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Pulmonary Hypertension Surveillance - Saudi Arabia, 2014

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Abstract

Pulmonary arterial hypertension (PAH) is a progressive life-threatening disease. Information about the incidence and prevalence of PH in Saudi Arabia remains limited.The aims of the present study were to estimate prevalence of PAH and compare clinical characteristics and the demographic of PH due to various causes in a Saudi population. Newly diagnosed cases of PH [defined as the mean pulmonary artery pressure > 25 mmHg at right heart cauterization (RHC)] were prospectively collected at a single tertiary care hospital from January 2013 and June 2014. Detailed clinical, demographic data and hemodynamic parameters were collected at the time of diagnosis. Results of the total 925 patients who underwent RHC, 368 were identified as having PH. At diagnosis the mean age was 37.8 ± 12.8 years, and there was a female preponderance of 62.4%. One hundred sixty five of the patients (44.8%) were classified as Idiopathic pulmonary arterial hypertension, ninety three (25.2%) as Congenital heart disease-associated pulmonary arterial hypertension, eighty nine (24.1%) as a Connective tissue disease-associated pulmonary arterial hypertension, twelve (3%) as Heritable pulmonary arterial hypertension), and nine (2.4%) as Portal hypertension-associated pulmonary arterial hypertension. Most of the patients were in stage III pulmonary hypertension. This data emphasize the current status of pulmonary arterial hypertension in Saudi Arabia. Patients having pulmonary arterial hypertension are much younger than patients described in other international records, but the course of the disease is still detected lately. A majority of patients showed severe functional and hemodynamic impairments. Screening of patients for PAH will help in early diagnosis and therapeutic intervention before significant end-organ damage occurs.

Key words : Hemodynamics, pulmonary arterial hypertension, prevalence, Saudi Arabia.

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a syndrome in which elevation of a blood pressure in the supplying lung blood vessels [1]. It is described as vasoconstriction and vascular obstruction that finally lead to increased pulmonary vascular resistance, right heart failure and a 15% annual mortality rate [2]. Its exact incidence is unknown, but annual rating incidence is 2-10 cases per million of population per year according to British, American, French, and Scottish [1-5]. Female to male ratio about 4:1. The disease is insidious, and patients are generally not diagnosed until they begin to suffer from symptoms of right heart failure. Pulmonary hypertension (PH), comprises a spectrum of diseases that are categorized into 5 groups: Group 1, idiopathic pulmonary hypertension (PAH); group 2, PH due to left heart disease (LHD); group 3, PH due to lung disease; group 4, connective tissue PH (CT-PH); and group 5, PH with unclear multifactorial mechanisms[7]. The understanding of PAH pathogenesis and the management of the disease have experience significant improvement during the last decade. Despite such advances, PAH accelerating and often fatal. The prediction markers in PAH include a combined measures that comprise clinical distinctive and physiological and hemodynamic parameters. The modified New York Heart Association (NYHA) functional class has been recognized as an important prognostic measure. Furthermore, exercise tolerance and physiological and hemodynamic markers are also crucial tools for classification of PAH patients as regard prognosis and therapeutic angle [8]. The load of PAH in the Middle East and Saudi Arabia is still obscure, and the disease distinguishing parameters are yet to be determined. The aims of the present study were to estimate prevalence of PAH and compare clinical characteristics and the demographic of PH due to various causes in a Saudi population.

MATERIALS AND METHOD

This study was approved by the Institutional Review Board/Ethics Committee of the College of Medicine, Prince Sattam Bin Abdulaziz University, Alkharj, Saudi Arabia. The present study describes the results of prospectively collected and longitudinally followed cohort of patient records from tertiary specialized pulmonary hypertension (PH) center, Prince Sultan Medical Military City and Cardiac Center (PSMMC & CC), in Saudi Arabia over a 2.5 year period from PAH June 2012 and December 2014. 925 patients records were specifically examined, all patients referred to the pulmonary hypertension unit with suspected or confirmed diagnosis of WHO group I disease (PAH) were screened by using echocardiograph. The diagnostic right heart catheterization (RHC) was essential to meet the study inclusion criteria.

Participants:

Patients diagnosed as PAH were eligible for registration if the definition of pulmonary hypertension (PH) group I PAH, as per the Nice 5th PH World Congress was fulfilled [10]. This includes patients with idiopathic PAH, heritable PAH, or PAH associated with congenital systemic-to-pulmonary shunts, connective tissue diseases PAH, portal hypertension PAH. A standard form was used to collect clinical information, including symptoms, smoking history, medication use, environmental history, occupational history, family history, and physical findings. Detailed blood testing, echocardiography, pulmonary function tests (PFTs), 6- minute walk test (6MWT), and computed tomography pulmonary angiography were included in the

systemic diagnostic evaluation when PH was suspected. PHA group I disease category was also identified at this stage. Physiological assessment at the time of diagnosis includes a six-minute walk test (6MWT), and echocardiographic evaluation for pericardial effusion and right ventricular function (TAPSE score). Using these data to categorize each patient as Pulmonary arterial hypertension first, then patients in whom an isolated coding of PAH was recorded in the absence of any explanatory concurrent diagnoses from prior hospitalizations were designated as having IPAH.

Individuals with a past or concurrent diagnosis of congenital systemic-to-pulmonary shunts were identified as having CHD-PAH. Similarly, patients with evidence of PAH related to systemic connective tissue disorders were designated as having CTD-PAH. Patients with evidence of PAH related to portal hypertension were designated as having Po-APAH, also Patients with evidence of PAH related to Heritable pulmonary arterial hypertension, were designated as having HPAH.

Data analysis:

Statistical analysis

Descriptive statistics in terms of mean, standard deviations and percentages were used to describe characteristics of the studied patients. Comparison of categorical variables was conducted by Chi-Square test or Fisher's exact test accordingly. After assessment of the normality distribution of variables, Student t-test and ANOVA test were used if the data had normal distribution whilst MannWhitney and KruskalWallis test were used in skewed data. A P-value less than 0.05 was considered a significant test. SPSS version 17 was used for all statistical analysis.

RESULTS

A total of 925 consecutive patients underwent RHC for suspected PH, of which, 557 patients did not have PH. In addition, 368 patients were identified as having PH and were divided into five groups according to the current classification of PH [Figure 1]. Comparison of demographic characteristics, clinical characteristics, and hemodynamic data among the five groups at the time of diagnosis are shown in table 1.

Demographics:

The mean age at diagnosis was 33.8±6.8 for males and 35.5±13 for female out of the 368 patients, 225 (61.1%) were female. Table 1 illustrates the type of pulmonary hypertension of the patients enrolled in the study.

Clinical characteristics:

Figure 2 illustrate the baseline clinical characteristics of the patients enrolled in the study. At the time of diagnosis, 107 patients (29.1%) were in modified NYHA functional class II, 196 patients (53.3%) were in functional class III, and 65 patients (17.6%) were in functional class IV. In the whole cohort of patients, 165 patients (44.8%) were diagnosed as IPAH, 93 patients (25.3%) as PAH associated with congenital heart disease

Figure 1: The Distribution of the Study Cohort.

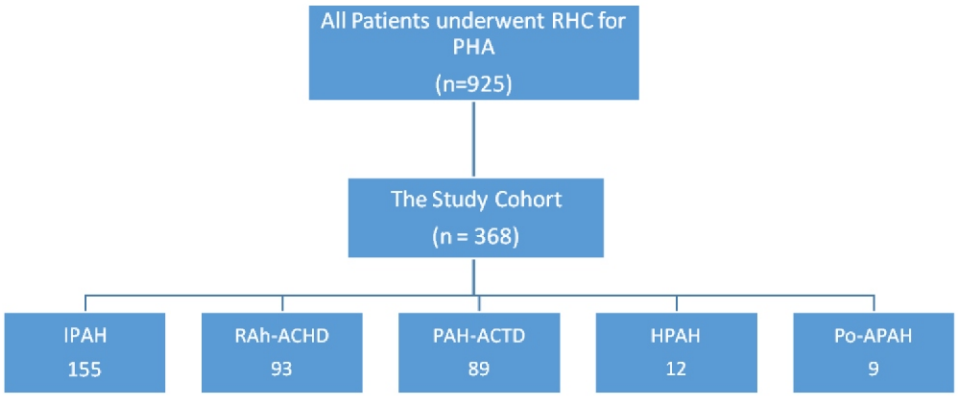

Table 1: Demographic profile, including type of pulmonary arterial hypertension, of Saudi populations (Data are presented as mean ±SD)

	Males		Females	
	Subjects N	Age yrs	Subjects N	Age yrs
Idiopathic PAH	62	40±5	103	38±3
Congenital PAH	38	31±6	55	29±4
Connective PAH	26	50±7	63	46±5
Heritable PAH	8	21±9	4	19±7
Portal hypertension PAH	9	37±7	0	0
Total	143	33.8±6.8	225	35.5±13

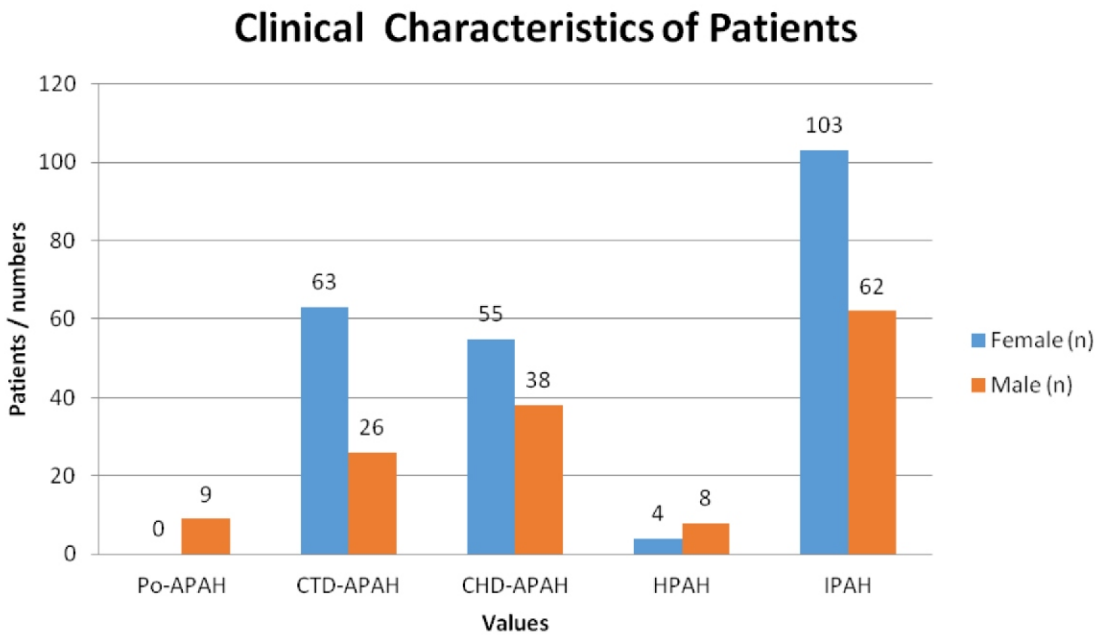

Figure 2: Clinical Characteristics of Patients.

IPAH = Idiopathic pulmonary arterial hypertension, CHD-APAH = Congenital heart disease-associated pulmonary arterial hypertension, CTD-APAH = Connective tissue disease-associated pulmonary arterial hypertension, HPAH = Heritable pulmonary arterial hypertension, Po-APAH = Portal hypertension-associated pulmonary arterial hypertension (portopulmonary hypertension).

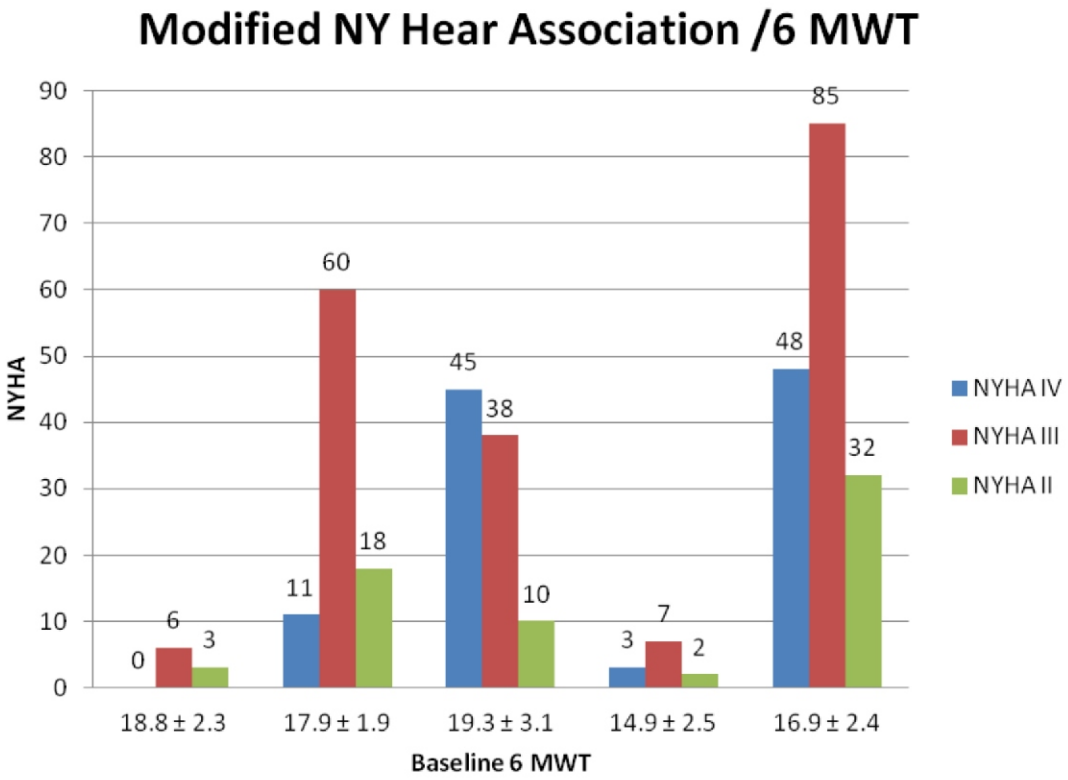

Figure 3: NYHA = Modified New York Hear Association, 6-MWT = 6-minute walk test.

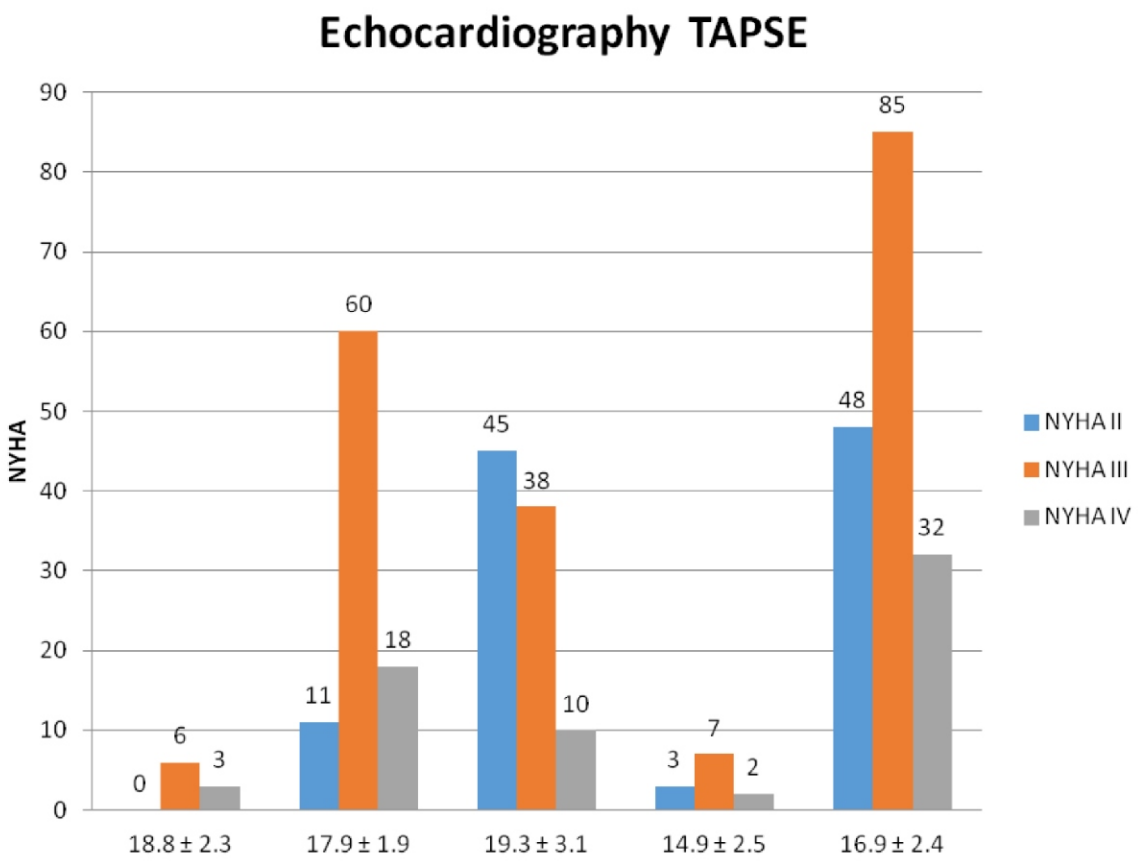

Figure 4: Echocardiography TAPSE = Tricuspid annular plain systolic excursion.

(CHD-A PAH), 89 patients (24.2%) as PAH associated with connective tissue disease (CTD -APAH),12 patients (3.2 %) as heritable pulmonary arterial hypertension (HPAH) [based on strong family history but genetic testing was not performed], and 9 patients (2.4%) as portopulmonary hypertension (PoPH) [all with hepatitis B virus and portal hypertension]. The HPAH subgroup patients were younger than the other sub groups, while the CTD APAH patients subgroup were the eldest and had more severe symptoms at diagnosis.

Exercise capacity had been evaluated at the time of diagnosis by six minutes walk test (6- MWT) [Figure 3] and Echocardiograph [Figure 4] results were available for all patients (100%) at the time of diagnosis.

DISCUSSION

The present study describes the characteristics of PAH in the largest population of patients in Saudi Arabia to date. The clinical characteristics used in this study were limited to the modified NYHA functional class since this clinical parameter was found to have prognostic significance both at baseline [9] and follow up [10]. The physiological characteristics included six minutes walk test (6-MWT), and TAPSE scoring as measured by echocardiography. 6MWT is a straightforward, safe, and reproducible test, which measures the distance walked in 6 minutes. It has been found to have a prognostic measure in PAH patients [10,11]. Similarly, TAPSE scoring have also been found to carry prognostic values [12,13]. The mean age of the whole cohort at the time of diagnosis was significantly lower than the mean age reported by other registries [4,6,14]. This can probably be explained by the young age of the Saudi Arabian population, as more than 50% of the whole Saudi population is younger than 20 years of age. About 70.9% of the patients were in functional class III or IV at presentation. This delayed diagnosis is consistent with similar findings reported in many studies [6,14]. Because baseline modified NYHA functional class is a well-recognized predictor of outcome in PAH patients, the long duration of symptoms before establishing the diagnosis indicates insufficient awareness about the disease in Saudi Arabia. Alhamad et al., has recently published a single-center experience in managing PH in Saudi Arabia [15]. In his cohort of 112 PH patients, only 12 (10.7%) belonged to group I PAH, and almost all of them were related to IPAH and PAH-ACTD. IPAH was the most common subtype of PAH in our study. This observation has been recognized by other international registries [4,16,17]. Our IPAH patients were predominantly female and significantly older than the HPAH and PAH-ACHD patients but younger than CTD -APAH- ($P < 0.001$ between the groups). PAH-ACHD patients were the second most common PAH subgroup and had the best physiological parameters compared to other groups. The high prevalence of PAH-ACHD in this cohort probably reflects the current practice of late detection of CHD patients in Saudi Arabia and delayed surgical corrections.

Despite a relatively long duration of symptoms, those patients were more likely to be in modified NYHA functional class II compared to other groups, although this did not reach the statistically significant level ($P = 0.08$ between the groups). Nevertheless, PAH-ACHD patients showed a significantly better physiological profile when compared to other PAH groups. PAH-ACTD patients were significantly older than the other groups ($P <$

0.001 between groups) and had the longest duration of symptoms before confirming the diagnosis ($P < 0.001$ between groups). This is presumably related to the presence of other comorbidities that might be associated with CTD and can also lead to pulmonary symptoms, such as interstitial lung disease, heart failure, or myopathy. Furthermore, PAH-ACTD patients had significantly more physiological limitation when compared to other PAH groups ($P < 0.001$). HPAH patients were the youngest among the groups. Both HPAH and PoPH patients had the shortest symptoms duration before establishing the diagnosis compared to other groups ($P < 0.001$). This is presumably related to the lower threshold for making the diagnosis because of involvement of other family members, and because of the severity of the symptoms.

CONCLUSION

This descriptive study emphasized the current status of pulmonary arterial hypertension in Saudi Arabia. Patients having pulmonary arterial hypertension still present very late in the course of the disease, and the majority of them display severe physiological and hemodynamic compromise. Of note, our patients are much younger when compared to the international registries.

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