Profile and Prediction of Severity of Rheumatic Mitral Stenosis in Children

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Abstrak

Di negara-negara berkembang seperti Indonesia, penyakit jantung reumatik (PJR) masih merupakan masalah kesehatan masyarakat. Stenosis mitral reumatik (SMR) dapat terjadi dengan cepat dan SMR berat dapat timbul pada umur sedini 15 tahun di negara Asia-Afrika. Pemeriksaan fisik tidak cukup akurat untuk menentukan derajat berat SMR. Penelitian ini untuk mengetahui gambaran klinis SMR pada anak, gambaran EKG dan foto Roentgen dada yang mungkin dapat memperkirakan derajat berat SMR sesuai ekokardiografi. Telah dilakukan penelitian 'cross-sectional' pada 28 pasien SMR di Bagian Ilmu Kesehatan Anak RSCM. Umur rata-rata adalah 13,5 tahun. Dua pasien tidak dapat disertakan dalam uji diagnostik karena pemeriksaan yang belum lengkap. Derajat berat SMR berdasarkan pengukuran luas katup mitral dengan ekokardiografi 2 D digolongkan dalam derajat ringan, sedang dan berat masing-masing terdapat pada 1, 15 dan 10 pasien. Prakiraan derajat berat SMR berdasarkan RVH dan RAD pada EKG menunjukan spesifisitas 75% dan nilai duga negatif 85,7%. Prakiraan derajat berat SMR berdasarkan analisis foto Roentgen dada menunjukkan sensitifitas 80%, spesifisitas 81,2% sedangkan nilai duga negatif adalah 86,7%. Kombinasi pemeriksaan EKG atau Foto Roentgen dada menunjukan sensitifitas yang tinggi yaitu 90%, yang berguna untuk menapis pasien SMR di daerah yang tidak mempunyai fasilitas ekokardiografi. Nilai duga negatif pemeriksaan kombinasi adalah 92%, yang berarti bila tidak didapatkan tanda SMR berat pada EKG atau foto Roentgen dada, kemungkinan besar bukan SMR berat.

Abstract

In developing countries such as Indonesia, rheumatic heart disease (RHD) is still an important community health problem. Rheumatic mitral stenosis (RMS) occurs more rapidly and severe RMS could occur at age as early as 15 years old in Asia-Africa country. The physical examination is not accurate enough to predict the severity of RMS. The aims of this study are to explore RMS clinical, ECG, CXR, echocardiographic features, and to evaluate the value of ECG or CXR as a diagnostic tool predict the RMS severity compared to echocardiography as a gold standard. Cross-sectional study was done on 28 RMS patients at Child Health Department Dr Cipto Mangunkusumo Hospital. Mean of age was 13.5 years. Unfortunately 2 patients were excluded from diagnostic test due to incomplete examination. The severity of RMS based on 2 D echo was classified as mild, moderate and severe in 1, 15 and 10 patients, respectively. The specificity of RMS severity prediction by RVH and RAD on ECG was 75%, and negative predictive value was 90.9%. Sensitivity of CXR in prediction of RMS severity was 80%, specificity was 81.2%, while negative predictive value was 86.7%. The combination of ECG or CXR gave 90% sensitivity that would be beneficial to screen RMS patient in rural area. The negative predictive value was 92%. This means that if there is no severe RMS sign on ECG nor CXR, then the RMS is most probably not severe.

Keywords : Rheumatic mitral stenosis, mitral valve area, 2D-echocardiography

In developing countries as Indonesia, rheumatic fever (RF) and rheumatic heart disease (RHD) are still an important community health problem. RHD potentially raises serious problem for patient, family, community as well as our country, because it strikes young and productive people and may influence the future human resource.[1] About one third of the children suffering from RF would have chronic sequel as RHD especially affecting the mitral valve which occur at a frequency of 75 - 98 %.[2,3,4,5] Mitral abnormality could be manifested as regurgitation, stenosis or both. In developed countries rheumatic mitral stenosis (RMS) occurred at least 5 - 10 years after the acute episode of RF;[6] but in developing countries, primarily in Asia Africa, RMS has more rapid clinical course and severe RMS could occur in patients at the age of 15 years.[7] Generally, RMS raises more problems and needs for earlier intervention than rheumatic mitral regurgitation (RMR).

Data on characteristic, clinical, electro-cardiographic (ECG), roentgenographic (CXR) and echocardiographic features of RMS in Indonesian children are

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still rare in literature. The physical examination is not accurate enough to predict the severity of RMS.[8] The ECG or CXR feature might be important as a diagnostic tool especially in predicting the RMS severity with certain accuracy as a reason to refer patient from rural area. The aims of this study are to evaluate the characteristic, clinical, ECG, CXR and echocardiographic features of RMS in Indonesian children; and to evaluate the value of ECG or CXR as a diagnostic tool to predict the RMS severity compared to echocardiography as a gold standard.

METHODS

This study was a cross-sectional study performed at The Child Health Department Dr Cipto Mangunkusumo Hospital, since December 1990 until April 1993. The inclusion criteria were patient's age among 4.5 - 18 years old and diastolic rumbling with presystolic accentuation at the apex. The exclusion criteria were (1) predominant mitral regurgitation, (2) other heart valve abnormalities which were more dominant such as severe aortic regurgitation (both criteria were excluded by clinical examination and supported by the presence of left ventricular hypertrophy (LVH) on ECG), and (3) severe chronic pulmonary disease as such as bronchiectasis and destroyed lung.

The sample size was calculated by formula[9]: $N = {}^4Z_\alpha^2 P (1-P) : W^2$. Z_α = the standard normal deviate for two tailed α, in this study the confidence level was 90%, so Z_α = 1.645. P= expected sensitivity/ specificity. W= total width of confidence interval, in this study was 0.3. N= sample size. If P was predicted as 0.7, then N would be 26.

The functional capacity of patients was classified according to The New York Heart Association (NYHA).[10]

The right ventricular hypertrophy (RVH) criteria on ECG were that used in the Pediatric Cardiology subdivision Child Health Department such as : R_1 > max (age > 30 months : R_1 > 19 mm), S_6 > max (age > 3 months: S_6 > 6 mm), R_1/S_1 > max (age 6 -15 years : R_1/S_1 > 0.8), T wave positive in V_1 after the third day, if R_1/S_1 > 1.0. The right axis deviation (RAD) was considered if the QRS axis > 110°. The prediction of severe RMS was based on the presence of RVH and RAD.

The prediction of RMS severity by CXR with Barium contrast was as follows:

1. mild: (a) cardiac silhouette was normal, unless left atrial appendage (LAA) enlargement was seen on AP projection,[11] (b) left atrial (LA) enlargement was seen on lateral or left anterior oblique projection[12-14]
2. moderate: mild criteria plus: (a) right ventricle enlargement, (b) moderate pulmonary hypertension: redistribution of pulmonary blood vessel (upper lobe = lower lobe)
3. severe: moderate criteria plus: (a) right atrial enlargement,[12,13] (b) severe pulmonary hypertension if any sign listed below was found: pulmonary artery trunk enlargement,[12,13] pulmonary blood vessel of upper lobe lower lobe,[7] Kerley A or B line,[12] alveolar oedema.[5,7]

The mitral valve orifice area (MVA) was measured by 2 D Toshiba Sonolayer echocardiography. The severity of RMS based on MVA was classified as follows: mild, if MVA was 2 - 2.5 cm[2]; moderate, if MVA was 1 - 2 cm[2]; severe, if MVA was less than 1 cm[2].

The diagnostic tests of ECG and CXR were compared to MVA measurement of 2 D echocardiography as gold standard. Diagnostic indices were sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. Confidence interval (c.i.) of diagnostic indices was calculated by formula : [15]

$$\text{c.i.} = \frac{2p + \theta^2 \pm \theta \sqrt{\theta^2 + 4p(1-p)}}{2 + 2\theta^2}$$

p   = proportion of diagnostic index
θ = $Z_{\alpha/2} : \sqrt{N}$
$Z_{\alpha/2}$ = normal standard deviate for 2 tailed α, in this study the confidence level was 90% so $Z_{\alpha/2}$ = 1.645

RESULTS

Patients' profile

Mean age was 13.5 (SD 2.0) years (range : 10 - 18 years). There were 15 male and 13 female patients. Mean weight was 32.48 (SD 8.35) kg. Mean height was 142.21 (SD 1.21) cm. Functional capacity was classified according to NYHA. Class I, II and III were found in 9, 12 and 7 patients respectively. The mean haemoglobin level was 12.3 (SD 0.96) g/dl (range: 10.3 - 14 g/dl). Mean haematocrite was 37.1 (SD 2.5) vol% (range : 32 - 42 vol%).

The ECG abnormalities

The ECG abnormalities were shown on Table 1. Left atrial enlargement was found in 21 out of 26 (80.77%) cases, while right ventricular enlargement was detected in 15 out of 26 (57.69%) patients. Right axis deviation was found in 12 cases (46.15%). Various ECG features of RMS patients according to RMS severity were shown in Table 4.

Table 1. ECG abnormalities in 26 RMS patients

Abnormalities	Cases	%
Right axis deviation	12	46.15
Rhythm : sinus tachycardia	14	53.85
atrial fibrillation	3	11.54
Left atrial enlargement	21	80.77
Right ventricular hypertrophy	15	57.69
Right atrial enlargement	9	34.62

The CXR abnormalities

The CXR abnormalities were seen in Table 2. Severe RMS was found in in 11 out of 26 (42.31%), while mild and moderate RMS were found in 15 out of 26 (57.69%) patients.

Table 2. CXR abnormalities in RMS patients

Abnormalities	Sum	%
Left atrial appendix enlargement	18	68.23
Left atrial enlargement	26	100
Right atrial enlargement	9	34.62
Left ventricular enlargement	15	57.69
Right ventricular enlargement	21	80.77
Cardiomegaly	23	88.46
Pulmonary hypertension:		
- moderate	13	50
- severe	11	42.31
Severity of RMS:		
- mild	2	7.69
- moderate	13	50
- severe	11	42.31

The 2 D echocardiography

The 2 D echocardiography examination of RMS severity was shown in Table 3. There were 10 severe RMS out of 26 patients (38.46%).

Table 3. RMS severity by 2-D echocardiography in 26 cases

RMS severity	Cases	%
Mild	1	3.85
Moderate	15	57.69
Severe	10	38.46

Table 4. ECG features according to echographic RMS severity

	RMS severity by echocardiography	
	Severe	No severe
LAE	1	7
RVH + RAD	2	1
LAE + RAVH + RAE + RAD	4	3
LAE + RAE	-	2
LAE + RVH	1	1
RVH	-	1
LAE + RVH +RAD	2	-
Normal	-	1
Total cases	10	16

The RMS severity prediction by RVH and RAD on ECG

The sensitivity, specificity, predictive value and accuracy of RVH and RAD were shown in Table 5.

Table 5. Diagnostic indices of RVH and RAD on ECG and RMS severity

	RMS severity by Echocardiography		
	Severe RMS	Non-severe RMS	Total cases
RVH + and RAD + ECG	8	4	12
RVH - RAD - RVH + RAD - RVH - RAD +	2	12	14
Total cases	10	16	26

Sensitivity = 80%   (c.i. 90% : 65% to 90%)
Specificity = 75%   (c.i. 90% : 59% to 86%)
Positive predictive value = 66.7% (c.i. 90% : 51% to 80%)
Negative predictive value = 85.7% (c.i. 90% : 71% to 94%)
Accuracy = 76.9% (c.i. 90% : 61% to 87%)

The RMS severity prediction by CXR analysis

The sensitivity, specificity, predictive value and accuracy of CXR analysis were shown in Table 6.

Table 6. Diagnostic index of CXR analysis and RMS severity

		RMS severity by Echocardiography		
		Severe RMS	Non-severe RMS	Total cases
C X R	Severe RMS	8	3	11
	Non-severe RMS	2	13	15
	Total cases	10	16	26

Sensitivity = 80% (c.i. 90% : 65% to 90%)
Specificity = 81.2% (c.i. 90% : 66% to 91%)
Positive predictive value = 72.7% (c.i. 90% : 57% to 84%)
Negative predictive value = 86.7% (c.i. 90% : 72% to 94%)
Accuracy = 80.8% (c.i. 90% : 65% to 90%)

The RMS severity prediction by ECG or CXR analysis

The sensitivity, specificity, predictive value and accuracy of ECG or CXR analysis were shown in Table 7.

Table 7. Diagnostic index of ECG or CXR analysis and RMS severity

		RMS severity by Echocardiography		
		Severe RMS	Non-severe RMS	Total cases
ECG or CXR	Severe RMS	9	5	16
	Non-severe RMS	1	11	10
	Total	10	16	26

Sensitivity = 90% (c.i. 90% : 76% to 96%).
Specificity = 69% (c.i. 90% : 53% to 81%).
Positive predictive value = 64% (c.i. 90% : 48% to 77%).
Negative predictive value = 92% (c.i. 90% : 79% to 97%).
Accuracy = 77% (c.i. 90% : 61% to 88%).

DISCUSSION

The limitations of this study

In this study period, there were 28 RMS patients who satisfied the inclusion and exclusion criteria. Unfortunately, 2 patients could not be included in the analysis because of incomplete examination. This diagnostic test study actually requires at least 26 patients for each sensitivity and specificity test. The limitation of the sample size would lower the confidence interval of the diagnostic indices. If the result of this study will be applied in the community population, then another study with 95% confidence level and narrower total width of confidence interval should be performed.

The patients' profile

The average age of RMS patients was 13.5 year and the youngest patient was 10 years old. In Asia and Africa, RMS can occur in patients of less than 20 years old, [16] moreover it has been reported in patients as young as 5 years old.[17] In contrary to the western literature that reported female predominance, sex ratio in this study was near equal or male was slightly predominant. The male and female ratio were 1.1 : 1. It agreed with the male predominance reported in a series of RMS patients undergoing Balloon Mitral Valvuloplasty in the Harapan Kita Cardiac Center. In Harapan Kita patients, the male and female ratio was 1.3 : 1.[18] It is also in accordance with Cherian report that in the developing countries RMS occurs in male and female near equally.[19]

In this study, there was no patient suffering from severe anemia that may influence the cardiovascular system. The cardiac output will continuously increase if the haematocrite level is less than 25 volume %,[20] the haemoglobin level is less than 7 g/dl or half of normal value.[21] None of our RMS patients showed such haematological abnormalities.

The ECG

The right axis deviation (RAD) was found in 14 patients, 8 of them suffered from severe RMS. In this study all patients who showed RAD, also showed RVH. RAD is generally found in RVH.[22]

Atrial fibrillation was found in 3 patients. This is in accordance with the literature that atrial fibrillation is rare in children and young people.[5]

In contrast to CXR examination that showed 26 patients with left atrial enlargement (LAE), electrocardiographically LAE was found only in 21 patients. This confirmed the literature report that ECG examination in RMS patients would disclose LAE in about 90% of the cases. [11]

Right atrial enlargement which was seen as P pulmonal wave was found in 9 patients. The P pulmonal wave was associated with increased pulmonary resistance.[7]

Right ventricular hypertrophy (RVH) was found in 15 patients. RVH was associated with severe RMS [23] and pulmonary hypertension. [7,8] Nevertheless, the absence of RVH does not exclude recently developing severe pulmonary hypertension.[8]

The CXR

Left atrial appendage (LAA) enlargement was found in 18 patients. The LAA enlargement was a pathognomonic sign of mitral valve disease due to RF. [4,24] The left atrial enlargement (LAE) was found in 26 patients. This confirmed the literature report that LAE was found in most RMS patients.[4]

Left ventricle enlargement was found in 15 patients who showed mild mitral regurgitation in Doppler echocardiography.

Right ventricular enlargement was found in 21 patients who showed either moderate or severe pulmonary hypertension. The right ventricle does enlarge in pulmonary hypertension.[5,7]

The moderate and severe pulmonary hypertension features were found in 13 and 11 patients.

The echocardiography

The RMS severity was evaluated on basis MVA measurement in 2 D echocardiography examination in adult patients. There is no classification of RMS severity based on children MVA currently. We applied the adult criteria in children.

In children, MVA (cm^2) correlates well with body surface area (BSA, in m^2) which is formulated as MVA = 4.83 x MVA - 0.07. [25] The predicted MVA of RMS patients in this study will be 4.11 to 6.91 cm2. Normal adult MVA is 4 - 6 cm2. The predicted MVA was slightly larger than normal adult MVA.

The RMS severity prediction by RVH and RAD on ECG

RVH is caused by pulmonary hypertension [5,7,26] and is found in severe RMS.[23] However, the absence of RVH does not exclude severe pulmonary hypertension. [8] The purpose of including RAD as one criteria in the prediction of severe RMS was to increase specificity and accuracy. If the RVH was used alone, it would give a specificity of 62.5% and an accuracy of 73.1%, while the combination would give 75% and 76.9% respectively.

In this study, sensitivity of RVH and RAD was 80% (c.i. 90% : 65% to 90%), specificity was 75% (c.i. 90% : 59% to 86%). Negative predictive value was 85.7% (c.i. 90% : 71% to 94%). This means that if there is no RVH and RAD on ECG examination in RMS patients, then RMS is most probably not severe.

The RMS severity prediction by CXR analysis

Pulmonary hypertension occurs in moderate or severe RMS. In moderate RMS, upper pulmonary lobe receives more blood perfusion than normal, so the upper pulmonary blood vessels appear to fill equally to blood vessels of the lower lung field. In severe pulmonary hypertension, the upper pulmonary lobe receives more blood than lower lobe. These pulmonary vascular changes are seen in the CXR. [5-7,27] The degree of pulmonary hypertension can be used to assess the severity of RMS.[6]

Sensitivity of CXR in the prediction of RMS severity was 80% (c.i. 90% : 65% to 90%), specificity was 81.2% (c.i. 90% : 66% to 91%). Negative predictive value had highest diagnostic value, i.e., 86.7% (c.i. 90% : 72% to 94%). This means that if there is no severe RMS sign on CXR film in RMS patient, then the RMS is most probably not severe.

The RMS severity prediction by ECG or CXR analysis

The RMS prevalence is relatively rare amongst RHD patients, i.e., about 5 - 10%. [5,6] In Pediatric Cardiology sub-division Child Health Department, the RMS prevalence is also rare. In this study, there were only 28 patients out of approximately 400 RHD patients examined. To screen RMS patients in the rural area, a sensitive diagnostic test is required to support clinical examination.

The ECG and CXR analyses were combined to increase the sensitivity. If either ECG or CXR analysis showed severe RMS sign, then the patients were grouped as severe RMS. The results are shown in table 7.

The sensitivity of combined examination was higher (90%) than the sensitivity of ECG (80%) or CXR analysis (80%) alone. The negative predictive value was also increased to 92%, in contrast to 85.7% in the ECG and 86.7% in the CXR analysis. The accuracy of combined examination was equal to the accuracy of ECG but slightly lower than the CXR analysis. The other diagnostic indices had lower value than ECG or CXR analysis. This might be caused by the increase of false positive cases and decrease of true negative cases.

CONCLUSION

The RMS severity criteria on CXR analysis and ECG examination are useful in predicting the RMS severity, especially in rural area where echocardiography facility is lacking. It may be beneficial in managing RMS patients especially in screening severe RMS patients for referral. To determine the indication for an invasive procedure, more accurate diagnostic procedure is needed such as echocardiography, which can be performed in the referral hospital.

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