Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2023 Feb 06; 11(C):57-61.
https://doi.org/10.3889/oamjms.2023.11223
eISSN: 1857-9655
Category: *C - Case Reports*
Section: *Case Report in Internal Medicine*

Unique Clinical Manifestation of Infective Endocarditis in Children: A Case Series

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Edited by: Igor Spiroski
Citation: Rahayuningsih SE, Kuswiyanto RB, Apandi P, Setiabudi D, Manurung BJ, Hasna M. Unique Clinical Manifestation Infective Endocarditis in Children: A Case Series. Open Access Maced J Med Sci. 2023 Feb 06; 11(C):57-61. https://doi.org/10.3889/oamjms.2023.11223
Keywords: Infective endocarditis; Children; Neonate
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Received: 22-Nov-2022
Revised: 24-Dec-2022
Accepted: 31-Jan-2023

Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist

Abstract

BACKGROUND: Infective endocarditis (IE) was a significant cause of morbidity and mortality, particularly in children with congenital heart disease (CHD). Infective endocarditis could occur in all ages with higher in children below 1-year-old, including neonates. Various clinical manifestations of IE in children make it difficult to make a prompt diagnosis and appropriate management. Finding in echocardiography could help clinicians determine the diagnosis of IE. Systemic embolization could cause many complications that may present as chief complaint underlying patient hospitalization.

CASE PRESENTATION: We present case series of diverse manifestation of IE in children in Bandung, West Java, Indonesia. Two cases had a history of structural heart disease, while one case with no history of any structural heart disease before.

CONCLUSION: Wide range of symptoms that could occur in children with IE, made it challenging to make a proper diagnosis

Introduction

The incidence of infective endocarditis (IE) in children was not as high as in adults but still contributed to one of the crucial causes of hospital admission in pediatric cardiology centers with substantial morbidity and mortality. Congenital heart disease (CHD) was the most common predisposing factor for IE in children; nevertheless, 8% to 10% of pediatric IE cases were developed without structural heart disease [1], [2], [3]. Prevention of IE was recommended to give antibiotics following the invasive procedure, especially to those with a high risk of IE. This could helpfully reduce the incidence of IE [2], [4]. Clinical characteristics of IE in children were challenging due to a wide range of signs and symptoms. Improvement of Duke criteria could help clinicians determine the diagnosis of IE in children; supporting examination as echocardiography could also improve diagnosis and monitoring of IE in children. Neurological complications, abscess, peripheral signs, and other complications could occur as a manifestation of IE in children due to bacteremia and systemic embolization [5]. Streptococci were the most common cause of IE, while staphylococcal infection may increase the risk of mortality in children. Culture negativity could not rule out the possibility of bacterial growth, and empiric antibiotics still must be given to those with IE for 2–6 weeks [6]. Infective endocarditis could also occur in neonates with higher mortality and different causative microorganism [7]. Here, we presented case series of distinctive features of IE in children from a single-center tertiary hospital in Bandung, West Java, Indonesia.

Clinical Summary

Case 1

A 6-day-old girl baby was referred to our hospital with a complaint of bradyarrhythmia. It was known first by prenatal ultrasonography (USG) at 8 months old pregnancy. The baby was born from a P4A0 mother, the second baby from twins by C-section due to fetal distress with a birth weight of 2470 g. The first twins had asymptomatic bradyarrhythmia in better condition. Heart rate was 60–80 bpm with the electrocardiogram (ECG) which showed complete atrioventricular (AV) block and right axis deviation.

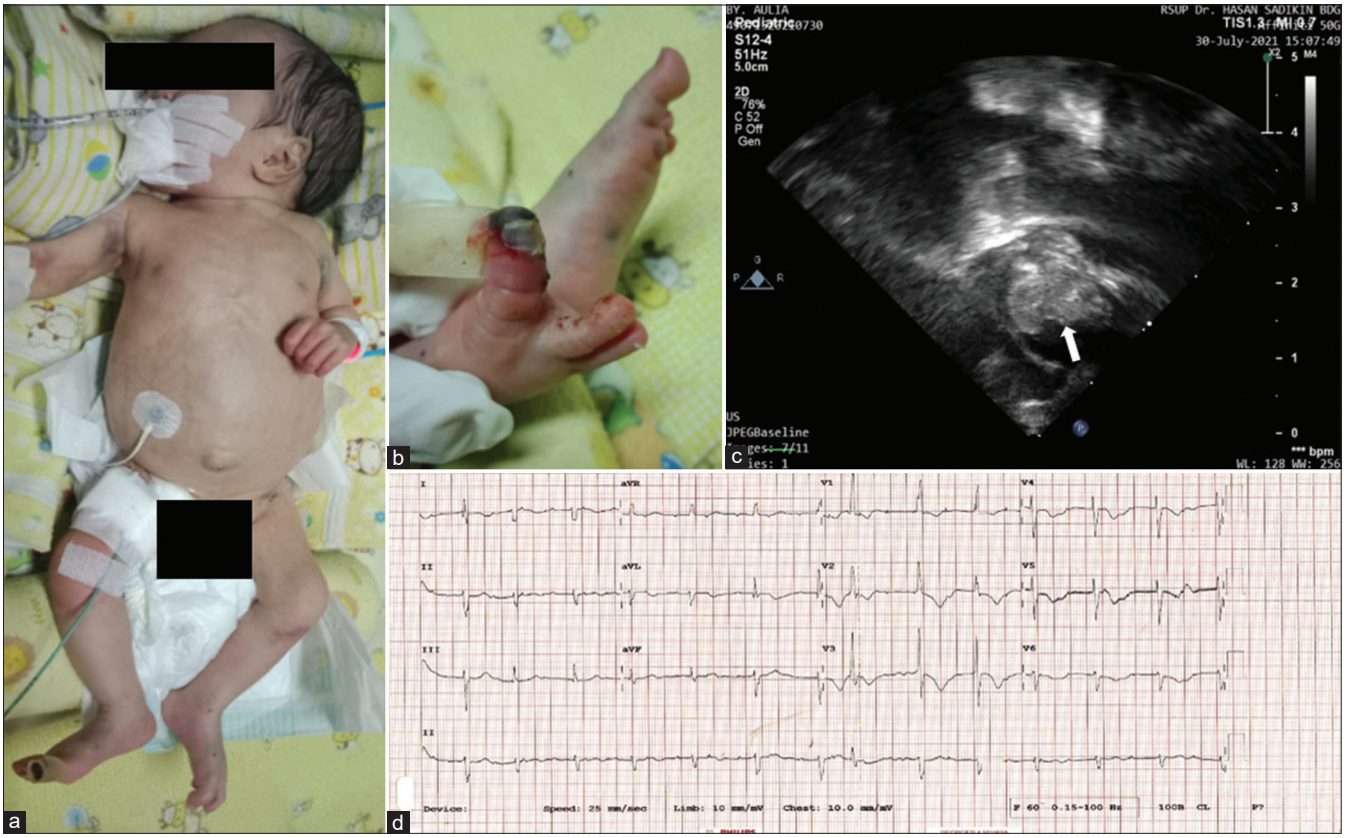

Figure 1: Clinical profile and supporting an examination of the patient. (a) The baby was 2 months old with TPM inserted from the right femoral vein, (b) gangrene of the right thumb of the foot, (c) echocardiography showed thrombus at left and right atrium with suspected vegetations at right ventricle (arrow), and (d) ECG showed complete AV block

The chest X-ray showed right pleura effusion with cardiomegaly. From laboratory examination, we found a low level of hemoglobin, hematocrit, and platelets, increasing of C-reactive protein (CRP), positive 3 for Anti Ro (SS-A), and Ro-52 recombinant. There was no history of SLE before in the mother. Echocardiography showed patent ductus arteriosus (PDA) with mild aortic valve regurgitation and mild pericardial effusion. The patient was diagnosed with neonatal systemic lupus erythematosus with complete AV block.

A temporary pacemaker (TPM) was installed on the baby while preparing for permanent pacemaker (PPM) if the baby's condition was better (Figure 1). Installation of TPM is carried out with high sterilization standards in a special room. During hospitalization, the blood culture always showed positive for bacterial isolate including *Klebsiella pneumoniae*, *Acinetobacter baumanii*, *Burkholderia cepacia*, and *Pseudomonas aeroginosa*. The antibiotics were given based on culture and sensitivity results. Then, we evaluated echocardiography at 2 months old; it showed thrombus at left and right atrium, suspected vegetations at right ventricle, and small PDA. We concluded that this baby had infective endocarditis. We added heparin for therapy in this patient. During monitoring, gangrene on the right thumb of the foot appeared with Doppler USG showed stenosis of dorsalis pedis artery. The baby was died at 2 months old due to respiratory failure with sepsis.

Case 2

A 12-year-old boy came to our hospital with a chief complaint of feeling tired easily. He also complained of palpitation with dyspnea that worsened in the past month. There was a history of fever and decreased body weight since 1 month before admission. At femur sinistra, there was a redness swelling that felt pain and getting more significant since 1 month. The complaint started with the history of falling in the rice field. The nutritional status of the patient was severe malnutrition. The patient was then hospitalized in a regional hospital for 3 weeks in the intensive care unit and carried out several examinations as a tuberculin skin test, rapid molecular test Xpert Mtb/Rif with result negative. Echocardiography, chest X-ray, and femur X-ray were also performed in the regional hospital. The patient was diagnosed with massive pericardial effusion caused by tuberculosis, infective endocarditis, mild tricuspid regurgitation, and abscess at femur sinistra. Then, the patient was referred to our hospital for further management.

At admission, there were fever, tachypnea, elevated jugular venous pressure, and systolic murmur grade III with punctum maximum in intercostal space

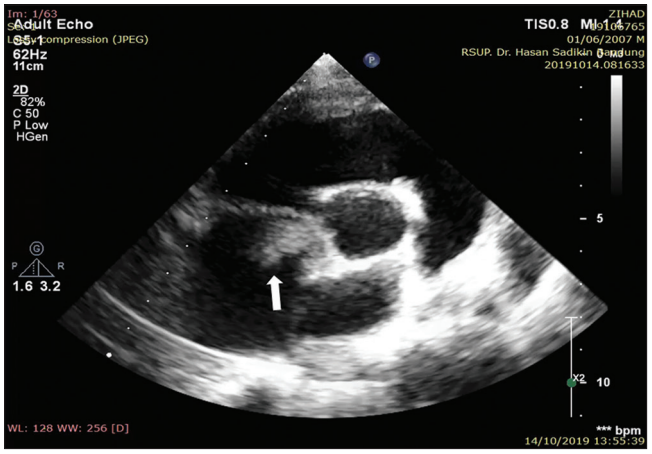

Figure 2: Echocardiography showed vegetation at the tricuspid valve with mild-to-moderate pericardial effusion (arrow)

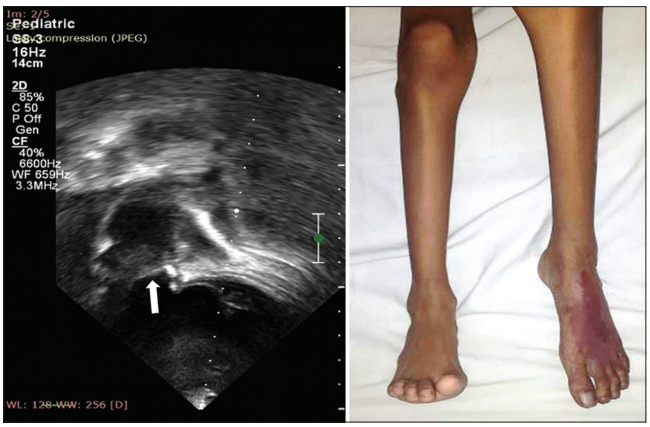

Figure 3: Echocardiography showed moderate PDA with multiple vegetations at the main pulmonary artery and left atrium (arrow) (a). Gangrene at the left foot as a complication of systemic embolism (b)

IV midclavicular sinistra found from the physical examination. There was an open wound with a red-yellowish discharge at the femur sinistra. Laboratory examination results showed leukocytosis, anemia, elevated C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). Blood culture showed *Burkholderia cepacia* that was sensitive with ceftazidime, cotrimoxazole, and meropenem. We performed echocardiography, and there was vegetation in the tricuspid valve with mild-to-moderate pericardial effusion (Figure 2). From pelvic X-Ray, we found subluxation of the hip joint with sclerotic lesion around ischium tuberosity and inferior pubic sinistra, lytic lesion in the head of femur sinistra, suggestive osteomyelitis. The result of biopsy from abscess of the femur was caseous necrosis suggested tuberculosis infection. We gave antibiotic consistent with blood culture result and antituberculosis drug to the patient. Debridement surgery was also performed for abscess in femur sinistra. After 6 weeks of intravenous antibiotics, we evaluated with echocardiography and showed vegetation improvement in the tricuspid valve. The patient was, then, discharged from the hospital with oral antibiotic and antituberculosis drug for 12 months in total.

Case 3

A 12-year-old girl was admitted to the hospital with a complaint of dyspnea and fever. She was diagnosed with PDA at the age of 6 years. Nutritional status was severe malnutrition. From the physical examination, there were tachycardia, tachypnea, diaphoresis, and elevated jugular venous pressure. There was a tooth cavity, and it was found to be reversible pulpitis. Laboratory examination showed leukocytosis with neutrophilia, hypoalbuminemia, and elevated CRP. Blood culture showed no bacterial growth. Echocardiography showed moderate PDA, multiple vegetation in the main pulmonary arteries, and left atrium (Figure 3). We diagnosed the patient with infective myocarditis and heart failure with PDA. The patient was treated with empiric intravenous antibiotics (ceftriaxone and gentamycin), heart failure therapy, and antipyretic.

On 4th day of hospitalization, the patient complained of pain in the left foot with the bluish-colored and cold left foot. We evaluated with Doppler ultrasonography (USG) and found arterial stenosis at popliteal, anterior tibial, posterior tibial, and left dorsalis pedis artery. The patient underwent transtibial amputation. During surgery, a thrombus was found at the posterior and anterior tibialis artery. After 35 days of hospitalization, we evaluated echocardiography and found no vegetation. At 2 months after discharge, the patient underwent transcatheter PDA closure.

Discussion

We present case series of diverse manifestation IE in children in Bandung, West Java, Indonesia. Two cases had a history of structural heart disease, while one case with no history of any structural heart disease before. Congenital AV block (CAVB) in neonatal SLE is caused by transplacental passage of maternal anti-Ro/SSA and/or anti-La/SSB autoantibodies [8]. CAVB is associated with high mortality rate. The mortality rate without pacing is 14–34% and lower with pacing condition. About 75% of neonates with CAVB required pacemaker in neonatal period. Fetal hydrops and ventricular rate <55 bpm are the risk factor of high mortality [9], [10]. Fetal AV block cases have a bad prognosis. Perinatal mortality rate CAVB is ranging between 5.5 and 25% of intrauterine fetal death, 9–37% rate postnatal deaths, and all survivor always require permanent cardiac pacing. CAVB related to CHD has worse prognosis than CAVB without CHD [11], [12]. Children with CHD were prone to have IE, particularly those who underwent invasive procedures, and antibiotic prophylaxis could help prevent it [13]. Wide range of symptoms that could occur in children with IE, made it challenging to make a proper diagnosis [5]. In

second case, we described IE case without heart defect. The literature information on IE in previously healthy children is relatively sparse, and the pathogenesis and underlying risk factors remain largely unknown. Lin *et al*. study over 20 years reported that over one-third (35.4%) of IE cases were patients without pre-existing heart disease [14].

As presented in this case series, symptoms could occur as part of IE or as a complication from systemic embolization. Malnutrition was found in most cases which could be one of the prognostic factors for patient with IE. Morbidity and longer hospitalization were associated with the malnourished patient as they tend to have a complication such as heart failure, sepsis, and coagulopathy as seen in our patients [15]. Echocardiography could give benefit to reduce mortality in children with IE, allowing early detection of IE, prompt management, and monitoring [16]. *Burkholderia cepacia* is a rare pathogen found in clinical infection, but we found as the cause of infective endocarditis in neonates. This finding was also reported by Yonas *et al*. [17]. *B. cepacia* was the causative organism of IE in neonates. *Burkholderia cepacia is* usually found in the environment and is related to infection in people with cystic fibrosis. Bacteria could inhale from the respiratory tract of a human [18]. However, in case 2, an open fracture in femur might be a port of entry for bacteria. In most IE cases in children, streptococci and staphylococci were still the primary causative organism [13], [16], [19], [20]. Blood culture was negative in 40% of IE cases but could not rule out diagnosis IE, and diagnosis should be made based on clinical and image findings. After 1 week of antibiotic treatment, blood culture could show no microorganism growth in most patients, as of antibiotic use, prior blood culture sampling might bias the result [5], [21], [22]. Besides, the blood culture positivity rate was lower in developing countries, contributing to increased mortality and morbidity rate as the sensitivity of blood culture should determine antibiotics treatment. Developing countries also had a lower incidence of children IE cases reported, and it might be due to limited resources to diagnose, difficulty health care access, so many cases might be underreported [23], [24], [25].

References

1. Baltimore RS, Gewitz M, Baddour LM, Beerman LB, Jackson MA, Lockhart PB, *et al.* Infective endocarditis in childhood: 2015 update: A scientific statement from the American Heart Association. Circulation. 2015;132(15):1487-515. http://doi.org/10.1161/CIR.0000000000000298

   PMid:26373317

2. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, *et al.* 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). Eur Heart J. 2015;36(44):3075-128. http://doi.org/10.1093/eurheartj/ehv319

   PMid:26320109

3. Kelchtermans J, Grossar L, Eyskens B, Cools B, Roggen M, Boshoff D, *et al.* Clinical characteristics of infective endocarditis in children. Pediatr Infect Dis J. 2019;38(5):453-8. https://doi.org/10.1097/INF.0000000000002212

   PMid:30346369

4. Khan O, Shafi AM, Timmis A. International guideline changes and the incidence of infective endocarditis: A systematic review. Open Heart J. 2016;3(2):e000498. http://doi.org/10.1136/openhrt-2016-000498

   PMid:27621836

5. Luca AC, Curpan AS, Adumitrachioaiei H, Ciobanu I, Dragomirescu C, Manea RS, *et al.*, editors. Difficulties in Diagnosis and Therapy of Infective Endocarditis in Children and Adolescents-Cohort Study. Basel, Switzerland: Multidisciplinary Digital Publishing Institute; 2021.

6. Cahill TJ, Jewell PD, Denne L, Franklin RC, Frigiola A, Orchard E, *et al.* Contemporary epidemiology of infective endocarditis in patients with congenital heart disease: A UK prospective study. Am Heart J. 2019;215:70-7. http://doi.org/10.1016/j.ahj.2019.05.014

   PMid:31299559

7. Smith JA, Kretovics E, Hartley J, Svenson A. Infective endocarditis of the aortic valve in a neonate. Prog Pediatr Cardiol. 2021;62(3):101372. https://doi.org/10.1016/j.ppedcard.2021.101372

8. Carrilho MC, Bravo-Valenzuela NJ, Júnior EA. Congenital complete atrioventricular heart block in a pregnant woman with Sjögren syndrome: Prenatal care follow-up and the challenge of intrauterine treatment. Rev Bras Ginecol Obstet. 2020;42(4):228-32. http://doi.org/10.1055/s-0040-1709738

   PMid:32330965

9. Baruteau AE, Pass RH, Thambo JB, Behaghel A, Le Pennec S, Perdreau E, *et al.* Congenital and childhood atrioventricular blocks: Pathophysiology and contemporary management. Eur J Pediatr. 2016;175(9):1235-48. http://doi.org/10.1007/s00431-016-2748-0

   PMid:27351174

10. Hansahiranwadee W. Diagnosis and management of fetal autoimmune atrioventricular block. Int J Womens Health. 2020;12:633-9. http://doi.org/10.2147/IJWH.S257407

    PMid:32884363

11. Cuneo BF, Ambrose SE, Tworetzky W. Detection and successful treatment of emergent anti-SSA-mediated fetal atrioventricular block. Am J Obstet Gynecol. 2016;215(4):527-8. http://doi.org/10.1016/j.ajog.2016.07.002

    PMid:27418449

12. Kuleva M, Le Bidois J, Decaudin A, Villain E, Costedoat-Chalumeau N, Lemercier D, *et al.* Clinical course and outcome of antenatally detected atrioventricular block: Experience of a single tertiary centre and review of the literature. Prenat Diagn. 2015;35(4):354-61. http://doi.org/10.1002/pd.4547

    PMid:25487821

13. Sun LC, Lai CC, Wang CY, Wang YH, Wang JY, Hsu YL, *et al.* Risk factors for infective endocarditis in children with congenital heart diseases-a nationwide population-based case control study. Int J Cardiol. 2017;248:126-30. http://doi.org/10.1016/j.ijcard.2017.08.009

    PMid:28811093

14. Lin YT, Hsieh KS, Chen YS, Huang IF, Cheng MF. Infective endocarditis in children without underlying heart disease.

J Microbiol Immunol Infect. 2013;46(2):121-8. http://doi.org/10.1016/j.jmii.2012.05.001

PMid:22727890

15. Harris CM, Albaeni A, Norris KC. Impact of malnutrition in patients with infective endocarditis. Nutr Clin Pract. 2021;36(2):472-9. http://doi.org/10.1002/ncp.10557

PMid:32700334

16. Willoughby ML, Basera W, Perkins SR, Comitis GAM, Fourie B, Lawrenson JB, *et al.* Infective endocarditis in infants and children in the Western Cape, South Africa: A retrospective analysis. Cardiol Young. 2019;29(10):1282-6. http://doi.org/10.1017/S1047951119002154

PMid:32167040

17. Yonas E, Damay V, Pranata R, Nusarintowati N. Infective endocarditis due to *Burkholderia cepacia* in a neonate: A case report. J Med Case Rep. 2018;12(1):120. http://doi.org/10.1186/s13256-018-1633-z

PMid:29734941

18. Lord R, Jones AM, Horsley A. Antibiotic treatment for *Burkholderia cepacia* complex in people with cystic fibrosis experiencing a pulmonary exacerbation. Cochrane Database Syst Rev. 2020;4(4):CD009529. http://doi.org/10.1002/14651858.CD009529.pub4

PMid:32239690

19. Ware AL, Tani LY, Weng HY, Wilkes J, Menon SC. Resource utilization and outcomes of infective endocarditis in children. J Pediatr. 2014;165(4):807- 12.e1. http://doi.org/10.1016/j.jpeds.2014.06.026

PMid:25064162

20. Niwa K, Nakazawa M, Tateno S, Yoshinaga M, Terai M. Infective endocarditis in congenital heart disease: Japanese National Collaboration Study. Heart. 2005;91(6):795-800. http://doi.org/10.1136/hrt.2004.043323

PMid:15894782

21. Lamas CC, Fournier PE, Zappa M, Brandão TJ, Januário-da-Silva CA, Correia MG, *et al.* Diagnosis of blood culture-negative endocarditis and clinical comparison between blood culture-negative and blood culture-positive cases. Infection. 2016;44(4):459-66. http://doi.org/10.1007/s15010-015-0863-x

PMid:26670038

22. Fournier PE, Thuny F, Richet H, Lepidi H, Casalta JP, Arzouni JP, *et al.* Comprehensive diagnostic strategy for blood culture-negative endocarditis: A prospective study of 819 new cases. Clin Infect Dis. 2010;51(2):131-40. http://doi.org/10.1086/653675

PMid:20540619

23. Math RS, Sharma G, Kothari SS, Kalaivani M, Saxena A, Kumar AS, *et al.* Prospective study of infective endocarditis from a developing country. Am Heart J. 2011;162(4):633-8. http://doi.org/10.1016/j.ahj.2011.07.014

PMid:21982654

24. Garg N, Kandpal B, Garg N, Tewari S, Kapoor A, Goel P, *et al.* Characteristics of infective endocarditis in a developing country-clinical profile and outcome in 192 Indian patients, 1992-2001. Int J Cardiol. 2005;98(2):253-60. http://doi.org/10.1016/j.ijcard.2003.10.043

PMid:15686775

25. Sadiq M, Nazir M, Sheikh SA. Infective endocarditis in children-incidence, pattern, diagnosis and management in a developing country. Int J Cardiol. 2001;78(2):175-82. http://doi.org/10.1016/s0167-5273(01)00374-6

PMid:11334662