

Accuracy of Preliminary Techniques in Diagnosis of Patients with Pulmonary Hypertension

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ABSTRACT

Background: Right heart catheterization is the gold standard in PH diagnosis, however it is invasive, costly and needs the experts so not all hospitals can carry out it. Therefore, an alternative diagnostic methods is required. **Aim:** to assess accuracy of Preliminary Methods in Diagnosis of pulmonary hypertension patients. **Patients and methods:** This cross-sectional study was carried out in Chest and cardiology departments at Zagazig University Hospitals on thirty moderate and severe PH patients during the period from July 2023 to February 2024. All patients were subjected to full history and clinical examination, laboratory investigations, ECG, Imaging techniques, trans thoracic Echocardiography, 6-minute walk distance test, Spirometric pulmonary function test and all patients also subjected RHC. **Results:** The mean age of studied patients was 41.5 ± 19.1 and range of age (18-65) years. 63.4% were females. Spirometric pulmonary function FEV1% and FVC% were significantly decreased in cases with severe PH compared to moderate PH patients. Right heart catheterization data analysis that Mean PAP was Severely elevated in (93.3%) of patients, PVR was high in 76.6%. Echocardiography showed sensitivity 82.1%, specificity 50% and accuracy 80% to discriminate severe PH . congenital heart diseases were the highest percent among the causes of PH in the studied patients 46.6% and only one case was Idiopathic PH 3.3%, PH patients with lung diseases were 4 (13.3%). **Conclusions:** Echocardiography shows high sensitivity (82.1%) and accuracy (80%) to discriminate severe PH . Significant decrease in spirometric pulmonary function test (FEV1, FVC) values in severe compared to moderate pulmonary hypertension patients.

Keywords: Preliminary Methods; Echocardiography; Pulmonary artery catheterization; Pulmonary hypertension

INTRODUCTION

The first meeting for pulmonary hypertension was arranged by the World Health Organization and took place in Geneva in October 1973. The unexpected rise in PH cases in Austria, Germany, and Switzerland over the previous era, which was linked to the use of the appetite suppressant aminorex, sparked interest in this subject. The meeting's outcomes were released in a 45-page paper. While the publication did not specifically provide a hemodynamic definition for pulmonary hypertension (PH), it included significant information about diagnosing PH. Thus, 1) pulmonary pressure measurement

requires right heart catheterization (RHC); 2) mPAP is not impacted by age and does not surpass 20 mmHg in healthy individuals; and 3) PH is clearly taken into consideration if mPAP exceeds 25 mmHg [1]. The European Society of Cardiology and the European Respiratory Society have released revised hemodynamic guidelines for the diagnosis and management of pulmonary hypertension (PH), which define PH as a resting mean pulmonary arterial pressure (mPAP) more than 20 mmHg [2]. All age groups may be affected by PH, and the present estimates shows a prevalence of approximately 1% of the world's population, with lung disorders, particularly chronic

obstructive pulmonary disease, coming in second. Left heart disease is the primary cause [3]. Definite diagnosis of catheterization of the right heart to assess the severity and hemodynamics, however it is invasive, costly and needs the experts so not all hospitals can carry out it [4]. so the aim of this study is to assess the accuracy of Preliminary Methods in Diagnosing pulmonary hypertension patients to improve the outcome.

METHODS

This cross-sectional study was carried out in Chest and cardiology departments at Zagazig University Hospitals during the period from July 2023 to February 2024 on 66 patients clinically suspected to have pulmonary hypertension, 12 were hemodynamically unstable, 23 refused RHC and one patient died before completing the steps of check up. 30 patients who met the inclusion criteria included in this study. After protocol approval by our Local Ethics Committee (IRB # 10961-19-7-2023). All patients provided written informed consent to participate in the study. Study protocol conformed to the ethical guidelines of the Declaration of Helsinki (1975) for studies involving humans.

Sample size: According to the rate of admission of suspected pulmonary hypertension patients to chest and cardiology departments per month, 11 patients in 6 months to be 66 cases as a comprehensive sample.

Inclusion criteria were age >18 years and moderate and severe pulmonary hypertension patients admitted to Zagazig University hospitals. Severity of pulmonary hypertension detected by Echocardiography moderate (mean PAP 50-70mmHg), Severe (mean PAP >70 mmHg) [5]. **Exclusion criteria were** Hemodynamically unstable patients [6]. Refuse Right heart. Catheterization. Death before complete all the steps of the study.

All patients were subjected to complete history taking including personal, complaint, present history including pulmonary hypertension symptoms (Dyspnea according to MMRC scale, fatigue, syncope, hemoptysis, chest pain) [7], drug, toxins, Past and family history. Full clinical examination (general and local chest examination) including signs of pulmonary hypertension (jugular vein

distension, prominent right ventricular impulse, loud pulmonary component of second heart sound, right sided third heart sound, tricuspid murmur, hepatomegaly and peripheral edema) [7].

Laboratory investigations at time of admission: Completed Blood Count (CBC), Renal function tests (RFTs), Liver function tests (LFTs), serum electrolyte, coagulation profile, troponin, In selected cases, serological studies include testing for parasitic infection, hepatitis viruses, HIV, thyroid function tests and collagen profile.

Electrocardiography (ECG). Chest radiographic techniques; Chest x-ray or HRCT Chest with or without contrast or CT pulmonary angiography. Pelvic and abdominal ultrasound. Transthoracic Doppler Echocardiography (picture of pulmonary hypertension including RA and RV dilatation, septal flattening, estimate systolic pulmonary artery pressure, PA dilatation, IVC diameter) [8]. 6-minute walk distance test. Spirometric pulmonary function test. Right heart catheterization.

6-minute walk distance test [9]: Base line vital signs and dyspnea was considered, timer was set, patient was at standing point and instructed how to proceed then allowed to walk unassisted for 6 minutes in the corridor of chest department and the total distance measured, The main predictor variables being gender, age and height. Normally ≥ 400 m.

Spirometric pulmonary function test[10]: Weight and height were measured, Test was explained for the patient, Nose clip attached and mouthpiece placed in mouth and the lips closed around the mouthpiece, normal breath few times then complete and rapid inhalation then maximal exhalation until no more air could be expelled while patient in upright posture. Duration of maneuver at least 6 second. Maneuver repeated 3 times, the best values of FEV1, FVC, FEV1/FVC were considered.

Right heart catheterization (Pulmonary artery catheterization) [11]: All patients were subjected to PAC (pigtail and multipurpose catheters) ranged in French sizes from 5F to 8F and are 110 cm long [12].

Lab consists of patient table, digital flat panel detector mounted on C-arm, viewing monitors,

real time ECG, blood pressure, oxygen saturation, injector pump catheters and defibrillator. The procedure was Performed by cardiologist and assistant physician, assistant nurses , Cath. lab technician [13].

Preparation: The patient was put on the table in the supine position after giving their informed consent. The access points were sanitized and covered in sterile materials. Chlorhexidine was employed to create a sterile access site. Sterile gowns, gloves, head caps, and facial protection would be necessary for the operating physician and the assistant. The access sheaths, catheters, and needles were flushed to prevent air from entering the systemic circulation. [14].

Technique : Subcutaneous injection of a local anesthetic was performed at the access point. A normal 18-gauge needle was used to create venous access at the femoral sites. A suitable-sized sheath was inserted into the vein and fastened. The pulmonary artery catheter was inserted 45 cm into the vein through the sheath. There would be a pulsatile right atrial waveform visible when the catheter entered the right atrium. Zeroing the system established a reference before pressure measurements were taken. In order for the air-fluid transducer to equalize with atmospheric pressure, it should be opened to air during the zeroing process. The air-fluid transducer had to be at the level of the heart when doing this. Right ventricular pressure was measured when the catheter was turned to face the right ventricle and the right atrial pressure waveform was acquired. To measure the pulmonary capillary wedge pressure, the catheter was then typically advanced to a wedge position. Pulmonary artery pressure could be measured by retracting the catheter a few millimeters into the pulmonary artery. It was optimal to measure all pressures at end-expiration. Using the distal port, a blood sample from the pulmonary artery was taken, and mixed venous oxygen saturation was measured. The procedure involved moving the pulmonary artery catheter into the superior or inferior vena cava in order to take blood samples and measure oxygen saturation levels. The right ventricle underwent the same measurement.

STATISTICAL ANALYSIS

Data management using SPSS IBM Corp. 2015 release. Version 23.0 of IBM SPSS Statistics for Windows. NY / Armonk: IBM Corp. The mean standard deviation (mean $\pm$ SD) and median (range) were used to represent quantitative data, while absolute frequencies (number) and relative frequencies (%) were used to convey qualitative data. To compare two groups of normally distributed variables, the t-test was employed. All tests were two-sided. P-value < 0.05 was considered statistically significant(S), and p-value ≥ 0.05 was considered statistically insignificant (NS).

RESULTS

The mean age of studied patients was 41.5 ± 19.1 and range of age (18-65) years. Gender was distributed as 63.4% females and 36.6% males (figure 1). All patients were complaining of Dyspnea. In this study regarding Echocardiography findings, 24 patients (80%) had severe pulmonary hypertension as regard Mean PAP. Severe tricuspid regurgitation in 9(30%) patients, abnormal ($<50\%$) EF% in 8(26.6%). As regard ECG, 8 (26.7%) patients had abnormal ECG findings. (Table1). The present study showed that 6-min walk distance test in all patients ranged from 122 to 310 with mean value 217.5 ± 45.57 , two patients could walk more than 300 during 6-min. (Table 2). This study reported that parameters of spirometric pulmonary function test FEV1% and FVC% were significantly decreased in cases with severe pulmonary hypertension compared to moderate pulmonary hypertension patients ($p < 0.05$). However, no significant difference was noted between FEV1/FVC and degree of pulmonary hypertension. ($p > 0.05$) (figure 2). Right heart catheterization data analysis from this study were that Mean PAP showed Severe elevation in (93.3%) of patients, pulmonary vascular resistance (PVR) was high in 76.6%, Pulmonary capillary wedge pressure estimated to be pre capillary PH in 66.6%, post capillary PH in 23.3% and combined post and pre capillary PH in 10% (Table 3). The present study showed that Chest x-ray, HRCT Chest, CTPA, ECG define slight agreement with PAC in diagnosis of PH (table 4).

Echocardiography showed sensitivity 82.1%, specificity 50% and accuracy 80% to discriminate severe pulmonary hypertension (Table 5).

The present study showed that congenital heart diseases were the highest percent among the

causes of pulmonary hypertension in the studied patients 46.6% and only one case was Idiopathic PH 3.3%, PH patients with lung diseases were 4 (13.3%) (Table 6).

Table (1): ECG and Echocardiography in the studied patients.

			n.	%	
ECG			Normal	22	73.3
			Abnormal ECG	8	26.7
ECHO	Mean PAP	Moderate	6	20.0	
		Severe	24	80.0	
		Mild	10	33.3	
	Tricuspid regurgitation	Moderate	9	30.0	
		Moderate to severe	2	6.7	
		Severe	9	30.0	
	Ejection fraction (EF%)	>50%	22	73.3	
		<50%	8	26.6	
		VSD	8	26.6	
	Other findings	ASD	7	23.3	
		MR	5	16.6	
		Dilatation RA and RV	21	70.0	
		Diastolic dysfunction	4	13.3	

Table (2): 6-min walk distance test (6MWD) among the studied patients.

6-min walk distance test (6MWD)		
Mean $\pm$ SD		217.5 $\pm$ 45.57
Range		122-310
Meters in walk test	<300 m	28(93.3%)
	$\geq$ 300 m	2 (6.7%)

Table (3): Right heart catheterization parameters in the studied patients.

			n.	%
Parameter	Mean Pulmonary artery pressure (Mean PAP)	Moderate elevation	2	6.7
		Severe elevation	28	93.3
		Normal	7	23.3
	Pulmonary vascular resistance (PVR)	High	23	76.6
		Mean ±SD range	16.67±11.4 11.1 (1.06-43.3)	
		Pulmonary capillary wedge pressure (PCWP)	Pre-capillary PH	20
	Post-capillary PH		7	23.3
	Combined post and precapillary PH		3	10.0

Table (4): Agreement of some preliminary Methods in Diagnosis of patients with Pulmonary Hypertension compared to gold standard " Right heart catheterization ":

Abnormal	Kappa		Agreement	
ECG	8/30(26.7%)	28/30(93.3%)	0.051	Slight
Chest X- ray	17/30(56.7%)	28/30(93.3%)	0.171	Slight
High-resolution CT chest	4/30(13.3%)	28/30(93.3%)	0.03	Slight
CT pulmonary angiography	2/30(6.7%)	28/30(93.3%)	0.01	Slight

Cohen's Kappa: a measure of agreement

Table (5): Accuracy of Echocardiography in the diagnosis of severe patients with pulmonary Hypertension comparing to gold standard “Right heart catheterization “ :

	Sensitivity	Specificity	PPV	NPV	Accuracy
Echo finding	82.1%	50.0%	95.8%	16.7%	80.0%

Table (6): Frequency distribution for the causes of pulmonary hypertension in the studied patients:

Causes		n.	%
1. Pulmonary arterial hypertension (PAH)	Congenital heart disease	14	46.6
	Idiopathic	1	3.3
	associated with connective tissue disease (SLE)	2	6.7
2. Pulmonary hypertension with left heart disease	Left ventricular systolic dysfunction	7	23.3
3. Pulmonary hypertension associated with lung disease	Interstitial lung disease	4	13.3
4. Pulmonary hypertension associated with pulmonary artery obstructions	Chronic thromboembolic pulmonary hypertension (CTEPH)	2	6.7

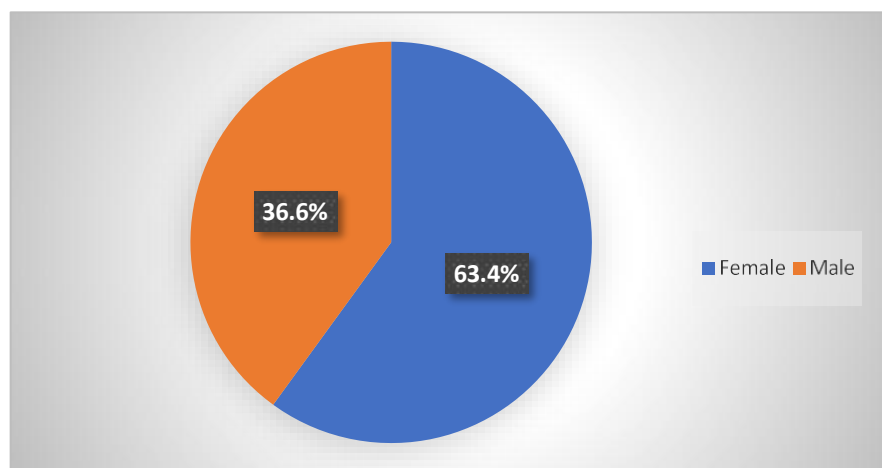


Figure (1): Females percent in studied patients were 63.4%.

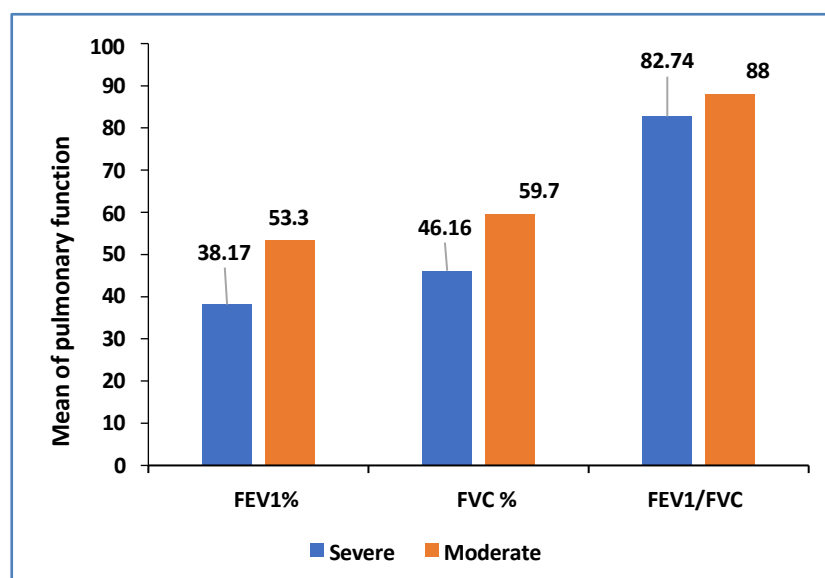


Figure (2): Relation between Spirometric Pulmonary function test and severity of pulmonary hypertension by echocardiography.

DISCUSSION

The prevalence of pulmonary hypertension (PH), a varied condition affecting 1% of the world's population, can reach 10% in those over 65. The rise in pulmonary pressure is linked to a significant increase in the risk of mortality and clinical deterioration, regardless of the underlying ailment [15].

This study revealed that the mean age of the studied patients was 41.5 ± 19.1 and range of age (18-65) years. Gender was distributed as 63.4% females and 36.6% males (female predominance) (figure 1), all patients were complaining of Dyspnea, 40% palpation, 16.6% chest pain, 26.6% hemoptysis and 6.6% syncopal attack. These results were consistent with **Humbert et al. [16]**, who stated that the patients' average age in the study was 47.5 ± 3.3 . The gender M/F ratio was distributed as 6/16 with female predominance.

In this study regarding Echocardiography findings, 24 patients (80%) had severe pulmonary hypertension as regard Mean PAP. Severe tricuspid regurgitation in 9(30%) patients, abnormal ($<50\%$) EF% in 8(26.6%). As regard ECG, 8(26.7%) patients had abnormal ECG findings (Table1). Consistent with this study, **Raymond et al. [17]** reported that for measuring right ventricular size and function, septal curvature, pericardial effusion, and tricuspid regurgitation severity in at least 75 patients, echocardiograms were of sufficient technical quality. In 70 patients, the maximal tricuspid regurgitant jet velocity could be measured. As well, this results were consistent with **Radwan et al. [18]**, regarding Echocardiography findings, Severe tricuspid regurgitation in 6 (15.0%) patients and abnormal EF% was 57.55 ± 11.07 . Also, **D'Alto et al. [19]** found that using transthoracic Doppler echocardiography, the mean SPAP $\pm$ SD was 59 ± 17 mmHg. **Fisher et al. [20]** who the mean RAP $\pm$ SD of individuals with different types of pulmonary hypertension was 9.4 ± 5 mmHg, according to a study by echocardiography.

The present study showed that **6-min walk distance test** in all patients ranged from 122 to 310 with mean value 217.5 ± 45.57 , two patients can walk more than 300 during 6-min. (Table 2).

In the same line, **Miyamoto et al. [21]** found that in individuals with PPH, the distance walked in 6 minutes was 297 ± 188 . **Deboeck et al. [22]**, on the other hand, sought to evaluate heart rate and ventilatory variables in 20 PAH patients during symptom-limited incremental maximal exercise testing using the 6MWT. They stated that 450 ± 22 meters was covered in 6 minutes of walking.

This study reported that parameters of **spirometric pulmonary function test FEV1% and FVC%** were significantly decreased in cases with severe pulmonary hypertension compared to moderate pulmonary hypertension patients ($p < 0.05$). However, no significant difference was noted between FEV1/FVC and degree of pulmonary hypertension. ($p > 0.05$) (figure 2). In agree with this result an earlier study **Thabut et al [23]** and **Scharf et al [24]** this shown the inverse relationship between pulmonary hypertension and FEV1%. According to **Jani et al. [25]**, the severity of pulmonary hypertension was associated with a reduction in spirometric values. Pulmonary hypertension became more severe as the spirometry values declined.

Right heart catheterization data analysis from this study were that **Mean PAP** showed Severe elevation in (93.3%) of patients, **pulmonary vascular resistance (PVR)** was high in 76.6%, **Pulmonary capillary wedge pressure** estimated to be pre capillary PH in 66.6%, post capillary PH in 23.3% and combined post and pre capillary PH in 10% (Table3).

Chest x-ray, HRCT chest, CTPA, ECG findings define slight agreement with PAC in diagnosis of PH (Table 4), In Chest x ray (Cardiomegally in 56.7%, dilated RA and RV in 20%, basal heterogeneous opacity in 13.3% pleural based opacity in 3.33% and enlarged pulmonary artery with regional oligemia in 6.6%). HRCT chest showed honeycombing and traction bronchiectasis in 13.3% and CTPA angiography demonstrated dilation in pulmonary arteries, eccentric organized thrombin adherent to the pulmonary arterial wall with intraluminal filling defect in 6.6%. Echocardiography showed sensitivity 82.1%, specificity 50% and accuracy 80% to discriminate severe pulmonary hypertension

(Table 5). **Soofi et al. [26]**, corresponded with this study and reported that the evaluation of PAPs and PAPm by echocardiography in RHC shows a strong sensitivity and a weak to moderate association with hemodynamic data. Furthermore, **Sohrabi et al. [27]** noted that individuals with pulmonary hypertension had a higher sensitivity for echo in diagnosing their condition. PAPm was measured in echo for 53% of the patients using a formula that included PAPs within 10 mmHg of PAPm obtained in RHC, and the means of the two values were similar. **Janda et al. [28]**, revealed that there was a 0.70 (95% CI 0.67 to 0.73; n = 27) connection between the systolic pulmonary arterial pressure measured by right cardiac catheterization and the value predicted via echocardiography. For the diagnosis of pulmonary hypertension, echocardiography had a sensitivity and specificity of 83% (95% CI 73 to 90) and 72% (95% CI 53 to 85; n = 12), respectively.

Jin-Rong et al. [29] conducted a recent meta-analysis and reported that the echocardiogram's pooled sensitivity and specificity for diagnosing pulmonary hypertension were 85% and 74%, respectively. **Farber et al. [30]**, showed that while echo and RHC had a decent association at one point, there was no correlation when measuring pulmonary hemodynamic changes precisely. **Mukerjee et al. [31]** confirmed that in individuals with a high pretest likelihood, the echocardiogram's involvement in ruling out pulmonary hypertension was insufficient.

According to **Habash et al. [32]**, there was a slight connection between the invasive and echocardiographic methods of measuring PAPs in the various patient subgroups that used an echocardiogram with a higher PAP cutoff. **Elmonim et al. [33]** reported that Right Heart Catheterization (RHC) is still the sole technique capable of fully and precisely diagnosing pulmonary arterial hypertension. The absence of pulmonary hypertension on echocardiogram doesn't rule out pulmonary hypertension and if suggested clinically and by other investigations and imaging techniques then it is appropriate to request RHC however, a more accurate diagnosis of the illness and its sequelae can be obtained by combining right cardiac

catheterization with echocardiography. **Wang et al [34]** showed that 43% of the patients had PAPs measured by an echocardiography and RHC that differed by less than 10 mmHg. Additionally, statistical techniques were created by **Fisher et al. [20]** for the Bland and Altman tests as well as other studies to improve the evaluation of the accuracy or equivalency of tests. With 95% limits of agreement (range from 138.8 to 240.0 mmHg), the bias for the echocardiographic estimations of the pulmonary artery pressures was 20.6 mmHg using Bland-Altman analysis. By defining an appropriate pulmonary artery pressure estimate as one that is within 10 mmHg of the catheterization measurement, 48% of the echocardiographic estimations met this criterion. In their opinion, Doppler echocardiography is still a crucial screening method for the assessment and ongoing treatment of pulmonary hypertension. Doppler echocardiography can considerably underestimate or overestimate pulmonary artery and right atrial pressures in specific patients. It is not always an accurate indicator of these values.

Similarly, in patients with interstitial lung disease undergoing lung transplant evaluation, **Arcasoy et al. [35]** found a good association between sPAP assessed by RHC and that calculated by Doppler echocardiography. Doppler echocardiography-derived sPAP was accurate (within 10 mmHg of RHC measurement) in only 48% of cases, despite a statistically strong correlation between that measured by RHC and that predicted by Doppler echocardiography. Additionally, a difference of more than 20 mmHg was found in 28% of cases between the sPAP measured by RHC and the estimate from Doppler echocardiography, and a difference of more than 30 mmHg in 9% of cases. The results of the mPAP measurements from catheterization and echocardiography were not substantially skewed, as was the case with **D'Alto et al. [19]**. When comparing the echocardiographic data to the gold standard catheterization measurements, there was a high degree of accuracy. The levels of agreement on the difference in means, which were quite significant, indicated that the echocardiographic measures had only

somewhat greater precision. Conversely, RVSP measured by Doppler echocardiography and sPAP by RHC were found to differ significantly in patients with PAH (66.4 ± 26.3 mmHg VS 72.1 ± 32.3 mmHg, $P = 0.035$). RVSP and mPAP by RHC were also found to differ significantly (66.4 ± 26.3 mmHg VS 45.9 ± 22.1 mmHg, $P < 0.01$).

Moreover, **Lafitte et al. [36]** found that systolic PAP from RHC was considerably higher than that from Doppler echocardiography in a similar manner. Nonetheless, there was discovered to be a substantial, robust, and positive association between the two measurements.

The present study showed that congenital heart diseases were the highest percent among the causes of pulmonary hypertension in the studied patients 46.6% and only one case was Idiopathic PH 3.3%, PH patients with lung disease were 4 (13.3%). (**Table 6**). All congenital heart diseases patients in this study above 18 years old with onset of symptoms since childhood, Their follow up were with cardiology staff. All COPD (21 patients) refused PAC. Similarly, **D'Alto et al. [19]** who evaluated looking ahead, it was shown that most patients with suspected pulmonary hypertension had left heart problems and either pulmonary arterial hypertension (PAH, 36%) or pulmonary venous hypertension (PVH, 40%). Ten (7%) of the patients had mPAPs of less than 25 mmHg at right cardiac catheterization, meaning they did not fit the diagnostic criteria for pulmonary hypertension. **Khalid et al. [37]** 16.6% of patients had pulmonary arterial hypertension, 6.6% had idiopathic PAH, 3.3% had ASD, 3.3% had chronic thromboembolic pulmonary hypertension, and 20% had pulmonary hypertension with unclear and/or multifactorial mechanisms, according to researchers who assessed the severity indicators and the impact of the most recent therapeutic recommendations on survival in pulmonary hypertension.

LIMITATIONS

Small sample included as 23 patients refused PAC and the short period of the study.

CONCLUSIONS

Echocardiography shows high sensitivity (82.1%) and accuracy (80%) with average specificity (50%) to discriminate severe pulmonary hypertension compared to gold standard "pulmonary artery catheterization". The role of Preliminary Methods as laboratory investigations and radiological techniques along with Doppler echocardiography to classify pulmonary hypertension patients for proper management. Significant decrease in spirometric pulmonary function test (FEV1, FVC) values in severe compared to moderate pulmonary hypertension patients.

RECOMMENDATIONS

Encourage cooperative work between cardiologists and pulmonologists in pulmonary hypertension to improve the outcome of patients. Spirometric pulmonary function test (FEV1, FVC) should be considered in pulmonary hypertension severity detection and follow up.

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