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Original Article

Epidemiologic profiles of subclinical rheumatic heart disease in school children

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Abstract

Background Rheumatic heart disease (RHD) causes premature deaths every year worldwide. Low socioeconomic level is considered to be a risk factor facilitating the transmission of airway infections due to *Streptococcus pyogenes*. Subclinical RHD is a stage of RHD in which heart valve abnormalities have occurred according to the *World Health Organization* (WHO) or *World Heart Federation* (WHF) classification but without any complaints to the subject. Echocardiography is used to screen subclinical RHD in several countries.

Objective To estimate the prevalence, risk factors, and echocardiographic features of subclinical RHD in children.

Methods This cross-sectional study was conducted on 250 elementary school children in Palembang, South Sumatera. We interviewed subject's parents about family characteristics, environment, and history of recurrent sore throat. Subjects underwent anthropometric examination, auscultation, and echocardiography. Diagnosis of RHD was based on WHO and WHF criteria.

Results Of 250 subjects, the prevalence of subclinical RHD was 8% (95%CI 4.8 to 11.6). Of the 20 subclinical RHD subjects, 15/20 met the possible RHD criteria, 5/20 met the probable RHD criteria, and none met the definite RHD criteria. Multivariate analysis showed that household crowding (OR 8.135; 95%CI 1.048 to 63.143; P=0.045), history of recurrent sore throat within the previous 6 months (OR 6,476; 95%CI 1.79 to 23.427; P=0.004) and age > 10 years (OR 3.167, 95%CI 1.184 to 8.471; P=0.022) significantly increased the risk of subclinical RHD.

Conclusion The prevalence of subclinical RHD in elementary school children is 8%. For echocardiographic features, most cases met the WHO/WHF possible RHD criteria. Factors significantly associated with the incidence of subclinical RHD are age > 10 years, household crowding, and history of recurrent sore throat in the previous 6 months. **[Paediatr Indones. 2020;60:334-40; DOI: 10.14238/pi60.6.2020.334-40].**

Keywords: *RHD; subclinical RHD; echocardiograpy; risk factor; school children*

Rheumatic heart disease primarily affects children between the ages of 5-15 years. It is estimated that there are more than 15 million cases of RHD worldwide, with 282,000 new cases and 233,000 deaths each year. While the rate of RHD in developed countries has decreased in the last five decades, it still causes high morbidity and mortality.[1] The prevalence of RHD in Indonesia in the year of 1981-1990 was 0.3-0.8 per 1,000 population. Based on *Global, Regional, and National Burden of Rheumatic Heart Disease* data from 1990-2015, Indonesia was classified as

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endemic, but the prevalence data was unclear.[2] The 65 RHD patients in Dr. Mohammad Hoesin Hospital, Palembang, South Sumatera, in the year of 2016-2017 exhibited varying degrees of severity. Subclinical RHD is a stage in the course of RHD, in which heart valve abnormalities occur without clinical symptoms.

Socioeconomic factors play an important role in RHD pathophysiology. Low levels of education and income with all their manifestations, such as ignorance, low quality housing and environment, household crowding, poor nutrition, and lack of access to health services lead to the transmission of recurrent *Streptococcus pyogenes* infections, which are responsible for causing RHD.[1,3,4]

Echocardiographic screening has increased the detection of RHD in endemic areas. Screening guidelines are based on the *2006 World Health Organization* (WHO) criteria/*National Institutes of Health and World Heart Federation* (WHF).[5,6] Prevalence study of subclinical RHD in India showed 20 cases per 1000 (95% CI 16.9 to 23.9), among children aged 5-15 years.[7] In Indonesia, especially in Palembang, South Sumatra, there is no data on the prevalence of subclinical RHD. Therefore, the purpose of this study was to determine the prevalence, risk factors, and echocardiographic features of subclinical RHD in school children in Palembang.

Methods

This cross sectional study was conducted in 8 elementary schools in Palembang, South Sumatera, from July to November 2019. The inclusion criteria of the study were children whose guardians or parents provided written informed consent. We excluded children who were diagnosed with infectious diseases with acute symptoms (fever, no appetite, nausea, vomiting, body weakness, etc.), children with symptoms of rheumatic fever (sudden high fever, severe sore throat with difficulty swallowing, rashes, abdominal pain, polyarthritis, Sydenham's chorea, subcutaneous node, or erythema marginatum).

A total of 250 students were enrolled. Subjects' demographic and anthropometric data were collected in the Pediatric Ward, Dr. Mohammad Hoesin Hospital, Palembang, South Sumatera. Socioeconomic status was categorized as low (parental income < Rp 3 million/month), medium (Rp 3 to 10 million/month), or high (>10 million/month).[8] Household crowding was assessed from the number of persons and the number of bedrooms in one house, crowded if occupants were more than normal. Normal household occupancy defined as 2 people in 1 room, 4 people in 2 rooms, and so on, except for children under 5 years old.[9] We assessed household crowding in the subject by interviewing their parents.

Parental education was considered to be low if the highest education attained was high school, and high if the highest education attained was beyond high school. History of recurrent sore throat was classified as occurring within the previous 6 months or >6 months/never. Nutritional status was defined by the *2000 CDC Growth Chart*. We examined subject's nutritional status using *2000 CDC Growth Chart* before echocardioagraphic was performed. We classified the nutritional status as well-nourished if the weight for height was between >90th-110th percentile, wasted if weigth for height was < 90th percentile, overweight if BMI was > 85th and < 95th percentile, and obesity if BMI was > 95th percentile.[10]

Diagnosis of subclinical RHD subjects was based on echocardiography (modified WHO and WFH) which was carried out in the Pediatric Ward Dr. Mohammad Hoesin Hospital along with other investigations. Subclinical RHD consisted of morphological abnormalities in the mitral and/or aortic valve, pathological mitral valve and pathological aortic valve, with at least 1 of these abnormalities without complaints.[2,6] Morphological features of RHD can be in the form of stiffness, restrictions or excessive movement of the mitral valve and/or aorta. Pathological mitral valve was defined as jet length >2 cm, velocity >3 m/s for one complete envelope, and pan-systolic jets in at least one envelope. Pathological aorta was defined as jet length >1 cm, velocity >3 m/s in early diastole, and pan-diastolic jets in at least one envelope). The 2006 WHO criteria were used to classify patients into categories of possible, probable, or definite subclinical RHD (**Table 1**).[5,6,11]

Characteristic data were presented as numbers (%), mean (SD), median, and range. Prevalence was reported with 95% confidence intervals. The distribution of variables was analyzed by Kolgomorov-Smirnov test. Bivariate analysis of risk factors of subclinical RHD was done with Chi-square test.

Table 1. Echocardiographic diagnosis of RHD according to the *2006 World Health Organization/National Institutes of Health Joint Criteria*[5]

Definite	Has cardiac murmur* AND significant mitral regurgitation and/or significant aortic regurgitation AND a thickened mitral valve and/or elbow deformity of the anterior mitral leaflet
Probable	Comes from a population in which RHD is endemic AND has cardiac murmur* AND either significant mitral regurgitation and/or aortic regurgitation OR thickened mitral valve and/or elbow deformity of the anterior mitral leaflet
Possible	Comes from a population in which RHD in endemic, has no cardiac murmur, AND has thickened mitral valve and/or elbow deformity of mitral valve and/or significant mitral and/or aortic regurgitation

*Consistent with any combination of mitral regurgitation or aortic regurgitation.

Multivariate analysis with binary logistic regression was done to determine which risk factors were significantly associated with subclinical RHD. Age, sex, nutritional status, household crowding, parental income, parental education, history of recurrent sore throat in the previous 6 months were assessed for possible relationships to subclinical RHD. Results with P values <0.05 were considered to be statistically significant. Data were analyzed using *SPSS version 16.0*, with 95% confidence intervals.

The study protocol have been reviewed and approved by the Ethical Committee of Dr. Mohammad Hoesin General Hospital, Palembang, South Sumatera.

Results

The 250 children enrolled had a mean age of 9.4 (SD 1.9) years (range 5-14 years), and consisted of 52.8% girls and 47.2% boys. Most subjects were well-nourished (52.8%), while 30% were wasted. Most subjects came from low-income families (74.8%) and lived in crowded housing (67.6%). The majority of parents had low educational levels (86.4% of fathers and 84% of mothers). History of recurrent sore throat in the previous 6 months was found in 50.4% subjects (**Table 2**).

Echocardiography revealed subclinical RHD in 20 (8%) subjects (95%CI 4.8 to 11.6). Types of valve abnormalities are shown in **Table 3**. Based on WHO criteria the 20 children with subclinical RHD were classifed as possible (15/20) or probable (5/20). None of them could be classified as definite.

The prevalence of subclinical RHD increased across age categories from 5.1% in children 5-10 years of age to 13% in children >10 years of age (OR 2.7; 95%CI 1.06 to 6.89; P=0.031). Children with subclinical RHD more commonly lived in crowded than uncrowded houses (OR 10.133; 95%CI 1.332 to 77.048; P=0.006). Children whose last episode of sore throat occurred within the previous 6 months had a higher risk of subclinical RHD (OR 6.291; 95%CI 1.794 to 22.052; P=0.001). There were no significant differences in between subjects with and without subclinical RHD, in terms of nutritional status, parental income, and parental education (**Table 4**).

Multivariate analysis using binary logistic

Table 2. Characteristics of subjects

Characteristics	(N=250)
Gender, n (%)	
Male	118 (47.2)
Female	132 (52.8)
Age	
Mean (SD), years	9.4 (1.9)
Range, years	5-14
5-10 years, n (%)	156 (63.4)
> 10 years, n (%)	94 (37.6)
Nutritional status, n (%)	
Well-nourished	132 (52.8)
Wasted	75 (30)
Overweight	30 (12)
Obese	13 (5.3)
Household crowding, n (%)	
Crowded	169 (67.6)
Not crowded	81 (32.4)
Family income, n (%)	
Low	187 (74.8)
Moderate	57 (22.8)
High	6 (2.4)
History of recurrent sore throat, n (%)	
Within the previous 6 months	126 (50.4)
Never	106 (42.4)
Prior to the previous 6 months	18 (7.2)
Parental education, n (%)	
Fathers	
Never attended school	3 (1.2)
Low	216 (86.4)
High	31 (12.4)
Mothers	
Never attended school	9 (3.6)
Low	210 (84)
High	31 (12.4)

regression revealed that the significant risk factors for subclinical RHD were crowded housing (OR 8.135; 95%CI 1.048 to 63.143; P=0.045), history of recurrent sore throat within the previous 6 months (OR 6.476; 95%CI 1.79 to 23.427; P=0.004), and age > 10 years (OR 3.167; 95%CI 1.184 to 8.471; P=0.022) (**Table 5**).

Table 3. Echocardiographic abnormalities

Variables	(n=20)
Valve abnormalities, n	2
Mitral regurgitation	3
Aortic regurgitation	8
Mitral and aortic regurgitation	5
Mitral, aortic and tricuspid regurgitation	2
Mitral, aortic, tricuspid and pulmonal regurgitation	
WHO criteria, n	
Definite	0
Probable	5
Possible	15

Discussion

In this cross-sectional study, we studied the prevalence, risk factors, and echocardiographic features of subclinical RHD in elementary school children in Palembang, South Sumatera. The previous pilot study in 25 elementary school children who underwent echocardiography found that 4 children (16%) had abnormalities in the mitral valve and/or aorta without symptoms (subclinical RHD). This number was quite high compared to the prevalences from previous studies.[7,12] Thus, we conducted a study with a larger sample size on possible risk factors for subclinical RHD.

The majority of subjects (52.6%) were female. The mean age of children was 9.4 years (range 5-14 years), with most subjects in the 5-10-year age group. The majority of subjects lived in crowded housing (67.6%), were well-nourished (53.8%), and came from

Table 4. Bivariate analysis of subclinical RHD and possible risk factors

Characteristic	Subclinical RHD			OR (95%CI)	P value
	Yes	No	Total		
Age, n (%)				2.7 (1.063 to 6.792)	0.031
>10 years	12	82	92		
5-10 years	8	148	158		
Household crowding, n (%)				10.133 (1.332 to 77.048)	0.006
Crowded	19	150	169		
Not crowded	1	80	81		
Gender, n (%)				1.732 (0.667 to 4.500)	0.25
Female	13	119	132		
Male	7	111	118		
Nutritional status, n (%)				0.476 (1.76 to 1.290)	0.137
Wasted	9	79	88		
Well-nourished	8	126	134		
Nutritional status, n (%)				0.529 (1.131 to 2.134)	0.364
Overweight	3	25	28		
Well-nourished	8	126	134		
History of recurrent sore throat, n (%)				6.291 (1.794 to 22.052)	0.001
Within the previous 6 months	17	109	126		
More than 6 months ago or never	3	121	124		
Family income, n (%)				1.089 (1.051 to 1.135)	0.465
Middle to lower	20	224	244		
High	0	6	6		
Maternal education, n (%)				1.299 (0.286 to 5.889)	0.734
Low	18	201	219		
High	2	29	31		
Paternal education, n (%)				2.86 (0.368 to 22.076)	0.295
Low	19	200	219		
High	1	30	31		

Table 5. Multivariate analysis of risk factors for subclinical RHD

Variables	Unadjusted		Adjusted	
	OR (95%CI)	P value	OR (95%CI)	P value
> 10 years of age	2.7 (1.063 to 6.792)	0.031	3.167 (1.184 to 8.471)	0.022
Crowded housing	10.133 (1.332 to77.048)	0.006	8.135 (1.048 to 63.143)	0.045
History of recurrent sore throat within the previous 6 months	6.291 (1.794 to 22.052)	0.001	6.476 (1.79 to 23.427)	0.004

Logistic regression, 95%CI

low-income families (74.8%). The socioeconomic status of our subjects may have been skewed as the majority of students from the randomly-chosen public schools were from crowded environments and had lower-middle economic status.

Echocardiographic examination revealed a subclinical RHD prevalence of 8% (95%CI 4.8 to 11.6). A study reported a prevalence of 2.04% in India in 2008-2010,[10] and another study reported 2.11% in a meta-analysis study in children 5 to <18 years from 1993-2014 in endemic areas.[11] The highest prevalence was in Tonga (3.33%). In India, 0.6-0.8 RHD cases per 1,000 children had symptoms, from subclinical RHD screening results of 20.4 per 1000 children and reported silent/subclinical RHD in 21.1 cases per 1000 children, about 7-8 times higher than clinical RHD (2.7 per 1000 children).[12] According to the *Global, Regional, and National Burden of Rheumatic Heart Disease* data in the year of 1990-2015, Indonesia is considered to be an endemic area for RHD.[13] Nationally, RHD rates have not been recorded to date. However, several teaching hospitals in Indonesia reported their RHD cases as follows: Dr. M. Djamil Hospital Padang, West Sumatera (January 2009 to December 2012) had 54 cases, Dr. Wahidin Sudirohusodo Hospital, Makassar, South Sulawaesi (January 2005 to December 2009) had 80 patients, and Dr. Hasan Sadikin General Hospital, Bandung, West Java, had 55 cases annually.[4,14] Subclinical RHD cases in Palembang were suspected to be higher at Dr. Mohammad Hoesin Hospital, Palembang, South Sumatera, as 65 RHD patients were treated with varying degrees of severity in 2016-2017 (unpublished data).

In 20 subjects with subclinical RHD, echocardiography revealed mitral regurgitation in 2 children, aortic regurgitation in 3 children, as well as mitral and aorta regurgitation in 15 children. Based on the 2006 WHO criteria, 15/20 children fulfilled the possible RHD criteria, 5/20 children fulfilled the probable RHD criteria, and no children fulfilled the definite criteria. A previous study in 72 subjects with subclinical and clinical RHD reported 65% subjects with possible RHD, 23% with probable, and 4,75 with definite, from a total of 5,006 children. They did not exclude patients with clinical symptoms.[5] In our study, no subjects met the criteria of definite RHD classification. Definite cases tend to have heart abnormalities that cause obvious clinical symptoms. In addition, our subjects were told to return to our facility if symptoms occurred before their scheduled evaluation. A previous study also provided secondary prophylactic therapy to subjects who met the definite criteria.[5] Moreover, an Indian study reevaluated the subclinical RHD children 1 year after the first echocardiography.[7] In our study, the 20 children with subclinical RHD were regularly followed up and educated at the pediatric cardiology clinic, with tracking and monitoring plans for the next 1 year.

Children over 10 years of age are known to have a higher risk for subclinical RHD (OR 3.167; 95%CI 1.184 to 8.471; P=0.022). A previous study found that definitive cases increased by more than 2% in children aged 10 to 13 years and less than 1% in children aged < 9 years, with possible and probable criteria subclinical RHD.[5] A meta-analysis showed an increase of subclinical RHD prevalence from 4.7/1,000 children at the age of 5 years to 21/1,000 for children at the age of 16 years.[12] Also, a study reported prevalences of 26.5/1,000 in children > 10 years of age (11-15 years), and 12.6/1,000 in children aged 5-10 years (OR 1.93; 95%CI 1.29 to 2.88; P=0.001).

History of recurrent sore throat within the previous 6 months was associated with an increased risk of subclinical RHD (OR 6.476; 95%CI 1.79 to 23.427; P=0.004). In our study, history of recurrent sore throat within the previous 6 months was common. Nonetheless, this variable may be subjective, since it

was dependent on subject/parent recall. Dajani stated that one-third of RHD patients denied any upper respiratory infections or sore throats, but antibody responses to streptococcal extracellular products were shown in almost all cases of rheumatic fever. Acute attacks of rheumatic fever were closely related to the magnitude of the antibody response. Many children experience episodes of pharyngitis each year, with 15-20% caused by group A streptococcus (GAS) and another 80% caused by viral infections.[15]

In our study, household crowding had a significant association with incidence of subclinical RHD (OR 10.133; 95%CI 1.332 to 77.048; P=0.006). A study found that kutcha house had a higher risk of subclinical RHD compared to concrete houses. However, we found no significant relationship between lower-middle family income and the incidence of subclinical RHD (OR 1.089; 95%CI 1.051 to 1.135; P=0.314), while they noted such an association.[7]

Our sample population mostly came from families with lower-middle economic status, which impacts household crowding and family knowledge of the importance of the adequate shelter and sanitation and facilitates transmission of airway infections due to Streptococcus pyogenes, which is responsible for RHD pathophysiology. In addition, respiratory tract infections due to GAS are often improperly treated, even by medical personnel. Genetic factors also certainly affect the immune response, but we did not examine it in our study.

Nutritional status was not significantly associated with subclinical RHD in our study. Similarly, a previous study found no significant difference in incidence of subclinical RHD in children with BMI <-2 and BMI > -2.[7] Nevertheless, RHD may affect nutritional status because of symptoms, the impact on metabolism, and difficulties in dietary intake.[16]

The main limitation of this study was possible recall bias on the history of recurrent sore throats. Multicenter study is needed to describe the RHD prevalence in the Indonesian pediatric population, with possible consideration for echocardiographic screening of at-risk children.

In conclusion, the prevalence of subclinical RHD is 8%. Most cases are categorized as possible subclinical RHD. Significant risk factors for subclinical RHD are age over 10 years, household crowding, and history of recurrent sore throat within the previous 6 months. Education about preventing recurrent *Streptococcus pyogenes* infection is important to limit transmission and RHD progression, including the importance of adequate shelter, handwashing, cough and sneeze etiquette, and seeking treatment at appropriate health facilities. Furthermore, medical personnel should be trained to evaluate and manage airway infection due to GAS.

Conflict of interest

None declared.

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