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Original Research Paper

A Correlative Study of Spirometric Parameters, ECG Changes, Lipid Profile and Diabetes in Chronic Obstructive Pulmonary Disease

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Introduction

Globally, about 3 million deaths occur every year because of this dreadful disease and the prevalence is increasing because of the mounting problem of tobacco smoking and it is projected that the deaths because of COPD will increase by 30% in the next 10 years. Moreover, above 90% of these deaths occur in middle and low income countries. Since the airway obstruction caused by COPD is irreversible and the available treatment modalities can only slow the progression of this disease, prevention is the only choice for control of COPD.

Exclusion criteria

Patients with known conditions like Bronchial asthma, congenital or acquired heart diseases, Bronchectasis, Pulmonary tuberculosis were excluded. Also patients with known Diabetes mellitus and Hypertension and Patients taking hypolipidemic drugs are also excluded

Depending upon the clinical symptoms and arterial blood gas findings COPD patients are divided into two extreme presentations. They are as follows:

1) Type A patients (pink puffers)
   - Have severe dyspnoea
   - Normal or low $PaCO_2$
   - Only a mild decrease in PaO_2 at rest and low DLCO
   - Hypoxaemic only at late stages, so no pulmonary hypertension, cor pulmonale, fluid retention and secondary polycythemia
   - Predominantly emphysematous type

2) Type B patients or blue bloaters
   - Cough with sputum production
   - Likely to develop hypoxemia and hypercapnia early
   - Hence pulmonary hypertension, cor pulmonale, fluid retention and secondary polycythemia are present
   - Predominantly bronchitic type

Have double the risk of mortality than type A patients[19]

Spirometry[29]

It is a Volume-Time curve and now-a-days it is computerized and the values are read in relation to the reference values. It is the robust test to identify the limitation of airflow in COPD. Decrease in FEV_1 with a decrease in FEV_1/FVC ratio is the most definitive criteria for diagnosis of COPD.

It is a simple non-invasive test to measure the amount of air a person can breathe out and the amount of time taken to do so.

1) FEV_1 (Forced expiratory volume in 1 second):

- The rate of decline in FEV_1 usually correlates well with severity of COPD, progression of the disease, reversibility of COPD, and susceptibility in cigarette smokers.
- It is also influence by age, sex, height and ethnicity and is best interpreted as the percentage of the predicted normal value.
- Above 55 years, in males it is usually 2.14 liters and in females 1.39 liters[30].

2) FVC (forced vital capacity)

- Above 55 years, in males it is usually 2.7 liters and in females 1.68 liters[30].

3) FEV_1/ FVC ratio:

- Above 55 years, in males it is usually 80% and in females 83%[30].
- In normal adults it is between 70 to 80% and the value of < 70% indicates the airflow limitation and COPD.

GOLD stage	Severity	Spirometry findings	Symptoms
0	At risk	Normal	Chronic cough, sputum production
I	Mild	$FEV_1 \geq 80\%$ predicted and $FEV_1/FVC < 0.7$	With or without chronic cough or sputum production
II	Moderate	$FEV_1 \geq 50\%$ but < 80% predicted and $FEV_1/FVC < 0.7$	With or without chronic cough or sputum production
III	Severe	$FEV_1 \geq 30\%$ but < 50% predicted and $FEV_1/FVC < 0.7$	With or without chronic cough or sputum production
IV	Very severe	FEV_1< 30% predicted and $FEV_1/FVC < 0.7$ Or FEV_1< 50% predicted with respiratory failure or signs of right heart failure	With or without chronic cough or sputum production

Effect of COPD on ECG recording[35,36,37,38,39,40,41,42]

The following are the changes in the electrical events of the heart

- The insulating effect of the voluminous lungs diminishes the transmission of electrical potentials to the registering electrodes
- The heart descends to the lower position in the thorax and this will alter the relative position of the electrodes as well.
- The right atrium and right ventricle become compromised because of the reduction of pulmonary vascular bed.

All these above mentioned changes lead to following manifestations

- Decreased magnitude of ECG deflections

The QRS and T wave deflections are diminished and there is loss of R wave amplitude in the precordial leads. The QRS axis tend to be oriented more obliquely to horizontal plane. The p waves however may beincreased in leads II, III and aVF due to right deviation of frontal p wave axis.

- Changes because of right atrial enlargement

1. The p wave axis is deviated towards the right of +60□□□It is commonly deviated to +90□
2. P pulmonale is reflected by tall and peaked p waves in leads II, III, and aVF and is due to right atrial enlargement. The p wave is directed away from the positive pole of lead aVL and thus be negative in their lead, the height of p wave will be □2.5mm.

- Abnormalities of QRS complex

1. There is frontal plane of QRS is commonly directed to +90degreesand because of pulmonary hypertension it may deviate to +120 degrees or even +150 degrees. This plane leads to S1Q3R3 pattern.

2. Sometimes it may be deviated towards left axis in 10% of cases between -60 degrees to -90 degrees.
3. The terminal S waves are prominent in leads I, II and III giving rise to S1,S2 and S3 syndrome. This reflects the posterior displacement of apex and sometimes in leads V4 to V6, wide and slurred S waves may appear.
4. The mean QRS axis can be displaced posteriorly so that it is more oblique to the horizontal plane.
5. The precordial QRS complexes are diminished and there is general loss of R wave amplitude in all precordial leads. Commonly all precordial leads show rs complexes. In severe cases, in leads v4 to v6, R/S may be less than 1mm and R wave amplitude in lead V6 may be less than 5 mm.
6. Occasionally, complete or incomplete right bundle branch block occurs and this may be transient during an acute exacerbation of emphysema or increase in oxygen desaturation.

- T wave abnormalities
  1. The frontal plane T wave axis is usually similar in direction to QRS axis and is commonly directed to +80 degrees to +90 degrees. This can be seen in lead I showing small T wave when compared to T wave in lead III.
  2. The T wave in overall is diminished in all leads and precordial leads show flat or slightly positive T waves.Inverted T wave can be seen in precordial leads when pulmonary hypertension is present. QT interval is not prolonged in cor pulmonale unlike other forms of heart failure.

ECG evaluation of pulmonary function

Increasing severity of COPD with increasing deterioration of lung function is reflected in ECG by the following changes:

1. Progressive right QRS axis deviation which in sometimes may reach right superior quadrant in severe cases
2. Progressive right axis deviation of P wave
3. R:S ratio becomes less than 5 mm in lead V6
4. There is increasing amplitude of P wave in leads II, III and aVF
5. Noticeable and pronounced Ta wave develops in leads II, III and aVF.

Lipid profile in COPD

Cigarette smoking is clearly the single most causative factor in COPD and about 85% of COPD is attributed to cigarette smoking[44]. Smoking affects lipid profile in the following ways:

1. The plasma α1 lipoprotein, cholesterol and triglycerides concentration are higher
2. HDL cholesterol is lower in smokers
3. Free fatty acid concentration tends to be variable but immediate increase of FFA occurs after inhalation of smoking due to stimulation of adrenal medulla
4. Nicotine increases the concentration of epinephrine in plasma and urinary excretion of catecholamines and their metabolites.
5. Plasma 11-hydroxycorticosteroids may be increased by 75% with heavy smoking.
6. Plasma cortisol concentration increases by 40% within 5 minutes of start of smoking
7. Smokers excrete more 5-hydroxy indole acetic acid than do non-smokers.

The following table shows the changes in concentration of various biochemical parameters due to smoking:

Parameter	Change in percentage
Albumin	3
Cholesterol	4
Glucose	10
Phospholipids	20
Triglycerides	20
Urea nitrogen	10

In a study done in USA, 1994, it was observed that higher HDL is associated with better lung function and total cholesterol had no association

while lower LDL was associated with better lung function.

According to Cirillo et al, increase in HDL was associated with increase in FEV_1 of 43ml and icrease in LDL decreased FEV_1 by 24ml and this was attributed to attenuation of inflammation by HDL and oxidative burden by LDL.

Fekete et al observed that triglycerides were lower in COPD females and Iribarren et al observed a significant inverse relationship between serum cholesterol and risk of death (upto 25%) in COPD patients.

Marquis et al found out that metabolic syndrome was much frequent in individuals with COPD as there was a overlap in the causative risk factors. On the contrary, Bahar et al observed there was no atherogenic lipid pattern in COPD patients and concluded that increased HDL levels can be due to the effect of drugs used for COPD.

Floren et al studied the lipid profile of COPD patients and found that increased HDL cholesterol was due to drugs like bambuterol as it increases the synthesis of HDL in liver and intestinal wall.

Diabetes and COPD[45,46]

There are many controversies between the interlinkage of type 2 diabete and COPD and either way COPD can predispose an individual to diabetes and concersely type II DM can also be a risk factor for development of COPD and has a influential role in outcomes of COPD

Hypoxia and glucose metabolism

Pancreatic beta cells may be damaged by hypoxia and hypoxia inducible factor plays a vital role and also long standing hypoxia affects the skeletal muscle insulin sensitivity affecting the uptake of glucose by muscles. Hypoxia causes increased epinephrine release and can cause glucose intolerance. Hypoxia also affects the adipocytes and decreases the production of adiponectin and increases plasminogen activator inhibitor-1 (PAI-1).

Hypoxia also causes increase in HIF-1alpha which induces adipose tissue fibrosis and insulin resistance. In muscles hypoxia causes damage to mitochondria and causes insulin resistance and also COPD patients show a shift in skeletal muscle fiber.

Also in COPD, the release of catecholamines are increased and thus they are prone for hyperglycemia. In addition, COPD patients have high levels of aldosterone and renin activity along with high vasopressin. Studies like Rana et al, Song et al, Feary et al and Bolton et al showed the positive relationship between COPD and further development of DM and all these studies show that individuals with COPD are at increased risk of diabetes. Patients with COPD had higher levels of insulin levels and inflammatory markers like CRP, IL-6 and receptors for TNF-α.

Effect of Diabetes on COPD[47]

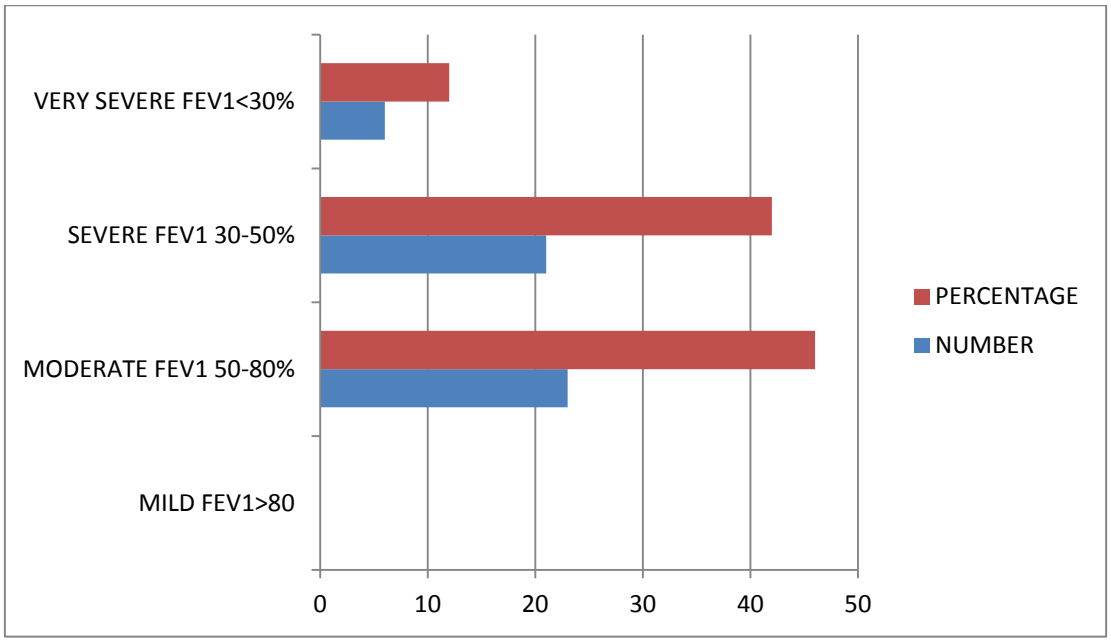
Diabetes independently affects the lung function and structure negatively and moreover diabetes can cause muscle and neuronal damage which reduces the lung function by affecting the respiratory muscles. It generally lowers the physical performance of the individuals and more so in case of COPD.

Diabetes affects the alveolar capillary membrane detrimentally and decreases the DLCO and $FEV_1$and similar to other microangiopathic conditions it causes vessel damage and hence the pulmonary vasculature becomes targeted.

Further diabetes is associated with presence of glucose in airway secretions and hence there is a high risk of pulmonary infections which can be deadly in COPD patients. Hence, diabetes is usually associated worse clinical outcomes in individuals with COPD. In addition patients with metabolic syndrome and obstructive sleep apnea syndrome have worse outcomes of COPD.

Moreover smokers with diabetes tend to have worsened alveolar gas exchange leading to hypoxia and changes in the alveolar membrane and capillary bed occurs secondary to diabetes. The pro-inflammatory state in DM with elevated fibrinogen and other inflammatory markers are risk factors for exacerbations frequently in COPD. Furthermore, anti-hyperglycemic medications improve DLCO and metformin and thiazolidine-diones improve FVC in diabetic patients.

FEV1/FVC %	NO.OF RESPONDANTS (n=50)	PERCENTAGE (100%)
Below 40%	1	2
41-50%	9	18
51-60%	19	38
61-70%	21	42



ECG CRITERIA	NO.OF RESPONDANTS (n=50)	PERCENTAGE (100%)
P wave axis >90 degrees	35	70
QRS axis >90 degrees	28	56
P wave height >2.5mm in lead II	25	50
R wave V1 >7 mm	3	6
R wave V6 < 5mm	19	38
Normal ECG	13	26

PARAMETER	MEAN VALUE	SD
Total cholesterol	188.62	33.708
HDL	38.66	9.503
VLDL	32.40	19.337
LDL	124.87	24.451
Triglycerides	138.26	45.645

Correlation of blood sugar levels with FEV1%

FBS >126mg% & PPBS>200mg%	NO.OF RESPONDANTS (n=50)	PERCENTAGE (100%)
YES	15	30
NO	35	70

Conclusion

Spirometry is the investigation to diagnose and stage COPD.

Smoking is associated with COPD and considered as a major risk factor.

Smoking cessation slow down the degree of pulmonary function deterioration and hence every patient should be adviced to quit smoking.

ECG changes correlated with severity of COPD and so ECG can be used as a bedside test for assessing severity.

Since smoking is also associated with dyslipidemia, there is no strong correlation between dyslipidemia and COPD severity.

There is increased prevalence of diabetes as the severity of COPD increases and presence of diabetes in COPD patients is associated with higher risk of hospitalization and mortality.

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