FIRST DAY PREDICTORS OF REQUIREMENT OF MECHANICAL VENTILATION IN COPD PATIENTS WITH ACUTE EXACERBATION

DISSERTATION SUBMITTED FOR

M.D GENERAL MEDICINE

BRANCH –I

APRIL 2017

THE TAMILNADU

DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI

CERTIFICATE FROM THE DEAN

This is to certify that this dissertation entitled **"FIRST DAY PREDICTORS OF REQUIREMENT OF MECHANICAL VENTILATION IN COPD PATIENTS WITH ACUTE EXACERBATION"** is the bonafide work of **Dr.DHANUS SADASIVAN NAIR** in partial fulfilment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for **M.D General Medicine Branch I** examination to be held in **April 2017.**

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THE DEAN

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Madurai.

CERTIFICATE FROM THE HOD/GUIDE

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Madurai.

DECLARATION

I **Dr.DHANUS SADASIVAN NAIR,** declare that, I carried out this work on **"FIRST DAY PREDICTORS OF REQUIREMENT OF MECHANICAL VENTILATION IN COPD PATIENTS WITH ACUTE EXACERBATION"** at the Department of Medicine, Govt. Rajaji Hospital during the period AUGUST 2015 to AUGUST 2016. I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree or diploma to any other University, Board either in India or abroad.This is submitted to The Tamilnadu Dr.M.G.R.Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D degree examination in General Medicine.

Place : Madurai

Dr.DHANUS SADASIVAN NAIR

Date:

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At the outset, I wish to thank our Dean **Dr. VAIRAMUTHU RAJU,** for permitting me to use the facilities of Madurai Medical College and Government Rajaji Hospital to conduct this study.

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I thank my friends and family who have stood by me during my times of need. Their help and support have always been invaluable to me. And last but not the least I would like thank the Lord Almighty for His grace and blessings without which nothing would have been possible.

ABBREVIATIONS

FEV1 - forced expiratory volume

FVC - forced vital capacity

COPD - chronic obstructive pulmonary disease

PFT -pulmonary function test

GOLD - global guidelines for obstructive pulmonary diseases

SHT - systemic hypertension

IU - international unit

T2DM - type 2 diabetic mellitus

ECG - Electrocardiogram

SD - Standard Deviation

CVA - cerebrovascular accident

CAD – coronary artery disease

CKD - chronic kidney disease

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading cause of mortality and the 12th leading cause of disability worldwide today. The worldwide prevalence of COPD is estimated at 9/1000 men and 7/1000 women. COPD commonly affects elderly adults with a prevalence of 15%. Studies involving COPD patients with acute exacerbations discovered a combined mortality of 20.3% with prevalence of mechanical ventilation at 9-67%.

India being a developing country, there is severe limitation of health care facilities and scarcity of availability of intensive health care facilities. Reforms in economic and health care fields have resulted in an increase in the life expectancy of Indian adults which in turn has lead to an increasing incidence of age related morbidities like COPD. The number of COPD patients who are at risk of developing acute respiratory failure and who may benefit from mechanical ventilation vastly outnumbers the critical care facilities available to deal with this burden. Hence, methods to stratify the patients based on need for intubation and mechanical ventilation are imperative.

In view of this current scenario, identification on the first day of admission, of those COPD patients with exacerbation who may require intubation and mechanical ventilation during the course of their hospital stay, will allow prompt arrangement and appropriate utilization of these scanty critical care facilities.

APACHE II (Acute Physiology and Chronic Health Evaluation II) is a severity-of-disease classification system , one of several ICU scoring systems. It is applied within 24 hours of admission of patient and calculated from 12 routine physiological measurements and 2 disease related variables. The APACHE II score ranges from 0 to 71 points, with the highest number of points pointing to a more severe form of disease.

Premorbid functional status is a measure of morbidity that indicates the severity of dyspnea, the degree of independence in performing everyday activities, which indicates the severity of the underlying COPD and associated conditions.

AIMS AND OBJECTIVES:

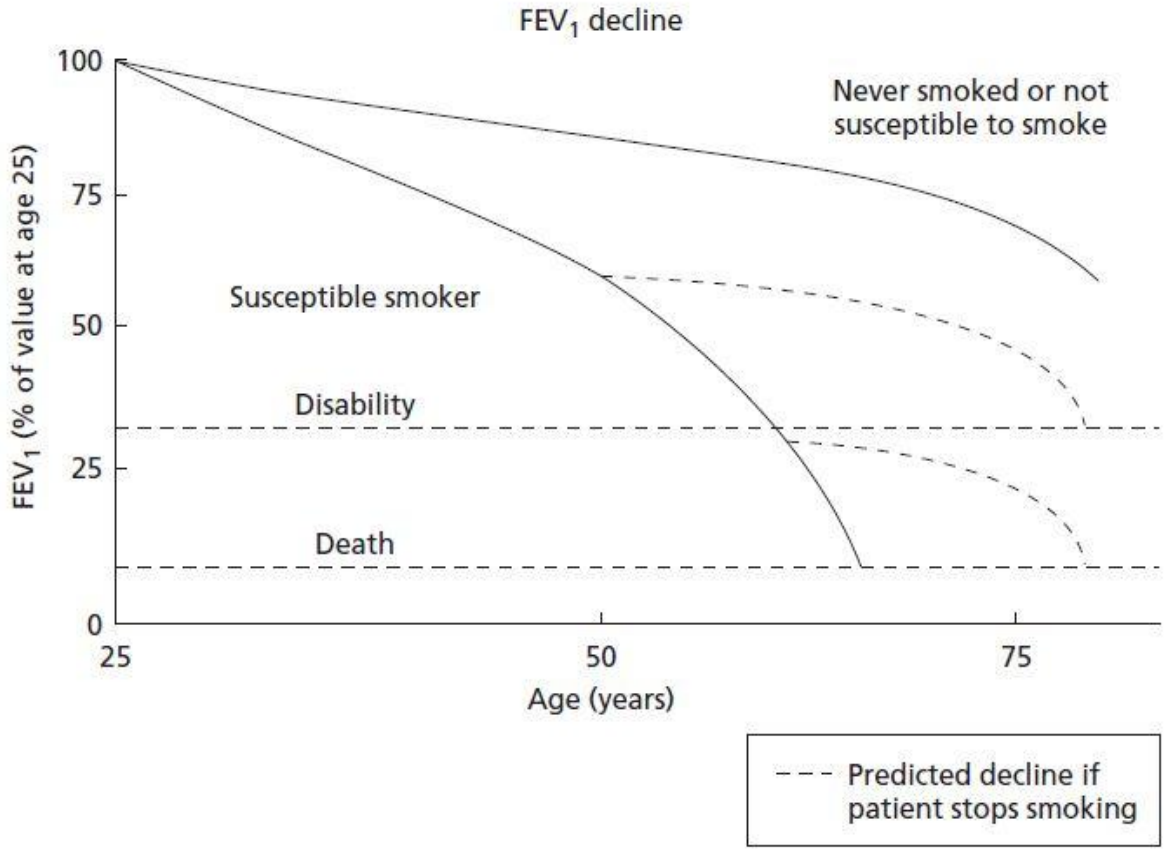
To identify the first day predictors of requirement of mechanical ventilation in COPD patients with acute exacerbation

REVIEW OF LITERATURE

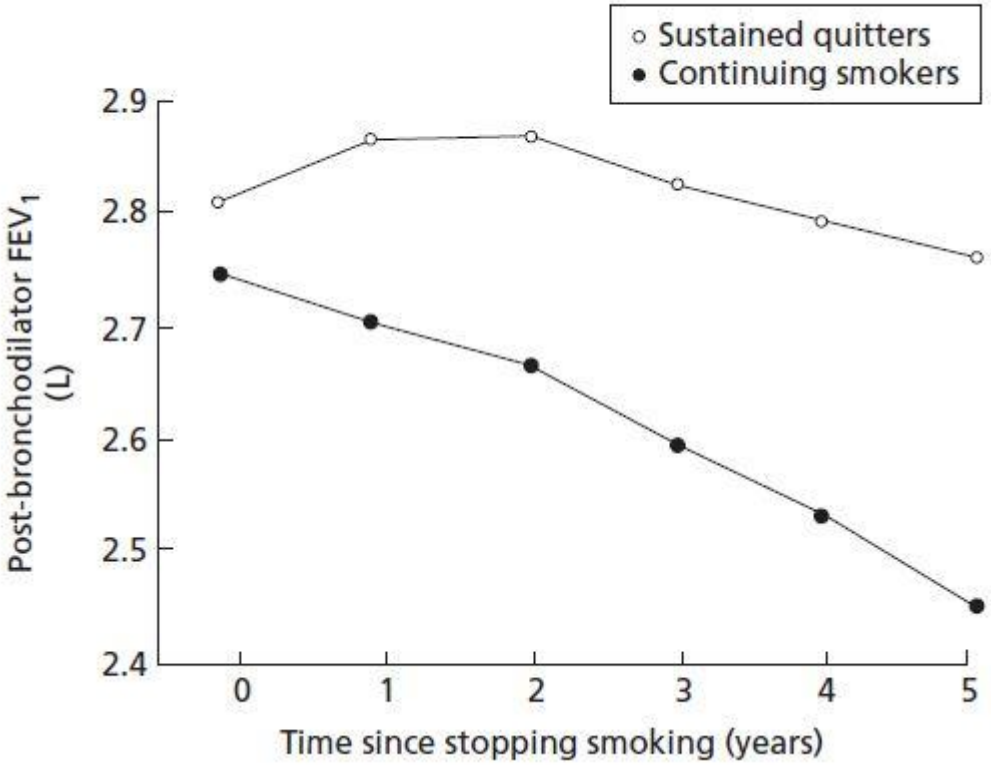
COPD has been defined as " a disease state characterised by airflow limitation that is not fully reversible." COPD includes *emphysema*, anatomically defined by the destruction and enlargement of distal airspaces; *chronic bronchitis*, clinically defined by chronic cough and sputum; and *small airways disease* causing bronchiolar narrowing.

RISK FACTORS-

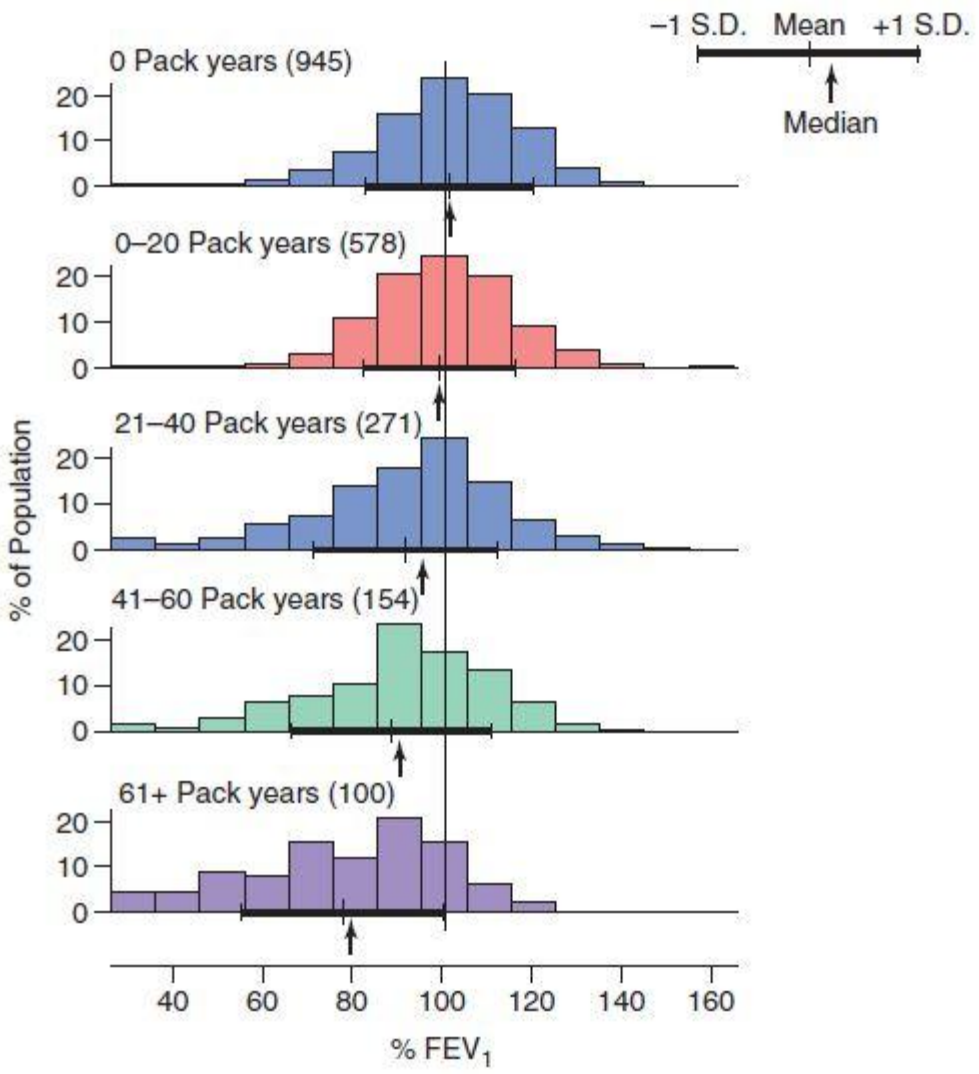
1) Cigarette smoking is definitively the most important identifiable causative factor of COPD. However, only 20% of smokers go on to develop clinically significant disease. Pack years of smoking is the most highly significant predictor of FEV1.



The above table depicts the effect of age on airflow obstruction in normal subjects and in susceptible cigarette smokers. Quitting the smoking habit will return the rate of decline to the normal trend.



Mean FEV1 after bronchodilator administration in ex-smokers who maintained abstinence compared with smokers who continued to smoke is depicted in the above chart.



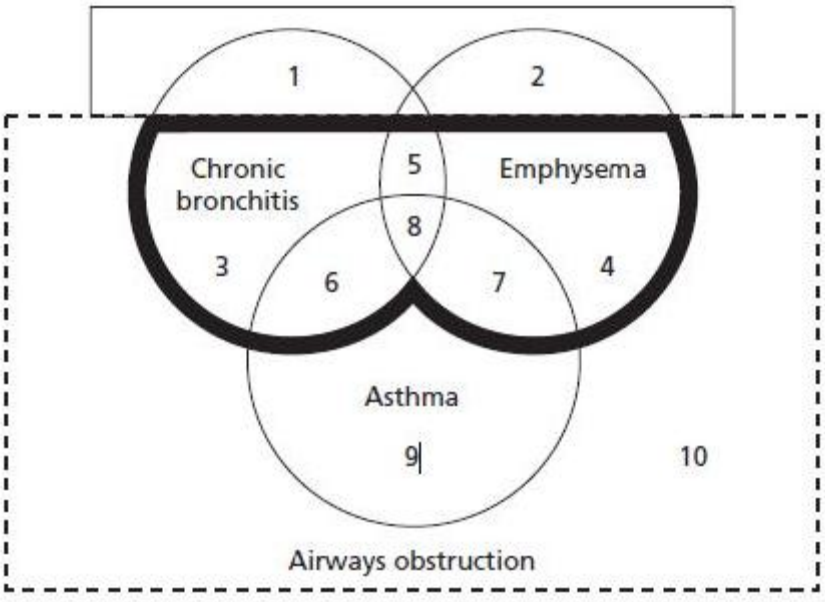
The above table depicts the distribution of (FEV1) values in general population, differentiated by packyears measuring duration of smoking.

Dose-response relationship between smoking intensity and FEV1 was identified, but marked differences in PFT was seen among smokers with similar duration and smoking habits.

2) Airway hyperresponsiveness, one of the characteristic features of bronchial asthma, is seen in many patients with COPD.

Overlap between asthma and COPD was the basis for the formation of Dutch hypothesis which proposes that asthma, emphysema and chronic bronchitis are variations of the same disease, altered by genetics and environment to produce these phenotypes.

The British hypothesis proposes that asthma is completely different from COPD- asthma being an allergic phenomenon and COPD the sequel of smoking related inflammation and damage.



A non proportional Venn diagram describing the relation between asthma, emphysema and chronic bronchitis/ the broken line rectangle includes all patients with airflow obstruction. Patients in subsets 1 and 2 have clinical or radiological features of chronic bronchitis or emphysema but do not have airflow obstruction and thus have a normal FEV1 and FEV1/FVC ratio. These patients are not classified as having COPD. Patients in subsets 6-8 have partially reversible airflow obstruction. Subsets 3-5 have no significant reversibility and patients in subset 8 have features of all three disorders. Those in subset 9 have completely reversible airflow obstruction and thus classified as asthma. Those in subset 10 have airflow obstruction due to specific causes like cystic fibrosis, bronchiectasis. Patients with COPD are those within the thick shaded band.

3) Ambient air pollution is a much less significant risk factor than cigarette smoking

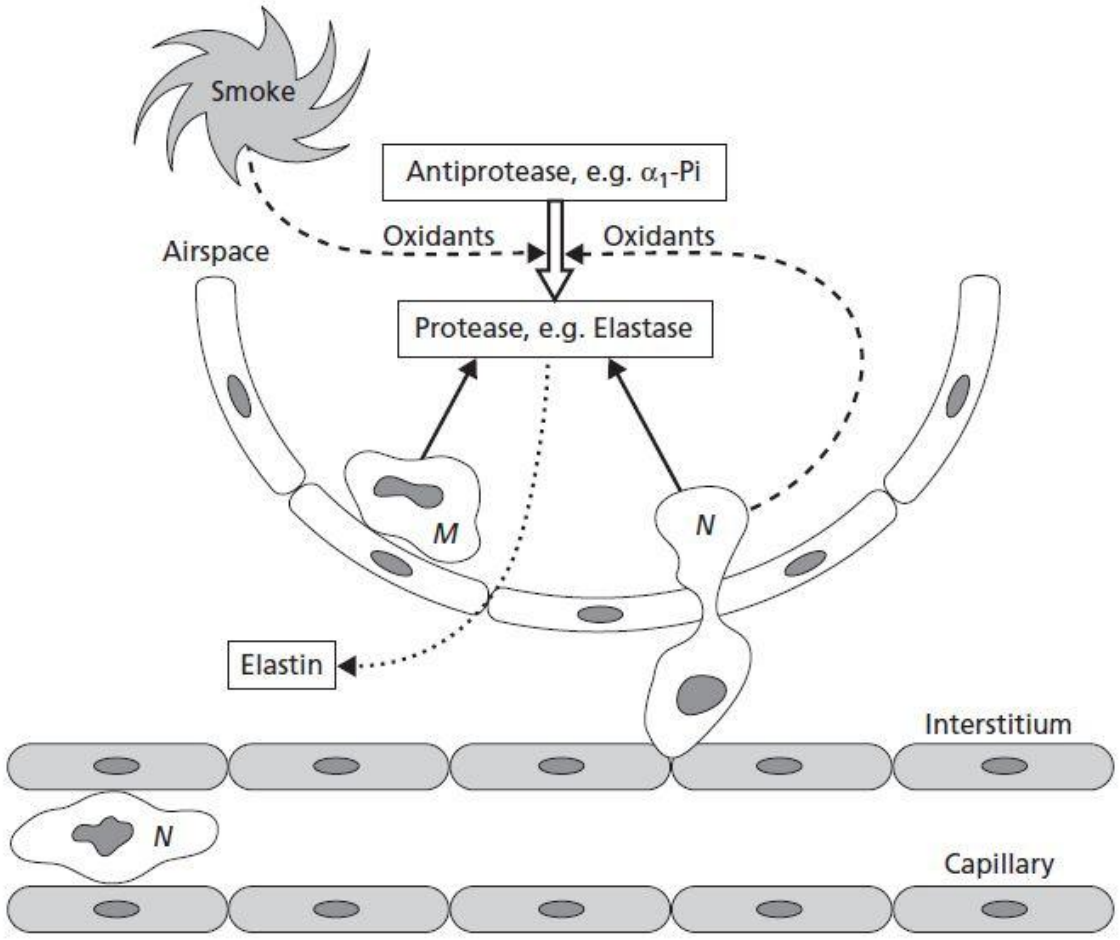
4) Passive smoking exposure has been linked to decreased lung function, but relation with COPD remains unproven

PATHOGENESIS OF COPD

Both chronic bronchitis and emphysema produce airway narrowing but evidence of obstruction need not be present. Airway obstruction is always seen by the time the patient becomes dyspnoeic. Airflow limitation, which is the major physiological change in COPD, can result from both small airway obstruction and emphysema.

PROTEASE- ANTIPROTEASE THEORY -

Cigarette smoke has a pro- oxidant effect, which makes neutrophils less deformable and causes neutrophil sequestration in the pulmonary capillaries. Activated neutrophils initially adhere to the endothelium and then migrate to the airspaces. The pro-oxidants from cigarette smoke or released by activated airspace neutrophils inactivate antiproteases , mainly elastase. Elastase enters the lung interstitium and destroys elastin , causing destruction and enlargement of distal airspaces.

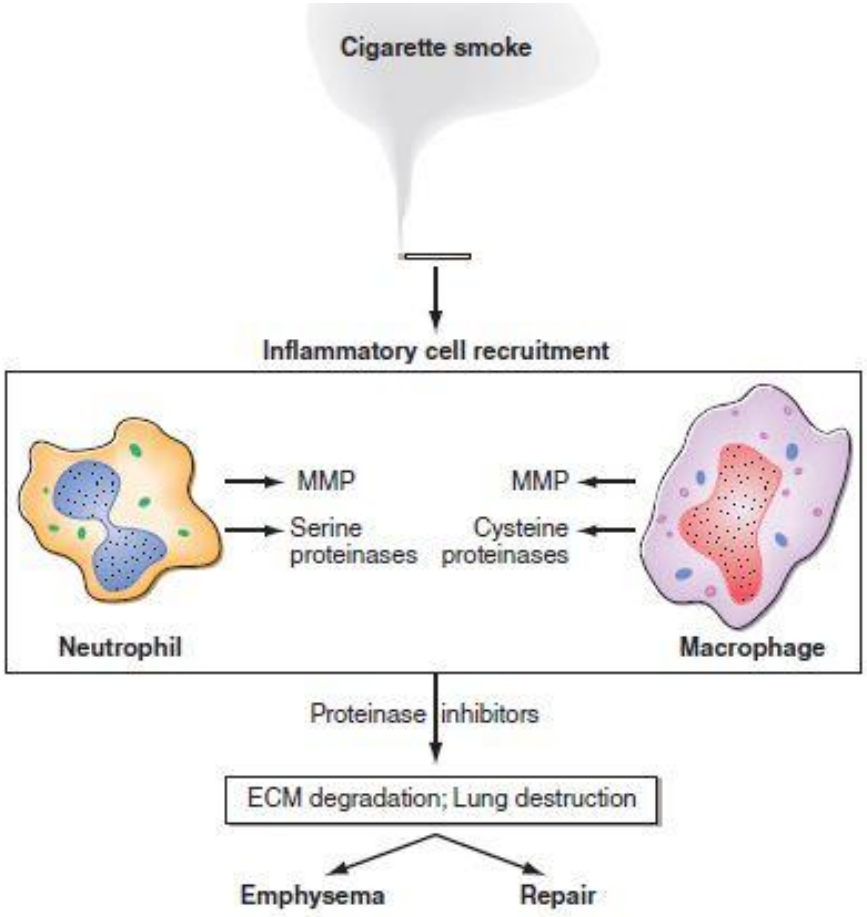


INFLAMMATION AND EXTRACELLULAR MATRIX HYPOTHESIS:-

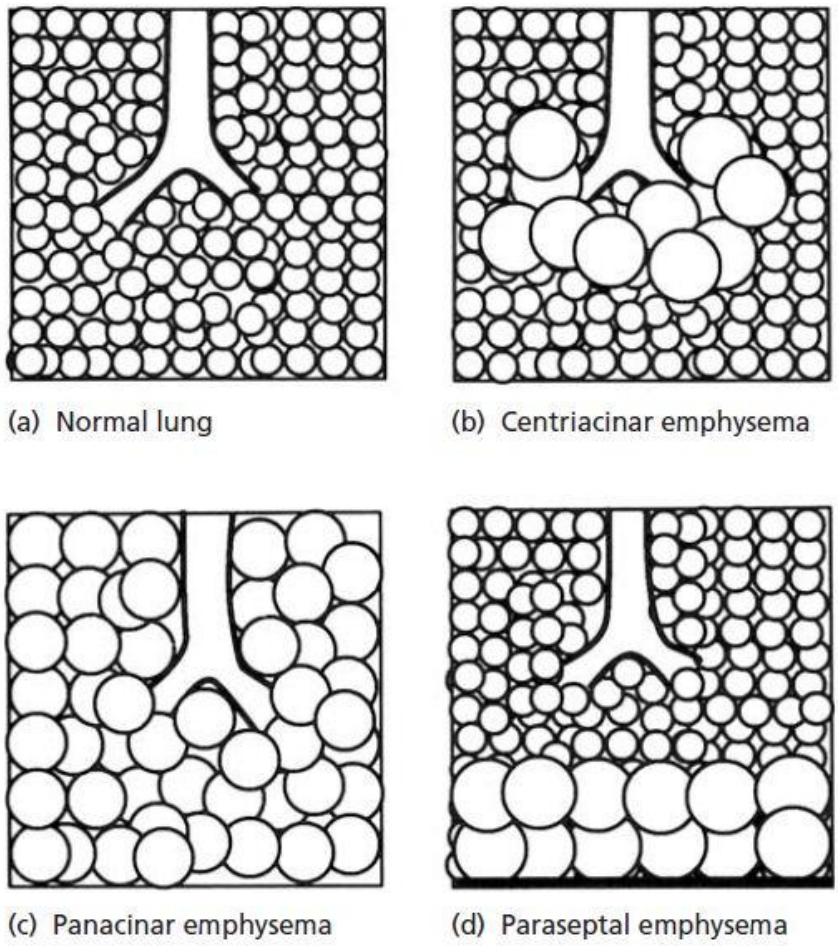
Macrophages and epithelial cells are activated on exposure to oxidants in cigarette smoke and produce chemokines that attract inflammatory cells, for example matrix metalloproteinases, IL-8 and TNF which lead to neutrophil recruitment.CD8+T cells are also recruited and release interferon inducible protein-10 (IP-10) which simulate macrophage production of macrophage elastase- matrix metalloproteinase-12.

Matrix metalloproteinases and serine proteinases (especially neutrophil elastase)

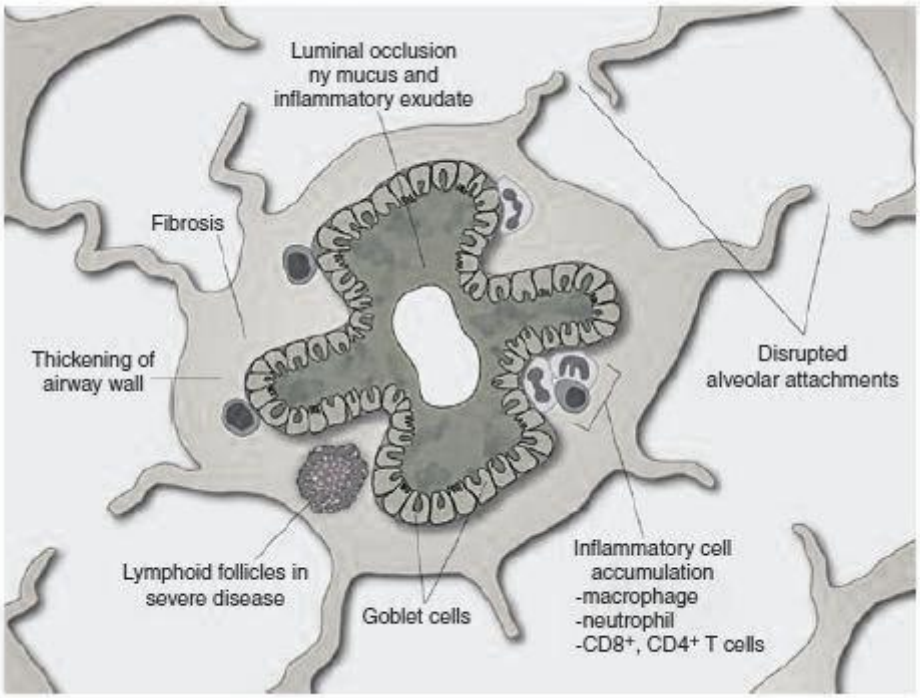
work synergistically by degrading the other's inhibitor and produce lung destruction.



TYPES OF EMPHYSEMA-



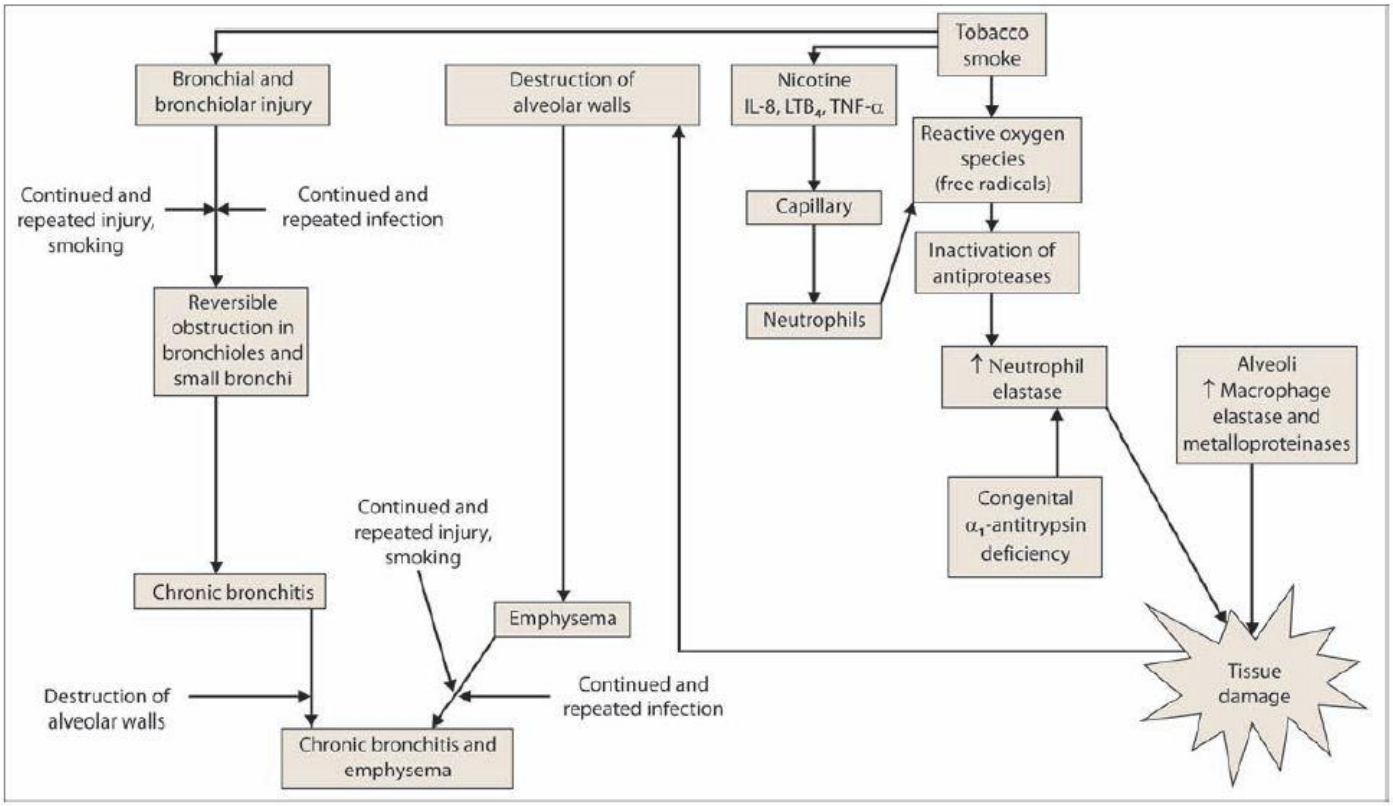
- Centriacinar- destruction of central acinus, commonly affect upper lobes, common in smokers
- Panacinar- widespread destruction of acinus, commonly affect lower zones, common in antitrypsin deficiency
- Paraseptal- affects the distal acinus, can cause spontaneous pneumothorax



The above picture demonstrates the multiple individual pathologies ultimately leading to small airway disease with reduction of FEV1.

CELL DEATH AND INEFFECTIVE REPAIR:-

Structural cell death caused by oxidants in cigarette smoke occurs through a number of mechanisms, including rt801 inhibition of mammalian target of rapamycin (mTOR), leading to cell death and proteolysis. Involvement of mTOR and other senescence indicators has funded recent theories that emphysema is a type of premature accelerated ageing of lung. Macrophage uptake of apoptotic cells is inhibited by cigarette smoke, which limits repair



PATHOPHYSIOLOGY OF COPD

Persistent reduction in forced expiratory flow rates is the most typical finding in COPD.

AIRFLOW OBSTRUCTION:-

Also known as airflow limitation, it is evaluated by spirometry, by forced

expiratory maneuvers after patient inhales to total lung capacity. Most important measurements are the volume of air exhaled in the first second of the forced expiratory maneuver (FEV1) and the total volume of air exhaled during the complete spirometric maneuver {Forced Vital Capacity (FVC)}. Airflow obstruction of COPD is identified by a persistently reduced FEV1/FVC ratio. Unlike bronchial asthma, the decreased FEV1 in COPD does not show improvements more than 15% in response to inhaled bronchodilators.

The airflow in forced exhalation depends upon the balance between elastic recoil of the lungs which assists flow and the airway resistance inhibiting flow. In COPD, maximal expiratory flow decreases as the lung empties because the parenchyma gives progressively less recoil and the airflow resistance increases due to decrease in airway cross sectional area.

HYPERINFLATION:-

Pulmonary function tests also measure lung volumes. “Air trapping” {increased residual volume and increased ratio of residual volume to total lung capacity} and increasing hyperinflation {increased total lung capacity} occurs in COPD. Hyperinflation is an initial compensatory mechanism which helps in maintaining maximal expiratory airflow, as the increased lung volume increases the elastic recoil and the airways enlarge decreasing the airway resistance.

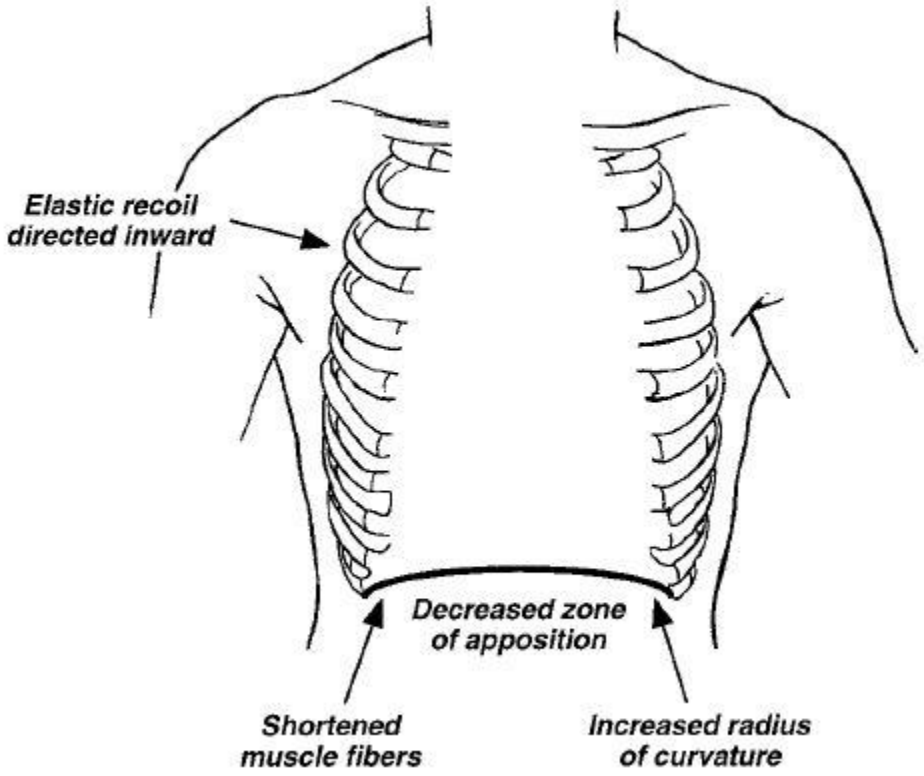
However, the flattening of diaphragm due to hyperinflation of lungs is adverse for the COPD patient:-

1) As diaphragm and abdominal wall are now closely apposed, positive abdominal pressure in inspiration can not be as effectively delivered to chest, which decreases rib cage movement and impairs inspiration.

2) The muscle fibres of the flattened diaphragm are shorter than normal and hence, less able to produce normal inspiratory pressures.

3) Flat diaphragm has increased radius of curvature ***r***, hence, increased tension ***t*** must be produced to maintain transpulmonary pressure ***p*** for tidal breathing- {LAPLACE LAW p=2t/r}

4) Inspiratory muscles must over work to overcome the resistance of the expanded thoracic cage.



The above diagram depicts the mechanisms by which flat diaphragm eventually contributes to COPD morbidity

GAS EXCHANGE:-

Partial pressure of oxygen in arterial blood PaO2 remains normal until FEV1 decreases to less than 50% of predicted. Increased PaCO2 occurs only when FEV1 decreases to less than 25% of predicted.

Pulmonary hypertension causing cor pulmonale and right ventricular failure occurs when FEV1 decreases to less than 25% of predicted with chronic hypoxemia (PaO2 < 55mm Hg).

Mechanism of development of Pulmonary Hypertension in COPD-

- Degeneration of the vascular bed in lungs
- Alterations in blood gas tension
- Alterations in lung mechanics
- Elevated cardiac output
- Alterations in blood volume
- Increased velocity of blood
- Changes in lung endothelium

Nonuniform ventilation and ventilation perfusion mismatch is characteristic of COPD, showing that the disease process is truly heterogenous. Ventilation perfusion mismatch is responsible for most of the reduction in PaO2 of COPD, which is why even modest elevations of inspired oxygen is so effective in correcting hypoxemia due to COPD, so much so that other problems should be looked for if hypoxemia is not corrected by modest levels of supplemental oxygen.

Systemic Features of COPD

Systemic features	*Possible mechanism*
Cachexia	TNF-α, IL-6, leptin
Muscle wasting	Apoptosis of skeletal muscle due to TNF-α
Polycythaemia	Chronic hypoxia
Anaemia	TNF-α
Depression	TNF-α, IL-6
Cardiovascular abnormalities	CRP, fibrinogen
Osteoporosis	? effect of corticosteroid therapy

Conditions suggesting alpha-1 anti-trypsin deficiency
Early-onset emphysema (age under 45 years)
Emphysema in a nonsmoker
Emphysema predominantly in lung bases (pan-acinar)
Necrotizing panniculitis (Weber-Christian disease)
c-ANCA positive vasculitis (e.g., Wegener's granulomatosis)
Family history of early onset emphysema or non-smoking–related emphysema
Bronchiectasis without other etiology

DIAGNOSIS:

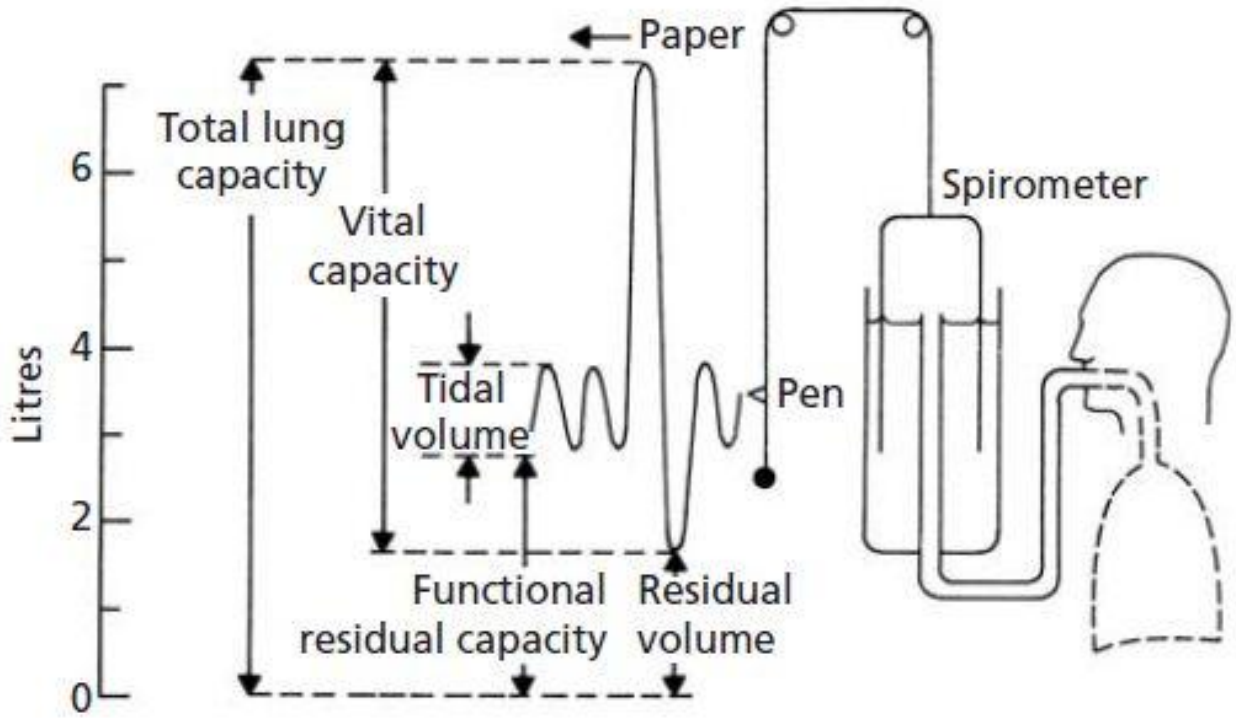
COPD must be thought of in patients with chronic complaints of cough, sputum production or dyspnea with history of smoking and exposure to risk factors.

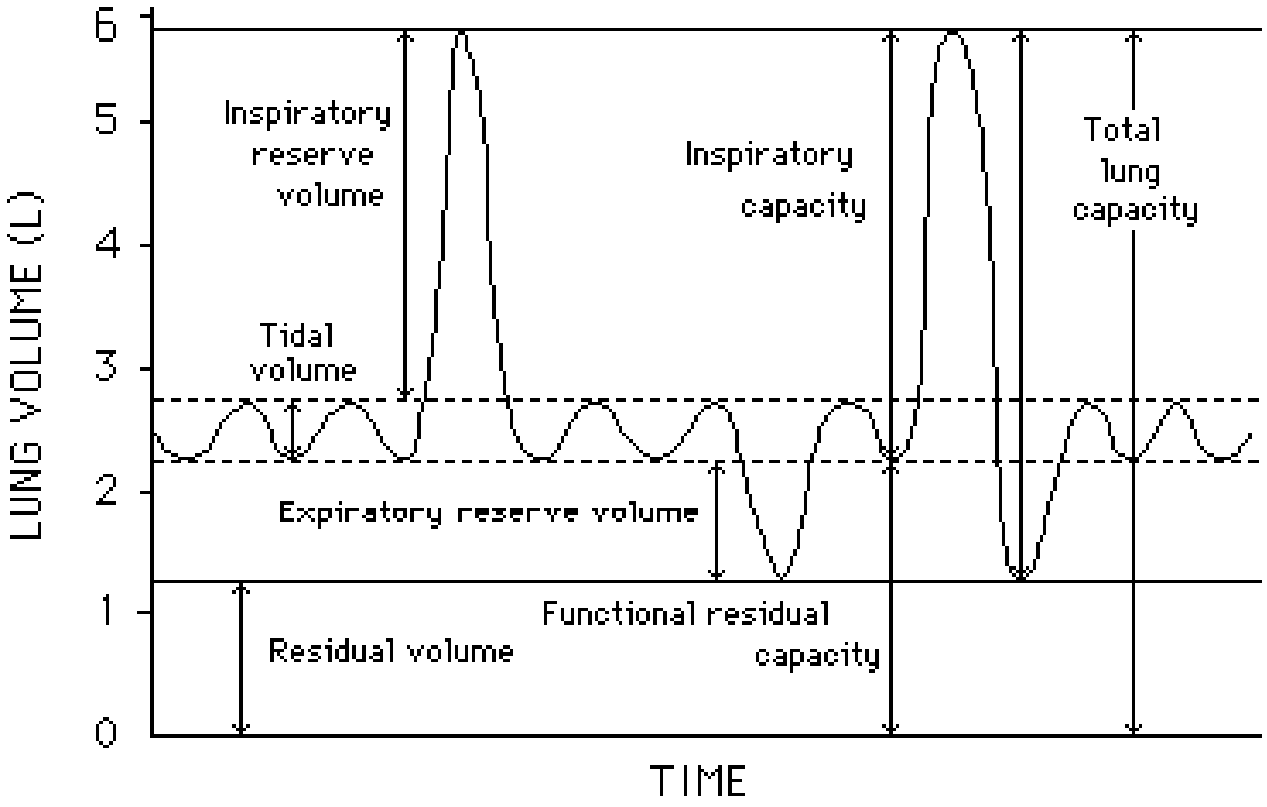
SEVERITY SCORES FOR RESPIRATORY DISEASES:-

Calculation of the BODE Index*				
	Points on the BODE Index			
Variable	0	1	2	3
FEV_1 (% predicted)	≥65	50–64	36–49	≤35
Distance walked in 6 min (meters)	≥350	250–349	150–249	≤149
MMRC dyspnea scale	0–1	2	3	4
Body-mass index (kg/M^2)	> 21	≥21		

Modified Medical Research Council Dyspnea Scale (MMRC Scale)	
Grade	**Description**
0	Not troubled with breathlessness except with strenuous exercise
1	Troubled by shortness of breath when hurrying on the level or walking up a slight hill
2	Walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level
3	Stops for breath after walking about 100 yards or after a few minutes on the level
4	Too breathless to leave the house or breathless when dressing or undressing

The diagnosis is made by spirometry.


Paper
Total lung capacity
Vital capacity
Tidal volume
Pen
Spirometer
Litres
6
4
2
0
Functional residual capacity
Residual volume



PULMONARY FUNCTION TESTING:

A post bronchodilator FEV1/ FVC < 0.7 confirms airway obstruction that is not completely reversible. Increased lung volumes may point to emphysema. PEFR is reduced, DLCO is normal or slightly reduced in patients with chronic bronchitis and severe reduction indicates associated severe emphysema.

According to GOLD guidelines, patients have been categorised into mild (stage 1),

moderate (stage 2), severe (stage 3) and very severe (stage 4) based on percentage predicted FEV1 of more than or equal to 80, 50 to 80, 30 to 50, less than or equal to 30, respectively.

COPD- GOLD criteria

GOLD Stage	SEVERITY	SPIROMETRY
I	Mild	FEV1/FVC<0.7 and FEV1 >80% predicted
II	Moderate	FEV1/FVC<0.7 and FEV1 >50% but <80% predicted
III	Severe	FEV1/FVC<0.7 and FEV1 >30% but <50% predicted
IV	Very Severe	FEV1/FVC<0.7 and FEV1 <30% predicted

IMAGING :

Chest X-ray may be normal or show emphysematous changes. It is very useful in ruling out other differential diagnoses and in detecting complications of COPD, including life threatening ones like pneumothorax. Patients with chronic bronchitis may have thick bronchial walls which appear as tubular or tram track shadows with increased vascular markings.

Chest X-ray in symptomatic emphysematous patients reveals dark hyperlucent lung fields with decreased vascular markings, characteristic bullae, flattened and pushed-down diaphragm and tube-like heart.

HRCT can readily detect emphysema but is not used routinely for the purpose of diagnosis. Contrast-enhanced computed tomography (CECT) chest may show a dilated pulmonary artery, indicating pulmonary hypertension.

ACUTE EXACERBATION:-

An exacerbation is defined as an episode of increased cough, dyspnea and altered volume and character of sputum, with or without other signs of disease.the frequency of exacerbations greatly affects quality of life of COPD patients, especially those with GOLD stage III or IV, who experience one to four exacerbations in a year.

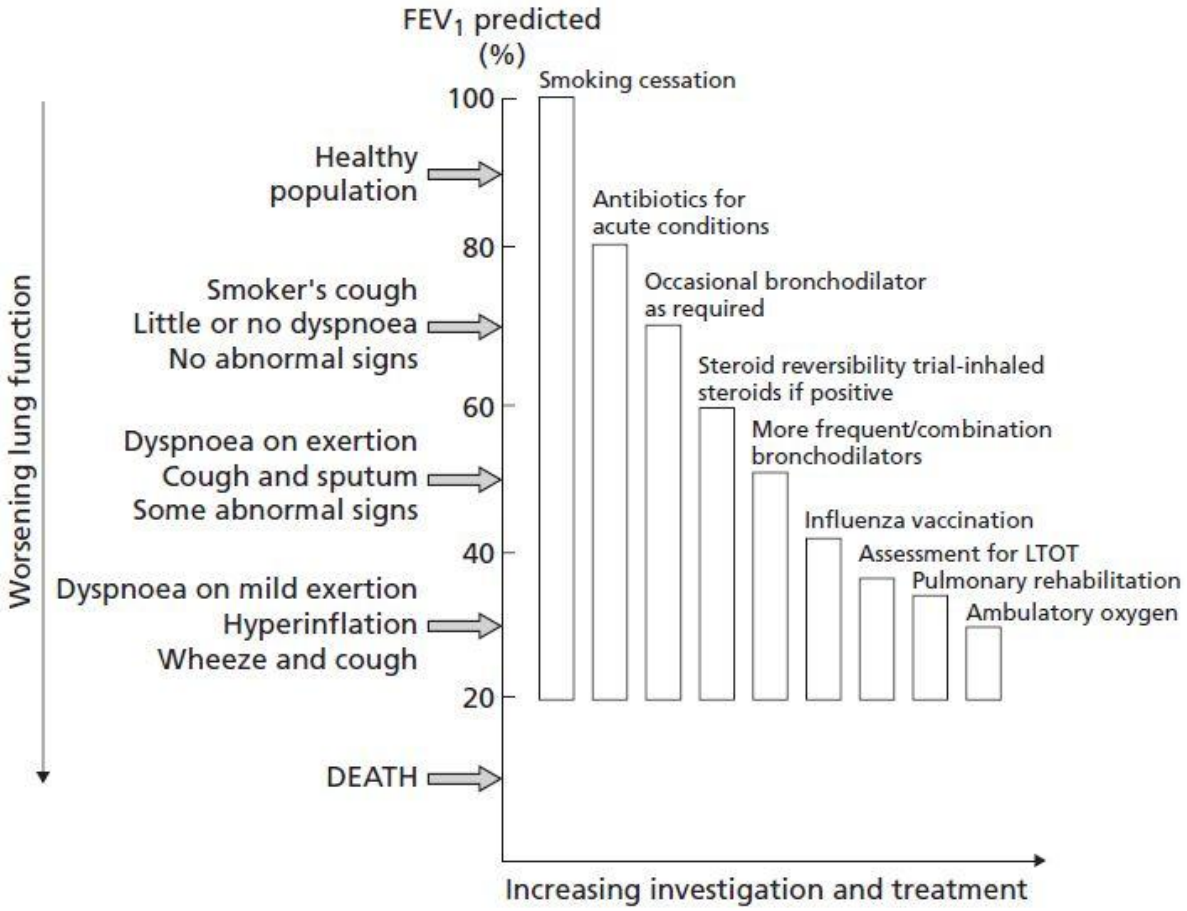
Chances of exacerbation in future are increased by a previous history of

exacerbation and an increased ratio of pulmonary artery diameter to aorta diameter on Chest CT.

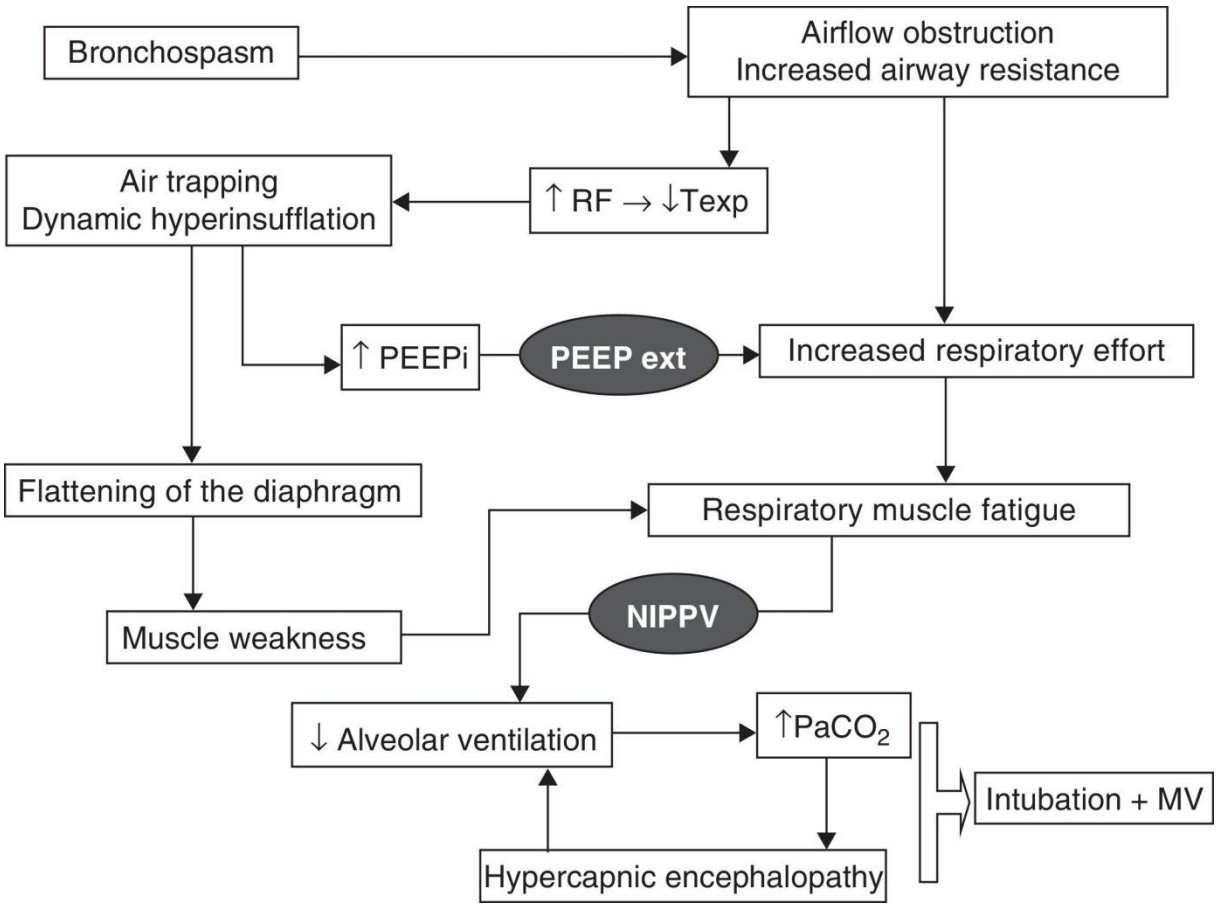
Bacterial infection accounts for more than half of exacerbations, with viral infections being involved in 30% and remaining 20 % cases having no obvious precipitating cause.

Prevention of exacerbations is achieved to a great degree of success with inhaled steroids, anticholinergics and long acting beta agonists.

Treatment is by inhaled beta agonists, along with anticholinergic agent, antibiotics, oral glucocorticoids and supplemental O2.



The above table shows the " Chronic Obstructive Pulmonary Disease Escalator"- treatments need to be escalated as the lung function progressively decreases.



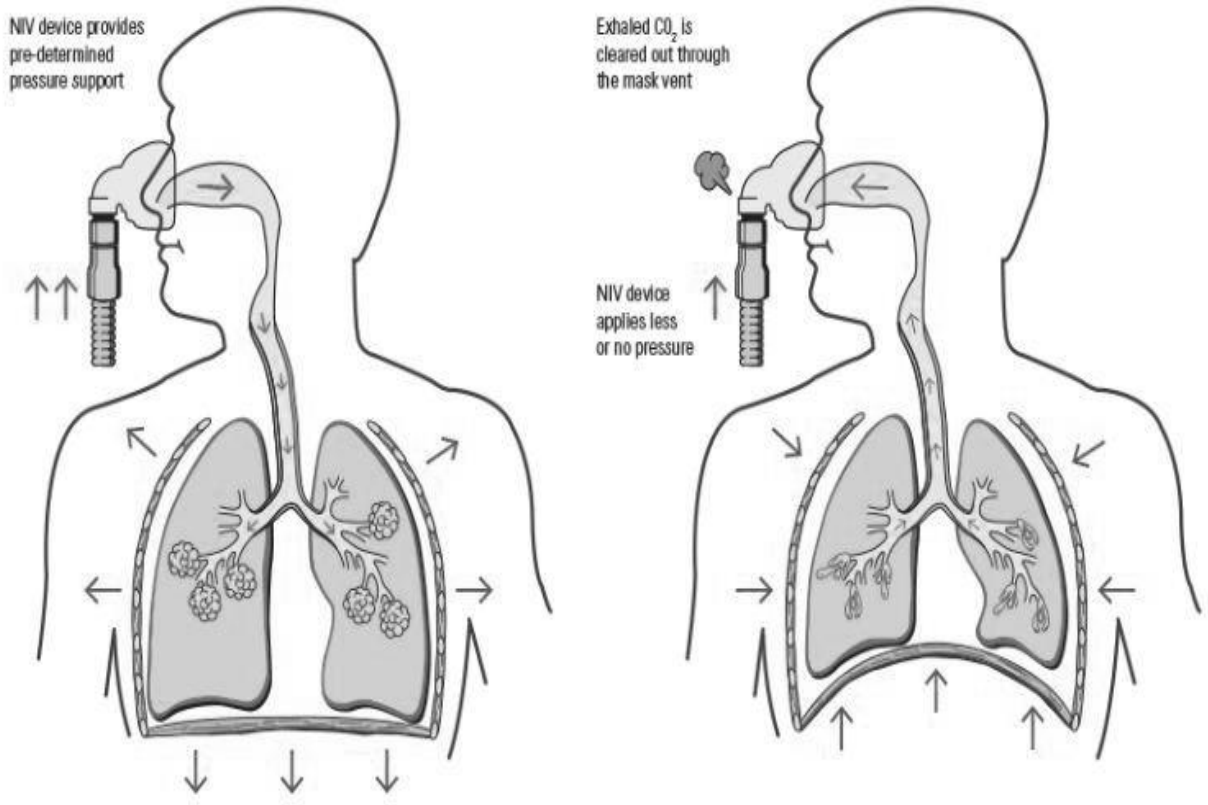
The above table depicts a summary of the physiopathology of the hypercapnic acute respiratory failure in COPD and the points where non invasive and mechanical ventilation acts in blocking these mechanisms.

<u>Non invasive Ventilation is indicated in-</u>

A. Moderate to severe dyspnea with evidence of increased work of breathing

B. Acute respiratory acidosis wih pH <7.35 and PaCO2> 45 mmHg

C. Respiratory rate >25



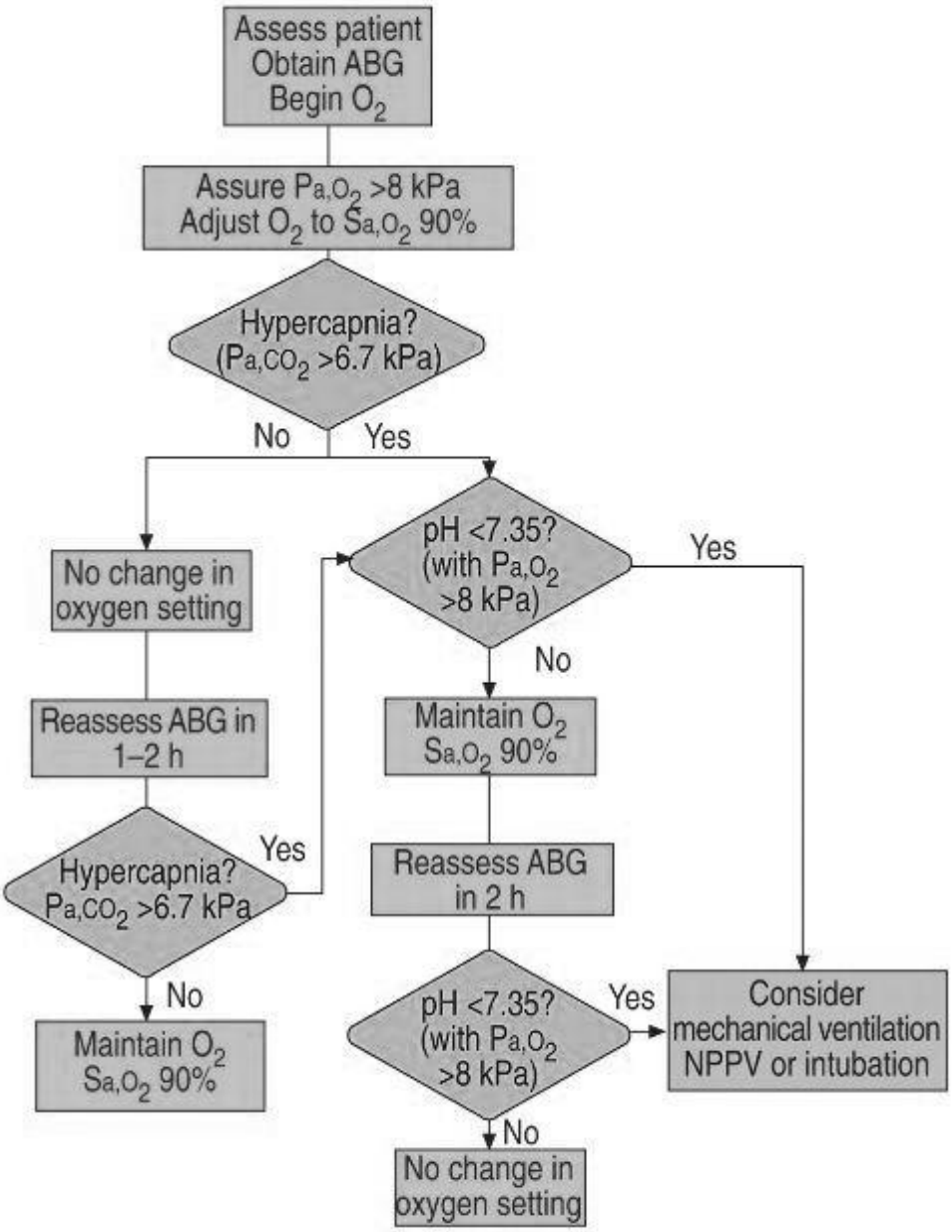
The above table depicts the lung mechanics in Non Invasive Ventilation and its usefulness in COPD

<u>Contraindications to NIV-</u>

A. Extreme obesity
B. Craniofacial trauma, recent facial surgery, burns
C. Nasopharyngeal abnormalities
D. Altered sensorium, uncooperative patients
E. Respiratory arrest
F. Shock
G. High chance of aspiration

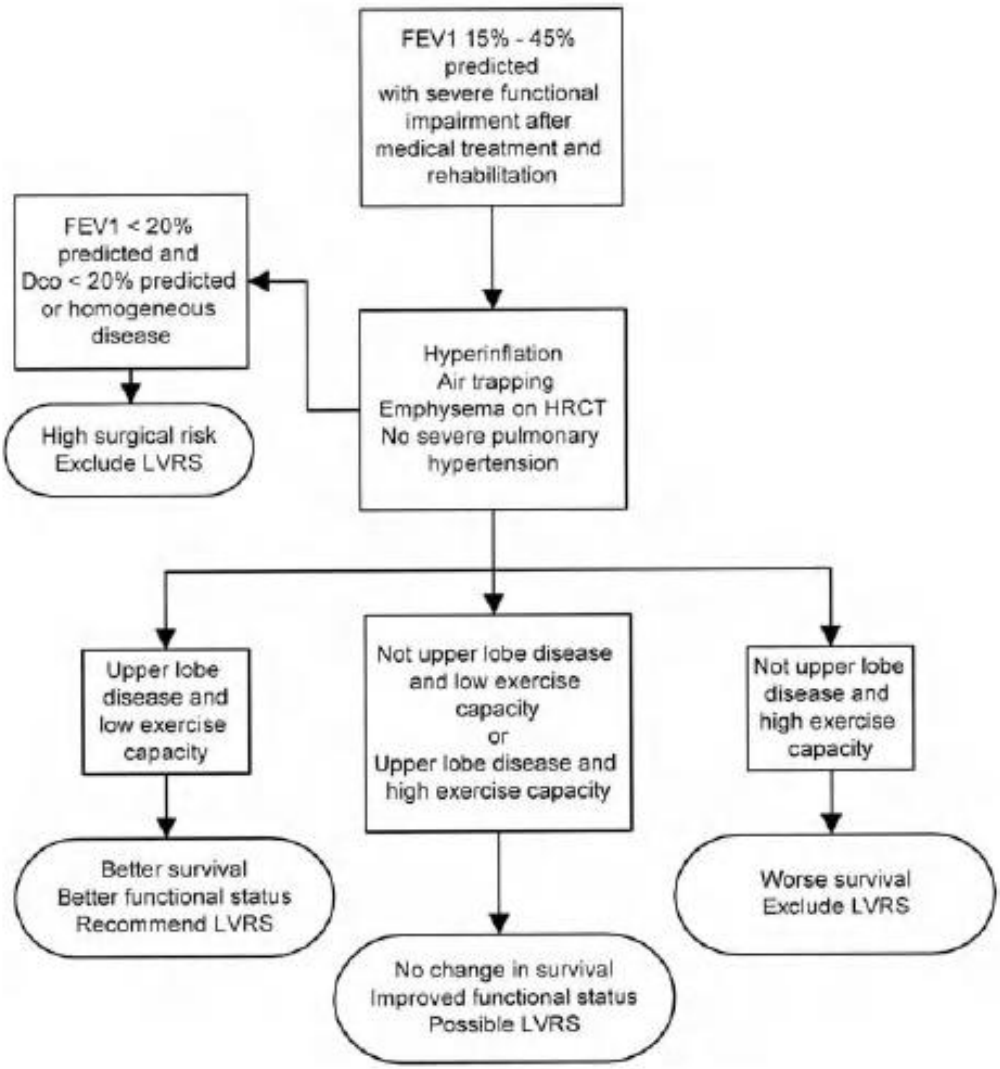
Indications for Mechanical Ventilation-

A. Contraindication or unresponsive to NIV
B. Severe dyspnea and increased work of breathing
C. Acute respiratory acidosis wih pH <7.25 and PaCO2> 60 mmHg
D. Respiratory rate >35
E. PaO2 <40mmHg
F. Associated comorbidities like cardiac disease, metabolic abnormalities, sepsis, pneumonia, pulmonary embolism, pneumothorax, large pleural effusion



The above flowchart depicts the management of respiratory failure in acute exacerbation of COPD and initiation of NIV and mechanical ventilation.

Lung Volume Reduction Surgery:-



LVRS involves reduction of lung volumes by 30% by freeing them from the apices. The residual lung expands and fills the thorax and hence elastic recoil is increased and airflow during expiration increases.

Smoking cessation, oxygen supplementation and LVRS are the only modes of treatment increasing survival in COPD patients.

ACUTE PHYSIOLOGY AGE AND CHRONIC HEALTH EVALUATION {APACHE} SYSTEMS I,II,III,IV

Knaus described the APACHE score in 1981, a physiologically based classification system for measuring severity of illness in groups of critically ill patients. It was widely used for comparing outcomes, evaluate new therapies and evaluate the utilisation of ICU facilities.

APACHE II, a simplified version was described in 1985 and was superseded by APACHE III in 1991 and APACHE IV in 2006, however, APACHE II has become the most widely used system all over the world for studying and reporting severity of illness.

APACHE II score is the sum of three components:-

1) an acute physiology score (APS)

2) a chronic health score based on premorbid states

3) a score based on patient's age

The 12 variables of APACHE II are collected in the first 24 hours after admission and they should represent the worst physiological values.

1) Age
2) Glasgow Coma Scale
3) Temperature
4) Heart rate
5) Respiratory rate
6) Mean arterial pressure
7) Packed cell volume
8) WBC Count
9) Arterial Ph
10) Serum Sodium
11) Serum Potassium
12) Serum Creatinine

13) A-a Gradient (if FiO2>0.5) or PaO2 (if FiO2 <0.5)

14) Chronic health problems { Cirrhosis/ NYHA –IV/Severe COPD/ Regular HD/ Immunocompromised}

TOTAL SCORE-

MATERIALS AND METHODS:-

TITLE: FIRST DAY PREDICTORS OF REQUIREMENT OF MECHANICAL VENTILATION IN COPD PATIENTS WITH ACUTE EXACERBATION

AIMS AND OBJECTIVES: To identify the first day predictors of requirement of mechanical ventilation in COPD patients with acute exacerbation

MATERIALS AND METHODS:

STUDY POPULATION:

The present study was conducted on 200 patients from General Medicine wards of Government Rajaji Hospital, Madurai during the period of March 2016 to August 2016.

INCLUSION CRITERIA:

1. All patients admitted with a primary admitting diagnosis of acute exacerbation of COPD.
2. All patients must have a Prior confirmed diagnosis of COPD on the basis of FEV1/FVC<0.70 and should be on regular follow up and treatment

3. Exacerbation of COPD was diagnosed on basis of worsening of atleast one of these symptoms- dyspnea, cough, sputum production

EXCLUSION CRITERIA:

1. Patients with underlying COPD admitted with another primary admitting diagnosis (eg. Stroke, Acute Myocardial Infarction) were excluded from the study
2. Patients with acute respiratory failure secondary to bronchiectasis, bronchial asthma, active/inactive tuberculosis, pneumothorax, pulmonary embolism, pulmonary edema were excluded from the study

ANTICIPATED OUTCOME: Endotracheal Intubation for Mechanical Ventilation

DATA COLLECTION: A previously designed proforma was used to collect the demographic and clinical details of the patients. All the patients were given detailed clinical evaluation, appropriate investigations.

The demographic profile collected by questionnaire at the time of admission included age, sex, smoking status. Patient vitals including heart rate, blood pressure and respiratory rate was recorded. Premorbid functional status for the last month according to the modified Menzies criteria was calculated from the patient

or relatives if the patient was unable to provide the details. Arterial blood gas analysis, liver function tests, renal function tests, serum electrolytes was done routinely for the patients. Acute Physiology and Chronic Health Evaluation II (APACHE II) score was calculated for each patient from the following data (Age, Temperature, Mean Arterial Pressure, Heart Rate, Respiratory Rate, FiO2, Arterial pH, Serum HCO3, Serum sodium, Serum Potassium, Serum Creatinine, Packed Cell Volume, WBC count, Glasgow Coma Scale).

Patients were promptly intubated if NIV was contraindicated or not responding to NIV, if they had severe dyspnea and increased work of breathing, if acute respiratory acidosis wih pH <7.25 and PaCO2> 60 mmHg was present, if respiratory rate was >35 or if PaO2 was <40mmHg.

LABORATORY INVESTIGATIONS:

Hemoglobin

WBC count

Blood Glucose

Bilirubin – Total, Direct, Indirect

SGOT, SGPT

Total Protein

Serum Albumin

Blood Urea

Serum Creatinine

Serum Sodium

Serum Potassium

Serum Calcium

Arterial Blood Gas Analysis (arterial pH, Serum Hco3)

SCORE CALCULATION

1) **Premorbid Functional Status (Modified Menzies Criteria)** (for the previous 1 month)

I. Independent- working/Living without help

II. Restricted- able to leave house but exercise is restricted

III. Housebound- rarely leaves house but able to do self care

IV. Bed/ chair bound- not able to do self care

2) Acute Physiology and Chronic Health Evaluation II (APACHE II) score

1) Age
2) Glasgow Coma Scale
3) Temperature
4) Heart rate
5) Respiratory rate
6) Mean arterial pressure
7) Packed cell volume
8) WBC Count
9) Arterial Ph

10) Serum Sodium

11) Serum Potassium

12) Serum Creatinine

13) A-a Gradient (if FiO2>0.5) or PaO2 (if FiO2 <0.5)

14) Chronic health problems { Cirrhosis/ NYHA –IV/Severe COPD/ Regular HD/ Immunocompromised}

TOTAL SCORE-

DESIGN OF STUDY: Prospective study

PERIOD OF STUDY: March 2016 To August 2016 (6 months)

COLLABORATING DEPARTMENTS:

- Department of Respiratory Medicine
- Department Of Biochemistry

ETHICAL CLEARANCE: Obtained

CONSENT: Individual written and informed consent.

ANALYSIS:STATISTICAL ANALYSIS.

CONFLICT OF INTEREST: NIL

FINANCIAL SUPPORT: SELF

PARTICIPANTS:

200 patients admitted with a primary diagnosis of acute exacerbation of COPD in General Medicine wards of Government Rajaji Hospital, Madurai from March 2016 to August 2016 were included in this study. All patients must have a Prior confirmed diagnosis of COPD on the basis of FEV1/FVC<0.70. Exacerbation of COPD was diagnosed on basis of worsening of atleast one of these symptoms- dyspnea, cough, sputum production. Patients with underlying COPD admitted with another primary admitting diagnosis (eg. Stroke, Acute Myocardial Infarction) were excluded from the study. Patients with acute respiratory failure secondary to bronchiectasis, bronchial asthma, active/inactive tuberculosis, pneumothorax, pulmonary embolism, pulmonary edema were excluded from the study

DEFINITIONS USED FOR THE STUDY:

1. COPD

A patient was taken to have COPD only if he/she described the typical history suggestive of COPD and was previously diagnosed to have COPD on the basis of pulmonary function test result FEV1/FVC<0.70. Only those COPD patients who were on regular followup and treatment were included in the study.

Exacerbation of COPD was diagnosed on basis of worsening of atleast one of these symptoms- dyspnea, cough, sputum production.

2. Smoking

A patient was termed as smoker if he/she described a history of tobacco smoking within the last twenty years. Those who stopped smoking completely before twenty years were not included as smokers. Pack years were used to describe the duration and magnitude of smoking habit.

3. Systemic Hypertension

A patient was termed to have hypertension if he/she was already diagnosed and was on anti-hypertensive drugs or if the systolic BP during hospital stay was

found more than or equal to 140 mm Hg and/ or the diastolic BP was more than or equal to 90 mm Hg (JNC VII).

4. Diabetes Mellitus

A patient was termed to have diabetes mellitus if he/she was already diagnosed or blood investigations revealed

- Fasting plasma glucose of more than or equal to 126 mg/dl
- OR
- 2 hour post-prandial plasma glucose more than or equal to 200 mg/dl
- OR
- Symptoms of diabetes mellitus plus random blood sugar more than 200 mg/dl

STATISTICAL ANALYSIS :

The information collected regarding all the selected cases were recorded in a master chart. Data analysis was done with the help of computer by using SPSS 16 software and Sigma Stat 3.5 version (2012).

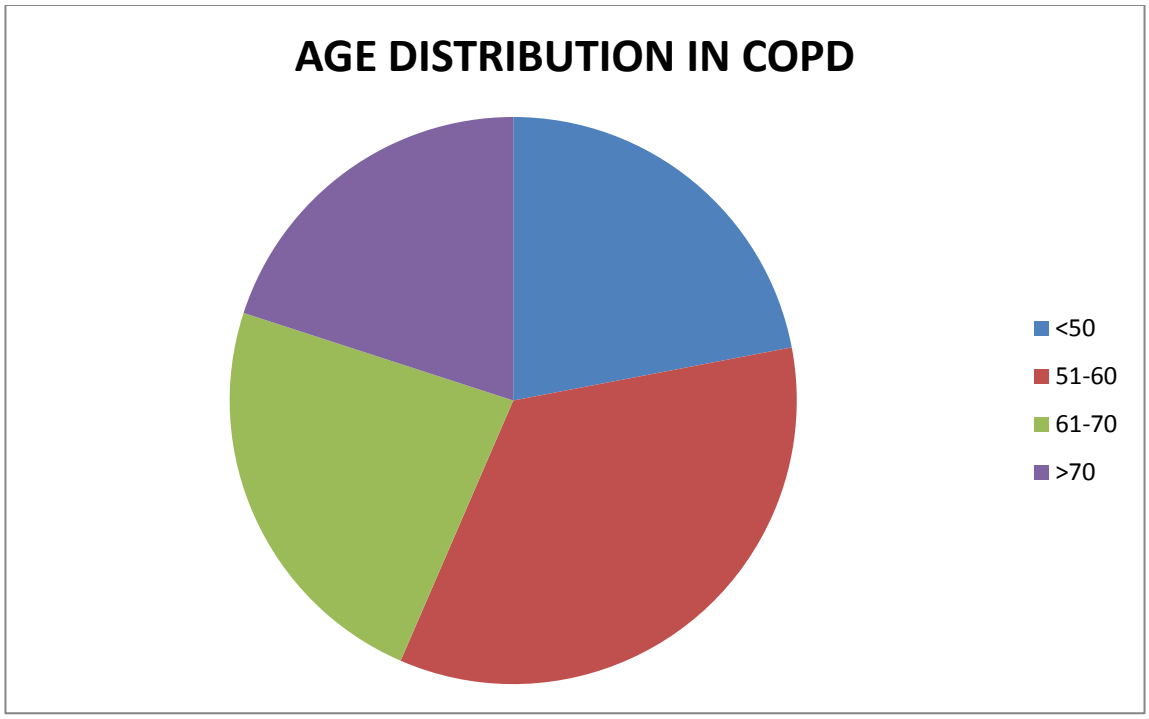
Using this software mean, standard deviation and ‘p’ value were calculated through One way ANOVA, Chi square test and P value of < 0.05 was taken as significant.

OBSERVATIONS AND RESULTS

AGE DISTRIBUTION IN COPD

Age	Number Of Cases
≤50	44
51-60	69
61-70	47
>70	40
Total	200

Of the 200 patients included in the study, 44 belonged to the age group (< 50 years) {22%}, whereas 156 patients {78%} were over 50 years of age. We already know COPD is a disease more affecting elderly persons. The findings of this study are similar to our earlier knowledge.


AGE DISTRIBUTION IN COPD
<50
51-60
61-70
>70

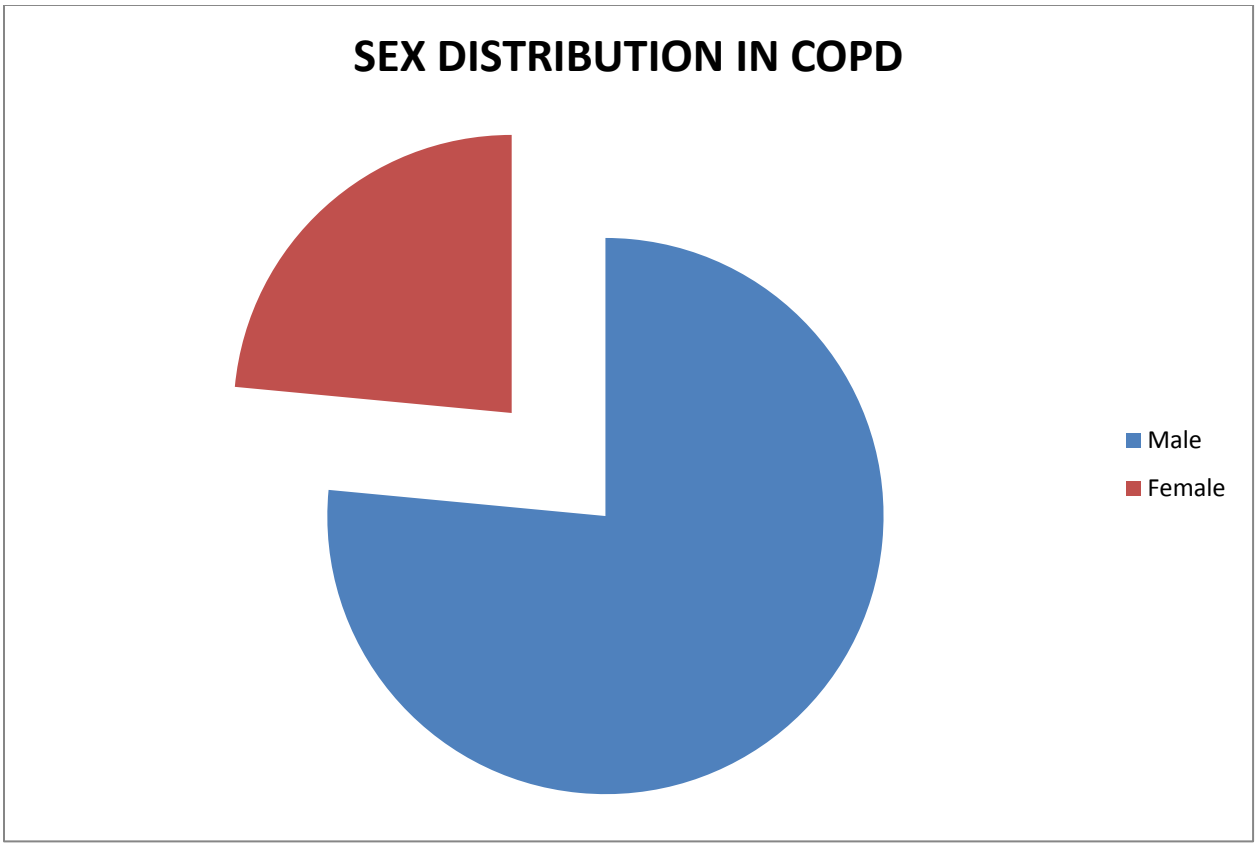
SEX DISTRIBUTION IN COPD

SEX	No Of Cases
Male	153
Female	47
Total	200

Of the total 200 COPD patients used in the study,

- Males were 153 (76.5%)
- Females were 47 (23.5%)

The prevalence of COPD, as we already know, is much more in males than females, probably due to higher prevalence of smoking in males. Our study also confirms the same.

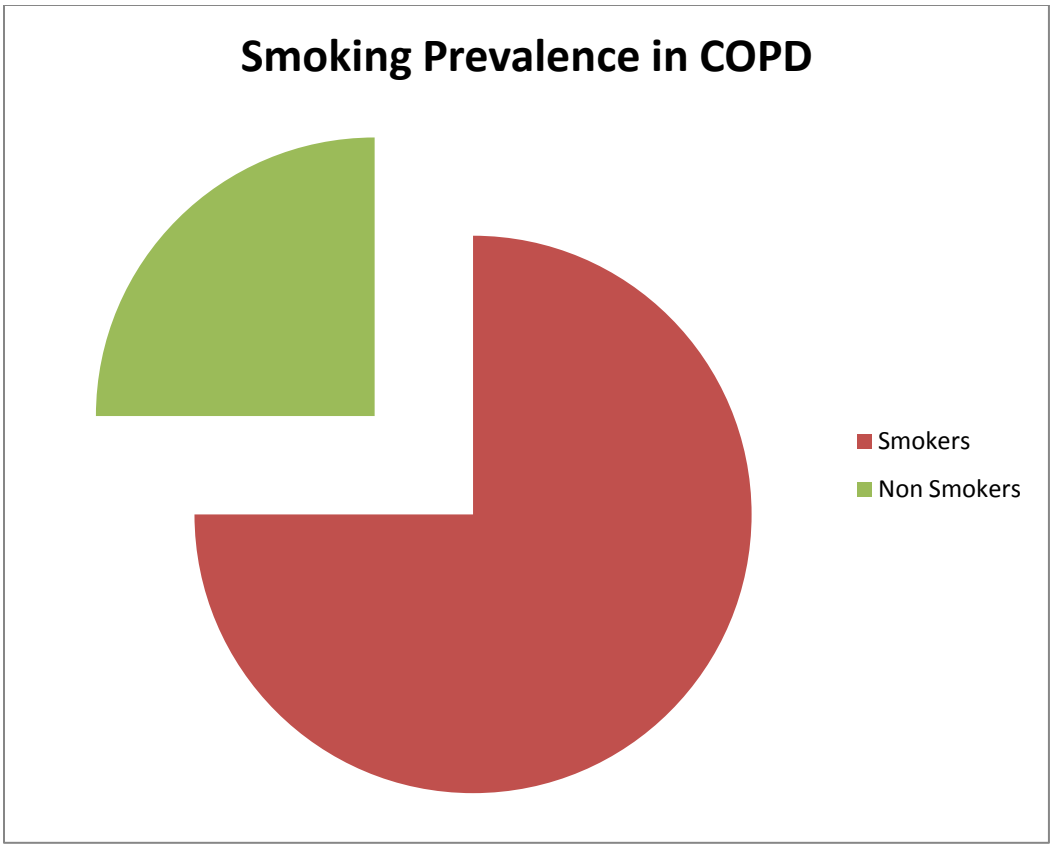

SEX DISTRIBUTION IN COPD
Male
Female

SMOKING IN COPD

SMOKING STATUS	**No Of Cases**
Smokers	150
Non Smokers	50
Total	200

As we already know, the major etiological factor in COPD is cigarette smoking.

In our study, smokers comprised 150 (75%) of the total 200 cases and hence our finding was in line with previous studies.


Smoking Prevalence in COPD
Smokers
Non Smokers

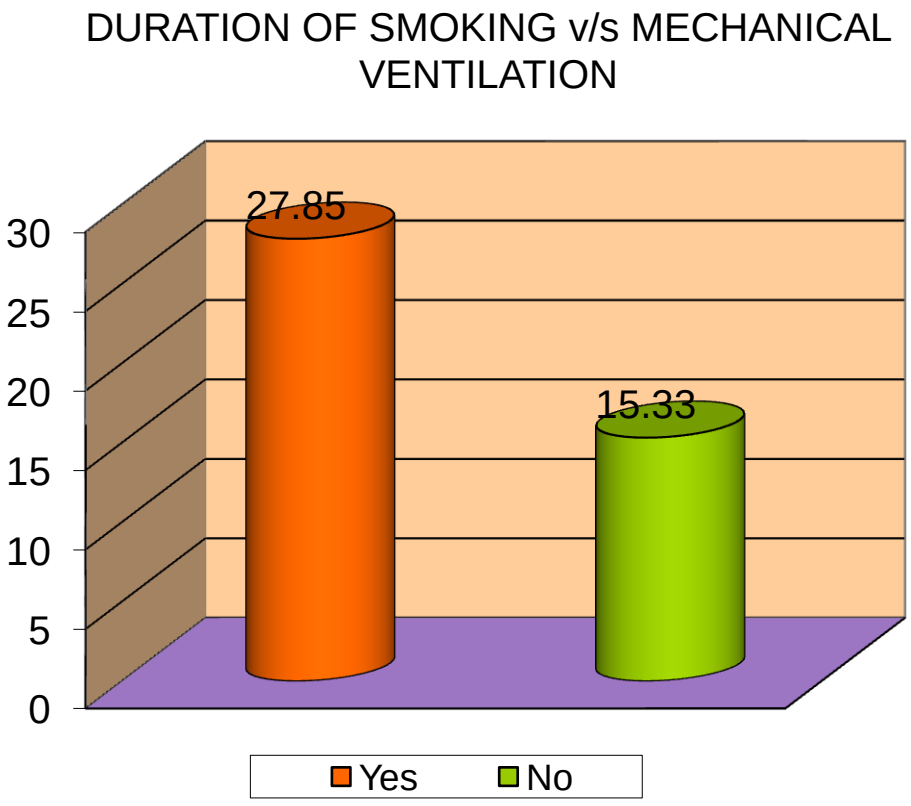
DURATION OF SMOKING v/s MECHANICAL VENTILATION

Pack years	**No Of Cases**	**MV**	**No MV**
1 - 10	55	0	55
11 - 20	54	10	44
21- 30	28	23	5
>30	13	9	4
Total	150	42	108
Mean		27.85	15.33
SD		6.99	6.81
P Value		<0.001	

In our study,

- none of the 55 cases who had smoked for 1-10 pack years eventually required mechanical ventilation
- 10 of the 54 cases (18.5%) with pack years11-20 needed mechanical ventilation
- 23 of the 28 (82.14%) with pack years 21-30 needed mechanical ventilation
- 9 of the 13 cases (69.2%) with pack years >30 needed mechanical ventilation

P value was found to be <0.001 which shows that the association between duration of smoking and the need for mechanical ventilation is significant. Hence COPD patients with long duration of smoking as measured by pack years are more likely to require mechanical ventilation in case of acute exacerbations.

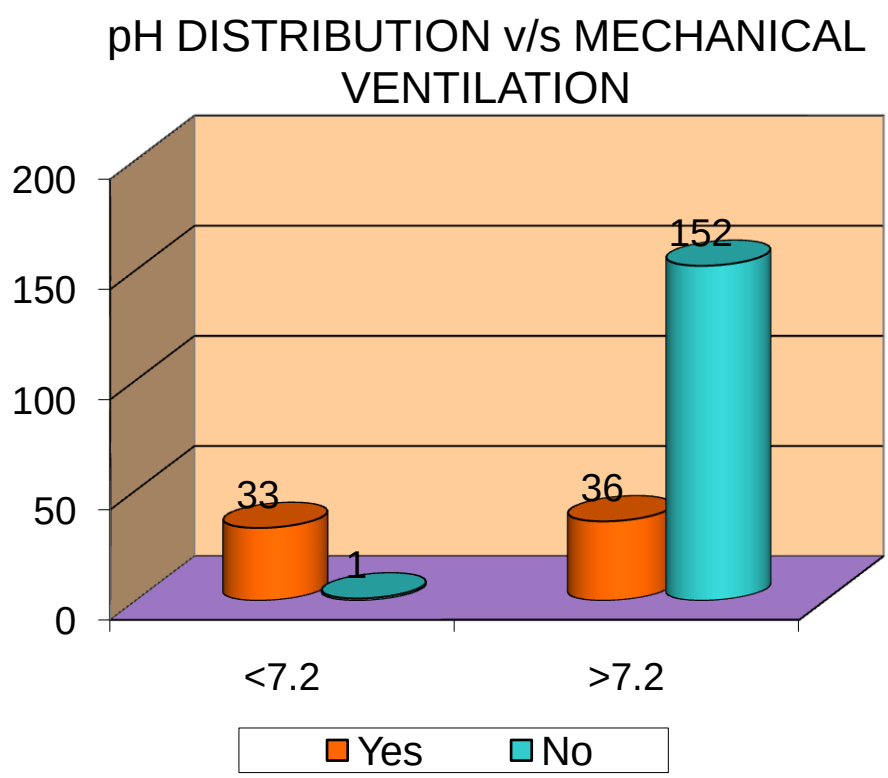


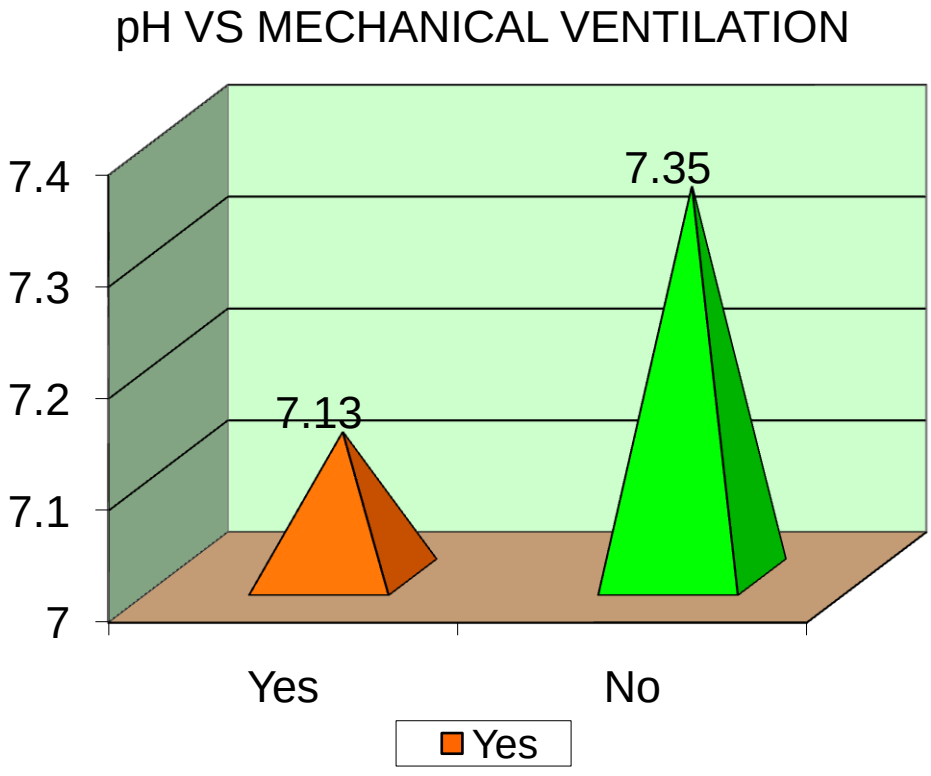
pH VERSUS NEED FOR MECHANICAL VENTILATION:-

Ph	**No Of Cases**	**MV**	**No MV**
≤7.2	34	33	1
>7.2	166	36	130
Total	200	69	131
Mean		7.13	7.35
SD		0.144	0.05
P'Value		<0.001	

Of the total 200 COPD patients, 34 had a pH of ≤7.2 , of whom 33 eventually needed mechanical ventilation (97.05%), whereas only 36 of 166 patients with pH >7.2 eventually needed mechanical ventilation (19.14%).

P value of <0.001 obtained by our study clearly indicates that pH ≤7.2 is an independent predictor for mechanical ventilation in COPD patients.


pH DISTRIBUTION v/s MECHANICAL VENTILATION
200
150
100
50
0
33
1
36
152
<7.2
>7.2
Yes
No

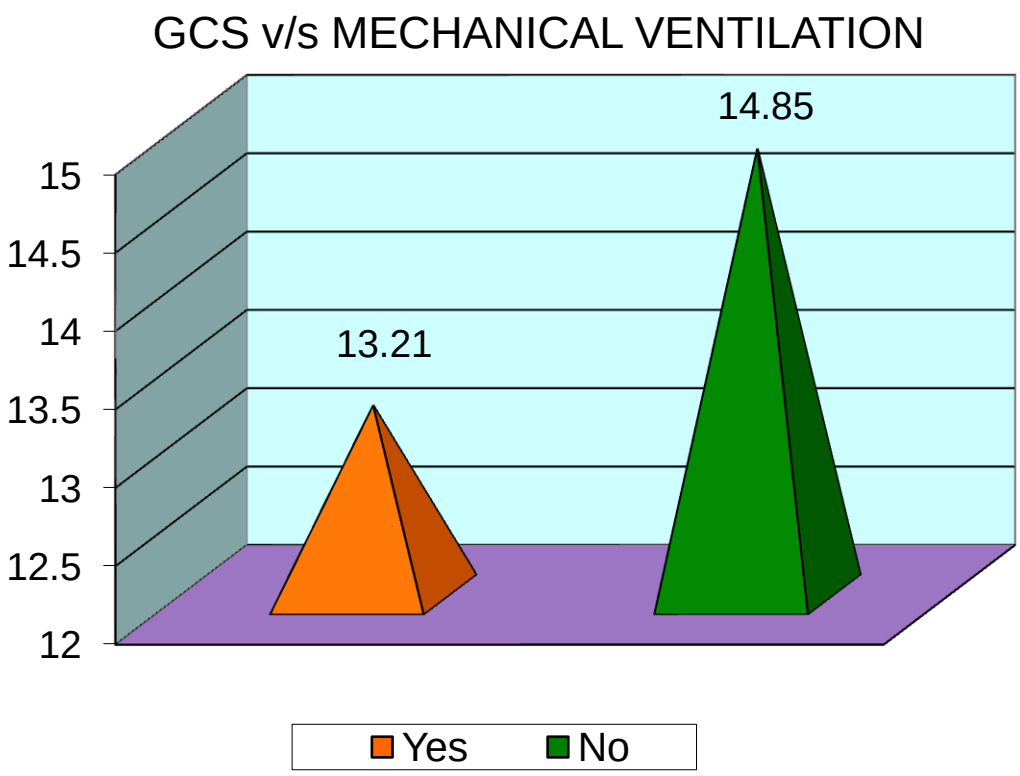

pH VS MECHANICAL VENTILATION
7.4
7.3
7.2
7.1
7
7.13
7.35
Yes
No
Yes

GLASGOW COMA SCALE VERSUS NEED FOR MECHANICAL VENTILATION:-

GCS	No Of Cases	Yes	No
<13	32	30	2
>13	168	17	151
Total	200	47	153
Mean		13.21	14.85
SD		1.19	0.43
P Value		<0.03	

Of the total 200 COPD patients, 32 had a GCS < 13 , of whom 30 (93.75%) eventually needed mechanical ventilation (97.05%), whereas only 17 of 168 patients with GCS >13 (10.11%) eventually needed mechanical ventilation.

P value of <0.03 obtained by our study clearly indicates that GCS< 13 is an independent predictor for need for mechanical ventilation in COPD patients.

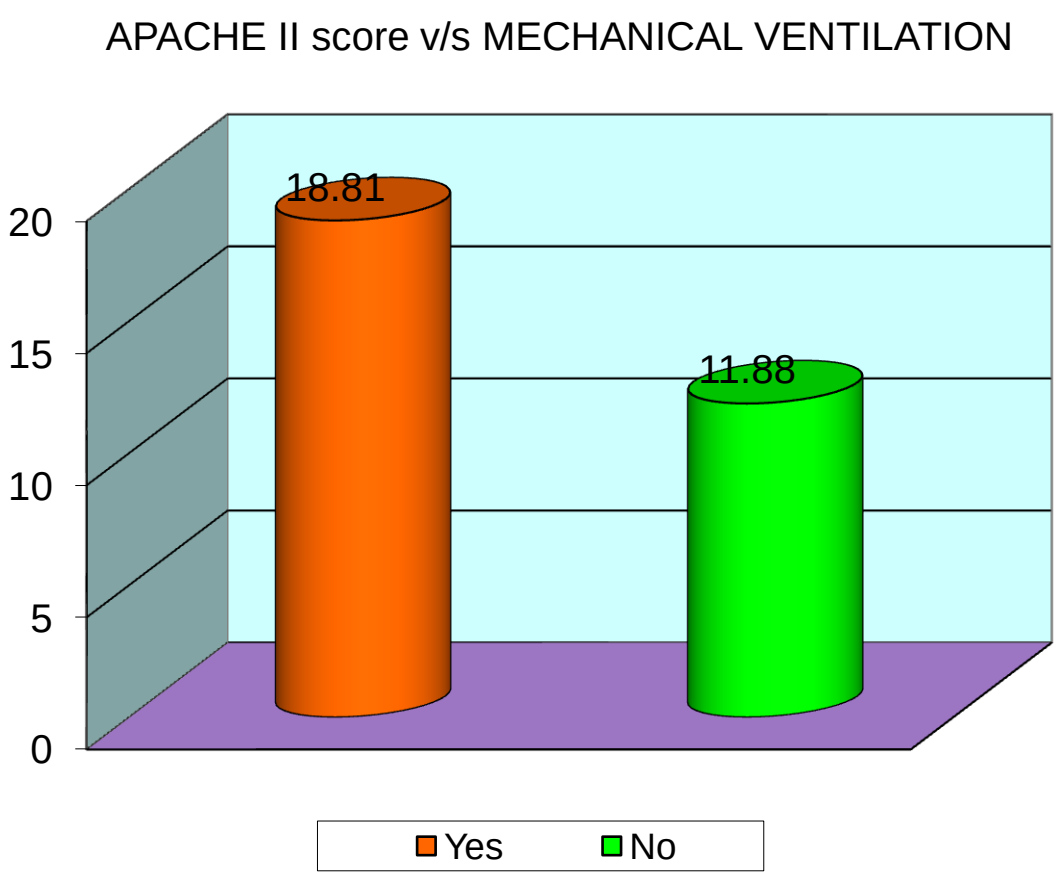

GCS v/s MECHANICAL VENTILATION
14.85
13.21
15
14.5
14
13.5
13
12.5
12
Yes
No

APACHE II SCORE VERSUS NEED FOR MECHANICAL VENTILATION:-

APACHE II	**No Of Cases**	**MV**	**No MV**
<15	137	7	130
>15	63	40	23
Total	200	47	153
Mean		18.81	11.88
SD		3.34	2.84
P'Value		<0.001	

Of the total 200 patients, 137 had an APACHE II score of < 15 on the day of admission, of which 7 {5.1%} eventually needed mechanical ventilation, whereas 63 patients had APACHE II score > 15 on the day of admission of whom 40 {63.4%} needed mechanical ventilation.

P value <0.001 obtained by our study indicates that APACHE II score >15 on the day of admission is an independent predictor of need for mechanical ventilation.

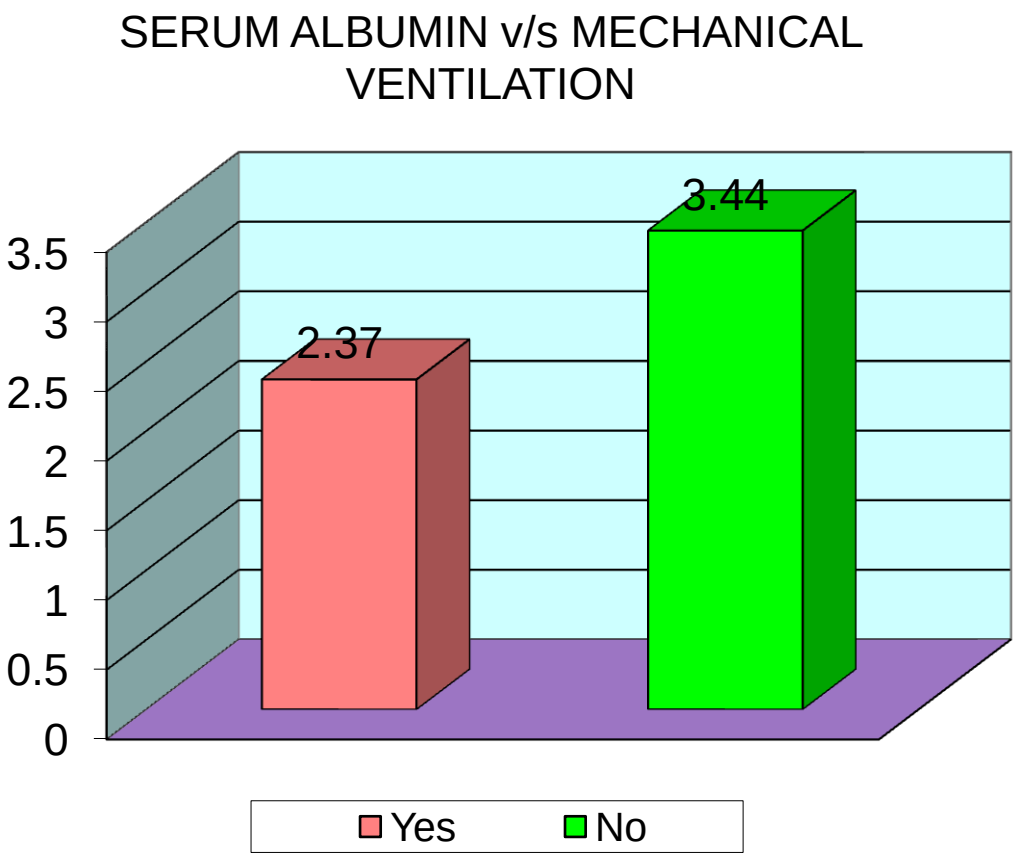

APACHE II score v/s MECHANICAL VENTILATION
18.81
11.88
20
15
10
5
0
Yes
No

SERUM ALBUMIN VERSUS NEED FOR MECHANICAL VENTILATION:-

SERUM ALBUMIN	**No Of Cases**	**MV**	**No MV**
<3	56	37	19
>3	144	10	134
Total	200	47	153
Mean		2.37	3.44
SD		0.65	0.54
P Value		<0.001	

Of the total 20 patients included in study, 56 had a serum albumin <3 g/dl on the day of admission of whom 37 {66.07%} were eventually given mechanical ventilation whereas 144 had serum albumin > 3 g/dl on the day of admission of whom 10 {6.94%} eventually needed mechanical ventilation.

P value < 0.001 indicates that serum albumin < 3 g/dl on the day of admission is an independent predictor of need for mechanical ventilation.


SERUM ALBUMIN v/s MECHANICAL VENTILATION
3.5
3
2.5
2
1.5
1
0.5
0
2.37
3.44
Yes
No

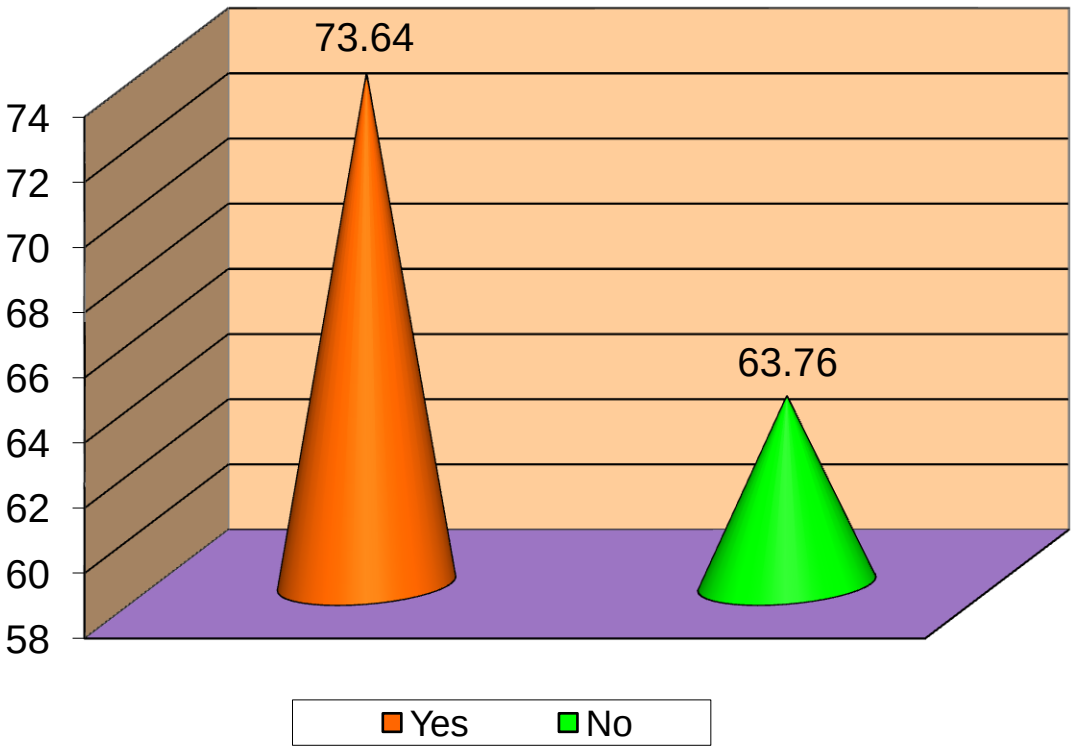
PaCO2 VERSUS NEED FOR MECHANICAL VENTILATION:-

PaCO2 (mm Hg)	**No Of Cases**	**MV**	**No MV**
<60	51	1	50
>60	149	46	103
Total	200	47	153
Mean		73.64	63.76
SD		5.27	6.19
P'Value		<0.001	

Of the total 200 patients, 51 had a PaCO2 of < 60mm Hg, of which1 patient eventually was given mechanical ventilation. 149 patients had a PaCO2 >60 mmHg, of whom 46 later had to be given mechanical ventilation (30.8%)

P value was <0.001 which indicates that PaCO2 > 60 mmHg on the day of admission is a significant independent predictor of need for mechanical ventilation.

PaCO2 v/s MECHANICAL VENTILATION



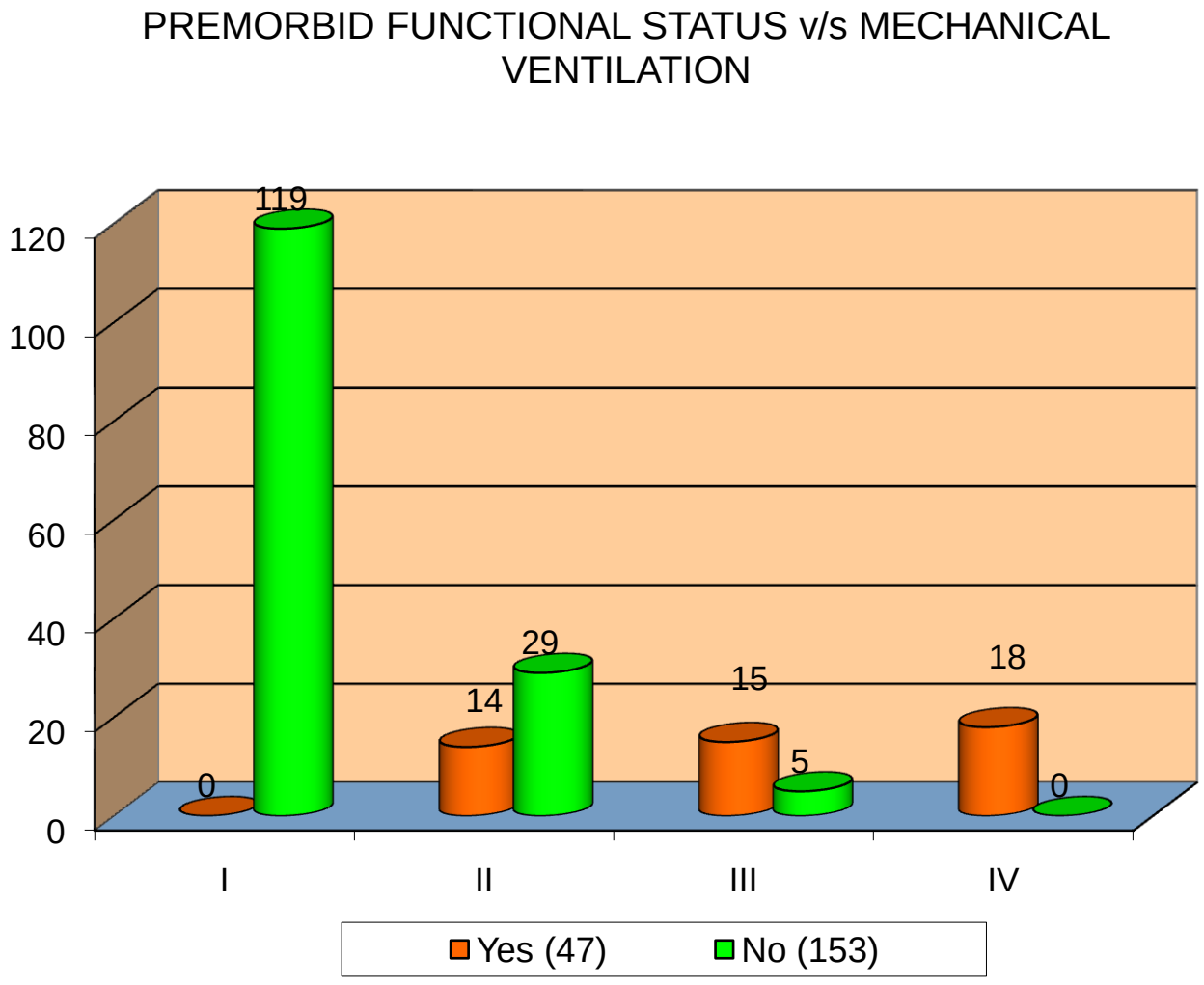
PREMORBID FUNCTIONAL SCORE VERSUS NEED FOR MECHANICAL VENTILATION:-

	Premorbid Functional Status			
MV	**I**	**II**	**III**	**IV**
Yes (47)	0	14	15	18
No (153)	119	29	5	0
TOTAL	119	43	20	18

I & II	14	148
III & IV	33	5
p value	0.035 Significant	

Of the total 200 patients, 119 were assigned as Grade I, with none of them needing mechanical ventilation, 43 were included in Grade II with 14 (32.5%) needing mechanical ventilation, 20 were in Grade III with 15 of them (75%) needing mechanical ventilation and 18 were in Grade IV with all (100%) needing mechanical ventilation eventually. Hence, 14 of the 152 patients in Grade I and II (9.2%) and 33 of the 38 patients (86.8%) in Grade III and IV needed mechanical ventilation.

P value of 0.035 is significant indicating that premorbid functional status of Grade III and IV is an independent predictor for need of mechanical ventilation.



DISCUSSION:-

In our study, majority (78%) of patients were over 50 years of age. We already know COPD is a disease more affecting elderly persons. The findings of this study are similar to our earlier knowledge.

In our study, majority (76.5%) of patients were males. The prevalence of COPD, as we already know, is much more in males than females, probably due to higher prevalence of smoking in males. Our study also follows the same prevalence pattern.

In our study, smokers comprised 150 (75%) of the total 200 cases. As we already know, the major etiological factor in COPD is cigarette smoking, hence our finding was in line with previous studies.

Madkour et al have earlier described smoking duration in pack years as a predictor of need for mechanical ventilation. In our study, P value of <0.001 shows that the association between duration of smoking and the need for mechanical ventilation is significant. Hence our findings follow the same trend as previous studies and COPD patients with long duration of smoking as measured by pack years are more likely to require mechanical ventilation in case of acute exacerbations.

Arterial Blood pH on the day of admission has been earlier studied by other groups. Khilnani et al have found pH <7.26 to be significant with respect to need

for mechanical ventilation. Hoo et al have also identified pH< 7.25 to be significant, with maximum rate of intubation with pH< 7.20. Kumar et al have found pH < 7.20 to be a significant predictor. In our study, a similar trend was found with 97.05% of patients with pH <7.2 on the first day eventually going for mechanical ventilation. Ventilation-perfusion mismatch, alveolar hypoventilation and respiratory muscle fatigue are reasons for acidosis in severe acute exacerbations.

Glasgow Coma Scale <9 has been identified by Ucgun et al as a significant predictor of mechanical ventilation. Our study has indicated a GCS < 13 to be significant. The lower threshold for our study is probably due to higher rates of intubation and relatively low availability of noninvasive ventilation.

APACHE II score> 22 has been described by Vitacca et al as significant in predicting need for mechanical ventilation. APACHE II > 23 was found significant by Ucgun et al while Kumar et al have identified an APACHE II score > 11.5 as independent predictor of intubation. Our study had a pattern more similar to the latter, with 63.4% of patients with APACHE >15 eventually needing mechanical ventilation.

Serum Albumin< 3.5 g/dl has earlier been found significant in predicting mechanical ventilation by Khilnani et al. Whereas in their study, Vitacca et al found albumin to have no significant relationship with mechanical ventilation. Our

study has paralleled the findings of Khilnani et al and indicates serum albumin < 3 g/dl to be significant predictor of intubation as 66.07% of patients with albumin <3g/dl on the first day needed mechanical ventilation. Serum Albumin is a proven marker of nutritional status of patients. COPD patients who are malnourished are more likely to go in for intubation and mechanical ventilation during an acute insult like an exacerbation. This explains the reason for the predictive ability of low serum albumin.

PaCO2 > 68 mm Hg has been described by Kumar et al as a significant predictor of mechanical ventilation. In our study, first day PaCO2 > 60 mm Hg has been found to be significant as 30.8% of patients with PaCO2 > 60 mm Hg needed mechanical ventilation during the course of their hospital stay. Ventilation-perfusion mismatch, alveolar hypoventilation and respiratory muscle fatigue are reasons for increased PaCO2 in severe acute exacerbations.

Premorbid functional status shows the severity of COPD as well as associated underlying comorbid conditions. Menzies et al have shown that premorbid status is the most significant factor in predicting outcome. Kumar et al showed that worse premorbid status can predict need for mechanical ventilation. In our study, 86.8% of patients with worse (Grade III and Grade IV) premorbid functional status according to modified Menzies score eventually required mechanical ventilation. Hence the finding in our study parallels the previous studies.

Hence, our study has found that duration of smoking in pack years, first day values of arterial blood pH, PaCO2, Glasgow Coma Scale, APACHE II score, serum albumin and premorbid functional status can be used to predict the need for mechanical ventilation in COPD patients with acute exacerbation.

LIMITATIONS:-

1. Relatively low availability of Non Invasive Ventilation during the course of the study may have led to a higher rate of intubation and mechanical ventilation.
2. Our centre being a tertiary care centre, COPD patients with more severity and thus with more need for mechanical ventilation are referred to us which may have influenced the results.

SUMMARY:-

The study "First Day Predictors Of Requirement Of Mechanical Ventilation In COPD Patients With Acute Exacerbation" was done to identify quantitative and qualitative variables which could help identify those patients who would eventually require mechanical ventilation, on the first day of admission itself, so as to help allocating scanty ICU facilities more effectively.

200 patients were included in the study according to the inclusion and exclusion criteria and evaluated on history, clinical and biochemical aspects, after obtaining the necessary institutional ethical clearance and informed consent from each patient. The data thus obtained was entered in Microsoft Excel Spreadsheet and subjected to statistical analysis.

In our study, 153 cases were males and 47 were females, probably due to increased prevalence of smoking among males. Majority (78%) cases were over 50 years of age which is in line with previous observations that COPD is a disease affecting the elderly more.

150 cases in our study were smokers (75%), which is coinciding with our previous knowledge that smoking is the major causative factor of COPD.

On the day of admission itself variables like arterial blood pH, $PaCO_2$, serum albumin, APACHE II score, Glasgow Coma Scale and duration of smoking in pack

years was measured and these values were entered into the spreadsheet for all patients. Each patient was followed up during the hospital stay and intubated if fulfilling the indications for mechanical ventilation. The above mentioned variables were compared between those cases managed without mechanical ventilation and those who ultimately required mechanical ventilation.

In our study the association between duration of cigarette smoking in pack years and the need for mechanical ventilation was found to be significant, hence COPD patients with long duration of smoking are more likely to require mechanical ventilation during acute exacerbation.

The association between low arterial blood pH (< 7.2) and the need for mechanical ventilation was found to be significant, hence COPD patients with more acidosis are more likely to require mechanical ventilation in an acute exacerbation.

The association between high PaCO2 (> 60mm Hg) on the day of admission and the need for mechanical ventilation was found to be significant, hence COPD patients with higher PaCO2 are more likely to require mechanical ventilation in an acute exacerbation.

Association between low GCS (<13) and the need for mechanical ventilation was significant, hence COPD patients with altered sensorium are likely to need mechanical ventilation in an acute exacerbation.

The association between high APACHE II score (>15) and the need for mechanical ventilation was significant, hence COPD patients with high APACHE II score on the day of admission are more likely to require mechanical ventilation.

The association between low serum albumin (<3g/dl) and the need for mechanical ventilation was found significant, hence COPD patients with less serum albumin are more likely to require mechanical ventilation in an acute exacerbation.

Association between premorbid functional status (Grade III and IV) as measured by modified Menzies scale and the need for mechanical ventilation was significant, hence COPD patients with higher premorbid score are more likely to require mechanical ventilation in an acute exacerbation.

Hence, our study has found that duration of smoking in pack years, first day values of arterial blood pH, PaCO2, Glasgow Coma Scale, APACHE II score, serum albumin and premorbid functional status can be used to predict the need for mechanical ventilation in COPD patients with acute exacerbation.

CONCLUSION:-

- Males comprise the majority of COPD cases, probably due to increased prevalence of smoking habit among males.
- Majority of cases are over 50 years of age, hence COPD is a disease affecting the elderly more.
- Majority of cases are smokers, which is in line with previous knowledge that smoking is the major causative factor for COPD.
- Long duration of smoking (as measured in pack years) is a significant predictor of need for mechanical ventilation in COPD patients with acute exacerbation.
- Low arterial blood pH on the day of admission (<7.2) is a significant predictor of need for mechanical ventilation in COPD patients with acute exacerbation.
- Altered sensorium on the day of admission (as measured by a low Glasgow Coma Scale {<13}) is a significant predictor of need for mechanical ventilation in COPD patients with acute exacerbation.
- A high APACHE II score on the day of admission (>15) is a significant predictor of need for mechanical ventilation in COPD patients with acute exacerbation.
- Low serum albumin on the day of admission (<3.5 g/dl) is a significant predictor of need for mechanical ventilation in COPD patients with acute exacerbation.

- High $PaCO_2$ (>60mm Hg) on the day of admission is a significant predictor of need for mechanical ventilation in COPD patients with acute exacerbation.
- Worse premorbid functional status (as measured by Grade III or IV on the modified Menzies score) is a significant predictor of need for mechanical ventilation in COPD patients with acute exacerbation.
- Hence, using these above mentioned variables, it is possible to classify according to severity and identify on the day of admission itself, those COPD patients with acute exacerbation who may, during their hospital stay, require mechanical ventilation.

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PROFORMA :-

Name:

Age / Sex:

IP / OP no:

Occupation:

Presenting complaints:

H/o increased dyspnea

H/o increased cough

H/o increased sputum production

Past History:

H/o CLD, DM, HT, CKD, CVD, DRUG INTAKE, THYROID DISORDER , EPILEPSY , HEPATITIS.

Personal history

alcoholic/ non alcoholic

smoker/ nonsmoker

Clinical Examination:

General examination	**Nutrition** **Glasgow Coma Scale** **Orientation** **Afebrile/Febrile** **Pallor/no pallor** **Cyanosis/ No cyanosis** **Clubbing/No clubbing** **Pedal edema / no pedal edema**
Vitals	**Temperature** **Pulse rate** **Blood pressure** **Respiratory rate** **Oxygen saturation**

RESPIRATORY SYSTEM	
CARDIOVASCULAR SYSTEM	
CENTRAL NERVOUS SYSTEM	

ABDOMEN	

Laboratory investigations:

1. Hemoglobin, complete blood count, platelet count
2. Blood urea, serum creatinine, blood glucose
3. Serum Sodium, Serum Potassium, Serum Calcium
4. Bilirubin – Total, Direct, Indirect
5. SGOT, SGPT, Total Protein, Serum Albumin
6. Arterial Blood Gas Analysis

Score Calculation

1. Premorbid Functional Status (Modified Menzies Criteria)

    I- Independent- working/Living without help

    II- Restricted- able to leave house but exercise is restricted

    III- Housebound- rarely leaves house but able to do self care

    IV- Bed/ chair bound- not able to do self care

2. Acute Physiology and Chronic Health Evaluation II (APACHE II) score

    1. Age
    2. Glasgow Coma Scale
    3. Temperature
    4. Heart rate
    5. Respiratory rate
    6. Mean arterial pressure
    7. Packed cell volume
    8. WBC Count
    9. A-a Gradient (if FiO2>0.5) or PaO2 (if FiO2 <0.5)
    10. Arterial pH
    11. Serum Sodium
    12. Serum Potassium
    13. Serum Creatinine
    14. Chronic health problems { Cirrhosis/ NYHA –IV/Severe COPD/ Regular HD/ Immunocompromised}

TOTAL SCORE-

Diagnosis

MASTER CHART-

	NAME	AGE	SEX	SMOKER (Pack years)	pH	GCS	PaCO2	PREMORBID FUNCTIONAL STATUS	SERUM ALBUMIN	APACHE II SCORE	MECHANICAL VENTILATION
1	A1	60	M	30	7.12	15	74	IV	2.9	21	YES
2	A2	50	M	25	7.3	15	78	IV	2.3	20	YES
3	A3	65	M	30	7.1	13	70	II	2.8	20	YES
4	A4	58	M	30	6.9	12	69	IV	3.2	20	YES
5	A5	56	M	30	6.92	14	78	III	1.7	18	YES
6	A6	52	M	25	7.1	13	80	II	2.5	17	YES
7	A7	75	M	35	7.05	15	82	II	3.1	19	YES
8	A8	58	M	15	6.9	14	68	IV	2.3	10	YES
9	A9	46	M	15	7.2	14	60	III	3.2	20	YES
10	A10	52	M	25	7.13	15	76	II	1.4	18	YES
11	A11	54	M	20	7.15	13	69	II	2.5	25	YES
12	A12	62	M	0	7.25	12	80	IV	2.2	16	YES
13	A13	56	M	40	7.35	12	78	III	3.3	18	YES
14	A14	49	M	25	7.33	13	69	IV	1.9	15	YES
15	A15	75	M	20	7.32	12	73	IV	1.2	25	YES
16	A16	67	M	30	7.34	12	78	IV	2.1	20	YES
17	A17	69	M	20	7.18	12	80	IV	2.3	23	YES
18	A18	64	M	30	7.2	12	82	IV	2.1	26	YES
19	A19	70	M	30	7.11	14	65	IV	2.8	20	YES
20	A20	62	M	20	7.15	12	68	II	2.5	24	YES
21	A21	60	M	15	7.17	13	69	III	1.5	23	YES
22	A22	59	M	20	7.21	13	70	IV	1.9	24	YES
23	A23	66	M	25	7.11	13	75	III	2.2	22	YES
24	A24	67	M	20	7.15	12	77	III	2.1	20	YES
25	A25	63	M	30	7.09	15	80	III	2.4	21	YES
26	A	58	M	25	7.13	12	71	III	2.2	16	YES
27	B	65	M	20	7.11	13	69	II	3.5	19	YES
28	C	52	F	0	7.12	15	70	IV	3.2	18	YES
29	D	46	M	35	6.9	13	74	III	2.8	20	YES
30	E	58	M	25	6.89	13	77	II	1.9	14	YES
31	F	72	F	0	7.21	11	69	II	1.4	20	YES
32	G	65	M	30	7.2	13	80	IV	2.5	17	YES

33	H	62	M	40	7.34	13	77	IV	3.4	16	YES
34	I	54	M	30	7.36	13	78	III	1.6	18	YES
35	J	75	M	35	7.22	14	80	II	2.8	16	YES
36	K	52	F	0	7.23	11	69	II	1.5	21	YES
37	L	68	M	40	7.25	15	72	IV	3.4	17	YES
38	M	80	M	40	7.13	15	78	III	2.2	15	YES
39	N	61	M	0	6.9	15	76	II	1.9	19	YES
40	O	56	F	25	6.92	15	72	II	1.4	16	YES
41	P	77	M	35	6.89	14	75	IV	3.1	21	YES
42	R	54	M	30	6.9	12	70	III	1.2	13	YES
43	S	64	M	30	7.05	12	65	IV	2.1	19	YES
44	T	48	M	30	7.11	12	77	III	3	18	YES
45	U	55	M	25	6.92	14	73	III	2.1	16	YES
46	V	78	M	30	7.34	13	64	III	2.4	15	YES
47	W	62	M	40	7.2	13	77	II	3.3	15	YES
48	X	81	M	30	7.21	14	80	III	1.6	20	NO
49	Y	52	M	0	7.35	14	78	III	2.2	18	NO
50	Z	55	F	25	6.92	14	70	II	1.4	17	NO
51	1	67	M	10	7.39	13	56	II	3.2	17	NO
52	2	88	M	10	7.36	12	58	II	3.6	13	NO
53	3	52	F	0	7.34	15	64	I	3.3	11	NO
54	4	74	M	10	7.32	15	50	I	3.6	14	NO
55	5	58	M	10	7.36	14	57	I	2.2	11	NO
56	6	82	M	20	7.37	15	58	II	3.3	17	NO
57	7	61	F	0	7.34	15	62	I	3.1	9	NO
58	8	74	M	10	7.28	14	64	I	3.5	12	NO
59	9	78	M	10	7.39	15	66	II	3.1	13	NO
60	10	55	F	0	7.37	15	65	II	3.5	13	NO
61	11	69	M	10	7.29	15	71	I	2.9	12	NO
62	12	81	M	20	7.3	15	58	II	3.1	8	NO
63	13	45	F	0	7.36	15	62	I	3.7	12	NO
64	14	54	M	10	7.37	15	55	I	4.1	13	NO
65	15	78	M	10	7.34	15	50	I	3.8	15	NO
66	16	64	M	40	7.36	14	48	I	3.3	13	NO
67	17	58	M	0	7.35	15	60	II	4.2	8	NO
68	18	45	F	0	7.39	14	63	I	3.8	17	NO
69	19	67	M	35	7.34	15	64	I	3.1	11	NO
70	20	45	F	10	7.35	15	66	II	3.2	7	NO
71	21	59	M	20	7.37	15	68	I	3.4	13	NO
72	22	72	M	25	7.34	15	70	I	3.5	11	NO
73	23	80	M	0	7.37	15	74	I	3.2	9	NO
74	24	52	F	0	7.36	15	58	I	3.1	14	NO

75	25	66	M	15	7.36	15	68	I	2.8	17	NO
76	26	58	M	10	7.39	15	64	II	4.6	9	NO
77	27	42	F	0	7.34	14	60	I	3.8	7	NO
78	28	76	M	20	7.37	15	72	I	3.8	17	NO
79	29	61	M	20	7.35	15	68	I	3.4	13	NO
80	30	45	M	10	7.37	15	64	II	3.8	12	NO
81	31	74	F	0	7.34	15	68	I	4.6	8	NO
82	32	52	M	0	7.33	15	60	I	3.5	12	NO
83	33	86	M	20	7.35	15	68	I	3.1	17	NO
84	34	45	M	20	7.39	15	60	II	2.8	13	NO
85	35	77	M	10	7.37	15	58	I	3.5	13	NO
86	36	54	M	10	7.37	15	64	I	3.2	11	NO
87	37	48	F	0	7.36	15	62	I	3.2	8	NO
88	38	42	M	20	7.34	14	63	I	3.8	12	NO
89	39	62	M	10	7.34	14	70	II	3.5	13	NO
90	40	68	M	20	7.37	15	72	II	3.3	13	NO
91	41	52	F	0	7.38	15	56	I	3.2	17	NO
92	42	53	M	10	7.39	15	58	I	4.1	17	NO
93	43	44	M	15	7.38	15	59	I	3.1	8	NO
94	44	60	M	10	7.38	15	67	I	3.1	7	NO
95	45	47	F	0	7.34	15	64	I	4.1	13	NO
96	46	41	M	20	7.24	15	65	I	4.5	8	NO
97	47	55	M	10	7.39	15	55	II	3.1	12	NO
98	48	61	F	0	7.36	15	50	I	2.7	9	NO
99	49	74	F	0	7.37	15	48	I	4.5	13	NO
100	50	46	M	10	7.39	15	55	I	4.1	17	NO
101	51	57	M	20	7.34	15	54	I	4.1	17	NO
102	52	71	M	0	7.36	15	55	I	4.5	12	NO
103	53	45	F	10	7.37	15	59	I	3.1	8	NO
104	54	48	M	10	7.36	15	60	I	3.2	11	NO
105	55	51	F	0	7.37	15	66	I	3.6	13	NO
106	56	58	M	15	7.34	15	58	I	3.6	13	NO
107	57	41	M	10	7.37	15	70	I	3.1	11	NO
108	58	78	M	0	7.37	15	58	I	4.5	17	NO
109	59	52	F	10	7.34	15	55	I	3.4	14	NO
110	60	64	M	40	7.36	15	60	I	3.1	13	NO
111	61	63	M	10	7.33	15	62	I	3.2	11	NO
112	62	56	F	0	7.37	15	72	I	3.7	11	NO
113	63	49	M	20	7.39	15	60	II	3.4	17	NO
114	64	41	M	15	7.38	15	55	I	3.3	12	NO
115	65	59	F	0	7.37	15	59	I	3.9	11	NO
116	66	71	M	10	7.37	15	60	III	3.5	10	NO
117	67	68	M	20	7.36	15	65	I	3.4	12	NO
118	68	59	M	10	7.37	15	68	II	3.6	14	NO

119	69	59	M	20	7.34	15	70	I	3.1	13	NO
120	70	41	F	0	7.36	15	70	I	3.9	11	NO
121	71	54	M	15	7.37	15	74	I	3.2	17	NO
122	72	47	F	10	7.28	15	60	I	3.4	16	NO
123	73	52	M	20	7.29	15	56	I	3.8	10	NO
124	74	63	M	15	7.39	14	45	I	2.1	13	NO
125	75	49	M	0	7.39	14	60	I	3.3	9	NO
126	76	42	F	0	7.34	15	50	I	3.1	11	NO
127	77	56	M	15	7.33	15	55	I	2.9	12	NO
128	78	54	M	10	7.36	15	58	I	3.2	12	NO
129	79	78	M	30	7.37	15	73	I	2.9	17	NO
130	80	64	M	20	7.29	15	70	I	3.3	13	NO
131	81	58	M	20	7.37	15	68	I	2.1	13	NO
132	82	45	F	0	7.32	15	66	II	3.9	9	NO
133	83	67	M	15	7.37	15	62	I	3.3	14	NO
134	84	45	F	10	7.33	15	60	II	2.3	11	NO
135	85	59	M	20	7.36	15	70	I	3.7	12	NO
136	86	72	M	25	7.34	15	67	I	2.4	9	NO
137	87	80	M	0	7.36	15	63	I	3.8	7	NO
138	88	52	F	0	7.39	14	64	I	3.3	13	NO
139	89	66	M	35	7.37	15	66	I	3.8	17	NO
140	90	58	M	10	7.39	15	70	I	3.3	12	NO
141	91	42	F	0	7.37	15	68	I	3.4	14	NO
142	92	76	M	20	7.34	15	63	II	3.6	10	NO
143	93	61	M	10	7.34	15	60	I	3.6	7	NO
144	94	45	M	10	7.37	15	74	I	3.5	9	NO
145	95	74	F	0	7.36	15	68	I	3.2	13	NO
146	96	52	M	0	7.36	15	64	I	3.4	11	NO
147	97	86	M	10	7.34	15	63	I	3.1	11	NO
148	98	45	M	20	7.33	15	68	II	3.7	12	NO
149	99	77	M	10	7.3	15	72	I	3.8	9	NO
150	100	54	M	10	7.39	15	65	I	3.2	7	NO
151	101	77	M	10	7.37	14	66	I	2.9	17	NO
152	102	51	F	0	7.39	15	60	I	3.9	13	NO
153	103	58	M	10	7.39	15	64	I	4.2	10	NO
154	104	41	M	10	7.34	15	66	I	4.2	9	NO
155	105	78	M	0	7.39	15	63	II	3.8	10	NO
156	106	52	F	10	7.35	15	68	I	3.9	10	NO
157	107	44	M	10	7.37	15	70	II	3.7	7	NO
158	108	63	M	10	7.36	15	68	I	3.2	9	NO
159	109	56	F	0	7.39	15	68	I	3.7	10	NO
160	110	49	M	20	7.34	15	71	I	3.9	11	NO
161	111	41	M	16	7.3	15	70	I	3.4	13	NO
162	112	59	F	0	7.35	15	66	I	3.8	10	NO

163	113	71	M	10	7.36	15	62	I	3.4	11	NO
164	114	68	M	10	7.34	15	70	II	3.9	9	NO
165	115	64	M	20	7.37	14	66	I	4.1	10	NO
166	116	59	M	20	7.34	15	61	I	3.2	10	NO
167	117	41	F	0	7.37	15	64	I	3.7	13	NO
168	118	54	M	15	7.39	15	60	I	3.3	11	NO
169	119	47	F	10	7.3	15	70	I	3.4	9	NO
170	120	52	M	20	7.36	15	75	I	3.7	10	NO
171	121	63	M	15	7.37	15	64	I	4.2	13	NO
172	122	49	M	0	7.32	15	62	I	3.6	10	NO
173	123	42	M	20	7.39	15	65	I	4.3	11	NO
174	124	62	M	10	7.35	15	63	III	3.9	11	NO
175	125	68	M	20	7.32	15	68	II	3.5	17	NO
176	126	52	F	0	7.28	15	68	I	3.3	9	NO
177	127	53	M	10	7.3	15	62	II	3.5	10	NO
178	128	64	M	20	7.36	14	65	I	3.2	12	NO
179	129	60	M	10	7.37	15	70	I	3.2	10	NO
180	130	47	F	0	7.36	15	60	I	4.1	9	NO
181	131	41	M	20	7.32	15	67	I	3.8	12	NO
182	132	55	M	10	7.39	15	60	I	3.8	10	NO
183	133	61	F	0	7.37	15	70	I	3.3	10	NO
184	134	74	F	0	7.37	15	75	I	3.2	9	NO
185	135	46	M	10	7.36	15	70	I	3.7	11	NO
186	136	57	M	10	7.38	15	65	I	3.3	12	NO
187	137	71	M	0	7.34	15	61	I	3.2	9	NO
188	138	45	F	10	7.38	15	65	I	3.1	13	NO
189	139	48	M	10	7.33	15	60	II	3.3	11	NO
190	140	55	F	10	7.38	14	62	I	2.8	9	NO
191	141	67	M	20	7.36	15	60	I	3.4	10	NO
192	142	88	M	10	7.32	15	62	I	3.9	14	NO
193	143	52	F	0	7.39	15	68	II	4.4	13	NO
194	144	74	M	20	7.34	14	70	I	2.5	9	NO
195	145	58	M	10	7.39	15	74	III	3.4	10	NO
196	146	82	M	20	7.32	15	62	I	2.6	16	NO
197	147	61	F	0	7.36	15	60	I	2.9	17	NO
190	148	66	M	15	7.28	15	63	I	3.8	10	NO
199	149	55	F	0	7.36	15	65	I	3.9	13	NO
200	150	69	M	20	7.3	15	70	II	3.8	11	NO

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ETHICS COMMITTEE CERTIFICATE

Name of the Candidate	:	Dr.Dhanus Sadasivan Nair,
Course	:	PG in MD., General Medicine
Period of Study	:	2014-2017
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	First day predictors of requirement of Mechanical Ventilation in COPD patients with acute exacerbation
Ethical Committee as on	:	27.07.2016

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

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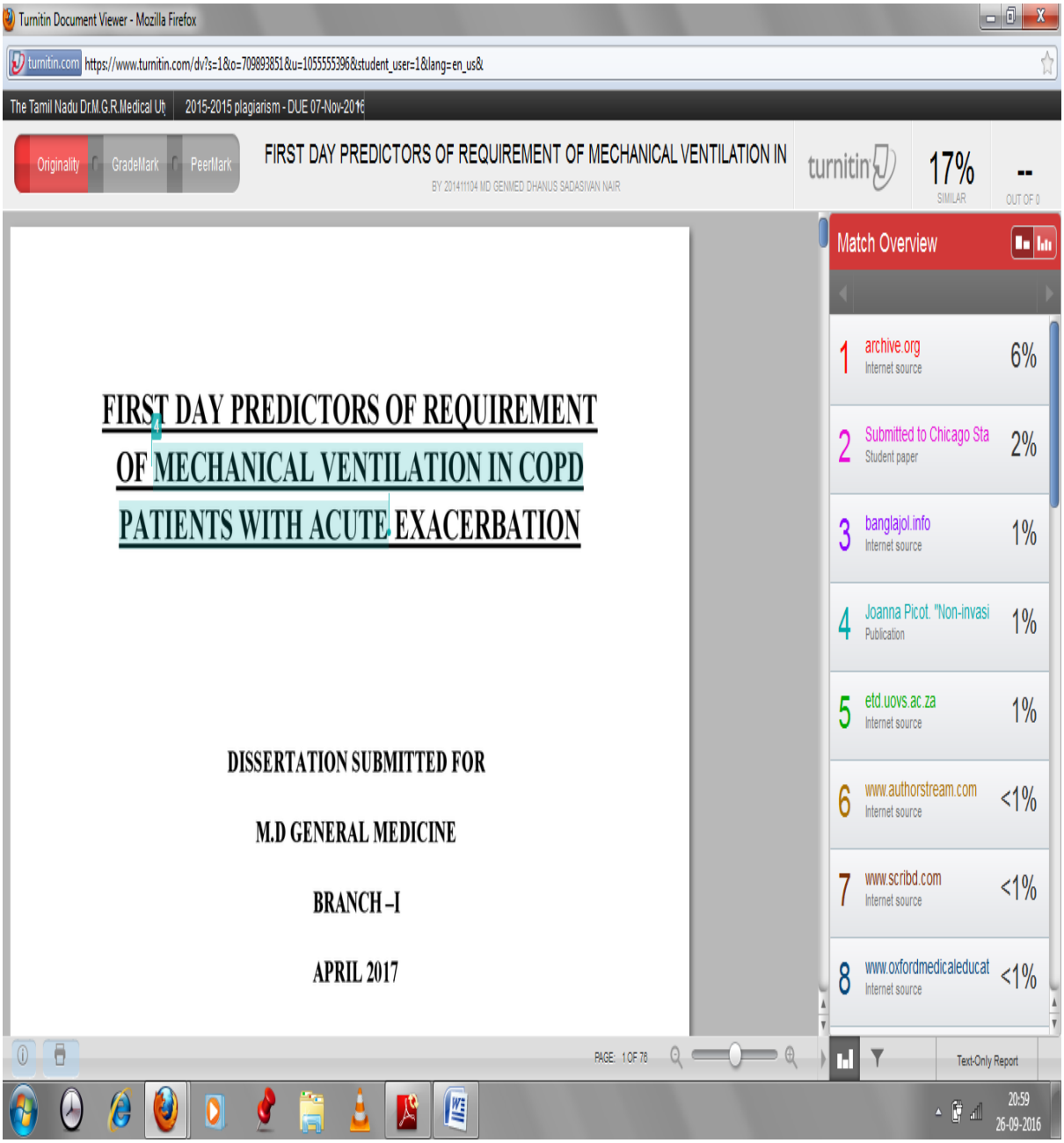
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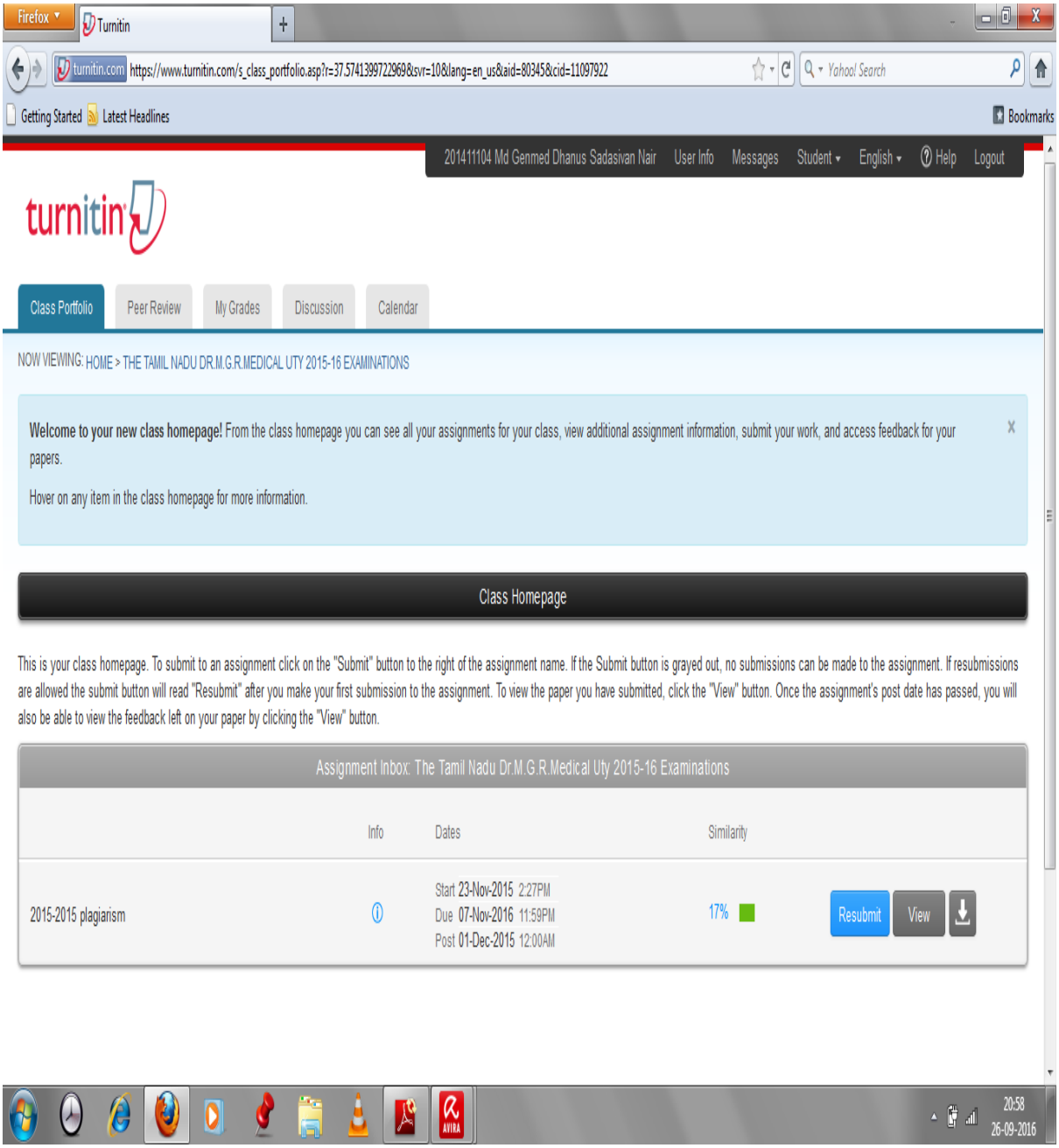
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