Abstract

Background: Chronic lung diseases (CLDs) are a major cause of chronic morbidity and mortality throughout the world. Many people suffer from this disease for years and die prematurely from it or its complications. Chronic lung diseases are chronic diseases of the airways and other parts of the lung. Some of the most common are asthma, chronic obstructive pulmonary disease (COPD), lung cancer, cystic fibrosis, sleep apnea and occupational lung diseases. Respiratory diseases affect all ages: children, teens, adults and elderly.

Aims of the study: This study was aimed to study and compare some demographic changes in hypoxic and non-hypoxic groups of patients with chronic lung diseases (CLDs) and to illustrate the correlations of pericardial effusion with hypoxia due chronic lung diseases and its correlation with severity of obstructive and restrictive lung diseases.

Design and method: The study was performed in Merja teaching hospital of Babylon province in the period from December 2010 to April 2012, the study included one hundred eighty two (182) patients with history of chronic lung diseases were studied clinically and by spirometry, pulse oximetry, electrocardiography and echocardiography. According to the results of oximeter, patients were divided into two groups, hypoxic and non-hypoxic group. Hypoxic group included 96 patients (mean age was 57.14±11.24, 66% was male) while the non-hypoxic group included 86 patients (mean age was 54.42±12.75, 62% was male).

Results and conclusions: The study also found that the numbers of patients with pericardial effusion (PE) were more in hypoxic group than non-hypoxic group, study also showed no significant correlation between PE and severity of hypoxia in both groups. Moreover, the study revealed no significant correlation between PE and severity of obstructive and restrictive diseases in both groups. In addition, there was significant correlation between PE and right ventricular systolic pressure (RVSP) in both groups.

Pericardial Effusion in Chronic Hypoxic Lung Diseases

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Introduction

Chronic lung diseases are a group of chronic diseases affecting the airways and the other structures of the lungs. Some of the most common are asthma, chronic obstructive pulmonary disease (COPD), lung cancer, cystic fibrosis, sleep apnea and occupational lung diseases. Respiratory diseases affect all ages: children, teens, adults and elderly. Most of these diseases are chronic in nature and all have a major impact not only on the individual with the disease, but on the family, the community, and the health care system [1]. Chronic lung diseases are divided into two types: Obstructive and restrictive lung diseases. Obstructive lung diseases are a category of respiratory diseases characterized by airway obstruction. It is generally characterized by inflamed and easily collapsible airways, obstruction to airflow, and frequent office visits and hospitalizations. Types of obstructive lung disease include; asthma, bronchiectasis, bronchitis and chronic obstructive pulmonary disease (COPD) [2]. Restrictive lung diseases are characterized by reduced lung volume, either because of an alteration in lung parenchyma or because of a disease of the pleura, chest wall, or neuromuscular apparatus. In physiological terms, restrictive lung diseases are characterized by reduced total lung capacity (TLC), vital capacity, or resting lung volume [3].

Chronic hypoxia is a condition in which tissues in the body are continuously deprived of oxygen over the course of months or years. It is typically characterized by the slow or gradual reduction in the oxygen supply of cells, tissues, and organ systems, often brought about by problems in the heart and lungs and the condition usually result in the decline of cell functions, and in the overall decline in health [4,5]. There is special character of chronic hypoxic lung diseases and PE.

Pericardial effusion is the presence of an abnormal amount of and/or an abnormal character to fluid in the pericardial space. It can be caused by a variety of local and systemic disorders, or it may be idiopathic [6].

Pericardial effusions can be acute or chronic, also it can be mild, moderate and severe or can be localized or surround all the heart and the time course of development has a great impact on the patient's symptoms. PE due to chronic hypoxic lung diseases occurs usually after development of pulmonary hypertension (PH). Treatment varies, and is directed at removal of the pericardial fluid and alleviation of the underlying cause, which usually is determined by a combination of fluid analysis and correlation with comorbid illnesses [7].

Pericardial effusion (PE) and pulmonary hypertension (PH):

The presence of pericardial effusion in PH usually represents...
advanced right heart failure and is associated with a poor prognosis. PE can be graded into small or mild (≤1 cm), moderate (2-3 cm) and large effusion (> 3 cm) [8]. Small or moderate pericardial effusion is present in up to 54% of patients [9]. Patients with cor pulmonale and circumferential pericardial effusion develop an atypical form of cardiac tamponade with isolated left heart compression. Pre-existing pulmonary arterial hypertension can modify the classic presentation. Symptoms and signs of right heart failure could already be present, so a high index of suspicion for tamponade is required in the presence of symptoms indicating worsening of right heart failure. When the pericardial pressure starts to increase in a patient with cor pulmonale, elevated pressure in right heart chambers prevent right atrial and ventricular compression, but while the pericardial pressure rises to the point to exceed left chambers pressure, this results first in diastolic collapse of left atrium and later on in left ventricle collapse due to a transient reversal of the transmural pressure. Signs of impaired filling of left ventricle ensue leading to a drop in cardiac output pressure [7, 10].

The most probable mechanism of accumulation of pericardial fluid in patients with PAH is transudation and impaired re-absorption of pericardial fluid due to elevated venous hydrostatic pressure in the setting of cor pulmonale. In the setting of PAH, large hemodynamically significant pericardial effusions might be treated surgically and/or conservative and it is known that prognosis of patients with this complication is poor [11, 12].

**Patients and Methods**

**Patients:**

The study was conducted in Merjan teaching hospital in Babylon Province during the period from December-2010 to April-2012. The study consisted of 182 patients with chronic lung diseases who were classified into two groups according to oxygen saturation (Spo2). The study was carried out on patients with chronic lung diseases (regardless of the individual diagnosis) with abnormal pulmonary function tests and history of the symptoms more than six months.

The patients involved in this study were either admitted in the wards or coming to the hospital as outpatients. Patients with a history of systemic hypertension, ischemic or valvular heart disease, or episodes of right-sided and/or left-sided cardiac failure, congenital heart disease, very poor echogenic subjects in whom meaningful echocardiographic examination could not be performed were excluded from the study, in addition to patients with anemia, chronic liver disease, peripheral vascular disease, and patient with pigment in the skin or nail.

All patients were subjected to: verbal agreement, full history, complete clinical examination, some needed investigations, packed cell volume (PCV), chest x-ray, electrocardiography (ECG), echocardiography (echo.), oxygen saturation (Spo2) as measured by pulse oximeter, and pulmonary function tests (PFT) as measured by spirometer.

According to the results of spirometry and oximetry, patients were classified into two groups. 1) **Hypoxic group** (chronic hypoxic lung disease+ hypoxemia): which involved patients with abnormal PFT along with arterial hypoxemia (Spo2 equal or less than
95% [8]). 2) Non-hypoxic group (chronic hypoxic lung disease + normoxemia): which consisted of patients with abnormal PFT and oxygen saturation more than 95%.

**Pulmonary function tests (PFTs):**

In this study, pulmonary function tests were carried out in all patients with the help of Mir spirometer connected to computer using Spirobank 2 software. It measures many parameters but we took the special parameters that are useful in differentiating obstructive from restrictive pulmonary diseases as shown in figure (1). Before doing the test, weight and height of each patient were measured then some needed informations like age, gender, race and smoking status in addition to weight and height for each patient were fed into the spirometer programme which automatically calculates the PFTs parameters that appear as predicted values according to the age, gender and race, weight and height. Three trials of the test were done for each patient until we get the result that is acceptable and reproducible. Type and severity of chronic respiratory diseases were also determined by the apparatus.

Cases that were involved in the study included patients with obstructive lung diseases that had FEV1/FVC < 70% and/or FEV1 % ≤ 80% of predicted and patients with restrictive lung diseases in which both FEV1 and FVC were reduced but the FEV1/FVC ratio was normal.

In this study, severity of obstructive diseases was graded according to FEV1% predicted while that of restrictive diseases was graded according to FVC% predicted according to table (1):

**Pulse oximetry:**

Oximetry were performed with a pulse oximeter (Spirobank 2) which records arterial haemoglobin saturation and heart rate.

To calculate the difference between full and empty capillaries, oximetry measures light absorption over a number of pulses, usually five. This causes the short delay before readings are obtained. An SpO2 of greater than 95% is generally considered to be normal [8].

**Procedure**

1. The procedure is performed by connecting the oximeter to the Mir spirometer to be switched on.
2. The hands should be clean. This will reduce transmission of microorganisms and body secretions. Anything that absorbs light may cause false-low readings and should be removed (dried blood, nail polish).
3. The probe was placed onto the finger, and the oximeter was turned on.
4. About 30 seconds was allowed for self-testing procedures and for detection and analysis of waveforms before values are displayed. Adequate arterial pulse strength is necessary for obtaining accurate SpO2 measurements. Oxygen saturation level and pulse rate are displayed in seconds on a lighted display screen. Blood pressure should also be measured and if below 90 mm Hg it results in false reading.

The pulse oximeter sensor was not applied on a finger of an arm that is using an automatic blood pressure cuff. Blood flow to the finger will be cut off whenever the cuff inflates. The most common cause of inaccurate SpO2 readings is movement.

Saturation values are averaged out over 5 to 20 seconds. The pulse rate is also calculated from successive pulsatile signals and averaged out over a similar variable period of time, depending on the particular monitor.

**Echocardiographic study:**

The echocardiography was performed for each patient using Philips (Envisor C, 2011) system (USA) echocardiographic device, with
a probe phasic array operating at 2.0 to 4 MHz, the echo examination takes about 15-20 minutes.

Transthoracic M-mode and two-dimensional images were obtained from parasternal long- and short-axis, apical four-chamber, and subcostal four-chamber views. While performing the echo test, patient was placed on supine and left lateral positions on the coach, the probe was placed on the anterior chest with use of jelly to ensure good images. In this study, a number of standard positions on the chest wall were taken that allow good penetration of ultrasound waves without too much masking by lung or ribs. These views include:

**Left parasternal view:**

**Long-axis view:** subject was placed in left lateral position, the probe placed on the anterior chest wall on the left side of the sternum and moved over the area until we get good image, the marker of the probe points to the right shoulder.

**Short-axis view:** the probe remains in the same location but the marker change to point toward the left shoulder to obtain images of the heart in transverse sections.

**Apical view:** 4-chamber view was mostly used, the probe placed at the cardiac apex and the marker point to the right shoulder. This gives the typical ‘heart-shaped’ 4-chamber view.

**Subcostal view:** patient in supine position and probe placed beneath the sternum, subject was asked to take deep inspiration and then stop in order the heart get down to be near the probe. This view was important in recording right atrial pressure by measuring inferior vena cava collapse with inspiration, also in diagnosing any interatrial septal shunt (patent foramen ovale).

In this study the following echo modes were used:

A. **Two-dimensional (2D) echocardiography:** it is used for defining anatomy, ventricular and valvular movement and for positioning for M-mode and Doppler echocardiography.

B. **Motion or m-mode echocardiography:** for measurement of dimensions.

C. **Doppler echocardiography:**

- **Continuous wave** used for determination of tricuspid regurgitation and aortic valve velocity time-integral (AV-VTI)
- **Pulsed wave** used for determination of left ventricular diastolic function.

Echocardiograms were reviewed to assess the pericardium, valvular anatomy and function, left- and right-sided chamber size, right and left ventricular ejection fraction. Tricuspid regurgitant flow was identified by color flow Doppler techniques, and the maximum jet velocity was measured by continuous wave Doppler without the use of intravenous contrast.

**Statistical analysis:**

All calculations and analysis were preformed using the Statistical Package for the Social Sciences (SPSS version 18). Clinical and echocardiographic data were expressed as mean ± standard deviation (SD) for continuous variables or as number and percentage for categorical variables. Student’s ‘t’ test was used to compare means of continuous variables between two groups. Chi square test was used to analyze categorical data and distribution of PE in both groups. For all tests p < 0.05 was considered statistically significant.

**Results**

The study involved 182 patients (96 in hypoxic group and 86 in non-hypoxic group), the non-hypoxic group acted as the control group, some needed investigations were done for exclusion like packed cell volume
(PCV) to exclude anemia and total serum bilirubin (TSB) to exclude jaundice and the results were normal in all groups. ECG was done for all patients to exclude ischemic heart disease.

**Demographic characteristics**

Table (2) shows demographic characteristics of patients in both hypoxic and non-hypoxic groups. The ages of patients ranged from 31-70 years. There was no significant difference in ages between the studied groups (P=0.152).

There was also no significant difference in gender between groups (P=0.5), most of patients were male (66% in hypoxic group and 62% non-hypoxic group).

**Pericardial effusion (PE) and its correlations:**

**Distribution of pericardial effusion in hypoxic and non-hypoxic groups:**

The study illustrated that there was significant difference in the distribution of PE between hypoxic and non-hypoxic groups as shown in table (3).

**Correlations between pericardial effusion (PE) and right ventricular systolic pressure (RVSP):**

The study illustrated significant correlation between right ventricular systolic pressure (RVSP) and pericardial effusion (PE) in both hypoxic and non-hypoxic groups as shown in tables 6 and 7.

**Correlations between pericardial effusion and severity of obstructive and restrictive diseases:**

The study also showed no significant correlation between pericardial effusion and severity of obstruction and restriction in both hypoxic and non-hypoxic groups as revealed in tables 8, 9, 10, and 11.

**Discussion**

**Patients characteristics:**

Patients that were selected for this study included those who have chronic lung diseases with a duration more than six months and they were divided into two groups (hypoxic and non-hypoxic) according to the results of oxygen saturation (Spo2), control healthy group was excluded from the study because large difference in readings between it and patients groups and this affect the results of comparisons and correlations between groups, in addition to that we studied the effects of hypoxia on patients and not on healthy population.

Patients were divided into groups according to the results of oximeter. Patients that had Spo2 equal or below 95% were put in hypoxic group, there was significant difference between both groups in oxygen saturation. In hypoxic group, only 27% had severe hypoxia (Spo2 below 90%).

There was no significant difference in the mean of ages between hypoxic and non-hypoxic groups, the mean age in hypoxic group was 57.14±11.24 while in non-hypoxic group it was 54.42±12.75.

In this study, most of patients were males in both groups, males form 66% (63/96) in hypoxic group and 62% (53/86) in non-hypoxic group. This higher incidence of diseases in males can be attributed to smoking.

**Pericardial effusion (PE) and its correlations:**

The presence of pericardial effusion has been shown to be a poor prognostic factor in several studies of patients with various forms of PAH [13, 14]. The study clarified that the number and percentage of patients who had PE was more in hypoxic group than non-hypoxic group with highly
significant differences between both groups. The percentage of patients with PE was 17% in hypoxic group, 6% in non-hypoxic group and the total percentage was 13% which was nearly similar to a study by [15] which was performed on patients with COPD and found the percentage 12% of patients. This difference in percentages between groups might be related to the effects of hypoxia. There was no significant correlation between PE and severity of hypoxia in both groups meaning that presence and severity of PE not increase with the decrease in oxygen saturation (increased hypoxia). In both groups, the patients had either no PE or mild PE, no moderate and severe PE were found and this is because severity of PE was associated with severity of RVSP and in this study only few patients got moderate and severe RVSP in both groups.

There was no correlation between PE with age and duration of symptoms, PE was associated more with RVSP than Spo2, there was highly significant relation between RVSP and PE.

Really, the physiology of the formation and removal of pericardial fluid is incompletely understood. However, fluid resorption is probably via an extensive venous circulation and a system of lymphatic plexuses that are located in the subepicardial region of the heart. These ultimately drain into the right atrium (RA) [16]. Elevation of RVSP cause elevation in RA pressure. Thus, it is likely that the pericardial effusion observed in patients with pulmonary hypertension is due to impaired venous and lymphatic drainage resulting from elevated right atrial pressure [17].

The study also showed no significant correlation between PE and severity of obstructive and restrictive diseases which could be because the severity of these diseases has no correlation with RVSP which was proved to be the cause of PE.

In the setting of PAH, a mild to moderate circumferential pericardial effusion is seen in up to half of patients, and is particularly common at the time of initial clinical presentation [18].

In general, a pericardial effusion typically indicates right heart decompensation, and is likely conferred on the basis of longstanding right atrial hypertension and impaired myocardial lymphatic drainage [19; 13].

**Conclusions**

From results of this study we conclude that there was highly significant correlation between PE and RVSP in both groups but there was no significant correlation between PE with severity of hypoxia and severity of obstructive and restrictive lung diseases in both study groups.

**Recommendations**

We recommend researchers to do further work on larger number of patients with chronic lung diseases and follow up study for those with PE to know the morbidity and mortality.

**References**

Figure 1 shows results of spirometry.

Table 1 Severity distribution in obstructive and restrictive groups

<table>
<thead>
<tr>
<th>Grade</th>
<th>Obstructive group (according to FEV1% predicted)</th>
<th>Restrictive group (according to FVC% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-80</td>
<td>mild</td>
<td>mild</td>
</tr>
<tr>
<td>40-59</td>
<td>moderate</td>
<td>moderate</td>
</tr>
<tr>
<td>&lt;40</td>
<td>severe</td>
<td>severe</td>
</tr>
</tbody>
</table>
### Table 2: Demographic characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Age (years) (mean± SD*)</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Male No. %</td>
</tr>
<tr>
<td>Hypoxic group</td>
<td>96</td>
<td>57.14±11.24</td>
<td>63  66</td>
</tr>
<tr>
<td>Non-hypoxic group</td>
<td>86</td>
<td>54.42±12.75</td>
<td>53  62</td>
</tr>
</tbody>
</table>

P value | NS** | NS | NS

*SD: standard deviation  **NS: Non-significant difference P>0.05

### Table 3: Distribution of pericardial effusion in study groups

<table>
<thead>
<tr>
<th></th>
<th>Hypoxic group</th>
<th>Non-hypoxic group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>96</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Negative</th>
<th>Positive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>80 (83)</td>
<td>16 (17)</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>81 (94)</td>
<td>5 (6)</td>
<td>86</td>
</tr>
</tbody>
</table>

P value | 0.003

### Table 4: Correlation between pericardial effusion (PE) and hypoxia in hypoxic group

<table>
<thead>
<tr>
<th>PE</th>
<th>N (96)</th>
<th>Spo2* Mean± SD**</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>80</td>
<td>91.035±4.0075</td>
<td>0.30</td>
</tr>
<tr>
<td>Positive</td>
<td>16</td>
<td>89.621±7.8087</td>
<td></td>
</tr>
</tbody>
</table>

*Spo2: oxygen saturation  **SD: standard deviation

### Table 5: Correlation between pericardial effusion (PE) and hypoxia in non-hypoxic group

<table>
<thead>
<tr>
<th>PE</th>
<th>N (86)</th>
<th>Spo2* Mean± SD**</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>81</td>
<td>96.550±0.7951</td>
<td>0.33</td>
</tr>
<tr>
<td>Positive</td>
<td>5</td>
<td>96.000±0.0000</td>
<td></td>
</tr>
</tbody>
</table>

*Spo2: oxygen saturation  **SD: standard deviation
Table 6 Correlation between right ventricular systolic pressure (RVSP) and pericardial effusion (PE) in hypoxic group

<table>
<thead>
<tr>
<th>PE</th>
<th>N (96)</th>
<th>RVSP* Mean± SD**</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>80</td>
<td>32.62±13.967</td>
<td>0.002</td>
</tr>
<tr>
<td>Positive</td>
<td>16</td>
<td>45.86±16.659</td>
<td></td>
</tr>
</tbody>
</table>

*RVSP: right ventricular systolic pressure  
**SD: standard deviation

Table 7 Correlation between right ventricular systolic pressure (RVSP) and pericardial effusion (PE) in non-hypoxic group

<table>
<thead>
<tr>
<th>PE</th>
<th>N (86)</th>
<th>RVSP* Mean± SD**</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>81</td>
<td>26.04±8.614</td>
<td>0.000</td>
</tr>
<tr>
<td>Positive</td>
<td>5</td>
<td>52.50±17.678</td>
<td></td>
</tr>
</tbody>
</table>

*RVSP: right ventricular systolic pressure  
**SD: standard deviation

Table 8 Relation between pericardial effusion (PE) and severity of obstruction in hypoxic group

<table>
<thead>
<tr>
<th>PE</th>
<th>N (96)</th>
<th>FEV1% pred. Mean± SD**</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>80</td>
<td>40.22±19.345</td>
<td>0.6</td>
</tr>
<tr>
<td>Positive</td>
<td>16</td>
<td>37.93±21.305</td>
<td></td>
</tr>
</tbody>
</table>

*FEV1% pred.: forced expiratory volume in one second as per cent predicted  
**SD: standard deviation

Table 9 Relation between pericardial effusion (PE) and severity of obstruction in non-hypoxic group

<table>
<thead>
<tr>
<th>PE</th>
<th>N (86)</th>
<th>FEV1% pred. Mean± SD**</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>81</td>
<td>66.76±14.760</td>
<td>0.1</td>
</tr>
<tr>
<td>Positive</td>
<td>5</td>
<td>50.50±21.920</td>
<td></td>
</tr>
</tbody>
</table>

*FEV1% pred.: forced expiratory volume in one second as per cent predicted  
**SD: standard deviation
Table 10  Relation between pericardial effusion (PE) and severity of restriction in hypoxic group

<table>
<thead>
<tr>
<th>PE</th>
<th>FVC% pred.* Mean±SD**</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>73.04±31.996</td>
<td>0.9</td>
</tr>
<tr>
<td>Positive</td>
<td>72.00±30.705</td>
<td></td>
</tr>
</tbody>
</table>

*FVC% pred.: forced vital capacity as per cent predicted
**SD: standard deviation

Table 11  Relation between pericardial effusion (PE) and severity of restriction in non-hypoxic group

<table>
<thead>
<tr>
<th>PE</th>
<th>FVC% pred.* Mean±SD**</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>95.81±23.534</td>
<td>0.08</td>
</tr>
<tr>
<td>Positive</td>
<td>66.50±40.305</td>
<td></td>
</tr>
</tbody>
</table>

*FVC% pred.: forced vital capacity as per cent predicted
**SD: standard deviation
Figure 3-9 (A) Gel electrophoresis of PCR of lukED amplicon product. Lane (S7, 8, 13, 15, 2, 22, 23, 26, 28, 31, 32, 36, 37, 41, 57, 59, S3, 17, 29, 36), Lane (B95), Lane (Ul60) isolate from ulcer, Lane (W79) isolate from wound. (B) Gel electrophoresis of Multiplex PCR of mecA and lukED amplicon product. Lane (S2, 7, 3, 13, 36) no. of isolates from skin, Lane (U173, U175) no. of isolates from urine, isolate from burn.