Clinical characteristics and the role of echocardiography in diagnosing acute rheumatic fever in patients referred to the Lady Ridgeway Hospital for Children, Colombo, Sri Lanka

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Abstract

Background: Acute Rheumatic Fever (ARF) is a systemic illness that may occur following group-A beta-haemolytic streptococcal pharyngitis in children. Rheumatic Heart Disease (RHD) is the most serious complication of ARF.

Objectives: To describe the demographic, socio-economical background and clinical profile in children with ARF referred to the Lady Ridgeway Hospital for Children (LRH), Sri Lanka, to assess the place of echocardiogram in diagnosis of ARF and to assess the predictive criteria to identify high risk patients with rheumatic carditis.

Method: Eighty patients with ARF formed cohort. Socio-demographic, clinical and laboratory characteristics were summarized using frequencies. Analysis was done to identify carditis risk predictors using Pearson Chi square test with 95% confidence interval. $p<0.05$ was considered significant.

Results: Of 80 children with ARF, 65 (81.3%) were on follow up for ARF and 15 (18.7%) were newly diagnosed patients. Seventy-one (88.8%) patients were diagnosed as having a definite episode of ARF, 7 (8.8%) as possible ARF and 2 (2.4%) as probable ARF. Most ARF patients were diagnosed between the ages of 5 to 10 years. Mean age was 9.5 years. Cohort showed a 1.75: 1 male: female ratio. Arthritis was the commonest major manifestation of ARF being seen in 73 (91.3%) children. Cardiac involvement occurred in 52 (65%) cases of which 34 (65%) were subclinical. Fever (>38^{0}C) occurred in 59 (73.8%) cases, erythrocyte sedimentation rate >30mm/hour in 74 (92.5%) and C-reactive protein above 3 mg/dl in 74 (92.5%) cases. Prolonged PR interval on electrocardiogram was seen in 8 (10%) patients. Increased rates of ARF were seen in children from urban, low-income, and crowded areas. When comparing the carditis group with the non-carditis group, low income, low maternal educational level, and low body mass index (BMI) showed positive correlation in predicting carditis.

Conclusions: In our study, arthritis was seen in 91% of children with ARF and carditis in 65%. Of children with carditis 65% were subclinical and diagnosed only with echocardiography. Low income, low maternal educational level and low BMI showed a positive correlation in predicting carditis.

(Key words: Acute rheumatic fever, Rheumatic carditis)

Introduction

Jones criteria have been used for diagnosing Acute Rheumatic Fever (ARF) since 1944[1]. It was modified in 1992 by the American Heart Association[2]. However, subclinical carditis was not mentioned in the modification but cannot be ignored since echocardiography is superior to auscultation. Thus, many cases were misdiagnosed who later developed rheumatic heart disease (RHD). American Heart Association did a successful revision in 2015 to avoid these pitfalls[3]. They introduced different diagnostic criteria for low risk and moderate/high risk populations. Today echocardiography is a must for all patients with suspected or confirmed ARF. In all populations subclinical carditis is a major criterion. For recurrent ARF separate specific criteria are provided. The Australian 2020 guidelines modified criteria for diagnosis of ARF and proposed additional criteria for high-risk groups[4]. In developed countries, ARF and RHD are not common health problems. There are minimal surveys for prevalence of RHD in developing countries. It has been shown that higher socio-economic status is associated with reduced prevalence of RHD[5]. In developing countries ARF is an enormous burden.

Objectives

To describe the demographic, socio-economical background and clinical profile in children with

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ARF referred to the Lady Ridgeway Hospital for Children (LRH), Sri Lanka, to assess the place of echocardiogram in diagnosis of ARF and to assess the predictive criteria to identify high risk patients with rheumatic carditis

Method

This is an observational cross-sectional study of patients diagnosed as ARF at LRH, Colombo, Sri Lanka. All patients with ARF referred to LRH from 2020 August to 2021 August were included in study. Children with suspected ARF without clinical criteria and negative echocardiography were excluded. No sample size was calculated as all children registered during the study period were eligible for inclusion. A data collection sheet in the format of a questionnaire was used to assess demographic data of the patient. All other data were collected from patient's referral letters, relevant hospital records and their clinic books at the time of first diagnosis. If the child was admitted to another hospital, data were collected from the relevant hospital records.

Ethical issues: Approval for the study was obtained from the Ethical Review Committee of the Sri Lanka College of Paediatricians (Ref. No. SLCP/ ERC/ 2020/18). Permission to conduct the study was obtained from the relevant authorities, including the ethical review committee at LRH, Colombo, Sri Lanka. Participation was voluntary after obtaining written informed consent from the legal guardians/ parents and written informed assent from children over 12 years of age**.** Adequate privacy was maintained during data collection and storage.

Statistical analysis: Data were analysed using SPSS. Socio-demographic, clinical and laboratory characteristics were summarized using frequencies and percentages. Analysis was performed to identify carditis risk predictors using a bivariate model with Pearson Chi square test with 95% confidence interval. $p<0.05$ was considered statistically significant. Graphs and tables were used to summarize data.

Results

A total of 80 patients with ARF referred to the Cardiology Department at LRH formed the cohort of this study. Of the children with ARF, 65 (81.3%) were being followed up for ARF and 15 (18.7%) were newly diagnosed patients. Diagnosis of ARF was based on modified Jones criteria with evidence of preceding recent streptococcal infection. All patients were examined according to a standard protocol consisting of a detailed medical history, general and special tests, including electrocardiogram (ECG), Doppler echocardiography, throat culture for Group-A beta-haemolytic streptococci and anti-streptolysin-O titre (ASOT). Seventy-one (88.8%) patients were diagnosed as definite episodes of ARF, 7 (8.8%) as possible ARF and 2 (2.4%) as probable ARF. Table 1 demonstrates the age and gender of patients with ARF. The mean age at presentation was 9.5 years. The cohort showed a 1.75: 1 male: female ratio. Ethnic distribution of the sample is demonstrated in figure 1.

Table 1

Age and gender of ARF patients (n=80)

Parameter	n (%)
Age at diagnosis (months)	
1-59	01 (01.3)
60-131	47 (58.8)
132-191	32 (40.0)
Gender	
Male	51 (63.8)
Female	29 (36.2)

ARF: Acute rheumatic fever

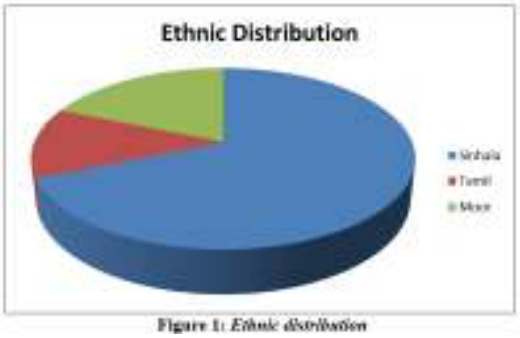

Figure 1: *Ethnic distribution*

Figure 2 demonstrates the geographic distribution of the patients with ARF who were referred to the LRH cardiology department. Of the patients 27.5% were from the Colombo district, 18.8% from the Gampaha district and 16.3% from the Puttalam district. As LRH is a tertiary care centre, ARF patients who need cardiac surgery will be coming to LRH from certain districts. Therefore, it will not represent the actual burden of disease of other provinces where paediatric cardiologists will manage them.

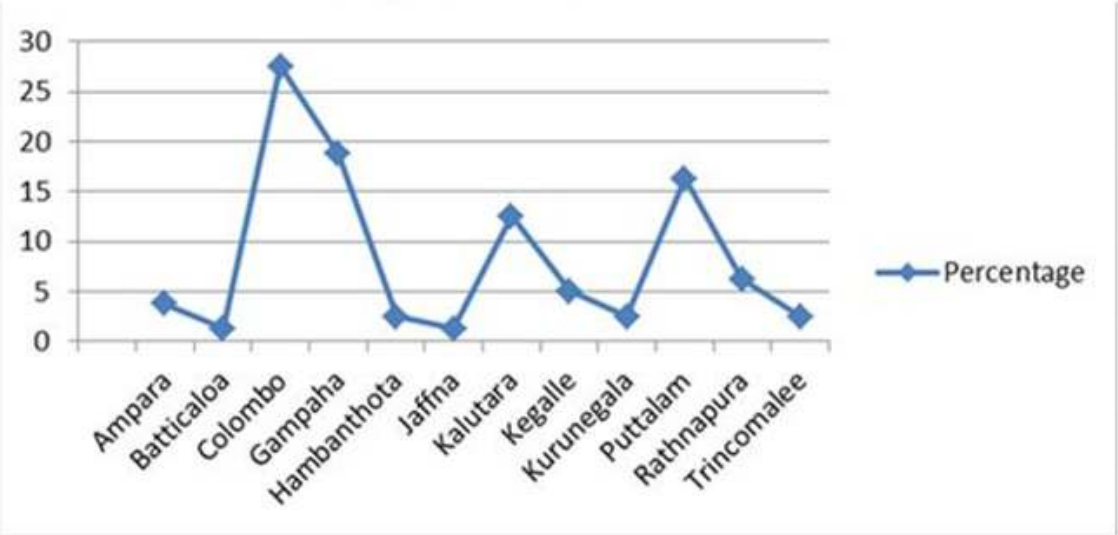

Figure 2: ***Geographic distribution of patients with acute rheumatic fever referred to the Lady Ridgeway Hospital for Children, Colombo, Sri Lanka***

In 47 (58.8%) cases, arthritis was associated with carditis. In 26 (32.5%) cases, arthritis was the only major Jones criterion. Arthritis associated with chorea and carditis was present in one (1.3%) case. None of the cases demonstrated arthritis alone with chorea as the major criteria. Of the patients with arthritis 39 (48.8%) had polyarthritis, and 7 (8.8%) had mono-arthritis.

Cardiac involvement was documented in 52 (65%) cases; it occurred alone in 4 (5%), with arthritis in 47 (58.8%), and with chorea in 1 (1.3%) patient. Among the 52 patients with carditis, 34 (65%) were subclinical carditis while 18 (34.6%) had clinical manifestations. The pattern of cardiac involvement was valvular in the majority. It was severe in the 6 (11.5%) cases who were referred for early surgery due to severe mitral regurgitation with significant left atrial and left ventricular dilatation and in the 13 (25%) cases who were started on anti-heart failure medications. The involvements of the mitral valve alone occurred in 40 (76%) cases in the form of mitral regurgitation (MR), while both aortic and mitral regurgitation were present in 12 (23%) cases, aortic valve regurgitation (AR) alone not being observed in any of the patients.

All children with rheumatic carditis were treated with a high dose of aspirin in the initial period and 2 (2.5%) needed oral steroids at the acute stage. The indications to start steroids in these children were heart failure and progression of valve lesion in spite of a high dose of aspirin. Table 2 shows the frequency of Jones criteria in patients with ARF.

Table 2

Jones criteria in patients with ARF (n=80)

Criteria	n (%)
Major Jones criteria	
Carditis	52 (65.0)
Arthritis	73 (91.3)
Chorea	02 (02.5)
Subcutaneous nodules	0 (0)
Erythema marginatum	0 (0)
Minor Jones criteria	
Clinical findings	
Fever more than 38^0C	59 (73.8)
Arthralgia	27 (66.3)
Laboratory findings	
Raised ESR > 30mm/hour	74 (92.5)
Raised CRP above 3 mg/dl	74 (92.5)
Prolonged PR interval on ECG	08 (10.0)

ARF: Acute rheumatic fever

All 80 patients had evidence of a preceding streptococcal infection in the form of raised ASOT. Throat culture for Group-A beta-hemolytic streptococci was done only in two patients and both were positive. Clinical evidence of preceding pharyngitis was noted in 65 (81.3%) patients. None had clinical evidence of scarlet fever. Recommended antibiotic treatment for recommended duration for preceding streptococcal infection was administered in 11 (13.8%) children. It is likely that manifestations of pharyngitis were interpreted as those of viral aetiology and antibiotic therapy was not administered in 12 (15%) patients. Fifteen (18.8%) patients had not been symptomatic prior to diagnosis of ARF. Amoxicillin was the commonest antibiotic therapy used in 26 (47%) patients followed by cephalexin in 6 (11%) and azithromycin in 5 (9.4%). A positive family history

of ARF was determined in one (1.3%) patient. Penicillin was administered intramuscularly in 78 (97.5%) children. Oral penicillin was administered in 2 (2.5%) children due to poor compliance to IM injection. Other antibiotics were not used in the study group. Fatal cases were not reported among the ARF patients.

Environmental and social factors associated with ARF were analysed in the study group. Of the 80 children with ARF, body mass index (BMI) was less than the 5th centile in 38 (47.5%), normal in 32 (40%), overweight in 9 (11.3%) and obese in one (1.3%). Sixty (75%) patients had five or more people per house and 3 (3.8%) had three or less people at home.

More than two people per living room was observed in 39 (48.8%) patients; 34 (42.5%) children were living two per room and one per room was observed in 7 (8.8%) patients. In 47 (58.8%) cases there were two children at home including the index case and in 14 (17.5%) cases there was only the index patient between 5-15 years of age. In 19 (23.75%) cases there were three or more children, including the index patient between 5-15 years of age. Separate kitchen for cooking was observed in 66 (82.5%) cases and no separate kitchen for cooking in 14 (17.5%). In 66 (62.5%) cases there was adequate gas emission at the kitchen but in 14 (17.5%) there was no gas emission at all. Passive smoking at home was observed in 42 (52.5%) cases. Majority of the 42 patients were from a low-income family receiving less than 25,000 per month. Figure 3 demonstrates the family income distribution of the children with ARF.

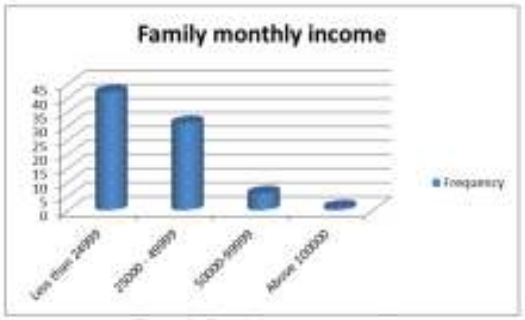

Figure 3: *Family income per month*

Most children with ARF had a low parental educational level.

Figure 4 demonstrates the pattern of parental educational level of the children with ARF.

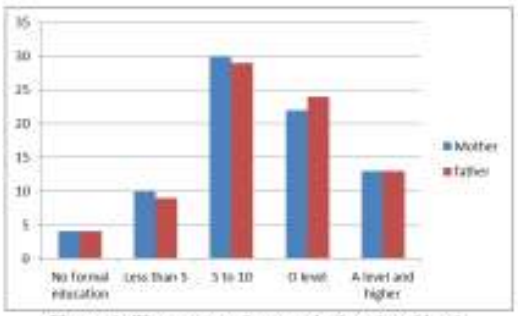

Figure 4: *The pattern of parental educational level*

When comparing the carditis group with the non-carditis group, low family income, low maternal educational level and low BMI showed positive correlation in predicting cardiac involvement (Table 3). However, age, gender, number of people per house, smoking, presence of arthritis, type of arthritis, presence of chorea, erythema marginatum, subcutaneous nodules, fever, elevated CRP and ESR did not demonstrate statistically significant correlation with cardiac involvement in the study population (Table 3).

Table 3
Variables predicting cardiac involvement in ARF

Factor	*p* value
Age category	0.25
Gender	0.124
Body mass index category	***0.017***
Number of people per house	0.12
Smoking	0.122
Family Income	***0.039***
Maternal education	***0.015***
Paternal education	0.058
Presence of arthritis	0.709
Type of arthritis	0.304
Presence of chorea	0.285
Presence of subcutaneous nodules	1
Presence of erythema marginatum	1
Degree of fever	0.97
C-reactive protein	0.061
Erythrocyte sedimentation rate	0.054

ARF: Acute rheumatic fever

Discussion

ARF is a systemic illness that may occur following group-A beta-haemolytic streptococcal pharyngitis in children. RHD, the most serious complication of ARF, is believed to result from an autoimmune response. Sex predominance of ARF varies in different parts of the world. There was female predominance in Nepal (64%) and Nigeria (52%)[6,7]. Male predominance was seen in Lebanon (58%)[8]. In a study in Sri Lanka ARF and RHD were commoner in boys[9]. Our study shows male predominance (63%) similar to a previous study done at LRH (57%)[9]. ARF is common in the 5-15-year age group. Mean age of diagnosis varies

between studies. In the Nepal study the mean age of diagnosis was 11.9 years and the youngest age of diagnosis was 5.9 years[6]. In our study mean age of diagnosis was 9.5 years with high prevalence in the 5-10-year age group. This may indicate that in our context younger populations are exposed to more group-A streptococcal disease.

Of the 80 patients 27.5% were from the Colombo district, 18.8% from the Gampaha district and 16.3% from the Puttalam district. As LRH is a tertiary care centre, ARF patients who need cardiac surgery only will be coming to LRH from certain districts. Therefore, the above distribution does not reflect the true distribution of ARF in Sri Lanka.

Arthritis was the major manifestation of ARF in this series in 73 (91.3%) children, similar to other studies[10]. Frequency of isolated arthritis as presenting symptom was 26 (32.5%) in this series similar to other studies[11]. Seven (8.8%) children presented as mono-arthritis similar to a previous study[12]. Although 26 (32.5%) children with isolated arthritis as a major criterion in association with minor criteria like fever and elevated ESR plus evidence of a recent streptococcal throat infection were included in our series, such children could be misdiagnosed as post-streptococcal reactive arthritis by other physicians.

Frequency of carditis in this series was 52 (65%) similar to other studies[10,13]. Mild carditis occurred in 46 (88.5%) children, 19 (36.5%) of whom developed severe carditis. Six (11.5%) cases were referred for early surgery due to severe mitral regurgitation with significant left atrial and left ventricular dilatation. However, our study shows that those needing surgical correction had to wait for a longer period due to non-availability of surgical correction on time. MR was the commonest echocardiographic finding in our study population similar to other studies[6,9]. MR and AR were the common findings in ARF while isolated aortic valve regurgitation was not reported in this series.

Increased rate of ARF was seen in children from urban, low-income, and crowded areas. Crowded living conditions, which are conductive to spread of respiratory infections, continue to be a predisposing factor. In addition, the associated poverty and low parental educational level leads to a delayed access to medical care. These socio-demographic features of our patients were similar to those from other countries[10,14,15]. In addition, malnourishment was shown to be associated with development of ARF in our study.

Lack of a history of preceding pharyngitis in 15 (18.8%) children in this series, similar to other series[10,16], is an important factor for persistence of ARF in the community; this is in addition to another important factor namely, poor compliance of patients to a full 10-day course of oral penicillin for treatment of bacterial pharyngitis[17,18]. Therefore, to optimise primary prevention of ARF, mass education of the population in general and the children in particular, is necessary using all resources available, including media.

As chest infections are now known to be strongly linked with air pollution, we investigated whether RHD might also be associated with air pollution. In our study we found that passive smoking was associated with 42 (52.5%) cases of ARF. The idea is supported by experimental work suggesting that air pollution impairs immune function. Domestic smoke exposure may increase the severity of streptococcal throat infections, so increasing the likelihood of developing RHD[19].

Carditis and resultant chronic RHD are the most serious manifestations of ARF and account for essentially all the associated morbidity and mortality[20]. RHD remains the commonest acquired heart disease in children in developing countries although its incidence had declined in developed countries over the past few decades. Not only increased incidence but also late presentation leading to severe valvular involvement contribute to the significant burden on paediatric cardiology and paediatric cardiac surgery units in developing countries. Cardiac involvement is reported to occur in 30-70% of patients with their first attack of ARF and higher rates and increasing severity with recurrence[20]. It is established that recurrent RF increases the risk of RHD[20]. However, the role of other factors contributing to development of carditis are not clearly defined. A study in Ukraine, considered a low-risk population with an incidence of ARF of one per 100, 000 population, showed that rural residence, which is associated with worse social conditions, was a significant risk factor for development of RHD[21]. Gender, employment status of parents, age, family status and overcrowding (number of people per house) did not have a significant influence on the development of RHD. In our study, when comparing the carditis with the non-carditis group, low family income, low maternal educational level and low BMI showed positive correlation in predicting cardiac involvement. However, age, gender, number of people per house, smoking, presence of arthritis, type of arthritis, presence of chorea, erythema marginatum, subcutaneous nodules, fever, elevated CRP and level of ESR did not demonstrate statistically significant correlation with cardiac involvement in ARF in the study population.

RHD in children still contributes a significant burden on cardiology and cardiac surgery in Sri

Lanka. Echocardiography must be done in all patients with suspected or confirmed ARF as there might be subclinical carditis. Increased rate of ARF was seen in children from urban, low-income, and crowded areas. Inadequate or lack of antibiotic treatment of streptococcal pharyngitis and undernutrition could potentially contribute to the ARF risk. To optimise primary prevention of ARF, mass education of the population in general and children in particular, is necessary using all resources available including the media especially in high risk areas.

There were some limitations. The data were collected from patients who were admitted or referred to LRH, Colombo Sri Lanka. In Sri Lanka LRH is the main tertiary care hospital for children with all the paediatric sub-specialities. However, paediatric cardiology services are available at Jaffna, Kurunegala, Kandy and Galle where ARF will be managed without referring to LRH. Thus, ARF cases from the above areas were not included in our study. Therefore, the study sample is not representative of ARF in Sri Lanka.

Conclusions

In our study, arthritis was seen in 91% of children with ARF and carditis in 65%. Of the children with carditis 65% cases were subclinical and were diagnosed only with echocardiography. Low income, low maternal educational level and low BMI showed a positive correlation in predicting cardiac involvement.

References

1. Jones TD. The diagnosis of rheumatic fever. *JAMA* 1944; **126**: 481-4. https://doi.org/10.1001/jama.1944.02850430015005

2. Guidelines for diagnosis of rheumatic fever. Jones Criteria, 1992 update. Special Writing Group of the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young of the American Heart Association. *Journal of the American Medical Association* 1992; **268**(15): 2069–73. https://doi.org/10.1001/jama.268.15.2069 PMid: 1404745

3. Gewitz M, Baltimore R, Tani L, *et al*. Revision of the Jones Criteria for the Diagnosis of Acute Rheumatic Fever in the Era of Doppler Echocardiography: A Scientific Statement from the American Heart Association. *Circulation* 2015; **131**: 1806–18. https://doi.org/10.1161/CIR.0000000000000205 PMid: 25908771

4. The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (3rd edition).

5. Steer AC, Carapetis JR, Nolan TM, Shann F. Systematic review of rheumatic heart disease prevalence in children in developing countries: the role of environmental factors. *Journal of Paediatrics and Child Health* 2002; **38**(3): 229-34. https://doi.org/10.1046/j.14401754.2002.00772.x PMid: 12047688

6. Sharma P, Shakya U, Sunita KC, Shrestha M. Clinical profile and management in children with rheumatic heart disease in a tertiary cardiac care centre of Nepal. *Nepalese Heart Journal* 2016; **13**(2): 33-6. https://doi.org/10.3126/njh.v13i2.15562

7. Sani MU, Karaye KM, Borodo MM. Prevalence and pattern of rheumatic heart disease in the Nigerian savannah: an echocardiographic study. *Cardiovascular Journal of Africa* 2007; **18**(5): 295–9.

8. Bitar FF, Hayek P, Obeid M, Gharzeddine W, Mikati M, Dbaibo GS. Rheumatic fever in children: A15-year experience in a developing country. *Pediatric Cardiology* 2000; **21**(2) 119-22. https://doi.org/10.3126/njh.v13i2.15562

9. de Silva KSH. Changing pattern of rheumatic fever in a paediatric ward: then and now. *Sri Lanka Journal of Child Health* 2010; **39**: 17-21. https://doi.org/10.4038/sljch.v39i1.1629

10. Al-Eissa YA, Al-Zamil FA, Al Fadley FA, Al Herbish AS, Al-Mofada SM, Al-Omair AO. Acute rheumatic fever in Saudi Arabia: mild pattern of initial attack. *Pediatric Cardiology* 1993; **14**(2): 89–92. https://doi.org/10.1007/BF00796986 PMid: 8469638

11. Williamson L, Bowness P, Mowat A, Ostman-Smith I. Lesson of the week: difficulties in diagnosing acute rheumatic fever-arthritis may be short lived and carditis silent. *BMJ* 2000; 320: 362–5.

https://doi.org/10.1136/bmj.320.7231.362
PMid: 10657336 PMCid: PMC1127146

12. Wilson E, Wilson N, Voss L, Morreau J, Lennon D. Monoarthritis in rheumatic fever. *Pediatric Infectious Disease Journal* 2007; **26**(4): 369–70. https://doi.org/10.1097/01.inf.0000259056.02569.0c
PMid: 17414410

13. Martins TB, Veasy LG, Hill HR. Antibody responses to Group A streptococcal infections in acute rheumatic fever. *Pediatric Infectious Disease Journal* 2006; **25**: 832–7. https://doi.org/10.1097/01.inf.0000232634.55883.d0
PMid: 16940843

14. Essop MR, Nkomo VT. Rheumatic and nonrheumatic valvular heart disease epidemiology, management, and prevention in Africa. *Circulation* 2005; **112**: 3584–91. https://doi.org/10.1161/CIRCULATIONAHA.105.539775
PMid: 16330700

15. Carapetis JR. Rheumatic heart disease in developing countries. *New England Journal of Medicine* 2007; **357**: 439–1. https://doi.org/10.1056/NEJMp078039
PMid: 17671252

16. Gerber MA, Baltimore RS, Eaton CB, Gewitz M, Rowley AH, Shulman ST, *et al.* Prevention of rheumatic fever and diagnosis and treatment of acute streptococcal pharyngitis. A scientific statement from American Heart Association. *Circulation* 2009; **119**: 1541–51. https://doi.org/10.1161/CIRCULATIONAHA.109.191959
PMid: 19246689

17. Gerber MA, Tanz RR. New approaches to the treatment of group A streptococcal pharyngitis. *Current Opinion in Pediatrics* 2001; **13**: 51–5. https://doi.org/10.1097/00008480200102000-00009
PMid: 11176244

18. Dajani AS. Adherence to physicians' instructions as a factor in managing streptococcal pharyngitis. *Pediatrics* 1996; **97**: 976–80.

19. Phillips DIW, Osmond C, Williams ML, Jones A. Air pollution in early life and adult mortality from chronic rheumatic heart disease. *International Journal of Epidemiology* 2017; **46**(4): 1107-14.

20. World Health Organization Rheumatic fever and rheumatic heart disease: report of a WHO Expert Consultation, Geneva, 29 October–1 November, 2001World Health Organization (2004)

21. Boyarchuk O, Komorovsky R, Kovalchuk T, Denefil O. (). Socio-demographic and medical predictors of rheumatic heart disease in a low-risk population. *Pediatria Polska* 2018; **93**(4): 325–30. https://doi.org/10.5114/polp.2018.77998