CLINICAL AND MICROBIOLOGICAL PROFILES OF INFECTIVE ENDOCARDITIS IN PEDIATRIC PATIENTS: A CROSS-SECTIONAL STUDY AT TIKUR ANBESSA SPECIALIZED HOSPITAL

By: DR. BEMNET ABERA (MD, PEDIATRICS AND CHILD HEALTH RESIDENT)

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Clinical and Microbiological profiles of Infective Endocarditis in Pediatric Patients: A Cross-Sectional Study at Tikur Anbessa Specialized Hospital

Advisors

Dr. Helen Mintesinot, MD Assistant professor of pediatrics and child health
Pediatric cardiologist.
Co Advisor Dr Elham Sani, MD Assistant professor of pediatrics and child health
Pediatric infectious sub specialist

Addis Ababa, Ethiopia

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Contents

List of acronyms

BP:	Blood pressure
CHD	Congenital heart disease
IE	Infective endocarditis
MUAC	Mid upper arm circumference
PR	Pulse rate
RR	Respiratory rate
SPo2	Oxygen saturation
TASH:	Tikur Anbessa Specialized hospital
T:	Temperature
PI:	Principal investigator
SD:	Standard deviation

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Abstract

Background: A serious infection of the heart's endocardial surface, including the heart valves, is known as infective endocarditis (IE). In young patients, IE is a rare but potentially fatal illness that needs to be diagnosed and treated right away. Improving outcomes requires an understanding of the clinical and microbiological features of IE in the pediatric context. These kinds of studies aid in the understanding of the local epidemiology of this uncommon but dangerous pediatric heart infection by physicians working in resource-constrained environments such as Ethiopia. The results can help develop diagnostic algorithms, direct empirical antibiotic therapy, and pinpoint areas where IE prevention and management in this patient population need to be improved.

Objectives: - This study aimed to describe the microbiological pattern, clinical manifestation, and outcome of infective endocarditis in pediatric patients attending Ethiopia's Tikur Anbessa Specialized Hospital, a tertiary care facility.

Methods: An institutional-based retrospective cross-sectional descriptive study was conducted, focusing on 61 medical records of pediatric patients admitted for infective endocarditis (IE) at TASH from January 2019 to January 2024. A self-administered and structured questionnaire was developed to encompass demographic, clinical, and echocardiography data from the medical records of the study subjects. The data were analyzed using SPSS version 27 software, and the findings were presented using tables and charts.

Result: This study includes a total of 61IE patients' more than half 35(57.4) were female. fever (52, 27.2%), shortness of breath (45, 23.6%), and cough (28, 14.7%) were the most common chief complaints .36 patients (59 %) were cured, 25 (59 %) died, with sepsis with multi-organ failure (13, 52%) being the leading cause of death. The average hospital stays for patients who died was 21.04 days (SD = 18.449), while the average stay for patients who were cured was 41.39 days (SD = 11.746). Length of hospital stay (Odds Ratio = 1.083, 95% CI = 1.030 to 1.138, p = 0.002) and presence of complications (Odds Ratio = 0.039, 95% CI = 0.005 to 0.345, p = 0.003) significantly affect the outcome

Conclusion:

Key words: IE, prevalence, Clinical, Microbiological profile, pediatrics, TASH, Ethiopia

1. Introduction

1.1. Background

Infective endocarditis, a condition involves the infection of the hearts surface and can affect one or more heart valves(1). Among children this disease is uncommon but significant, with an estimated occurrence rate ranging from 0.05 to 0.12, per 100,000 children (2, 3). In cases infective endocarditis is frequently linked to heart issues artificial heart devices and weakened immune systems (4)

The clinical presentation of IE in children is highly conditioned by age. In adolescents, the symptoms and findings are quite similar to the ones seen in adult patients: fever, loss of appetite, and malaise as evidence of a systemic infectious process. A history of congenital heart disease or previous cardiac defects that may or may not have required surgical correction may increase suspicion (5). A new murmur or a change in a previous murmur may be heard. In cases of subacute onset, it is common to find progressive deterioration in functional class, with persistent fatigue, malaise, or growth retardation. Patients with IE may present evidence of acute heart failure due to valve destruction (1). Regarding systemic manifestations, there may be renal immunological involvement (glomerulonephritis), seizures, or cerebral infarction due to cerebral embolisms. Immunological phenomena (Osler nodes, Janeway spot(5). Early diagnosis and appropriate antimicrobial therapy are crucial to improve patient outcomes, as IE carries a high mortality rate, especially in developing countries.

The microbiology of IE in the pediatric population studied in sub Saharan african, Patients with microbiology-positive infective endocarditis reported the causative microorganism to be Staphylococcus aureus (28·1%), coagulase-negative staphylococcus (13·2%), viridans streptococci (27·5%), and enterococci (9·1%). Haemophilus, Aggregatibacter, Cardiobacterium‹ hominis, Eikenella corrodens, and Kingella microorganisms represented 3·5% and fungi (Candida or Aspergillus species) represented 7·2% of identified microorganisms with Staphylococcus species and Streptococcus species being the most commonly reported causative agents. However, the specific microbiological profile may vary depending on the local epidemiology and patient characteristics (6).

In developing countries the occurrence of endocarditis (IE) is typically more frequent, than in developed nations. This difference is probably because of challenges in healthcare access late detection and a higher occurrence of conditions such as heart disease. The global estimate for IE incidence ranges from 0.43 to 0.69 cases, per 100,000 children(5). This low incidence makes it difficult to obtain evidence regarding the best diagnostic and therapeutic approach of IE at those ages(5).

In Sub-Saharan Africa, including Ethiopia, the epidemiology of IE in children has been understudied, with limited data available on the clinical features, microbiology, and outcomes of this disease(7). The annual incidence estimated to be about 2–12 cases per 100 000 people(8)

In children, rheumatic heart diseases (RHD), bacteremia from hospital-acquired infections, and congenital heart disease (CHD) are the main risk factors for infection-related echocardiography (IE). At the moment, patients without underlying heart disease are more susceptible to IE due to longer-term central venous catheter use and more invasive procedures(9). But further explanation is needed on the particular risk variables and how much of an impact they have in the Addis Ababa TASH local setting.

Understanding the clinical and microbiological characteristics of IE in the pediatric population at Addis Ababa TASH, a major referral hospital in Ethiopia, is important to guide empiric antimicrobial therapy, improve diagnostic strategies, and ultimately enhance the management and outcomes of these patients in a resource-limited setting.

1.2 Statement of the problem

In low resource settings such, as Ethiopia, pediatric infective endocarditis (IE) can be a potentially deadly condition. While IE has been extensively researched in countries there is a lack of data regarding its characteristics and prevalence in sub Saharan Africa specifically, in Ethiopia.

In order to develop efficient management methods in Ethiopia, has to have a deeper understanding of the regional clinical and microbiological features of pediatric IE. Among the particular knowledge gaps that need to be filled are:

Epidemiology and incidence of pediatric IE at TASH: There is currently a lack of adequate documentation regarding the incidence and disease burden of IE in the pediatric population that TASH serves.

Clinical profile and risk factors: In the Ethiopian setting, the typical presenting symptoms, underlying predisposing factors, and consequences linked to pediatric IE are not well-characterized.

Microbiological profile and antimicrobial susceptibility patterns: The choice of the most suitable antibiotic therapy may be impacted by the lack of clarity surrounding the causative microorganisms and antimicrobial resistance profiles that cause IE in Ethiopian children.

The clinical and microbiological profile of pediatric IE at TASH shall thoroughly be studied in order to fill in these gaps. The research findings can offer important guidance for evidence-based clinical practice and the distribution of healthcare resources in order to improve outcomes for this susceptible population.

1.3 Rationale of the study

The upcoming research, on the microbial traits of endocarditis (IE) in children at Tikur Anbessa Specialized Hospital (TASH) holds significant value.

Increasing knowledge about epidemiology; This study will offer insights into the frequency, occurrence and impact of pediatric IE in the TASH area data that could inform the development of healthcare strategies and allocation of resources, at both local and national levels

Understanding the microbiological environment: Selecting the right empirical and targeted antibiotic treatment will be guided by identifying the responsible microorganisms and their antimicrobial resistance patterns, thereby improving treatment effectiveness

To slow the spread of antibiotic resistance, knowledge of the local microbiological epidemiology can also inform infection control procedures and antimicrobial stewardship initiatives.

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2. Literature Review

A potentially fatal condition affecting the heart's endocardium and cardiac valves, infected endocarditis is brought on by infectious pathogens. Over the past five years, there has been an increase in its occurrence worldwide, indicating that it remains a significant source of cardiac infection(6).

The mortality rate of IE is remarkably high, with an in-hospital mortality rate of up to 22% and a 5-year mortality rate of 45% worldwide. Hospital mortality emphasizes the significance of the prompt diagnosis of this disease. Despite advances in diagnostics and therapeutics, the prognosis of IE remains poor (4)

The diagnosis and treatment of IE can be difficult in underdeveloped nations like Ethiopia, where the majority of health institutions are understaffed. It is also possible for IE instances to go unnoticed. There aren't many published studies on IE in children in sub-Saharan Africa. A few of them revealed variations in infective endocarditis patterns as compared to high-income nations(7). According to other reports, IE in children is constantly evolving in terms of underlying diseases, risk factors, causative agents, clinical symptoms, course of treatment, and result(6).

Numerous factors, such as the high prevalence of underlying cardiac issues, delayed diagnosis, restricted access to specialized care, and the emergence of antibiotic-resistant infections, can be blamed for the subpar outcomes observed in these settings.

While the incidence and clinical characteristics of IE are well documented in high-income countries, sub-Saharan Africa, and Ethiopia, remains under-researched (7). Numerous studies have shed insight on the unique clinical and microbiological characteristics of pediatric IE in settings with limited resources.

Children in developing nations typically have more advanced disease when they first arrive compared to those in high-income countries. These conditions are frequently made worse by embolic events, heart failure, and increased rates of intra-cardiac abscess formation(4).

The underlying conditions determine which pathogens are causal. Furthermore, the epidemiology of IE has changed in the last several decades. Worldwide, S. aureus continues to be the most common causing infection in both adults and children. Additionally common are streptococci infections, mostly of the viridans group. Staphylococcus species are the most prevalent in

youngsters, particularly in those without heart problems. Streptococcus species come in second. Nonetheless, Streptococcus, a member of the viridans group, is the most frequent cause in children with underlying heart disease. Children rarely get infection from Gram-negative germs, just like adults do (5)

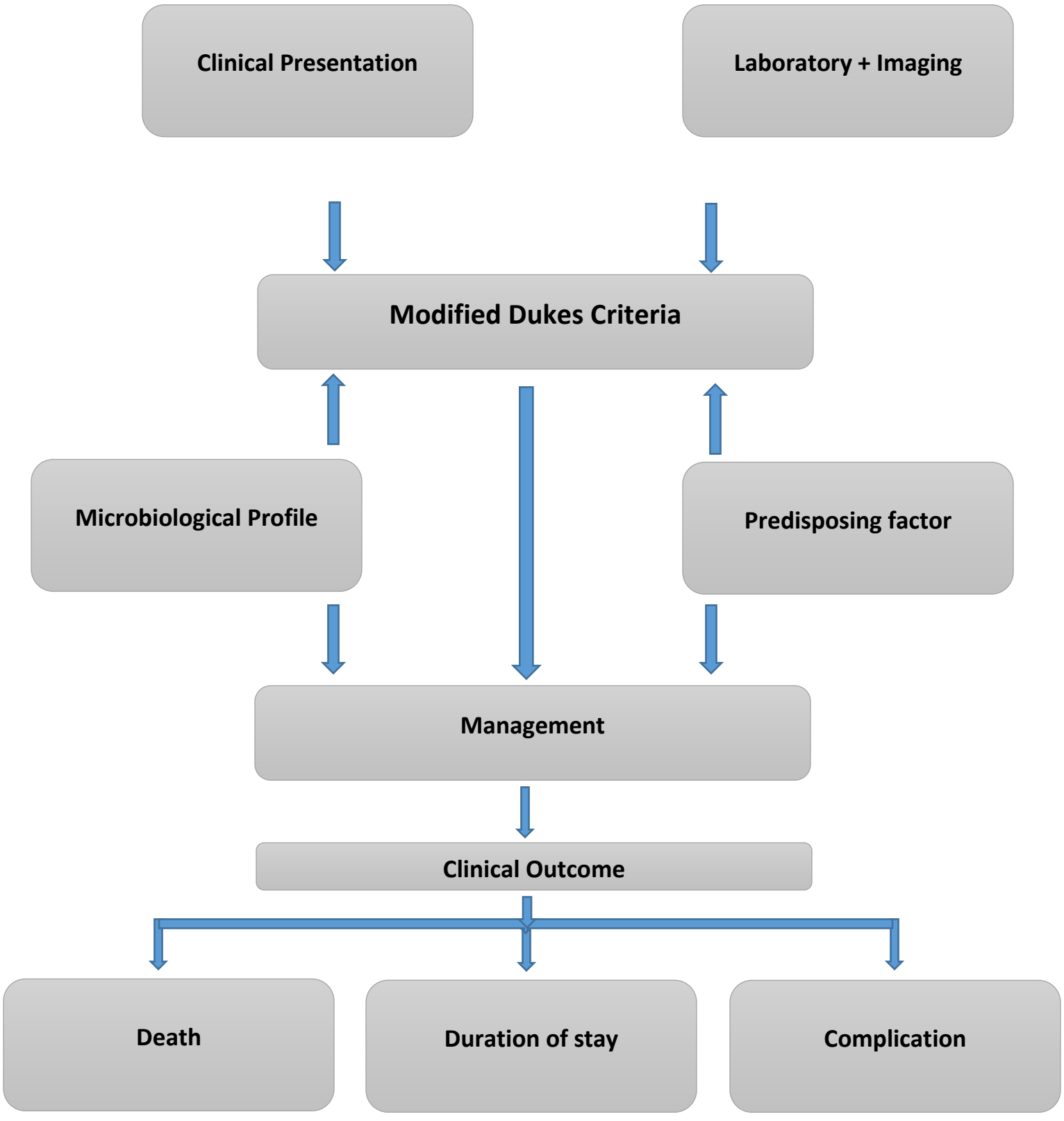
Reviews revealed that childhood infective endocarditis is linked to high mortality rates, particularly in low- and middle-income nations where in-hospital mortality rates are high (20–25%), as well as high morbidity. Despite advancements in diagnosis and treatment options, the incidence of IE is still on the rise globally. Over the past ten years, the risk factors for developing IE have changed. Increased rates of device-related infections accompanied developments in interventional cardiology with devices in high-income nations. Nowadays, about 20% of occurrences of endocarditis are related to prosthetic valve endocarditis(11)

There is an urgent need for enhanced access to modern diagnostic modalities, effective antibiotic stewardship programs, and specialist cardiac care to address the global burden of infective endocarditis in the pediatric population. The startling difference in results between environments with plenty and limited resources serves as evidence of this.

The clinical and microbiological features of pediatric IE remain poorly recognized, despite Tikur Anbessa Specialized Hospital (TASH) being Ethiopia's largest tertiary care institution. A hospital-based assessment conducted in TASH between 2008 and 2013 revealed that 25.0% of patients experienced complications such as systemic embolization, and 7.3% of patients had an IE case fatality. Additionally, all patients had an underlying cardiac disease, with 51 percent having CHD and 49 percent having RHD. Sixty-six percent of them had congestive heart failure (CHF), a dangerous illness. Only 13% of the samples obtained a positive blood culture result. Before having their blood cultures, three-fourths of the cases had taken one or more antibiotics.(12) However, little research has been done on the distinct risk factors, presenting symptoms, underlying etiologies, and causative microorganisms of the TASH pediatric populatio n. Closing this information gap is critical to improving outcomes for Ethiopian children with IE and guiding evidence-based care approaches.

To offer a comprehensive assessment of the clinical and microbiological characteristics of pediatric IE is the aim of the proposed study. In addition to supporting efforts for infection control and antimicrobial stewardship, this evaluation will help guide the development of diagnostic and treatment regimens that are appropriate for the situation.

Figure 1: conceptual frame work



3. Objective

3.1. General objective

- To describe the microbiological pattern, clinical characteristics, and outcome of infective endocarditis in pediatric patients attending Ethiopia's Tikur Anbessa Specialized Hospital, a tertiary care facility.

3.2. Specific objectives

- To provide an overview of the clinical features and demographics characteristics of pediatric patients diagnosed at TASH
- To investigate the distribution of the microorganisms and their patterns of antibiotic susceptibility, in the pediatric population at TASH.
- To investigate the outcome and in-hospital results for pediatric patients at TASH who have infective endocarditis.

4. Method and Materials

4.1. Study area and period

The study was conducted at Tikur Anbessa specialized tertiary hospital from September 1 to December 30, 2024, established in 1974 and administered by Addis Ababa University. It is the largest and oldest teaching hospital in Ethiopia, providing teaching for approximately 300 medical students and 350 residents every year. It has over 800 beds in surgical, gynecology and obstetrics, internal medicine, pediatrics, and emergency department wards combined. The hospital also has an outpatient department (OPD) and specialized referral clinics. The hospital has cardiac ICU rooms, as well as specific surgical, medical, and pediatric ICU units. The hospital offers diagnostic and treatment facilities for approximately 370,000 to 400,000 patients per year.

The pediatric department, one of the major departments with its different sub-units, contains 7 wards, PICU & CICU, Regular OPD, and 11 specialized referral clinics out of which our study concerns with cardiac and infectious department. Cardiac department is led by 4 senior consultants & 6 fellows and Infectious-disease team is led by 3 seniors. The pediatric department serves approximately 54,000 patients per year across all units. Within the wards and ICU, there are an average of 360 pediatric patients per month. The department has a total of 183 beds.

Pediatric cardiac patients are referred from all corners of the country. TASH is the only government owned hospital where pediatric cardiac surgery is done. Pediatric cardiology unit is staffed with consultant pediatric cardiologists and fellows. Pediatric residents and cardiac fellows are assigned on rotation bases. The unit offers inpatient and outpatient care, diagnostic tests, mission based cardiac surgeries and 2-3 thoracotomy and open surgery done by local cardiothoracic team weekly.

4.2. Study design

- A 5-year hospital based retrospective cross-sectional study was carried out.

4.3 Study period:

- The study was conducted from January 2019 up to November 30, 2024.

4.4. Population

4.4.1. Source population

- All pediatric IE cases who were admitted to TASH.

4.4.2. Study population

- All pediatric IE cases who were admitted to TASH from January 2019 to November 30, 2024

4.5. Eligibility

4.5.1 Inclusion

- All admitted pediatrics IE cases aged 0–14 years will be included.

4.5.2 Exclusion criteria

- Patients with incomplete record (>10% of the variable) and lost card
- cases that did not fulfill the criteria (rejected IE cases)

4.6. Sample size determination

4.6.1. Sample size determination

With the general assumption that this study will be presented with a level of confidence of 95% and 1% precision, single population proportion formula was used to calculate the sample size .

Sample size: $N=\frac{Z^2P(1-P)}{d^2} = \frac{(1.96)^2*0.00015*(1-0.00015)}{(0.01)^2} = 5.76$

Where: N= the minimum sample size

p=considering the overall prevalence IE from global data 15 case per 100,000 population

d= the level of precision (margin of error)

z= the value at 95% confidence level

4.6.2. Sampling methods:

Given that the initial sample size of 6 falls below the minimum required for research which is 30, we expanded our data collection to include all patients admitted and treated for infective endocarditis during the study period who met the inclusion criteria. Ultimately, 61 patients who were admitted and treated during this time were included in the study.

4.6 Data Collection Tool and Procedures

The medical record number (MRN) and IE diagnosed children age less than or equal to 14 years who were admitted at Tikur Anbessa specialized hospital was collected from the health management information system (HMIS) registration book of the hospital within the study period. HMIS record of the hospital was used. Demographic, clinical, and echocardiographic data were collected using questionnaires developed by a data collector. The principal investigator then reviewed the charts from the pediatric cardiac clinic to gather additional data. A Google Form was utilized to collect the information, with the data stored on the Gmail server.

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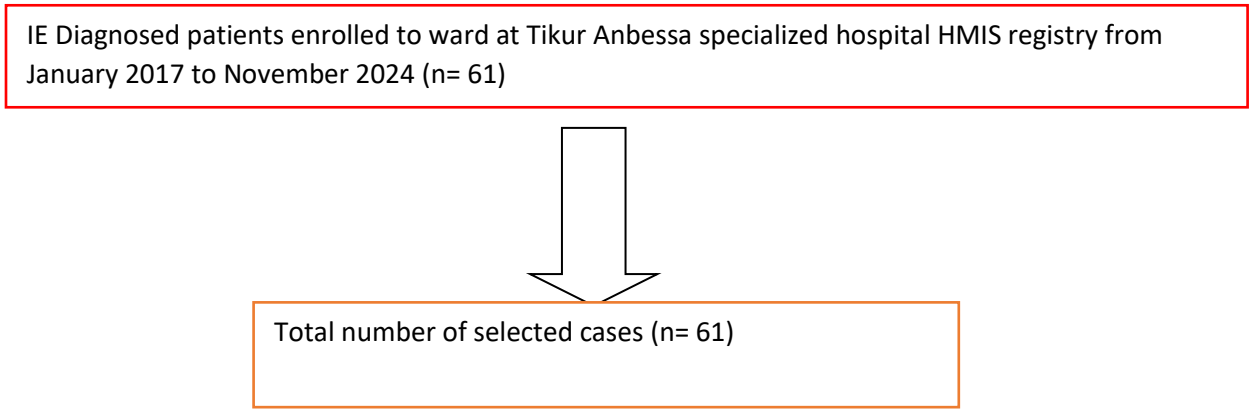

Figure 2 data collection prouder

4.7 Data Quality control and management

To ensure the quality of data, Google form was used. Each question was properly coded; The collected data were checked for completeness and consistency on each day of data collection by principal investigator.

4.8. Variables

4.8.1 Outcome variable

- Outcome of IE

4.8.2 Explanatory variables

- **Socio-demographic data**: age, sex, address, residence,

- **Clinical Data** (chief compliant, Duration of symptoms, Previous Admission, cardiac illness, predisposing factor physical findings, imaging Ecco)
- **Microbiological Profile**
- **Laboratory tests**
- **Management**

4.9. Operational Definition

- **Infective endocarditis (IE):** Infective endocarditis is defined as an infectious process affecting the endocardial surface of the heart, including native heart valves, prosthetic heart valves, and other intracardiac structures.
- **Diagnostic criteria:** Patients will be diagnosed with IE based on the modified Duke criteria, which include clinical, microbiological, and echocardiographic findings.(1)
- **Pediatric population:**
    - Patients aged 14 years or younger at the time of IE diagnosis.

4.10. Data processing and Analysis

After data collection with Google form, each filled form were checked for completeness and exported to SPSS version 27 for analysis. Mean, and standard deviation were used to describe Continuous data; and frequency and percentage were used to describe categorical data. Bi varable and multivariable regression was used to study association between outcome and potential factors. Statistical significance will be taken for a p-value of < 0.05 for all statistical tests. Finally, the results were presented using text, table, and charts.

4.11. Ethical consideration

Ethical clearance was obtained from the Department of Research and Ethical Review Committee (DRERC). Then an official letter of support and ethical clearance was submitted to the Record office. Confidentiality was maintained at all levels of the study, besides only the MRN number of study participants were used without mentioning the name and the collected information was kept in a secured place.

4.12. Dissemination and utilization of results

The finding of this research will be submitted to Addis Ababa university health science and medical college,departement of pediatrics and child health and will be presented during the final defense for partial fulfillment of speciality. The finding of the study will also be shared for other concerned bodies. Subsequently an attempt will be made to present the findings on different review meetings, seminars, and workshops. Furthermore, the manuscript will be published on peer reviewed journals.

5 Result

5.1 Sociodemographic character

This study includes a total of 62 patients, with a majority being female (35, 57.4%). The mean age of the patients was 7.09 ± 4.39. More than one third of them were in \ aged 5 to 10 years (22, 36.1%), followed by those older than 10 years (19, 31.1%). Geographically, nearly half of the patients (30, 49.2%) are from the Oromia region. As for patient records, a significant portion are new cases (38, 62.3%), while repeat patients make up a smaller percentage (23, 37.7%). *The details of sociodemographic characteristics is presented in Table 1.*

Table 1 Sociodemographic characteristics of study population

Sociodemographic Variable		Frequency	Percent
Age Group	< 1 Year	12	19.7
	2 to 5 Year	8	13.1
	5 to 10 Year	22	36.1
	> 10 Year	19	31.1
	Total	61	100.0
Sex	Male	26	42.6
	Female	35	57.4
	Total	61	100.0
Place of residence (Region)	Addis Ababa	24	39.3
	Oromia	30	49.2
	Amhara	1	1.6
	Former SNNPR	6	9.8
	Total	61	100.0
Patient record	New	38	62.3

	Repeat	23	37.7
	Total	61	100.0

5.2 Clinical characteristics

In our study, fever (52, 27.2%), shortness of breath (45, 23.6%), and cough (28, 14.7%) were the most common chief complaints, with chest pain (32, 16.8%) and body swelling (20, 10.5%) also being frequently reported. Other symptoms included urine color change (5, 2.6%), body weakness (5, 2.6%), and orthopnea (3, 1.6%) Fig 1. Most patients (35, 57.4%) experienced symptoms for 2 weeks or less, while 20 (32.8%) had symptoms for 3 to 5 weeks. Only a small percentage had symptoms lasting 6 to 9 weeks (4, 6.6%) or longer than 9 weeks (2, 3.3%). In terms of previous hospital admissions, 13 (21.3%) had been admitted before, with the majority (7, 53.8%) having been admitted twice. Additionally, 5 (38.5%) had been admitted once, and 1 (7.7%) had been admitted four times.

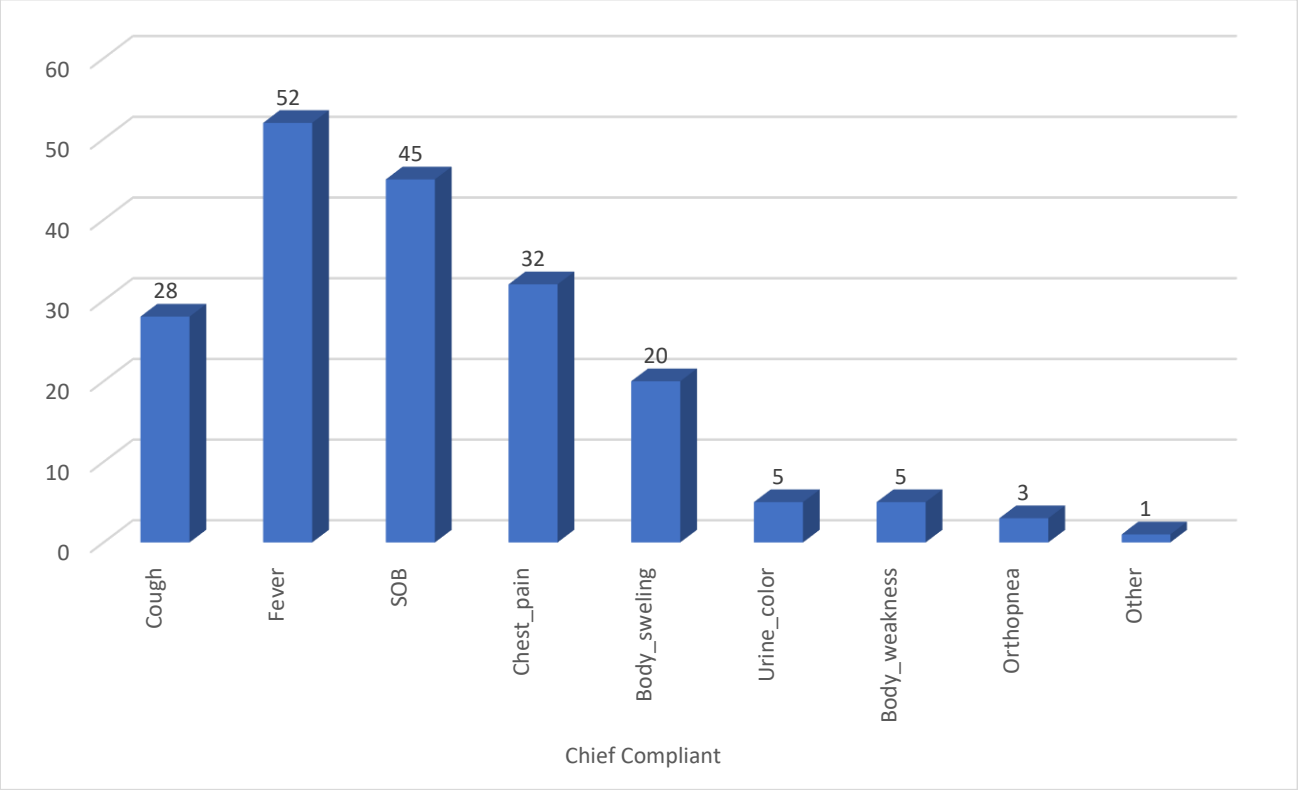

Fig 3 chief complaints

The majority of patients (57, 93.4%) had a history of cardiac illness, while only 4 (6.6%) did not. Among those with cardiac illness, the types were classified as either congenital or acquired. Congenital heart disease was present in 34 patients (59.6%), while acquired heart disease affected 23 patients (40.4%). Within congenital heart disease, acyanotic conditions were more common, with 23 patients (67.6%), and cyanotic conditions affected 11 patients (32.4%). Among the acyanotic conditions, the most common diagnosis was PDA (11, 47.8%), followed by VSD (7, 30.4%). Other conditions like AVSD, coarctation of the aorta, and VSD with pulmonary stenosis were less frequent. In the cyanotic group, Tetralogy of Fallot (TOF) was the most common condition (6, 54.5%), followed by D-Transposition of the Great Arteries (DTGA) (3, 27.3%). TAPVR were also present in 2 patient. For acquired heart disease, rheumatic heart disease was predominant (22, 95.7%), with only 1 patient (4.3%) having cardiomyopathy.

Table 2 Clinical Characteristics

Variables		**Frequency**	**Percent**
cardiac illness	Yes	57	93.4
	No	4	6.6
	Total	61	100.0
Type of Cardiac illness	Congenital Heart Disease	34	59.6
	Acquired Heart disease	23	40.4
	Total	57	100.0
congenital	Cyanotic	11	32.4
	A cyanotic	23	67.6
	Total	34	100.0
A cyanotic	AVSD	2	8.7
	Coarctation of aorta	1	4.3
	Coarctation of aorta and PDA	1	4.3
	PDA	11	47.8
	VSD	7	30.4
	VSD and pulmonary stenosis	1	4.3
	Total	23	100.0
cyanotic	D-Transposition of the Great Arteries (DTGA)	3	27.3
	Tetralogy of Fallot (TOF)	6	54.5
	TAPVR	2	18.2
	Total	11	100.0
Acquired	Cardiomyopathies	1	4.3
	Rheumatic heart disease	22	95.7

	Total	23	100.0

In our study most common predisposing factors for cardiac illness were poor oral hygiene (22, 64%). Other factors included surgery, infective endocarditis, and prolonged hospitalizations, each contributing 11.8 % (4 cases). Regarding physical findings, edema was the most common (35, 34.7%), followed by splenomegaly (29, 28.7%) and new or worsening heart murmur (23, 22.8%). Less frequent findings included clubbing (10, 9.9%), focal neurological deficit (3, 3.0%), and petechial rash (1, 1.0%). Table 3

Table 3 Predisposing factors and clinical findings

		Frequency	**Percent**
Predisposing Factor	Surgery	4	11.8%
	Infective Endocarditis	4	11.8%
	Poor Oral Hygiene	22	64%
	Prolonged Hospitalizations	4	11.8%
Total		34	100.0%
Physical Finding	Clubbing	10	9.9%
	Edema	35	34.7%
	Focal Neurological Deficit	3	3.0%
	New or Worsening Heart Murmur	23	22.8%
	Splenomegaly	29	28.7%
	Petechial Rash	1	1.0%
Total		101	100.0%

All patients (61, 100%) underwent echocardiography. Among these, 32 patients (52.5%) had findings suggestive of infective endocarditis (IE), while 29 patients (47.5%) did not. Of the 32 patients with IE findings, vegetation was present in all cases (32, 100%). Additionally, valvular regurgitation was observed in 24 patients (75%), while 8 patients (25%) did not have valvular regurgitation. Lastly, abscess formation was rare, with only 2 patients (6.3%) showing evidence of it, while 30 patients (93.8%) did not. Table 4

Table 4 Echocardiographic findings

		Frequency	Percent
Echocardiography	Yes	61	100.0
Echocardiography finding of IE	No	29	47.5
	Yes	32	52.5
	Total	61	100.0
Vegetation		32	100.0
Valvular regurgitation	No	8	25.0
	yes	24	75.0
	Total	32	100.0
Abscess formation	No	30	93.8
	yes	2	6.3
	Total	32	100.0

5.3 Microbiological Profile

Our finding revealed that the vast majority of patients (58, 95.1%) had blood cultures sent. Among those who had blood cultures, 31 patients (50.8%) had the cultures taken prior to receiving antibiotics, while 30 patients (49.2%) had cultures sent after starting antibiotic treatment. The majority of cultures involved 2 bottles (59, 96.7%), with only 2 patients (3.3%) having 4 bottles.

Regarding the identification of causative pathogens, 20 patients (32.6%) had an identified pathogen, while 41 patients (67.2%) did not. Of those 20 patients, 18 (85.7%) had atypical pathogens, and 2 (14.3%) had typical pathogens. The typical pathogens included Enterococcus, Streptococcus viridans, each found in one patient (5%). Atypical pathogens included Bacillus, Brucellosis, Acinetobacter, Klebsiella pneumoniae, and Pseudomonas aeruginosa, among others. The most frequent atypical pathogen was Staphylococcus Aureus (6, 30%) followed by CONS (5, 25.4%).

For antimicrobial susceptibility testing, 13 patients (65%) had their pathogens tested, and susceptibility results were reported for a variety of antibiotics. Amikacin (17.9%) was the most frequently effective antibiotic, followed by vancomycin (14.3%) and ciprofloxacin (14.3%). The presence of antibiotic resistance was noted in 9 patients (69.2%), with resistance detected to several

antibiotics, including cefepime (17.2%), ceftriaxone (17.2%), and gentamicin (13.8%). Other resistant antibiotics included clindamycin, penicillin, and erythromycin.

Table 5 Blood culture

		Frequency	Percent
Blood culture sent	No	3	4.9
	Yes	58	95.1
	Total	61	100.0
Blood culture sent prior to antibiotics	No	30	49.2
	Yes	31	50.8
	Total	61	100.0
Number of bottles	2	59	96.7
	4	2	3.3
	Total	61	100.0
Causative pathogen identified	No	41	67.2%
	Yes	20	32.6%
	Total	61	100.0
Causative pathogen	Atypical	18	90%
	Typical	2	10%
	Total	20	100.0
Typical	Enterococcus	1	5%
	Streptococcus Viridian	1	5%
Atypical	Bacillus	1	5%
	Brucellosis	1	5%
	CONS	5	25%
	K.aeorgnisa	2	10%
	K.pneumoniae	2	10%
	Pseudomonas aerognosa	1	5%
	S. Aureus	6	30%
	Total	20	100.0
Antimicrobial susceptibility testing results	No	7	35.0
	Yes	13	65.0
	Total	20	100.0
susceptibility	Amikacin	5	17.9%
	Meropenem	1	3.6%
	Cefepime	3	10.7%
	Ceftriaxone	3	10.7%
	Ciprofloxacin	4	14.3%
	Gentamicin	3	10.7%

	Doxycycline	1	3.6%
	Amoxicillin	1	3.6%
	Clindamycin	1	3.6%
	Oxacillin	2	7.1%
	Vancomycin	4	14.3%
Total		28	100.0%
Presence of antibiotic-resistant	No	4	30.8
	Yes	9	69.2
	Total	13	100.0
Resistance	Cefepime	5	17.2%
	Ceftriaxone	5	17.2%
	Meropenem	1	3.4%
	Gentamicin	4	13.8%
	Ceftazidime	2	6.9%
	Ciprofloxacin	1	3.4%
	Cotrimoxazole	1	3.4%
	Clindamycin	3	10.3%
	Erythromycin	3	10.3%
	Oxacillin	1	3.4%
	Penicillin	3	10.3%
Total		29	100.0%

Regarding laboratory findings: Hemoglobin/Hematocrit (Hgb/Hct) levels were decreased for age in 51 patients (83.6%), while 10 patients (16.4%) had levels normal for age. Regarding Erythrocyte Sedimentation Rate (ESR), 52 patients (85.2%) had elevated levels, 8 patients (13.1%) had normal levels, and 1 patient (1.6%) had unknown results. Renal Function Tests (RFT) revealed elevated levels in 21 patients (34.4%), while 40 patients (65.6%) had normal levels. For Urinalysis, RBCs > 5 HPF were found in 34 patients (55.7%), while 27 patients (44.3%) had no significant RBCs.

Table 6 Ancillary Laboratory tests

		Frequency	**Percent**
Hgb/Hct	Decreased for Age	51	83.6
	Normal for Age	10	16.4

	Total	61	100.0
ESR	Elevated	52	85.2
	Normal	8	13.1
	Unknown	1	1.6
	Total	61	100.0
RFT	Elevated	21	34.4
	normal	40	65.6
	Total	61	100.0
Urinalysis (RBC>5HPF)	No	27	44.3
	Yes	34	55.7
	Total	61	100.0

5.4 Management and Outcomes

Regarding Management, gentamycin (39, 28.7%) was the most commonly prescribed antimicrobial therapy, followed by ampicillin (27, 19.9%) and vancomycin (31, 22.8%). The majority of patients (23, 37.7%) received therapy for 28 days, while others were treated for varying durations, including less than 28 days (18, 29.5%) and 42-56 days (11, 18%). A small group underwent surgical procedures (4, 6.6%), such as abscess removal, PDA ligation, and vegetation removal. The most common complications were heart failure (31, 44.9%), renal complications (17, 24.6%), and sepsis with multi-organ dysfunction (12, 17.4%). Table 7

Table 7 Management and out comes

		Frequency	**Percent**
Type of Antimicrobial therapy	Ampicillin	27	19.9%
	Ceftriaxone	16	11.8%
	Gentamycin	39	28.7%
	Cefepime	5	3.7%
	Vancomycin	31	22.8%
	Meropenem	13	9.6%
	Metronidazole	3	2.2%
	Amikacin	2	1.5%
Total		136	100.0%
Duration of antimicrobial therapy	<28 Days	18	29.5
	28 Days	23	37.7
	28-42 Days	6	9.8
	42 Days	1	1.6
	42-56 Days	11	18.0

	56-84 Days	2	3.3
	Total	61	100.0
Surgical procedures	No	57	93.4
	Yes	4	6.6
	Total	61	100.0
Type of procedure	Abscess removal and PDA Ligation	1	25.0
	Abscess drainage	1	25.0
	PDA ligation and closure	1	25.0
	Vegetation removed	1	25.0
	Total	4	100.0
Complications	Embolic Pneumonia	8	11.6%
	Heart Failure	31	44.9%
	Conduction Abnormalities	1	1.4%
	Renal Complication	17	24.6%
	Sepsis with MOD	12	17.4%
Total		69	100.0%
Outcome	Cured	25	41.0
	Died	36	59.0
	Total	61	100.0
Immediate cause of death	Cardiogenic shock	3	12.0
	Conduction abnormality (Arrythmia)	2	8.0
	Heart failure	4	16.0
	Refractory heart failure	1	4.0
	Renal failure	2	8.0
	Sepsis with multiorgan failure	13	52.0
	Total	24	100.0

While 36 patients (59 %) were cured, 25 (59 %) died, with sepsis with multi-organ failure (13, 52%) being the leading cause of death, followed by heart failure (4, 16.0%) and cardiogenic shock (3, 12.0%). The average hospital stays for patients who died was 21.04 days (SD = 18.449), while the average stay for patients who were cured was 41.39 days (SD = 11.746)

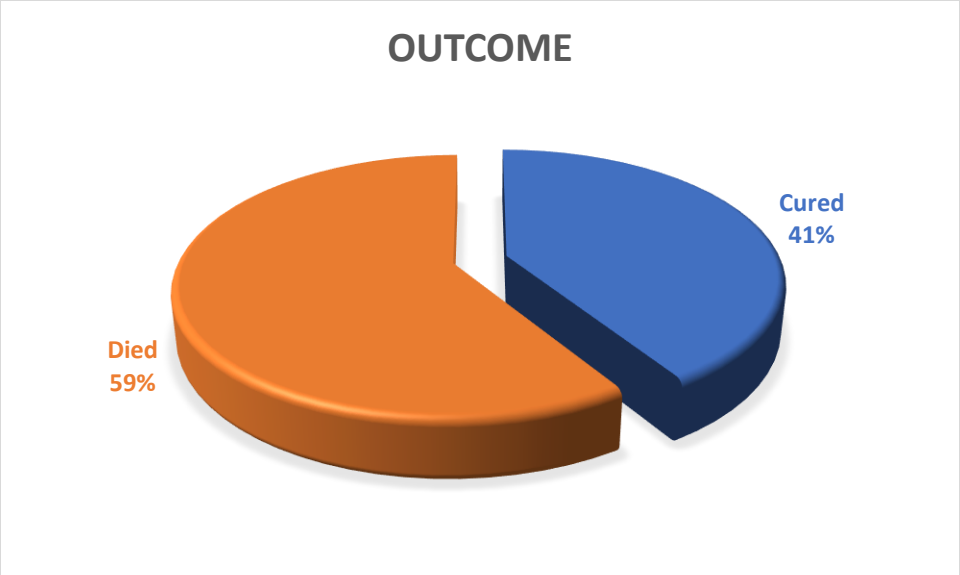

Fig 4 Out come

5.5 Factor affecting the outcome

In this study we assessed factor that affects the outcome, variables such as: - Duration of symptom, Length of hospital stay, Blood culture, Causative pathogen identified, complication and Resistance were analyzed first by bivariable analysis. Based on the p-value (< 0.25) of the bivariable analysis, the following variables were identified as candidate variables for the multivariable analysis these are: complication and Length of hospital stay

The multivariable analysis revealed that, with cure as the outcome, shows that each additional day of hospital stay increases the odds of recovery by 8.3% (Odds Ratio = 1.083, 95% CI = 1.030 to 1.138, p = 0.002). In contrast, the presence of complications significantly decreases the odds of being cured by 96.1% (Odds Ratio = 0.039, 95% CI = 0.005 to 0.345, p = 0.003).

6. Discussion

This study was a five-year retrospective hospital-based cross-sectional study, conducted in Tikur Anbessa specialized Hospital pediatrics Cardiac clinic involving records of sixty one pediatrics cardiac patients from January 2019 to November 30, 2024.

This study conducted on 61 patients who fulfil definite criteria based on modified Dukes criteria for IE. It has demonstrated a majority being female (35, 57.4%). The largest age group consists of patients aged 5 to 10 years (22, 36.1%), followed by those older than 10 years (19, 31.1%). Geographically, nearly half of the patients (30, 49.2%) are from the Oromia region. A significant portion of the records are new cases (38, 62.3%), while repeat patients make up a smaller percentage (23, 37.7). In our study, the majority of pediatric IE cases were observed in children aged 5-10 years (22, 36.1%). This aligns with findings from India, where a similar age distribution has been noted, indicating that younger children are particularly vulnerable to this condition. In contrast, reports from the USA suggest a broader age range of affected individuals more commonly affecting children >11 years, with cases often seen in older children and adolescents as well. Our data showed a higher prevalence of IE in females (35, 57.4%), which is consistent with trends observed in India. This may suggest a potential gender predisposition to the disease or differences in healthcare-seeking behaviors. Conversely, the USA has reported a more balanced sex distribution among pediatric IE cases, highlighting potential cultural or environmental factors influencing these outcomes.

The clinical presentation of pediatric infective endocarditis primarily includes fever (27.2%), shortness of breath (23.6%), and cough (14.7%). Among the presenting symptoms, fever was observed in the vast majority of our patients which is similar to observations from earlier literature (3, 4). However, absence of fever cannot rule out the diagnosis of IE as patients without fever may still have IE. Meanwhile, Sebastian et al. (2022) highlighted the challenges in diagnosis, particularly the variability in clinical presentation, which resonates with our study's observation of diverse symptoms such as fever, shortness of breath, and cough.

A significant proportion of patients had underlying cardiac conditions, with 59.6% having congenital heart disease, 40.4% with acquired heart disease, and 6.6% presenting with non-cardiac causes, mirroring findings from Indian studies that emphasize the role of these pre-existing conditions in the development of IE. However, the USA data often includes a wider range of

underlying health issues, such as prosthetic heart valves, intravenous drug use immunocompromised states, which may not be as prevalent in our cohort. Highlighting the critical role of cardiac conditions in the disease's etiology.

This study provides a comprehensive analysis of pediatric infective endocarditis in Ethiopia, contributing to the growing body of literature on this critical condition. Our findings align with previous research conducted in Ethiopia, particularly the study by Moges et al. (2015), which reviewed cases of infective endocarditis in children in Addis Ababa. Similar to our results, their study highlighted a predominance of congenital heart disease as a significant underlying condition, emphasizing the role of pre-existing cardiac abnormalities in the etiology of infective endocarditis.

Blood culture was sent for 31 patients (50.8%) prior to initiation of antibiotics and for the 30 patients (49.2%) blood culture sent after initiation of antibiotics(antibiotics is initiated either at TASH or from referring hospital). This indicates that just over half of the patients had their blood cultures taken before the initiation of antibiotic therapy, which is crucial for accurately identifying pathogens. Regarding the identification of causative pathogens, 21 patients (34.4%) had an identified pathogen, while 40 patients (65.6%) did not. This high rate in our series could be attributed to prior antibiotics therapy and lack of optimal culture techniques.

This shift of pattern from the usual prevalence of streptococci species has been reported in recent studies (1, 4). It seems that in the last decade staphylococci have exceeded the streptococci species in causing IE with concomitant decrease in the incidence of Streptococci viridian. In our current study, S. aureus was identified in (6, 30%) of cases, while previous studies reported Enterococcus. Previous studies showed that culture negative endocarditis accounts for 30–45% of all cases of IE (4). Which is in line with a study from USA, with a significant presence of Staphylococcus aureus and enterococci.

Out of the 20 patients tested for antimicrobial susceptibility: identified pathogens were susceptible to **Amikacin:** 5 (17.9%), **Meropenem:** 1 (3.6%), **Cefepime:** 3 (10.7%), **Ceftriaxone:** 3 (10.7%), **Ciprofloxacin:** 4 (14.3%), **Gentamicin:** 3 (10.7%) and **Vancomycin:** 4 (14.3%) and Resistance Patterns demonstrated from this study 13 patients (65.0%) **Cefepime:** 5 (17.2%), **Ceftriaxone:** 5 (17.2%), **Meropenem:** 1 (3.4%), **Gentamicin:** 4 (13.8%), **Ciprofloxacin:** 1 (3.4%), **Cotrimoxazole:** 1 (3.4%), **Clindamycin:** 3 (10.3%) and **Penicillin:** 3 (10.3%).This data indicates a concerning level of antimicrobial resistance among the identified pathogens, highlighting the

importance of careful selection of antibiotic therapy based on susceptibility testing. Regarding Management, gentamicin (39, 28.7%) was the most commonly prescribed antimicrobial therapy, followed by ampicillin (27, 19.9%) and the majority of survivors has been taking these two drugs. while surgical procedures were performed in a small percentage of cases (6.6%).

The study identified several complications in the patient population, including heart failure (44.9%), renal complications (24.6%), embolic pneumonia (11.6%), sepsis with multiple organ dysfunction (17.4%), and conduction abnormalities (1.4%), highlighting the serious nature of infective endocarditis and its potential to affect multiple organ systems, leading to significant morbidity and mortality in pediatric patients.

Our current data indicates that the mortality rate for pediatric infective endocarditis at Tikur Anbessa Specialized Hospital is 39.3%. Comparatively, previous studies in Ethiopia have shown a slightly lower mortality rate of around 7.3%(4), while research conducted in Tanzania reported mortality rates of approximately 30% and Global outcomes for infective endocarditis in children report in-hospital mortality rates ranging from 20% to 25%(11). This highlights the concerning severity of pediatric infective endocarditis in our setting, emphasizing the need for improved diagnostic and therapeutic strategies.

Overall, this study not only reinforces existing knowledge regarding the epidemiology and management of infective endocarditis but also highlights the specific challenges faced in the Ethiopian context. By comparing our findings with those from other research, we stress the necessity for tailored strategies that consider local healthcare dynamics, ultimately aiming for improved patient outcomes in pediatric infective endocarditis.

7. Limitations of the study

Due to incomplete registration of patient information and data management system in the study hospitals, some variables that were not included under the study and small sample size of the study makes this study's result questionable, the fact that it's a single center study and the retrospective nature of study are limitations.

8. Conclusion

This five-year retrospective hospital-based cross-sectional study conducted at Tikur Anbessa Specialized Hospital provides valuable insights into the epidemiology, clinical presentation, management, and outcomes of pediatric infective endocarditis (IE) in Ethiopia. The study, which included 61 pediatric patients meeting the modified Duke criteria for IE, revealed a predominance of female patients (57.4%) and a higher prevalence of cases among children aged 5–10 years (36.1%). Geographically, nearly half of the patients (49.2%) were from the Oromia region, reflecting potential regional disparities in disease burden or healthcare access.

The clinical presentation of pediatric IE was consistent with global trends, with fever, shortness of breath, and cough being the most common symptoms. However, the absence of fever in some cases underscores the diagnostic challenges associated with this condition.

A significant proportion of patients had underlying cardiac conditions, particularly congenital heart disease (59.6%), highlighting the critical role of pre-existing cardiac abnormalities in the development of IE. Blood culture results revealed that only 34.4% of patients had an identified pathogen, with *Staphylococcus aureus* being the most common causative agent (30%).

The high rate of culture-negative endocarditis (65.6%) may be attributed to prior antibiotic use and suboptimal culture techniques, emphasizing the need for improved diagnostic protocols, including early blood culture collection and the use of specialized media. Antimicrobial susceptibility testing revealed concerning levels of resistance, particularly to commonly used antibiotics such as cefepime and ceftriaxone, underscoring the importance of tailored antibiotic therapy based on susceptibility testing.

The study also identified significant complications associated with pediatric IE, including heart failure (44.9%), renal complications (24.6%), and sepsis with multiple organ dysfunction (17.4%), reflecting the severe morbidity and mortality associated with this condition. The mortality rate in this cohort was 39.3%, higher than rates reported in previous Ethiopian studies and global data, highlighting the urgent need for improved diagnostic and therapeutic strategies in this setting.

In comparison with international studies, our findings align with global trends in terms of clinical presentation and underlying risk factors but also reveal unique challenges specific to the Ethiopian context, such as limited access to advanced diagnostic tools and high rates of antimicrobial

resistance. The study underscores the importance of early recognition, timely intervention, and a multidisciplinary approach to managing pediatric IE, as emphasized in global literature. Furthermore, the integration of advanced imaging techniques and adherence to updated diagnostic criteria, such as the 2023 modified Duke criteria, are critical for improving diagnostic accuracy and patient outcomes.

In conclusion, this study contributes to the growing body of literature on pediatric infective endocarditis, particularly in low-resource settings. It highlights the need for context-specific strategies to address the unique challenges faced in Ethiopia, including improved diagnostic capabilities, antimicrobial stewardship, and enhanced multidisciplinary care. By addressing these gaps, we can work toward reducing the morbidity and mortality associated with pediatric IE and improving the overall quality of care for affected children.

9. Recommendations

Based on the findings of the study, the following recommendations are forwarded

Decreasing the likelihood of bacteremia by prompt treatment of other infections, regular checks for good oral hygiene and the absence or presence of dental carries should help to reduce the occurrence of IE especially in children with underlying structural heart disease.

A high index of suspicion remains essential in making a diagnosis of IE, more so as many of our patients presented with non-specific symptoms and signs.

Community awareness campaigns should educate parents and caregivers about the signs and symptoms of infective endocarditis, promoting early medical consultation.

Implementing robust antimicrobial stewardship programs will help optimize antibiotic use and reduce resistance development.

The findings emphasize the necessity for future retrospective and multicenter research to better understand the disease

To improve the Management of pediatric infective endocarditis, it is essential to prioritize timely blood culture collection before the initiation of antibiotic therapy, improvement in techniques of microbiology culturing techniques so that we enhance pathogen identification. Establishing special communication with the laboratory to ensure the use of appropriate media for pathogen growth is crucial for accurate diagnosis.

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Annex I: Checklists

Section I. Socio-demographic data

1. ID no----------

2. MRN----------

3. Age of child----------

4. Sex Male

Female

5. Place of residency Rural

Urban

6. Patient record New

Repeat

Section II; Clinical Data

1. Duration of illness before Diagnosis
2. Date of Admission
3. Previous admission

I. No II. Yes If yes specify Frequency--------

Ward Emergency ICU

4. Predisposing factor

Congenital heart disease	I. No	II. Yes
If Yes	Cyanotic	Acyanotic
Rheumatic heart disease	I. No	II. Yes
Does the patient underwent surgery	I. No	II. Yes
IV drug use	I. No	II. Yes
Prosthetic heart valve/ cardiac surgery	I. No	II. Yes
Other conditions	I. No	II. Yes If yes specify

5. Presenting symptoms

Fever	I. No	II. Yes
Osler's Nodes	I. No	II. Yes
Janeway Lesion	I. No	II. Yes
Splenomegaly	I. No	II. Yes
Heart murmur	I. No	II. Yes
Embolic events	I. No	II. Yes
Heart failure	I. No	II. Yes

6. Echocardiographic findings

Vegetation size and location

Valvular regurgitation

Abscess formation

Section III. Microbiological Profile

1. Causative pathogen(s) identified
2. Method of pathogen identification blood culture

3. Antimicrobial susceptibility testing results
4. Presence of antibiotic-resistant strains

Section IV. Management and Outcomes

1. Antimicrobial therapy (e.g., type, duration)
2. Surgical interventions (e.g., valve repair or replacement, abscess drainage)
3. In-hospital complications (e.g., stroke, heart failure, renal failure)
4. In-hospital mortality
5. If death cause of death
6. Length of hospital stay

Annex II: Declaration form

I, the undersigned, declare that this thesis is my original work, has not been presented for a degree in this or any other university and that all sources of materials used for the thesis have been fully acknowledged.

Name: _____

Signature: _____

Name of the institution: _____

Date of submission: _____

This thesis has been submitted for examination with my approval as university advisors.

Name and Signature of the first advisor

_____

Name and Signature of the second advisor

_____

Name and Signature of the internal examiner

_____