SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Cardiology

Infectious Endocarditis in Children: Epidemiological, Clinical, Paraclinical and Therapeutic Profile

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DOI: 10.36347/sasjm.2022.v08i10.003 | **Received:** 25.07.2022 | **Accepted:** 21.08.2022 | **Published:** 04.10.2022

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Abstract **Original Research Article**

Introduction: Infective endocarditis (IE) in children is a serious pathology with high mortality and morbidity. The aim of our study was to describe the clinical, microbiological, therapeutic and evolutionary characteristics of infective endocarditis in children. ***Materials and methods:*** This is a retrospective study, listing all children aged less than 15 years, diagnosed in pediatric cardio consultation and hospitalized in the department of Pediatrics A-Mother and Child Hospital of Marrakech for infective endocarditis between 2010 and 2020. Clinical, paraclinical and therapeutic data were collected for each case using an exploitation form. ***Results:*** During the study period, 25 children presented with infective endocarditis, with a sex ratio equal to 1.08. The mean age of the patients was 9 years and 6 months. Underlying heart disease was found in 76% of cases. A cardiac murmur was noted in 96% of cases, and the most frequent germs were Staphylococcus and Streptococcus. Cardiac ultrasound revealed endocardial vegetations in 72% of the children. Intravenous antibiotic therapy was initiated in all children for a median of 45 days, and an indication for valve replacement was given in 16% of cases. According to the modified Duke criteria, 28% of the infective endocarditis cases were definite and the evolution was favorable in 80% of the children. The most frequent complications were valve failure, heart failure, and embolic complications, and death in 5 cases. ***Conclusion:*** The analytical study concluded that embolic complications, heart failure and neurological complications are predictive of mortality. Therefore, its management must be multidisciplinary, early and adequate.

Keywords: Infective endocarditis - Congenital heart disease - Echocardiography - Treatment - Child.

INTRODUCTION

Infective endocarditis is defined as the transplantation of a microorganism (usually a bacterium) onto an endocardium that has most often been previously damaged.

It has been on the rise for several decades, with a prevalence ranging from 0.42 to 1.35 per 1000 admissions in pediatric wards [1, 2]. This is associated with profound changes in the population susceptible to endocarditis, with a decrease in the prevalence of rheumatic fever in developed countries [3], an improvement in the survival of children with congenital heart disease [4], and an increase in the frequency of occurrence of endocarditis in healthy hearts.

The pathophysiology of infective endocarditis involves complex interactions between circulating microorganisms, the injured valvular endothelium, and the host immune system.

The main lesions of infective endocarditis are vegetations that cause embolisms and destruction of the valvular or perivalvular tissue that causes acute regurgitation [5].

The diagnosis of infective endocarditis can sometimes be difficult to establish. It is based on the Duke criteria [6], recently modified according to the latest ESC 2015 recommendations [7], to provide a more precise definition of infective endocarditis (Table 1 and 2).

The prevention of IE remains a difficult problem. Prophylactic measures, although well codified, are not always possible or effective and, above all, are not always applied. Hence the imperative need to regularly inform patients and their families about the risk of endocarditis and to remind them at each consultation that they must remain vigilant.

Our objective was therefore to describe this endocarditis on a clinical, microbiological and therapeutic level through a series of 25 cases with a review of the literature.

ANNEX

Table 1: Definition of infective endocarditis according to the modified Duke criteria [7]

Definite infective endocarditis
Critères pathologiques : o Microorganisms identified by culture or histological examination of vegetation, embolized vegetation or intracardiac abscess o o Pathological lesions: presence of vegetation or intracardiac abscess with histological confirmation of active endocarditis Critères cliniques : o 2 major criteria o 1 major and 3 minor criteria o 5 minor criteria
Possible infective endocarditis
o 1 major and 1 minor criterion o 3 minor criteria
Infective endocarditis not retained
o Certain alternative diagnosis o Resolution of infective endocarditis syndrome with antibiotic therapy for 4 days or less o No evidence of infective endocarditis at surgery or autopsy after 4 days or less of antibiotic therapy o No criteria for possible infective endocarditis

Table 2: Modified Duke criteria for the diagnosis of infective endocarditis (IE) [7]

Major criteria
Positive blood cultures for IE: • Microorganisms typical for IE in 2 separate blood cultures: Streptococcus viridans, Streptococcus bovis, HACEK group bacteria, Staphylococcus aureus; or Community Enterococci, in the absence of a primary infection site. • Microorganisms not typical for IE but isolated in persistent positive blood cultures (at least 2 blood cultures separated by 12 h or 3/3 blood cultures, or a majority' of positive blood cultures out of more than 4 taken within at least 1 h) • 1 positive blood culture for Coxiella burnetii or a phase I Ig G antibody titer > 1:800 *Evidence of endocardial damage :* • Positive cardiac ultrasound for AR (transesophageal cardiac ultrasound recommended in patients with prosthetic valves, in those defined as possible AR based on clinical criteria or who have complicated AR) defined as: intracardiac oscillating mass on a valve, on the path of a reflux or on prosthetic material or abscess or new prosthetic valve dehiscence. • New murmur of valve insufficiency (worsening and/or modification of a known murmur is not sufficient) • Prosthetic fixation in PET or PNN. • Paravalvular lesion confirmed on cardio-scan.
Minor criteria
• Predisposing cardiac pathology or intravenous drug abuse • Fever > 38.8C. • Vascular phenomena: arterial embolisms, septic pulmonary infarcts, mycotic aneurysms, intracranial or conjunctival hemorrhage, Janeway lesions. • Immunological phenomena: glomerulonephritis, false Osler's panic, Roth nodules, positive rheumatoid factor. • Positive blood culture but not meeting major criteria or positive serology for an active condition with a germ compatible with IE.
HACEK group : Haemophilus spp, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, Kingella kingae.

MATERIALS AND METHODS

1. Methodology

This is a retrospective study, including all children under 15 years of age with infective endocarditis, diagnosed in the cardiology department of ERRAZI Hospital and hospitalized between January 2010 and December 2020, in the pediatrics department A - Mother and Child Hospital - CHU Mohammed VI of Marrakech. The records of patients hospitalized with the diagnosis of infective endocarditis were indexed from the registers and archives of the service.

2. Evaluation criteria

2.1. Clinical evaluation criteria:

The data studied concerned the age, sex of the child, medical history, and clinical history leading to the diagnosis of endocarditis.

Among the functional signs presented by the child at the time of diagnosis, alteration of the general condition and the notion of fever were sought.

The presence of a heart murmur, splenomegaly (indicative of an infectious syndrome), and immunologic signs (Roth nodule, Osler's false

panariasis, or Janeway's erythematous placard) was noted.

Hemodynamic or embolic complications were collected. Finally, a possible infectious portal of entry (presence of a venous route, skin invasion or deep sinus or dental infection) was identified.

2.2. Paraclinical evaluation criteria

The results of chest radiography (to look for cardiomegaly or a parenchymal focus), electrocardiogram (to identify a cardiac conduction disorder or signs of myocardial ischemia), and trans-thoracic (TTE) or trans-esophageal (TEE) cardiac echocardiography were noted.

Regarding cardiac echography, the presence of vegetation or complications, at the time of diagnosis or during the course of the disease, was sought.

The results of the initial biological work-up were also taken into account, in particular to look for an inflammatory syndrome or disseminated intravascular coagulation (DIC).

We were also interested in the germs detected in the blood cultures, as well as in the other samples, mainly intraoperative samples in case of surgery.

Finally, if a radiological extension work-up in search of an embolic or septic complication had been performed, the results were collated.

2.3. Therapeutic evaluation criteria

We collected the mode of administration and duration of the different antibiotic treatments prescribed during the episode of endocarditis.

The evolution of the disease was evaluated (sterilization of the blood cultures, disappearance of the biological inflammatory syndrome and results of the control cardiac echography).

The total duration of hospitalization was noted. Finally, for each child included, we were able to classify infective endocarditis according to the modified Duke criteria.

3. Statistical analysis

A descriptive analysis of the study population was performed. Quantitative variables were presented as medians and extremes and qualitative variables as numbers and percentages.

RESULTATS

1. Epidemiological data

We collected 25 children with infective endocarditis hospitalized in our facility over a 10-year period. The mean age of our patients was 9 years and 6 months, with extremes ranging from 3 months to 14 years. Five patients (20% of cases) were less than 2 years old.

There was a slight male predominance (Figure 1), with a sex ratio that was equal to 1.08 (12 girls and 13 boys).

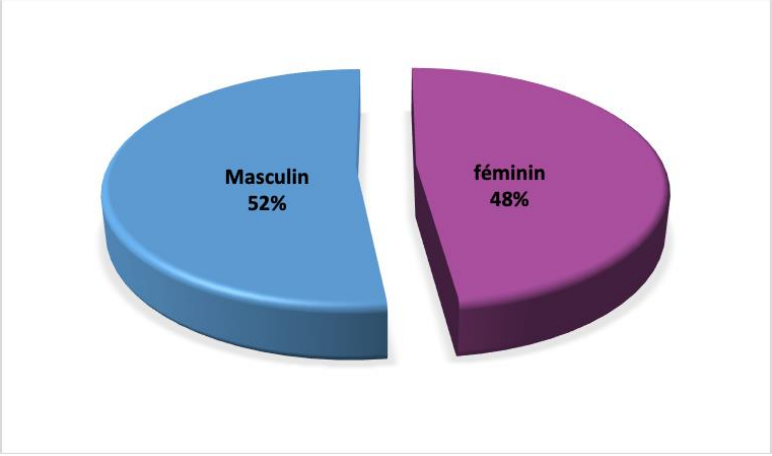

Figure 1: Gender distribution

In our series, six patients had endocarditis in a healthy heart (24%), while the remaining cases (76%) had pre-existing heart disease, 31% of which was rheumatic carditis (Figure 2).

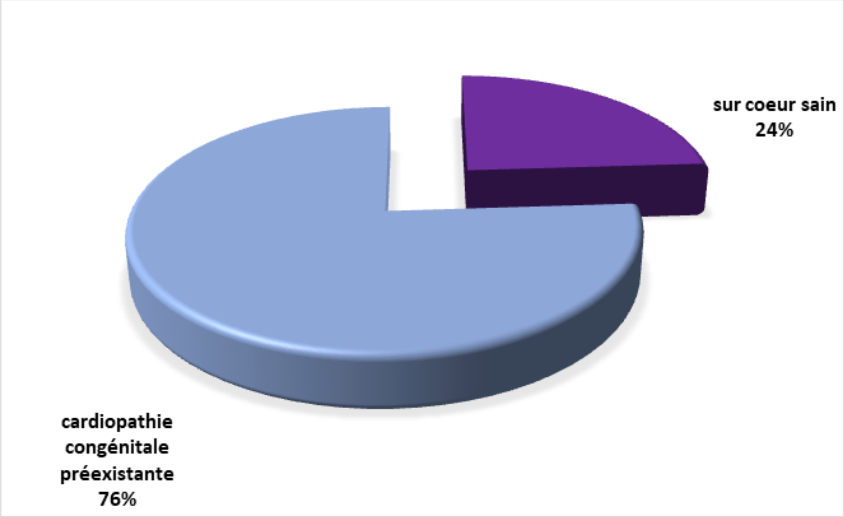

Figure 2: Distribution according to cardiac involvement

IVC was the most frequent abnormality in our series, present in 39.5% of patients followed for congenital heart disease, and 32% of all children with infective endocarditis.

Table 3 highlights the different congenital heart diseases found in our series.

Table 3: Classification of congenital heart disease found in our series

Cardiopathie congénitale	**Type de Cardiopathie congénitale**	**Nombre**	**Pourcentage**	**Traitement déjà établis**
Shunt gauche-droit (Non cyanogène)	CIV	8	**39.5%**	Cerclage (1cas) Fermeture (1 cas)
	CIA	4	**20%**	Fermeture (1 cas)
	CANAL ATERIEL PERSISTANT	2	**9%**	Double ligature du CA (1 cas)
	CAV	2	**9%**	Cerclage (1cas)
	MALADIE D'EBSTEIN	1	**4.5%**	-
	STENOSE PULMONAIRE	1	**4.5%**	-
Shunt droit-gauche (Cyanogène)	TETRALOGIE DE FALLOT	1	**4.5%**	-
	MALPOSITION DES GROS VAISSEAUX	2	**9%**	-

Among the six patients with rheumatic carditis, 3 had mitral insufficiency, i.e., 50%, and the rest had polyvalvulopathy responsible for moderate to severe mitral and aortic insufficiency (Fig 3).

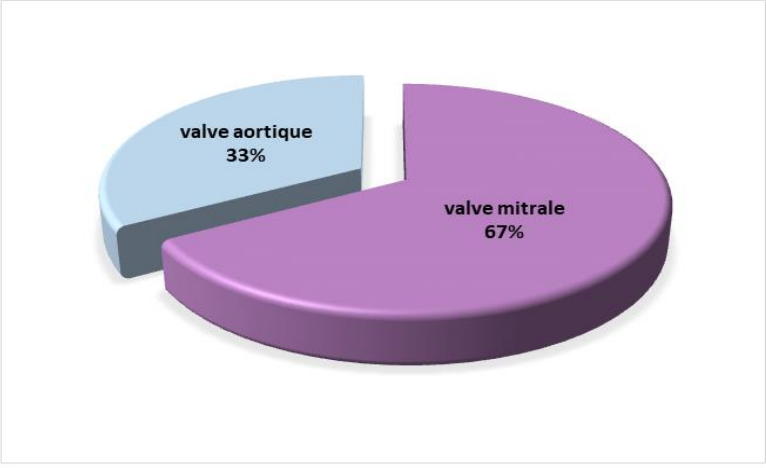

Figure 3: Distribution according to the type of valve affected in patients followed for rheumatic carditis

The mean time from symptom onset to consultation was 25 days. For only one patient, infective endocarditis was reported postoperatively with a delay in onset of symptoms of 30 days.

The portal of entry was found or suspected in 11 children (44%), dental in 45%, ENT in 27%, urinary in 20% and postoperative in 9% (Figure 4).

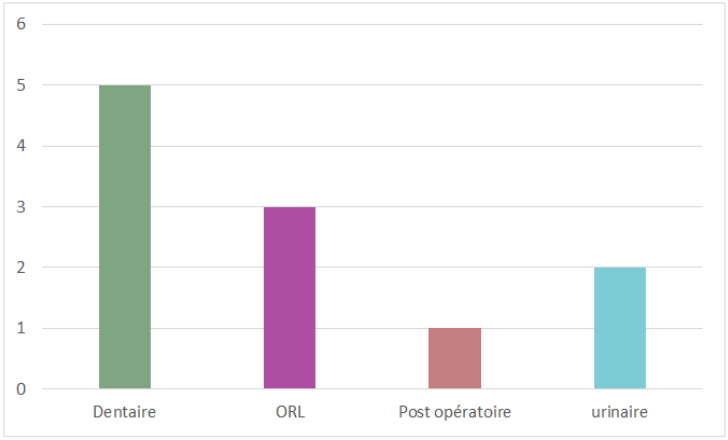

Figure 4: The portal of entry for infective endocarditis found in our series

2. Clinical outcomes

All patients had functional signs. Fever was the most frequent reason for consultation in 88% of cases with a median duration of 18 days (2-30 days), followed by alteration of general condition in 84% of patients (Figure 5).

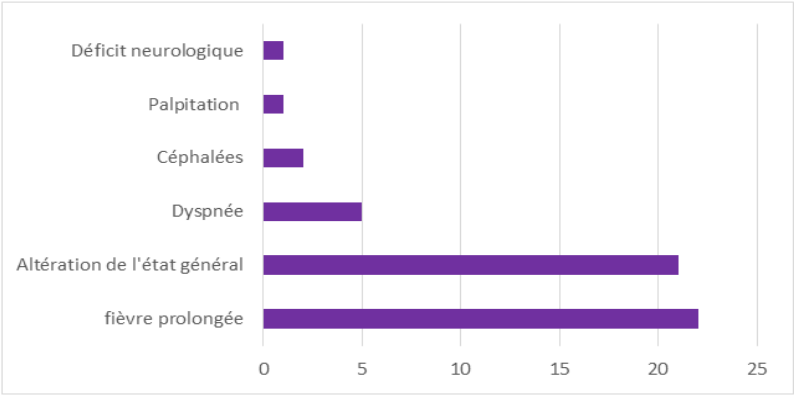

Figure 5: Distribution by reason for consultation.

Five children presented with polyarthralgias of inflammatory appearance involving mainly the large joints, one child complained of HTIC syndrome with headache, jet vomiting and photophobia.

Signs of chronic respiratory insufficiency with peribuccal cyanosis and digital hippocrasis were found in a girl of 06 years old, who had an unoperated tetralogy of Fallot (Figure 6).

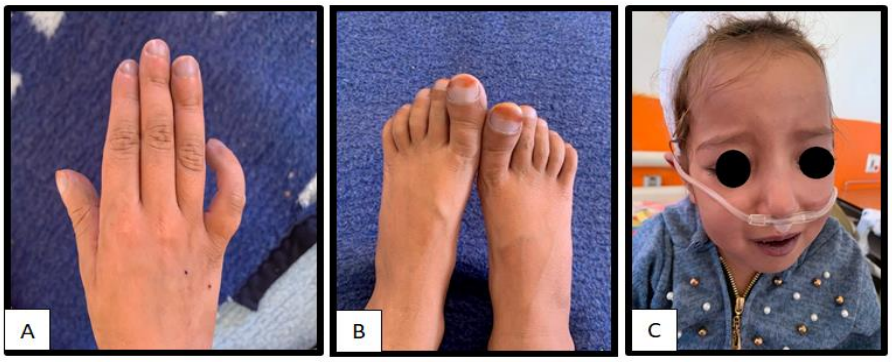

Figure 6: 6-year-old child, followed for non-operated tetralogy of Fallot; (A) and (B) digital hippocrasis with cyanosis of the extremities; (C) Peri oral cyanosis

Heart murmur was the most common finding on clinical examination. It was present in 24 out of 25 children (96%).

Four patients in our series (16%) had signs of cardiac insufficiency (hepatomegaly, turgidity of the jugular veins and hepatojugular reflux) at the time of diagnosis.

Statural and weight delay was found in 5 children (20% of our series).

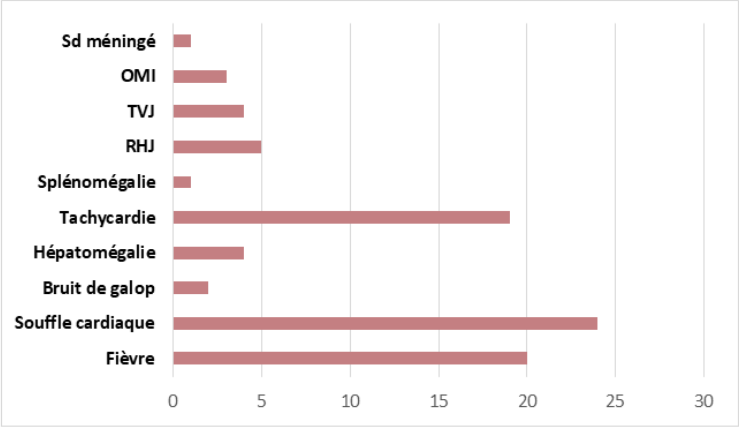

Figure 7: Physical signs found at the time of diagnosis.

3. Paraclinical Results

Twenty-two of 25 children (88%) had a biological inflammatory syndrome.

We reported hyperleukocytosis in 15 patients (60% of cases) and leukopenia in 2 patients (8% of cases). Thrombocytopenia less than 100,000 per cubic millimeter was present in 10 of 25 children, including 3 in the setting of DIC.

C-reactive protein (CRP) was performed in all our patients, positive in 22 children, The median C-reactive protein (CRP) level was 92 mg/l (4-268 mg/l).

The pro-calcitonin was requested only for 2 patients of our series, returned positive.

All our patients had undergone trans-thoracic echocardiography, with a mean time between admission and completion of 3.1 days. The most common valvular lesions in our series were vegetations: 18 cases, 72% of our series, and one case of partial rupture of a cord found in a single patient.

These vegetations were mobile in 12 cases (66.6% of cases). Their size was between 05 and 10 mm in 10 children and more than 10 mm in 8 children. The vegetations affected the mitral valve in 09 cases (50%), the tricuspid valve in 4 cases (22%), the aortic valve in 3 cases (17%), the aortic and mitral valve in 2 cases (11%) (Figure 8).

Left ventricular ejection fraction was impaired in 10% of cases, ranging from 30% to 50%.

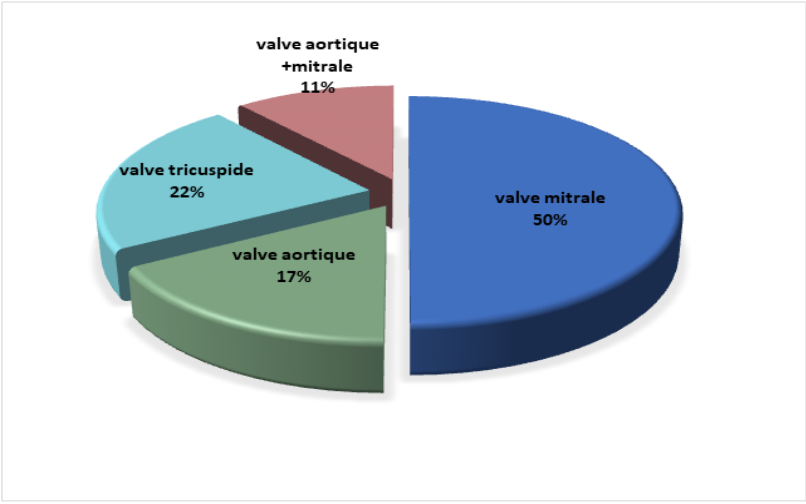

Figure 8: The location of endocardial vegetations in our series

Blood cultures were performed for all patients in our series, with a mean number of 3 (extremes ranged from 1 to 12). The average time to perform blood cultures was 2 days after admission (with extremes of 0 and 9). At least one or more blood cultures were positive in 12 cases (50%). The ratio of positive blood cultures was 1 to 2 patients.

Table 4: Patients with positive blood cultures noted in our series

Nombre de malades	Nombre des HC réalisées	Nombre de cultures positives	Germe isolé
Patient 1	3	**3**	*streptococcus*
Patient 2	2	**1**	*Staph aureus*
Patient 3	3	**2**	*Staph coagulase négatif*
Patient 4	2	**1**	*Staph aureus*
Patient 5	1	**1**	*Staph aureus*
Patient 6	2	**2**	*Staph aureus*
Patient 7	1	**1**	*streptococcus*
Patient 8	3	**3**	*Staph coagulase négatif*
Patient 9	12	**11**	*Staph coagulase négatif*
Patient 10	5	**5**	*Echoli*
Patient 11	8	**5**	*Staph aureus*
Patient 12	3	**2**	*Enterobacter*

Staphylococcus aureus was the most incriminating germ in infective endocarditis, found in 41% of positive blood cultures (Figure 9).

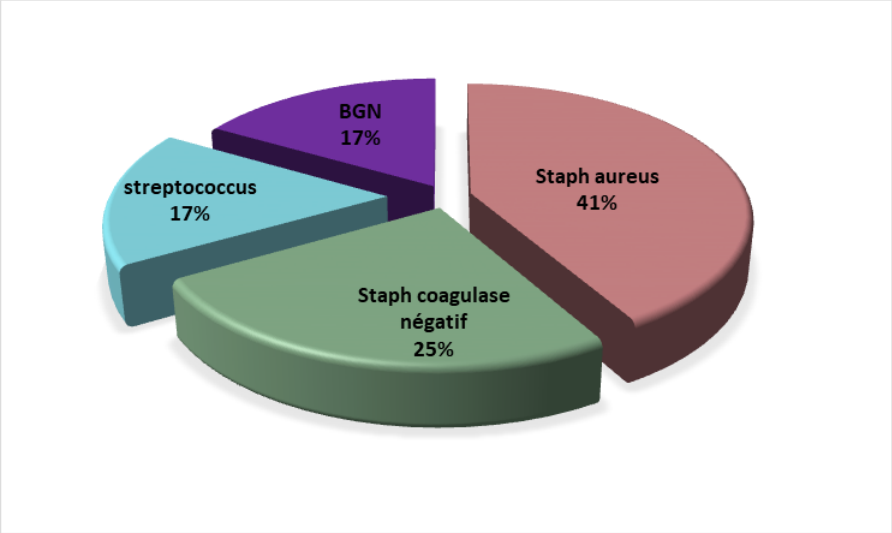

Figure 9: Germs involved in infective endocarditis

In only one patient, infective endocarditis due to staphylococcus aureus was noted in the aftermath of the pulmonary artery cerclage operation.

4. DUCK criteria

According to the modified Duke criteria, definite infective endocarditis was found in 7 children (28%) by the demonstration of 2 major clinical criteria (positive blood culture with specific germs + presence of endocardial lesions on echo-cardium) (Figure 10).

Eighteen children (72%) had presented with possible endocarditis, based on the combination of one major and 2 minor criteria (pre-existing heart disease and prolonged fever above 38.8C°).

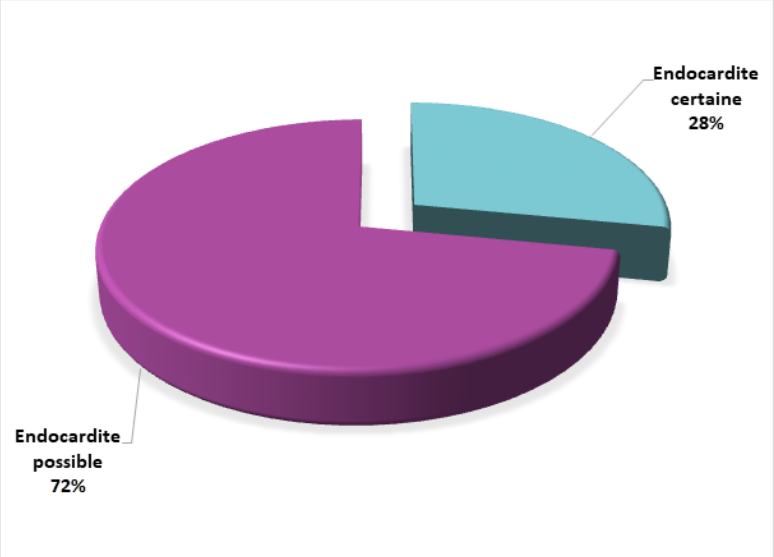

Figure 10: Infectious endocarditis according to the modified DUCK criteria

5. Taking charge

All patients in our series had received a combination of broad-spectrum intravenous antibiotic therapy. The median duration of intravenous antibiotic therapy was 45 days (15-60 days), the child with Enterobacter endocarditis died after 15 days of antibiotic therapy.

A probabilistic antibiotic therapy was initially prescribed; taking into consideration the cases with a found or suspected portal of entry.

Blood cultures were negative in 52% of the cases, and antibiotic therapy was prescribed in 90% of the cases with C3G at a dose of 80-100mg/kg/d for 6 weeks + Gentamycin at a dose of 5mg/kg/d for 2 weeks.

In each case, after obtaining the results of the blood cultures, the curative antibiotic therapy was adapted to the germs (Table 5):

Table 5: Treatment of blood culture positive infective endocarditis

Germe isolé	Traitement médial entretenu	Posologie	Durée
Staphylocoque aureus (3)	C3G + Gentamycine	**100mg/kg/j** **5mg/kg/j**	6 semaines 2 semaines
Staphylocoque aureus (1)	Amoxicilline- ac clav Gentamycine	**100mg/kg/j** **5mg/kg/j**	4 semaines 2 semaines
Staphylocoque aureus résistant au beta lactamine	Vancomycine Gentamycine	**30mg/kg/j** **5mg/kg/j**	6 semaines 2 semaines
Staphylocoque coagulase négatif (3)	C3G + Gentamycine	**100mg/kg/j** **5mg/kg/j**	7 semaines 2 semaines
Streptococcus (2)	C3G + Gentamycine	**80mg/kg/j** **5mg/kg/j**	7 semaines 2 semaines
Entérocoque (1)	Amoxicilline- ac clav Gentamycine	**100mg/kg/j** **5mg/kg/j**	4 semaines 2 semaines
Echoli (1)	C3G + Gentamycine	**100mg/kg/j** **5mg/kg/j**	6 semaines 2 semaines

Corticosteroid therapy at a dose of 2mg/kg/d was prescribed in cases of infective endocarditis on rheumatic valve disease for a period of 3 weeks.

Treatment was stopped in a patient with Echoli endocarditis due to drug toxicity causing renal failure secondary to drug tubulopathy, with a GFR of 9.

The indication for valve replacement was established in 4 patients, (16% of the cases in our series). The indications for surgery were:

- Severe valve insufficiency (1 case of coagulase-negative Staphylococcus endocarditis + 1 case of Staphylococcus aureus endocarditis).
- Persistent embolic risk (1 case of Staphylococcus aureus endocarditis + 1 case with negative blood culture).

Evolution

The evolution was marked by an improvement of the clinical state in 64%, the average time to obtain an apyrexia was 8 days in our series, and an average duration of hospitalization of 40.8 days.

One or more complications were noted in 10 cases (40% of cases):

- 4 patients presented hemodynamic disorders,
- 3 patients had severe valve failure,
- 1 patient presented neurological complications (brain abscess)
- 2 patients presented embolic complications (the location of the emboli was cerebral and renal).

The evolution was fatal in 5 cases in our series (20% of patients), secondary to septic shock in one case, nosocomial pneumonia in the second, rupture of a mycotic aneurysm in the third, and global cardiac failure in 2 cases.

DISCUSSION

Infective endocarditis (IE) is characterized by ulcerative-vegetative lesions of the endocardium, valvular and secondarily parietal, following the transplantation of a bacterial or more rarely fungal microorganism to the endocardium. In children, IE is rare as it accounts for 0.40 to 1.35 ‰ of admissions to pediatric services [8]. The mean age in our series was 09 years and 06 months, with 5 patients (20% of cases) being younger than 2 years.

Studies that have attempted to estimate the incidence of this condition are rare [8-10]. In recent decades, there has been an increase in AR in children and the average age of those with this disease has decreased. This may be related to many factors: surgery of patients with heart disease at an early age, increased life expectancy of patients with complex congenital heart disease, more frequent use of central lines (responsible for AR in structurally normal hearts and in young or immunocompromised children), and in particular improved diagnostic and therapeutic techniques [8-10].

We found that nearly a quarter of the patients in our series (24%) had structurally normal hearts and half had underlying congenital heart disease (52%). This situation is closer to that of developed countries than to that of the third world. In developed countries, there is a regression of rheumatic heart disease to congenital heart disease and structurally normal hearts. Most developing countries are currently in a progressive epidemiological transition. This transition is characterized by the emergence of postoperative endocarditis, IE in structurally normal hearts and congenital heart disease [11-13], but the impact of rheumatic heart disease is still significant to this day.

"Corrected" heart disease, not operated or having had palliation, is affected by bacterial grafting [3]. Surgical repair is supposed to reduce or even cancel the risk. This is the case unless there are no residual lesions [14]. Repair of congenital heart disease, especially if it is complex, may involve the placement of prosthetic valves or pacemakers, which carries a high risk of infection. It may also leave valvular lesions or other shunts at risk, although lower, but not zero.

Sometimes repair removes any residual lesion and negates the risk of infective endocarditis (e.g., patch closure of interventricular communication). But it is important to know that corrective surgery does not routinely eliminate the risk of IE [14].

Unoperated ventricular septal defect should not be underestimated (39.5% in our series). It is classified as a moderate risk heart disease, but its prevalence is high. It is the most common congenital heart disease of AR, followed by patent ductus arteriosus [15]. Transplantation is sometimes performed on a structurally normal heart, especially in acute infant forms in the setting of prolonged medical resuscitation [3].

Fever is an almost constant sign [3, 8, 13]. It is present in 98% of cases (88% of children in our study). It can be the sign of appeal and can take on all aspects (moderate and prolonged or high associated with chills). Cardiac auscultation is only suggestive when it confirms the appearance of a heart murmur or shows a change in intensity and/or tone of a previously known heart murmur. Murmur changes are not common, but are of great diagnostic value. They may be the first warning sign, but often appear secondarily, sometimes after sterilization of the lesions [16]. Extracardiac manifestations of AR in children are less frequent than in adults [15]. Left heart IE should be suspected in the presence of clinical signs of left ventricular dysfunction, in a septic setting, with an abnormal cardiac pattern on chest radiography.

Along with blood culture, echocardiography is the key investigation to confirm the morphology of the infection. It assists in the therapeutic management of patients with suspected IE. It should be remembered that an initial normal echocardiogram does not rule out the diagnosis of IE. It is desirable to repeat the examination a few days later, if diagnostic doubt persists [17]. It should also be remembered that the diagnosis may not be definitive in complex heart disease with multiple valve abnormalities.

In the present study, blood cultures were negative in 13 cases (50%). This high percentage may be explained by previous antibiotic therapy, faulty performance methods, and faulty culture. In developing countries, the proportion of AEs with negative blood cultures remains high, due to the over prescription of

antibiotics in the pediatric population and defective means of diagnosis. This is also due to infection with a germ that is difficult to culture (intracellular bacteria or bacteria belonging to the HACEK group) or a fungal infection, for which the sensitivity of blood cultures is only 54% [18].

Blood cultures should be taken prior to initiation of antibiotic therapy in any febrile child without an obvious site of infection with a heart murmur, congenital heart disease, or history of IE [19]. Unexpectedly and indiscriminately prescribed antibiotics may delay the diagnosis and underestimate the causative germ. In our study, blood cultures were taken early, the average time to take blood cultures was 2 days after admission (with extremes of 0 and 9) for the majority of patients.

According to the literature, Gram-positive Cocci are the most isolated organisms in patients with IE, and our results were consistent (10 of 12 of the positive cultures isolated a Gram-positive Cocci). Among the other germs, it should be noted that the frequency of gram-negative and HACEK bacilli has been increasing over the past 20 years, as has fungal endocarditis.

The infectious portal of entry is most often suspected rather than actually identified [15]. Thus, all localized infections, regardless of site, including streptococcus or staphylococcus, are potential entry points for IE in high-risk children [20]. It remains unknown in one third of cases [21]. In our series, the portal of entry was unknown in 56% of cases, dental in 20%, urinary in 8%, ENT in 12% and postoperative in 4%.

The immediate evolution of IE can include numerous complications. These complications are frequent, sometimes revealing, which makes the severity of the disease. In our series 4 children presented hemodynamic disorders, two of them died.

Valvular insufficiency and heart failure represent the common complications of AR and the serious causes of death [2, 18]. Conduction disorders and supraventricular arrhythmias also have a negative significance. They indicate extension of the infection and formation of abscesses that damage the atrio-ventricular and intra-ventricular conduction pathways [22].

In the present study, 2 patients (8%) had embolic complications, which occur in 22% to 50% of AEs according to the literature [18, 23, 20]. Embolisms often involve major arterial beds, including the lungs, coronary arteries, spleen, intestine, and extremities. Up to 65% of embolisms involve the central nervous system and are the most serious in terms of vital and functional prognosis: second leading cause of death [24].

None of our patients had a recurrence. The actual risk of AR recurrence varies from 2% to 6% [7]. There are two main types of recurrence: relapse and reinfection. Although not systematically differentiated in the literature, the term "relapse" refers to a repetition of an IE episode caused by the same microorganism, whereas "reinfection" describes an infection caused by another microorganism. There is no rule regarding the time between episodes, but it is generally shorter for a relapse than for a reinfection. In general, a recurrence caused by the same species within 6 months of the initial infection defines relapse; whereas subsequent events suggest reinfection [25].

Five of our patients died (20%). The cause of death was congestive heart failure in 2 patients, sepsis in one patient, nosocomial pneumonia in one patient, and rupture of a mycotic aneurysm in the other.

From our analytical study, we retained that the occurrence of embolic and/or hemodynamic and/or neurological complications are predictive factors of mortality during IE. The most common prognostic factors are comorbid cardiac conditions, type of microorganism involved (staphylococcus aureus and fungal infections) [26], location (left heart), increase in the size of the vegetations, acute nature of the onset of endocarditis, and complications (heart failure, renal failure, neurological involvement, or rhythmic and conduction disorders). In the most recent studies in developed countries, mortality has decreased: 4-7% in recent American studies [22, 27] and 6% in a recent Italian registry [28].

Therapeutic management of IE should be aimed at eradicating the organism from the bloodstream and vegetations (to prevent relapse). It should also treat extensive and destructive cardiac lesions and additional cardiac complications (to reduce morbidity and mortality). In this context, antibiotic therapy alone is not sufficient; other therapeutic means (in particular surgery) are often necessary.

Antibiotic therapy is well codified (molecules, duration and follow-up) according to the isolated or suspected causal germ. The occurrence of clinical events may require a revision of the antibiotic therapy or a complementary surgical attitude. The surgical indications are also codified.

The current trend is towards earlier surgery that favors valve repair [7, 29]. The three main complications of AR are also the three main surgical indications retained by the new ESC recommendations: heart failure, uncontrolled infection and systemic embolism [7].

It should be remembered that persistence or re-escalation of fever does not always mean that antibiotic therapy is ineffective. This febrile state may be secondary to certain complications of the AE, to hypersensitivity to antibiotics; to other complications related to the treatment (catheter infection for example) or to intercurrent pathologies.

The 2015 European recommendations aim to restrict the indications for antibiotic prophylaxis for the most at-risk patients, in the most exposed invasive procedures. In addition to prophylaxis, they emphasize the importance of oral hygiene, information about the patient at risk of endocarditis and their knowledge of suspected IE symptoms [7].

CONCLUSION

Infective endocarditis in children is much rarer than in adults. It can affect children with healthy hearts, but especially children with heart defects. It can also be a way to discover pre-existing heart disease. If infective endocarditis is suspected, microbiological samples and TTE should be performed as a first line of defence, especially when there is an underlying pathological condition such as immune deficiency. Specialized management is required.

All pediatricians, cardiologists and general practitioners should be aware of the various signs suggestive of IE. In particular, they should be aware of a febrile patient with cardiac disease who has no obvious infectious focus and any combination of heart murmur and fever. Despite significant progress in terms of bacteriological diagnosis and surgical management in the acute phase, IE in children remains a serious pathology with a high mortality rate. Its management must be multidisciplinary, early and adequate.

BIBLIOGRAPHIE

1. Ashkenazi, S., Levy, O., & Blieden, L. (1997). Trends of childhood infective endocarditis in Israel with emphasis on children under 2 years of age. *Pediatric cardiology*, *18*(6), 419-424.
2. Alshammary, A., Hervas-Malo, M., & Robinson, J. L. (2008). Pediatric infective endocarditis: has Staphylococcus aureus overtaken viridans group streptococci as the predominant etiological agent?. *Canadian Journal of Infectious Diseases and Medical Microbiology*, *19*(1), 63-68.
3. Ferrieri, P., Gewitz, M. H., Gerber, M. A., Newburger, J. W., Dajani, A. S., Shulman, S. T., ... & From the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the American Heart Association Council on Cardiovascular Disease in the Young. (2002). Unique features of infective endocarditis in childhood. *Circulation*, *105*(17), 2115-2126.
4. Milazzo Jr, A. S., & Li, J. S. (2001). Bacterial endocarditis in infants and children. *The Pediatric infectious disease journal*, *20*(8), 799-801.
5. Le Guillou, S., Casalta, J. P., Fraisse, A., Kreitmann, B., Chabrol, B., Dubus, J. C., & Bosdure, E. (2010). Endocardite infectieuse sur cœur sain chez l'enfant: étude rétrospective de 11 cas. *Archives de pédiatrie*, *17*(7), 1047-1055.
6. Durack, D. T., Lukes, A. S., Bright, D. K., & Service, D. E. (1994). New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. *The American journal of medicine*, *96*(3), 200-209.
7. Habib, G., Lancellotti, P., Antunes, M. J., Bongiorni, M. G., Casalta, J. P., Del Zotti, F., ... & Zamorano, J. L. (2015). 2015 ESC guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the European Society of Cardiology (ESC) endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *European heart journal*, *36*(44), 3075-3128.
8. Lefèvre, M., & Guérin, P. (2004). Endocardites de l'enfant et du petit enfant. *EMC-Cardiologie-Angéiologie*, *1*(3), 242-255.
9. Jortveit, J., Eskedal, L., Klcovansky, J., Døhlen, G., & Holmstrøm, H. (2019). Prevalence of infective endocarditis in children. *Tidsskrift for Den norske legeforening*.
10. Yakut, K., Ecevit, Z., Tokel, N. K., Varan, B., & Ozkan, M. (2020). Infective endocarditis in childhood: a single-center experience of 18 years. *Brazilian Journal of Cardiovascular Surgery*, *36*, 172-182.
11. Tseng, W. C., Chiu, S. N., Shao, P. L., Wang, J. K., Chen, C. A., Lin, M. T., ... & Wu, M. H. (2014). Changing spectrum of infective endocarditis in children: a 30 years experiences from a tertiary care center in Taiwan. *The Pediatric infectious disease journal*, *33*(5), 467-471.
12. Wang, W., Sun, H., Lv, T., & Tian, J. (2014). Retrospective studies on pediatric infective endocarditis over 40 years in a mid-west area of China. *Cardiology*, *128*(2), 88-91.
13. Jortveit, J., Klcovansky, J., Eskedal, L., Birkeland, S., Døhlen, G., & Holmstrøm, H. (2018). Endocarditis in children and adolescents with congenital heart defects: a Norwegian nationwide register-based cohort study. *Archives of Disease in Childhood*, *103*(7), 670-674.
14. Cahill, T. J., Jewell, P. D., Denne, L., Franklin, R. C., Frigiola, A., Orchard, E., & Prendergast, B. D. (2019). Contemporary epidemiology of infective endocarditis in patients with congenital heart disease: a UK prospective study. *American Heart Journal*, *215*, 70-77.
15. Rushani, D., Kaufman, J. S., Ionescu-Ittu, R., Mackie, A. S., Pilote, L., Therrien, J., & Marelli, A. J. (2013). Infective endocarditis in children with congenital heart disease: cumulative incidence and predictors. *Circulation*, *128*(13), 1412-1419.

16. Day, M. D., Gauvreau, K., Shulman, S., & Newburger, J. W. (2009). Characteristics of children hospitalized with infective endocarditis. *Circulation*, *119*(6), 865-870.
17. Sochowski, R. A., & Chan, K. L. (1993). Implication of negative results on a monoplane transesophageal echocardiographic study in patients with suspected infective endocarditis. *Journal of the American College of Cardiology*, *21*(1), 216-221.
18. Ellis, M. E., Al-Abdely, H., Sandridge, A., Greer, W., & Ventura, W. (2001). Fungal endocarditis: evidence in the world literature, 1965–1995. *Clinical Infectious Diseases*, *32*(1), 50-62.
19. Bitar, F. F., Jawdi, R. A., Dbaibo, G. S., Yunis, K. A., Gharzeddine, W., & Obeid, M. (2000). Paediatric infective endocarditis: 19-year experience at a tertiary care hospital in a developing country. *Acta paediatrica (Oslo, Norway: 1992)*, *89*(4), 427-430.
20. Di Filippo, S., Sassolas, F., & Bozio, A. (1998). La prévention de l'endocardite infectieuse chez l'enfant. Situation et protocoles actuels. *Archives de pédiatrie*, *5*(7), 785-792.
21. Jomaa, W., Ali, I. B., Abid, D., Ernez, S. H., Abid, L., Triki, F., ... & Maatouk, F. (2017). Clinical features and prognosis of infective endocarditis in children: Insights from a Tunisian multicentre registry. *Archives of cardiovascular diseases*, *110*(12), 676-681.
22. Franco-Paredes, C., Workowski, K., & Harris, M. (2002). Infective endocarditis-endarteritis complicating coarctation of the aorta. *The American journal of medicine*, *112*(7), 590-592.
23. Coward, K., Tucker, N., & Darville, T. (2003). Infective endocarditis in Arkansan children from 1990 through 2002. *The Pediatric infectious disease journal*, *22*(12), 1048-1052.
24. Bitar, F. F., Jawdi, R. A., Dbaibo, G. S., Yunis, K. A., Gharzeddine, W., & Obeid, M. (2000). Paediatric infective endocarditis: 19-year experience at a tertiary care hospital in a developing country. *Acta paediatrica (Oslo, Norway: 1992)*, *89*(4), 427-430.
25. Chu, V. H., Sexton, D. J., Cabell, C. H., Barth, R. L., Pappas, P. A., Singh, R. K., ... & Woods, C. W. (2005). Repeat infective endocarditis: differentiating relapse from reinfection. *Clinical infectious diseases*, *41*(3), 406-409.
26. Martin, J. M., Neches, W. H., & Wald, E. R. (1997). Infective endocarditis: 35 years of experience at a children's hospital. *Clinical infectious diseases*, *24*(4), 669-675.
27. Wilson, W. R., Giuliani, E. R., Danielson, G. K., & Geraci, J. E. (1982, March). Management of complications of infective endocarditis. In *Mayo Clinic Proceedings* (Vol. 57, No. 3, pp. 162-170).
28. Esposito, S., Mayer, A., Krzysztofiak, A., Garazzino, S., Lipreri, R., Galli, L., ... & for the Italian Pediatric Infective Endocarditis Registry. (2016). Infective Endocarditis in Children in Italy from 2000 to 2015. *Expert review of anti-infective therapy*, *14*(3), 353-358.
29. Buratto, E., & Konstantinov, I. E. (2021). Aortic valve surgery in children. *The Journal of Thoracic and Cardiovascular Surgery*, *161*(1), 244-250.