The COngenital HeARt Disease in adult and Pulmonary Hypertension (COHARD-PH) registry: a descriptive study from single-center hospital registry of adult congenital heart disease and pulmonary hypertension in Indonesia

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Abstract

Backgrounds The COngenital HeARt Disease in adult and Pulmonary Hypertension (COHARD-PH) registry is the first congenital heart disease (CHD) and PH registry in Indonesia. The study aims to describe prevalence, demographics, and hemodynamics data of adult CHD and PH in Indonesia.Methods The COHARD-PH registry is a hospital-based, single-center, and prospective cohort registry which includes adult patients with CHD and CHD-related PH. The patients were enrolled consecutively. We evaluate the registry patients from July 2012 until July 2018. The enrolled patients underwent clinical examination, electrocardiography, chest x-ray, 6 minute walking test, laboratory measurement, and transthoracic and transoesofageal echocardiography. Right Heart Catheterization (RHC) was performed to measure hemodynamics and confirmed the diagnosis of pulmonary artery hypertension (PAH).Results We registered 803 patients during the study. The majority were young-adult females. The majority of CHD was secundum ASD (79.0%). The main symptom was dyspneu on effort. The majority (78.1%) already develops signs of PH assessed by echocardiography. The Eisenmenger syndrome was encountered in 17.3% subjects. Based on the RHC, 67.8% subjects had developed PAH. Patients with PAH were significantly older, lower peripheral oxygen saturation, lower 6 minute walking distance, and higher NTproBNP. There was an increased of PAH prevalence according to age range, with the highest prevalence between 51 and 60 years old.Conclusions The COHARD-PH registry is the first Indonesian adult-CHD and PH registry. The incidence, demographics data, and hemodynamics data of this registry reflects situation in developing countries which need to be compared with similar registries from developed countries.

Background

The prevalence of adult congenital heart disease (CHD) in developed countries raises due to improved survival attributed to successful surgical and medical management in childhood.[1] Currently, the estimated number of adults with CHD exceeds the number of children and adolescents with CHD.[1] This number continues to increase, as does the complexity of CHD patients surviving to adult life.[2] As medical management and surgical procedures continue to advance, children previously deemed unsuitable for cardiac surgery are undergoing corrective and/or palliative procedures. As a result, an increasing population of children with CHD is surviving into adulthood, many of whom will require further medical or surgical management for residual or progressive complications.[2] The abovementioned condition happen in develop countries, whereas in less develop countries a significant number of adults with CHD exposed because they feel symptom due to complication that urge them seek medical help.

One of the devastating complications of CHD is pulmonary hypertension (PH) which occurs in about 10% of the CHD populations.[3] Pulmonary hypertension is defined as an increase in mean pulmonary artery pressures (mPAP) ≥25 mmHg at rest.[4] {Galiè, 2015 #2}{Galiè, 2015 #2}Based on the current clinical classification of PH, CHD may cause pulmonary artery hypertension (PAH) which is defined as a group 1 in this classification.[4] The PAH or PH group 1 is a clinical group which is

characterised by hemodynamic parameter as pre-capillary PH (mPAP ≥25 mmHg with pulmonary artery wedge pressure (mPAWP) ≤15 mmHg) and pulmonary vascular resistance (PVR) >3 Wood units (WU).[4] The hemodynamic measurement by right heart catheterization (RHC) is mandatory to diagnose PAH and to assess the recommendation of defect closure. The implications of CHD-related PH are limited functional capacity, increased risk of arrhythmias, right heart failure, and increased mortality.[5]

The populational based registries in developed countries indicate that the prevalence of CHD-related PH is approximately 5%–10%.[6,7,8] The systemic-to-pulmonary shunt CHD bears the increased risk to develop CHD-related PH.[5,8] The CHD-related PH is a result of the systemic-to-pulmonary shunt at both the pre-tricuspid level (atrial septal defect (ASD)) and the post-tricuspid level (such as ventricle septal defect (VSD), patent ductus arteriosus (PDA), and aortopulmonary (AP) window) which cause the chronic increased flow to the pulmonary vessels. The consequences of increased blood flow to the pulmonary vessels are endothelial dysfunction, pulmonary vascular remodeling, increased pulmonary artery pressure and increased pulmonary vascular resistance.[9]

Indonesia, a developing country and one of the most populous countries in the world, until currently does not have national registry in regards of the CHD-related PH in adult. The prevalence and incidence of CHD-related PH are still unknown; despite in clinical practice adult patients with undetected and delayed diagnosis of CHD are frequent.[10] Compared with registry from developed countries, the situation regarding the adult CHD-related PH in developing countries are quite different.[11,12,13] The COngenital HeARt Diseases in adult and Pulmonary Hypertension (COHARD-PH) registry was initiated since 2012 to be the first registry done in Indonesia to describe adult CHD and CHD-related PH populations. This registry is a hospital-based registry performed in Dr. Sardjito Hospital, Jogjakarta, Indonesia, which is a national referral hospital for cardiovascular disease in the region. The current study aims to describe the prevalence, demographics, clinical presentation, and hemodynamics characteristics of adults patients with CHD and CHD-related PH registered in the COHARD-PH registry.

Methods

Subjects

This registry, COngenital HeARt Diseases in adult and Pulmonary Hypertension (COHARD-PH) registry, is a single-center, observational, and prospective registry which enrolls adult patients with CHD and CHD-related PH. The adult patients presented in Dr. Sardjito Hospital, Jogjakarta, Indonesia with suspected CHD and CHD-related PH were undergone a series of examinations to confirm the CHD and CHD-related PH diagnosis. The subjects are enrolled consecutively from outpatients clinics, inpatients wards, and echo-lab. The enrollment and follow-up have been performed from July 2012 until currently. This study was evaluated the patients of COHARD-PH registry from July 2012 until July 2018. This registry enrolls adult patients with age ≥ 18 years old.

Procedures

Patients were interviewed, underwent physical examination, electrocardiography (ECG) examination, and chest x-ray examination. The suspected CHD patients were confirmed by transthoracic echocardiography (TTE) as the initial examination. By TTE, the probability of PH was also assessed based on current guideline.[4] The bubble test was performed in selected cases if the TTE examination was dubious regarding septal defects/shunts. Transoesofageal echocardiography (TOE) was performed in patients with confirmed ASD and VSD by TTE examination. The TTE and TOE examination were conducted with G.E Vivid 7 (G.E Healthcare, U.S.A), G.E Vivid S6 (G.E Healthcare, U.S.A) or Phillips HD 15 (Philips N.V, The Netherland). The image acquisitions were conducted by three experience sonographers. The validation and confirmation of TTE and TOE examinations were performed by cardiologist consultants in our center dedicated to the registry. The image acquisition, validation and confirmation are in accordance with E.A.E and A.S.E guidelines. The 6 minute walking test to measure the distant of walking was performed for baseline of the registry.

Right heart catheterisation (RHC) was subsequently performed in patients after being confirmed as CHD by TTE and TOE and enrolled for the registry. The RHC was performed by cardiologist consultants using standard procedures in non-sedated patients. The purpose of RHC was to measure hemodynamics, diagnose pulmonary artery hypertension (PAH) and decide the closure procedure for septal defects/shunts. The cardiac output was determined by indirect Fick method, as per hospital protocol. The flow ratio was calculated with the formula: pulmonary blood flow (Qp)/systemic blood flow (Qs)= (aorta saturation - mixed vein (MV) saturation)/(pulmonary vein (PV) saturation-pulmonary artery (PA) saturation). A MV saturation was calculated from: ((3 x superior vena cava saturation) + inferior vena cava saturation)/4. The pulmonary vascular resistance index (PVRi) was derived from the formula: (mPAP – mean left atrial pressure (mLAP) (or mPAWP)/Qp. A Qp was calculated from the formula: O_2 consumption (ml/min)/(1.36x10xhemoglobin level x ((PV saturation-PA saturation)/100). The PAH diagnosis was established when mPAP $\geq$25 mmHg, PVR >3 WU and PAWP $\leq$15 mmHg.[4] The diagnosis of Eisenmenger syndrome was established hemodynamically when Qp/Qs <1 and PVRi >8 WU.m^2 .[4]

Patients with simple defects such as ASD, VSD, PDA, AVSD, patent foramen ovale (PFO), and AP window were included in this study. The combined defects and other defect types were categorized as multiple defects. Patients with high probability of PH by TTE without confirmed CHD were excluded from the COHARD-PH registry (they included in other PH registry). Complex congenital heart diseases were excluded from the registry. The signs of Eisenmenger syndrome (desaturasion and bidirectional shunt from TTE) was noted and later confirmed by RHC.

The blood sample was collected from each patient by venipuncture in peripheral veins and during RHC. The blood sample was centrifuged and stored in -80º for further analysis. The hemoglobin and haematocrit levels were measured from routine hemocytometer. The NTproBNP measurement was performed using a electrochemiluminescence immunoassay (ElecsysProBNP II) and performed in Cobas e immunoassay analyzer (Roche Diagnostics, Germany).

Data Collection

The research assistants dedicated to the registry collect and compile the data and subsequently input the data to the electronic case report form of the COHARD-PH registry database. The baseline characteristics of patients were collected, comprising demographic data and clinical data. The ECG and chest X-ray results were documented. The TTE and TOE data were collected, comprising the type of CHD, dimension of right atrium (RA) and right ventricle (RV), left ventricle ejection fraction, tricuspid valvular regurgitation gradient (TVRG), and estimated mPAP. The 6 minute walking distance was collected. The laboratory data were also compiled. The RHC data were collected, comprising mPAP, mPAWP, mRAP, PVRi, and flow ratio.

The signed informed consents were acquired for each patient to be included in the registry. The ethics committee of Faculty of Medicine, Public Health and Nursing Universitas Gadjah Mada and Dr. Sardjito Hospital had approved the registry protocol.

Statistics Analysis

We performed the descriptive analysis of the data. The continuous data was presented in mean and standard deviation (SD) or median and interquartile range (IQR) depended on normality data distribution after tested with the Shapiro Wilk or Kolmogorov Smirnov test. The categorical data was presented in percentage. The group comparison was conducted with Student T test and Chi-square test according to the type of data. A $p < 0.05$ was deemed statistics significance.

Results

From July 2012 until July 2018, we have registered data from 803 patients who had the confirmed diagnosis as septal defects/shunts CHD. The clinical characteristics of the patients were shown in table 1. The mean age of the subjects at first diagnosis was 35 years. The majority of patients were females, which comprised of 78.5% of all patients. Normal and underweight body mass categories were predominant. Mean peripheral O_2 saturation was 95.4%. The WHO functional class was predominantly class II (46.0% of subjects), only the minority of patients had worse WHO functional class (15.1%). The mean 6 minute walking distance was 354.4 meters. Only 2.9% of subjects had defect closure (by surgery or device) in time of enrollment. The high probability of PH by TTE examination was predominant (78.1 %). The signs of Eisenmenger syndrome were encountered in 17.3 % of subjects. The laboratory result showed mean haemoglobin level was 13.8 g/dL, hematocrit 41.9% and median NTproBNP level 504.5 pg/mL. The main symptoms were dyspneu on effort (38.1%), easily fatique (17.7%), palpitation (10.1 %) and chest pain (9.1 %). As many as 13.1% subjects did not report any symptoms during first enrollment.

The majority of CHD type was secundum ASD (79.0%). Other CHD types were perimembranous VSD (6.7%), PDA (4.6%), doubly-committed subarterial (DCSA) VSD (3.4%), sinus venosus ASD (1.6%), primum ASD (1.5%), PFO (1.2%), AVSD (0.4%) and AP window (< 0.1%). The subjects with multiple defects were comprised of 1.2% of subjects. The majority of subjects had undergone RA and RV dilatation, with mean RA diameter of 46.1 mm and RV diameter of 43.0 mm. The mean mPAP based on

TTE examination was 36.1 mmHg. The mean of peak tricuspid velocity is 3.9±2.5 m/s. The mean left ventricle ejection fraction was 68.1%. Table 2 showed the result of TTE and TOE procedures.

The RHC had been performed in 503 subjects (62.6%) and confirmed that 341 subjects (67.8 %) had developed PAH. The haemodynamics data from RHC showed mean mPAP was 40.8 mmHg, mean PVRi was 9.2 WU.m^2, and mean flow ratio (Qp/Qs) was 2.7. Table 3 showed the result of RHC procedure.

Table 4 shows the comparison of clinical and laboratory parameter between CHD-related PAH and those without PAH. Patients with PAH had significantly older age at first diagnosis (36.5±12.9 vs. 32.6±12.0 years old, p=0.001), lower peripheral oxygen saturation (94.8±5.6 vs. 97.5±3.2 %, p <0.001), lower 6 minute walking distance (337.8±99.7 vs. 394.2±83.8 meter, p <0.001), higher hemoglobin level (14.0±2.2 vs. 13.4±1.9 g/dL, p=0.002) and higher NTproBNP level (median: 793.8 vs. 120.5 pg/mL, p <0.001). There was an incremental increased of PAH prevalence according to age range, with the highest prevalence in age between 51 and 60 years old (table 5).

Discussion

We reported the first hospital-based registry of adults with CHD and CHD-related PH in Indonesia in which comprise the complete diagnostic work-up. The COHARD-PH registry is a single center registry in Dr. Sardjito Hospital, a national referral center for cardiovascular disease in Indonesia. The COHARD-PH registry has been started in July 2012 and still on going until recently. Within the duration of five years, July 2012 – July 2018, the number of patients enrolled were 803 adults with CHD. The majority of CHD in this registry was ASD, followed by VSD and PDA. Young adult females (ages between 21-40 years old) were predominant in our registry. Most patients were symptomatic, with majority in WHO functional class II. By echocardiography, the prevalence of probability of PH was 78.1 %. Further confirmation with RHC measurement, the COHARD-PH registry showed that 67.8% subjects had developed PAH.

In our registry, the majority of CHD was ASD. This is similar with other study that in adult registry, ASD was the most common.[1] Most patients come to our medical facility when they already had a complaint, with shortness of breath and easily fatique among the most common complaint. This characteristic is similar to previous study where the patient was already in advanced condition and had limited activity.[13,14] Since in our registry the most prevalent CHD was ASD, the patients remain asymptomatic for decades. Therefore, the symptoms that appear later will urge the patients to consult doctor and visit hospital. The main symptom of patients was associated with the development of PAH, which later confirmed with RHC procedure. The early finding of CHD-related PAH are often not easy to recognize due to the unknown precise period of PAH.[11] The chronic systemic-to-pulmonary shunt is a congenital malformation causing blood overflow in the pulmonary vasculature from infancy, and if left untreated properly may give rise to PAH in adult life. The majority of our patients was untreated cases, and probably undetected cases in their childhood period. They come to our hospital in their delayed and progressed diseases.

Our registry showed that patients were predominantly young adult females. This observation was consistent with other registries.[3,6,7,13,15,16,17] The mean age of patients in our registry during first enrollment was 35 years old. The facts that most cases were ASDs, in which at younger age there had been no complaints. In ASD clinical presentation, the pulmonary hypercirculation and right heart volume overload induces PAH after a longer period of time, which is different with VSD or PDA.[6] The patients with VSD and PDA were symptomatic in earlier years of age and have more evident signs, probably before reaching adulthood, therefore mostly detected in childhood and adolescent period.[12] Our hospital register in pediatric patients indicated that VSD was the most prevalence in childhood.[18] Moreover, 72.7% patients were asymptomatic for a long period of time (> 2 decades). Mostly in the third decades of life, the PAH complication starts to clinically manifest and urge the patients to visit the hospital.

The echocardiographic data showed that majority of the patients was categorized in high probability of PH and confirmed PAH by RHC, which is a gold standard for diagnosis of PH and PAH. Almost 70% of our patients already developed PAH based on RHC. This data is much higher than data from other registries, especially registries from developed countries. The striking difference is likely due to late presentation and selection bias, because the patients were enrolled at our hospital mostly due to signs and symptoms they suffer. Currently, in Indonesia there was no early screening and detection of asymptomatic CHD, therefore many patients were undetected until they come to visit medical facilities due to complication.

The patients with PAH had worse clinical characteristics as compared to those without PAH. They were in young adult age and older than patients without PAH. Their functional capacities, measured by WHO class, 6 minute walking distance and peripheral oxygen saturation, were worse. The NTproBNP level, the sole biomarker for prognostication of PH, was higher in patients with PAH as compared with those without. Among CHD-associated PAH, it should be noted that four difference clinical subgroup have been proposed which reflects different pathophysiology and prognosis.[4,12,16] Patients with small defect-associated PAH had similar outcome with Eisenmenger syndrome which was better than the outcome of patients in which PAH develops or persists after closure of the defect.[16,17] The large defects with prevalent systemic-to-pulmonary shunts have better survival as compared with other clinical types.[12,16]

The definite management of CHD is closing the defect with either percutaneous defect closure or open heart surgery for those who still meet the closing criteria. While for those who have experienced CHD-PAH, medical therapy is mandatory by administration of pulmonary vasodilator medication as target drugs therapy.[4] Recently, more than ten specific PAH drugs are available across the world.[4] However, in Indonesia, only three drugs are available in the market, which are prostacyclin analogue (beraprost and illoprost) and PDE5 inhibitor (sildenafil). Unfortunalety, only beraprost is so far covered by the national insurance. This current study do not report the medications and procedures performed to the patients. The descriptive analysis of baseline data of this registry is reported here, whereas the intervention and outcome will be reported in the future. The registry data that showed predominant CHD-associated PAH in young adult female patients, give valuable evidence for further action by medical practitioner and government in developing countries such as the regulation in the prevention and early

detection/screening for CHDs during infancy and childhood. Furthermore, the availability of more drugs for treating PAH complication also a consideration to be implemented.

Limitations

The registry is a hospital based registry therefore patients who enrolled in the registry were those who development symptoms. Although cannot represent the population in the community, the registry reflects real world condition of undetected congenital disease earlier in Indonesia. The procedure for hemodynamic evaluation, i.e. RHC, was limited by hospital standard procedures and timeframe, therefore not all patients in the registry were completely performed RHC. However, the majority of patients had been performed RHC is an accomplishment of this registry.

Conclusions

The COHARD-PH registry is the first Indonesian adult CHD and CHD-related PH registry reported. The incidence, demographics data, clinical presentation, and hemodynamics of this hospital-based registry are indicative of real world situation in developing countries which needed to be compared with other CHD-related PH and PH registries, both from developed and developing countries.

Abbreviations

AP: aortopulmonary

ASD: atrial septal defect

CHD: congenital heart disease

COHARD-PH: The COngenital HeARt Disease in adult and Pulmonary Hypertension

DCSA: doubly-committed subarterial

ECG: electrocardiography

IQR: interquartile range

mLAP: mean left atrial pressure

mPAP: mean pulmonary artery pressures

PDA: patent ductus arteriosus

PFO: patent foramen ovale

PH: pulmonary hypertension

PVR: pulmonary vascular resistance

PVRi: pulmonary vascular resistance index

RA: right atrial

RHC: right heart catheterization

RV: right ventricle

Qp: pulmonary blood flow

Qs: systemic blood flow

SD: standard deviation

TEE: Transoesofageal echocardiography

TTE: Transthoracal echocardiography

TVRG: tricuspid valvular regurgitation gradient

VSD: ventricle septal defect

WU: Wood units

Declarations

Ethics approval and consent to participate

The Medical and Health Research Ethic Committee Faculty of Medicine, Public Health and Nursing Universitas Gadjah Mada approved this study. All patients provided written informed consent prior to enrollment in accordance with the 1975 Declaration of Helsinki.

Consent for publication

Not applicable

Availability of data and material

The registry and research data produced and analysed during the study are not publicly available due to patient confidentiality but are available from the corresponding author on request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

LKD, ABH and DWA initiated the registry, conceptualized the study outline, drafted and revised the manuscript. ADK drafted manuscript and performed statistics analysis. VCD, MS, MRH, and ADP collected data, maintained eCRF and drafted the manuscript. All authors have read and approved the final manuscript.

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Tables

Table 1. Demography, Clinical and Laboratory Characteristics of COHARD-PH Registry Patients

Characteristics	Total (n=803)
Age at First Enrollment (years) [mean±SD]	35.3±13.3
Gender [n (%)]	
Males	173 (21.5)
Females	630 (78.5)
Body Mass Index [n (%)]	
Underweight (<18.5 kg/m^2)	326 (44.5)
Normal (18.5-24.9 kg/m^2)	331 (45.2)
Overweight (≥25.0 kg/m^2)	76 (10.4)
Blood Pressure (mmHg) [mean±SD]	
Systolic	111.6±16.7
Diastolic	73.1±11.3
Oxygen saturation (%) [mean±SD]	95.4±5.6[a]
6 Minute Walk Distance (meter) [mean±SD]	354.4±104.5[b]
WHO Functional Class [n(%)]	
I	278 (38.9)
II	329 (46.0)
III-IV	108 (15.1)
Hemoglobin (g/dL) [mean±SD]	13.8±2.2[c]
Hematocrit (%) [mean±SD]	41.9±17.2[c]
NTproBNP (pg/mL) [median(IQR)]	504.5(144.8-1732.8)[d]
Pulmonary hypertension (by TTE) [n(%)]	627 (78.1)
Eisenmenger Syndrome [n (%)]	139 (17.3)
Post Defect Closure [n (%)]	24 (2.9)
Main symptoms [n (%)]	
Dyspneu on effort	306 (38.1)
Easily fatigue	142 (17.7)
Palpitation	81 (10.1)
Chest pain	73 (9.1)
Cough	44 (5.5)
Chest discomfort	12 (1.5)
Syncope	8 (1.0)
Leg swelling	6 (0.7)
Headache	6 (0.7)
Fever	5 (0.6)
Others	15 (1.9)
None	105 (13.1)

[a] data of 658 patients; [b] data of 567 patients; c data of 513 patients; [d] data of 336 patients

Table 2. Echocardiography Characteristics of COHARD-PH Registry Patients

Echocardiographic Findings	Total (n=803)
Congenital anomaly [n (%)]	
Primum ASD	11 (1.5)
Secundum ASD	577 (79.0)
Sinus venosus ASD	12 (1.6)
Patent foramen ovale	9 (1.2)
Perimembranous VSD	49 (6.7)
Doubly-committed subarterial VSD	25 (3.4)
Atrioventricular septal defect	3 (0.4)
Patent ductus arteriosus	34 (4.6)
Aortopulmonary window	1 (<0.1)
Multiple defects	9 (1.2)
mPAP(mmHg) [mean±SD]	36.1±15.7
TVR velocity (m/s) [mean±SD]	3.9±2.5
RA diameter (mm) [mean±SD]	46.1±8.4
RV diameter (mm) [mean±SD]	43.0±8.7
Left ventricle EF (%)	68.1±8.8

ASD: atrial septal defect; VSD : ventricular septal defect; mPAP : mean pulmonary artery pressure; TVR : tricuspid valve regurgitation; RA : right atrium; RV : right ventricle; EF : ejection fraction

Table 3. Hemodynamic Data from Right Heart Catheterization of COHARD-PH Registry Patients

Right Heart Catheterization Result	Total (n=503)
mPAP (mmHg) [mean±SD]	40.5 ± 22.2
PVRi (Wood Unit.m^2) [mean±SD]	9.2 ± 12.8
Flow Ratio [mean±SD]	2.7 ± 2.1
PAH [n (%)]	341 (67.8)
PAH Severity [n (%)]	
None	162 (32.2)
Mild	126 (25.0)
Moderate	115 (22.9)
Severe	100 (19.9)

mPAP : mean pulmonary artery pressure; PVRi : pulmonary vascular resistance index; PAH : pulmonary artery hypertension

Table 4. Characteristics of COHARD-PH Registry Patients based on the PAH Diagnosis

Characteristics	No PAH (n=162)	PAH (n=341)	P value
Age at First Enrollment (years) [mean±SD]	32.6±12.0	36.5±12.9	0.001
Gender [n (%)]			
Males	32 (19.8)	62 (18.2)	0.535
Females	130 (80.2)	279 (81.8)	
Body Mass Index [mean±SD]	20.2±3.2	19.4±7.4	0.212
Blood Pressure (mmHg) [mean±SD]			
Systolic	110.5±14.9	110.7±17.4	0.805
Diastolic	72.9±10.9	72.9±11.7	0.882
Oxygen Saturation (%)[mean±SD]	97.5±3.2	94.8±5.6	<0.001
6 Minute Walk Distance (meter)[mean±SD]	394.2±83.8	337.8±99.7	<0.001
WHO Functional Class [n(%)]			<0.001
I	94 (57.7)	107 (31.5)	
II	60 (36.8)	177 (52.1)	
III-IV	9 (5.5)	56 (16.4)	
Hemoglobin (g/dL) [mean±SD]	13.4±1.9	14.0±2.2	0.002
Hematocrit (%) [mean±SD]	42.9±3.3	42.0±6.5	0.652
NTproBNP (pg/mL) [median(IQR)]	120.5(56.8-209.5)	793.8(296.4-2070.3)	<0.001
Congenital Anomaly [n (%)]			0.166
Primum ASD	0 (0)	4 (1.2))	
Secundum ASD	129 (79.6)	294 (86.2)	
Sinus venosus ASD	5 (3.1)	8 (2.4)	
Patent foramen ovale	0 (0)	1 (0.3)	
Perimembranous VSD	12 (7.4)	7 (2.1)	
Doubly-committed subarterial VSD	5 (3.1)	6 (1.8)	
Atrioventricular defect	0 (0)	1 (0.3)	
Patent ductus arteriosus	0 (0)	1 (0.3)	
Aortopulmonary window	0 (0)	1 (0.3)	
Multiple defects	1 (0.6)	4 (1.2)	

PAH: pulmonary artery hypertension, ASD: atrial septal defect; VSD : ventricular septal defect; WHO: world health organisation

Table 5. Age Distribution Based of CHD-associated PAH

Age (years)	Congenital heart diseases (n)	PAH (n)	PAH Percentage (%)
17-20	59	32	54.2
21-30	160	105	65.6
31-40	120	78	65.0
41-50	91	66	72.5
51-60	55	46	83.6
>61	18	14	77.8
Total	503	341	67.6

CHD: congenital heart disease; PAH : pulmonary artery hypertension

Supplementary Files

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- STROBEchecklistcrosssectional.docx