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Infective endocarditis in children with heart diseases at Jakaya Kikwete Cardiac Institute, Tanzania: a cross-sectional study

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Abstract

Background Infective endocarditis (IE) in children with pre-existing heart conditions is a life-threatening disease entity associated with significant morbidity and mortality. In our cardiac setting, the management outcomes of children with IE are not well documented. We therefore aimed to document the clinical profile and treatment outcomes of children with IE attended at the Jakaya Kikwete Cardiac Institute (JKCI).

Methods This was a hospital-based cross-sectional study with longitudinal follow-up conducted among children with IE diagnosed by Modified Duke's Criteria at the JKCI from November 2021 to November 2023. A structured questionnaire was used to collect patients' socio-demographic and clinical data.

Results During the study period, 1,546 children were admitted to the JKCI. A total of 30 children with IE were enrolled, of these half ($n=16$, 53%) were aged 10 to 18 years, with a median of 10 yrs (Inter quartile range, IQR: 6.5–12.2 yrs). Twelve children (40%) and nearly half ($n=14$, 47%) had fever and used antibiotic therapy respectively. Majority of participants had anaemia ($n=26$, 87%) and heart failure ($n=21$, 70%). Nine children (30%) had positive blood cultures and *S. aureus* was the most frequently isolated organism ($n=7$). Ten patients (33%) developed acute kidney injury (AKI), and eleven (37%) children died during the hospital stay.

Conclusion In our setting, in-hospital mortality due to IE among children with heart diseases is high. Heart failure and anaemia were the common presentations of IE. Furthermore, AKI was observed to be the leading in-hospital non-cardiac complication.

Keywords Infective endocarditis, Heart disease, Children, JKCI, Tanzania

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Introduction

Infective endocarditis (IE) is an uncommon but serious microbial infection of the endocardium whose incidence ranges from 0.05 to 6.1 per 1000 children globally [1, 2]. Mortality associated with IE is reported to be higher in low- and middle- income countries compared to the developed world, however, limited studies have been conducted in these countries [3–8].

Diagnosis of IE is made by using the modified Duke's criteria [1], however, there are challenges of early diagnosis due to non-specific symptoms at presentation such as low-grade fevers and arthralgias [9]. Nevertheless, there are reported limitations with the above criteria such as negative blood cultures results and normal echocardiographic findings despite the presence of IE [1]. Consequently, a high index of suspicion is highly required especially in patients with reported risk factors including structural heart diseases or presence of prosthetic material [6, 9–11].

IE with negative bacterial blood cultures have been frequently reported in various studies, this is partly attributed to antimicrobial pre-treatment which reduces the yield of blood culture up to 60% [10–13]. Other factors are limited culture techniques for growing fastidious and rare organisms especially in developing countries or intracellular organisms that cannot be cultured [1, 13]. Microorganisms such as *Staphylococcus aureus* and *Streptococcal viridans* remain the leading causative bacteria in the paediatric population [13–16].

Empirical antibiotics for IE can be initiated before the identifiable agent is recovered with several considerations such as a prior history of antibiotic use, whether the native valve or prosthetic valve is involved and if its community or hospital-acquired infection [10]. However, in some cases surgical intervention may be indicated.

Despite advancements in diagnostics, treatment and preventive measures, the affected children have been reported to suffer from several complications including heart failure, systemic embolization or renal failure [6, 10, 17].

Our centre attends children with heart diseases from different areas of the country, however, we do lack local data on IE as it is in other low-income countries. Therefore, this study aimed to determine the clinical characteristics and the outcomes of children with IE.

Methods

Study design and setting

This was a hospital-based cross-sectional study with a longitudinal follow-up conducted in a paediatric cardiology unit at the JKCI, Tanzania from November 2021 through November 2023. JKCI is a 150-bed capacity national referral and teaching centre providing specialized cardiac services for adults and children. It is the only centre offering open cardiac surgery in Tanzania with seven paediatric cardiologists and two paediatric cardiac surgeons.

Study population and inclusion criteria: All children with heart conditions aged 1 month to 18 years were admitted to the paediatric unit during the study period. Those who fulfilled the modified Duke criteria were enrolled in the study. However, those who met the "rejected IE" criteria were excluded.

Study variables and measurements

Age, sex, prior antibiotic therapy, echocardiographic (ECHO) findings (valvular/perivalvular/periprosthetic lesions characteristics of IE by transthoracic ECHO), laboratory findings, IE treatment initiation and completion, treatment regimen, observed complications (heart failure, AKI, systemic embolization) and mortality were recorded.

Echocardiographic features of IE include vegetations, defined as an oscillating or non-oscillating intracardiac mass on a valve or other cardiac structure or prosthetic materials. Other features were; intracardiac abscess, pseudoaneurysm, valvular perforation and dehiscence of prosthetic intracardiac materials [10].

Mortality and observed complications (acute kidney injury, stroke, heart failure) were determined during the follow-up over the hospital stay until discharge.

The cut-off point to define anaemia was haemoglobin levels below 11 g/dl according to WHO guideline [18]. Severe anaemia was classified as haemoglobin levels below <7 g/dl.

Sample collection and testing

Five millilitres (mls) of blood were aseptically drawn from each enrolled child. Three mls of blood were inoculated into the BacT/Alert PF (Paediatric) bottle and the remaining 2 mls were sent for complete blood count and clinical chemistry analyses.

to conduct this study was obtained from the Ethics Review Committee of the Jakaya Kikwete Cardiac Institute (Ref.No.AB.123/307/01 C/32). Informed consent of participation in the study was obtained from the patients and /or their legal guardians and children above 7 years assent was obtained.

Data management and analysis

Data collection was done using a standardized structured questionnaire. Data entry and analysis were done using SPSS software version 23. Descriptive statistics were summarized into frequencies and proportions.

Results

In a period of two years, 1,546 children were admitted to the JKCI, and of these 30 children with IE were diagnosed. The hospital prevalence of infective endocarditis was 1.94%. Most of the children ($n=29$) were found to have definite IE and the remaining one patient had probable IE (Definite, $n=29$) (Fig. 1).

Out of 30 recruited children 16 (53%) were males and half (53%) were aged 10 to 18 years with a median of 10 years (IQR: 6.5–12.2 yrs). Twelve children (40%) and nearly half ($n=14$, 47%) had fever and used antibiotic therapy respectively. The majority of patients had anaemia ($n=26$, 87%), of which six children had severe form. About a third of the study participants ($n=10$, 34%) had acyanotic congenital heart disease and a quarter ($n=8$, 26%) had rheumatic heart disease. All children had blood cultures done, however, only nine (30%) yielded positive results with *S. aureus* as the predominant isolate ($n=7$). Out of twenty-nine participants who had vegetations, nearly two-thirds ($n=19$, 63%) had measured less than 10 mm and about half ($n=15$, 50%) were located on the left side of the heart. Nonetheless, six out of 30 children presented with glomerulonephritis. All children were on antibiotic therapy, however, two-thirds of them ($n=21$, 70%) were on antibiotic therapy for more than 6 weeks. Furthermore, only one child underwent surgery due to heart failure and uncontrolled infection (Table 1).

Heart failure was the commonest complication ($n=21$, 70%) followed by acute kidney injury ($n=10$, 33%) and systemic embolization (17%). About two-thirds of study participants (73%) spent more than 28 days in the ward and eleven children (37%) died during the hospital stay (Table 2).

Out of eleven children who died, eight and seven of them had vegetation of more than 10 mm, on the left side of the heart respectively. Eight children had significantly elevated white cell count. In a further review of causes of death, eight patients died of multi-organ failure (Table 3).

Discussion

This study demonstrates the clinical characteristics and hospital outcomes of the children with IE admitted at JKCI. In two years, 30 children were admitted due to IE, heart failure and anaemia were the common presenting clinical features. A significant number of children had prolonged hospital stays with a mortality of approximately 37%.

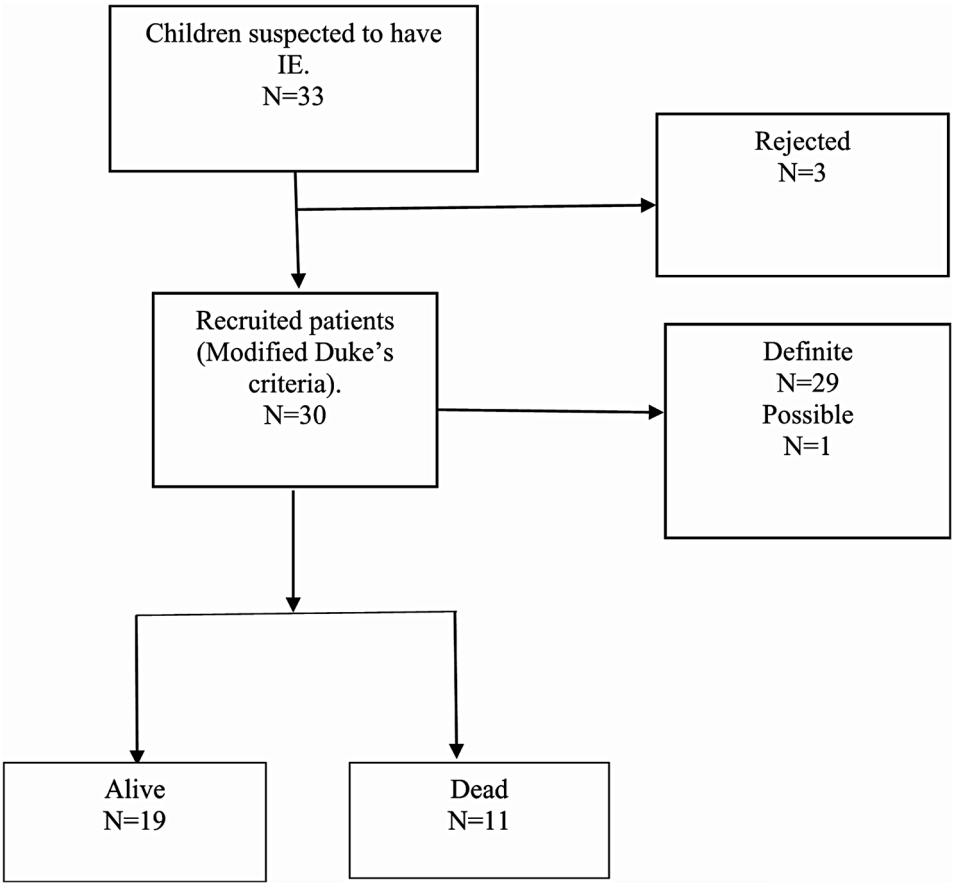

Fig. 1 Flow diagram showing the recruitment of study participants and their outcomes

Table 1 Clinical characteristics of children with infective endocarditis at JKCI in Tanzania, 2021–2023 (N = 30)

Variable	Category	Frequency (%)
Age (yr)	1- < 5	4 (13)
	5-<10	10 (33)
	10–18	16 (53)
Sex	Male	16 (53)
Fever	Yes	12 (40)
Prior antibiotic use	Yes	14 (47)
Anaemia	Yes	26 (87)
	Non severe	20 (67)
	Severe	6 (20)
	< 10 mm	19 (63)
	≥ 10 mm	10 (33)
Vegetation location**	Left side of the heart	15 (50)
	Right side of the heart	14 (47)
Blood culture result	Positive	9 (30)
Isolated organism*	*S. aureus*	7 (78)
	S. viridans	1 (11)
	K. pneumoniae	1 (11)
Underlying cardiac diagnosis	VSD	5 (17)
	PDA	5 (17)
	TOF	5 (17)
	TGA	1 (3)
	RHD	8 (26)
	Other	6 (20)
Glomerulonephritis	Yes	6 (20)
Prolonged antibiotic therapy (> 6 weeks)	Yes	21 (70)

*Out of positive blood culture, **Out of those with vegetations

VSD: Ventricular septal defect; PDA: Patent ductus arteriosus; TOF: Tetralogy of Fallot; TGA: Transposition of great arteries; RHD: Rheumatic heart disease

Table 2 Clinical complications and outcomes of children with infective endocarditis at JKCI in Tanzania, 2021–2023 (*N* = 30)

Variable	Frequency (%)
Clinical complications	
Heart failure	
Yes	21 (70)
No	9 (30)
Acute kidney injury	
Yes	10 (33)
No	20 (67)
Systemic embolization	
Yes	5 (17)
No	25 (83)
Outcomes	
Mortality	
Yes	11 (37)
No	19 (63)
Length of stay	
< 28 days	8 (27)
28 days and above	22 (73)

The present study shows significantly high in-hospital mortality despite timely management. Our finding is comparable to various studies conducted in developing countries, where high mortality was also reported [7, 13, 19–21]. On the contrary, a study conducted in Addis Ababa [11] reported a low fatality rate, the discrepancy can probably be differences in patients' clinical presentations. In this cohort, a great number of demised children presented in critically ill states with multi-organ involvement and needed admission to the intensive care unit (ICU). The majority of the IE lesions (vegetations) in children who died were either large or located on the left side of the heart, these features reported to predict poor outcome among the affected children [1].

Diagnosis of IE needs a high index of suspicion especially for those with risk factors presenting with fever. A significant number of our patients presented with heart failure and fever upon admission. Fever and congestive heart failure are reported to be the most frequent clinical presentations in patients with IE [1]. This aligns with previous studies [10, 22, 23] where fever and congestive heart failure are often reported.

As in previous reports [3, 5], IE reported to follow bimodal age distribution thus peaks in infancy and late adolescence. In the present study, half of the children with IE were aged 10 years and above. We observed a few numbers of children in the neonatal group since children below 28 days are cared for in the neonatal unit and our cardiac paediatric ward, we only admit neonates when scheduled for cardiac surgery.

In this study, blood culture-negative IE (BCNIE) was significant, only one-third of children had positive blood culture, with *S. aureus* being the most common organism, which is comparable to what is reported in the literature [1, 10]. A significant BCNIE in our study can be explained by a few reasons, including prior antibiotic use, as nearly half of our patients were on antibiotics before admission. Another reason is limited culture techniques for growing fastidious and rare organisms especially in developing countries.

We also observed a substantial number of children developing acute kidney injury (AKI), which is one of the reported non-cardiac complications. These children were those who needed urgent intensive care, however, none required needed dialysis treatment. The above findings were comparable with other previous reports [3, 24].

This study had some limitations, including the small number of participants, which limits further statistical analysis. Secondly, due to financial constraints, the studied patients did not meet the standard of at least three sets for blood culture analysis as per modified Duke's criteria.

Table 3 Socio-demographics and clinical characteristics of demised children with infective endocarditis at JKCI in Tanzania, 2021–2023 (N = 11)

Patient	Age	Sex	Underlying cardiac lesion	Vegetation size	Vegetation location	WBC on admission (× 10^3 / μL)	Blood culture result	Cause of Death
1	5 yrs	M	RHD	< 10 mm	Left	14.8	*S. aureus*	Multi-organ failure
2	1 mo	M	TGA	≥ 10 mm	Right	11.8	*Klebsiella pneumoniae*	Multi-organ failure
3	12 yrs	F	RHD	≥ 10 mm	Left	10.9	*S. aureus*	Multi-organ failure
4	15 yr	M	DCM	< 10 mm	Left	7.3	Negative	Multi-organ failure
5	9 yrs	M	VSD	< 10 mm	Right	43.4	*S. aureus*	Multi-organ failure
6	13 yrs	F	VSD	≥ 10 mm	Left	14.1	*S. aureus*	Multi-organ failure
7	12 yrs	M	RHD	≥ 10 mm	Left	9.3	*S. aureus*	Multi-organ failure
8	1 yr	F	TOF	≥ 10 mm	Right	14.7	*S. aureus*	Intractable cyanotic spells
9	5 yrs	F	DCM	≥ 10 mm	Left	12.5	Negative	Unknown
10	10 yrs	M	RHD	≥ 10 mm	Left	45	Negative	Multi-organ failure
11	15 yrs	M	VSD	≥ 10 mm	Right	36	Negative	Multi-organ failure

RHD: Rheumatic heart disease; TGA: Transposition of great arteries; DCM: Dilated cardiomyopathy; WBC: White cell count

Conclusion

Infective endocarditis though occurs infrequently, the present study demonstrates its high in- hospital mortality among the affected children. Heart failure and anemia were the common presenting clinical features. Furthermore, AKI was the leading in-hospital non-cardiac complication.

Abbreviations

AKI	Acute kidney injury
BCNIE	Blood culture negative infective endocarditis
CHD	Congenital heart disease
ECHO	Echocardiography
ESC	European society of cardiology
IE	Infective endocarditis
ICU	Intensive care unit
PDA	Patent ductus arteriosus
RHD	Rheumatic heart disease
TOF	Tetralogy of Fallot
VSD	Ventricular septal defect

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Author contributions

ZEK, ANS and FFF were involved in conceptualization. ZEK wrote the first manuscript draft. DAN, NGM, ANS, FFF and SDK provided contributions in reviewing the manuscript. All authors have read and approved the final version of the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval and consent to participate

Ethical approval to conduct the study was obtained from Ethics Review Committee of the Jakaya Kikwete Cardiac Institute (Ref. No.AB.123/307/01 C/32). All patients received treatment as per standard Institutional policies. We are confirming that all methods were carried out per relevant guidelines and regulations. Informed consent of participation in the study was obtained from the patients and /or their legal guardians and the children above 7 years, assent was obtained if they agreed to participate in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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