ORIGINAL RESEARCH

To study the correlation of venous blood lactate level and 6 minute walk test in stable COPD Patients in tertiary health care centre

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ABSTRACT
Aim: To study the correlation of venous blood lactate level and 6 minute walk test in stable COPD Patients in tertiary health care centre
Materials & methods: Study was conducted on 50 patients from the Department of Respiratory Medicine at Index Medical College, Research centre and Hospital, Indore and all the tests was perform with due permission from the Institutional Ethical Committee and informed consent from the subjects or their legal relatives. Subjects was included on the basis of their diagnosis of COPD as per GOLD guidelines & laboratory test of venous blood lactate level.
Result: Fifty participants were recruited and 74% of them were male. The median age of all the participants was 60.48 years. Based on the Severity classification, 12(24%) of them were mild, 21(42%) moderate, 7(14%) severe and 10(20%) very severe. The participants were under regular treatment. The median of 6MWT was 280.00 m (IQR 67-53.25, 375–205 m). For Normal Lactic acid the Mean 6MWT was 336.75 mtrs for 12 samples of Group A of COPD Severity Group, 20 of Group B, 4 of Group C & 1 of Group D. For Abnormal Lactic acid the Mean 6MWT was 171.92 mtrs for 0 samples of Group A of COPD Severity Group, 1 of Group B, 3 of Group C & 9 of Group D.
Conclusion: In conclusion, in COPD patients 6MWT is useful test to assess severity of disease. Our study has shown that 6MWT correlates well with pulmonary function and quality of life in patients with COPD. 6MWT can be used as a novel index in the evaluation of functional status of COPD. More importantly, steps might give additional indication in addition to distance traveled about the risk of lung hyperinflation. Considerably more work will be needed to investigate the link between steps and hyperinflation in patients with COPD.
Keywords: COPD, 6MWT

Introduction
As the fourth biggest cause of death, chronic obstructive pulmonary disease is becoming more and more important for global public health. Estimations of Global Initiative for Chronic Obstructive Lung Disease (GOLD) suggest that COPD will rise to the third most common cause of death worldwide by 2020. Not only a leading cause of death, following a late diagnosis of COPD, majority of the patients experience a temporary or permanent decrease in the quality of life.[1-4] In this modern era smoking rate is high among young generation, still women using chulla in homes, industrial workers working unprecautionally in industries lead to early age Chronic Obstructive Pulmonary Disease (COPD) and increase the prevalence and mortality rate of COPD. [4,5] Lung

parenchyma, pulmonary vasculature, and central and peripheral airways all exhibit pathological alterations that are typical of COPD. Chronic airflow limitation is attributed to the narrowing of the small airway lumen due to morphological changes and a decrease in lung elastic recoil due to parenchyma destruction. At present, although pulmonary function testing (PFT) is still the accepted standard for the confirmation and clinical grading of COPD, the results can be affected by a patient's age and other health factors, and PFT is associated with a relatively large margin of error. Additionally, in some patients with already abnormal small-airway function (diameter 2 mm), particularly in the early stages of the disease, PFT may be normal.[6]

Materials & methods
All patients >40 years of age admitted in Chest ward of Index Medical College, Indore with diagnosis of a COPD between JAN 2021 to MAY 2022 .Study was conducted on 50 patients from the Department of Respiratory Medicine at Index Medical College, Research centre and Hospital, Indore and all the tests was perform with due permission from the Institutional Ethical Committee and informed consent from the subjects or their legal relatives. Subjects was included on the basis of their diagnosis of COPD as per GOLD guidelines & laboratory test of venous blood lactate level.

Inclusion Criteria :
Ill patients older than 40 years of both sexes admitted to the respiratory ward.

Exclusion Criteria :
*   Patients younger than 40 years.
*   Use of any of these therapeutic interventions such as epinephrine, methformin, nucleoside analogs in HIV and high volume hemofilteration(HVHF) with lactate buffered replacement fluids.
*   Patients with acute renal failure or acute pancreatitis.

Results
The subjects were in the age range of 40 to 70 years with a Mean age of 60.48 and Standard Deviation of 10.06, out of which 37 were Males & 13 Females. The majority lies in the age group of 40 – 60 years (20 in nos,; 40% of the total sample). The Sample size of 50 has 13 Female Patients & 37 Male Patients for Study. Male patients formed 74% of the total and were observed as some were smokers, whereas, female patient were all non-smokers.

Table 1 : Chronic obstructive pulmonary disease severity grade

Group	Frequency	Percentage
Group A (Mild)	12	24%
Group B (Moderate)	21	42%
Group C (Severe)	07	14%
Group D (Very Severe)	10	20%

The sample has 42% (21 patients) in Group B Moderate and 24% (12 patients) in Mild Category. The Very Severe Group covers 20% (10 patients) from the Total.

Table 2 : Smoking habits

Smoker	Frequency	Percentage
NO	16	32%
YES	34	68%

The Smokers were 34 in total and all were Males. All the Female patients were non- smokers. The 32% samples are non-smokers, including all female patients. Out of remaining 68%, 12 (24%) patients, all male, were in the habit of smoking 31– 40 packs per year. packs per year. The 10% (5 patients) of the patients were smoking8 – 10 packs per year.

Table 3 : Chest x-ray findings of copd patients

Result	Frequency	Percentage
ABNORMAL	39	78%
NORMAL	11	22%

The Chest X-Ray findings of COPD were found to be Abnormal in 78% (39 patients). These COPD findings were because of various reason in addition to Smoking also. As 9 out of 13 female patients, all non-smokers revealed Abnormalities in their Chest X- ray. Out of the sample size of 50 (100%0, 6 (12%) were under the category of Obese & 13 (26%) were under-weight. 4 females were under-weight & 2 female patients were Obese, and 9 male patients were under-weight & 4 male were Obese.

Table 4 : mMRC GRADE DISTRIBUTION

mMRC Grade	Frequency	Percentage
0	7	14%
1	16	32%
2	14	28%
3	10	20%
4	3	6%
MEAN 1.72 ± 1.13		

mMRC (Modified Medical Research Council) Dyspnoea Scale is taken as 5 Grades 0,1,2,3,4. The samples falling in Grade 1 - Dyspnoea when hurrying or walking up a slight hill : are the highest 16 (32%) and lowest being in Grade 4 - Too dyspnoeic to leave house or breathless when dressing : only 3 (6%), out of total 50 patients.

Table 5: Gender wise 6 minute walk test

6MWT Grades	Frequency	Total Percentage
< 101	2	4%
101 - 200	11	22%
201 - 300	17	34%
301 - 400	10	20%
> 400	10	20%

The 6 minute Walk Test were done for all the Patients; out of the 50 patients list, maximum 17 (34%) patients covered a distance between 201 – 300 mtrs. The minimum distance of less than 100 mtrs were covered by only 2 patients.

Table 6 : Age v/s gender distribution

Age Group	Gender	Frequency	Percentage	Mean
40 - 50 yrs	Male	7	14%	44.75 ± 2.82
	Female	2	4%	
51 - 60 yrs	Male	9	18%	55.27 ± 2.71
	Female	4	8%	
61 - 70 yrs	Male	15	30%	65.25 ± 2.71
	Female	6	12%	
> 71 yrs	Male	6	12%	76 ± 4.62
	Female	1	2%	

The maximum Male 15 (30%) falls in the age group of 61–70 years; The minimum age of Male patients is 41 years & maximum being 84 years; female patients are 43 years & maximum age of 73 years. All 13 Female patient are Non-Smokers with 3 male Patients. Remaining 34 male patients are all Smokers. The Chest X-Ray findings of COPD were found to be Abnormal in 78% (39 patients). Out of these, 30 (60%) are Male patients. 7 male patients had their Chest X-ray Normal for findings of COPD. These COPD findings were because of various reason in addition to Smoking. As 9 out of

13 female patients, all non-smokers revealed Abnormalities in their Chest X-ray. Out of 50 sample size, maximum of 16 (32%) of Male patients covered a distance of 201 – 300 mtrs.; with only 1 female patient. No female patient covered less than 100 mtrs.; 4 female & 6 male patients covered more than 400 mtrs.

Table 7 : Age-wise COPD severity distribution

Age Group	Gender	Group A	Group B	Group C	Group D
40 - 50 yrs	Count	1	5	2	0
	%	2%	10%	4%	0%
50 - 60 yrs	Count	2	7	1	5
	%	4%	14%	2%	10%
60 - 70 yrs	Count	6	8	3	3
	%	12%	16%	6%	6%
>= 70 yrs	Count	3	1	1	2
	%	6%	2%	2%	4%

The COPD Severity Group of Very Severe Grade has 10 patients [5 from age group of 50 – 60 yrs; 3 from 60 – 70 yrs& 2 from 70+ yrs.] Group A (Mild) comprised of 12 patients; Age group of 60 – 70 yrs has 6 patients in Group A, 8 patients in Group B (moderate) and 3 each in Group C & D resp.

Table 8 : gender-wise COPD severity group distribution

Gender	Gender	Group A	Group B	Group C	Group D
	Count	5	4	3	1
Female	%	10%	8%	6%	2%
	Count	4	11	18	4
Male	%	8%	22%	36%	8%

Group D (very Severe) has 4 Male patients & 1 Female patient. Group C (Severe) has 18 Male patients & 3 Female patients. Group A (Mild) has 4 Male & 5 Female patients. Group B (Moderate) has 11 Male patients & 4 Female Patients.

Table 9 :COPD severity group in smokers

Smoking Habits	Gender	Group A	Group B	Group C	Group D
	Count	6	7	2	1
NO	%	12%	14%	4%	2%
	Count	6	14	5	9
YES	%	12%	28%	10%	18%

The Smokers group falls more in Group B : 14 in numbers, followed by Group D - 9 patients; 6 patients in Group A and 5 in Group C.

Table 10 : lactic acid values v/s copd severity group

COPD Severity Group v/s Lactic Acid Report						F	p-value
Lactic Acid		Group A	Group B	Group C	Group D	F	p-value
NORMAL	Count	12	20	4	1	2.60	0.158
	%	24%	40%	8%	2%		
ABNORMAL	Count	0	1	3	9	4.69	0.073
	%	0%	2%	6%	18%		

The patient having Normal Lactic acid falls in Group A (12) & Group B (20); The patient with high Lactic acid falls in Group D (9) & Group C (3). Although the Lactic acid is Normal, Group C & Group D has 4 & 1 patient respectively. Whereas Group A patient has no abnormal Lactic acid patients, whereas Group B has 1 patient.

Table 11 : Chest x-ray finding v/s COPD severity

COPD Severity Group v/s CXR COPD Findings						F	p-value
CXR Findings		Group A	Group B	Group C	Group D	F	p-value
NORMAL	Count	8	3	0	0	2.12	0.1954
	%	16%	6%	0%	0%		
ABNORMAL	Count	4	18	7	10	10.48	0.0177
	%	8%	36%	14%	20%		

The Abnormal Chest X-ray i.e. with findings of COPD covered maximum of 18 patients in Group B (Moderate) and 10 in Group D (Very Severe). Normal Chest X-Ray covered 8 in Group A (Mild) category & 3 in Group B (Moderate) with nil in Severe & Very Severe Categories. The under-weight patients, totaling 13 in numbers, has 4 patients in Group D, 3 in Group A; No patient in Obese category is in Group D of COPD Severity. A total of 6 Obese patients falls in Group A (1), Group B (2) & Group C (3). Except the Obese category, all the findings are Non-significant (less than .05)

Table 12 :mMRC grades v/s COPD severity group distribution

COPD Severity Group v/s mMRC Grade					F	p-value
mMRC Grade	Group A	Group B	Group C	Group D	F	p-value
0	7	0	0	0	1.000	0.3559
1	5	11	0	0	2.341	0.1768
2	0	10	4	0	2.194	0.1890
3	0	0	3	7	2.272	0.1823
4	0	0	0	3	1.000	0.3559

Table 13: 6 Minute walk test v/s COPD severity group distribution

COPD Findings Group v/s 6 minute Walk Test						F	p-value
6MWT Grades		Group A	Group B	Group C	Group D	F	p-value
< 101	Count	0	0	0	2	1	0.35
	%	0%	0%	0%	4%		
101 - 200	Count	0	0	4	7	2.61	0.15
	%	0%	0%	8%	14%		
201 - 300	Count	2	11	3	1	3.45	0.11
	%	4%	22%	6%	2%		
301 - 400	Count	1	9	0	0	1.31	0.29
	%	2%	18%	0%	0%		
> 400	Count	9	1	0	0	1.31	0.29
	%	18%	2%	0%	0%		

11 Patient belonging to Group B covered a distance of 201 – 300 mtrs in 6 minute Walk Test. 9 patient from the same Group covered 301 – 400 mtrs. 7 patients in Group D covered a distance of 101 – 200 mtrs.

Table 14 :6 MINUTE WALK TEST V/S LACTIC ACID VALUES

6MWT	Lactic Acid Values	Count	%
< 101	2.80	2	4%
101 - 200	2.50	10	20%
201 - 300	1.70	17	34%
301 - 400	1.00	12	24%
> 400	0.60	9	18%

Patients in study with Normal Lactic acid covered a distance of more than 350 mtrs. With COPD severity & Abnormal Lactic acid, patient covered less than 200 mtrs.

Discussion

The ability to walk for a distance is an easy way to measure exercise capacity in patients with cardiac and pulmonary diseases. 6MWT is found to be an effective way of assessing exercise tolerance. There have been few studies correlating 6MWD with spirometry in different chronic pulmonary diseases like ILD, COPD. However, there has been no comprehensive study which correlates both the 6MWD as well as pre and post exercise arterial blood gases with spirometry parameters in all the chronic pulmonary diseases as a whole. Besides there has also been no study that removes the confounding factors like age, gender, weight and height while correlating the 6MWD with chronic pulmonary diseases. In our study these confounding factors were removed by calculating percent predicted 6MWD using Enright et al., formula and Indian reference equation [7,8].In our study the 6 minute Walk Test were done for all the Patients; out of the 50 patients list, maximum 17 (34%) patients covered a distance between 201 – 300 mtrs. The minimum distance of less than 100 mtrs were covered by only 2 patients. Group A & Group B of COPD severity have 12 & 20 samples having Normal Lactic acid; The patient with high Lactic acid falls in Group D (9) & Group C (3). Enright PL et al was done similar study.[7]The Global Initiative for Chronic Obstructive Lung Disease (GOLD) defined COPD as "a common preventable and treatable disease characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and co morbidities contribute to the overall severity in individual patient".[9] in our study the Normal Lactic acid values, Mean distance covered in 6MWT is 341.38 mtrs with 36 samples. The normal Lactic acid values samples have 3 samples from Group C & 1 from Group D. For Abnormal Lactic acid values, it was 171.78 mtrs with sample size of 14, comprising of Group C & Group D of COPD Severity Grade, except 1 from Group B. The observation of wide range of values of Venous Lactate levels can be attributed to the small sample size and unequal distribution levels of Airflow Limitation among the study population. It is further observed that the baseline venous blood lactate levels do not show any significant correlation with increasing Stage of COPD. It suggests that the mechanisms regulating lactate concentration were unaffected by the increasing degree of damage found in COPD. Though it has been stated in literature that the lactate level at rest in COPD is higher than that of healthy individuals, it does not necessarily imply that the values of Baseline Lactate levels would increase in line with the degree of pulmonary damage. [10] This finding was in line with that of other authors.[11,12 However the Net Change in lactate levels after stress of sub maximal exercise (Six Minute Walk Test) showed significant positive correlation with progressively higher stages of COPD.The mMRC grade of +1 [Dyspnoea when hurrying or walking up a slight hill] contributed to the maximum of 16 (32%) sample size, followed by mMRC grade of +2 [Walks slower than people of the same age because of dyspnoea or has to stop for breath when walking at own pace] – 14 (28%) samples. Minimum was for grade +4[Too dyspnoeic to leave house or breathless when dressing] – only 3 (6%) Samples. In 6 minute Walk Test, the maximum is for the 201 – 300 Group with 13 (26%) Males and minimum 2 (4%) Males in < 101 6MWT Group. Females contributed to 4 (8%) each in 201 – 300 &> 400 6MWT group, followed by 3 in 301 – 400 & 2 in 101 – 200 Group respectively. No female patient covered less than 100 mtrs.; 4 female & 6 male patients covered more than 400 mtrs. A similar study was done by Forey BA et al. [13]The postulated etiology for significant rise in lactate levels are altered muscle morphology, altered metabolic regulation of muscle, an impaired oxidative phosphorylation and ATP resynthesis, with early activation of anerobic glycolysis within the contracting muscles. Tobacco smoking is the main cause of obstructive pulmonary disease.[13] Other important environmental factors associated with COPD are outdoor air pollution, occupational exposure to dusts and fumes, biomass smoke inhalation, exposure to second-hand smoke and previous tuberculosis. [14] While it was not our aim to compare the behavior of COPD patients with that of healthy individuals, but rather the impairment seen with COPD progression, the use of a control group could have provided other important information. Equally so, it would have been better had the groups representing different levels of obstruction contained a greater number of homogeneous individuals.

Conclusion

In conclusion, in COPD patients 6MWT is useful test to assess severity of disease. Our study has shown that 6MWT correlates well with pulmonary function and quality of life in patients with COPD.

6MWT can be used as a novel index in the evaluation of functional status of COPD. More importantly, steps might give additional indication in addition to distance traveled about the risk of lung hyperinflation. Considerably more work will be needed to investigate the link between steps and hyperinflation in patients with COPD.

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