"CORRELATION OF HYPERGLYCEMIA AND ITS OUTCOME IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE – A CROSS SECTIONAL STUDY"

By

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Under the Guidance of

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DECLARATION

I hereby declare that this dissertation entitled **"CORRELATION OF HYPERGLYCEMIA AND ITS OUTCOME IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE – A CROSS SECTIONAL STUDY"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. B. SRINIVAS** MD Professor, Department of Medicine, Jawaharlal Nehru Medical College, Nehru Nagar, Belgaum – 10.

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LIST OF ABBREVIATIONS USED

AECOPD	–	Acute Exacerbation of Chronic Obstructive Pulmonary Disease
CHF	–	Congestive Heart Failure
COPD	–	Chronic Obstructive Pulmonary Disease
DALYS	–	Disability Adjusted Life Years
D_{Lco}	–	Diffusion Capacity of Lung for Carbon Monoxide
FEV1	–	Forced Expiratory Volume in 1 second
FRC	–	Functional Residual Capacity
GOLD	–	Global Initiative for Chronic Obstructive Pulmonary Disease
h/o	–	history of
HR	–	Hazards Ratio
ICU	–	Intensive Care Unit
K-W test	–	Kruskal Wallis Test
MRC	–	Medical Research Council
RBS	–	Random Blood Sugar
RR	–	Relative risk
UK	–	United Kingdom
URTI	–	Upper Respiratory Tract Infection
V/Q	–	Ventilation by Perfusion Ratio

ABSTRACT

Background and Objectives

Chronic obstructive pulmonary disease (COPD) is a common, costly and preventable disease and is at present the fifth leading cause of death globally. The present study was undertaken to determine the relationship between blood glucose concentrations and clinical outcomes in patients admitted with AECOPD.

Methods

The present one year cross sectional study was conducted in Department of Internal and Respiratory Medicine, at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during January 2008 to December 2008 on 85 patients admitted with the diagnosis of AECOPD. Detailed history, clinical examination, blood investigations were performed. To establish the severity of exacerbation clinical questionnaire was used with gold classification alongwith arterial blood gas analysis and blood glucose measurements at the time of admission were noted.

Results

In this study majority of the patients were males (84.70%). Forty percent of the patients were in the age group of 61 to 70 years. All the patients (n=85) complained of Dyspnea (Grade 4 to Grade 5). Out of the total 85 patients, 94% of male patients (n=68) were smokers and 6% (n=4) were nonsmokers. The smoking index in stage II patients was 230, in stage III it was 240 and in stage IV patients it was 270. The Median length of stay for all the patients in stage IV COPD was eight days. As the value of admission RBS increased so did the

median length of stay in the hospital (p=0.002). Median length of stay for all the patients in stage III was six days (p=0.150) and in stage II patients it was five days (p=0.6309). The median length of stay of patients among the diabetic group was more than that of nondiabetic group (0.0002).

Conclusion

The study can be concluded that higher the admission RBS, longer was the median duration of stay in the hospital for patients with severe COPD.

Key words

Acute exacerbations with chronic obstructive pulmonary disease; Chronic obstructive pulmonary disease; Diabetes mellitus; Duration of hospital stay.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common, costly and preventable disease and is at present the fifth leading cause of death globally. The estimate in 2002 suggests worldwide prevalence of COPD to be 11.6/1000 in men and 8.7/1000 in women. According to the estimate of the Global Burden of Disease Study, by the year 2020, COPD is likely to become the fifth leading cause of Disability Adjusted Life Years (DALYS), moving ahead from 12th position it occupied in 1990. Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) estimates suggest that COPD will rise from sixth to the third most common cause of death worldwide by 2020.[1]

Chronic obstructive pulmonary disease is more in countries where smoking is highly prevalent. Sadly Smoking is turning out to be a menace on the rise in India. It has been estimated that 2500 Indians die everyday from smoking related diseases, one in every 40 seconds.[2]

In this context, strategies to reduce mortality and length of stay from acute exacerbation of COPD (AECOPD) are urgently required. Previous studies have shown that in-hospital mortality from AECOPD is predicted largely by fixed factors such as older age,[3,4] male sex, co-morbidity, higher income,[4] and arterial pH.[3] It is not known whether hyperglycaemia, which is remediable, predicts outcomes of hospitalisation for AECOPD. Hyperglycaemia is of interest as it is associated with poor outcomes from acute hospital admission for other conditions.[5-9]

In a study of 2030 adults admitted to general hospital wards, newly discovered hyperglycaemia (admission or fasting blood glucose >7 mmol/l (126 mg%) or two random blood glucose measurements >11.1 mmol/l (200mg%) was associated with higher in-hospital mortality (16%) than established diabetes mellitus (3%) or normal blood glucose (1.7%).[10] Furthermore, hospital stay was longer and admission to the intensive care unit (ICU) was more frequent in those with new hyperglycaemia. Hyperglycaemia has also been associated with adverse outcomes from acute myocardial infarction,[6] ischaemic or haemorrhagic stroke,[7] surgery,[8] and trauma.[9]

Hyperglycaemia is thus associated with a poor outcome from a wide range of acute illnesses. However, the relationship between blood glucose levels and clinical outcomes in AECOPD has not been fully established. Furthermore, recently published national UK guidelines[11] do not comment on whether blood glucose should be measured or controlled in the management of AECOPD.

Hyperglycaemia is associated with a poor outcome from a wide range of acute illnesses. However, the relationship between blood glucose levels and clinical outcomes in AECOPD has not been fully established. Furthermore, published national United Kingdom (UK) guidelines[11] do not comment on whether blood glucose should be measured or controlled in the management of AECOPD. A higher baseline glucose level at the time of presentation predicts significantly higher long-term mortality, independent of a history of diabetes, and is a risk factor that may be modifiable with aggressive treatment. Determination of blood sugar is a simple procedure, requires no expertise, is inexpensive and

importantly, It is a correctable factor, having a bearing on morbidity and mortality.

Hence the present study was undertaken to determine the relationship between blood glucose concentrations and clinical outcomes in patients admitted with AECOPD.

OBJECTIVES

To study the correlation of hyperglycemia and its outcome in patients with AECOPD admitted under Respiratory Medicine and Internal Medicine General Wards of KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belgaum over a period of one year.

REVIEW OF LITERATURE

Critically ill patients who require intensive care for more than five days carry 20% risk of death and significant morbidity. Hyperglycemia and insulin resistance are common in critical care settings, even observed in those without preexisting diabetes. Newly detected hyperglycemia (admission or fasting blood glucose more than 126 mg/dl or two random blood glucose more than 200 mg/dl) in one study[10] was associated with higher in-hospital mortality (16%) than established diabetes (three percent) or normal blood glucose (1.7%). The risk of in-hospital complications and ICU death increase by three percent for each 20 mg/dl increase in blood glucose above 100 mg/dl.

Hyperglycemia per se, for example in myocardial infarction (MI) showed, admission blood glucose of more than eight to 10 mM/L (144 to 180 mg/dl) was associated with increased incidence of congestive heart failure (CHF) or cardiogenic shock in patients without diabetes. Diabetic patients with random blood glucose of more than 10 to 11 mM/L (180 to 198 mg/dl) had a moderately increased risk of death [relative risk (RR) 1.7].[6]

Two landmark studies in Surgical ICU (2001) and Medical ICU (MICU) (2006) in Belgium compared outcomes maintaining random blood glucose between 80-110 mg/dl (intensive group) versus 180-200 mg/dl (conventional group). In surgical intensive care unit (SICU), intensive insulin therapy reduced in-hospital mortality by 34%, septicemia by 46%, acute renal failure (ARF) requiring dialysis or hemofiltration by 41%, packed cell transfusion by 50%, critical illness polyneuropathy by 44% and less requirement for prolonged

mechanical ventilation.[12] In MICU, intensively treated group had significantly reduced morbidity, prevented kidney injury, and helped in early weaning from ventilator and early discharge from MICU.[13]

Neurological outcomes after acute ischemic stroke in diabetics are significantly worse as compared with non diabetics. Even among non diabetics, prospective analyses have shown significantly worse outcome with admission blood glucose of more than 120 mg/dl (43% regained employment) than blood glucose less than 120 mg/dl (76% regained employment).[14] In one study[15] admission blood glucose of more than 130 mg/dl in acute stroke had been associated with both short-term and long-term mortality at 1month [Hazards ratio (HR) 1.87], one year (HR 1.75), six year (HR 1.41). All remained hyperglycemic with mean blood glucose of 206 mg/dl. Meta-analysis of 32 studies relating acute post-stroke glucose levels to survival revealed three fold increased risk of in-hospital or 30 day mortality with admission blood glucose of more than 108-144 mg/dl.

Perioperative glycemia in patients undergoing coronary artery bypass (CABG) has been shown to be an independent predictor of deep sternal wound infections and mortality in diabetics. Lowest mortality is seen when blood glucose is less than 150 mg/dl.[16]

Hyperglycemia has been associated with poor outcomes in patients with acute exacerbations of COPD. In one study, blood glucose quartile independently predicted adverse clinical outcomes instead of underlying severity of COPD.[17]

Blood glucose of 11.1 mM/L (more than 200 mg/dl) was associated with longer hospital stay and increased mortality. Blood glucose concentrations above 6.7 to 9.7 mM/L (120.6 to 174.6 mg/dl) are associated with glucose concentrations of one to 11 mM/L (18 to 198 mg/dl) in bronchial aspirates (normally extremely low). These patients were shown more likely to suffer from infection especially methicillin resistant staphylococcus aureus.

PATHOGENESIS OF HYPERGLYCEMIA IN COPD

Blood glucose is increased in acute illness due to a combination of metabolic effects such as raised plasma catecholamine and glucocorticoid hormone concentrations and increased peripheral insulin resistance.[18] Increased blood glucose concentrations in AECOPD could therefore simply be a marker for more severe illness which, in turn, results in adverse clinical outcomes. Blood glucose concentrations also rise with corticosteroid treatment for AECOPD,[19] hence increased blood glucose concentrations could reflect administration of steroids at larger doses or for longer in people who are more unwell, who have poor clinical outcomes. Regression analysis in other studies suggest that control of blood glucose levels, rather than insulin dose used to treat this hyperglycemia, was responsible for the clinical benefits observed.[20] These findings imply that increased glucose concentrations could have a direct detrimental effect on outcomes.

Hyperglycaemia could have adverse effects in acute illness through cellular glucose overload and oxidative stress. In acute illness, cytokines, hormones and hypoxia upregulate expression and membrane localisation of

glucose transporters in many cell types.[21] Cellular glucose overload results in increased glucose metabolism, in turn increasing superoxide and peroxynitrite production which may impair mitochondrial activity.[21] In support of this, ultrastructural abnormalities were observed in hepatic mitochondria obtained at liver biopsy from ICU patients with hyperglycaemia, whereas virtually no mitochondrial abnormalities were detected in patients where normoglycaemia was maintained therapeutically.[22] Mitochondrial toxicity of glucose in diverse cells could account for the broad spectrum of organ and tissue dysfunction associated with hyperglycaemia in acute illness.[12]

Thus hyperglycemia in acute illness occurs due to combination of defects mainly increase in stress hormones like catecholamines and glucocorticoid and increased peripheral insulin resistance. In acute illness cytokines, hormones, and hypoxia lead to cellular glucose overload, which in turn increase superoxide and free radical formation which impair mitochondrial activity. Mitochondrial toxicity of glucose in various cells contribute to widespread organ and tissue dysfunction.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Introduction

Chronic obstructive pulmonary disease (COPD) remains a major public health problem. It is the fourth leading cause of chronic morbidity and mortality in the United States, and is projected to rank fifth in 2020 in burden of disease worldwide, according to a study published by the World Bank/World Health Organization.

COPD prevalence, morbidity, and mortality vary across countries and across different groups within countries but, in general, are directly related to the prevalence of tobacco smoking, although, in many countries, air pollution resulting from the burning of wood and other biomass fuels has also been identified as a COPD risk factor. The prevalence and burden of COPD are projected to increase in the coming decades due to continued exposure to COPD risk factors and the changing age structure of the world's population.

Epidemiology

In the past, imprecise and variable definitions of COPD have made it difficult to quantify prevalence, morbidity, and mortality. Furthermore, the underrecognition and underdiagnosis of COPD lead to significant underreporting. The extent of the underreporting varies across countries and depends on the level of awareness and understanding of COPD among health professionals, the organization of health care services to cope with chronic diseases, and the availability of medications for the treatment of COPD.[23]

Prevalence

Many sources of variation can affect estimates of COPD prevalence, including sampling methods, response rates, quality control of spirometry and whether spirometry is performed pre or post-bronchodilator. Despite these complexities, data are emerging that enable some conclusions to be drawn regarding COPD prevalence. A prevalence study in Latin America,[24] a systematic review and meta-analysis of studies performed in 28 countries between 1990 and 2004,[25] and an additional study from Japan[26] provide evidence that the prevalence

of COPD (Stage I, mild COPD and higher) is appreciably higher in smokers and ex-smokers compared with nonsmokers, in those older than 40 years compared with those younger than 40 years, and in men compared with women.

Morbidity

Morbidity measures traditionally include physician visits, emergency department visits, and hospitalizations. Although COPD databases for these outcome parameters are less readily available and usually less reliable than mortality databases, the limited data available indicate that morbidity due to COPD increases with age and is greater in men than in women.[27,28] COPD in its early stages (Stages I and II) is usually not recognized, diagnosed, or treated, and therefore may not be included as a diagnosis in a patient's medical record. Morbidity from COPD may be affected by other comorbid chronic conditions[29] (for example, musculoskeletal disease, diabetes mellitus) that are not directly related to COPD but nevertheless may have an impact on the patient's health status, or may interfere with COPD management. In patients with more advanced disease (Stages III and IV), morbidity from COPD may be misattributed to another comorbid condition.

Mortality

COPD is one of the most important causes of death in most countries. The Global Burden of Disease Study[30,31] has projected that COPD, which ranked sixth as the cause of death in 1990, will become the third leading cause of death worldwide by 2020. This increased mortality is driven by the expanding epidemic

of smoking and the changing demographics in most countries, with more of the population living longer.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Definition

COPD is defined as a disorder characterized by abnormal tests of expiratory flow that do not change markedly over periods of several months observation.[32] It comprises chronic bronchitis and emphysema.

- Chronic bronchitis is defined as "a condition in which there is coughing up of sputum on most days for at least three months of the year for two successive years".[33]

- Emphysema is defined as a "condition of the lung characterized by abnormal permanent enlargement of the air spaces distal to terminal bronchiole, accompanied by destruction of their walls and without obvious fibrosis".[34]

Prevalence studies of COPD are normally based on values of percentage predicted forced expiratory volume in one second (FEV_1). Forced expiratory volume in one second values decline with increase in age, particularly in smokers. Males are more frequently affected than females. COPD increases in frequency with increase in age after 49 years. Prevalence peaks in seventh and eighth decades. The estimated prevalence of COPD worldwide were 1013/100000 population.[35] Most of the mortality from COPD occurs in the over 65 age group mortality rates tend to be higher in urban areas than rural areas.[36]

Etiology

Chronic hyper secretion of mucous and persistent airflow obstruction

Chronic hypersecretion of mucous and progressive, persistent airflow obstructions occur in COPD patients. The persistent cough and sputum production results from Bronchial gland enlargement in the proximal conducting airways and is to an extent improvable, where as the persistent airflow obstruction arises from damage to the peripheral airways and airspaces and is persistent.

Risk factors

Major risk factors are smoking, air pollution, occupation, respiratory illness, α_1 antitrypsin deficiency.

Cigarette smoking

Cigarette smoking is the single most important identifiable etiological factor in COPD. The greater the total tobacco exposure, the greater the risk of developing COPD. British Thoracic Society (BTS)[37] guidelines suggest that most patients with COPD have at least a 20 pack year smoking history. On an average, cigarette smokers have a high annual rate of decline in FEV_1 of about 50 ml/Year. Stopping cigarette smoking does not produce a substantial improvement in FEV_1 but the subsequent rate of decline is decreased.

Air pollution

World Health Organization (WHO) expert committee on air pollution concluded that high concentration of Sulfur dioxide (150 $\mu g/m^3$) or similar concentrations of particulate air pollution, measured as black smoke, were associated with increased morbidity in COPD.

Protease inhibitor deficiency

Laurell and Eriksson[38] in 1963 were the first to describe the association between α_1 antitrypsin deficiency and development of early-onset Emphysema. The incidence of α_1 antitrypsin deficiency in a population study of patients presenting with COPD was one to two percent but rose to greater than 50% in patients with severe disease who were less than 40 years of age.[39] The onset of dyspnea and death occur at a younger age in smokers with α_1 antitrypsin deficiency.

Occupation

There is a causal link between occupational dust exposure and the development of mucous hypersecretion. Occupational dust exposure results in rapid decline in FEV_1. Studies of coal-miners indicate a relationship between the exposure to dust and longitudinal decline in FEV_1.[40] Welding fumes and cadmium exposure also causes COPD.

Chronic bronchopulmonary infection

Recurrent bronchopulmonary infections result in damage to the airways and progressive airways destruction.[41] Chest illness in childhood may have an association with chronic respiratory morbidity and impaired respiratory function in adulthood.[42] Early childhood illnesses like whooping cough, bronchiolitis or pneumonia in the first year of life were associated with a significant reduction in FEV_1 measured in the first decade.[43]

Growth and nutrition

Recent studies suggested that nutrition might affect both the growth and decline in ventilatory function. Mortality from chronic respiratory diseases correlated inversely with birth weight and weight at one year of age.[43]

Pathology

The pathological changes in patients with COPD are complex and occur in both the large and small airways, and in the alveolar compartment. Three major types of emphysema are recognized according to the distribution of enlarged airspaces within the acinar unit. They are centriacinar emphysema, panacinar emphysema and periacinar emphysema. The hypertrophy of mucous glands is mainly seen in the larger bronchi and is evenly distributed through out the lungs.[44] Smaller peripheral bronchi may be thickened and distorted by scar tissue. The airway epithelium is characterized by squamous metaplasia, atrophy of ciliated cells and hypertrophy of mucus glands. Small airways show narrowing of lumina, including goblet cell hyperplasia, mucosal and submucosal

inflammatory cells, edema, peribronchial fibrosis, intraluminal mucus plugs and increased smooth muscle. CD8+ T lymphocytes and B lymphocytes characterize the inflammatory infiltrate. The marked thickening of subepithelial lamina reticularis which is characteristic of asthma, is absent in COPD.

Pathogenesis

Cigarette smoke may alter elastase-antielastase balance in the lungs. Neutrophil elastase[45,46] and α_1 antitrypsin deficiency are the main players in this protease-antiprotease imbalance. COPD may be genetically determined by such factors as the cellular response to tobacco, Bronchial hyperreactivity, variations in neutrophil and macrophage protease activity, protease inhibitor function and lung matrix injury and repair.

The mechanisms for the development of pulmonary emphysema include;

1. *Increased protease burden* due to increase sequestration and migration of neutrophils into the lungs in smokers, increased amounts of elastase present in neutrophils from smokers, enhanced degranulation causing more connective tissue injury.

2. *Decreased antiprotease function* due to functional deficiency of α_1 antitrypsin in the airspaces produced by smoking due to oxidation of methionine-358 residue at the active site of α_1 antitrypsin molecule. This can occur by a direct oxidative effect of cigarette smoke or by oxidants released from activated airspace leucocytes.[47,48]

3. *Decreased elastin synthesis* the concentrations of the elastin cross-linking peptide desmosine and elastin peptides are elevated in patients with COPD.[49] Lysyl oxidase activity is reduced by cigarette smoking and may contribute to emphysema by preventing elastase repair.[50]

Cigarette smoke produces oxidative stress causing inflammation and COPD. It also inactivates α_1 antitrypsin, thus helping elastase to degrade elastin and act as chemoattractant and up regulates adhesion molecules. Smoke and elastase increase the expression of proinflammatory nuclear transcription factor κB and interleukin 8 that recruits neutrophils, basophils, eosinophils and T lymphocytes. Macrophages and mast cells produce Transforming growth factor β causing fibrogenesis. Smoke also leads to lipid peroxidation and DNA damage.

Pathophysiology

Airflow limitation

Airflow limitation and increased airways resistance may be caused by loss of elastic recoil, increased collapsibility of small airways through loss of radial traction on airways or to increased resistance due to intrinsic narrowing of small airways.

Hyperinflation

Loss of the elastic recoil of lung results in higher Functional Residual Capacity (FRC). The residual volume and FRC are almost always higher than normal. Prolongation of expiration in association with obstruction would lead to dynamic increase in FRC (dynamic hyperinflation), if inspiration is initiated

before the respiratory system reaches its static balance point. Dynamic hyperinflations cause flattening of diaphragm and places it at a mechanical disadvantage.

Impaired pulmonary gas exchange

The underlying structural abnormalities in COPD result in disturbance of pulmonary gas exchange. Ventilation-perfusion (V_A/Q) mismatching is the most important cause of impaired pulmonary gas exchange in COPD. Other causes, such as alveolar hypoventilation, impaired alveolar-capillary diffusion of oxygen and increased shunt, are of much less importance. The distribution of ventilation is very uneven in patients with COPD. A reduction of blood flow is produced by several mechanisms, including local destruction of vessels in alveolar walls as a result of emphysema, hypoxic vasoconstriction in areas of severe alveolar hypoxaemia and passive vascular obstruction as a result of increased alveolar pressure and distension.

Patients with COPD have been divided on clinical grounds and blood gas abnormalities into two extreme presentations. Type A patients or 'pink puffers' have severe dyspnea, a normal or low $Paco_2$, only a mild decrease in Pao_2 at rest, and a low D_{LCO}. These patients are hypoxaemic only at a late stage in the disease and therefore do not develop pulmonary hypertension, cor pulmonale and consequently fluid retention and secondary polycythaemia. In contrast, 'blue bloaters' or type B patients present with cough and sputum production and are likely to develop hypoxaemia and hypercapnia earlier in the course of their disease, and hence cor pulmonale, fluid retention and polycythaemia. The 'pink

puffers' were thought to have predominantly emphysema and the 'blue bloaters' were the bronchitic type as described by Burrows and colleagues.[51]

Small airway narrowing causes a decrease in ventilation of their distal alveolar acini. When alveolar capillaries remain intact, this results in mismatching of ventilation and blood flow, reduced ventilation-perfusion ratios and mild-moderate hypoxemia. With emphysema, destruction of alveolar walls may decrease alveolar capillary perfusion as well, better preserving ventilation-perfusion matching and PaO_2.

There is a broad relationship between spirometry and blood gases in patients with COPD, where $Paco_2$ rises when the FEV_1 falls below 1.5 L.[52]

Table 1: Patterns of disease in advanced COPD

	Type A: Pink Puffer (Emphysema Predominant)	**Type B: Blue Bloater (Bronchitis Predominant)**
History and physical examination	Major complaint is dyspnea, often severe, usually presenting after age 50. Cough is rare, with scant clear, mucoid sputum. Patients are thin, with recent weight loss common. They appear uncomfortable, with evident use of accessory muscles of respiration. Chest is very quiet without adventitious sounds. No peripheral edema.	Major complaint is chronic cough, productive of mucopurulent sputum, with frequent exacerbations due to chest infections. Often presents in late 30s and 40s. Dyspnea usually mild, though patients may note limitations to exercise. Patients frequently overweight and cyanotic but seem comfortable at rest. Peripheral edema is common. Chest is noisy, with rhonchi invariably present; wheezes are common.
Laboratory studies	Hemoglobin usually normal (12-15 g/dL). Pao_2 normal to slightly reduced (65-75 mm Hg) but Sao_2 normal at rest. $Paco_2$ normal to slightly reduced (35-40 mm Hg). Chest radiograph shows hyperinflation with flattened diaphragms. Vascular markings are diminished, particularly at the apices.	Hemoglobin usually elevated (15-18 g/dL). Pao_2 reduced (45-60 mm Hg) and $Paco_2$ slightly to marked elevated (50-60 mm Hg). Chest radiograph shows increased interstitial markings (“dirty lungs”), especially at bases. Diaphragms are not flattened.

	Type A: Pink Puffer (Emphysema Predominant)	Type B: Blue Bloater (Bronchitis Predominant)
Pulmonary function tests	Airflow obstruction ubiquitous. Total lung capacity increased, sometimes markedly so. D_L co reduced. Static lung compliance increased.	Airflow obstruction ubiquitous. Total lung capacity generally normal but may be slightly increased. $D_L$co normal. Static lung compliance normal.
Special evaluations V/Q matching	Increased ventilation to high V/Q areas, i.e., high dead space ventilation.	Increased perfusion to low V/Q areas.
Hemodynamics	Cardiac output normal to slightly low. Pulmonary artery pressures mildly elevated and increase with exercise	Cardiac output normal. Pulmonary artery pressures elevated, sometimes markedly so, and worsen with exercise.
Nocturnal ventilation	Mild to moderate degree of oxygen desaturation not usually associated with obstructive sleep apnea.	Severe oxygen desaturation frequently associated with obstructive sleep apnea.
Exercise ventilation	Increased minute ventilation for level of oxygen consumption. Pao_2 tends to fall, $Paco_2$ rises slightly.	Decreased minute ventilation for level of oxygen consumption. Pao_2 may rise; $Paco_2$ may rise significantly.

Pulmonary circulation

Changes in the pulmonary circulation occur characteristically in the peripheral arteries in patients with COPD.[53,54] Among the earliest change in

pulmonary vasculature that develops as airflow limitation worsens, is thickening of the intima of the small pulmonary arteries.[54,55] Pulmonary arterial hypertension develops late in the course of COPD, with the development of hypoxaemia and usually hypercapnia. It is the major cardiovascular complication of COPD and is associated with development of right ventricular hypertrophy (cor pulmonale). Pulmonary vessels constricts in response to alveolar hypoxia. Repeated desaturation may cause pulmonary hypertension.

Renal and Hormonal Dysfunction

The most consistent change in renal function in patients with hypoxic COPD, particularly those with edema, is a reduction in renal blood flow.[56] Chronic hypoxemia and hypercapnea cause increased circulation levels of norepinephrine, renin and aldosterone and decreased levels of antidiuretic hormone. Renal arterial endothelium defects in COPD patients, shifts renal blood flow the cortex to the medulla and impairing renal functional reserve. Changes in hormonal balance in patients with COPD include activation of renin-angiotensin-aldosterone system and elevation of circulating catecholamines.[57,58]

Cachexia

Cachexia is due to caloric intake failing to keep pace with energy expenditures associated with increased work of breathing. Hypoxemia leads to increased circulating levels of Tumor Necrosis Factor α (TNF α).

Peripheral muscle dysfunction

Protein and muscle are lost as part of wasting in advanced COPD. Proximal limb girdle muscles of upper and lower extremities are particularly affected.

Osteoporosis

Loss of bone density is common in advanced COPD. Vertebral fractures are common.

Breathing adaptations in patients with COPD

As a result of the respiratory muscle dysfunction in patients with COPD, patients with severe disease adopt a characteristic breathing pattern during tidal breathing, consisting of rapid frequency and a small tidal volume. This pattern helps to avoid the development of respiratory muscle fatigue but predisposes patients to the development of hypercapnia.[59]

Natural history of COPD

Patient will have an abnormal FEV_1 in middle age, usually early in the fifth decade. COPD is characterized by an accelerated decline of FEV_1 with aging. Annual loss of FEV_1 in COPD patients is between 50 and 100 ml per year. Majority of patients experience exertional dyspnea when FEV_1 less than 40% predicted and dyspnea at rest, CO_2 retention and cor pulmonale is FEV_1 less than 25% predicted. COPD is punctuated by episodic exacerbations. Exacerbation is described as worsening of previously stable disease characterized by increased

dyspnea, wheeze, cough and sputum volume, tenacity and with worsening gas exchange and ventilation- perfusion relationships. Most COPD exacerbations are due to acute tracheobronchitis, usually infectious. Most infections are primarily bacterial. Exacerbation may be triggered by left ventricular failure, cardiac arrhythmias, pneumothorax, pneumonia and pulmonary thromboembolism. Exacerbations do not cause accelerated declines of FEV_1 over time.

Clinical features

Symptoms

The characteristic symptoms of COPD are breathlessness on exertion, sometimes accompanied by wheeze and cough, which is often productive.[60] Breathlessness is usually the most disabling of these symptoms. Most patients have a smoking history of at least 20 pack-years before symptoms develop, commonly in the fifth decade. It is characteristic of COPD that patients progress through the clinical stages of mild, moderate, and severe disease. Breathlessness is the symptom that causes most disability and is associated with loss of lung function over time.[61] The appearance of breathlessness indicates moderate to severe impairment of airway function. By the time the patients seeks medical advice the FEV_1 has usually fallen to one to 1.5 L in an average man. Breathlessness can be assessed on the MRC scale.[62]

A productive cough occurs in upto 50% of cigarette smokers.[63] In most patients with COPD, cough precedes the onset of breathlessness or appears with it. The MRC questionnaire uses cough as preceding symptom of chronic bronchitis. The frequency and severity of cough generally do not correlate with

the degree of functional impairment, but recent studies did indicate an association between cough and the development of airflow limitation.[64]

Wheeze is common but not specific to COPD since it is due to turbulent airflow in large airways from any cause.

Patients with COPD often complain of chest tightness during exacerbations of breathlessness, particularly due to exercise.

Haemoptysis in association with purulent sputum may be due to inflammation or infection.

Weight loss and anorexia are features of severe COPD and are thought to result form both a decrease in calorie intake and hypermetabolism.[65] Depression is common in patients with severe COPD.[66] Sleep quality is impaired in advanced COPD.[67]

Physical signs

The physical signs in patients with COPD depend on the degree of airflow limitation and pulmonary overinflation. Variable degrees of tachypnoea may be present depending on the type of clinical presentation. Prolonged forced expiratory time (more than five seconds) can be a useful indicator of airway obstruction. In early disease the only abnormal physical finding may be wheeze on forced expiration and a forced expiratory time prolonged beyond six seconds.

Cyanosis may be present indicating hypoxaemia. The flapping tremor associated with hypercapnia is neither sensitive nor specific.

The breathing pattern is often characteristic with a prolonged expiratory phase, some patients adopting pursed-lip breathing on expiration, which may reduce expiratory airway collapse[68] and may even improve oxygenation.[69] The use of accessory muscles of respiration, particularly the sternomastoids, is often seen in advanced disease. In the later stages of COPD the chest is often barrel shaped with kyphosis and an apparent increased antero-posterior diameter, horizontal ribs, prominence of the sternal angle and a wide subcostal angle. As a result of elevation of sternum, the distance between the suprasternal notch and the cricoid cartilage may be reduced and an inspiratory tracheal tug may be detected, due to contraction of the low flat diaphragm.[70] The horizontal position of diaphragm acts to pull in the lower ribs during inspiration (Hoover's sign).[71] Increased intrathoracic pressure may result in indrawing of the suprasternal and supraclavicular fossae and of the intercostal muscles. Coarse inspiratory crackles and rhonchi are heard over the lung fields, especially at the bases. Patients with severe airflow obstruction may adopt tripod sitting posture to gain better mechanical advantage for their compromised respiratory muscles. A rise in jugular venous pressure may be seen on expiration. With pulmonary hypertension a loud P_2, along with a right ventricular heave and a murmur of tricuspid regurgitation may be found. Cor pulmonale and right heart failure may be evidenced by dependant edema and enlarged tender liver. If right sided pressures are very high, neck veins may elevate instead of collapse with inspiration (Kussmaul's sign).

On percussion of the chest there is decreased hepatic and cardiac dullness, indicating overinflation. Breath sounds may have prolonged expiratory phase or may be uniformly diminished particularly in advanced stages of disease.

Radiographic findings

As COPD progress, abnormalities reflect emphysema, hyperinflation and pulmonary hypertension.

Emphysema increased lucency of the lungs. In smokers, these changes are more prominent in upper lobes, while in α_1 AT deficiency, they are more likely in basal zones. Local translucencies more than 1 cm diameter and surrounded by hairline arcuate shadows indicate the presence of bullae and are highly specific for emphysema.

With hyperinflation chest becomes vertically elongated with low flattened diaphragms. The heart shadow is vertical and narrow.

In pulmonary hypertension the right heart border may become prominent.

Computed technology has greater sensitivity and specificity for emphysema.

Staging of COPD

A simple spirometric classification of disease severity into four stages is recommended (Table 2).[72] Spirometry is essential for diagnosis and provides a useful description of the severity of pathologic changes in COPD.

Specific spirometric cut points (for example, post-bronchodilator FEV_1/FVC ratio less than 0.70 or FEV_1 less than 80, 50, or 30% predicted) are used for purposes of simplicity; these cut points have not been clinically validated. A study in a random population sample found that the post-bronchodilator FEV_1/FVC exceeded 0.70 in all age groups, supporting the use of this fixed ratio.[73] However, because the process of aging does affect lung volumes, the use of this fixed ratio may result in overdiagnosis of COPD in the elderly, especially in those with mild disease.

The characteristic symptoms of COPD are chronic and progressive dyspnea, cough, and sputum production. Chronic cough and sputum production may precede the development of airflow limitation by many years. This pattern offers a unique opportunity to identify smokers and others at risk for COPD, and to intervene when the disease is not yet a major health problem. Conversely, significant airflow limitation may develop without chronic cough and sputum production.

Stage I – Mild COPD

Characterized by mild airflow limitation (FEV_1/FVC less than 0.70, FEV_1 more than or equal to 80% predicted). Symptoms of chronic cough and sputum production may be present, but not always. At this stage, the individual is usually unaware that his or her lung function is abnormal.

Stage II - Moderate COPD

Characterized by worsening airflow limitation (FEV1/FVC < 0.70, 50% =/< FEV1 < 80% predicted), with shortness of breath typically developing on exertion and cough and sputum production sometimes also present. This is the stage at which patients typically seek medical attention because of chronic respiratory symptoms or an exacerbation of their disease.

Stage III – Severe COPD

Characterized by further worsening of airflow limitation (FEV_1/FVC less than 0.70, 30% less than or equal to FEV_1 less than 50% predicted), greater shortness of breath, reduced exercise capacity, fatigue, and repeated exacerbations that almost always have an impact on patients' quality of life.

Stage IV - Very severe COPD

Characterized by severe airflow limitation (FEV_1/FVC less than 0.70, FEV_1 less than 30% predicted or FEV_1 less than 50% predicted plus the presence of chronic respiratory failure). Respiratory failure is defined as an arterial partial pressure of O_2 (PaO_2) less than 8.0 kPa (60 mm Hg), with or without an arterial partial pressure of CO_2 ($PaCO_2$) greater than 6.7 kPa (50 mm Hg) while breathing air at sea level. Respiratory failure may also lead to effects on the heart such as cor pulmonale (right heart failure). Clinical signs of cor pulmonale include elevation of the jugular venous pressure and pitting ankle edema. Patients may have stage IV COPD even if their FEV1 is greater than 30% predicted, whenever

these complications are present. At this stage, quality of life is very appreciably impaired and exacerbations may be life threatening.

Table 2: Spirometric classification of chronic obstructive pulmonary disease severity based on post bronchodilator FEV_1

Stages	FEV_1
Stage I: Moderate	$FEV_1/FVC < 0.70$
	$FEV_1 \geq 80\%$ predicted
Stage II: Moderate	$FEV_1/FVC < 0.70$
	$50\% \leq FEV_1 < 80\%$ predicted
Stage III: Severe	$FEV_1/FVC < 0.70$
	$30\% \leq FEV_1 < 50\%$ predicted
Stage IV: Very severe	$FEV_1/FVC < 0.70$
	$< FEV_1 < 30\%$ predicted or FEV1 $< 50\%$ predicted plus chronic respiratory failure*

*Respiratory failure: Arterial partial pressure of oxygen (Pao_2) < 8.0 kPa (60 mm Hg) with or without arterial partial pressure of CO_2 ($Paco_2$) > 6.7 kPa (50 mm Hg) while breathing air at sea level.

Diagnosis

Initial diagnosis

A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease. The diagnosis should be confirmed by spirometry.

Key indicators for conidering a diagnosis of chronic obstructive pulmonary disease

- Dyspnea
    - Progressive (worsens over time).
    - Usually worse with exercise.
    - Persistent (Present every day).
    - Described by the patient as an increased effort to breathe, heaviness, air hunger or gasping.
- Chronic cough
    - May be intermittent and may be unproductive.
- Chronic sputum production
    - Any pattern of chronic sputum production may indicate COPD.
- History of exposure to risk factors, especially
    - Tobacco smoke
    - Any pattern of chronic sputum production may indicate COPD.
- History of exposure to risk factors, especially;
    - Tobacco smoke.
    - Occupational dusts and chemicals.

- Smoke from home cooking and heating fuels.

ASSESSMENT OF SYMPTOMS

Dyspnea, the hallmark symptom of COPD, is the reason most patients seek medical attention and is a major cause of disability and anxiety associated with the disease. As lung function deteriorates, breathlessness becomes more intrusive. Chronic cough, often the first symptom of COPD to develop[74] and often predating the onset of dyspnea, may be intermittent, but later is present every day, often throughout the day. In some cases, significant airflow limitation may develop without the presence of a cough. Patients with COPD commonly raise small quantities of tenacious sputum after coughing bouts. Wheezing and chest tightness are nonspecific symptoms that may vary between days, and over the course of a single day. An absence of wheezing or chest tightness does not exclude a diagnosis of COPD. Weight loss, anorexia, and psychiatric morbidity, especially symptoms of depression and/or anxiety, are common problems in advanced COPD.[75,76]

Medical history

A detailed medical history of a new patient known or believed to have COPD should assess the following:

- Exposure to risk factors
- Past medical history, including asthma, allergy, sinusitis, or nasal polyps; respiratory infections in childhood; other respiratory diseases
- Family history of COPD or other chronic respiratory disease

- Pattern of symptom development
- History of exacerbations or previous hospitalizations for respiratory disorder
- Presence of comorbidities, such as heart disease, malignancies, osteoporosis, and muscloskeletal disorders, which may also contribute to restriction of activity.[77]
- Appropriateness of current medical treatments
- Impact of disease on patient's life, including limitation of activity, missed work and economic impact, effect on family routines, feelings of depression or anxiety.
- Social and family support available to the patient.
- Possibilities for reducing risk factors, especially smoking cessation.

Physical examination

Although an important part of patient care, a physical examination is rarely diagnostic in COPD. Physical signs of airflow limitation are usually not present until significant impairment of lung function has occurred[78,79] and their detection has a relatively low sensitivity and specificity.

Measurement of airflow limitation (Spirometry)

Spirometry should be undertaken in all patients who may have COPD. Spirometry should measure the volume of air forcibly exhaled from the point of maximal inspiration (FVC) and the volume of air exhaled during the first second of this maneuver (FEV_1), and the ratio of these two measurements (FEV_1/FVC) should be calculated. Spirometry measurements are evaluated by comparison

with reference values[80] based on age, height, sex, and race. Patients with COPD typically show a decrease in both FEV1 and FVC. The presence of airflow limitation is defined by a post-bronchodilator FEV_1/FVC less than 0.70. This approach is pragmatic in view of the fact that universally applicable reference values for FEV_1 and FVC are not available. Where possible, values should be compared with age-related normal values to avoid overdiagnosis of COPD in the elderly.[81] Using the fixed ratio (FEV_1/FVC) is particularly problematic in patients with milder COPD who are elderly because the normal process of aging affects lung volumes.

Assessment of COPD severity

Assessment of COPD severity is based on the patient's level of symptoms, the severity of the spirometric abnormality, and the presence of complications such as respiratory failure, right heart failure, weight loss, and arterial hypoxemia.

Additional investigations

For patients diagnosed with stage II moderate COPD and beyond the following additional investigations may be considered.

Bronchodilator reversibility testing

Despite earlier hopes, neither bronchodilator nor oral glucocorticosteroid reversibility testing predicts disease progression, whether judged by decline in FEV_1, deterioration of health status, or frequency of exacerbations[82,83] in patients with a clinical diagnosis of COPD and abnormal spirometry.[83] In some cases (For

example, a patient with an atypical history such as asthma in childhood and regular night waking with cough or wheeze), a clinician may wish to perform a bronchodilator and/or glucocorticosteroid reversibility test.

Chest X-ray

An abnormal chest X-ray is seldom diagnostic in COPD unless obvious bullous disease is present, but it is valuable in excluding alternative diagnoses and establishing the presence of significant comorbidities, such as cardiac failure. Computed tomography (CT) of the chest is not routinely recommended. However, when there is doubt about the diagnosis of COPD, high-resolution CT scanning might help in the differential diagnosis. In addition, if a surgical procedure such as lung volume reduction is contemplated, a chest CT scan is necessary because the distribution of emphysema is one of the most important determinants of surgical suitability.[84]

Arterial blood gas measurement

In advanced COPD, measurement of arterial blood gases while the patient is breathing air is important. This test should be performed in stable patients with FEV_1 less than 50% predicted or with clinical signs suggestive of respiratory failure or right heart failure.

α_1 – antitrypsin deficiency screening.

In patients who develop COPD at a young age (less than 45 year) or who have a strong family history of the disease, it may be valuable to identify

coexisting α_1-antitrypsin deficiency. This could lead to family screening or appropriate counseling.

DIFFERENTIAL DIAGNOSIS

In some patients with chronic asthma, a clear distinction from COPD is not possible using current imaging and physiologic testing techniques, and it is assumed that asthma and COPD coexist in these patients. In these cases, current management is similar to that of asthma. Other potential diagnoses are usually easier to distinguish from COPD.

Table 3: Differential diagnosis of COPD

Diagnosis	Suggestive features
COPD	Onset in midlife Symptoms slowly progressive Long history of tobacco smoking Dyspnoea during exercise Largely irreversible airflow limitation
Asthma	Onset early in life (Often childhood) Symptoms vary from day to day Symptoms at night/early morning Allergy, rhinitis and/or eczema also present Largely reversible airflow limitation
Congestive heart failure	Non specific basic crackles on auscultation Chest X ray shows dilated heart, pulmonary edema, pulmonary function tests indicate volume restriction not airflow limitation
Bronchiectasis	Large volumes of purulent sputum Commonly associated with bacterial infection Coarse crackles, clubbing on auscultation Chest X ray / CT shows bronchial dilatation, bronchial wall thickening.
Tuberculosis	Onset all ages Chest X ray shows lungs infiltrate Microbiological confirmation High local prevalence of tuberculosis
Obliterative bronchiectasis	Onset in younger age, non smokers May have history of rheumatoid arthritis or fume exposure CT on expiration shows hypodence areas
Diffuse panbronchiectasis	Most patients are male and non smokers Almost all have chronic sinusitis Chest X ray and HRCT show diffuse small centrilobular nodular opacities and hyperinflation

Acute exacerbations

Introduction

COPD is often associated with exacerbations of symptoms.[85,86,87] An exacerbation of COPD is defined as ‘‘an event in the natural course of the disease characterized by a change in the patient’s baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD.[88,89]

Exacerbations are categorized in terms of either clinical presentation (number of symptoms[86]) and/or heath care resources utilization.[88]

The impact of exacerbations is significant and a patient’s symptoms and lung function may both take several weeks to recover to the baseline values.[90]

The most common causes of an exacerbation are infection of the tracheobronchial tree and air pollution[91] but the cause of approximately one-third of severe exacerbations cannot be identified. The role of bacterial infections is controversial, but recent investigations have shown that at least 50% of patients have bacteria in high concentrations in their lower airways during exacerbations.[92,93] Development of specific immune responses to the infecting bacterial strains and the association of neutrophilic inflammation with bacterial exacerbations, also support the bacterial causation of a proportion of exacerbations.[94,95]

Diagnosis and assessment of severity.

Medical history

Increased breathlessness, the main symptom of an exacerbation, is often accompanied by wheezing and chest tightness, increased cough and sputum, change of the color and/or tenacity of sputum, and fever. Exacerbations may also be accompanied by a number of nonspecific complaints, such as tachycardia and tachypnea, malaise, insomnia, sleepiness, fatigue, depression, and confusion. A decrease in exercise tolerance, fever, and/or new radiologic anomalies suggestive of pulmonary disease may herald a COPD exacerbation. An increase in sputum volume and purulence points to a bacterial cause, as does prior history of chronic sputum production.[86,95]

Assessment of severity

Assessment of the severity of an exacerbation is based on the patient's medical history before the exacerbation, preexisting comorbidities, symptoms, physical examination, arterial blood gas measurements, and other laboratory tests. Physicians should obtain the results of previous evaluations, where possible, to compare with the current clinical data. Specific information is required on the frequency and severity of attacks of breathlessness and cough, sputum volume and color, and limitation of daily activities. When available, prior arterial blood gas measurements are extremely useful for comparison with those made during the acute episode, as an acute change in these tests is more important than their absolute values. Thus, where possible, physicians should instruct their patients to bring the summary of their last evaluation when they

come to the hospital with an exacerbation. In patients with stage IV COPD, the most important sign of a severe exacerbation is a change in the mental status of the patient and this signals a need for immediate evaluation in the hospital.

Spirometry and PEF

Even simple spirometric tests can be difficult for a sick patient to perform properly. These measurements are not accurate during an acute exacerbation; therefore, their routine use is not recommended.

Pulse oximetry and arterial blood gas measurement

Pulse oximetry can be used to evaluate a patient's oxygen saturation and need for supplemental oxygen therapy. For patients that require hospitalization, measurement of arterial blood gases is important to assess the severity of an exacerbation. A PaO_2 less than 8.0 kPa (60 mm Hg) and/or SaO2 less than 90% with or without $PaCO_2$ more than 6.7 kPa (50 mm Hg) when breathing room air indicate respiratory failure. In addition, moderate to severe acidosis (pH less than 7.36) plus hypercapnia ($PaCO_2$ more than six to eight kPa, 45 to 60 mm Hg) in a patient with respiratory failure is an indication for mechanical ventilation.[96]

Chest X-ray and ECG

Chest radiographs (posterior/anterior plus lateral) are useful in identifying alternative diagnoses that can mimic the symptoms of an exacerbation. An ECG aids in the diagnosis of right heart hypertrophy, arrhythmias, and ischemic episodes. Pulmonary embolism can be very difficult to distinguish from an exacerbation, especially in advanced COPD, because right ventricular

hypertrophy and large pulmonary arteries lead to confusing ECG and radiographic results. A low systolic blood pressure and an inability to increase the PaO_2 above 8.0 kPa (60 mm Hg) despite high-flow oxygen also suggest pulmonary embolism. If there are strong indications that pulmonary embolism has occurred, it is best to treat for this together with the exacerbation.

Other laboratory tests

The complete blood count may identify polycythemia (hematocrit 55%) or suggest bleeding. White blood cell counts are usually not very informative. The presence of purulent sputum during an exacerbation of symptoms is sufficient indication for starting empirical antibiotic treatment. Streptococcus pneumoniae, Hemophilus influenzae, and Moraxella catarrhalis are the most common bacterial pathogens involved in COPD exacerbations. If an infectious exacerbation does not respond to the initial antibiotic treatment, a sputum culture and an antibiogram should be performed. Biochemical test abnormalities can be associated with an exacerbation and include electrolyte disturbances (for example, hyponatremia, hypokalemia), poor glucose control, or metabolic acid base disorder. These abnormalities can also be due to associated comorbid conditions.

DIFFERENTIAL DIAGNOSES

Patients with apparent exacerbations of COPD who do not respond to treatment[90,97] should be reevaluated for other medical conditions that can aggravate symptoms or mimic COPD exacerbations, including pneumonia, congestive heart failure, pneumothorax, pleural effusion, pulmonary embolism,

and cardiac arrhythmia. Noncompliance with the prescribed medication regimen can also cause increased symptoms that may be confused with a true exacerbation. Elevated serum levels of brain-type natriuretic peptide, in conjunction with other clinical information, can identify patients with acute dyspnea secondary to congestive heart failure and enable them to be distinguished from patients with COPD exacerbations.[98,99]

METHODOLOGY

The present study was conducted on the patients admitted with the diagnosis of AECOPD under the Department of Internal Medicine and Respiratory Medicine General Wards of KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the period of January 2008 to December 2008.

Study design

One year cross-sectional study.

Study period

The present study was conducted during January 2008 to December 2008.

Method of collection of data

Source of Data

Patients admitted with the diagnosis of AECOPD under the Department of Internal Medicine and Respiratory Medicine General Wards of KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the study period.

Sample size

Eighty five (85) patients admitted with the diagnosis of AECOPD admitted under Internal Medicine and Respiratory Medicine General Wards.

Sampling procedure

The study included 85 patients admitted with the diagnosis of AECOPD based on the 80% of average last three year admissions at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Selection Criteria

Inclusion Criteria

- All the patients admitted with AECOPD irrespective of their admission glycemic status. COPD was designated by premorbid pulmonary function testing when available. In the absence of documented air flow obstruction we used clinical criteria, clinical history with compatible physical findings and/or evidence of hyperinflation on chest radiograph in support of the diagnosis of COPD. Once the patient was stabilized the patients were subjected for spirometric studies and his/her COPD status confirmed. In patients with COPD, acute exacerbation was diagnosed by the following criteria.

    - Recent rapid worsening of dyspnoea
    - Increase in Sputum Purulence
    - Increase in Sputum Volume

Exclusion Criteria

- Patients with Bronchial Asthma, Interstitial Lung Disease and Bronchiectasis.

- Patients of AECOPD with myocardial infarction/CVA/requiring surgery.
- Patients not willing to participate in the study.

Procedure

The study was approved by the Ethical and Research Committee of J. N. Medical College, Belgaum. Patients who fulfilled the inclusion criteria were selected for the study. The selected patients were briefed about the nature of the study and informed consent was obtained (Annexure–I). The consented patients after being included in the study were subjected to detailed clinical examination according to predesigned and pretested proforma (Annexure-II).

Further, first and foremost an attempt to establish the severity of exacerbation by clinical questionnaire and examination supported by appropriate blood investigations as well as the severity of pre-existing COPD was done by the use of gold classification. Blood glucose measurements at the time of admission were noted. The patients were followed up in the hospital over time, until they were discharged or till death ensued. A composite adverse outcome was defined as, death or length of stay longer than the median length of stay for analysis. Since this study included all subjects who came with AECOPD irrespective of their admission glycemic levels this study automatically included normoglycemic subjects who were compared as controls with hyperglycemic subjects who otherwise matched in their severity of COPD.

Instruments/Tools

Socio demographic and clinical data sheet

This sheet was used to collect the patient's socio demographic data, including age, gender, educational status, residential status, socioeconomic status, past history, family history, personal history and details of general physical examination.

Interventions

- RBS using hexokinase method.
- Serum HbA1C levels.
- Peak Expiratory flow metry.
- Spirometry.
- Sputum microbiological examination.
- Chest X-ray.
- ECG.
- Full blood counts.
- Routine urine analysis.
- Arterial blood gas analysis.
- Mini renal profile.

Statistical Methods

- Kruskal Wallis Test
- Man Whitney Test
- Test of Proportions

RESULTS

The present study was conducted on the patients admitted with the diagnosis of AECOPD under the Department of Internal Medicine and Respiratory Medicine General Wards of KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the period of January 2008 to December 2008. Eighty five (85) patients admitted with the diagnosis of AECOPD during the study period. The observations made were recorded and findings were tabulated as follows.

Table 4: Gender wise distribution

Sex	Patients	
	Number	Percentage
Male	72	84.70%
Female	13	15.30%

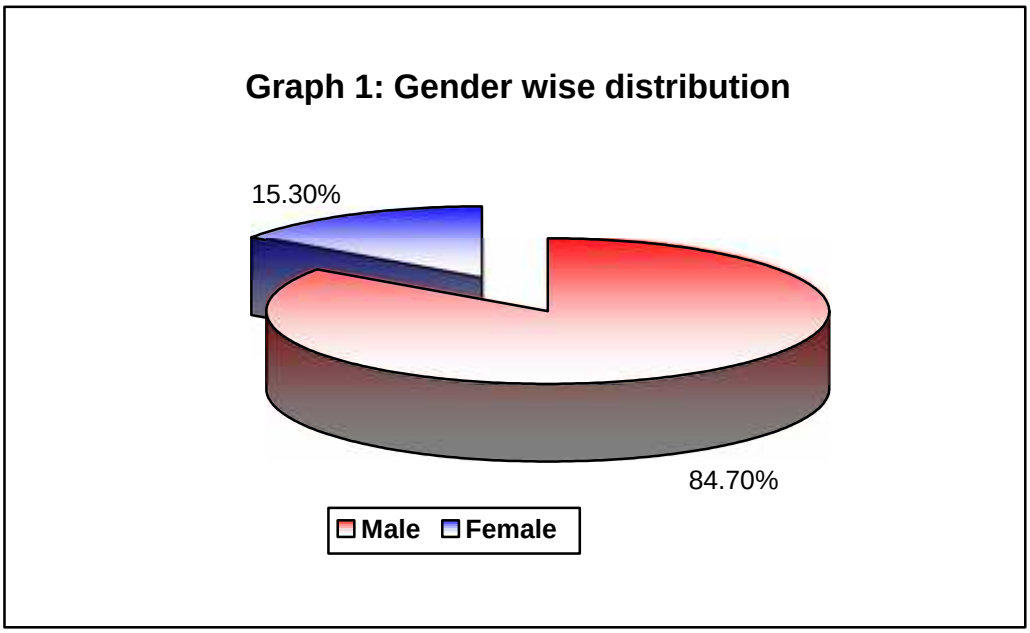
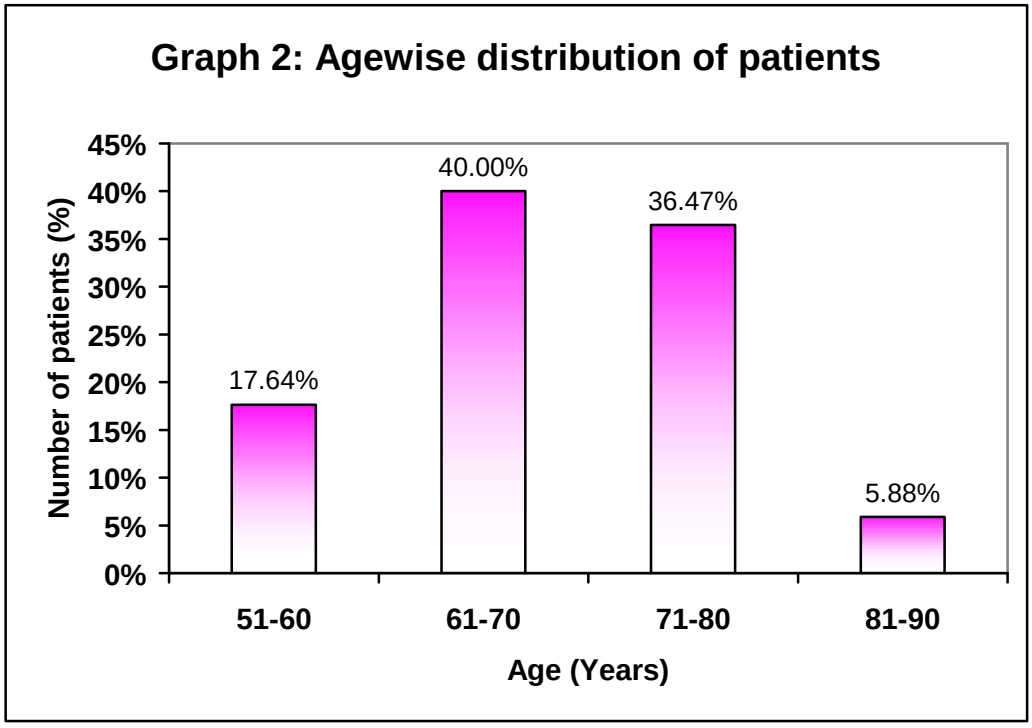


Table 5: Agewise distribution of patients

Age (Years)	Patients	
	Number	**Percentage**
51 – 60	15	17.64%
61 – 70	34	40.00%
71 – 80	31	36.47%
81 – 90	05	5.88%



In the present study, 17.64% (n=15) patients fell into the age group of 51 to 60 years, 40% (n=34) patients fell into the age group of 61 to 70 years, 36.47% (n=31) patients fell into the age group of 71 to 80 years, 5.88% (n=5) patients fell

into the age group of 81 to 90 years and the mean age of the population under study was 70.03 +/- 18.25 years.

Table 6: Symptoms

Symptoms	Patients	
	Number	**Percentage**
Dyspnoea	85	100%
Wheeze	64	75.29%
Cough with expectoration	52	61.17%
Fever	52	61.17%
History of URTI	27	31.76%

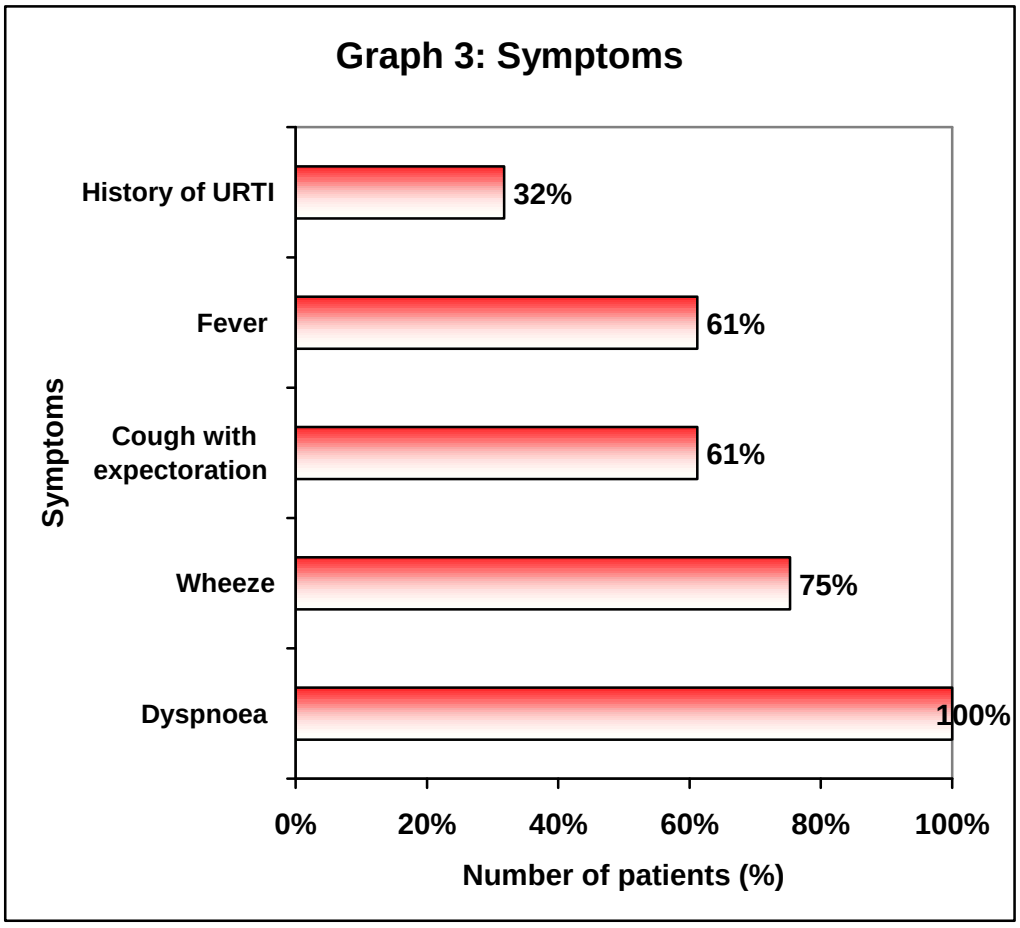
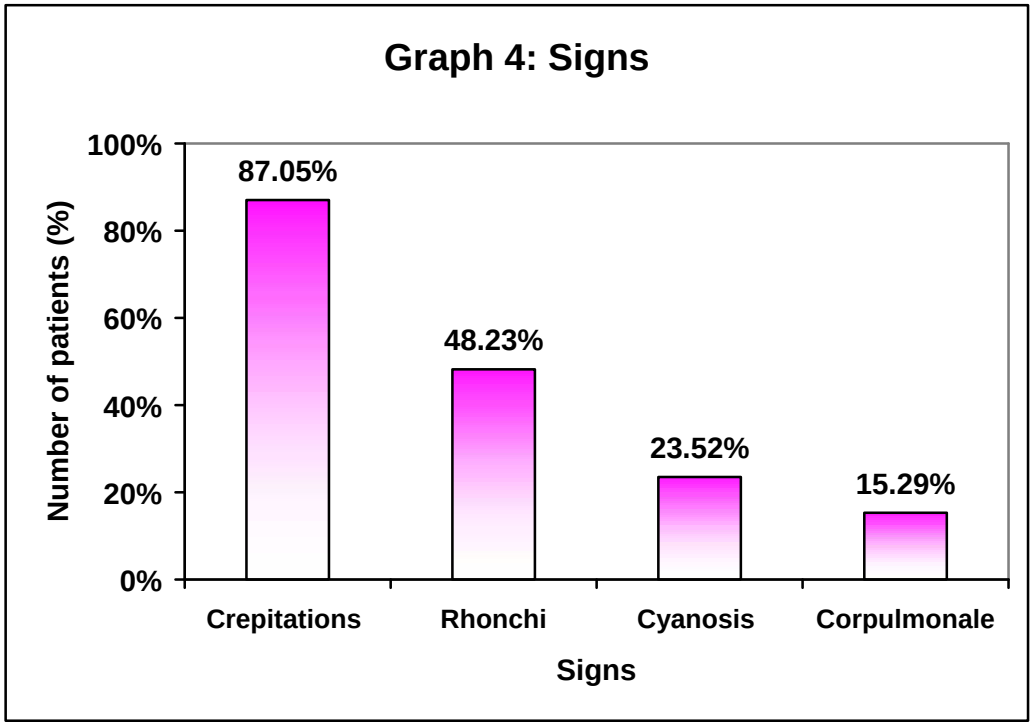


Table 7: Signs

Signs	Patients	
	Number	**Percentage**
Crepitations	74	87.05%
Rhonchi	41	48.23%
Cyanosis	20	23.52%
Corpulmonale	13	15.29%

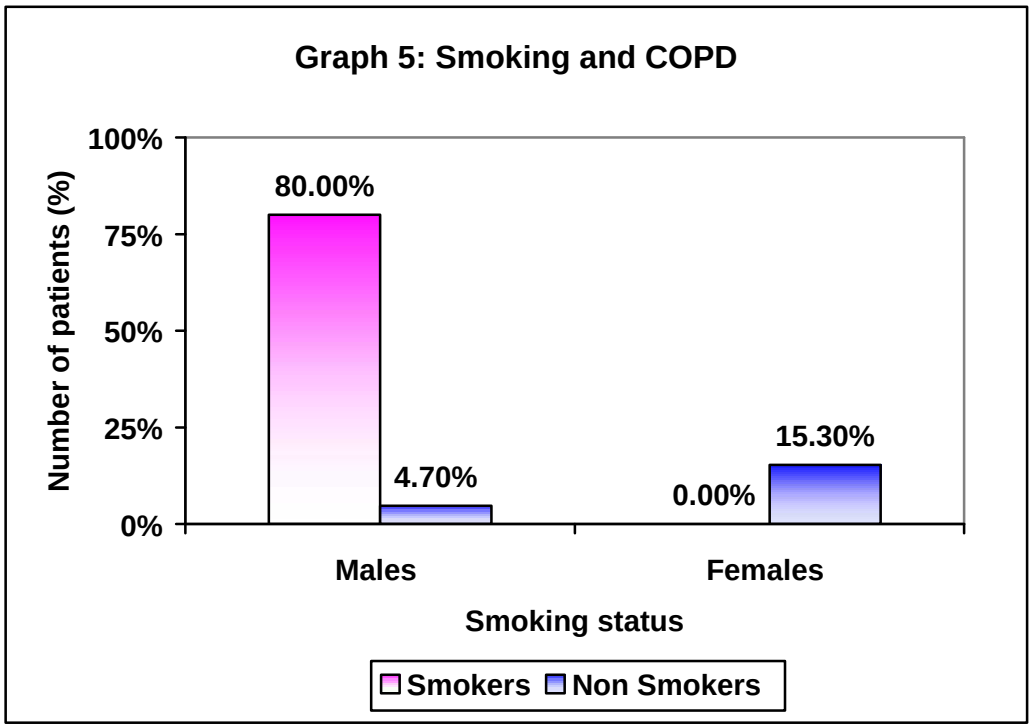


In the present study, out of the total 85 patients, All patients (n=85) complained of Dyspnea (Grade 4 to Grade 5 according to MRC dyspnea scale), 75.29% of patients (n=64) had history of wheeze, 61.17% of patients (n=52) complained of cough with expectoration and fever, 31.76% of patients (n=27) had history of upper respiratory tract infection, 87.05% of patients (n=74) had

wide spread scattered crepitations, 48.23% of patients (n=41) had scattered polyphonic rhonchi, 23,52% of patients (n=20) had central cyanosis and 15.29% of patients (n=13) were in corpulmonale.

Table 8: Smoking and COPD

Signs	Males		Females		Total	
	No	Percentage	No.	Percentage	No.	Percentage
Smokers	68	80.00%	00	0%	68	80%
Non smokers	04	4.70%	13	15.30%	17	20%



In the present study, out of the total 85 patients, 94% of male patients (n=68) were smokers and 6% (n=4) were nonsmokers. None of the female patients smoked but had significant history of exposure to cooking fuels in their

past. In the smoking population (n=68), the average number of pack years was 20 and the average smoking index was 314.

Table 9: Classification of patients according to GOLD criteria

Signs	Number of patients (%)	Median length of stay (Days)
Stage 1	00 (0%)	-
Stage 2	09 (10.58%)	5.0
Stage 3	31 (36.47%)	6.0
Stage 4	45 (52.94%)	8.0

p=0.0001*

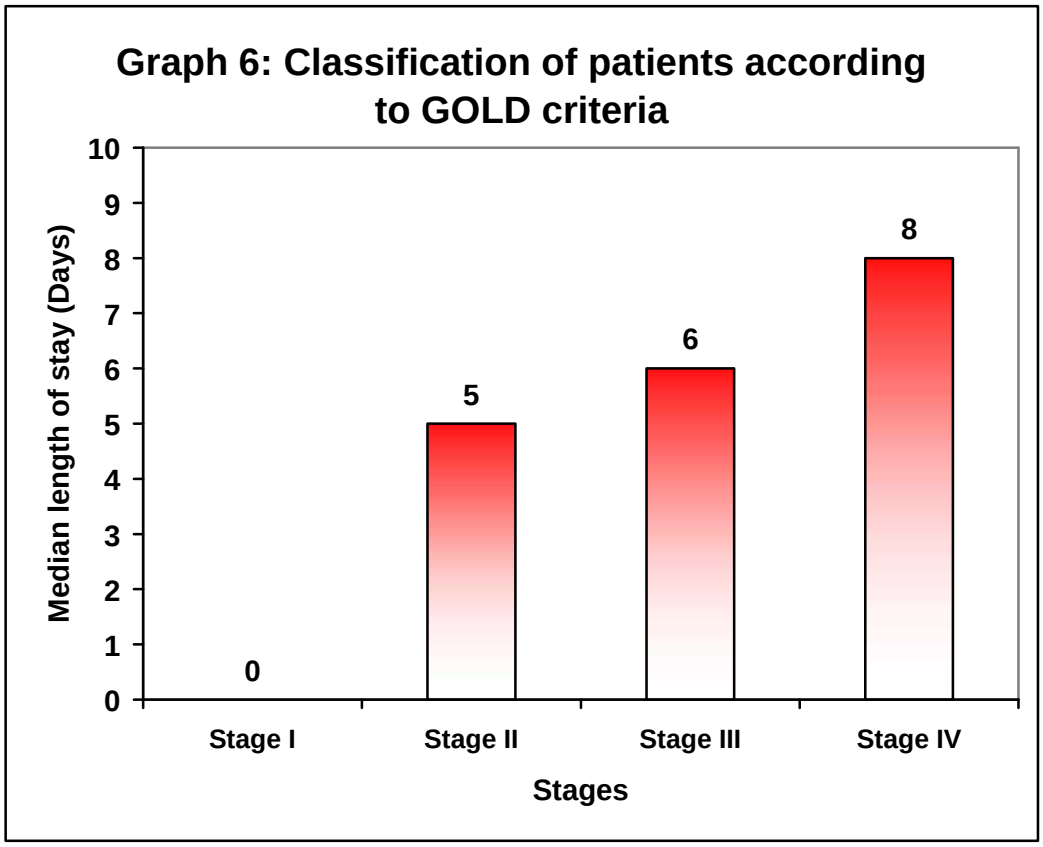
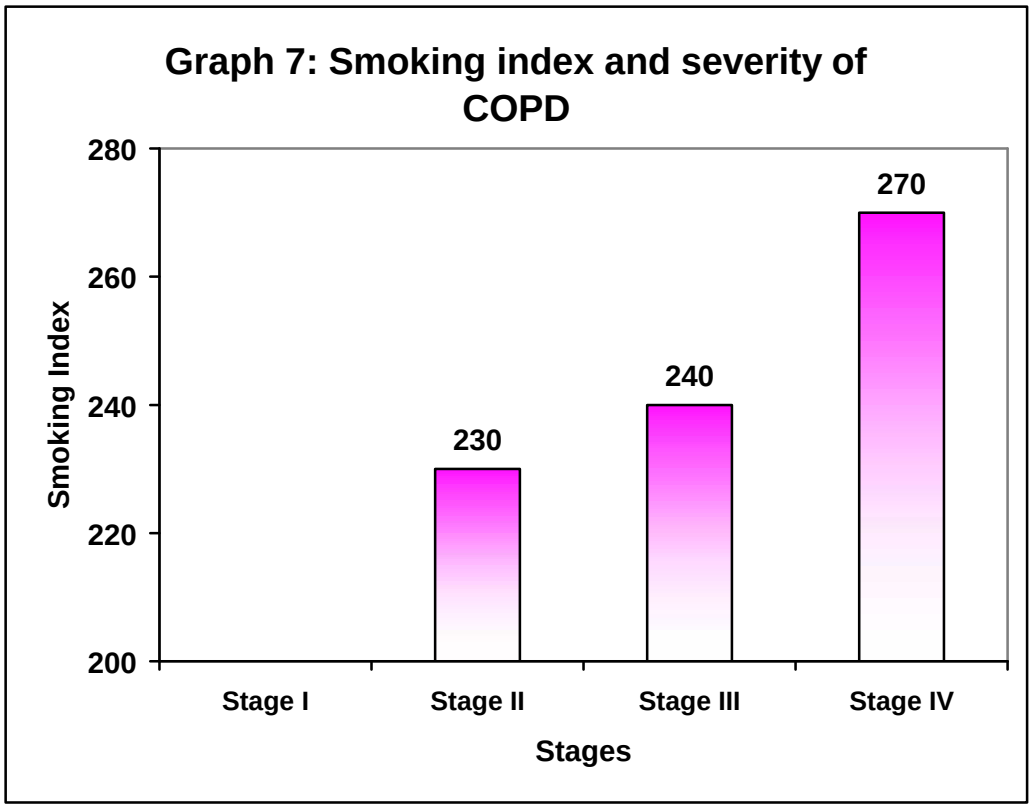


Table 10: Smoking Index and Severity of COPD

Stages	Smoking index
Stage 1	00
Stage 2	230
Stage 3	240
Stage 4	270

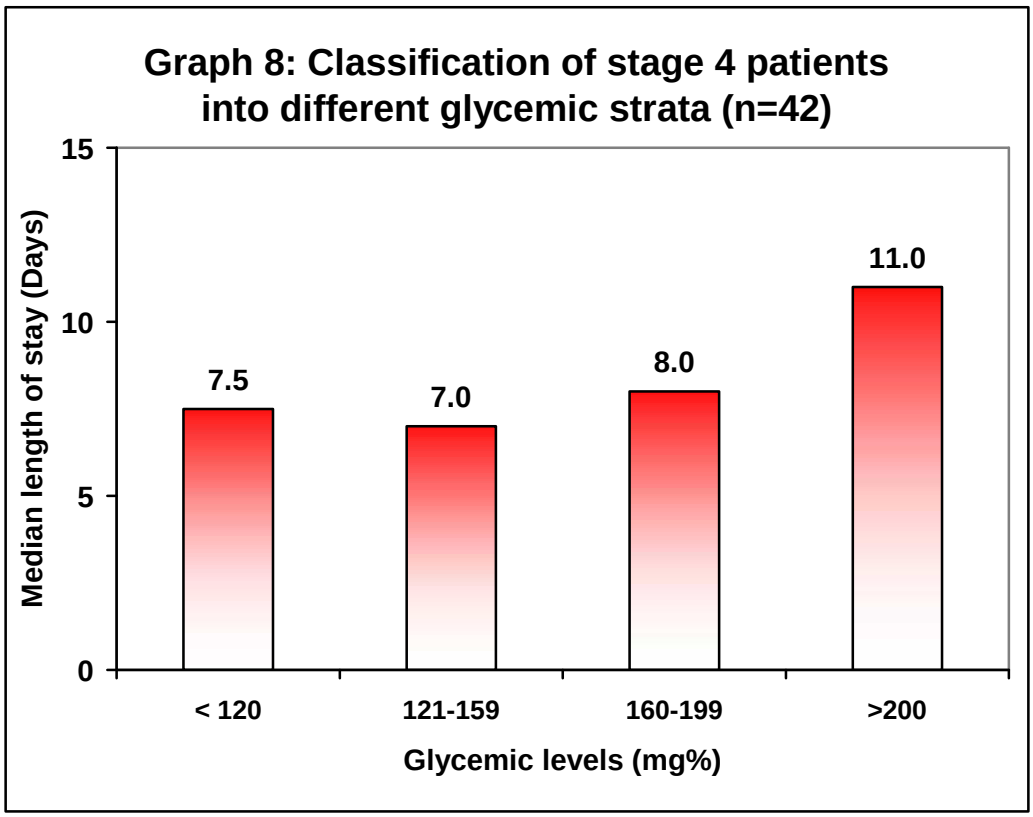


The smoking index in stage II patients was 230, in stage III it was 240 and in stage IV patients it was 270. There were no patients in stage I COPD. As the smoking index increased, so did the severity of COPD.

Table 11: Classification of stage 4 patients into different glycemic strata (n=42)

Glycemic levels (mg%)	Number of patients	Median length of stay (Days)
< 120	08	7.5
121 – 159	10	7.0
160 – 199	11	8.0
≥ 200	13	11.0

p=0.0029*



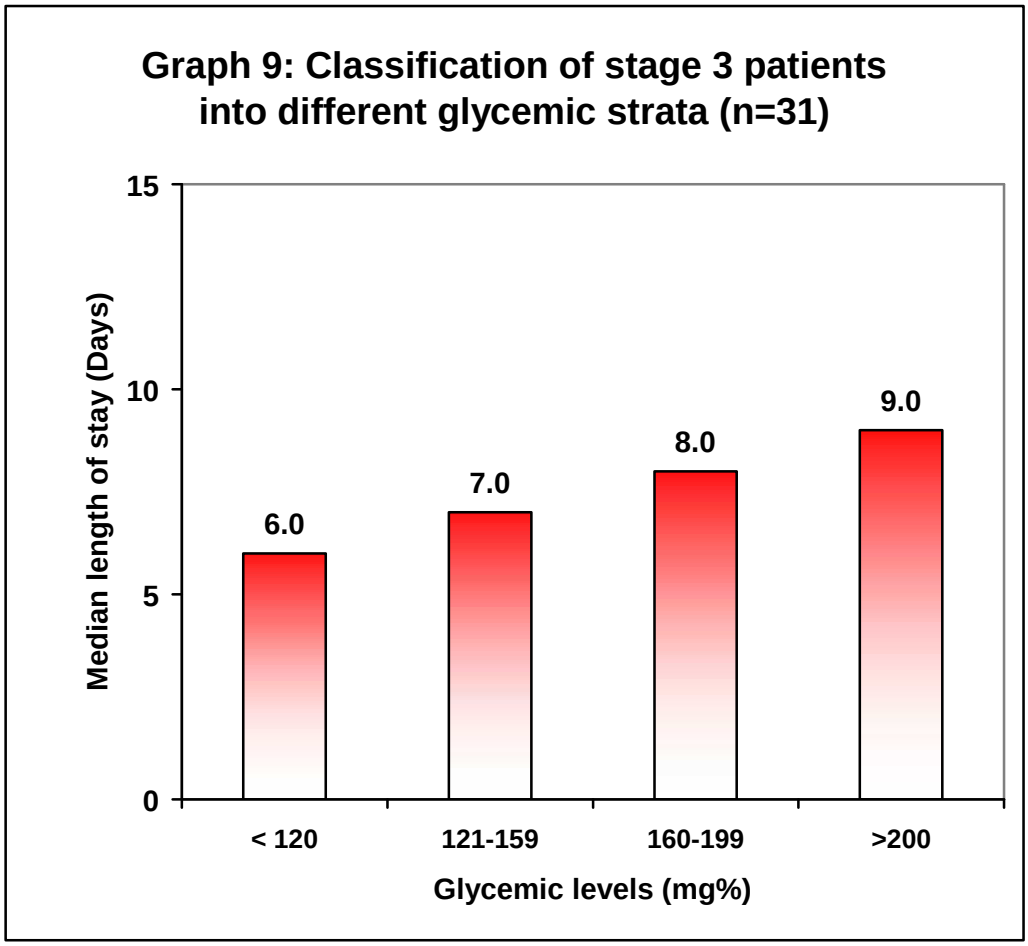
In the present study, the Median length of stay for all the patients in stage four COPD was 8 days. As the value of admission RBS increased so did the median length of stay in the hospital. Using Kruskal-wallis test, there is non homogeneity among the medians of the above four groups and thus P value was statistically significant (P = 0.0029*).

Three patients expired in a total of 85 patients. The crude mortality rate of this study was 3.53%. These three patients belonged to stage 4 group as indicated by their past medical records. The mortality rate for stage 4 group of patients was 7.14%. For the purpose of statistical analysis these three patients who expired were not considered in calculating the median length of stay.

Table 12: Classification of stage 3 patients into different glycemic strata (n=31)

Glycemic levels (mg%)	Number of patients	Median length of stay (Days)
< 120	11	6.0
121 – 159	05	7.0
160 – 199	06	8.0
≥ 200	09	9.0

p=0.1506

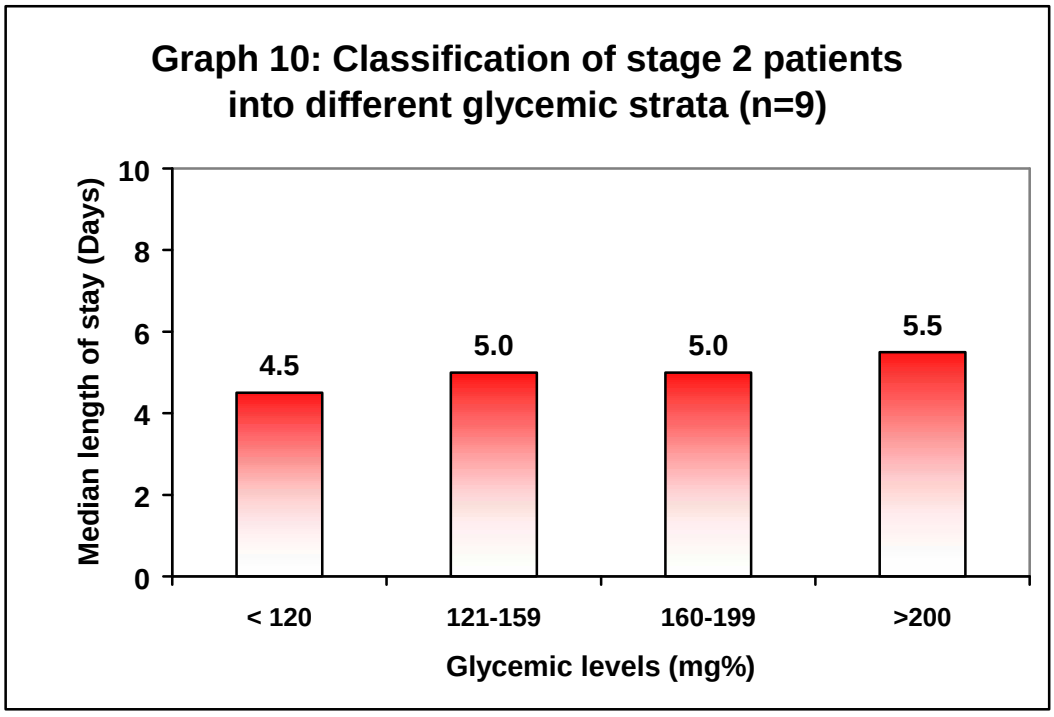


In the present study, the Median length of stay for all the patients in stage three was 6 days. As the value of admission RBS increased, so did the median length of stay in the hospital. Using Kruskal-Wallis test, there is homogeneity among the median of the above four groups and thus cannot be considered statistically significant. (p=0.1506)

Table 13: Classification of stage 2 patients into different glycemic strata (n=9)

Glycemic levels (mg%)	Number of patients	Median length of stay (Days)
< 120	02	4.5
121 – 159	04	5.0
160 – 199	01	6.0
≥ 200	02	5.5

p=0.6309

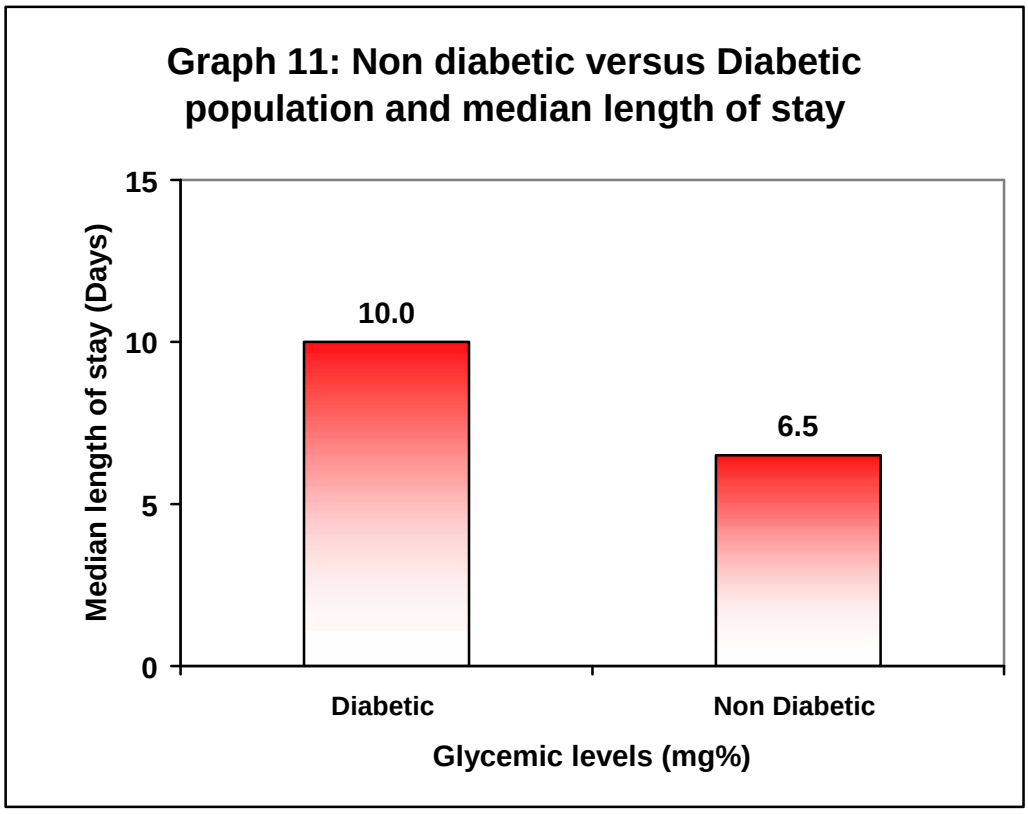


In the present study, the Median length of stay for this group is 5 days. Using K-W test, it is found that there is homogeneity among medians of the above four groups. P = 0.6309, which is statistically not significant.

Table 14: Non diabetic versus Diabetic population and median length of stay

Glycemic levels (mg%)	Number of patients (%)	Median length of stay (Days)
Diabetics	35 (41.18%)	10
Non diabetics	50 (58.82%)	6.5

p=0.0002*



In the present study, the median length of stay of patients among the Diabetic group was more than that of nondiabetic group with a P value of 0.0002* which was statistically significant. Man Whitney test was used to compare various parameters, between Diabetic and non Diabetic populations.

Table 15: Gram stain/culture/corpulmonale/respiratory failure and artificial ventilation

Culture	Non diabetics	Diabetics	p value
Gr. Stain positive	2	11	<0.001*
Culture positive	2	10	<0.001*
Cor pulmonale	4	9	0.026*
Respiratory failure	9	7	0.816
Artificial ventilation	2	5	0.90

In the present study, 11 patients in the diabetic group had demonstrable organisms in sputum, on Gram staining as compared to two in nondiabetic group, with P value of less than 0.001 which was statistically significant. 10 patients in the Diabetic group had demonstrable sputum cultures compared to only 2 in the non diabetic group, with P value of less than 0.001 which was again statistically significant. Nine patients in the Diabetic group had corpulmonale as compared to four in the diabetic group, with P = 0.026, which was statistically significant.

Seven patients in the Diabetic group as compared to nine in the non diabetic group had respiratory failure but p=0.816 is statistically not significant. Five patients in the Diabetic group required artificial ventilation, as compared to two in the non diabetic group but p=0.09. Hence, it was not statistically significant.

Table 16: Sub group analysis of the Diabetic group (n = 35)

Parameters	Status	Number of patients	Median length of stay (Days)	p value
Gram stain	Positive	11	11	0.3556
	Negative	24	9.5	
Culture	Positive	10	11	0.3710
	Negative	25	9	
Cor pulmonale	Present	9	11	0.4850
	Absent	26	9.5	
Respiratory failure	Present	7	11	0.6143
	Absent	28	10	
Artificial ventilation	Required	5	11	0.4795
	Not required	30	10	

In the present study, sub group analysis of the diabetic group revealed longer median length of stay among patients with, sputum Gram Stain positive, Culture positive, Patients in whom corpulmonale was present, Patients who were in Type 2 respiratory failure and Patients who required artificial ventilation. However this difference was not statistically significant ($p>0.05$).

DISCUSSION

COPD is one of the leading causes of morbidity and mortality worldwide. Strategies to reduce mortality and length of stay from AECOPD are urgently required. Previous studies have shown that in hospital mortality form AECOPD is predicted largely by fixed factors such as older age[3,4] male sex, co-morbidity, higher income[4] and arterial pH.[3] Hyperglycemia at the time of presentation is associated with a poor outcome in a wide range of acute illness. The relationship between blood glucose levels and clinical outcomes in AECOPD has not been fully established.

The present study was undertaken to determine the relationship between admission blood glucose concentrations and clinical outcomes in patients admitted with AECOPD. A composite adverse outcome was defined as death or length of stay longer than the median length of stay for analysis. A total of 85 patients were included in this study. 84.7% patients were males and the rest females. All the patients were between the age group of 51 to 90 years. The mean age of the population under study was 70.03 ± 18.25 years. This was similar to the observation made in a prospective study[100] carried out in 1997 at a acute care teaching referral center, in the province of Barcelona, Spain where the mean age of the population under study was 72.2 ± 9.25 years.

Out of the total 85 patients, All patients complained of Dyspnea (Grade IV to Grade V according to MRC dyspnea scale), 75.29% of patients had history of wheeze, 61.17% of patients complained of cough with expectoration and fever, 31.76% of patients had history of upper respiratory tract infection, 87.05% of

patients had wide spread scattered crepitations, 48.23% of patients had scattered polyphonic rhonchi, 23.52% of patients had central cyanosis and 15.29% of patients were in corpulmonale. Clinical presentation of AECOPD observed in the present study was similar to that reported from studies reported from other parts of the world.[101,102,103]

Out of the total number, 80% of patients were smokers and 20% nonsmokers. The average number of pack years in the smoking population was 20 and the average smoking index was 314. As the smoking index increased, so did the severity of COPD. This is in accordance with the well known fact that, more heavier the smoking habit, more earlier is the rate of development and severity of COPD.

The total numbers of patients were divided into different groups depending on their severity of COPD according to the GOLD criteria.[72] As the severity of COPD increased so did the median length of stay in the hospital (p=.0001*). This was in accordance with the observations noted in a Turkish study,[104] wherein 81 patients were studied, and the group which had more severe COPD had a slightly longer length of stay in the hospital than patients in the group with less severe COPD.

In each stage of COPD, Patients were further divided into different glycemic strata, according to their admission RBS levels and the outcome studied. Among the stage IV group of patients, as the admission RBS increased, so did the median length of stay in the hospital (p=0.0029*). This was in accordance with the observations made in other similar studies in different acute

illnesses, wherein it was opined that admission hyperglycemia is an independent predictor of morbidity and/or mortality in patients admitted for acute coronary syndromes, ischemic stroke, heart failure, community acquired pneumonia, trauma, and a variety of surgical procedures.[6,7,9,10,17,105-109] However, in stage III and stage II patients this association was not found, probably because, not only admission hyperglycemia is a factor in deciding the outcome of COPD, but also various other factors play an equally important role.

Three patients expired in a total of 85 patients. The crude mortality rate of this study was 3.53%. These three patients belonged to stage IV group as indicated by their past medical records. The mortality rate for stage IV group of patients was 7.14%. This was in accordance with observations done in various other studies, which showed mortality to be as low as 2.5% in a cross sectional study done in USA in the year 1996,[4] to as high as 30% in another study done in 1993 in USA.[103]

Out of the total of 85 patients, 41.18% were in the diabetic group, which comprised of both known diabetics as well as patients with new hyperglycemia. They had a longer median length of stay in the hospital in comparison with non diabetics (p=0.0002*). Thus COPD patients with diabetes as a comorbidity had more adverse outcome than those without. This was in accordance with a similar prospective study[110] done in Lexington, USA wherein 20,296 subjects were studied and the authors concluded that, Lung function impairment was associated with a higher risk of comorbid disease, which contributed to a higher risk of adverse outcomes of mortality and hospitalisations. One another, two year prospective study[111] done in year 2000 in five university hospitals in the Nordic

countries showed, in a total of 416 patients who were hospitalized for an acute COPD exacerbation, diabetes was a risk factor for mortality. Previous studies have shown that patients with diabetes had a higher mortality rate after acute myocardial infarction[112] and cardiogenic shock[113] than did non-diabetic patients. Studies on COPD patients with co-morbidity and the relationship to mortality have shown conflicting results. One study[100] found a relation, whereas two other studies[114,115] reported no correlation between mortality and COPD with comorbidity.

Hyperglycaemia could also cause adverse outcomes from AECOPD by predisposing to infection through systemic or local effects on host immunity or bacterial growth. In the current study we found that the diabetic population had more number of sputum gram stain positive ($p<0.001$*) for organisms and culture growth positive ($p<0.001$*) than in the non diabetic group. Systemic immune defects in people with diabetes are well documented and include decreased neutrophil and macrophage chemotaxis, phagocytosis, and killing and impairment in complement and cytokine responses to infection.[116] It has been shown that local glucose concentrations in human airway secretions are normally extremely low.[117] However, when blood glucose is raised above a threshold of 6.7 to 9.7 mmol/l, glucose becomes detectable in airway secretions at concentrations of one to 11 mmol/l.[117,118] Patients intubated in ICUs who had glucose in bronchial aspirates were more likely than those without glucose in bronchial aspirates to have respiratory pathogens detected in aspirates, particularly methicillin resistant Staphylococcus aureus.[119] The major organisms isolated in the current study were S. pneumonia, S. aureus and K. pneumonia.

Cor-pulmonale was diagnosed if there was ECG (p-pulmonale; right axis deviation; right ventricular hypertrophy) evidence of right ventricular hypertrophy/dilatation.[101] In the current study, a strong association was found between, "patients who were diabetic with COPD and presented in corpulmonale" than patients who were "non diabetic with COPD and not in cor pulmonale (p=0.026*)". This was in accordance with observations made in a study conducted in Belarusian state medical university,[120] wherein 55 AECOPD patients with type 2 diabetes mellitus had higher values of pulmonary hypertension compared to patients with COPD alone who were otherwise matched in all other respects. The main morphologic substrate leading to lung pathology in DM is diabetic microangiopathy. It is the part of the pathologic process in pulmonary tissue. The lung changes are the same as in diabetic microangiopathy in other organs (kidney, eyes), but it expressiveness is less and these changes develop later than in other organs. The disorders of micro-circulation as well as nervous regulation present in DM favor to the changes for the worsening of pulmonary circulation. A long period of time in COPD evolution with episodes of acute exacerbations leads to the profound disorders of microcirculation which play the important role in the development of hypoxic PH in COPD. These disorders in DM become the additional and unfavorable factor in the case of such combined pathology (COPD plus DM). The aggravating disorders of microcirculation become the additional and burden factor which makes worse the present structural and functional disorders of bronchi and lungs in the case of combination of COPD and DM. Thus DM has a negative influence on pulmonary hemodynamics.

In the present study seven patients in the Diabetic group as compared to nine in the non diabetic group had respiratory failure but p=0.816, which is statistically not significant. In a Prospective study conducted at a tertiary referral centre in Tirupati,[101] clinical presentation and predictors of outcome was studied in 116 patients presenting with severe AE-COPD requiring admission to the medical intensive care unit between January 2000 and December 2004. patients who presented with AE-COPD who also had type II diabetes mellitus and respiratory failure, died suggesting that complications related co-morbid conditions also contribute to the morbidity and mortality However we did not find any association between patients with comorbidity of type II diabetes mellitus and respiratory failure faring poorly against euglycemic patients with respiratory failure alone. We also did not find any significant correlation between patients (n=5) in the Diabetic group who required artificial ventilation, as compared to patients (n=2) in the non diabetic group who did not require artificial ventilation (p=0.09), probably because of the small number of the study group which required mechanical ventilation as the criteria for intubation were not standardized, and noninvasive ventilation was infrequently utilized at our hospital during the period of study. Endotracheal intubation and assisted mechanical ventilation were initiated when pharmacologic and other non-ventilatory treatments failed to reverse clinically significant respiratory failure.

CONCLUSION

The conclusion arrived at from our study are that higher the admission RBS, longer was the median duration of stay in the hospital for patients with severe COPD. The diabetic population comprising of both known and new hyperglycemic patients had more positive sputum gram staining, cultures and were found more to be in cor pulmonale. The mortality rate was also very high in patients, with severe COPD and higher admission RBS levels (more than 200 mg%).

SUMMARY

In the present study we intended to determine the relationship between admission blood glucose concentrations and adverse clinical outcome defined as, Death or length of stay longer than the median length of stay for the study group, in patients admitted with AECOPD. The study was conducted in 85 cases of AECOPD admitted at KLES Dr. Prabhakar Kore Hospital and MRC Belgaum during the year 2008/2009. The cases were divided into different groups depending on the severity of COPD and in each group, depending on their admission RBS levels they were further divided into different glycemic strata and outcome compared. A secondary analysis, by dividing the total number of patients into diabetic and non diabetic groups was also made. The results are as follows.

- Patients with higher smoking Index had more severe COPD.
- As the severity of COPD increased, so did the median length of stay in the hospital.
- In the stage 4 patients as the admission RBS increased, so did the median length of stay in the hospital.
- The median length of stay in the hospital was significantly more in the diabetic group than that of the non-diabetic group.
- Patients of the diabetic group had more positive sputum gram stain and culture results and were significantly more in cor pulmonale than patients in the non diabetic group.

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ANNEXURE I

CONSENT FORM

"CORRELATION OF HYPERGLYCEMIA AND ITS OUTCOME IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE – A CROSS SECTIONAL STUDY"

Objective and purpose of the study

This research is intended to study the correlation of hyperglycemia and its outcome in patients with acute exacerbation of COPD. The principal investigator of the study is Dr. Deepak Patil under the guidance of Dr. B. Srinivas. My co-operation will be of great help to patients with chronic obstructive pulmonary disease.

Procedure

If I agree to be part of the research study I will be asked the relevant history and will be subjected to relevant clinical examination and investigations. I will also have to give blood, sputum and urine samples for the necessary investigations

Risk and Benefits

The only risk and possible discomfort I might get is while taking blood from my arm for the investigations. It may cause swelling, pain, redness, bruising or infection (rarely happens) at the site from where the blood is drawn.

Alternatives

Taking part in this study is voluntary. I may choose not to take part in this study, or if I decide to take part I can later change my mind and withdraw from the study. My decision is will not change the present or future health care or other services that I receive. The study doctor or sponsor may stop my participation in this study any time. If I choose not to take part in the study I will receive the standard treatment for patients with my condition.

Privacy and Confidentiality

All information collected about me during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify me in this research record. Information from this study may be published but my identity will be confidential in any publication.

Institution / Sponsor's policy

Does not apply to this research

Financial incentives for participation

I will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MS degree, review and publishing.

If I have any questions about my rights as a participant I may call Dr. V. D. Patil, Principal and Chairman, J.N.M.C Ethical Committee for Human Research phone number 0831-2471350.

Consent Statement

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read, or it has been read to me, this entire consent form, and have had all my questions answered.

Name of the Participant or legally authorised representative : _____

Signature / Thumb print _____

In case of the queries during study or in future you may contact following person

Principal investigator : Dr. Deepak C. Patil

Guide : Dr. B. Srinivas

Name of the Witness _____

Signature _____

Investigator Name and Signature _____

Date: Place:

ANNEXURE II - PROFOMA

Title: Correlation of hyperglycemia and its outcome in patients with acute exacerbation of chronic obstructive pulmonary disease – A cross sectional study.

Principal Investigator: Dr. Deepak C. Patil

Sr. No.	:	I.P. No	:
Name	:	Age	:
Sex	:	Occupation	:
Address	:	Ward	:
Date of Admission	:	Date of discharge/death:	
Duration of COPD	:		

History of present illness

Cough :

Sputum

Quality :

Quantity :

Breathlessness :

(Grading according to Medical Research Centre Scale)

Wheezing :

Fever :

History of upper respiratory tract infection :

Recent exposure to dust / smoke / fume :

Symptoms suggestive of diabetes mellitus : Polyuria / polydipsia /polyphagia

Co-morbid illness

Pulmonary tuberculosis : Diabetes Mellitus :

Hypertension :

Personal History

Smoking

Type :

Pack years :

Smoking index :

Alcoholism :

Treatment History

β2 agonist :

Xanthine derivatives :

Oral steroids :

Inhalational drugs :

β2 agonists :

Anticholinergics:

Corticosteroids:

Oxygen :

H/o of vaccine immunization:

Antidiabetics :

Family History

Asthma : Atopy :

Allergy :

General Examination

Height : Weight :

Dependent edema : Conjunctival suffusion:

Lymphadenopathy : Cyanosis :

Clubbing : Diaphoresis :

Single breath count :

Vital data

Pulse rate : Blood Pressure :

Temperature : Respiratory rate :

Jugular venous pressure : Pulses Paradoxus :

Systemic Examination

Respiratory system

Barrel shaped chest : Purse lip breathing :

Accessory muscle use : Suprasternal indrawing:

Paradoxical abdominal movements: Intercostal indrawing :

Intensity of breath sounds: Tracheal tug :

Wheeze: Crepitations :

Hyper-resonant note on percussion:

Cardiovascular system

Right ventricular heave :

Pulmonary flow murmurs :

Second heart sound :

Per abdomen

Hepatomegaly :

Splenomegaly :

Ascites :

Central nervous system

Investigations

1. Hemoglobin :
2. Total leukocyte count :
3. Differential leukocyte count :
4. Erythrocyte sedimentation rate :
5. RBC count :
6. Platelets :

II. a. Random blood sugar using Hexokinase method :

b. Serum HbA_1C

III. Blood urea :

IV Sr. Creatinine :

V. Sr. Electrolytes :

VI. Urine analysis :

VII. ABG :

VIII. Sputum

Gram stain :

Culture and sensitivity :

AFB stain :

IX. Chest X-ray :

X. ECG :

XI Peak expiratory flow meter (ml)

AM :

PM :

XII. Spirometry :

	Pred (L)	**Actual (L)**
FVC		
FEV1		
FEV1/FVC		

XIII. BODE Index

Treatment given

Oxygen :

β2 agonist :

Parenteral steroids :

Xanthine derivatives :

Inhalational drugs :

Antibiotics :

Mechanical ventilation:

Non-invasive :

Invasive :

Antidiabetics :

Length of stay in the hospital :

Outcome :

ANNEXURE III - MASTER CHART

Sl. No.	IP. No.	Age (Years)	Sex	Date of admission	Date of Discharge	Cough with expectoration	MRC Grade	Wheeze	Fever	URTI	History of hypertension	History of diabetes mellitus	Smoking index	Cyanosis	Crepts	Rhonci	Cor Pulmonale	Haemoglobin (gm%)	Total leukocyte count (/cmm)	Blood Urea (mg/dL)	Serum Creatinine (mg/dL)	Serum sodium (meq/L)	Serum potassium (meq/L)	Urinary tract infection	pH	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	HCO_3 (meq/L)	Random blood sugar (mg/dL)	HBA1c (%)	Sputum Gram stain	Sputum Culture	Height (Cms)	FEV_1(P) Litres	FEV_6(P) Litres	FEV_1(A) Litres	FEV_6(A) Litres	FEV_1/FEV_6(A)	Percentage of predicted FEV1	GOLD Staging	Hospital Stay (Days)	Outcome
1	265865	58	M	1/17/2008	1/24/2008	-	3	-	-	+	-	+	0	-	-	+	-	12.5	12950	23	0.8	130	3.8	-	7.38	86.0	34.5	24.6	225	8.00	-	-	168	2.44	3.08	1.17	1.80	0.65	48	3	7	I
2	266410	74	F	1/21/2008	2/2/2008	-	4	+	-	-	+	+	0	-	+	+	+	10.4	17800	69	1.7	144	5.2	-	7.338	85.0	36.7	25.0	245	10.20	-	-	155	1.30	1.86	0.36	0.55	0.66	28	4	12	I
3	270541	75	M	4/25/2008	4/30/2008	+	4	+	+	+	-	-	300	-	+	-	-	11.7	35700	64	0.7	132	4.3	+	7.354	92.0	36.0	23.0	90	6.00	-	-	174	2.20	2.93	1.01	1.49	0.68	46	3	5	I
4	270586	82	M	4/25/2008	5/7/2008	-	4	+	+	+	-	-	150	+	+	-	-	13	14200	42	1.2	140	3	-	7.23	78.6	94.7	39.3	248	6.40	-	-	169	1.85	2.55	0.83	1.28	0.65	45	4	12	I, cpap
5	270648	66	M	4/26/2008	5/2/2008	+	4	+	-	-	-	-	0	-	+	+	-	13	3900	28	0.8	131	3.8	-	7.243	98.0	33.4	24.8	151	6.20	-	-	170	2.30	2.97	0.64	1.00	0.64	28	4	7	I
6	270684	75	M	4/26/2008	5/9/2008	-	3	+	+	-	-	+	250	-	-	+	-	10.5	10700	48	2.1	143	3.5	-	7.342	95.5	35.0	26.8	198	10.40	+	-	180	2.41	3.19	1.08	1.81	0.60	45	3	13	I
7	270758	60	M	4/27/2008	5/3/2008	+	4	+	+	-	-	-	150	-	+	+	-	7.9	14600	40	0.8	131	5	-	7.256	99.0	33.2	26.4	250	6.80	-	-	173	2.56	3.25	1.68	2.52	0.67	66	2	6	I
8	271048	75	M	4/29/2008	5/13/2008	+	3	+	-	+	-	-	200	-	+	-	-	10.3	8900	18	0.7	142	4.2	-	7.385	43.3	74.6	25.0	124	5.60	-	-	170	2.06	2.76	0.95	1.63	0.58	46	4	14	I, cpap
9	271089	60	M	4/29/2008	5/9/2008	+	4	+	-	+	-	+	240	-	-	+	-	12	12400	42	1.4	131	4.2	-	7.334	94.6	36.0	22.4	131	9.00	-	SPN	174	2.59	3.29	1.24	1.97	0.63	48	3	10	I
10	271127	60	M	4/30/2008	5/8/2008	+	4	+	-	-	-	+	180	+	+	+	-	11	9200	22	0.9	131	4.8	-	7.386	94.8	46.0	25.0	350	8.40	-	-	170	2.45	3.12	0.61	0.97	0.63	25	4	8	I
11	271465	52	F	5/3/2008	5/9/2008	+	4	+	-	-	-	-	0	+	-	+	+	12	10200	36	1.1	129	3.7	-	7.39	95.0	42.0	24.0	118	6.20	-	-	150	1.66	2.17	0.41	0.61	0.67	25	4	6	I
12	271502	80	M	5/3/2008	5/12/2008	+	4	+	+	-	-	-	300	-	-	+	-	14	6800	44	1.2	130	4.5	-	7.367	94.0	34.0	24.5	228	6.40	+	-	176	2.14	2.89	0.60	0.88	0.68	28	4	9	I
13	271581	58	M	5/4/2008	5/8/2008	-	4	-	+	+	-	-	200	-	+	+	-	13	11200	22	0.8	131	4.2	-	7.324	97.8	43.0	26.0	100	6.00	-	-	175	2.68	3.38	1.15	1.83	0.63	43	3	4	I
14	272667	60	M	5/13/2008	5/19/2008	-	4	+	-	+	+	-	320	-	+	-	+	14	6800	50	1.2	141	4.2	-	7.355	92.6	34.0	22.0	140	4.80	-	-	155	1.93	2.47	0.48	0.75	0.64	25	4	6	I
15	272882	65	M	5/14/2008	5/19/2008	-	4	-	-	-	-	-	225	-	+	+	-	14	10400	42	1.1	130	3.6	-	7.345	98.0	35.6	23.0	208	5.80	-	-	168	2.25	2.91	1.69	2.60	0.65	75	2	5	I
16	273233	63	M	5/17/2008	5/25/2008	+	3	-	+	+	-	-	320	-	+	-	-	11	14800	28	0.8	135	4.4	-	7.35	82.0	60.0	36.5	174	5.40	-	-	161	2.06	2.66	0.82	1.37	0.60	40	4	8	I, cpap
17	273486	76	F	5/19/2008	5/29/2008	+	4	+	+	-	-	-	0	-	+	+	-	10.5	12200	30	0.9	138	3.9	-	7.412	87.5	42.0	28.0	222	7.00	-	-	150	1.15	1.69	0.32	0.53	0.61	28	4	10	I
18	274291	70	M	5/26/2008	6/3/2008	-	4	+	+	+	-	-	300	-	+	+	-	12.9	18300	71	1.5	142	3	-	7.41	83.0	46.2	28.9	155	6.00	-	-	163	1.95	2.58	0.56	0.98	0.57	29	4	8	I
19	274396	66	M	5/27/2008	5/9/2008	-	4	+	+	-	-	+	300	-	+	+	-	11	7300	31	1	138	4.6	-	7.386	85.6	38.2	24.5	252	6.20	+	-	154	1.74	2.28	0.83	1.34	0.62	48	3	13	I
20	274641	70	M	5/28/2008	6/4/2008	+	4	+	-	-	-	-	300	-	+	+	-	11.4	8600	22	0.8	130	3.2	-	7.36	88.0	35.0	28.0	120	5.60	-	-	170	2.19	2.88	0.65	1.16	0.56	30	4	7	I
21	274783	61	M	5/29/2008	6/8/2008	-	3	+	-	-	-	+	250	-	-	+	-	12	10800	32	1.2	140	4.2	-	7.28	89.0	36.0	27.5	395	8.20	-	-	164	2.22	2.83	0.99	1.46	0.68	45	3	10	I
22	275241	65	M	6/2/2008	6/10/2008	+	3	+	+	+	-	-	175	-	+	-	-	13.6	14200	32	1.4	144	3.2	-	7.412	86.0	33.6	27.8	194	6.40	-	CM	168	2.25	2.91	0.63	0.93	0.68	28	4	8	I
23	275635	65	M	6/7/2008	6/16/2008	+	3	+	+	-	-	-	200	-	+	-	-	14.6	15600	52	1.4	132	5.2	+	7.352	84.6	35.4	28.0	240	5.70	-	KPN	168	2.25	2.91	0.50	0.71	0.70	22	4	9	I
24	275967	65	M	6/9/2008	6/11/2008	+	3	+	+	-	-	-	300	+	+	+	+	12.3	18600	32	1.8	144	3.2	-	7.162	54.0	56.0	26.0	280	10.20	-	-	168	2.25	2.91	0.56	0.91	0.62	25	4	2	E, InVent
25	276995	61	M	6/14/2008	6/21/2008	+	3	+	+	-	-	-	180	-	+	-	-	13.6	12600	38	0.9	136	4.2	-	7.368	88.2	34.5	26.5	180	5.80	+	-	168	2.36	3.01	0.66	0.99	0.67	28	4	7	I
26	277138	75	M	6/14/2008	6/20/2008	-	4	+	+	-	-	-	150	-	+	-	-	15.6	14200	32	1.4	132	3.6	-	7.354	96.8	36.0	26.8	90	6.10	-	-	165	1.89	2.54	0.83	1.22	0.68	44	3	6	I
27	277186	70	F	6/14/2008	6/22/2008	-	3	-	+	-	-	-	0	-	+	-	-	11.8	12200	42	1.4	132	4.2	-	7.364	92.4	32.0	25.6	170	5.50	-	-	160	1.49	2.08	0.45	0.66	0.68	30	4	8	I
28	277332	65	M	6/16/2008	6/23/2008	+	4	+	+	-	-	-	300	-	+	+	-	13.8	11800	32	0.9	132	4.2	-	7.378	98.0	35.4	22.6	166	5.80	-	-	165	2.15	2.78	0.56	0.96	0.58	26	4	7	I
29	278170	79	F	6/20/2008	6/29/2008	+	4	+	+	-	-	+	0	-	+	-	-	15.6	8600	42	1.3	132	3.8	+	7.364	97.0	36.5	24.8	240	10.80	-	-	156	1.22	1.79	0.56	0.95	0.59	46	3	9	I
30	278924	75	M	6/22/2008	6/25/2008	-	3	+	-	-	-	-	250	-	+	-	-	13.6	8900	32	1.2	132	4.2	-	7.345	98.2	32.0	22.5	140	6.20	-	CM	175	2.24	2.97	1.79	2.60	0.69	80	2	3	I
31	279474	80	M	6/25/2008	7/5/2008	-	4	+	-	-	-	+	400	-	+	-	-	14.6	9800	24	0.6	132	4.8	-	7.29	91.5	38.0	28.8	188	7.40	-	-	183	2.39	3.20	1.00	1.48	0.68	42	3	10	I
32	281480	69	M	6/28/2008	12-Jul	+	4	+	+	-	+	+	500	+	+	+	+	15.4	12800	32	0.6	126	4.6	-	7.284	84.6	48.0	24.0	222	6.80	-	CM	165	2.05	2.69	0.49	0.70	0.70	24	4	14	I
33	281506	71	M	6/28/2008	7/3/2008	+	4	+	-	-	-	-	500	-	+	-	-	13.8	12200	32	1.2	140	3.6	-	7.34	98.0	36.0	24.8	112	5.40	-	-	170	2.17	2.85	1.43	2.10	0.68	66	2	5	I

Sl. No.	IP. No.	Age (Years)	Sex	Date of admission	Date of Discharge	Cough with expectoration	MRC Grade	Wheeze	Fever	URTI	History of hypertension	History of diabetes mellitus	Smoking index	Cyanosis	Crepts	Rhonci	Cor Pulmonale	Haemoglobin (gm%)	Total leukocyte count (/cmm)	Blood Urea (mg/dL)	Serum Creatinine (mg/dL)	Serum sodium (meq/L)	Serum potassium (meq/L)	Urinary tract infection	pH	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	HCO_3 (meq/L)	Random blood sugar (mg/dL)	HBA1c (%)	Sputum Gram stain	Sputum Culture	Height (Cms)	FEV_1(P) Litres	FEV_6(P) Litres	FEV_1(A) Litres	FEV_6(A) Litres	FEV_1/FEV_6(A)	Percentage of predicted FEV1	GOLD Staging	Hospital Stay (Days)	Outcome
34	281989	78	M	6/30/2008	7/12/2008	+	4	+	-	-	-	+	200	+	+	+	+	15.6	14200	32	1.2	128	4.2	+	7.234	70.0	56.0	28.0	220	7.60	+	-	175	2.16	2.90	0.56	0.99	0.57	26	4	12	I
35	282151	65	M	7/1/2008	7/8/2008	+	3	+	-	-	-	-	375	+	+	+	-	14.6	8600	52	1.2	128	3.6	-	7.312	90.8	38.6	23.8	134	6.00	-	-	165	2.15	2.78	0.54	0.88	0.61	25	4	7	I
36	282417	72	F	7/2/2008	7/6/2008	-	3	+	-	-	-	-	0	-	+	-	-	11.8	14200	32	0.8	142	4.2	-	7.368	88.3	36.5	28.0	100	5.60	-	-	156	1.36	1.93	0.64	0.94	0.68	47	3	4	I
37	282733	76	M	7/3/2008	7/10/2008	+	3	+	+	-	-	-	250	-	+	-	-	14.6	12800	28	0.9	132	4.2	-	7.334	88.0	38.6	24.6	120	5.50	-	-	168	1.97	2.65	0.55	1.00	0.55	28	4	7	I
38	284461	60	M	7/8/2008	7/19/2008	+	3	+	+	-	-	-	250	+	+	+	+	15.8	10800	52	1.4	124	3.6	-	7.316	72.0	46.0	26.0	270	8.60	+	CM	162	2.17	2.77	0.61	0.87	0.70	28	4	11	I
39	289010	79	F	7/13/2008	7/20/2008	-	4	+	-	+	+	-	0	-	+	-	-	13.6	16800	52	1.2	144	4.6	-	7.318	82.0	42.5	26.5	180	5.90	-	-	155	1.20	1.79	0.31	0.60	0.52	26	4	7	I
40	289991	70	M	7/16/2008	7/22/2008	-	3	-	-	+	+	-	150	-	+	-	-	13.6	18200	32	0.8	140	3.8	-	7.334	80.0	38.0	23.0	90	6.10	-	-	162	1.91	2.53	0.80	1.27	0.65	42	3	6	I
41	291349	80	M	7/18/2008	7/29/2008	-	4	-	+	-	-	+	450	-	+	-	-	13.6	15600	16	0.6	134	3.8	-	7.3	82.0	36.0	27.0	280	10.80	-	CM	172	2.00	2.72	0.92	1.31	0.70	46	3	11	I
42	291929	70	M	7/24/2008	8/2/2008	+	3	+	+	-	-	-	300	+	+	+	-	15.6	11800	48	1.2	132	3.8	-	7.388	84.0	34.0	25.0	110	5.80	-	-	172	2.26	2.96	0.61	1.01	0.60	27	4	9	I
43	292319	84	M	7/27/2008	7/29/2008	+	4	+	+	-	+	+	450	+	+	+	+	13.8	14200	52	0.6	130	4.2	-	7.116	70.0	56.0	18.0	380	11.20	+	SA	158	1.41	2.02	0.35	0.60	0.58	25	4	2	E, InVent
44	292778	73	M	7/29/2008	8/5/2008	-	3	-	-	+	-	-	250	-	+	-	-	13.8	18200	40	1.2	132	4.2	-	7.356	86.5	38.0	28.0	160	5.80	-	-	168	2.05	2.72	0.59	0.96	0.62	29	4	7	I
45	293268	70	M	8/5/2008	8/19/2008	+	3	+	+	+	-	+	250	+	+	+	-	15.6	13200	32	1.2	140	4.2	-	7.288	78.6	42.0	22.0	280	10.20	-	-	158	1.74	2.36	0.71	1.29	0.55	30	4	14	I
46	293511	78	M	8/7/2008	8/17/2008	-	3	+	+	-	-	+	150	-	+	+	-	13.8	8900	20	0.9	132	4.2	-	7.378	88.0	36.5	29.0	198	7.20	-	-	172	2.06	2.77	0.62	0.95	0.65	30	4	10	I
47	293596	70	M	8/7/2008	8/13/2008	+	3	+	-	+	-	-	300	-	+	-	-	14.2	9800	42	0.8	134	3.8	-	7.324	93.4	40.0	24.0	110	6.00	-	-	170	2.19	2.88	1.05	1.60	0.66	48	3	6	I
48	293732	75	M	8/8/2008	8/16/2008	+	4	+		-	-	-	450	+	+	-	+	13.6	12600	32	1.4	128	3.8	-	7.314	70.0	47.0	24.0	154	6.20	-	-	170	2.06	2.76	0.58	0.99	0.58	28	4	8	I
49	294012	70	M	8/10/2008	8/15/2008	-	3	-	-	+	-	+	0	-	-	+	-	12.5	12900	23	0.8	130	3.8	-	7.368	96.4	38.0	24.0	225	8.00	-	-	170	2.19	2.88	1.05	1.59	0.66	48	3	5	I
50	294518	66	M	8/13/2008	8/19/2008	+	3	+	+	+	-	-	300	-	+	+	-	13	3900	20	0.8	140	3.8	-	7.398	94.5	32.6	28.6	151	6.00	-	-	180	2.65	3.40	0.85	1.28	0.66	32	3	6	I
51	294979	64	M	8/15/2008	8/22/2008	+	3	-	+	+	+	-	350	-	+	+	-	11.5	11600	30	1	142	4.2	-	7.286	89.6	52.0	24.6	180	5.80	-	-	172	2.42	3.08	0.73	1.11	0.65	30	4	7	I
52	295395	60	M	8/18/2008	8/28/2008	+	3	-	+	-	-	-	0	-	+	-	-	10	36500	40	0.9	128	3.6	-	7.412	96.0	24.0	18.0	131	6.10	-	-	168	2.38	3.03	0.87	1.32	0.66	36	3	10	I
53	295952	81	F	8/20/2008	8/26/2008	-	3	-	+	+	-	-	0	-	+	-	-	10.6	7800	32	1.4	134	3.8	-	7.345	94.5	36.5	24.5	120	5.20	-	-	165	1.75	2.43	0.78	1.16	0.68	45	3	6	I
54	296316	65	M	8/22/2008	9/4/2008	+	3	+	+	-	+	+	420	+	+	+	-	8	12800	56	1.02	134	3.8	-	7.41	90.5	42.0	18.0	180	5.50	-	-	178	2.60	3.34	0.72	1.07	0.67	27	4	13	I
55	296694	65	M	8/24/2008	8/30/2008	+	3	+	-	-	-	-	325	-	+	+	-	13.5	11600	48	1.2	140	4.2	-	7.404	92.8	30.8	26.5	130	5.80	-	-	169	2.29	2.95	0.86	1.39	0.62	37	3	6	I
56	297723	60	M	9/4/2008	9/13/2008	+	3	+	+	-	-	+	450	+	+	+	-	13	10800	43	0.6	136	4.2	+	7.348	94.6	34.5	24.0	350	10.30	-	-	170	2.45	3.12	0.78	1.41	0.55	31	3	9	I
57	298128	55	M	9/7/2008	9/21/2008	+	3	+	+	-	-	-	600	-	+	-	-	10.3	14300	16	0.6	140	4.2	-	7.317	99.0	36.8	25.6	100	4.80	-	-	173	2.63	3.31	1.26	1.91	0.66	48	3	14	I
58	298955	68	M	9/11/2008	9/20/2008	+	3	+	+	-	-	-	400	+	+	+	-	12	14500	100	1.6	144	4.6	-	7.406	92.6	32.5	24.6	100	6.20	-	-	176	2.46	3.18	0.49	0.95	0.51	19	4	9	I
59	299245	68	M	9/13/2008	9/20/2008	-	3	-	+	-	-	-	375	-	+	-	-	11	7300	31	1	136	4.2	-	7.218	90.0	48.0	22.0	153	6.20	-	-	176	2.46	3.18	0.71	1.05	0.67	28	4	7	I
60	299990	80	F	9/18/2008	9/23/2008	-	4	+	+	-	-	+	0	-	+	-	-	15.6	8600	42	1.3	132	3.8	+	7.246	92.4	34.8	26.4	240	10.80	-	-	156	1.44	2.03	0.69	1.02	0.68	48	3	5	I
61	300545	80	F	9/20/2008	9/26/2008	-	3	-	+	-	-	-	0	-	+	-	-	11.8	12200	42	1.4	132	4.2	-	7.365	96.5	36.5	27.8	170	6.20	-	-	160	1.58	2.21	0.67	1.01	0.66	43	3	6	I
62	300963	76	M	9/22/2008	30-Sep	+	3	-	+	-	-	-	480	-	+	+	-	7.8	4200	52	0.6	142	3.6	-	7.388	98.6	34.5	26.8	110	5.70	-	-	168	1.97	2.65	0.55	0.80	0.68	28	4	8	I
63	301286	70	M	9/24/2008	9/29/2008	+	3	+	-	-	+	+	600	-	+	-	-	12.9	13000	41	0.8	131	4.9	-	7.382	88.0	37.5	24.7	220	7.80	-	-	182	2.61	3.39	0.92	1.87	0.49	35	3	5	I
64	301330	80	F	9/24/2008	10/14/2008	-	4	+	+	+	+	-	0	-	+	-	-	11	9500	40	1.2	134	3.8	+	7.366	82.5	58.0	26.0	110	6.20	-	-	165	1.76	2.42	0.56	1.30	0.43	31	4	10	I
65	301550	88	M	9/26/2008	10/2/2008	-	4	-	+	+	-	+	300	-	+	-	-	13.6	7800	56	1.5	130	4.2	-	7.224	92.5	34.6	25.5	160	8.40	-	-	178	2.01	2.79	0.98	1.51	0.65	49	3	6	I
66	302213	70	M	10/1/2008	10/6/2008	+	4	+	-	-	-	-	500	-	+	-	-	13.8	12200	32	1.2	140	3.6	-	7.386	97.6	32.5	26.6	112	5.80	-	-	170	2.20	2.88	0.97	1.55	0.62	44	3	5	I

Sl. No.	IP. No.	Age (Years)	Sex	Date of admission	Date of Discharge	Cough with expectoration	MRC Grade	Wheeze	Fever	URTI	History of hypertension	History of diabetes mellitus	Smoking index	Cyanosis	Crepts	Rhonci	Cor Pulmonale	Haemoglobin (gm%)	Total leukocyte count (/cmm)	Blood Urea (mg/dL)	Serum Creatinine (mg/dL)	Serum sodium (meq/L)	Serum potassium (meq/L)	Urinary tract infection	pH	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	HCO_3 (meq/L)	Random blood sugar (mg/dL)	HBA1c (%)	Sputum Gram stain	Sputum Culture	Height (Cms)	FEV_1(P) Litres	FEV_6(P) Litres	FEV_1(A) Litres	FEV_6(A) Litres	FEV_1/FEV_6(A)	Percentage of predicted FEV1	GOLD Staging	Hospital Stay (Days)	Outcome
67	302811	64	M	10/7/2008	10/14/2008	+	3	+	-	-	-	-	375	+	+	+	-	14.6	8600	52	1.2	128	3.6	-	7.382	94.0	36.5	26.3	134	5.40	-	-	165	2.18	2.81	0.61	1.02	0.60	28	4	7	I
68	303127	78	M	10/10/2008	10/21/2008	+	4	-	+	-	+	-	375	+	+	-	+	8	19800	48	1.1	124	3.6	-	7.318	90.0	45.0	24.0	217	6.40	+	CM	175	2.16	2.90	0.60	1.00	0.60	27	4	11	I
69	303427	75	M	10/13/2008	10/26/2008	-	3	-	-	+	-	+	400	-	+	-	-	10.5	10700	48	1.2	132	4.2	+	7.382	84.6	38.2	24.3	199	7.20	+	SPN	180	2.41	3.19	0.86	1.50	0.57	35	3	13	I
70	303603	72	M	10/17/2008	10/28/2008	+	4	-	+	-	-	-	350	+	+	-	-	11.5	14800	18	0.5	140	3.6	-	7.212	86.0	55.0	26.4	303	10.60	+	SPN	168	2.07	2.74	0.55	0.79	0.69	26	4	11	I,cpap
71	304433	80	M	10/25/2008	11/3/2008	+	4	+	+	-	+	+	400	-	+	-	-	10	18900	40	1.1	130	4.2	-	7.312	88.0	55.0	18.0	228	7.80	+	SPN	170	1.93	2.64	0.58	0.96	0.60	29	4	9	I,cpap
72	304443	86	M	10/25/2008	10/31/2008	+	4	+	+	+	-	-	300	-	+	-	-	13.5	18800	64	0.7	132	4.2	+	7.386	86.5	35.6	27.0	110	5.60	-	-	174	1.92	2.66	0.86	1.31	0.66	45	3	6	I
73	304752	70	M	10/27/2008	10/28/2008	+	4	+	+	+	-	-	600	+	+	-	+	12.3	2800	56	1.8	124	4.2	-	7.236	50.0	56.0	26.0	340	6.20	-	-	168	2.12	2.79	0.85	1.70	0.50	40	4	1	E
74	304948	73	M	10/29/2008	11/13/2008	+	3	+	+	-	-	+	360	+	+	+	+	12	13200	58	1.02	126	4.2	-	7.336	90.5	36.5	22.4	154	8.20	-	-	172	2.19	2.89	0.60	0.88	0.68	27	4	15	I
75	305239	70	M	11/3/2008	11/11/2008	-	4	+	+	-	-	-	300	-	+	-	-	15.8	18000	37	0.9	140	3.6	-	7.4	82.0	46.2	28.9	184	5.40	-	-	163	1.91	2.58	0.52	0.86	0.60	27	4	8	I
76	306151	60	F	11/12/2008	11/17/2008	+	4	+	+	-	-	-	0	-	+	-	-	12.5	12400	32	0.9	140	4	-	7.386	93.4	35.0	25.5	156	6.20	-	-	150	1.49	2.01	1.01	1.45	0.70	68	2	5	I
77	306551	70	F	11/16/2008	11/21/2008	+	4	+	+	-	-	-	0	-	+	-	-	10.8	12000	38	0.6	136	3.6	+	7.338	92.0	33.0	26.8	140	5.40	-	-	154	1.36	1.92	0.98	1.51	0.65	72	2	5	I
78	306905	78	M	11/20/2008	11/26/2008	+	4	+	+	+	-	-	300	-	+	-	-	13.5	18800	64	0.7	132	4.2	+	7.332	97.5	42.0	28.0	110	5.80	-	-	174	2.13	2.86	0.60	0.91	0.65	28	4	6	I
79	307569	57	M	11/27/2008	12/2/2008	+	4	+	+	-	+	+	180	-	+	-	-	14	14600	40	0.8	132	4.6	-	7.402	88.0	34.5	26.5	160	6.80	+	-	173	2.64	3.32	1.27	1.81	0.70	48	3	5	I
80	308539	76	M	12/7/2008	12/12/2008	+	3	+	-	+	-	-	200	-	+	+	-	12.4	8800	18	0.7	140	3.6	-	7.394	83.0	32.5	25.4	120	6.10	-	-	170	2.04	2.73	0.82	1.41	0.58	40	3	5	I
81	308738	70	M	12/9/2008	12/15/2008	+	5	+	+	-	-	+	450	-	+	+	+	15.4	18400	32	0.9	128	3.6	+	7.422	88.5	36.5	30.0	156	7.40	-	-	174	2.33	3.05	0.65	0.98	0.67	28	4	6	I
82	308947	60	M	12/10/2008	12/14/2008	-	4	-	+	+	-	-	200	-	-	+	-	13.6	11800	28	0.9	134	4	-	7.346	94.5	32.5	28.8	120	5.50	-	-	175	2.63	3.33	1.84	2.92	0.63	70	2	4	I
83	309096	76	M	12/11/2008	12/17/2008	+	4	+	+	-	-	-	300	-	+	+	-	16.4	18600	44	1.2	130	3.8	-	7.267	90.6	44.0	30.0	140	5.80	+	-	176	2.21	2.99	1.66	2.54	0.65	75	2	6	I
84	309140	66	M	12/11/2008	12/18/2008	+	4	+	+	-	+	-	300	-	+	+	-	14.6	12800	46	1.2	132	4.2	-	7.388	89.0	35.5	26.5	140	6.20	-	-	165	2.12	2.76	0.96	1.71	0.56	45	3	7	I
85	309952	60	M	12/21/2008	12/26/2008	-	3	+	-	+	-	-	450	-	+	+	-	12.8	12000	23	0.8	135	4.2	-	7.325	86.5	36.5	24.6	180	5.20	-	-	168	2.38	3.03	1.79	2.59	0.69	75	2	5	I

ANNEXURE III - KEY TO MASTER CHART

-	–	Negative / Absent
+	–	Positive / Present
CM	–	Comensals grown
Cmm	–	Cubic millimeter
Cms	–	Centimeter
cpap	–	Continuous Positive Airway Pressure
E	–	Expired
F	–	Female
FEV_1(A)	–	Forced Expiratory Volume in 1 Second of the Actual Patient
FEV_1(P)	–	Predicted Forced Expiratory Volume in 1 Second for age, height and sex
FVC(A)	–	Forced Vital Capacity of the Actual Patient
FVC(P)	–	Predicted Forced Vital Capacity for age, height and sex
gm%	–	Gram percent
GOLD	–	Global initiative for chronic obstructive pulmonary disease
HBA1c	–	Glycated Hemoglobin levels
HCO_3	–	Serum Bicarbonate levels
I	–	Improved
InVent	–	Invasive Ventilation
IP. No.	–	In Patient Number
KPN	–	Klebsiella pneumonia isolated

M	–	Male
meq/L	–	Milli equivalents per litre
Mg/dL	–	Milligrams per deci litre
mm Hg	–	Millimeter mercury
MRC	–	Medical Research Council
$PaCO_2$	–	Partial Pressure of Carbon Dioxide in arterial blood
PaO_2	–	Partial Pressure of Oxygen in arterial bood
SA	–	Staphylococcus aureus
Sl. No	–	Serial Number
SPN	–	Streptococcus pneumonia isolated
URTI	–	Upper Respiratory Tract Infection