

Infective endocarditis in children-pattern, diagnosis, management and short term outcome in Sudan

Abstract

Introduction: Infective Endocarditis (IE) in children is relatively rare but causes significant morbidity and mortality when it occurs. The incidence of IE in children is increasing worldwide.

Objective: To identify pattern, management and short outcome of IE in Sudanese children.

Methods: Retrospective notes review of all the children from birth to 16 years old, diagnosed with IE at Ahmed Gasim Children's hospital, Khartoum North, Sudan. During the 12 month period starting from January 2017. All children who fulfilled Dukes criteria for Definite or Possible IE were included in the study.

Results: During the study period 6260 children were admitted to Ahmed Gasim Children's hospital, 47 patients fulfilled Dukes criteria for IE; Three patients were labelled as Definite and 44 as Possible, The majority of the patients were over five years old.

Of the 47 patients enrolled in the study, 34% had normal hearts and 66.0% were known to have structural cardiac disease; out of them, 17 patients (54.8%) were known to have Rheumatic heart disease (RHD) and 14 patients (45.2%) were known to have Congenital Heart Disease (CHD). The hospital mortality was 21.3%.

Conclusion and Recommendation: IE in Sudanese children is not rare and is associated with high hospital mortality, the health professionals should have a high index of suspicion to diagnose IE echocardiography and blood culture should be done whenever the possibility of endocarditis is entertained. The children, parents and caregivers of children with structural heart disease should be educated about IE's presentation and prevention.

Keywords: infective endocarditis, children, Sudan

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Introduction

Infective endocarditis (IE) is defined as an infection of the endothelial surface of the heart, which mainly involves heart valves, the mural endocardium, or septal defects.¹ All cases of IE evolve from a commonly shared process of bacteraemia, that allows the organisms to reach the endothelial surface of the heart, then adherence of the organisms to the surface and eventual invasion of the valvular leaflet and other tissues e.g. septal defects.² IE is associated with substantial morbidity and mortality; it is a serious condition and can be fatal if not treated early and aggressively. Although it is relatively rare in children in comparison to adults,³ studies from the West have shown that the incidence of IE in children is increasing due to the improved survival of children with complex CHD.⁴

Paediatric Infective endocarditis in the developing countries mainly occurs in the predisposing setting of RHD, followed up by CHD.⁵ Risk factors for IE include the presence of structural heart disease, prosthetic heart valve, intravenous drug use, and a recent history of invasive procedures. IE should be suspected in patients with unexplained fevers, night sweats, or signs of systemic illness. Diagnosis is made using the Duke criteria, which include clinical, laboratory, and echocardiographic findings.⁶ Despite advances in medical, surgical and critical care interventions, infective endocarditis remains a disease that is associated with considerable morbidity and mortality.³

Historically infective endocarditis was caused by *streptococcus viridans*, but recently other organisms such as *staphylococcus aureus*

are becoming more common, these changes will have implications for the choice of antibiotics and create additional therapeutic problems in the management of this potentially life threatening infection.⁷ Sudan, like other developing nations, has problems regarding rampant poverty, ignorance, late presentation, delayed diagnosis, availability and affordability of investigations e.g. Blood culture and cost of treatment.

We do not have data about IE in Sudanese children; to the best of our knowledge this is the first study to attempt to address this issue.

Objective

To identify pattern, management and short outcome of IE in Sudanese children.

Methods

Retrospective notes review of all the children from birth to 16 years old; diagnosed to have IE at Ahmed Gasim Children's hospital, Khartoum North, Sudan. During the 12 months period from January 2017 - December 2017. All children who fulfilled Dukes criteria for Definite or Possible IE were included in the study.⁶

Statistical analysis

Data was analysed using IBM SPSS version 25.0. Descriptive statistics presented in term of frequency tables with percentages and graphs, Bi variable analysis was performed to assess the relationship between the different characteristics of the patients and P value of 0.05

or less was considered statistically significant. Data was represented after analysis in form of uni-variable tables, cross tabulation (bi variable tables), figures and narrative illustration.

Results

During the study period there were a total of 6260 hospital admissions, 47 children were identified to have the diagnosis of IE and all of them were included in the study. There were 24 females (51.1%) and 23 males (48.9%) in the study group. The majority of the study group were in the age group over five years of age, in which there were 32 patients (68.1%). In the one to five years of age category there were 11 patients (23.4%), there were two patients (4.3%) in the six months to one year category and two patients (4.3%) younger than six months (Figure 1).

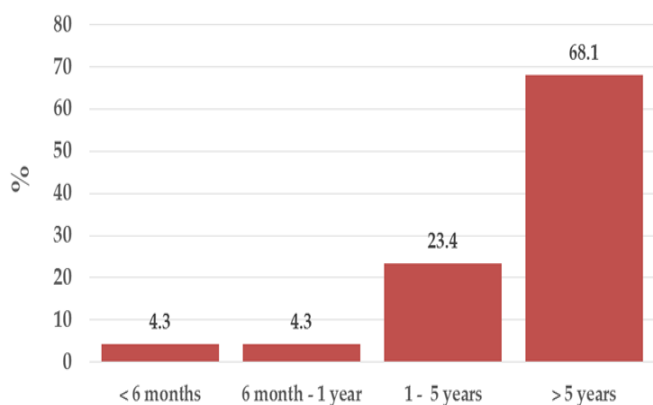


Figure 1 Study Group Age Distribution (n = 47).

Of the 47 patients in the study, 16 patients (34%) have normal hearts and 31 patients (66%) were known to have structural cardiac disease; out of them 17 patients (54.8%) were known to have RHD and 14 patients (45.2%) were known to have CHD. Out of the 31 patients with structural heart disease, only 17 patients (54.8%) were on regular follow up.

Only two patients (4.3%) had history of cardiac surgery more than 6 months prior to admission, both had ventricular septal defect closure.

18 patients (38.3 %) of the study group were from outside of Khartoum state and 29 patients (61.7%) were from Khartoum state (Table 1).

Table 1 Area of Residence (n = 47)

Characteristics	Categories	Frequency	Percent
State of residence	Khartoum	29	61.7
	Kordufan	5	10.6
	Darfour	5	10.6
	Kassala	2	4.3
	Algazira	2	4.3
	White Nile	2	4.3
	Gedarif	1	2.1
	River Nile	1	2.1

Clinical presentation: 42 patients (89.4%) patients presented with prolonged fever, 32 patients (68.1%) presented with symptoms and signs of heart failure, 26 patients (55.3%) presented with cough, 11 patients (23.4%) have new/changing heart murmur and two patients (4.2%) have splenomegaly (Figure 2).

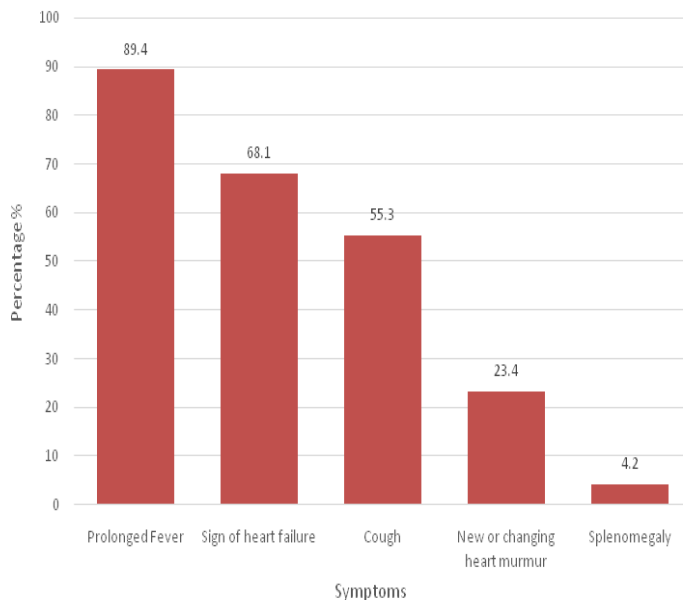


Figure 2 Clinical Presentation (n = 47).

Regarding Investigations, 11 patients (23.4%) had echocardiography, all the patients who had echocardiography showed vegetation. Eight patients (17%) had blood culture done, out of the eight patients who had blood culture done four came back as positive, three grew *staph aureus* and one grew *strep viridians* (Table 2).

Table 2 Blood Culture timing and results (n = 8)

Results of blood culture	Categories	Frequency	Percent
Timing of blood culture from admission	< 48 Hours	2	25
	48 Hours - 7 Days	4	50
	> 7 Days	2	25
Result of blood culture	Positive	4	50
	No Growth	4	50
Isolated organism (n = 4)	staph aureus	3	75
	streptococcus viridance	1	25

Two patients had sample for culture collected less than 48 hours after admission, four patients had samples taken two to seven days after admission and two patients had samples taken more than seven days (Table 2).

Testing of urine for microscopic hematuria was done in 23 patients (48.9%) of all study groups, testing showed a positive result in eight patients (17.0%), and 15 patients (31.9 %) showed a negative result (Figure 3).

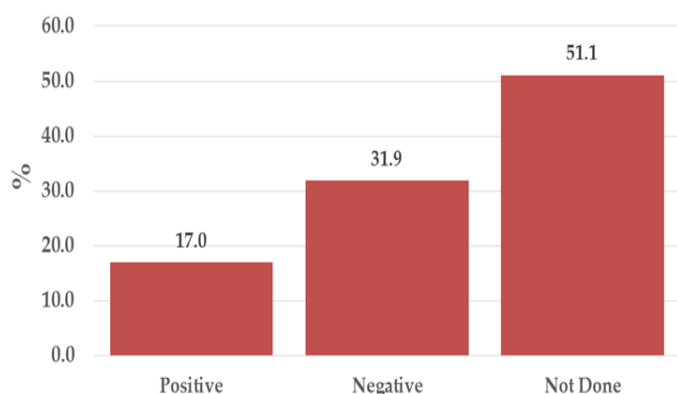


Figure 3 Microscopic Haematuria (n = 47).

39 patients (83%) received Ceftriaxone and Vancomycin, five patients (10.6%) received Benzyl Penicillin and Gentamycin and three patients (6.4%) received Meropenem (Table 3).

Table 3 Antibiotics used (n = 47)

Treatment	Frequency	Percent
Benzyl Penicillin and Gentamycin	5	10.6
Ceftriaxone and Vancomycin	39	83
Meropenem	3	6.4
Total	47	100

24 patients (51.1%) received iv antibiotics for less than two weeks, 12 patients (25.5%) received iv antibiotics between two to four weeks and 11 patients (23.4%) received iv treatment for 6 weeks (Table 4).

Table 4 Duration of treatment (n = 47)

Categories	Frequency	Percent
< 2 Weak	24	51.1
2 - 4 Weeks	12	25.5
6 weeks	11	23.4

36 patients (76.6%) had been discharged in good conditions, 10 patients (21.3%) died and one patient (2.1%) developed Cerebrovascular Accident (CVA). From those who died, five of them (50%) died within a week of admission.

The most common cause of death was cardiogenic shock in eight patients (80.0%), and respiratory failure in two patients (20.0%).

From all of the study group only three (6.4%) were diagnosed to have Definitive IE according to Dukes criteria (Table 5).

Table 5 Diagnosis According to Duke Criteria (n = 47)

Diagnosis - according to Duke criteria	Frequency	Percent
Definitive	3	6.4
Possible	44	93.6
Total	47	100

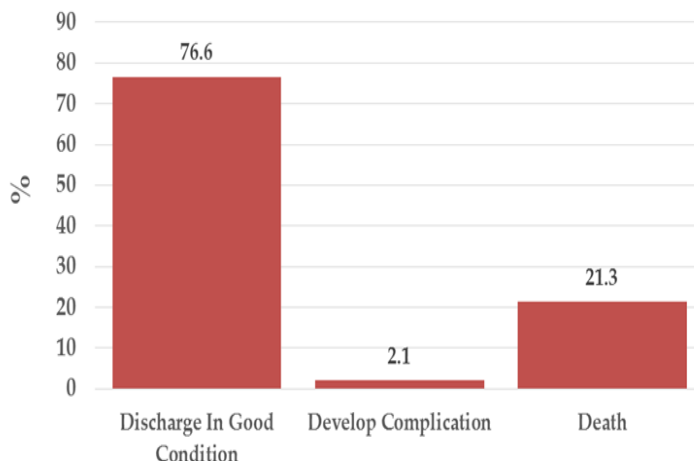


Figure 4 Short Term Outcome (n = 47).

Discussion

This study aimed to identify diagnosis, management and short outcome of IE at Ahmed Gasim Children’s hospital; during the study period, 6260 patients were admitted, 47 patients were identified to have IE according to Dukes criteria. Three patients fulfilled the criteria for Definite endocarditis and 44 were classified as Possible; IE admission rate was 7.5: 1000 admission, this figure is high compared to other countries even in Africa, a large multicentre study from USA from 2003 to 2010 showed the annual incidence rate in the United States was 0.05- 0.12 cases per 1000 paediatric admissions, CHD has been associated with increased risk of periodontal infection and this in turn increased the risk of endocarditis in CHD cases. Previous studies from Ahmed Gasim hospital showed that Sudanese children with CHD are at increased risk of severe gingivitis and caries compared to the children without CHD.^{9,10}

There was almost equal number of males to females with a ratio of 1:0.9, and most of the patients were over five years old (Figure 1). 34% of patients with IE had no structural heart disease, the diagnosis of IE in structurally normal heart in children can be delayed, as the index of suspicion will be very low; this figure is similar to studies from Africa. 66% of the patients were known to have structural heart defects, out of them 54.8% were known to have RHD and 45.2% were known to have CHD, so we still see more of RHD than CHD; this pattern is similar to the pattern reported in sub-Saharan Africa.¹¹ In the developing world, RHD is the major player and still represent a challenge⁵ while in the developed world the endocarditis secondary to RHD account for only 5 - 10% of cases.⁴

Out of the 31 children with structural heart disease, only 17 patients (54.8%) were on regular follow up, this figure is quite low and an alarming figure; all children with heart disease should be encouraged and strongly advised to attend follow up clinics.

The most common symptoms of IE are prolonged fever and cough while the two most common signs are the signs of heart failure and new or changing murmur (Figure 2).

Only 23.4% of patients have echocardiography done which is quite a low figure, considering that these patients were treated as endocarditis and all of them should have had an echocardiography;¹² interestingly all patients who have had echocardiography showed suggestive features of endocarditis.

Only 8 patients (17%) had blood culture done which is a very low number as well, and only 25% of them were done within 48 hours, the blood culture was positive in four patients out of the eight patients who has blood culture done, this yield of 50 % is low and could be explained by the delay in taking blood cultures and prior antibiotic; around 40% of the patients are from areas outside Khartoum (Table 1) and invariably they have received antibiotics in their local hospital. Blood culture is very crucial for the diagnosis and for guiding the antibiotic management,¹² Blood cultures should be collected for patients with fever of unknown origin, especially if they have pathological heart murmur, a history of heart disease, or previous endocarditis.¹³

Echocardiography and blood culture are very fundamental investigations and should be carried out on any child who is suspected to have endocarditis, and the figure of 23.4% for Echocardiography and 17% for Blood culture are quite low. We think it is a safe assumption that the incidence of IE would have been higher if all children with prolonged fever; especially if no focus of infection was found, with or without history of structural heart disease have had these two investigations done. We think the reason for the low numbers of echocardiography and blood culture is the issue of cost, as the parents and the caregivers have to pay for these tests which are relatively expensive for most of them.

In all of the studies, patients who met the definite criteria are two to three times more than the possible criteria.^{3,11} In our study there was only three Definite cases and 44 Possible cases; this reverse ratio in our study could be explained by the low number of echocardiography and the blood culture done.

The organism grown was Staph Aureus in three patients (75%) and Strep Viridins in one patient (25%) (Table 2), studies from the developed and developing countries are showing this trend as well with emergence of Staph Aureus as the most frequent organism.^{2,4,11,14} None of our patients had a long line, which is a risk factor for Staph endocarditis.

Testing of urine for microscopic haematuria was done in 23 patients (48.9%), out of the tested one there was a positive result in eight patients (34.8%), and a negative result in 15 patients (65.2 %) (Figure 3), urine testing is a cheap and a very useful test in cases of suspected endocarditis.

Regarding the management, most of the patients (83%) received a combination of Ceftriaxone and Vancomycin and about half of the patients received intravenous treatment for two weeks in hospital (Table 3& 4). Ceftriaxone is becoming popular because it could be given to stable patients on ambulatory basis. We think the choices of antibiotic needs to be based on microbiological studies, hence it is very important to do blood culture to guide the treatment.^{13,14}

36 patients (76.6%) had been discharged in good conditions, 10 patients (21.3%) died and one patient (2.1%) developed Cerebrovascular accident (CVA). The mortality figure are comparable to studies from Africa^{11,15} and Asia.⁵ The hospital mortality in USA was 2-5%^{5,16} which is far away from our figure.

Limitation

This is a retrospective study and there was no long term follow up.

Conclusion and recommendations

IE in Sudanese children is not rare and is associated with a high mortality, the scarce availability and the high cost of investigations

like echocardiography and blood culture may reduce the number of diagnosed patients, meaning we are most likely looking at the tip of the iceberg.

Health professionals should have a high index of suspicion to diagnose endocarditis. One third of endocarditis cases were in children with normal hearts, so a normal heart does not rule out IE. Echocardiography and blood culture should be done whenever the possibility of endocarditis is entertained blood culture should be taken as soon as possible and before antibiotics are commenced. There is a shift of organism towards staph aureus and hence the management should be guided by the microbiological investigations.

RHD is still contributing to IE in children and preventive measures like primary and secondary prophylaxis of Rheumatic Fever should decrease the associated short term and long-term morbidity and mortality.

The children, parents and caregivers of children with structural heart disease should be educated about preventive measures of endocarditis e.g. antibiotics before bacteremic procedures, good dental hygiene and the need for regular follow up.¹³

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