Introduction
1: INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) has been seen as a multi-systemic rather than a respiratory system disease \(^{(1)}\). It is acknowledged that the inflammation which occurs and installs in COPD leads to remodeling of the airway, with consequent impaired pulmonary mechanism and obstructed air flow \(^{(2)}\).

Chronic obstructive pulmonary disease (COPD) has been variously labeled in the past as chronic bronchitis (CB) and emphysema, chronic nonspecific respiratory disease, chronic airway obstruction (CAO), chronic airflow limitation (CAL) and chronic obstruction lung disease (COLD) depending upon the understanding of the pathophysiology and clinical features of the syndrome of chronic cough and/or airways obstruction. It is only in the last century that the disease has been better understood. Yet, the confusion in the terminology has persisted till now. COPD is presently accepted as an overall umbrella term for a variety of clinical disorders with chronic bronchitis at the one and emphysema at the other end of the spectrum \(^{(3)}\).

Globally, COPD has emerged as the major cause of morbidity and mortality expected to become the 3\(^{rd}\) most leading cause of death and the 5\(^{th}\) leading cause of loss of ‘Disability Adjusted Life Years’ (DALYs) as per projection of the Global Burden of Disease Study (GBDS). The region-wise projections for the developing countries including India were even worse \(^{(3)}\).

Extra pulmonary manifestations in COPD, in addition to pulmonary component, are common. It has been observed in the ECLIPSE study that co morbidities were significantly higher in patients with COPD than in smokers and never smokers \(^{(4)}\). The important co morbidities associated with COPD are cardiovascular disorders (coronary artery disease and chronic heart failure, hypertension),
metabolic diseases (diabetes mellitus, metabolic syndrome and obesity), bone disease (osteoporosis and osteopenia), stroke, lung cancer, cachexia, skeletal muscle weakness, anemia, depression and cognitive decline \(^{(5)}\) \(^{(6)}\).

Worldwide, COPD affects 329 million people or nearly 5% of the population. In 2011, it ranked as the fourth leading cause of death, killing over 3 million people \(^{(7)}\). The number of deaths is projected to increase due to higher smoking rates and an aging population in many countries \(^{(8)}\) which has resulted in an estimated economic cost of $2.1 trillion in 2010 \(^{(9)}\).

It is generally known that a substantial portion of patients with chronic obstructive pulmonary disease (COPD) develop lactic acidosis early in exercise and at very low work rates \(^{(10)}\) \(^{(11)}\) \(^{(12)}\). Lactic acidosis is unfavorable, since it puts additional stress on these patients’ limited ventilatory system during exercise. Recently, evidence has become available that a reduced oxidative capacity of skeletal muscle correlates with the accelerated lactate (La) response to exercise in COPD \(^{(13)}\).

It has been described that COPD patients develop early lactic acidosis during lower limb exercises, which enhances the ventilator output and imposes certain limits to the exercise tolerance \(^{(14)}\).

1.1: EXERCISE AND LACTATE

The effect of lactate production on acidosis has been the topic in the field of exercise physiology. The production of lactate does result in a hydrogen ion, potentially resulting in a fall in pH. However, the hydrogen ion is quickly buffered by bicarbonate which forms an intermediary in the blood stream which is quickly converted into water and carbon dioxide. CO\(_2\) is transported to the lungs and exhaled to
maintain acid-base status. This is the reason for the increased respiratory rate with the accumulation of lactate in the blood.

This process can be written as chemical equation:

\[
\text{Lactic Acid} \rightarrow \text{dissociates} \rightarrow \text{Lactate} + \text{H}^+
\]

\[
\text{H}^+ + \text{HCO}_3^- \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{H}_2\text{O} + \text{CO}_2 \quad (\text{CO}_2 \text{ is expired by the lungs to maintain pH}).
\]

The bicarbonate buffering system is extremely efficient at removing the acidifying hydrogen ion and expelling it from the body in the form of carbon dioxide. The only remaining by product of anaerobic metabolism is lactate.

Increase in partial pressure of CO₂, PCO₂ also causes an increase in [H⁺]. During exercise, the intramuscular lactate concentration and PCO₂ increase, causing an increase in [H⁺], and thus a decrease in pH. Strenuous anaerobic exercise causes a lowering of pH and pain, called acidosis.

The by-product of anaerobic glycolysis, lactate, has traditionally been thought to be detrimental to muscle function. However, this appears likely only when lactate levels are very high. Elevated lactate levels are only one of many changes that occur within and around muscle cells during intense exercise that can lead to fatigue. Fatigue, that is muscular failure, is a complex subject. Elevated muscle and blood lactate concentrations are a natural consequence of any physical exertion. The effectiveness of anaerobic activity can be improved through training \(^{(15)}\) \(^{(16)}\).

- At slightly higher exercise intensity than lactate threshold a second increase in lactate accumulation can be seen and is often referred to as the onset of blood lactate accumulation or OBLA. OBLA generally occurs when the concentration of blood lactate reaches about 4mmol/L \(^{(17)}\).
Owing to its major and better recognized burden from both individual and societal perspectives, chronic obstructive pulmonary disease (COPD) is an area of intensive epidemiological, fundamental and clinical research, leading to the publication of more than 10,000 papers each year in the PubMed database. Among these, many report important advances in the understanding of and care for COPD. Epidemiological aspects are the topic of another manuscript in this issue of the European Respiratory Review\(^{(18)}\).

Patients with COPD have generally limited exercise capacity because of the reduced ventilatory capacity. During a progressive exercise test, generally a patient with COPD will reach his maximum work rate earlier and be unable to continue exercise\(^{(11)}\).

Most often, treatment of the dyspnoea of patients with COPD is designed to improve pulmonary mechanics by the use of medicine and control or reduce the chances of infection. However, reduction of the metabolic acidosis during the exercise by exercise training is also an important approach to reduce the ventilatory drive and ultimately exertional dyspnoea and improve the exercise capacity of a patient\(^{(11)}\).

In patients with COPD strength and endurance exercise capacity are impaired\(^{(19)}\)\(^{(20)}\). Exercise capacity may be affected by many factors such as ventilator limitation, dynamic hyperinflation and diminished oxygen uptake in the lung\(^{(21)}\). In addition, impaired exercise capacity could be caused by factors outside the lung, such as early lactate production\(^{(10)}\)\(^{(22)}\)\(^{(23)}\), muscle dysfunction and cardiovascular deconditioning (e.g. higher heart rate and lower stroke volume during exercise)\(^{(24)}\)\(^{(25)}\) which may at least be partially induced by sedentary lifestyle due to dyspnoea\(^{(26)}\).
In so many study it is shown that early lactate is the one of the factor for the exercise limitation in the COPD patients but how early it starts accumulating in the COPD patients compared to normal individual and how fast it is eliminated by CO₂ production is also important as this will determine the duration of exercise so the focus of this study is mainly to compare the rate of production and recovery of lactate in the COPD and in normal individual after an exercise.