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To compare and contrast the levels of various metabolites and risk/stress factors in chronic obstructive pulmonary disease (COPD) with and without diabetes vs healthy controls- A study protocol..

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ABSTRACT

COPD is a progressive lung disorder characterized by persistent airflow limitation and systemic inflammation. Its burden is compounded when associated with comorbidities such as diabetes mellitus (DM), which share overlapping risk factors and pathophysiological mechanisms. This study aims to compare and contrast metabolic, oxidative stress, and inflammatory biomarker profiles among COPD patients with diabetes, COPD patients without diabetes, and healthy controls. A hospital-based cross-sectional observational design will be employed at the Department of Biochemistry, Datta Meghe Institute of Higher Education & Research, Wardha, India, over a three-year period. Participants aged 25–60 years will be included, and fasting blood samples will be analyzed for glucose, HbA1c, total protein, albumin, lipid profile, reactive oxygen species (ROS), antioxidant enzymes (SOD, GPx), ferritin, ceruloplasmin, and cytokines (TNF-α, IL-6, CRP). Pulmonary function (FEV1, FEV1/FVC) and functional capacity (6-minute walk test) will also be assessed. Data will be analyzed using descriptive and inferential statistics, with correlation analyses exploring associations between glycemic/lipid indices and inflammatory/oxidative markers. This will be the first comparative study in an Indian setting evaluating systemic metabolite and inflammatory profiles in COPD patients with and without diabetes, generating pilot data for risk prediction models and providing insights relevant to low- and middle-income country populations.

KEYWORDS: COPD, Diabetes Mellitus, Oxidative Stress, Inflammatory Biomarkers, Metabolites..

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is an umbrella term for progressive lung diseases, not ably including chronic bronchitis and emphysema. COPD is primarily caused by tobacco smoking; however, other contributory factors include alpha-1 antitrypsin (AAT) deficiency, second-hand smoke, air pollution, and occupational exposure to dust and fumes[1].COPD is the third leading cause of death globally, with 3.23 million deaths recorded in 2019.Over 70% of COPD cases in high-income countries are attributed to tobacco smoking. In low- and middle-income countries (LMICs), tobacco use accounts for 30–40% of cases, while household air pollution remains a significant contributor.COPD symptoms often worsen when associated with comorbidities such as diabetes, cancer, pneumonia, cardiovascular disease, osteoporosis, and mental health issues like depression and anxiety[2]. Generally, COPD leads to restricted airflow and impaired lung function due to inflammation and damage to lung tissue. Symptoms include cough, breathlessness, wheezing, and fatigue[3]. The WHO includes COPD in its Global Action Plan for the prevention and control of non-communicable diseases (NCDs), as well as in the United Nations' 2030 Agenda for Sustainable Development[4].

This study focuses specifically on COPD patients who are smokers with and without diabetes in comparison to healthy control subjects.

REVIEW OF LITERATURE

COPD is traditionally classified as a pulmonary disorder characterized by airflow limitation. However, recent perspectives emphasize its systemic inflammatory nature[5]. When mortality due to comorbidities is considered, the disease presents an even graver health burden. Risk factors include air pollution, aging, infections, asthma, and low socioeconomic status[6].

Metabolic disorders such as Type 2 Diabetes Mellitus and Metabolic Syndrome are prevalent and contribute to increased morbidity. Glucose metabolism is more frequently impaired in COPD patients than in non-COPD individuals. Age, lifestyle, and genetic predisposition link these conditions[7]. Obesity, physical inactivity, genetic factors, and smoking are among the principal risk factors for T2DM[8].

Contrasting studies show regional variation in the COPD-DM association. For instance, while some research confirms increased DM burden in COPD patients, others, such as a **Korean study**, found no significant link possibly due to a higher proportion of underweight individuals in the sample[9]. Additionally, COPD patients have an increased incidence of myocardial infarction, depression, lung cancer, and osteoporosis[10].

Obesity impacts pulmonary mechanics by reducing expiratory reserve volume (ERV) and functional residual capacity (FRC). Moreover, adipose tissue exacerbates inflammation by producing cytokines like TNF-α and IL-6[11]. COPD patients often present with comorbidities even without diabetes, including cardiovascular and cerebrovascular diseases[12].

IL-6 and TNF-α have strong links to insulin resistance and T2DM[13]. **Botelho et al. demonstrated** IL-1α's role in neutrophilic inflammation due to smoke exposure in animal models[14]. Research shows elevated IL-6 levels in COPD patients, correlating with disease severity, although generalization is limited due to sample-specific factors[15]. Further studies affirm IL-6 as a predictor of COPD risk, though genetic associations remain inconclusive[16].

Tkacova et al. linked increased CD40 expression in adipose tissue to COPD severity and hypoxia, suggesting adipose dysfunction may amplify systemic inflammation and insulin resistance. Elevated inflammatory markers such as CRP and TNF-α are well-established in COPD High white blood cell count and CRP levels also predict T2DM and COPD morbidity[17].

Rationale / Need for the Study

COPD and diabetes share pathogenic mechanisms. This study explores metabolomic and inflammatory differences in COPD patients with and without diabetes to improve early diagnosis and targeted interventions, especially in LMICs.

Hypotheses

This study tests whether COPD patients with diabetes differ significantly in metabolite, oxidative stress, and inflammatory profiles from other groups. It also examines correlations between glycemic/lipid indices and oxidative-inflammatory markers. The null hypothesis assumes no significant group differences or associations among these biomarkers within COPD patients.

AIMS AND OBJECTIVES

Aim:

To compare and integrate metabolic, oxidative stress, inflammatory, and functional biomarker profiles in COPD patients with and without diabetes versus healthy controls, and to explore their translational relevance for early risk stratification.

Objectives:

1. To evaluate and compare plasma/serum biomarkers (glucose, HbA1c, proteins, lipid profile, ROS, antioxidants-SOD/GPx, ferritin/ceruloplasminand cytokines—TNF-α, IL-6, CRP) across the three groups.
2. To analyze the correlation between HbA1c and lipid indices with oxidative and inflammatory markers, lung function (FEV1, FEV1/FVC), and functional capacity (6-minute walk test) in COPD patients.

Material and Methods

Study Design:Hospital-based cross-sectional observational study

Site: Department of Biochemistry, Datta Meghe Institute of Higher Education & Research, Sawangi (Meghe), Wardha, Maharashtra, India.

Duration:3 years

Inclusion Criteria:

- Adults aged 25–60 years with clinically diagnosed COPD (with/without T2DM)
- Smokers and non-smokers
- Age-matched healthy controls

Exclusion Criteria:

- Use of hypolipidemic, hormonal, or steroid medications
- Pregnancy or lactation
- Chronic or acute inflammatory diseases

Sample Size Calculation:

$$N = \left(\frac{Z_{1-\alpha/2} + Z_{1-\beta}}{0.5 \times \ln\left(\frac{1+r}{1-r}\right)} \right)^2 + 3$$

Number of groups = 3 (Healthy, COPD−DM, COPD+DM)
Sample Collection:5 ml venous blood (after 12–14 hours fasting), collected using aseptic precautions.

Methodology

Standardized laboratory protocols for glucose, HbA1c, total protein, albumin, globulin, lipid profile.Inflammatory & Oxidative Stress Markers:Assayed via commercially available ELISA kits for ROS, SOD, GPx, ferritin, ceruloplasmin, TNF-α, IL-6, and CRP. Kit selection will depend on sensitivity and availability at the time of testing.

Statistical Analysis
Software: SPSS v23 (USA Inc.)
Descriptive Statistics: Mean and standard deviation
Chi-square test: Categorical variables
Student's t-test: Comparison between two groups
Pearson's correlation coefficient: Relationship among biomarkers

Expected Outcomes / Novelty

- First comparative study assessing systemic metabolite, oxidative, and inflammatory biomarkers in COPD with and without diabetes
- Pilot data to develop multi-marker risk prediction models.

Contextual relevance for underrepresented LMIC populations in the global COPD-diabetes research framework.

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