Demographic and clinical characteristics of pulmonary hypertension cases and the awareness of the disease among chest physicians in Abassia Chest Hospital

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Abstract Rational: To date in Egypt there is no available national registry for PH cases therefore this study had two objectives, first to record the clinical characteristics and demographics of PH cases in a single center study that hopefully could be a stepping stone in the development of a national registry. The second objective was to assess the awareness of the physicians of the disease.

Methods: It included two parts, the first a retrospective descriptive study of 52 patients diagnosed as PH who were admitted to Abassia Chest Hospital in the period between January 2011 and December 2012. The second part comprised a prospective assessment of the awareness of 40 specialized chest physicians who worked in Abassia Chest Hospital using a questionnaire.

Results: Among the 52 patients the mean age was 55.8 ± 13.25 years, 28 females (53.8%) and 24 males (46.2%) and a mean cigarette smoking index of 78.5 (±33.3). The patients suffered from slight respiratory acidosis with a mean pH of 7.3 (± 0.03) explained by the elevated mean PaCO2 of 49.9 (± 8.6) mmHg and hypoxemia explained by a mean PaO2 of 73.6 (± 12.7) mmHg, and a mean SO2 of 83.9 (± 5)%. According to NYHA, 40 (76.9%) presented in FC III and 12 (23.1%) FC IV. ECHO assessment records revealed an elevated right ventricular systolic pressure (RVSP) with an estimated mean of 61.4 (± 12.4) mmHg, tricuspid regurge was the most common valve affection in 38 (73%) of the cases while 18 (34.6%) had left ventricular diastolic dysfunction and left ventricular hypertrophy. Almost all of the diagnosed patients with PH 43/52 (82.6%) were classified as group 3 that is PH due to lung diseases and/or hypoxemia. COPD contributed to slightly

Keywords Pulmonary hypertension; Echocardiography; Demographic; Registry; Chronic obstructive pulmonary diseases; Awareness.

Abbreviations: PH, pulmonary hypertension; NYHA, New York Heart Association; FC, functional class; CXR, chest X-ray; ABG, arterial blood gases; ECG, electrocardiograph; ECHO, echocardiography; TR, tricuspid regurge; RVSP, right ventricular systolic pressure; COPD, chronic obstructive pulmonary disease; RHC, right heart catheterization; CTEPH, chronic thromboembolic pulmonary hypertension; IHD, ischemic heart disease; CRF, chronic renal failure; ILD, interstitial lung diseases; PE, pulmonary embolism; WHO, World Health Organization; SD, standard deviation; CCB, calcium channel blockers; ACEI, angiotensin converting enzyme inhibitors.

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more than half of the 29 (55.7%) cases meanwhile the other half was shared between variable lung diseases. PH due to left sided heart failure (group 2) was the second common cause 5/52 (9.6%) followed equally by patients with chronic thromboembolism (CTEPH) (group 4) 2/52 (3.8%) and patients with idiopathic pulmonary hypertension (group 1) 2/52 (3.8%). Among the 40 physicians enrolled in the survey only 15 (37.5%) acknowledged that they found PH a commonly diagnosed disease in their practice. As regards the method of investigation; 34 (85%) decided on ECHO only but 5 (12.5%) recommended both ECG and ECHO. To reach a confirmed diagnosis of PH only 2 (5%) selected right heart catheterization while 35 (87.5%) chose elevated RVSP > 25 mmHg and 3 (7.5%) didn’t know. None of the physicians conducted clinical trials on PH medications also none of them have previously referred any of the PH cases for heart and lung transplant and only 1 physician referred 1 case for thrombo-endarterectomy. Lastly 34 (85%) of the physicians didn’t attend any educational meeting concerning PH, the remaining 4 (10%) attended one meeting and 2 (5%) attended two meetings.

Conclusion: In conclusion the study provides information on the clinical and epidemiological features of PH in Egypt as a primary pilot study. It highlights the fact that awareness about the disease is still lacking among physicians and/or health care providers and late detection continues to be a threat for optimum management of PH.

Clinical impact: It unveiled the urgent need for a large scale registry not only national but also regional using uniform diagnostic criteria based on the latest published guidelines.© 2015 The Authors. Production and hosting by Elsevier B.V. on behalf of The Egyptian Society of Chest Diseases and Tuberculosis. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Pulmonary hypertension (PH) is a devastating disorder of the cardiovascular system leading to right heart failure and death. Although it was known for the last 100 years, only in the last 25–15 years a better understanding of pathogenesis and risk factors has led to new diagnostic and therapeutic approaches and hence to an increased interest in the detection of this incurable disease associated with poor survival and prognosis [1–3]. The profile of PH varies throughout the world therefore obtaining data about epidemiology, follow-up and prognosis is invaluable to improve therapy and assess outcome parameters [4].

Major advances in the diagnosis and management of PH have been in constant evolution and these achievements were marked by the different World Symposia on Pulmonary Hypertension (WSPH). The complexity of the recent international guidelines for the diagnosis and assessment of patients with PH during the 5th WSPH in 2013 as well as the published data that the majority of PH cases are still diagnosed in a late stage manifesting the urgent need to increase the awareness of the doctors to achieve a better understanding of this multi-system disorder [5].

To date in Egypt there is no available national registry for PH cases therefore this study had two objectives, first to record the clinical characteristics and demographics of PH cases in a single center study that hopefully could be a stepping stone in the development of a national registry. The second objective was to assess the awareness of the physicians of the disease.

Subjects and methods

This study was conducted in Abassia Chest Hospital in the period between January 2011 and December 2012

It included two parts, the first a retrospective descriptive study of 52 patients diagnosed as PH who were admitted to the Abassia Chest Hospital in the period between January 2011 and December 2012. It is important to note that although current guidelines recommend right heart catheterization (RHC) for the diagnostic evaluation of patients with PH, the diagnostic approach in this study was established mainly in the presence of clinical suspicion based on the accepted definitions and trans-thoracic echocardiography recording high pulmonary artery systolic pressure (PASP > 50 mmHg) as the RHC wasn’t available [6].

The second part comprised a prospective assessment of the awareness of 40 specialized chest physicians who worked in the Abassia Chest Hospital using a questionnaire [7].

The questionnaire included 18 questions as follows:

(1) Is PH a common finding you met with?
(2) What are the common diseases that are complicated by PH that you usually examine?
(3) How do you suspect that your patient developed PH?
(4) Do you care for chest X-ray findings in PH?
(5) Do you investigate for pulmonary hypertension if you suspect it?
(6) How do you investigate?
(7) Do you usually ask for echocardiography as a routine in cases suspected to develop pulmonary hypertension?
(8) When do you suspect idiopathic pulmonary hypertension?
(9) When do you diagnose idiopathic pulmonary hypertension as a final diagnosis?
(10) Do you refer your patient to a specialized center or are you the one who cares?
(11) What year did you begin caring for patients with PH?
(12) How many PH patients do you currently treat?
(13) Do you require all patients to undergo right heart catheterization with vasodilator testing prior to prescribing a therapy for PH?
(14) What therapies do you prescribe for pulmonary hypertension?
(15) Do you conduct clinical trials on PH medications?
(16) Have you referred patients for lung or heart/lung transplant?
(17) Have you referred patients for pulmonary thromboendarterectomy?
(18) Which educational meetings regarding PH have you attended in the last two years?

Statistical analysis

Parametric data were expressed as mean ± standard deviation (SD), minimum, maximum, and range, while non-parametric data were expressed as number, and percentage. Chi-square was used to study the relation between non-parametric variables. Two tailed \( p \) value of <0.001 was considered highly significant, and \( p < 0.05 \) was considered significant. Statistical analyses were performed utilizing Statistical Package for Social Sciences software (SPSS for Windows, version 15.0; SPSS Inc., Chicago, IL).

Results

Results of the studied population

The total number of the studied patients were 52 with a mean age of 55.8 ± 13.25 years, among them 28 females (53.8%) and 24 males (46.2%), most of the females 26 (92.8%) didn’t work whereas 19 (79.1%) of the males worked in different occupations. As regards the residency the majority lived in Cairo governorate 32 (61.5%) followed by Qalyubia governorate 7 (13.5%) then Giza governorate 6 (11.5%) and 7 (13.5%) in others. 23 (44.2%) of the cases were cigarette smokers with the mean 3.9 (± 1.6) pack/day and mean cigarette smoking index of 78.5 (± 33.3). The clinical characteristics of the recorded patients are illustrated in Table 1 from which it is evident that based on the World Health Organization (WHO) modification of the New York Heart Association (NYHA) classification of PH [7] all the patients presented late in FC III 40 (76.9%) and FC IV 12 (23.1%). Among the studied group co-morbid conditions were present as highlighted in Fig. 1.

ABG findings for the patients revealed that all patients suffered from slight respiratory acidosis with a mean pH of 7.3 (± 0.03) explained by the elevated mean PaCO2 of 49.9 (± 8.6) mmHg and hypoxemia explained by a mean PaO2 of 73.6 (± 12.7) mmHg, and a mean SO2 of 83.9 (± 5)%. The mean HCO3 was 28.5 (± 33.3) mmol/L and the mean ABE was 5.19 (± 6.6) mEq/L.

Among the 52 ECG reports collected two predominant findings were noticed equally in the form of right axis deviation and P pulmonale in 33 (63%).

Retrospective ECHO assessment records revealed an elevated right ventricular systolic pressure (RVSP) with an estimated mean of 61.4 (± 12.4) mmHg, tricuspid regurgue was the most common valve affection in 38 (73%) of the cases while 18 (34.6%) had left ventricular diastolic dysfunction and left ventricular hypertrophy. It is important to note that some of the patients had more than one abnormality detected. The clinical classification of PH among the cases is summed in Table 2.

Referring to Table 2 it can be established that almost all the diagnosed patients with PH 43/52 (82.6%) were classified as

<table>
<thead>
<tr>
<th>Table 1</th>
<th>The clinical characteristics of the recorded patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pulmonary symptoms</strong></td>
<td>Number</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>52</td>
</tr>
<tr>
<td>Wheeze</td>
<td>21</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>12</td>
</tr>
<tr>
<td>Cough</td>
<td>15</td>
</tr>
<tr>
<td>Expectoration</td>
<td>11</td>
</tr>
<tr>
<td>Chest pain</td>
<td>2</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>2</td>
</tr>
<tr>
<td><strong>Clinical examination</strong></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>12</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>10</td>
</tr>
<tr>
<td>Irregular pulse</td>
<td>4</td>
</tr>
<tr>
<td>Central cyanosis</td>
<td>22</td>
</tr>
<tr>
<td>Elevated jugular venous pulse</td>
<td>40</td>
</tr>
<tr>
<td>Lower limb edema</td>
<td>47</td>
</tr>
<tr>
<td>Wheezes</td>
<td>40</td>
</tr>
<tr>
<td>Crackles</td>
<td>25</td>
</tr>
<tr>
<td>S2*: loud and splitting</td>
<td>11</td>
</tr>
<tr>
<td>S3^: loud and splitting</td>
<td>12</td>
</tr>
<tr>
<td>TR#: murmur</td>
<td>24</td>
</tr>
<tr>
<td><strong>WHO/NYHA</strong> functional class</td>
<td>Number</td>
</tr>
<tr>
<td>I</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>40</td>
</tr>
<tr>
<td>IV</td>
<td>12</td>
</tr>
</tbody>
</table>

\( S2^* \): second heart sound; \( S3^* \): third heart sound; \( TR^* \): tricuspid regurgue; WHO/NYHA*: World Health Organization modification of New York Heart Association functional classification.

Figure 1 Co-morbidity prevalence.
group 3 that is PH due to lung diseases and/or hypoxemia. COPD contributed to slightly more than half of the cases (55.7%) meanwhile the other half was shared between variable lung diseases as represented in Fig. 2.

Analysis of the data emphasized that all the patients (100%) received antibiotics, diuretics [Frusemide and/or Spironolactone] in 45 (86.5%), calcium channel blockers [Diltiazem] in 35 (67.3%), angiotensin converting enzyme (ACE) inhibitors [Captopril] in 13 (25%), Phosphodiesterase inhibitors (PDE5) Sildenafil in 17 (32.7%), bronchodilators in 38 (73%), steroids in 11 (21.2%) and lastly anticoagulants [heparin and/or warfarin] in 5 (9.6%). These medications were given either singly or in combinations.

Results of the questionnaire

Among the 40 physicians enrolled in the survey only 15 (37.5%) acknowledged that they found PH a commonly diagnosed disease in their practice and the majority 32 (80%) recorded that it is usually a complication for COPD while 13 (32.5%) credit it to ILD. Lower limb edema and/or elevated jugular venous pressure were the commonest two clinical findings that 35 (87.5%) physicians agreed upon when asked when to suspect the patient developed PH whereas 15 (37.5%) referred to the development of unexplained dyspnea and only 4 (10%) considered the presence of P-pulmonale and right axis deviation in ECG. It is significant to mention that each physician had more than one answer. Moreover 31 (77.5%) physicians cared to inspect the chest X-ray findings, almost all the physicians 37 (92.5%) concurred on investigating the patients to confirm the diagnosis of PH once suspected. As regards the method of investigation; 34 (85%) decided on ECHO only but 5 (12.5%) recommended both ECG and ECHO. Idiopathic PH was suspected by the presence of unexplained dyspnea with normal CXR as stated by 30 (75%) physicians, the rest 10 (25%) were not knowledgeable. To reach a confirmed diagnosis of PH only 2 (5%) selected right heart catheterization while 35 (87.5%) chose elevated RVSP > 25 mmHg and 3 (7.5%) did not know. Regarding the referral of the PH cases to specialized centers only 11 (27.5%) agreed; 10 (25%) physicians start to care for PH cases since the year 2005, 4 (10%) started since 2000 and 2 (5%) did not. Furthermore 14 (35%) of the physicians were managing > 30 patients, 7 (17.5%) were managing 20–30 patients, 11 (27.5%) were managing 1–10 patients and 8 (20%) weren’t managing any at the time of the questionnaire. Only 6 (15%) of the involved physicians requested right heart catheterization with vasodilator testing prior to prescribing a therapy for PH. As regards the different types of medications prescribed it is illustrated in Fig. 3. None of the physicians conducted clinical trials on PH medications also none of them have previously referred any of the PH cases for heart and lung transplant and only 1 physician referred 1 case for thromboendarterectomy. Lastly and unfortunately 34 (85%) of the physicians didn’t attend any educational meeting concerning PH, the remaining 4 (10%) attended one meeting and 2 (5%) attended two meetings.

Discussion

This study recorded that the mean age of the enrolled patient was (55.8 ± 13.25) years demonstrating that PH is now more frequently diagnosed in elderly patients matching with studies done by Gartman et al. [8] (55 ± 10) years and Fayngersh et al. [9] (63 ± 10.2) years. In addition it was in agreement with many registries as the Scottish-SMR [10] (52 ± 12) years, the Spanish [11] (52 ± 12) years and the US REVEAL [12] (50 ± 14) years although their selected population involved only group 1. However it wasn’t in accord with the NIH registry [13] (36 ± 15) years nor the new Chinese registry [14] (36 ± 13) years. The changing phenotype of PH could be explained by the fact that the NIH registry of the selected

Table 2 The clinical classification of PH among the studied cases.

<table>
<thead>
<tr>
<th>Type</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH due to lung diseases and or hypoxemia</td>
<td>43</td>
<td>82.6</td>
</tr>
<tr>
<td>(G3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PH due to left heart disease [G2]</td>
<td>5</td>
<td>9.7</td>
</tr>
<tr>
<td>Chronic thromboembolic PH (CTEPH) [G4]</td>
<td>2</td>
<td>3.8</td>
</tr>
<tr>
<td>Idiopathic PH [G1]</td>
<td>2</td>
<td>3.8</td>
</tr>
</tbody>
</table>

G: group; PH: pulmonary hypertension.
population was only idiopathic pulmonary hypertension cases meanwhile the dissimilarity from the Chinese registry could be related to the different healthcare environment independent to the disease expressions The female predominance (53.8%) in this study though not much, was also consistent with the previous registries [10–12]. Data in this study revealed that (50%) half of the diagnosed female patients were housewives and lived in the capital city Cairo. This could be attributed to the better awareness of the urban doctors than the rural ones as well as the abundance of specialized medical centers and hospitals distributed all over the vast city. Cigarette smoke-induced pulmonary hypertension is associated with evidence of oxidative vascular damage by reactive nitrogen species leading to pulmonary vascular remodeling [15]. This was witnessed by the presence of 23 (44.2%) cigarette smokers among the cases with a mean of 3.9 (± 1.6) packs/day and a mean cigarette smoking index of 78.5 (± 33.3). As regards the co-morbid diseases hypertension (46.2%) and type II diabetes mellitus (17.3%) were the commonest conforming with the findings of Ling et al. [16]. There is no pathognomonic clinical sign of PH; clinical presentation is related either to right heart failure or to associated diseases. Persistent dyspnea on exertion is the most frequent symptom; and it is present in almost all patients even in the presence of mild hemodynamic abnormalities. Dyspnea usually starts insidiously and is often neglected by patients who explain the delay of around two years in establishing the diagnosis of PH [17]. The study showed that dyspnea was the most prevalent symptom being manifested by all patients (100%), followed by chest wheeze (40.4%), cough (28.8%) orthopnea (23.1%), chest pain (3.8%), hemoptysis (3.8%), and elevated body temperature (7.7%) showing concordance with results of Ling et al. [16], Edelman [18] and Jing et al. [14]. Baseline functional class (FC) is an important correlate and predictor of survival. The modified New York Heart Association (NYHA) FC is a simple, reproducible and clinically important assessment tool and prognostic measure in PH patients both at the time of diagnosis and in follow up [19]. The cases in this study were classified according to the NYHA FC into two groups. The majority fitted in FC III (76.9%) and only 12/52 (23.1%) into FC IV corresponding to the findings of Hurdman et al. [20] who found that 47% of patients were FC III at diagnosis superior to 20% who were in FC IV. It was also matching the results of Soliman et al. [21] as all studied groups resided in FC III (36%) and FC IV (55%). The study registered that lower limb edema (90.4%) was the most prevalent sign followed by congested neck vein (77%) then wheeze (76.9%). Cardiac examination revealed that TR murmur was the commonest (46.2%) followed by audible S3 (23.1%), accentuated S2 (21.2%) and Splitting of S2. This did not agree with Colman et al. [22] and Jing et al. [14] who both found that the sign most associated with PH was a loud pulmonic component of the second heart sound (P2). The ABG analysis for the patients revealed that all the patients suffered from slight respiratory acidosisis with a mean pH of 7.3 (± 0.03) explained by the elevated mean PaCO2 of 49.9 (± 8.6) mmHg and hypoxemia explained by a mean PaO2 of 73.6 (± 12.7) mmHg, and a mean SO2 of 83.9 (± 5%). The mean HCO3 was 28.5 (± 6.9) mmol/L and the mean ABE was 5.19 (± 6.6) mEq/L. The hypoxemia could be regarded as either a causal factor for PH as sustained alveolar hypoxia induces pulmonary vascular remodeling or a consequence of the disease itself [23]. The hypoventilation might be related to affection of ventilatory reserve by PH or the fact that the majority of the cases where COPD similarly to the results of Soliman et al. [21] and Hurdman et al. [20]. Among the 52 ECG reports collected two predominant findings were noticed equally in the form right axis deviation and P pulmonale in 33 (63%) and this agreed with Jing et al. [14] and Bossone et al. [6].

The right ventricle plays an important role in the morbidity and mortality of patients presenting with signs and symptoms of cardiopulmonary disease. However, the systematic assessment of right heart function is not uniformly carried out. This is due partly to the enormous attention given to the evaluation of the left heart, lack of familiarity with ultrasound techniques that can be used in imaging the right heart, and a paucity of ultrasound studies providing normal reference values of right heart size and function [24]. Unfortunately this applies to this study since data were collected retrospectively; ECHO assessment of the right heart was defective and represents one of the limitations of this study. The diagnostic methodology used in the studies was not always the same; some used echocardiography as a sole diagnostic tool, while others used right heart catheterization (RHC) as it is considered the “gold standard” for the diagnosis of PAH [25]. In this study retrospective ECHO assessment records revealed an elevated right ventricular systolic pressure (RVSP) with an estimated mean of 61.4 (± 12.4) mmHg, tricuspid regurge was the most common valve affection in 38 (73%) of the cases while 18 (34.6%) had left ventricular diastolic dysfunction and left ventricular hypertrophy. It is important to note that some patients had more than one abnormality detected.

PH due to lung diseases and/or hypoxia (group 3 according to the updated classification of PH) constituted the majority of cases 43/52 (82.6%) mostly chronic obstructive pulmonary disease (COPD) 29/52 (55.7%). PH due to left sided heart failure was the second common cause 5/52 (9.6%) followed equally by patients with chronic thromboembolism (CTEPH) (group 4) 2/52 (3.8%) and patients with idiopathic pulmonary hypertension (group 1) 2/52 (3.8%). The results didn’t conform with the findings of many studies as Mueller-Mottet et al. [26], Idrees et al. [27] 2014 and Jansa et al. [28] 2014. The discrepancies in the results could be attributed to many factors, firstly the variable populations, enrollment pattern and cohort size among the different studies. Secondly the profile of PH and patients characteristics varies around the world. Thirdly group 3 (PH due to chronic lung disease and/or hypoxia) and group 2 (PH due to left heart diseases) represent an increasing part of the clinical practice especially among cases admitted to chest hospitals where this study took place.

Analysis of medications received by the patients emphasized that all patients 52 (100%) received antibiotics, followed by diuretics [Fresmade and/or Spironolactone] in 45 (86.5%), calcium channel blockers [Dilatazem] in 35 (67.3%), angiotensin converting enzyme (ACE) inhibitors [Captopril] in 13 (25%), Phosphodiesterase inhibitors (PDE5) Sildenafil in 17 (32.7%), bronchodilators in 38 (73%), steroids in 11 (21.2%) and lastly anticoagulants [heparin and/or warfarin] in 5 (9.6%). These medications were given either singly or in combinations. Data from all over the world indicate that the majority of patients are still diagnosed in a late stage of the disease, and this is not expected to change in the near future Hoeper et al. [29]. Consequently another aim of this thesis was to conduct a survey to evaluate the awareness of pulmonary hypertension among chest physicians in Abbasia Chest Hospi-
tal. This questionnaire was crafted to better understand referrals, diagnosis and treatment patterns of the patient population with suspected pulmonary hypertension among health care providers. This will help to identify the pitfalls in the practice and the needed tools and/or evidence based programs to ensure early diagnosis and goal oriented therapy in pulmonary hypertension patients. The questionnaire included 18 questions about the prevalence (Q1, 12 and 2), caring about pulmonary hypertension as a disease (Q11), clinical picture (Q3), investigations (Q8, 4–9 and 13) and treatment of pulmonary hypertension (Q10, 14–18). The outcome of the questionnaire reflected defective awareness as regards the diagnosis and management of the disease and lack of continuous medical education in this field reflected the fact that 85% of the physicians didn’t attend educational meetings regarding pulmonary hypertension in the last 2 years.

The limitations of this study could be attributed mainly to two factors:

1. The unavailability of the RHC at the facility where the study was performed.
2. The systematic assessment of the right heart side using ECHO was not uniformly carried out therefore retrospective collection the data was perplexing.

Conclusion

In conclusion the study provides information on the clinical and epidemiological features of PH in Egypt as a primary pilot registry. It was demonstrated that PH due to lung diseases and/or hypoxia (group 3 according to the updated classification of PH) constituted the majority of cases 43/52 (82.6%) mostly chronic obstructive pulmonary disease (COPD) 28/52 (53.8%). Echocardiography provides several variables which correlate with right heart hemodynamics including PAP, and should be used as a non invasive screening tool but not as a substitute to the RHC. Female gender, smoking, COPD and hypertension were the most prevalent risk factors for PH among the studied patients. Combination of nonspecific therapy was the mainstay in treating pulmonary hypertension. Furthermore it highlights the fact that awareness about the disease is still lacking among physicians and/or health care providers and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large and late detection continues to be a threat for optimum management of PH. Lastly it unveiled the urgent need for a large

Conflict of interest

There is no conflict of interest.

References


Demographic and clinical characteristics of pulmonary disease


