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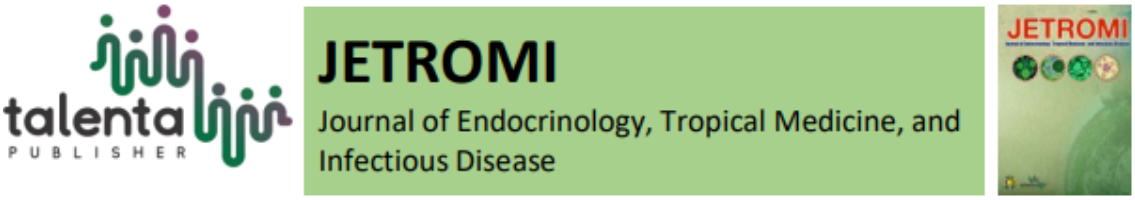

Prevalence of Valvular Heart Disease and Pulmonary Hypertension in Children in Rantau-Prapat City, North Sumatra, Indonesia

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ABSTRACT

Background: Valvular heart disease and pulmonary hypertension (PH) are two distinct but often interconnected cardiac conditions that can affect children and encompass abnormalities of the heart's valves such as the aortic, mitral, tricuspid, and pulmonary valves, and can present with symptoms such as chest pain, fatigue, and dyspnea. In contrast, PH refers to elevated blood pressure in the pulmonary arteries. Routine screening for these conditions is needed for prompt diagnosis and management. This study was conducted to obtain data on children with valvular heart disease or PH who participated in the Community Service Program of the Department of Cardiology and Vascular Disease, Universitas Sumatera Utara.

Method: This study was a descriptive study conducted through a cross-sectional study design. Data was collected from interviews and on-the-spot examination with validated measurement tools. Data was analyzed using SPSS version 26. Categorical variables were presented using frequency (n) and percentage (%), and numerical variables with normally distributed data were presented with mean and standard deviation (SD). In non-normally distributed data, numerical variables were presented using the median and interquartile range.

Results: There were 157 children included in this study. Most subjects were female (n=94, 59.9%) in the age range 12 to 16 years old. Most subjects (n=152, 96.8%) had normal mitral valves, three subjects had anterior mitral valve prolapse (1.9%), one subject (0.6%) had anterior mitral valve thickening and one subject (0.6%) had mild mitral regurgitation. 10 subjects (5.7%) had pulmonary regurgitation. Two subjects had tricuspid regurgitation (1.2%). No subjects had any aortic abnormalities. No subjects had a PH.

Conclusion: In the children population in Rantau-Prapat City, most subjects with valve abnormalities had mitral and pulmonary valve abnormalities. No subjects had aortic valve abnormalities or PH.

Keywords: Valvular heart disease, pulmonary hypertension, mitral valve, tricuspid valve, pulmonary valve, children

ABSTRAK

Latar Belakang: Penyakit katup jantung dan hipertensi pulmonal (HP) adalah dua kondisi jantung yang berbeda tetapi sering saling berhubungan yang dapat mempengaruhi anak-anak

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dan mencakup kelainan katup jantung seperti katup aorta, mitral, trikuspid, dan pulmonal, dan dapat hadir dengan gejala seperti nyeri dada, kelelahan, dan dispnea. Sebaliknya, HP mengacu pada tekanan darah tinggi di arteri pulmonalis. Skrining rutin untuk kondisi ini diperlukan untuk diagnosis dan manajemen yang cepat. Penelitian ini dilakukan untuk mendapatkan data anak penderita penyakit katup jantung atau PH yang mengikuti Program Pengabdian Masyarakat Departemen Kardiologi dan Penyakit Vaskular Universitas Sumatera Utara.

Metode: Penelitian ini merupakan penelitian deskriptif yang dilakukan melalui desain studi potong lintang. Data dikumpulkan dari wawancara dan pemeriksaan langsung dengan alat pengukuran yang divalidasi. Data dianalisis menggunakan SPSS versi 26. Variabel kategoris disajikan menggunakan frekuensi (n) dan persentase (%), dan variabel numerik dengan data terdistribusi normal disajikan dengan rata-rata dan standar deviasi (SD). Dalam data yang tidak berdistribusi normal, variabel numerik disajikan menggunakan rentang median dan interkuartil.

Hasil: Terdapat 157 anak yang dilibatkan dalam penelitian ini. Sebagian besar subjek adalah perempuan (n = 94,59,9%) dalam rentang usia 12 hingga 16 tahun. Sebagian besar subjek (n = 152,96,8%) memiliki katup mitral normal, tiga subjek memiliki prolaps katup mitral anterior (1,9%), satu subjek (0,6%) memiliki penebalan katup mitral anterior dan satu subjek (0,6%) memiliki regurgitasi mitral ringan. 10 subjek (5,7%) memiliki regurgitasi paru. Dua subjek memiliki regurgitasi trikuspid (1,2%). Tidak ada subjek yang memiliki kelainan aorta. Tidak ada subjek yang memiliki HP.

Kesimpulan: Pada populasi anak-anak di Kota Rantau-Prapat, sebagian besar subjek dengan kelainan katup memiliki kelainan katup mitral dan paru. Tidak ada subjek yang memiliki kelainan katup aorta atau HP.

Kata kunci: Penyakit katup jantung, hipertensi pulmonal, katup mitral, katup trikuspid, katup pulmonal, anak

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1 Introduction

Valvular heart disease (VHD) is a significant contributor to physical disability and a decline in quality of life. It stands as a leading cause of cardiovascular health problems and death worldwide. Understanding the geographical and temporal trends in VHD epidemiology is crucial for improving clinical practices and crafting effective health policies for both primary and secondary prevention. While population-based studies are a suitable method for assessing disease prevalence, they require comprehensive echocardiographic examinations in a large, representative sample of the population. Additionally, they heavily rely on routinely collected data, including diagnostic codes. This approach may be less reliable, as post-mortem analyses have shown that the actual prevalence of VHD is much higher than what is clinically recorded and reported. Population-based data is typically collected only when VHD is at least moderately severe or clinically relevant, often when patients are referred for diagnostic tests due to symptoms or clinical indications. Moreover, limited access to VHD diagnostic techniques likely leads to significant underreporting, particularly in low or middle-income/resource-poor countries. Lastly, the specific causes of VHD can be misclassified, especially in regions where rheumatic heart disease (RHD) is prevalent and VHD classification is susceptible to error. RHD remains the most common primary cause of VHD globally. The most disadvantaged and economically challenged populations at regional, national, and subnational levels continue to face high mortality rates due

to RHD. Despite substantial reductions in global poverty over the past few decades, the prevalence of RHD has been steadily increasing since 1990, affecting 40.5 million people in 2019.[1] While RHD is considered rare in Western countries, it's worth noting that in 2019, there were approximately 152.700 new cases and 2.3 million people living with RHD across the European Society of Cardiology (ESC) member countries. There is a clear correlation between income levels and RHD incidence, with middle-income countries experiencing twice the incidence compared to high-income ones.[2] Conversely, degenerative VHD (especially aortic and mitral) and infectious endocarditis are more predominant in high-income countries. The incidence of calcific aortic valve disease (CAVD) has increased sevenfold in the last 30 years, with rates four times higher in high-income countries compared to middle-income ones. Similarly, the absolute prevalence of primary mitral regurgitation (PMR) has significantly increased over the past two decades (by 70% between 1990 and 2017), as well as the global absolute prevalence of non-rheumatic endocarditis (by 44% since 1990).[3]

Severe valvular heart disease (VHD) causes a gradual rise in pressure within the left ventricle (LV) during filling, along with increased pressure in the left atrium (LA). This leads to a passive elevation in pressure in the pulmonary veins, resulting in isolated postcapillary pulmonary hypertension (Ipc-PH), which can still be reversed at this stage. However, if there is further constriction of the pulmonary blood vessels or structural changes with Ipc-PH, the condition may become irreversible.[4] This study aims to screen for valvular heart disease and pulmonary hypertension children in to ensure the best care through a multidisciplinary team

2 Method

This research was a descriptive study with a cross-sectional research design of people who participated in the examination at the Community Service Program of the Department of Cardiology and Vascular Disease, Universitas Sumatera Utara. The study was held on June 12, 2023, at one of the most populated Junior High Schools in Rantau-Prapat City, North Sumatera, Indonesia. The criteria of the samples are children between the ages of 10 to 15 years old. Informed consent will then be obtained from legal guardians or the parents of each child. Demographic variables such as age and sex were obtained by interviewing the participants, and the study was conducted after obtaining approval (ethical clearance).

A structured form was used to collect social demographic information (age, gender), parental information (parents' education level, parents' monthly income, family amenability), environmental surroundings and household information (available rooms, number of extended family members), anthropometric information (body weight, height, BMI), resting portable 12 lead ECG testing and echocardiographic information provided by handheld Echocardiography. The electrocardiograph (ECG) was obtained by using a KardiaMobile machine connected by Bluetooth to a mobile phone. The data obtained was ECG rhythm, if it was sinus or atrial

fibrillation. Echocardiography examinations using Lumify Handheld echocardiography will be performed on consented children at their schools. Body weight and height were measured by the GEA ZT-120 body weight scale that had been validated. Body mass index (BMI) was obtained by dividing the body weight by body height square. This study was conducted in line with the requirements of the Declaration of Helsinki. There will be no targeting survey study conducted before this study.

Statistical Analysis

All data were processed and analyzed statistically using SPSS ver.26. Categorical variables are presented with frequency (n) and percentage (%). Numeric variables are presented with mean and standard deviation (SD) values for normally distributed data. As for the normal non-distributed data numerical variables are presented with the middle value (median) and the interquartile range.

3 Results

Of the 157 children, 94 children (59.9%) were female and 63 children (59.9%) were male. The mean age in this study was 13.87 years with a mean weight of 48.1 kg and a mean height of 148.12 cm. Most children (66.2%) had normal body mass index. Based on family background, most of the children grew up in a family with last educational status in senior high school (58% vs 54.8%), monthly income less than Rp3 million (52.9%), 2 rooms in the house (53.5%) and history of occasional flu in the family around one time per month (53.5%). (Table 1)

Table 1 Demographic characteristic

Variable	Frequency (n = 157)	Percentage (%)
Age (Mean±SD), years	13.8 ± 0.8	
Sex		
Male	63	40.1
Female	94	59.9
Body weight (Mean±SD), kg	48.1 ± 9.7	
Body height (Mean±SD), cm	148.1 ± 9.5	
BMI		
Underweight	27	17.2
Normal weight	104	66.2
Obese	26	16.6
Paternal recent educational status		
Didn't go to school	1	0.6
Elementary	15	9.6
Junior High School	22	14.0
Senior High School	91	58.0
Bachelor	27	17.2
Master degree	1	0.6
Maternal recent educational status		
Didn't go to school	1	0.6
Elementary	23	14.6
Junior High School	24	15.3
Senior High School	86	54.8
Bachelor	23	14.6
Master degree	0	0
Monthly income		
< 3 million rupiah	83	52.9
3-10 million rupiah	73	46.5
>10 million rupiah	1	0.6
Number of bedrooms in the house		
No bedroom	24	15.3
2 bedrooms	84	53.5
3 bedrooms	5	3.2
>3 bedrooms	44	28.0
History of flu in the family		
No history	47	29.9
Seldom (one time / 3 months)	13	8.3
Occasional (one time/month)	84	53.5
Frequently (one time/week)	13	8.3

Based on echocardiography examination, 142 children (90.4%) had no valve disorders, 5 children (3%) had mild regurgitation on the pulmonary valve, and 2 children (1.3%) had trivial regurgitation on the pulmonary. The other valvular heart disease that discovered were: 1 child (0.6%) had mild Tricuspid Regurgitation, 1 child (0.6%) had mild Mitral Regurgitation, 1 child (0.6%) had AML Thickness (>3mm), 1 child (0.6%) had AML prolapse without regurgitation, 1 child (0. 6%) had AML Prolapse + Thickening > 3mm, 1 child (0.6%) had PR mild + TR Mild, 1 child (0.6%) had AML Thickening + MR mild, and 1 child (0.6%) had MR Mild + PR Mild + TR Mild. Of the participants, 100% of children had normal aortic valves, intact intraventricular septum, normal heart chamber dimensions, normal IVC, and normal MPA. There was only one child (0.6%) had a secundum ASD defect with RA-RV dilatation. No child with PDA and pulmonary hypertension was found. Based on our examination of the valve abnormalities, 3 children (1.8%) were suspected of Rheumatic Heart Disease and 1 child (0.6%) was suspected as Degenerative Myxomatous. We notified each parent about the suspected underlying disease and

valve abnormalities and facilitated them to a cardiologist in each district general hospital for further treatments and follow-up. (Table 2)

Table 2 Sample clinical characteristic

Variable	Frequency (n = 157)	Percentage (%)
Valve abnormalities		
Normal	142	90.4
PR mild	5	3.0
PR trivial	2	1.3
TR mild	1	0.6
MR mild	1	0.6
AML Thickness (>3mm)	1	0.6
AML prolapse without regurgitation	1	0.6
AML Prolapse + Thickening > 3mm	1	0.6
PR mild + TR Mild	1	0.6
AML Thickening + MR mild	1	0.6
MR Mild + PR Mild + TR Mild	1	0.6
Aortic valve		
Normal	157	100
Abnormal	0	0
IAS		
Intact	156	99.4
Defect	1	0.6
IVS		
Intact	157	100
Defect	0	0
PDA		
Not Found	157	100
Heart camber		
Normal	157	100
Abnormal	0	0
IVC		
Normal	157	100
Abnormal	0	0
MPA		
Normal	157	100
Dilatation	0	0
Suspected etiology		
Suspected Rheumatic Heart Disease	3	1.8
Degenerative Myxomatous	1	0.6

IAS, Interatrial Septum; IVS, Interventricular Septum; PDA, Patent Ductus Arteriosus; AML, Anterior Mitral Leaflet; AR, Aortic Regurgitation; MR, Mitral Regurgitation; PR, Pulmonary Regurgitation; TR, Tricuspid Regurgitation; IVC, Inferior Vena Cava; MPA, Main Pulmonary Artery; EKG, Elektrokardiogram; PVC, Premature Ventricular Contraction

4 Discussion

According to the European Society of Cardiology (ESC) and European Respiratory Society (ERS) guidelines, pulmonary hypertension (PH) is characterized by a resting mean pulmonary arterial pressure (mPAP) equal to or exceeding 25 mmHg, as determined through right heart catheterization (RHC). However, a suggestion emerged during the 6th World Symposium on Pulmonary Hypertension (WSPH) in Nice, 2018, proposing a lower threshold of 20 mmHg for mPAP. This recommendation is based on data from healthy individuals, indicating that the typical

resting mPAP ranges from 14 ± 3 mmHg, with an upper limit of around 20 mmHg. Deviating from this mean value by two standard deviations would imply that an mPAP above 20 mmHg falls into the category of abnormal pulmonary arterial pressure (beyond the 97.5th percentile). However, a mPAP of 20 mmHg alone is not enough to lead to pulmonary vascular disease. Therefore, the task force has proposed incorporating a pulmonary vascular resistance (PVR) of 3 Wood units (WU) or higher into the definition. It's important to note that the definition of PH may evolve in the future, and we will adhere to current guidelines and the recommendations from the 6th WSPH.[4]

It is anticipated that the burden of VHD will continue to rise in the coming decades, leading to a further deterioration in associated health problems and mortality rates. Several factors contribute to the shifts in geographical and temporal trends in VHD epidemiology, including the aging Population. As global life expectancy improves, certain VHD conditions traditionally associated with aging, like calcific aortic valve disease (CAVD) and degenerative mitral regurgitation (MR), have more time to develop symptoms and be identified. Additionally, advancements in VHD treatment have led to better long-term survival rates, contributing to an overall increase in prevalence.[5] The availability of imaging techniques and the accessibility of diagnosis and treatment play a crucial role.

Conditions like rheumatic heart disease (RHD), linked to poverty, inequality, and limited healthcare resources, continue to rise despite reductions in extreme poverty rates. This increase is likely due to greater global awareness, improved access to echocardiography for diagnosis, enhanced availability of treatment, and subsequent improvements in survival rates in many low-income countries. Similarly, in middle- and high-income nations, the widespread use of advanced echocardiography equipment, improved operator proficiency, and a shift towards prevention-focused healthcare systems have made it easier to diagnose degenerative VHDs, even in mild and asymptomatic cases.[3] In the screening, we found 3 children (1.8%) suspected of RHD. As the population in rural areas of South Asia is largely of lower economic status and a lower literacy rate, this could be a reason for the higher prevalence of RHD in rural areas than in urban areas.[5] Warm and humid climatic conditions might be responsible for the higher prevalence of rheumatic fever and RHD. In this screen, we found a history of occasional flu in the family that might raise the risk in children but needs further investigation.[7] Mitral valve lesion was the majority of valve abnormalities in our study which was similar to studies from many countries (India, Australia, and Europe). Mitral valve lesions were linked to rheumatic heart disease, by circulating autoantibody that binds to the surface endothelium of the mitral valve and enhances the vascular cell adhesion protein 1 expression. The activated endothelium will facilitate T-lymphocytes to infiltrate the sub-endothelium of the valve and lead to inflammation. The inflammation will expose the extracellular matrix which makes the damage to the valves worse.[8] Mitral

regurgitation will occur two decades earlier than mithan stenosis and become the most common valve lesion in children under 18 years old.[9]

The global shift towards urbanization and changing economic activities has exposed more individuals to various cardiovascular risk factors, both traditional and non-traditional. Factors such as smoking, hypertension, obesity, diabetes, air pollution, and stress are strongly associated with VHD, particularly calcific aortic stenosis (AS). In high-income countries with declining fertility rates and an aging population, there is a growing need for young immigrant populations to support the workforce and provide care for the elderly. However, immigrants often face socioeconomic challenges compounded by health disparities stemming from discrimination and racism. They are more likely to have RHD, a condition typically rare in high-income countries, and are at higher risk of developing early cardiovascular disease, including VHD.[10]

The tricuspid valve (TV), which was once overlooked, has recently gained increased attention. Tricuspid regurgitation (TR) has become a growing public health concern, affecting over 4% of individuals over the age of 75 in a clinically significant way.[11] Despite the rising interest, there is a lack of comprehensive global epidemiological data. National screening studies have shown varying prevalence rates: nearly 4% of individuals over 75 have clinically relevant TR. In the UK, around 2.7% of older individuals were found to have moderate to severe TR, while in China, the prevalence was only 1.1% among patients of a similar age.[11] TR independently predicts higher mortality and morbidity rates, with a 3-year survival rate of approximately 58%. Mortality rates increase with the severity of TR. Unfortunately, over 90% of TR patients do not undergo specific operative treatment for the regurgitation and are considered only for general optimal medical treatment (OMT), with outcomes varying. On the other hand, traditional surgery poses a significant mortality risk, with over 10% in-hospital mortality. Therefore, given the bleak prognosis associated with TR, it is crucial to promptly refer patients for the most effective treatment available.[11]

Multivalvular heart disease (MHD) is characterized by the presence of faulty valves in two or more areas of the heart, either due to leakage or narrowing. Despite being quite common, there is a notable scarcity of evidence-based recommendations for its clinical management in the current literature. Improvements in living conditions, nutrition, and access to medical care, particularly the widespread use of penicillin, have led to a significant shift in the predominant causes of MHD. While rheumatic heart disease (RHD) was the primary cause at the start of the 21st century, the EuroObservational VHD II survey indicates a substantial decrease in RHD cases in developed countries over the years. With an aging population, degenerative causes have become more prevalent, accounting for approximately 60% compared to RHD's 20.5%.[12]

Echocardiography is valuable in patients with confirmed or suspected pulmonary hypertension (PH) as it allows for the identification of increased pressure in the right chambers, assessment of

right ventricular changes due to heightened afterload, evaluation of left ventricular size and function, and measurement of systolic pulmonary artery pressure (PAP).[13]

If certain parameters such as left and right ventricular size and function (including wall motion), presence of intracardiac shunts, pericardial effusion, tricuspid regurgitation (TR) jet velocity (i.e., <2.8 m/s), inferior vena cava diameter (i.e., <2.1 cm), and pulmonary acceleration time (i.e., >100 ms) fall within normal ranges or are absent, it is reasonable to exclude PH. However, if any of these parameters are abnormal or if several are close to normal values, current expert consensus suggests conducting a more detailed echocardiographic assessment, including a more quantitative analysis of cardiac hemodynamics and chamber sizes and function.[13]

Pediatric treatment algorithms for PH are almost all derived by extrapolating safety and efficacy from the adult PH literature. Extrapolation is necessary because very few targeted PAH therapies have been rigorously studied in children, therefore most of these therapies do not have either a U.S. Food and Drug Administration (FDA) or European Medicines Agency (EMA) approved indication for pediatric use and instead must be used “off-label”. This is suboptimal as pediatric patients with PH may differ from adults in their response to therapies. (14,15) Nonetheless, off-label treatment is not unusual in children with complex diseases,[16] and given the poor prognosis, represents a preferred alternative to no treatment at all.

5 Conclusion

In the children population in Rantau-Prapat City, most subjects with valve abnormalities had mitral and pulmonary valve abnormalities. No subjects had aortic valve abnormalities or PH.

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