Durack, A. S. Lukes, D. K. Bright et al., "New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings," *The American Journal of Medicine*, vol. 96, no. 2, pp. 200–209, 1994
2. Correa de Sa DD, Tleyjeh IM, Anavekar NS, et al. Epidemiological trends of infective endocarditis: a population-based study in Olmsted County, Minnesota. *Mayo Clin Proc* 2010; 85:422-6. [Erratum, *Mayo Clin Proc* 2010; 85:772.]
3. Duval X, Delahaye F, Alla F, et al. Temporal trends in infective endocarditis in the context of prophylaxis guideline modifications: three successive population-

based surveys. *J Am Coll Cardiol* 2012; 59:1968-76.

4. Fedeli U, Schievano E, Buonfrate D, Pellizzer G, Spolaore P. Increasing incidence and mortality of infective endocarditis: a population-based study through a record-linkage system. *BMC Infect Dis* 2011; 11:48.

5. Federspiel JJ, Stearns SC, Peppercorn AF, Chu VH, Fowler VG Jr. Increasing US rates of endocarditis with *Staphylococcus aureus*: 1999-2008. *Arch Intern Med* 2012; 172:363-5.

6. Sy RW, Kritharides L. Health care exposure and age in infective endocarditis: results of a contemporary population based profile of 1536 patients in Australia. *Eur Heart J* 2010; 31:1890-7.

7. Murdoch DR, Corey GR, Hoen B, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. *Arch Intern Med* 2009; 169:463-73.

8. Selton-Suty C, Célard M, Le Moing V, et al. Preeminence of *Staphylococcus aureus* in infective endocarditis: a 1-year population-based survey. *Clin Infect Dis* 2012; 54:1230-9.

9. Tleyjeh IM, Abdel-Latif A, Rahbi H, et al. A systematic review of population based studies of infective endocarditis. *Chest* 2007; 132:1025-35.

10. Fournier PE, Thuny F, Richet H, et al. Comprehensive diagnostic strategy for blood culture-negative endocarditis: a prospective study of 819 new cases. *Clin Infect Dis* 2010; 51:131-40.

11. Houpiikian P, Raoult D. Blood culture negative endocarditis in a reference center: etiologic diagnosis of 348 cases. *Medicine (Baltimore)* 2005; 84:162-73.

12. Stehbens WE, Delahunt B, Zuccollo JM. The histopathology of endocardial sclerosis. *Cardiovasc Pathol* 2000; 9:161-73.

13. Brouqui P, Raoult D. Endocarditis due to rare and fastidious bacteria. *Clin Microbiol Rev* 2001; 14:177-207.

14. Li JS, Sexton DJ, Mick N, et al. Propose modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000; 30:633-8.

15. Greub G, Lepidi H, Rovey C, et al. Diagnosis of infectious endocarditis in patients undergoing valve surgery. *Am J Med* 2005; 118:230-8.

16. Lepidi H, Coulibaly B, Casalta JP, Raoult D. Autoimmunohistochemistry: a new method for the histologic diagnosis of infective endocarditis. *J Infect Dis* 2006; 193:1711-7.

17. Botelho-Nevers E, Thuny F, Casalta JP, et al. Dramatic reduction in infective endocarditis-related mortality with a management-based approach. *Arch Intern Med* 2009; 169:1290-8.

18. Morris AJ, Drinković D, Pottumarthy S, MacCulloch D, Kerr AR, West T. Bacteriological outcome after valve surgery for active infective endocarditis: implications

for duration of treatment after surgery. Clin Infect Dis 2005; 41:187-94.

19. Habib G, Hoen B, Tornos P, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC): endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. Eur Heart J 2009; 30:2369-413.
20. R. S. Math, G. Sharma, S. S. Kothari et al., "Prospective study of infective endocarditis from a developing country," *The American Heart Journal*, vol. 162, no. 4, pp. 633–638, 2011.
21. S. S. Kothari, S. Ramakrishnan, and V. K. Bahl, "Infective endocarditis—an Indian perspective," *Indian Heart Journal*, vol. 57, no. 4, pp. 289–294, 2005.
22. N. Garg, B. Kandpal, S. Tewari, A. Kapoor, P. Goel, and N. Sinha, "Characteristics of infective endocarditis in a developing country- clinical profile and outcome in 192 Indian patients, 1992–2001," *International Journal of Cardiology*, vol. 98, no. 2, pp. 253–260, 2005.
23. Hill EE, Herijgers P, Claus P, et al. Infective endocarditis: changing epidemiology and predictors of 6-month mortality: a prospective cohort study. Eur Heart J 2007; 28:196.
24. Al-Mogheer B, Ammar W, Bakoum S, et al. Predictors of inhospital mortality in patients with infective endocarditis. The Egypt Heart J 2012. Article in press.
25. Murdoch DR, Corey GR, Hoen BL. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century. Arch Intern Med. 2009; 169:463.
26. Chaudhary R. Active infective endocarditis observed in an Indian Hospital 1981-91. Am J Cardiol. 1992; 70:1453-8.
27. Baddour LM, Wilson WR, Bayer AS. Infective endocarditis: Diagnosis, antimicrobial therapy, and management of complications. A statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association. Circulation. 2005; 111:e394.
28. Kabde VR, Bidwai PS, Berry JN, Agarwal KC. Clinical and bacteriological studies in infective endocarditis. Indian Heart J. 1970; 22:318-32.
29. Agarwal RK, Gupta R, Agarwal SC, Dwivedi M. Bacterial endocarditis-its diagnostic problems. J Assoc Physicians India. 1981; 29:745-50.
30. Bayer AS, Bolger AF, Taubert KA. Diagnosis and management of infective endocarditis and its complications. Circulation. 1998; 98:2936.
31. Hoen B, Alla F, Selton-Suty C, et al. Changing profile of infective endocarditis: results of a 1-year survey in France. JAMA 2002; 288:75–81.
32. Yiu KH, Siu CW, Lee KL, Fong YT, et al. Emerging trends of community acquired infective endocarditis. Int J Cardiol 2007; 121: 119–22.

33. Rivas P, Alonso J, Moya J, et al. The impact of hospital-acquired infections on the microbial etiology and prognosis of late-onset prosthetic valve endocarditis. *Chest* 2005; 128:764–71.
34. Tariq M, Karim B. *Int J Collaborative Res Intern Med Public Health* 2009; 1(3):84–99.
35. Yousuf RM, How SH, Fauzi ARM, et al. Infective endocarditis in the east coast of peninsula Malaysia: a two year retrospective survey from Kuantan. *JK-Practitioner* 2006; 13(1):5–8.
36. Steckelberg JM, Wilson WR. Risk factors for infective endocarditis. *Infect Dis Clin North Am* 1993; 7:9–19.
37. Klug D, Balde M, Pavin D, Hidden-Lucet F, et al. Risk factors related to infections of implanted pacemakers and cardioverter-defibrillators: results of a large prospective study. *Circulation* 2007; 116:1349–55.
38. Rehman S, Ghulam Shabbier, Shahid M. Clinical presentation of infective endocarditis. *J Postgrad Med Inst* 2002; 16: 55–63.
39. Chen CH, Lo MC, Hwang KL, et al. Infective endocarditis with neurological complication: 10 year experience. *J Microbiol Immunol Infect* 2001; 34:119–24.
40. Zamorano J, Sanz J, Almeria C, et al. Difference between endocarditis with true negative blood cultures and those with previous antibiotic treatment. *J Heart Valve Dis* 2003; 12:256–60.
41. Mylonakis E, Calderwood SB. Infective endocarditis in adults. *N Engl J Med* 2001; 345:1318–30.
42. C. Rostagno, G. Rosso, F. Puggelli et al., “Active infective endocarditis: clinical characteristics and factors related to hospital mortality,” *Cardiology Journal*, vol. 17, no. 6, pp. 566–573, 2010.
43. J. C. Castillo, M. P. Anguita, M. Ruiz et al., “Changing epidemiology of native valve infective endocarditis,” *Revista Espanola de Cardiologia*, vol. 64, no. 7, pp. 594–598, 2011.
44. Kini V, Logani S, Ky B. Transthoracic and transesophageal echocardiography for the indication of suspected infective endocarditis: Vegetations, blood cultures and imaging. *J Am Soc Echocardiograph*. 2010; 23:396.
45. Tornos P, Iung B, Permanyer-Miralda G, et al. Infective endocarditis in Europe: lessons from the Euro heart survey. *Heart* 2005; 91:571–5.
46. Van Le, Gill S. Serious complications after infective endocarditis. *Dan Med Bul* 2010; 57(10).
47. Habib G. Management of infective endocarditis. *Heart* 2006; 92:124–30.
48. Nashmi A, Memish ZA. Infective endocarditis at a tertiary care centre in Saudi Arabia: review of 47 cases over 10 years. *East Mediterr Health J* 2007; 13:64–71.
49. Erbay AR, Erbay A, Canga A, et al. Risk factors for in-hospital mortality in infective endocarditis: five years’ experience at a tertiary care hospital in Turkey. *J Heart Valve Dis* 2010; 19(2):216.
50. Ruotsalainen E, Sammalkorpi K, et al. Clinical manifestations and outcome in *Staphylococcus aureus* endocarditis among injection drug users and non addicts: a prospective study of 74 patients. *BMC Infect Dis* 2006; 6:137.
51. Miyake M, Hatta K, Kameyama T, et al. Infective endocarditis developing as uremia. *Intem Med* 2005; 44:598–60