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Pediatric infective endocarditis at a referral children's hospital during 19-year period: Trends and Outcomes

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Abstract

Background: We noted an increase in infective endocarditis (IE) cases in recent years. The purpose of the study was to examine the changes in incidence, risk factors, microbiology, complications and outcome of IE in our patient population.

Methods: Records of children < 18 years with discharge diagnosis of IE during 2002-2020 at Children's Hospital of Michigan, Detroit were reviewed. Modified Duke criteria were used to determine "definite" and "possible" IE cases.

Results: 101 patients with IE were identified, representing annual incidence of 4.9/10,000 admissions. During 2002-2011 (early period), the incidence was 2.8/10,000 (33 cases). However, during 2012-2020 (late period), the incidence was 7.0/10,000 (68 cases): a 2.5-fold increase. Males were 53.4%. The age range was 1 mo – 17 yrs (median 6 yrs). Of 101 patients, 37 (36.6%) met criteria for definitive and 64 (63.4%) for possible IE. The most common predisposing conditions included congenital heart disease (CHD) (50.5%), central venous catheter (CVC) (25.7%), and immunosuppression (13.9%). CHD was more frequent in the late period (41/68, 60.3%) compared to early period (10/33, 30.3%) (p = 0.0059). Cardiac surgery had been performed in 28/51 (55%) prior to IE diagnosis. CVC related infections were more frequent in the early period (16/33, 48.5%) than the late period (10/68, 14.7%), (p = 0.0005). Overall, 16 (15.8) cases were culture negative. In culture-positive IE, *S. aureus* was most common (33/101, 32.7%) followed by streptococci (17), *S. epidermidis* (10), Gram negative bacilli (8), Enterococci (7), fungi (5) and HACEK group (4). Causative organisms were similar in both periods except for fungal organisms (5) and *B. henselae* (1) in the late period only. Valve replacement or valvuloplasty were performed in 19 (18.8%) patients. Complications included acute kidney injury (9) and emboli to the brain (10) and to the lungs (7). Mortality occurred in 15 (14.8%): 8 had CHD, 5 had CVC and 1 had fulminant MRSA infection.

Conclusion(s): Most of our IE patients had underlying medical conditions. The higher incidence of IE during the late period is likely due to an increase in the number of patients with complex cardiac conditions who underwent surgery at our institution. S. aureus was the predominant pathogen followed by streptococci. Mortality rate in our patients was 14.8%.

Background

- In children, hospitalization rates due to IE are estimated at 1: 1300 to 2000 admission annually
- Regional and national prevalence estimates of endocarditis vary significantly. Mortality rate using Kid's Inpatient Database was estimated at 3.5%
- Underlying rheumatic heart disease was a major risk factor associated with infective endocarditis
- More recently, congenital heart disease with recent surgical intervention has been identified as a common risk factor for infective endocarditis. Other predisposing conditions include central venous catheters and Intravenous drug use

AIMS

- To determine the incidence of bacterial endocarditis in children (<18 years) at Children's Hospital of Michigan during the period 2002-2020
- To determine the spectrum of risk factors and bacterial pathogens associated with bacterial endocarditis in Children's Hospital of Michigan during the study period

Methods

- Records of patients aged < 18 years with discharge diagnosis of IE during 2002-2020 were reviewed
- Modified Duke criteria were used to determine "definite" and "possible" IE cases
- Demographics, risk factors: underlying cardiac conditions, presence of CVC, immunosuppression, recent dental procedure identified
- Clinical, microbiological and echocardiographic findings were reviewed
- Statistical analysis of different clinical variables and frequencies was performed using SPSS

Results

Demographics

- **Study period: January 2002 – December 2020**
- **Number of patients: 101**
- **Age: Range 1 month - 17 y (median 6 y)**
- **Gender:**
  - **Male 54 (53.5%)**
  - **Female 47 (46.5%)**
- **Ethnicity:**
  - **African American 52 (50.5%)**
  - **Caucasian 29 (28.7%)**
  - **Hispanic 6 (5.9%)**
  - **Others/unknown: 14 (13.9%)**

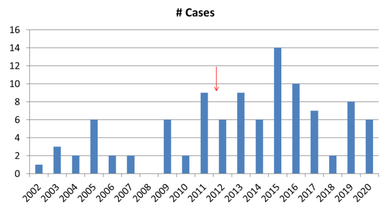
Diagnosis by Duke criteria

- **Definite IE: 37 (36.6%)**
- **Possible IE: 64 (63.4%)**
- **Abnormal echocardiograms: 63/101 (62.4%)**
- **Overall, 16/101 (15.8) were culture negative**

Predisposing conditions

- **Congenital heart disease (CHD): 51 (50.5%)**
  - **28/51 (55%) had prior cardiac surgery (palliative/corrective)**
  - **Interval range prior to IE diagnosis: 12d - 13y**
- **CVC or Ventriculoatrial (VA) shunt: 26 (25.7%)**
- **Immunosuppression: 14 (13.9%):**
  - **Malignancy/chemotherapy: 6**
  - **DiGeorge syndrome: 5**
  - **Primary immunodeficiency: 3**
- **Rheumatic heart disease: 2 (2%)**
- **Preceding dental procedure: 3 (3%)**

Figure1: Yearly distribution of patients with endocarditis



Incidence

Overall incidence: 4.9/10,000 admissions

Early period (2002-2011): 2.8 cases/10,000 admissions

Late period (2012-2020): 7.0 cases/10,000 admissions

2.5-fold increase

Early vs Late period

- **Congenital heart disease (CHD) was more frequent as underlying condition during the late study period (41/68, 60.3%) vs the early period (10/33, 30.3%) (p = 0.0059)**
- **However, CVC and V-A shunt related infections were more frequent in the early period (16/33, (48.5%) vs the late period (10/68, 14.7%) (p = 0.0005)**

Clinical/Lab findings

Heart murmur 39 (38.6%)
Splenomegaly 6 (5.9%)
Petechiae 1 (1%)
Immunological phenomenon 4 (4%)
Embolic phenomenon 3 (3%)

Leukocytosis 31 (30.7%)
Bandemia 21 (20.8%)
Anemia 58 (57.4%)
Thrombocytopenia 21 20.8%
Thrombocytosis 4 (4%)
CRP elevation 60 (59.4%)
Abnormal liver function 27 (26.7%)
Abnormal kidney function 17 (16.8%)

Results

Microbiology in 101 patients with IE

	Total	2002-2011	2012-2020	p-value
Patients #	101	33	68	
Culture negative	16	4 (12.1%)	12 (17.6%)	0.48
Culture positive	85	29 (87.9%)	56 (82.3%)	0.48
S. aureus	33	10	23	
MSSA	23	7 (21.2%)	16 (23.5%)	0.79
MRSA	10	3 (9.1)	7 (10.3%)	0.85
VGS	13	5 (15.2%	8 (11.8%)	0.63
S. epidermidis	10	5 (15.2%)	5 (7.4%)	0.22
Gram negatives	8	1 (3.0%)	7 (10.3%)	0.20
Enterococcus sp.	7	4 (12.1%)	3 (4.4%)	0.15
Fungal	5	0 (0.0%)	5 (7.4%)	NA
HACEK	4	1 (3.0%)	3 (4.4%)	0.74
S. penumoniae	2	1 (3.0%)	1 (1.5%)	0.60
NV streptococci	2	2 (6.0%)	0 (0.0%)	NA
B. henselae	1	0 (0.0%)	1 (1.5%)	NA
Incidence: case/10,000 admissions	4.9	2.8	7.0	
Cardiac conditions	51	10 (30.3)	41 (60.3%)	0.0059
CVC/VA shunt	26	16 (48.5%)	10 (14.7)	0.0005

MSSA: Methicillin susceptible *Staphylococcus aureus*
MRSA: Methicillin resistant *Staphylococcus aureus*
VGS: Viridans group streptococci
HACEK: *Haemophilus species, Aggregatibacter actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae.*
NV: Nutritionally variant

Most common organism: *Staphylococcus aureus*

Causative organisms were similar between Early & Late periods except: Fungal organisms: 0 in early period vs 5 patients in late period

***Bartonella henselae*: 1 patient in late period**

Treatment

Penicillin
Third generation cephalosporins
Vancomycin
Oxacillin
Rifampin
Carbapenem
Gentamicin
Micafungin

Duration: 4-6 weeks in most cases

Underlying cardiac conditions in 51 patients

Underlying cardiac condition	Number
Ventricular septal defect	17
Cyanotic congenital heart disease	12
Tetralogy of Fallot	11
Atrial septal defect	5
Patent ductus arteriosus	4
Tricuspid regurgitation	2
A-V canal defect	2
Mitral regurgitation	1

Interventions/surgery

Catheter Removal	18
Valve Replacement	**13**
Valvuloplasty	**6**
Pulmonary artery banding	2
Thrombus removal	17
VSD mass removal	6

Complications	Number
Acute kidney injury AKI	9
Emboli	
Brain	10
Splenic infarct	1
Periphery	1
Lung	7
Liver Abscess	1
Osteomyelitis	1
Mortality within 1 year of diagnosis	**15**

Valves involved

Valve	Frequency
Mitral valve	18
Tricuspid valve	19
Pulmonary valve	3
Aortic valve	1
Prosthetic valve	3

Mortality: organisms and underlying conditions

Age at time of diagnosis	Organism	Predisposing condition	Year
28 days	*S. epidermidis*	CVC	2005
13 months	*S. epidermidis*	CVC, TPN dependent	2013
17 years	MRSA	Eczema, MRSA sepsis	2013
6 years	Negative	St Jude prosthetic valve	2012
4 months	MRSA	Complete AV canal defect	2011
5 years	Negative	TOF	2014
7 days	MRSA	Rt ventricular hypoplasia	2014
2 years	*C. albicans*	CVC, TPN dependent, hypogammaglobulinemia	2014
11 years	*C. kruzei*	CVC, chemotherapy, malignancy	2015
2 months	*Klebsiella pneumoniae*	Pulmonary atresia, pulmonary valve stent stenosis	2020
2 months	*Klebsiella oxytoca*	TOF, absent pulmonary valve, PA conduit stenosis	2019
11 years	*Streptococcus intermedius*	Situs ambiguous, failed Fontanne stent	2017
7 months	*E. faecalis*	CVC, TPN dependent	2020
11 years	Negative	Morbid obesity	2015
3 months	*S. epidermidis*	PDA. Pulmonary hypertension	2016

Mortality occurred in 15 (14.8%):
8 had CHD
5 had CVC
1 had fulminant MRSA infection

Conclusions

- **The majority of our IE patients had underlying medical conditions including CHD, indwelling CVCs & immunosuppression**
- **The higher incidence of IE during the late period is likely due to an increase in the number of patients with complex cardiac conditions who underwent surgical intervention**
- ***Staphylococcus aureus* (33%) was the predominant causative pathogen followed by streptococci (13%)**
- **Mortality rate in our study patients was 14.8%. Underlying conditions may have been a contributing factor.**