

**CHRONIC OBSTRUCTIVE PULMONARY DISEASE SEVERITY  
AND ITS ASSOCIATION WITH SERUM MAGNESIUM LEVELS  
AMONG PATIENTS AT MOI TEACHING AND REFERRAL  
HOSPITAL, ELDORET**

**BY**

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## DECLARATION

### Student's Declaration:

This research thesis is submitted to the School of Medicine as part of the fulfillment of the requirements of the Masters of Medicine degree in Internal Medicine, Moi University.

I declare that this is my original thesis and that it has never been presented for a degree in any other university.

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## DEDICATION

First and foremost, I dedicate this work to **Allah, the Almighty**, for granting me the strength, patience, and wisdom to see this journey through. Without His countless blessings and mercy, none of this would have been possible.

To my beloved wife, **Anzal Garat Hassan**,

Your unwavering love, understanding, and constant support have been my pillar through every challenge. Thank you for standing beside me through it all.

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This work is as much yours as it is mine.

## ABSTRACT

**Background:** Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory condition characterized by persistent airflow limitation and chronic symptoms such as dyspnea, cough, and sputum production. Magnesium plays a critical role in bronchodilation, neuromuscular function, and inflammatory modulation. Hypomagnesemia has been linked to increased COPD severity and exacerbation frequency. However, local data exploring this association remains limited. This study assessed the relationship between serum magnesium levels and COPD severity among patients at Moi Teaching and Referral Hospital (MTRH).

**Objectives:** To determine COPD severity and its association with serum magnesium levels among COPD patients in MTRH.

**Methods:** A hospital-based cross-sectional study was conducted at MTRH from January to June 2023, enrolling 102 COPD patients aged  $\geq 40$  years from outpatient and inpatient departments. Diagnosis was confirmed by spirometry (post-bronchodilator  $FEV_1/FVC < 0.70$ ), and patients were staged according to GOLD severity (I–IV). Serum magnesium was classified as hypomagnesemia ( $< 0.7$  mmol/L), normomagnesemia ( $0.7–1.05$  mmol/L), or hypermagnesemia ( $> 1.05$  mmol/L). Data were analyzed using STATA v16. Categorical variables were reported as frequencies and percentages; continuous variables as means  $\pm$  SD. Associations were tested using Chi-square and logistic regression, with adjusted odds ratios (aOR) and 95% confidence intervals. Ethical approval was obtained from the Moi Teaching and Referral Hospital/Moi University Institutional Research and Ethics Committee (MTRH/MU-IREC).

**Results:** The mean age of participants was  $71.3 \pm 14.8$  years, with females comprising 60.8% of the study population. Biomass exposure was nearly universal (99%), while 43.1% had a history of cigarette smoking. The overall mean serum magnesium level was  $0.77 \pm 0.12$  mmol/L (range: 0.47–1.14 mmol/L). Patients with mild to moderate COPD (GOLD stages I–II) had a higher mean magnesium level ( $0.82 \pm 0.09$  mmol/L) compared to those with severe to very severe COPD (GOLD stages III–IV), who had a mean level of  $0.74 \pm 0.12$  mmol/L. Hypomagnesemia ( $< 0.7$  mmol/L) was identified in 31 patients (30.4%), with 93.5% of them classified as having GOLD stage III or IV disease. There was a statistically significant association between hypomagnesemia and increased COPD severity ( $p = 0.001$ ). Multivariate logistic regression analysis revealed that patients with hypomagnesemia had significantly higher odds of severe COPD (adjusted odds ratio [aOR] = 27.3; 95% CI: 4.38–170.19). Hypermagnesemia ( $\geq 1.05$  mmol/L) was observed in only two patients (1.96%): one with GOLD stage II and another with GOLD stage IV, limiting meaningful interpretation. All participants were referred for routine clinical follow-up, with treatment plans tailored to the severity of their COPD.

**Conclusions:** Hypomagnesemia was strongly associated with advanced COPD stages, suggesting it may serve as a potential marker of disease severity and a possible target for further clinical attention.

**Recommendations:** Routine screening of serum magnesium levels may be considered in the evaluation of COPD patients, particularly those with more severe disease. Further research, including randomized controlled trials, is warranted to determine whether correction of hypomagnesemia can lead to improved clinical outcomes.

**Key Words:** COPD, serum magnesium levels, hypomagnesemia, spirometry, GOLD classification, exacerbations, bronchodilation, Moi Teaching and Referral Hospital (MTRH).

### ABBREVIATIONS OF TERMS

|                        |                                                         |
|------------------------|---------------------------------------------------------|
| <b>AATD</b>            | Alpha-1 Antitrypsin Deficiency                          |
| <b>ACE</b>             | Angiotensin-Converting Enzyme                           |
| <b>AF</b>              | Atrial Fibrillation                                     |
| <b>AOR</b>             | Adjusted Odds Ratio                                     |
| <b>ARBs</b>            | Angiotensin Receptor Blockers                           |
| <b>BBs</b>             | Beta-Blockers                                           |
| <b>BMI</b>             | Body Mass Index                                         |
| <b>CAT</b>             | COPD Assessment Test                                    |
| <b>CCBs</b>            | Calcium Channel Blockers                                |
| <b>CI</b>              | Confidence Interval                                     |
| <b>CKD</b>             | Chronic Kidney Disease                                  |
| <b>COPD</b>            | Chronic Obstructive Pulmonary Disease.                  |
| <b>CRP</b>             | C-reactive protein                                      |
| <b>DALYs</b>           | Disability Adjusted Life years                          |
| <b>DLCO</b>            | Diffusing Capacity of the Lungs for Carbon Monoxide     |
| <b>DM</b>              | Diabetes Mellitus                                       |
| <b>DVT</b>             | Deep Vein Thrombosis                                    |
| <b>ECOPD</b>           | Exacerbation of Chronic Obstructive Pulmonary Disease   |
| <b>FEV<sub>1</sub></b> | Forced Expiratory Volume at 1 second                    |
| <b>FVC</b>             | Forced Vital Capacity                                   |
| <b>GINA</b>            | Global Initiative for Asthma                            |
| <b>GOLD</b>            | Global initiative for chronic obstructive lung disease. |
| <b>GSTP1</b>           | Glutathione S-Transferase Pi 1                          |
| <b>HAART</b>           | Highly Active Antiretroviral Therapy                    |
| <b>HFrEF</b>           | Heart Failure with reduced Ejection Fraction            |

|                        |                                                            |
|------------------------|------------------------------------------------------------|
| <b>HRCT</b>            | High-Resolution Computed Tomography                        |
| <b>ICS</b>             | Inhaled Corticosteroids                                    |
| <b>IL-6</b>            | Interleukin 6                                              |
| <b>IQR</b>             | Interquartile Range                                        |
| <b>IREC</b>            | Institutional Research and Ethics Committee                |
| <b>LABA</b>            | Long-acting Beta 2 agonist.                                |
| <b>LAMA</b>            | Long-Acting Muscarinic Antagonist                          |
| <b>LMICs</b>           | Low and Middle Income Countries                            |
| <b>LTOT</b>            | Long-Term Oxygen Therapy                                   |
| <b>LTRA</b>            | Leukotriene Receptor Antagonists.                          |
| <b>MDI</b>             | Metered-Dose Inhaler                                       |
| <b>Mg<sup>2+</sup></b> | Magnesium                                                  |
| <b>MMP12</b>           | Matrix Metalloproteinase 12                                |
| <b>mMRC</b>            | Modified Medical Research Council (dyspnea scale)          |
| <b>MOPC</b>            | Medical Outpatient Clinic                                  |
| <b>MTRH</b>            | Moi Teaching and Referral Hospital                         |
| <b>MTRH/MU-IREC</b>    | Moi Teaching and Referral Hospital/Moi University          |
| <b>NACOSTI</b>         | National Commission for Science, Technology and Innovation |
| <b>NHLBI</b>           | the U.S. National Heart, Lung, and Blood Institute         |
| <b>NO</b>              | Nitrogen Dioxide                                           |
| <b>OHA<sub>s</sub></b> | Oral Hypoglycemic Agents                                   |
| <b>PE</b>              | Pulmonary Embolism                                         |
| <b>PHTN</b>            | Pulmonary Hypertension                                     |
| <b>PM</b>              | Particulate Matter less than 2.5 micrometers in diameter   |
| <b>PPIs</b>            | Proton Pump Inhibitors                                     |

|                                |                                                          |
|--------------------------------|----------------------------------------------------------|
| <b>Pre-COPD</b>                | Pre Chronic Obstructive Pulmonary Disease                |
| <b>PRISm</b>                   | Preserved Ratio Impaired Spirometry                      |
| <b>REDcap</b>                  | Research Electronic Data Capture                         |
| <b>RHF</b>                     | Right Heart Failure                                      |
| <b>ROMK</b>                    | Renal Outer Medullary Potassium channel                  |
| <b>SABA</b>                    | Short-Acting Beta <sub>2</sub> -Agonist                  |
| <b>SAMA</b>                    | Short-Acting Muscarinic Antagonist                       |
| <b>SD</b>                      | Standard Deviation                                       |
| <b>SGLT2</b>                   | Sodium-Glucose Cotransporter 2                           |
| <b>SGRQ</b>                    | St. George's Respiratory Questionnaire                   |
| <b>SPSS</b>                    | Statistical Package for the Social Sciences              |
| <b>SSA</b>                     | Sub Saharan Africa                                       |
| <b>STATA</b>                   | Data Analysis and Statistical Software                   |
| <b>T2DM</b>                    | Type 2 Diabetes Mellitus                                 |
| <b>TNF-<math>\alpha</math></b> | Tumor Necrosis Factor alpha                              |
| <b>TRPM6/7</b>                 | Transient Receptor Potential Melastatin 6 and 7 channels |
| <b>UOR</b>                     | Unadjusted Odds Ratio                                    |
| <b>VTE</b>                     | Venous Thromboembolism                                   |
| <b>WHO</b>                     | World Health Organization                                |

## DEFINITION OF TERMS

### **Chronic Obstructive Pulmonary Disease (COPD).**

COPD is a heterogeneous, progressive respiratory disease characterized by chronic respiratory symptoms such as dyspnea (shortness of breath), chronic cough, and sputum production, caused by persistent abnormalities in the airways (including bronchitis and bronchiolitis) and/or alveoli (emphysema). These changes lead to irreversible and progressive airflow limitation, often due to long-term exposure to noxious gases or particles (B. Celli et al., 2022). Diagnosis is confirmed using the GOLD recommended post bronchodilator spirometric criterion of  $FEV_1/FVC$  ratio  $< 0.70$  (GOLD, 2024).

### **FEV<sub>1</sub> (Forced Expiratory Volume in One Second).**

This is the volume of air exhaled forcefully in the first second during a spirometry test. It is used to assess the degree of airway obstruction and to classify the severity of COPD (Pauwels et al., 2001).

### **FVC (Forced Vital Capacity).**

FVC is the total amount of air exhaled during the spirometry test after taking a full deep breath. The  $FEV_1/FVC$  ratio is critical in diagnosing obstructive airway diseases such as COPD (Pauwels et al., 2001).

### **FEV<sub>1</sub>/FVC Ratio**

The  $FEV_1/FVC$  ratio is the proportion of a person's vital capacity that they are able to exhale in the first second of forced expiration to the full forced vital capacity. A post-bronchodilator  $FEV_1/FVC$  ratio of less than 0.70 is diagnostic of airflow obstruction in COPD. It is a central parameter in identifying and classifying obstructive airway diseases such as COPD (Pauwels et al., 2001).

**Exacerbation of Chronic Obstructive Pulmonary Disease (ECOPD).**

An exacerbation refers to an acute worsening of respiratory symptoms, typically dyspnea, cough, and increased sputum production, that occurs over a period of less than 14 days. It is usually associated with tachypnea, tachycardia, and increased airway or systemic inflammation. These episodes are commonly triggered by airway infections, air pollution, or other environmental or physiological insults (B. R. Celli et al., 2021).

**Magnesium ( $Mg^{2+}$ ).**

Magnesium is a divalent intracellular cation vital for numerous physiological functions, including neuromuscular transmission, muscle contraction, enzymatic activity, and immune modulation. In respiratory health, it plays a key role in regulating bronchial smooth muscle tone, reducing airway hyperresponsiveness, and maintaining normal respiratory muscle function. Hypomagnesemia has been linked to increased airway resistance and poor outcomes in patients with obstructive lung diseases (Zeki et al., 2011).

**Hypomagnesemia.**

Hypomagnesemia refers to a condition in which serum magnesium concentration falls below the normal range, typically  $<0.7$  mmol/L or  $<1.7$  mg/dL. It may result in neuromuscular dysfunction, muscle cramps, arrhythmias, and impaired bronchodilation, particularly in patients with chronic respiratory conditions (Elin, 2010). According to Youssef et al. (2022), hypomagnesemia is prevalent among COPD patients and may be associated with increased disease severity (Youssef et al., 2022).

**Spirometry.**

Spirometry is a non-invasive pulmonary function test that measures the volume and speed of air that can be inhaled and exhaled. It is the gold standard for diagnosing

COPD, as it allows for objective assessment of airflow obstruction and monitoring of disease progression (GOLD, 2024).

**GOLD Criteria.**

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria provide internationally accepted guidelines for the diagnosis, classification, and management of COPD. These include spirometric thresholds for airflow limitation, symptom burden evaluation using tools such as the COPD Assessment Test (CAT), and exacerbation history to guide therapy decisions (GOLD, 2024).

## **OPERATIONAL DEFINITION**

### **COPD Severity**

In this study, COPD severity is categorized based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2024 classification. Patients are grouped into four stages according to post-bronchodilator  $FEV_1$  as follows:

- GOLD 1 (Mild):  $FEV_1 \geq 80\%$  predicted
- GOLD 2 (Moderate):  $50\% \leq FEV_1 < 80\%$  predicted
- GOLD 3 (Severe):  $30\% \leq FEV_1 < 50\%$  predicted
- GOLD 4 (Very Severe):  $FEV_1 < 30\%$  predicted

This variable is treated as a categorical variable with four levels, indicating increasing severity of airflow limitation (GOLD, 2024).

### **Acute exacerbation of COPD**

Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) is defined as worsening of patient's symptoms such as increased dyspnea, cough or change in amount, and purulence of sputum from normal state (GOLD 2021). Anthonisen study classified AECOPD into three types depicted in the table below (Wong et.al, 2008);

### **Anthonisen criteria for AECOPD classification**

| Type I (severe)                                                                                            | Type II (moderate)       | Type III (mild)                                                                                                                                                                                                                                                                               |
|------------------------------------------------------------------------------------------------------------|--------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| All three symptoms:<br>1. Increased sputum volume<br>2. Increased sputum purulence<br>3. Increased dyspnea | Any two symptoms present | One of the symptoms present plus at least one of the following:<br>1. An upper respiratory tract infection in the past 5 days.<br>2. Increased wheezing<br>3. Increased cough<br>4. Fever without an obvious source.<br>5. A 20% increase in respiratory rate<br>6. Heart rate above baseline |

### Serum Magnesium Levels

Serum magnesium levels are classified into three categories based on standard reference intervals used in respiratory and metabolic studies:

- Normomagnesemia: 0.70–1.05 mmol/L (1.7–2.6 mg/dL)
- Hypomagnesemia: < 0.70 mmol/L (< 1.7 mg/dL)
- Hypermagnesemia: >1.05mmol/L(>2.6mg/dL)

This variable is treated as a categorical variable with three levels reflecting magnesium status (Elin, 2010) (Zeki et al., 2011).

### Smoking Status

- Never Smoker: An individual who has smoked fewer than 100 cigarettes in their lifetime and does not currently smoke.
- Former Smoker: An individual who has smoked at least 100 cigarettes in their lifetime but no longer smokes.

- **Current Smoker:** An individual who has smoked at least 100 cigarettes in their lifetime and currently smokes cigarettes daily or occasionally (Cornelius et al., 2023).

**PRISm (Preserved Ratio Impaired Spirometry)**

Defined as a spirometric pattern where the FEV<sub>1</sub>/FVC ratio is  $\geq 0.70$ , indicating no obstruction, but the FEV<sub>1</sub> is  $< 80\%$  predicted. This reflects impaired lung function without classic airflow limitation and is associated with respiratory symptoms, increased cardiovascular risk, and a predisposition to developing COPD (GOLD, 2024).

**Pre-COPD**

Refers to individuals with a preserved FEV<sub>1</sub>/FVC ratio ( $\geq 0.70$ ) who do not meet spirometric criteria for COPD but exhibit early signs of lung disease. These may include symptoms (e.g., chronic cough, dyspnea), imaging abnormalities (e.g., emphysema or airway thickening), or physiologic changes e.g., decreased Diffusing Capacity of the Lungs for Carbon Monoxide (DLCO) or gas trapping. Pre-COPD helps identify at-risk individuals before irreversible obstruction develops (GOLD, 2024).

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## CHAPTER ONE

### 1.0 INTRODUCTION

#### 1.1 Background

Chronic Obstructive Pulmonary Disease (COPD), a chronic lung disease characterized by persistent respiratory symptoms and airflow limitation, is a progressive and debilitating condition marked by breathlessness, chronic cough, and sputum production. These manifestations result from structural changes in the airways such as bronchitis and bronchiolitis and in the alveolar regions such as in emphysema, leading to airflow limitation that is largely irreversible. Globally, COPD remains a major contributor to morbidity, disability, and premature death, especially in low and middle income countries (B. Celli et al., 2022).

Chronic bronchitis, defined by a productive cough lasting for at least three months in two consecutive years, is predominantly due to mucus hypersecretion and airway inflammation. Emphysema, in contrast, involves alveolar wall destruction and enlargement of airspaces, impairing gas exchange by reducing surface area and elastic recoil. These two pathologies often coexist within the same individual and collectively define the clinical and pathological spectrum of COPD (GOLD, 2024).

The diagnosis of COPD is primarily based on spirometry, which remains the gold standard. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), a post-bronchodilator forced expiratory volume in one second to forced vital capacity ( $FEV_1/FVC$ ) ratio of less than 0.70 confirms persistent airflow limitation (Labaki & Rosenberg, 2020). The GOLD classification system grades disease severity based on percentage predicted  $FEV_1$ , providing a standardized framework for staging

and therapeutic decision-making. Table 1.1 outlines this classification system, which is used in this study to stratify patients by disease severity (GOLD, 2024).

**Table 1.1: Global Initiative for Chronic Obstructive Lung Disease (GOLD) Classification Based on Post-Bronchodilator FEV1**

| GOLD            | Severity    | FEV1 Percentage                   |
|-----------------|-------------|-----------------------------------|
| <b>GOLD I</b>   | Mild        | $FEV1 \geq 80\%$ predicted        |
| <b>GOLD II</b>  | Moderate    | $50\% \leq FEV1 < 80\%$ predicted |
| <b>GOLD III</b> | Severe      | $30\% \leq FEV1 < 50\%$ predicted |
| <b>GOLD IV</b>  | Very Severe | $FEV1 < 30\%$ predicted           |

GOLD was established in 1998 through collaboration between the World Health Organization (WHO), the U.S. National Heart, Lung, and Blood Institute (NHLBI), and a panel of international experts, with the aim of standardizing the prevention, diagnosis, and management of COPD (GOLD, 2024). Despite these global guidelines, COPD remains underdiagnosed and undertreated, especially in low and middle income countries (LMICs), where access to spirometry and other diagnostic tools is limited (GOLD, 2024). As of 2021, COPD was the fourth leading cause of death globally, accounting for approximately 3.5 million deaths representing 5% of all global deaths (WHO, 2024). Nearly 90% of COPD-related deaths in individuals under 70 occurred in LMICs, underscoring global health disparities (WHO, 2023). Prevalence estimates suggest COPD affects 9% to 12% of the global population, with 300–400 million individuals affected. This number is projected to increase by 23% by 2050, particularly among women and vulnerable groups due to ongoing exposure to risk factors like tobacco and indoor pollution (Boers et al., 2023).

In sub-Saharan Africa (SSA), the burden of COPD is rising rapidly. Between 1990 and 2019, the number of cases increased by 117%, with an estimated 10.3 million people affected. Household air pollution from biomass fuels remains a leading risk factor for COPD morbidity and mortality in SSA (Alemayohu et al., 2023). In Kenya, these challenges are evident at institutions such as Moi Teaching and Referral Hospital (MTRH), where COPD is often diagnosed clinically due to limited access to spirometry. This leads to inadequate disease classification and contributes to gaps in local epidemiological data (Binegdie et al., 2022).

While smoking is the leading global risk factor, GOLD (2024) acknowledges a broader array of causes, including biomass exposure, occupational hazards, early life developmental impairments, prior tuberculosis, and chronic asthma. This etiotype based classification better reflects the complexity of COPD, particularly in LMICs where multiple risk factors frequently coexist (GOLD, 2024). The pathogenesis involves chronic inflammation of the airways and lung parenchyma, leading to narrowing of small airways and alveolar destruction. Key inflammatory mediators include neutrophils, macrophages, and CD8+ T lymphocytes. These processes result in structural changes such as goblet cell hyperplasia, fibrosis, and alveolar attachment loss, reducing airflow and impairing gas exchange (Rodrigues et al., 2021). Inflammation can extend systemically, contributing to comorbidities such as cardiovascular disease, skeletal muscle wasting, osteoporosis, metabolic syndrome, and depression (Matsunaga et al., 2020).

Clinically, COPD presents with cough, sputum production, chest tightness, and exertional dyspnea. Acute exacerbations, defined as episodes of worsening respiratory symptoms often triggered by infections or environmental irritants, are associated with

accelerated decline in lung function, increased mortality, and elevated healthcare costs (GOLD, 2024). Management involves pharmacologic and non-pharmacologic strategies. Medications such as bronchodilators, inhaled corticosteroids, and phosphodiesterase 4 inhibitors are used to relieve symptoms and reduce exacerbations. Non-pharmacological interventions include smoking cessation, pulmonary rehabilitation, nutritional support, influenza and pneumococcal vaccination, and long term oxygen therapy (GOLD, 2024).

Given COPD's systemic manifestations, emerging research has explored the role of micronutrients in disease progression. Magnesium, a vital intracellular cation, has attracted interest due to its physiological roles in over 300 enzymatic processes including neuromuscular function, inflammation modulation, and energy metabolism. In respiratory function, magnesium acts as a calcium antagonist, reducing smooth muscle contraction, acetylcholine release, and mast cell degranulation, thereby exhibiting bronchodilatory and anti-inflammatory properties (Makwana et al., 2022).

Hypomagnesemia, defined as serum magnesium  $<0.7$  mmol/L, has been linked to frequent exacerbations, increased hospitalizations, and poor symptom control in COPD patients (Shivanthan & Rajapakse, 2014). Potential contributors include poor dietary intake, systemic inflammation, corticosteroid use, and diuretics. Although supplementation has shown benefits in some studies, findings remain inconclusive and there is no established guideline on its use in COPD management (Zanforlini et al., 2022) (do Amaral, 2008). In Kenya, access to serum magnesium testing is limited, contributing to a lack of data on the potential relationship between magnesium deficiency and COPD severity. Addressing this gap could inform more targeted management strategies in resource limited settings.

## 1.2 Problem Statement

Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of morbidity and mortality globally, posing a substantial public health challenge. In 2012 alone, nearly 3 million deaths were attributed to COPD, with approximately 90% occurring in low- and middle-income countries (LMICs), where access to diagnostic and therapeutic resources remains limited (GOLD, 2024). In Kenya, COPD continues to place a significant burden on the healthcare system, especially in tertiary institutions such as Moi Teaching and Referral Hospital (MTRH). Clinical diagnosis often occurs in the absence of spirometric confirmation, leading to underdiagnoses, misclassification of disease severity, and suboptimal management strategies (Binegdie et al., 2022).

Magnesium, an essential intracellular cation, plays a pivotal role in neuromuscular function, bronchial smooth muscle tone, and inflammatory modulation. Emerging evidence suggests that magnesium deficiency may contribute to increased disease severity, frequent exacerbations, and poorer clinical outcomes in COPD patients. For instance, a study by do Amaral et al. (2008) observed that COPD patients with lower serum magnesium levels were more likely to present with severe clinical symptoms and required longer hospital stays, suggesting a potential link between hypomagnesemia and disease burden (do Amaral, 2008).

Nonetheless, the clinical relevance of serum magnesium levels in COPD remains unclear. Although magnesium supplementation was associated with reductions in systemic inflammatory markers, Zanforlini et al. (2022) found no significant improvement in quality of life or exercise capacity among patients with stable COPD (Zanforlini et al., 2022).

Moreover, current evidence is largely drawn from high-income settings, with minimal data from African populations (Igwe et al., 2025). In Kenya, while magnesium is sometimes used empirically in the management of COPD, there are no published context-specific guidelines or robust local studies to support this practice. This gap highlights the need to investigate the association between serum magnesium levels and COPD severity in resource-constrained environments. Such evidence is critical for informing clinical decision-making and optimizing COPD care in settings like MTRH.

### **1.3 Justification**

Chronic Obstructive Pulmonary Disease (COPD) continues to impose a substantial and escalating burden on global health systems, ranking as the fourth leading cause of death worldwide (WHO, 2024). This burden is disproportionately felt in low- and middle-income countries (LMICs), where over 90% of COPD-related deaths occur, largely due to limited access to preventive interventions such as smoking cessation programs and vaccinations, as well as therapeutic measures including bronchodilators, corticosteroids, and oxygen therapy (GOLD, 2024). In Kenya, the impact of COPD is significant and growing, yet remains underappreciated and underreported due to the lack of robust surveillance systems and research. At Moi Teaching and Referral Hospital (MTRH), COPD is a frequently encountered respiratory condition. However, most patients are diagnosed based on clinical symptoms rather than objective measurements like spirometry. The absence of spirometry testing compromises the accuracy of COPD severity classification, which is crucial for guiding appropriate therapeutic decisions and improving long-term outcomes.

The diagnosis and management of COPD are further complicated by comorbid conditions and micronutrient deficiencies, which may influence disease progression

and exacerbation frequency. Among these, magnesium has emerged as a potentially important yet understudied factor. Magnesium is an essential intracellular cation involved in smooth muscle relaxation, neuromuscular transmission, and modulation of inflammatory pathways, all of which are relevant to the pathophysiology of COPD (Makwana et al., 2022). Hypomagnesemia has been implicated in increased airway hyperresponsiveness, impaired bronchodilation, and heightened inflammation, thereby potentially exacerbating COPD symptoms and contributing to frequent exacerbations (Shivanthan & Rajapakse, 2014). Despite these biologically plausible mechanisms, serum magnesium levels are not routinely assessed in COPD patients, and their clinical relevance remains unclear, particularly in sub Saharan Africa (Shah et al., 2010).

In Kenya, there is a glaring lack of local data examining the relationship between serum magnesium levels and COPD severity. This mirrors findings from other low and middle income settings where micronutrient monitoring remains underprioritized (Ahmadi et al., 2022). This knowledge gap hinders the development of evidence-based guidelines on magnesium assessment and supplementation in COPD care. While magnesium is sometimes used empirically in the management of acute bronchospasm or COPD exacerbations in some clinical settings, there is no published local evidence or standardized protocol guiding its use in Kenya or similar resource-constrained environments (GOLD, 2024). Understanding whether low serum magnesium levels correlate with increased disease severity could provide clinicians with a simple, cost-effective biomarker to enhance COPD risk stratification and therapeutic planning in resource limited settings.

This study seeks to fill this critical evidence gap by systematically evaluating serum magnesium levels among COPD patients stratified by disease severity using GOLD

criteria. It will provide foundational data on the prevalence of hypomagnesemia across different stages of COPD and assess its potential utility in clinical assessment and management. In doing so, the study could lay the groundwork for future research, including prospective studies and randomized controlled trials aimed at determining the efficacy of magnesium supplementation as an adjunctive therapy in COPD management. Ultimately, the findings may contribute to improved, context-specific care pathways for COPD patients in Kenya and similar LMIC settings, aligning with broader global health goals to reduce the burden of chronic respiratory diseases through better diagnosis and targeted treatment.

#### **1.4 Hypothesis**

There is a statistically significant association between severe COPD and serum magnesium levels.

#### **1.5 Research Question**

1. What is the distribution of COPD severity among patients attending MTRH?
2. What are the serum magnesium levels among COPD patients at MTRH?
3. What is the association between serum magnesium levels and COPD severity among patients at MTRH?

#### **1.6 Objective**

##### **1.6.1 Broad Objective**

To determine COPD severity and its association with serum magnesium levels among patients with COPD in MTRH.

##### **1.6.2 Specific Objective**

1. To stratify patients with COPD at MTRH according to severity, based on the GOLD 2023 criteria using post-bronchodilator FEV<sub>1</sub> % predicted.

2. To determine serum magnesium levels among COPD patients in MTRH.
3. To evaluate COPD severity and its association with serum magnesium levels among COPD patients in MTRH.

## **CHAPTER TWO**

### **LITERATURE REVIEW**

#### **2.0 Introduction**

Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory disorder characterized by persistent airflow limitation and an enhanced chronic inflammatory response in the airways and lungs. It is a leading cause of morbidity and mortality worldwide and presents a significant public health burden (GOLD, 2024).

The literature review in this chapter explores the current understanding of COPD, including its definition, causes, clinical presentation, disease burden, pathophysiology, diagnosis, management strategies, and common comorbidities.

Given the multifactorial nature of COPD, recent research has highlighted the role of micronutrients such as magnesium, which is crucial for smooth muscle function, neuromuscular conduction, and inflammatory modulation. Studies have shown that serum magnesium levels are associated with COPD severity and clinical outcomes, though this relationship remains incompletely characterized in many populations (Zeki et al., 2011) (Zanforlini et al., 2022).

This chapter will therefore also examine the role of magnesium in pulmonary health and its potential association with COPD severity. By synthesizing current knowledge, this review sets the foundation for the present study, which seeks to assess the association between serum magnesium levels and COPD severity.

## **2.1 Chronic Obstructive Pulmonary Disease (COPD)**

### **2.1.1 Background**

Chronic obstructive pulmonary disease (COPD) is ranked as the fourth leading cause of death worldwide (WHO, 2024). COPD is a collection of conditions with different causes, physiological effects and pathogenic mechanisms (Rennard & Drummond, 2015).

Increase in COPD prevalence globally makes its exacerbation an important phenomenon for patients and clinicians to manage. Resulting to a mounting interest in preventing its exacerbation as well as designing optimal COPD treatment approaches (Singh et al., 2012).

According to Kshirsagar & Patil, 2021 hypomagnesemia during acute exacerbation is correlated with the increased frequency of acute exacerbation in COPD (Kshirsagar & Patil, 2021).

COPD is diagnosed by the GOLD criteria which defines COPD as a condition with postbronchodilator FEV<sub>1</sub>/FVC ratio of <0.70 depicting airflow limitation in COPD patients. After identification of airflow limitation patients are further categorized into four GOLD stages according to the FEV<sub>1</sub>%: GOLD 1 - mild: FEV<sub>1</sub> ≥80% predicted, GOLD 2 - moderate: 50% ≤ FEV<sub>1</sub> <80% predicted, GOLD 3 - severe: 30% ≤ FEV<sub>1</sub> <50% predicted and GOLD 4 - very severe: FEV<sub>1</sub> <30% predicted (Arkhipov et al., 2017).

### **2.1.2 Definition of COPD**

Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, expectoration) due to persistent abnormalities of the airways (bronchitis, bronchiolitis), and/or alveoli (emphysema), that often results in progressive airflow limitation (B. Celli et al., 2022).

### 2.1.3 Burden of COPD

According to the World Health Organization's global health estimates, chronic obstructive pulmonary disease (COPD) ranked as the fourth leading cause of death globally, accounting for approximately 3.23 million deaths in 2019 (Li et al., 2023).

Despite its significant impact, respiratory diseases such as COPD have historically received less attention and funding compared to other major contributors to global mortality and morbidity (Lopez-Campos et al., 2016).

In Kenya, COPD contributes to a comparable burden of Disability-Adjusted Life Years (DALYs) as stroke, ischemic heart disease, and epilepsy, yet it remains highly underdiagnosed and undertreated. Analysis of hospital data from 2012 to 2016 across all 47 counties indicated that COPD accounted for approximately 0.3% of deaths (102,110 out of 323 total recorded deaths), substantially lower than the global average of 5% (Kariuki & Gathecha, 2018). This discrepancy likely reflects underdiagnosis and gaps in routine clinical recognition of COPD.

As per Kshirsagar & Patil 2021 majority (72%) of COPD patients in acute exacerbation had hypomagnesemia, while 28% had normal or high magnesium level. The odds of hypomagnesemia were 6.54 times more during exacerbation than when they had stable COPD. Patients with hypomagnesemia had 9.34 times higher risk of increased number of exacerbations compared to those patients with normal or high magnesium level. Hypomagnesemia during acute exacerbation is therefore correlated with increased frequency of acute exacerbation in COPD (Kshirsagar & Patil, 2021).

In a study conducted by Singh et.al ,2012 on serum magnesium level in COPD patients attending a tertiary hospital, 17 patients (34%) of the 50 studied had hypomagnesemia, while 33 (66%) of the COPD patients had normomagnesemia (Singh et al., 2012).

### 2.1.4 Etiology and Risk Factors of COPD

The pathophysiology of Chronic Obstructive Pulmonary Disease (COPD) reflects a complex and heterogeneous disease process involving chronic inflammation, airway remodeling, and progressive airflow limitation. In recognition of this complexity, the GOLD 2024 report introduced refined etiotypes; COPD-G (genetic), D (developmental), C (cigarette smoke), P (pollution), I (infections), A (asthma), and U (unknown causes) highlighting the diverse and overlapping origins of COPD. These etiotypes underscore the multifactorial nature of COPD pathogenesis, which arises from interactions between environmental exposures and individual susceptibility. Understanding the underlying mechanisms and risk factors associated with each etiology is essential for tailoring prevention and treatment strategies (GOLD, 2024).

COPD is the result of a multifaceted interplay of long-term cumulative exposure to noxious gases and particles, combined with a variety of host factors including genetics, airway hyper-responsiveness and poor lung growth during childhood. The risk of developing COPD is related to the following factors (Momtazmanesh et al., 2023).

#### 2.1.4 .1 Genetic factors (COPD-G)

Genetic susceptibility plays a significant role in COPD development, particularly through rare variants like alpha-1 antitrypsin deficiency (AATD) and common polymorphisms in genes regulating oxidative stress and tissue remodeling. Notably, *glutathione S-transferase pi 1* (GSTP1) is involved in oxidative stress response, while *matrix metalloproteinase 12* (MMP12) contributes to extracellular matrix remodeling. The most well-characterized genetic risk factor, AATD (PiZZ genotype), confers a 5–10-fold increased risk of COPD due to uncontrolled protease-mediated lung destruction, while MMP12 variants influence disease progression through altered matrix degradation. Emerging evidence suggests these genetic factors interact with

environmental exposures (e.g., smoking) to accelerate lung function decline, highlighting the importance of personalized risk assessment in high-risk populations (Silverman, 2020).

#### **2.1.4.2 Tobacco smoking (COPD-C)**

Globally, tobacco smoking remains the predominant risk factor for COPD, responsible for approximately 80% of cases. The study demonstrated that smokers face a 12-fold increased risk of developing COPD compared to non-smokers, underscoring the critical need for targeted smoking cessation programs. While occupational hazards and genetic factors contribute to disease burden, tobacco control emerges as the most impactful strategy for COPD prevention (Carreras et al., 2021).

Chronic exposure to tobacco smoke represents the most significant modifiable risk factor for COPD, with cigarette smokers demonstrating markedly worse respiratory outcomes compared to non-smokers. Research indicates smokers experience substantially higher rates of lung function impairment (6.4-fold increased COPD prevalence), accelerated annual FEV1 decline (56.8 mL/year vs 22.7 mL/year in non-smokers), and greater COPD-related mortality. These risks extend to secondhand smoke exposure (2.1-fold increased COPD risk) and alternative tobacco products, while emerging evidence suggests similar pulmonary consequences from chronic marijuana use, albeit through distinct pathological mechanisms (Salvi & Barnes, 2009).

While traditional cigarette use remains dominant, other forms of smoking and inhalational exposure are increasingly recognized as clinically relevant contributors to COPD risk. These include waterpipe (shisha) smoking, cigar and pipe smoking, electronic cigarettes (vaping), marijuana use, and exposure to secondhand tobacco smoke. Evidence suggests that waterpipe users inhale larger volumes of smoke per

session, often resulting in carbon monoxide exposure comparable to or exceeding that of cigarette smoking(Waziry et al., 2017). Electronic cigarette aerosols contain nicotine, volatile aldehydes, and ultrafine particles capable of inducing airway inflammation, with emerging research linking chronic vaping to obstructive lung changes(Gotts. et,al, 2019). Marijuana smoking has been associated with chronic bronchitis symptoms and airway injury, though via mechanisms distinct from tobacco (National Academies of Sciences, Engineering, and Medicine, 2017). Additionally, secondhand smoke increases COPD risk by approximately twofold, particularly among individuals with prolonged household exposure(Rosen et al., 2015). In low- and middle-income settings, biomass smoke exposure also interacts with tobacco smoke to exacerbate airway inflammation and contribute significantly to COPD burden (Assad et al., 2016).

Collectively, these findings emphasize that COPD risk extends beyond conventional cigarette smoking to a spectrum of combustible and non-combustible inhalational exposures, underscoring the need for comprehensive and inclusive smoking cessation and exposure-reduction strategies.

### **2.1.4 .3 Pollution (COPD-P)**

#### **2.1.4 .3 .1 Indoor air pollution**

Indoor air pollution from biomass fuel combustion (e.g., wood, charcoal) for cooking and heating in poorly ventilated homes disproportionately affects women in low- and middle-income countries (LMICs), contributing to COPD development. While research on biomass-related COPD remains limited, preliminary evidence suggests that interventions such as transitioning to cleaner fuels (e.g., liquefied petroleum gas) or improving ventilation may reduce COPD risk in non-smoking populations (Kurmi et al., 2010).

#### **2.1.4 .3 .2 Occupational exposures**

Occupational exposures to hazardous substances, including industrial chemicals, fumes, and particulate matter (both organic and inorganic), represent a significant yet often overlooked contributor to COPD development. Emerging evidence indicates that workplace-related inhalational risks account for approximately 15-20% of COPD cases, with particularly strong associations observed in agricultural, mining, and manufacturing sectors. These exposures induce persistent airway inflammation and accelerated lung function decline, independent of smoking status, highlighting the need for improved workplace safety measures and targeted pulmonary surveillance for high-risk occupations (Blanc et al., 2019).

#### **2.1.4.3.3 Outdoor air pollution**

Outdoor air pollution contributes to COPD pathogenesis through chronic exposure to particulate matter (PM<sub>2.5</sub>), nitrogen dioxide (NO<sub>2</sub>), and ozone, though its impact is less pronounced than smoking or occupational hazards. López-Campos et al. (2016) highlight that air pollution exacerbates existing COPD by inducing oxidative stress and systemic inflammation, rather than being a primary etiological factor. While long-term exposure may accelerate lung function decline, the population-attributable risk remains

modest (10–15% of cases) compared to tobacco smoke. The authors emphasize that pollution reduction strategies, particularly in urban areas could mitigate COPD exacerbations and slow disease progression, especially in vulnerable populations with pre-existing respiratory conditions (Lopez-Campos et al., 2016).

#### **2.1.4 .4 Lung growth and development (COPD-D)**

Early-life determinants of lung development significantly influence COPD risk in adulthood. Compromised lung growth due to low birth weight, childhood respiratory infections (e.g., tuberculosis, severe pneumonia), or environmental exposures (e.g., secondhand smoke) may lead to persistently reduced lung function. These factors potentially establish a lower baseline lung function trajectory, rendering individuals more vulnerable to accelerated decline when exposed to additional risk factors like smoking or air pollution later in life. This "developmental origins" hypothesis suggests that up to 30% of COPD cases may originate from impaired lung development during critical growth periods (Svanes et al., 2010).

#### **2.1.4.5 Asthma and airway hyper-reactivity (COPD-A)**

Emerging evidence suggests that asthma, particularly when poorly controlled or persistent into adulthood, may predispose individuals to COPD development through chronic airway remodeling and accelerated lung function decline. Patients with a history of asthma exhibit a 3- to 5-fold increased risk of fixed airflow obstruction, with airway hyperresponsiveness and recurrent exacerbations contributing to progressive irreversible damage. This asthma-COPD overlap phenotype underscores the importance of early and aggressive asthma management to mitigate long-term obstructive lung disease risk (Papi et al., 2020).

#### **2.1.4 .6 Infections (COPD-I)**

Early-life respiratory infections represent a significant risk factor for COPD development, with epidemiological studies demonstrating that severe childhood pneumonia is associated with persistent reductions in lung function that progress to airflow obstruction in adulthood. The proposed mechanisms include impaired alveolar development during critical growth periods and chronic airway remodeling secondary to infection-induced inflammation. Cohort studies estimate that individuals hospitalized for childhood respiratory infections have 2-3 times greater risk of developing COPD, independent of smoking status, suggesting these early insults may establish a vulnerable pulmonary substrate for subsequent environmental exposures (Allinson et al., 2016).

#### **2.1.4 .7 COPD of Unknown Cause- COPD-U**

Chronic Obstructive Pulmonary Disease of Unknown Cause (COPD-U) refers to a subset of patients who present with persistent airflow limitation and structural lung abnormalities characteristic of COPD yet lack any of the commonly recognized risk factors. These include smoking, biomass fuel exposure, occupational hazards, childhood lower respiratory tract infections, or hereditary disorders such as alpha-1 antitrypsin deficiency. Despite this, patients with COPD-U frequently experience progressive dyspnea, chronic cough, and exacerbations that mimic those seen in typical COPD cases. (GOLD, 2024) (Salvi & Barnes, 2009)

The 2024 Global Initiative for Chronic Obstructive Lung Disease (GOLD) report formally recognizes COPD-U as a distinct etiological category and emphasizes the need for focused research into its mechanisms, diagnostic biomarkers, and treatment modalities. Without clear diagnostic criteria and greater clinical awareness, individuals

with COPD-U may remain underdiagnosed and excluded from research and care pathways.(B. Celli et al., 2022).

A better understanding of COPD-U is crucial for accurately characterizing the global burden of COPD and advancing individualized care. Addressing this gap in knowledge can help tailor preventive and therapeutic strategies to populations that do not fit the traditional COPD risk profile (GOLD, 2024)

#### **2.1.4 .8 Age and sex**

Advanced age and female sex are independent risk factors for COPD development and progression. Epidemiological studies demonstrate that lung function decline accelerates after age 50, with women exhibiting greater susceptibility to tobacco smoke-induced airway damage compared to men at equivalent exposure levels. This sex disparity may reflect anatomical differences (smaller airways), hormonal influences, and variations in smoke metabolism, leading to more severe symptoms and faster FEV1 decline in aging women (Martinez, 2007).

#### **2.1.4 .9 Socioeconomic status**

Lower socioeconomic status is independently associated with increased COPD prevalence and severity, though the exact mechanisms remain multifactorial. Poverty correlates with a 2- to 3-fold higher risk of airflow obstruction, likely mediated by cumulative exposures to indoor/outdoor pollutants (e.g., biomass smoke, industrial emissions), higher rates of smoking, poor nutrition, and limited healthcare access. Crowding and recurrent respiratory infections in childhood may further compromise lung development, creating a lifelong vulnerability. While socioeconomic status itself is not causative, it serves as a proxy for intersecting environmental, behavioral, and structural determinants that collectively drive COPD disparities. (Prescott & Vestbo, 1999).

#### **2.1.4 .10 Chronic bronchitis**

Chronic bronchitis represents a significant independent risk factor for the development of chronic obstructive pulmonary disease (COPD), as it is associated with progressive airflow obstruction even in non-smokers. The pathophysiological progression involves three interrelated mechanisms: (1) chronic airway inflammation leading to irreversible airway remodeling, (2) mucus hypersecretion that promotes recurrent infections and neutrophil-mediated damage, and (3) an accelerated decline in forced expiratory volume in one second (FEV<sub>1</sub>), as documented in longitudinal studies. Patients with the chronic-bronchitis (bronchitic) phenotype of COPD have been shown to experience more frequent exacerbations, greater respiratory symptoms, and worse quality of life compared to non-bronchitic COPD subjects(Wu et al., 2020). These findings underscore the importance of early intervention in chronic bronchitis, as timely management may mitigate COPD progression in susceptible individuals(Kim & Criner, 2013).

#### **2.1.5 COPD Clinical presentation**

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory condition characterized by a persistent limitation in airflow and an enhanced chronic inflammatory response in the airways and lungs. The clinical presentation encompasses a range of respiratory and systemic symptoms that significantly impact patients' quality of life. Common features include chronic cough, sputum production, and exertional dyspnea, which tend to worsen over time. Systemic manifestations such as fatigue, weight loss, and muscle wasting may also occur, particularly in advanced stages. These symptoms vary in severity and frequency among individuals and are often influenced by the underlying phenotype and comorbidities (GOLD, 2024).

#### **2.1.5.1 Dyspnea**

Dyspnea is the most common and characteristic symptom of COPD — often starting as breathlessness during exertion and gradually progressing to breathlessness at rest as the disease advances and airflow limitation increases. The Medical Research Council (MRC) Dyspnea Scale is commonly used to assess the severity of dyspnea and guide clinical management decisions (Jones et al., 2009).

#### **2.1.5.2 Cough and Prolonged Sputum Production**

A persistent cough with sputum production is another common symptom of chronic obstructive pulmonary disease (COPD). Initially, the cough may be intermittent, but it often becomes more frequent and productive as the disease progresses. Chronic sputum production is particularly characteristic of the chronic bronchitis phenotype of COPD, defined clinically as a productive cough lasting for at least three months in each of two consecutive years in the absence of other causes (Wedzicha & Seemungal, 2007).

#### **2.1.5.3 Wheezing and Chest Tightness**

Patients with chronic obstructive pulmonary disease (COPD) frequently report chest tightness and wheezing, a high-pitched whistling sound produced during breathing, particularly during exacerbations. These symptoms are typically caused by airflow obstruction and bronchial hyperresponsiveness. Although less common than cough or dyspnea, chest tightness and wheezing may indicate disease progression and should not be overlooked (Miravittles & Ribera, 2017).

#### **2.1.5.4 Fatigue and Exercise Intolerance**

Fatigue is one of the most commonly reported systemic symptoms in chronic obstructive pulmonary disease (COPD) and often leads to reduced physical activity and exercise intolerance. This symptom is multifactorial in origin, driven by systemic inflammation, skeletal muscle deconditioning, and the increased energy expenditure

associated with the elevated work of breathing. Fatigue in COPD is strongly associated with impaired health-related quality of life (HRQoL) and significantly limits functional capacity and daily activities (Spruit et al., 2013).

#### **2.1.5.5 Acute Exacerbations of COPD**

Acute exacerbations of chronic obstructive pulmonary disease (COPD) are defined as episodes of worsening respiratory symptoms, such as increased dyspnea, sputum volume, or purulence that exceed normal day to day variation and often require changes in therapy, including hospitalization. These exacerbations are commonly triggered by respiratory infections and exposure to environmental pollutants. Frequent exacerbations are associated with a more rapid decline in lung function, increased healthcare utilization, reduced health related quality of life (HRQoL), and higher mortality risk (Wedzicha & Seemungal, 2007).

#### **2.1.5.6 Psychological Symptoms in COPD**

Patients with chronic obstructive pulmonary disease (COPD) have a higher prevalence of psychological disorders, particularly anxiety and depression, compared to the general population. These conditions are associated with increased healthcare utilization, reduced adherence to treatment, and a heightened perception of dyspnea. Addressing mental health is essential for holistic COPD management, as untreated psychological symptoms can negatively impact clinical outcomes and quality of life (Donovan et al., 2017).

#### **2.1.5.7 Sleep Disturbances in COPD**

Patients with chronic obstructive pulmonary disease (COPD) frequently experience sleep disturbances, including insomnia, nocturnal hypoxemia, and fragmented sleep architecture. These issues are often caused by nighttime symptoms such as coughing

and dyspnea, which contribute to poor sleep quality and increased daytime fatigue. Sleep impairment in COPD is also associated with reduced health related quality of life (HRQoL). Management strategies include optimizing bronchodilator therapy, addressing comorbid sleep disorders, and, in selected cases, administering nocturnal oxygen therapy (Romero-Corral et al., 2010).

#### **2.1.5.8 Impact of COPD on Quality of Life**

Chronic obstructive pulmonary disease (COPD) significantly impairs quality of life across physical, emotional, and social domains. The cumulative burden of symptoms such as dyspnea, fatigue, and sleep disturbances limits daily functioning and contributes to psychological distress. To evaluate this impact and guide patient centered care, tools such as the COPD Assessment Test (CAT) and the St George's Respiratory Questionnaire (SGRQ) are commonly used (Jones et al., 2009).

#### **2.1.6 Pathophysiological Mechanisms of COPD with Emphasis on Magnesium Homeostasis**

The pathophysiology of chronic obstructive pulmonary disease (COPD) is multifactorial, involving persistent airway inflammation, mucociliary dysfunction, and structural remodeling of the airways, all of which contribute to progressive airflow limitation (Rodrigues et al., 2021).

Magnesium ( $Mg^{2+}$ ), the second most abundant intracellular cation after potassium, plays a crucial role in numerous enzymatic and physiological processes. Its role in pulmonary physiology is increasingly recognized. Magnesium contributes to bronchodilation by modulating calcium ion influx at nerve terminals, thereby inhibiting acetylcholine release, stabilizing T lymphocytes, and preventing mast cell degranulation, all of which attenuate airway inflammation (Kshirsagar & Patil, 2021).

Experimental studies support this bronchodilatory effect. For example, Spivey et al. (1990) demonstrated that magnesium chloride induced dose-dependent relaxation of isolated rabbit tracheal smooth muscle, likely via calcium antagonism, thereby reducing bronchial tone (Spivey et al., 1990).

Magnesium deficiency may also enhance bronchial hyperresponsiveness. Dominguez et al. (1998) found a strong association between reduced intracellular magnesium levels and increased bronchial reactivity, suggesting a regulatory role for magnesium in airway smooth muscle tone (Dominguez et al., 1998).

Clinically, hypomagnesemia has been reported in patients with acute exacerbations of COPD. In a prospective study at El-Hussein University Hospital, Makled et al. (2019) found significantly lower levels of sodium, potassium, magnesium ( $1.85 \pm 0.17$  mEq/L), and chloride in COPD patients compared to healthy controls, possibly due to metabolic effects of infection and medication use, such as  $\beta_2$ -agonists, diuretics, and corticosteroids (Makled et. al, 2019).

Aziz et al. (2005) similarly observed hypomagnesemia in patients with COPD exacerbations, especially those receiving systemic corticosteroids, suggesting a drug-induced component (Aziz et al., 2005).

Magnesium homeostasis is tightly regulated by the kidneys. Van Laecke (2019) emphasized that renal magnesium wasting, commonly induced by loop and thiazide diuretics, or proton pump inhibitors (PPIs), and is a major cause of hypomagnesemia. Conversely, hypermagnesemia may occur in patients with renal insufficiency receiving magnesium-containing medications (Van Laecke, 2019).

Long-term PPI use is a recognized iatrogenic cause of hypomagnesemia. Famularo et al. (2013) reported that 10–15% of chronic PPI users developed clinically significant magnesium deficiency. Proposed mechanisms include impaired intestinal absorption via disruption of TRPM6/7 channels (Transient Receptor Potential Melastatin 6 and 7), which are magnesium-permeable ion channels essential for active magnesium absorption in the colon and distal convoluted tubule. TRPM6 is mainly expressed in epithelial cells of the intestine and kidney, while TRPM7 is widely expressed and possesses a kinase domain. Dysfunction of these channels leads to impaired absorption and paradoxical renal magnesium loss. Risk increases in the elderly and those using diuretics, and complications of severe hypomagnesemia include arrhythmias and refractory seizures (Famularo et al., 2013).

Magnesium deficiency is also associated with potassium wasting and can make hypokalemia refractory to correction. This occurs through enhanced distal potassium secretion mediated by increased activity of the renal outer medullary potassium (ROMK) channel. However, magnesium deficiency alone is not sufficient to cause hypokalemia; contributing factors like elevated aldosterone or increased sodium delivery are often required (Huang & Kuo, 2007).

### **2.1.7 Diagnosis and Assessment of COPD**

The diagnosis of chronic obstructive pulmonary disease (COPD) is based on a combination of clinical evaluation and objective measurements. A comprehensive clinical history is essential, with common symptoms including chronic cough, sputum production, and progressive dyspnea. To quantify symptom severity and its impact on daily life, validated instruments such as the COPD Assessment Test (CAT) and the Modified Medical Research Council (mMRC) dyspnea scale are widely used. These

tools help monitor disease progression and inform treatment decisions (Ertan Yazar et al., 2022).

Physical examination may reveal signs consistent with COPD, such as a barrel-shaped chest, reduced breath sounds, prolonged expiratory phase, and the use of accessory muscles during respiration. Although these findings are not pathognomonic, they provide supporting evidence when interpreted alongside history and spirometric data (Sarkar et al., 2019).

Spirometry remains the gold standard for confirming the diagnosis of COPD. It measures the volume and flow of air that can be inhaled and exhaled, providing an objective assessment of lung function. COPD is defined by a post-bronchodilator FEV<sub>1</sub>/FVC ratio of less than 0.70 (GOLD, 2024). This threshold helps distinguish COPD from other obstructive lung diseases and is integral to disease staging and management. For borderline values (FEV<sub>1</sub>/FVC between 0.60 and 0.80), GOLD recommends repeat testing and careful interpretation to avoid over-diagnosis in older adults and under-diagnosis in younger individuals (Agustí et al., 2023).

Bronchodilator reversibility testing may further aid in distinguishing COPD from asthma. While asthma often demonstrates marked reversibility, COPD is characterized by airflow limitation that is not fully reversible. However, partial reversibility may be present in some COPD patients, and test results should be interpreted within the clinical context (Jones et al., 2009)

Radiological investigations, particularly high-resolution computed tomography (HRCT) and chest X-rays, are valuable in assessing the extent of parenchymal damage and excluding alternative diagnoses. HRCT is particularly effective in identifying

emphysematous changes and bronchial wall thickening associated with COPD. These imaging modalities play a critical role in differentiating COPD from conditions such as bronchiectasis, asthma, and congestive heart failure (Washko, 2010).

In low- and middle-income countries (LMICs), the lack of access to spirometry poses significant diagnostic challenges. Clinicians often rely on symptom history and physical examination in such settings. Innovative strategies, including the deployment of portable spirometry devices and telemedicine platforms, are being explored to improve diagnostic accuracy and accessibility in resource-constrained environments (GOLD, 2024).

### **2.1.8 Comorbidities in COPD**

Chronic obstructive pulmonary disease (COPD) is frequently accompanied by multiple comorbidities that contribute significantly to disease burden, reduce quality of life, and complicate clinical management. These comorbidities are not simply coincidental but share overlapping pathophysiological mechanisms such as systemic inflammation, oxidative stress, and endothelial dysfunction (Trinkmann et al., 2019). Their presence influences not only the severity of respiratory symptoms but also increases the frequency of exacerbations and the risk of mortality, warranting a comprehensive, multidisciplinary approach to care (GOLD, 2023).

#### **2.1.8.1 Cardiovascular Comorbidities**

Among the most prevalent comorbidities in COPD are cardiovascular diseases (CVD), including hypertension, ischemic heart disease, heart failure, and arrhythmias. COPD patients have a significantly elevated risk of cardiovascular events, even after adjusting for smoking history and age. The inflammatory burden in COPD is thought to accelerate atherosclerosis and endothelial dysfunction, fostering the development of

CVD(Curkendall et al., 2006). Notably, the coexistence of COPD and CVD leads to increased hospital admissions, higher healthcare costs, and a worsened prognosis(Trinkmann et al., 2019).

#### **2.1.8.2 Metabolic Disorders**

Metabolic disturbances including metabolic syndrome and type 2 diabetes mellitus (T2DM) are prevalent in individuals with COPD, affecting approximately 21–62% of patients and contributing to heightened systemic inflammation. A meta-analysis found that up to 30% of COPD patients have concurrent T2DM, which is linked to poorer pulmonary outcomes, increased hospitalization rates, and elevated mortality (Catana et al., 2025). Chronic inflammation, marked by elevated TNF- $\alpha$ (Tumor Necrosis Factor alpha), IL-6 (Interleukin 6), and CRP (C-reactive protein), promotes insulin resistance, while hyperglycemia and oxidative stress further impair lung function and delay recovery (Rogliani et al., 2015). Moreover, the use of high-dose inhaled corticosteroids has been associated with a 34% increased risk of diabetes onset or progression in COPD patients (Catana et al., 2025).

#### **2.1.8.3 Osteoporosis and Fracture Risk**

Osteoporosis is another important comorbidity, especially in patients with advanced COPD or those undergoing prolonged corticosteroid therapy. Chronic inflammation, nutritional deficiencies, and reduced physical activity further increase the risk of low bone mineral density. Research has shown that up to one-third of COPD patients may have osteoporosis, predisposing them to vertebral and rib fractures that impair respiratory mechanics (Peng et al., 2023). Proactive screening and management of bone health are crucial to reducing morbidity in this patient population (Janson et al., 2021).

#### **2.1.8.4 Mental Health disorders**

Psychological comorbidities, particularly anxiety and depression, are highly prevalent in COPD, affecting up to 60% of patients in some cohorts. These conditions negatively impact self-care behaviors, medication adherence, and response to pulmonary rehabilitation (Martínez-Gestoso et al., 2022). They also contribute to increased dyspnea perception and healthcare utilization. Despite their impact, mental health disorders often go unrecognized in routine COPD care, underlining the need for routine psychological screening and timely intervention (Tselebis et al., 2016).

#### **2.1.8.5 Other Notable Comorbidities**

Chronic obstructive pulmonary disease (COPD) is frequently accompanied by a spectrum of comorbid conditions that further compromise patient outcomes. Pulmonary hypertension (PH), a frequent complication in advanced COPD, significantly worsens hypoxemia and reduces exercise tolerance—up to 39% of patients may be affected leading to poorer survival unless detected early (Barberà et al., 2003). Routine echocardiographic screening is recommended to facilitate early therapeutic intervention, notably in hypoxia-driven (Group 3) PH, where effective disease

management has been shown to improve functional outcomes and prognosis (Paudyal et al., 2025).

Gastroesophageal reflux disease (GERD) and obstructive sleep apnea (OSA) are also highly prevalent; GERD affects approximately 11–28% of COPD patients and is strongly associated with recurrent exacerbations, while OSA present in 10–30% of patients contributes to nocturnal hypoxia and daytime fatigue, particularly in those with overlap syndrome (Voulgaris et al., 2021). OSA affects up to 30% of COPD patients, though prevalence estimates in overlap syndrome vary widely from 3% to 66%, depending on disease severity and diagnostic methods (Kang et al., 2024). Patients with both COPD and OSA experience notably more severe nocturnal oxygen desaturation than individuals with either condition alone, leading to greater daytime fatigue, higher risk of pulmonary hypertension, and increased cardiovascular risk (Arvan & Sankari, 2025). Additionally, anemia occurs in 10–30% of COPD cases, further reducing oxygen-carrying capacity and exacerbating dyspnea and exercise limitation (Alisamir et al., 2022). Dyslipidemia a key component of metabolic syndrome has been observed in over a third of COPD patients ( $\approx 35\%$ ) and may contribute to chronic inflammation and cardiovascular risk; statin therapy has shown promise in reducing COPD exacerbations (Chen, 2023).

These multifaceted comorbidities illustrate the systemic reach of COPD and underscore the need for a holistic care model. Integrating routine echocardiography for PH, screening for sleep-disordered breathing, monitoring hematologic and metabolic parameters, and managing lipid abnormalities with statins and lifestyle interventions can attenuate symptom burden and reduce hospitalization rates. This aligns with the GOLD 2024 emphasis on comprehensive care that transcends pulmonary-limited

frameworks, promoting coordinated multidisciplinary treatment that addresses the full scope of COPD-related morbidities(GOLD, 2024).

#### **2.1.8.6 Clinical Implications**

The presence of multiple comorbidities in COPD necessitates an integrated, multidisciplinary approach to diagnosis and treatment. Rather than addressing COPD as a solely pulmonary condition, clinicians must adopt a systemic perspective, incorporating cardiometabolic, musculoskeletal, and psychological assessments into routine care. Early detection and management of comorbidities not only improve quality of life but also reduce exacerbation frequency and mortality rates(GOLD, 2024). Effective care coordination among pulmonologists, cardiologists, endocrinologists, and mental health professionals is critical for optimizing outcomes.

#### **2.1.9 Management of COPD**

The management of chronic obstructive pulmonary disease (COPD) involves a multidimensional approach, including pharmacological interventions such as bronchodilators, corticosteroids, and oxygen therapy, as well as non-pharmacological strategies such as pulmonary rehabilitation, smoking cessation, and patient education. The primary goals are to reduce symptom burden, decrease the frequency and severity of exacerbations, and improve health-related quality of life. According to the Global Initiative for Chronic Obstructive Lung Disease, individualized treatment based on symptom severity and exacerbation risk is essential for optimal outcomes (GOLD, 2024).

### 2.1.9.1 Pharmacological Management

Pharmacotherapy remains the mainstay of COPD treatment. The GOLD 2023 report introduced a simplified classification, ABE, to stratify treatment based on the patient's symptoms and exacerbation history(GOLD, 2023). In this system:

- Group A includes patients with few symptoms and low risk of exacerbation. These patients are recommended to start with a single long-acting bronchodilator either a long-acting beta-2 agonist (LABA) or a long-acting muscarinic antagonist (LAMA)(GOLD, 2023).
- Group B includes patients with more symptoms but still a low risk of exacerbations. Dual bronchodilation with LABA + LAMA may be initiated if monotherapy does not control symptoms(GOLD, 2023).
- Group E includes patients with frequent or severe exacerbations. Initial treatment with LABA + LAMA is recommended, with the addition of inhaled corticosteroids (ICS) forming triple therapy (LABA + LAMA + ICS) in cases where blood eosinophil counts are  $\geq 300$  cells/ $\mu$ L or there is a history of asthma (GOLD, 2023).

This stepped approach is supported by multiple clinical trials. For instance, the IMPACT trial demonstrated that triple therapy significantly reduces moderate to severe exacerbations compared to dual therapy (Lipson et al., 2018).

Long-acting bronchodilators have been shown to improve lung function and exercise capacity and reduce hospitalizations (Calverley et al., 2007)

Beyond bronchodilators and ICS, other pharmacological agents include:

- Roflumilast, a phosphodiesterase-4 inhibitor, beneficial in patients with chronic bronchitis and frequent exacerbations (Martinez et al., 2018).
- Long-term macrolide antibiotics such as azithromycin, which may reduce exacerbation frequency in selected patients due to their anti-inflammatory and antibacterial properties (Albert et al., 2011).

#### **2.1.9.2 Non-Pharmacological Management**

Non-pharmacological interventions complement pharmacological therapy and are essential in COPD management.

Smoking cessation is the most effective intervention for preventing disease progression and mortality. Clinical trials have shown that smoking cessation slows the decline in lung function and reduces mortality among COPD patients (Anthonisen et al., 2005). GOLD (2023) recommends combining behavioral counseling with pharmacologic aids such as varenicline or nicotine replacement therapy (GOLD, 2023).

Pulmonary rehabilitation is highly effective in improving dyspnea, exercise capacity, and quality of life. Comprehensive programs involve exercise training, nutritional counseling, education, and psychosocial support, with significant reductions in hospitalizations and exacerbations (Spruit et al., 2013) (McCarthy et al., 2015).

Preventive strategies such as vaccination against influenza and pneumococcal infections are essential in reducing the frequency of exacerbations (GOLD, 2024). In advanced stages, long-term oxygen therapy (LTOT) improves survival in patients with chronic hypoxemia (Casaburi et al., 2018). Nutritional support and the management of comorbidities, including anxiety and depression, are also vital to holistic care. Malnutrition is associated with poorer outcomes, and early nutritional intervention can

enhance respiratory muscle strength and immune response (Raizada, 2014). Meanwhile, untreated depression and anxiety can significantly affect treatment adherence and quality of life (Soler-Cataluña et al., 2005).

#### **2.1.10 Magnesium and Its Role in COPD**

Magnesium ( $Mg^{2+}$ ), a divalent cation integral to numerous physiological processes, has garnered attention as a potentially modifiable factor in the management of chronic obstructive pulmonary disease (COPD). Its role extends beyond simple electrolyte balance to include modulation of bronchial smooth muscle tone, regulation of inflammatory signaling, mitochondrial bioenergetics, and maintenance of skeletal muscle function (Petit et al., 2023). These pathways intersect directly with the core pathophysiological mechanisms of COPD, such as airflow limitation, systemic inflammation, and respiratory muscle dysfunction (Altura & Altura, 1996).

Recent literature suggests that individuals with COPD may be particularly susceptible to magnesium deficiency due to a combination of inadequate dietary intake, gastrointestinal and renal losses, and polypharmacy, including the use of diuretics and proton pump inhibitors (al-Ghamdi et al., 1994). Emerging data also suggest that lower serum magnesium levels may be linked with increased disease severity, frequent exacerbations, and poorer functional outcomes (Kshirsagar & Patil, 2021) (Makwana et al., 2022).

This section synthesizes current evidence surrounding magnesium's physiological functions, the prevalence and consequences of hypomagnesemia in COPD, and its therapeutic potential when administered acutely or chronically. Moreover, it explores the micronutrient's impact on health-related quality of life and outlines key considerations regarding dosing and safety.

### **2.1.10.1 Physiological Role of Magnesium**

Magnesium ( $Mg^{2+}$ ), the body's fourth most abundant cation, acts as a cofactor in over 600 enzymatic reactions essential for energy production, nucleic acid synthesis, and protein metabolism. Although the majority is stored in bones (~60%) and skeletal muscles (~20%), even the small serum fraction critically supports homeostasis (Altura & Altura, 1996).

Within the airways, magnesium antagonizes calcium influx via voltage-dependent and receptor-operated channels, curtailing acetylcholine release and facilitating smooth muscle relaxation thereby promoting bronchodilation (Petit et al., 2023). It also exerts anti-inflammatory effects by suppressing nuclear factor- $\kappa$ B activation and reducing pro-inflammatory cytokines like IL-6 and TNF- $\alpha$  (Yang et al., 2021). In skeletal muscles,  $Mg^{2+}$  is vital for ATP stabilization and efficient cross-bridge cycling, supporting diaphragmatic strength and endurance a key determinant of dyspnea in COPD (do Amaral, 2008). Additionally, it provides cardiovascular benefits by modulating myocardial excitability and vascular tone, potentially mitigating arrhythmias and pulmonary hypertension seen in COPD (Altura & Altura, 1996).

### **2.1.10.2 Hypomagnesaemia in COPD**

Hypomagnesemia is commonly defined as a serum magnesium level below 0.7 mmol/L (or <1.7 mg/dL). This electrolyte disturbance frequently occurs in patients with COPD, driven by multifactorial etiologies. First, malnutrition a common comorbidity in moderate-to-severe COPD due to hypermetabolic demands and reduced dietary intake significantly lowers total body magnesium stores. Second, chronic gastrointestinal losses, often due to diarrhea or malabsorption syndromes, as well as increased renal

excretion secondary to loop or thiazide diuretics, contribute further to magnesium depletion (al-Ghamdi et al., 1994).

In addition, polypharmacy is prevalent among COPD patients. Drugs such as proton pump inhibitors (PPIs), aminoglycosides, and certain bronchodilators may impair magnesium absorption or enhance renal wasting. Systemic inflammation, a hallmark of COPD, is also believed to redistribute magnesium into cells or exacerbate urinary losses through hormonal mechanisms. Thus, COPD patients are at increased risk for both absolute and relative magnesium deficiency, which may worsen their clinical status and functional capacity (DiNicolantonio et al., 2018).

#### **2.1.10.3 Therapeutic Potential of Magnesium in COPD**

Magnesium sulfate has garnered interest as a potential adjunctive therapy in the management of acute exacerbations of COPD due to its physiological role in bronchodilation and modulation of airway reactivity. Administered either intravenously or through nebulization, magnesium sulfate exerts a bronchodilatory effect by antagonizing calcium-mediated smooth muscle contraction, reducing bronchial hyperresponsiveness, and enhancing the efficacy of  $\beta_2$ -agonists (Shivanthan & Rajapakse, 2014). These properties are particularly beneficial in acute settings where patients may exhibit suboptimal response to conventional bronchodilators such as salbutamol or ipratropium bromide (Skorodin et al., 1995).

A number of randomized controlled trials and meta-analyses have explored the use of magnesium in acute respiratory conditions, with evidence showing improved pulmonary function parameters such as FEV<sub>1</sub> and peak expiratory flow rate (PEFR) in patients receiving magnesium sulfate in addition to standard care. While most robust data comes from asthma populations, similar pathophysiologic mechanisms support its

potential utility in COPD exacerbations (Solooki et al., 2014). However, the magnitude of benefit in COPD appears to be more modest and less consistent across studies (Edwards, 2012).

Despite these findings, the GOLD 2024 guidelines currently do not endorse the routine use of magnesium in the maintenance phase of COPD, citing limited evidence of long-term efficacy and a need for further targeted trials (GOLD, 2024). Although robust data on the direct link between serum magnesium and COPD severity are still limited, one cross-sectional study found that serum magnesium levels decreased progressively across GOLD stages, with more advanced disease (stage III/IV) associated with lower magnesium concentrations (Sreekumar & Velayudhan, 2021). Therefore, measuring magnesium status could meaningfully aid in stratifying patients and guiding individualized management strategies.

#### **2.1.10.4 Magnesium, Quality of Life, and Functional Status**

Beyond its well-known role in acute exacerbation management, magnesium may also influence the broader clinical trajectory of COPD, particularly in relation to quality of life and functional capacity, areas directly linked to disease severity. Hypomagnesemia is associated with systemic symptoms such as fatigue, muscle cramps, and impaired immune defense (Louie et al., 2013), which can contribute to reduced exercise tolerance and increased susceptibility to respiratory infections. In patients with moderate to severe COPD, these consequences can perpetuate the cycle of inactivity and deconditioning, often referred to as the "dyspnea inactivity deconditioning" loop. This phenomenon has been linked to skeletal muscle dysfunction and diminished contractile properties of the limb muscles, which are more pronounced in advanced COPD (Debigaré et al., 2003).

Magnesium deficiency may also exacerbate physical limitations and negatively affect patient-reported outcomes, as reflected in scores on instruments like the COPD Assessment Test (CAT) and the St. George's Respiratory Questionnaire (SGRQ). A randomized controlled trial by Zanforlini et al. (2022) assessed the effects of oral magnesium supplementation (300 mg/day magnesium citrate) in stable-phase COPD patients over a 6-month period. The study found that while magnesium supplementation was associated with reduced systemic inflammation, it did not result in significant improvements in quality-of-life scores or exercise capacity (Zanforlini et al., 2022). Similarly, research by Abou Youssef et al. (2022) demonstrated that stable COPD patients had significantly higher serum magnesium levels compared to those experiencing exacerbations, and a threshold of 1.91 mg/dL could predict exacerbations with high sensitivity and specificity. Given that poor nutritional status is frequently observed in patients with severe COPD, low magnesium levels may still serve as a marker of disease burden (Youssef et al., 2022). Although magnesium supplementation is not currently recommended as standard therapy in stable COPD, emerging evidence suggests it may have potential benefits in patients with documented hypomagnesemia or those at high risk of exacerbations, warranting further investigation (Zanforlini et al., 2022).

#### **2.1.10.5 Clinical Considerations and Research Gaps**

Despite increasing interest in magnesium's role in COPD pathophysiology and progression, several clinical and methodological challenges hinder its routine clinical application. A key limitation is the absence of standardized protocols for assessing magnesium status. Most studies measure total serum magnesium, which may not accurately represent intracellular or biologically active magnesium. Additionally,

laboratory reference ranges differ, and no universally accepted threshold defines magnesium deficiency in respiratory disease (Elin, 2010).

Compounding these challenges is the variability in study designs and outcome measures used in trials evaluating magnesium supplementation. Many of these studies focus on short-term outcomes during acute COPD exacerbations, leaving the chronic effects of magnesium levels—particularly their association with COPD severity—underexplored (Zanforlini et al., 2022). However, these findings have not yet been incorporated into current practice guidelines (GOLD, 2024).

Moreover, the bulk of existing literature originates from high income countries, which limits the generalizability of findings to low- and middle-income settings such as Kenya, where nutritional deficiencies and underdiagnosis of COPD are more prevalent.

Limited access to spirometry, biochemical testing, and structured rehabilitation programs in resource constrained settings further hampers the ability to identify patients who might benefit from magnesium assessment or supplementation. Additionally, the absence of guidance in national and international treatment protocols, including those by GOLD and the Kenya Ministry of Health, highlights significant evidence to practice gap.

To bridge this gap, well powered, context specific studies are needed to investigate magnesium's utility as both a biomarker and potential therapeutic adjunct in COPD. Future research should also assess how magnesium status interacts with common COPD comorbidities such as cardiovascular disease, diabetes, and malnutrition. Establishing locally relevant data could inform clinical decision making and help

integrate magnesium related interventions into broader COPD management strategies, particularly for populations at risk of severe disease.

#### **2.1.11 Conclusion**

This literature review highlights that COPD is a complex, multifactorial respiratory condition with diverse causes, presentations, and burdens. It underscores the significant role of environmental, genetic, and socioeconomic factors in COPD development and progression. Importantly, it identifies magnesium as a potentially influential micronutrient in COPD severity due to its role in muscle function and inflammation. However, existing research on magnesium's association with COPD remains limited, justifying further investigation, particularly in underrepresented populations, to better understand this relationship and inform clinical management.

## **CHAPTER THREE**

### **3.0 METHODOLOGY**

#### **3.1 Introduction**

This chapter outlines the methodological framework employed to investigate the association between the severity of Chronic Obstructive Pulmonary Disease (COPD) and serum magnesium levels among patients receiving care at Moi Teaching and Referral Hospital (MTRH). A cross-sectional study design was utilized to collect and analyze data from adult patients diagnosed with COPD.

The chapter provides a detailed description of the study setting, design, target population, sample size determination, eligibility criteria, sampling technique, and study procedures. It also outlines the variables of interest, and the strategies used for data collection, management, and analysis. Both descriptive and inferential statistical methods, including univariate, bivariate, and multivariate analyses, were employed to evaluate associations.

This methodology was designed to ensure scientific rigor and uphold ethical standards. It aimed to comprehensively capture clinical characteristics, spirometric parameters, and serum magnesium levels, and to explore how these variables relate to the severity of COPD.

#### **3.1 Study Setting**

The study was conducted at Moi Teaching and Referral Hospital (MTRH) in the chest clinic, the medical wards (both male and female) and the medical outpatient clinic (MOPC). MTRH is a National/International Referral Hospital offering outpatient, inpatient and specialized medical services with bed capacity of 1020 specialized beds, average of 1300 inpatients at any time and 1500 outpatient per day. The hospital is

located along Nandi Road in Eldoret, Uasin Gishu County and serves 23 counties in Kenya, parts of Eastern Uganda, South Sudan, Tanzania and Democratic Republic of Congo with a population of over 24 million people.

MTRH also serves as the Teaching Hospital for Moi University College of Health Sciences that trains both undergraduate Medical Students and several Master's in Medicine specialist programs with over 240 postgraduate students (Registrars) distributed across several programs.

The chest clinic is run on Thursdays every week with approximately 15 patients out of which 4 are COPD patients making a total of 16 COPD patients in a month. While on average the medical wards admit approximately 4 patients per month, on the other hand in the MOPC on average 4 patients are seen monthly.

### **3.2 Study Design**

A cross-sectional study of COPD patients presenting at the chest clinic, MOPC and the medical inpatient wards (male and female).

### **3.3 Study Population**

All adult patients aged 40 years and above documented with history of COPD.

### **3.4 Sample Size**

The primary objective of this study was to evaluate the relationship between the severity of Chronic Obstructive Pulmonary Disease (COPD) and serum magnesium levels among patients receiving care at Moi Teaching and Referral Hospital (MTRH). This research was informed by prior findings, including a study by Singh et al. (2012) conducted in India, which reported that 34% (17 of 50) of COPD patients exhibited hypomagnesemia, while the remaining 66% (33 of 50) had normal serum magnesium levels (normomagnesemia).

Data collection for the current study was conducted over a six-month period, spanning from January 2023 to June 2023. Throughout this timeframe, all study procedures were carried out according to the approved research protocol. These procedures included participant recruitment, administration of structured questionnaires, physical examinations, spirometry testing (both pre- and post-bronchodilator), and blood sampling for laboratory analysis.

At MTRH, approximately 24 COPD patients are attended to each month across various units, including the chest clinic, the medical outpatient clinic (MOPC), and the inpatient medical wards. Over the six-month data collection period, this translated to an estimated pool of 144 eligible patients. However, because the accessible population was smaller than the originally calculated sample size, a consecutive sampling approach was adopted. This method involved enrolling all eligible and consenting patients who presented during the study period until the required sample size was achieved.

To determine our sample size for the study, we used Fisher's formula (Fisher, 1998)

$$\text{Unlimited population: } n = \frac{z^2 \times \hat{p}(1-\hat{p})}{\epsilon^2}$$

$$\text{Finite population: } n' = \frac{n}{1 + \frac{z^2 \times \hat{p}(1-\hat{p})}{\epsilon^2 N}}$$

**n:** Sample size before finite population correction: This is the initial sample size calculated using Fisher's formula, assuming an infinite or sufficiently large population.

**Z:** Standard normal deviation: For a 95% confidence interval (CI), this corresponds to a z-value of 1.96 (the critical value from the standard normal distribution).

**P:** Proportion of the population estimated to have the characteristic of interest:

In your example, **P = 0.34**, which comes from the study by Singh et al., 2012, where 34% of COPD patients were found to have hypomagnesemia.

**1-p:** Proportion of the population without the characteristic: If **P = 0.34**, then **1 - P = 0.66** represents the proportion of COPD patients without hypomagnesemia.

**ε(epsilon):** is the margin of error set at 0.05. = Margin of error: This represents the maximum acceptable difference between the sample estimate and the true population parameter. You've correctly set this at **0.05**, or 5%.

**n':** Desired sample size after finite population correction: This is the adjusted sample size when accounting for the fact that you're working with a finite population, which is necessary when the population size is relatively small.

**N:** Population size: This is the total number of individuals in the population you're studying (for example, the total number of COPD patients at MTRH).

### Step 1: Unlimited population sample size using Fisher's Formula

$$\text{Unlimited population: } n = \frac{z^2 \times \hat{p}(1 - \hat{p})}{\epsilon^2}$$

$$n = \frac{(1.96^2 \times 0.34(1 - 0.34))}{0.05^2}$$

$$n = \frac{3.8416 \times 0.2244}{0.0025}$$

$$n = \frac{0.8623}{0.0025} = 344.92$$

$$n \approx 345$$

### Step 2: Finite population

$$\text{Finite population: } n' = \frac{n}{1 + \frac{z^2 \times \hat{p}(1-\hat{p})}{\varepsilon^2 N}}$$

$$n' = \frac{n}{1 + \frac{z^2 \times \hat{p}(1-\hat{p})}{\varepsilon^2 N}}$$

$$n' = \frac{345}{1 + \frac{3.8416 \times 0.2244}{0.0025 \times 144}}$$

$$n' = \frac{345}{3.395}$$

$$n' = 101.6$$

$$n \approx 102$$

The required minimum sample size was **102 subjects**.

### 3.5 Eligibility Criteria

#### 3.5.1 Inclusion Criteria

1. Patients diagnosed with COPD based on spirometry (FEV1/FVC|<0.7) and clinical assessment.
2. Adult patients  $\geq 40$  years with a diagnosis of COPD confirmed by spirometry according to GOLD criteria.
3. Patients who give informed consent to blood tests for magnesium levels and spirometry.

#### 3.5.2 Exclusion Criteria

1. Patients with other pulmonary diseases such as Asthma, Interstitial lung disease, Active Tuberculosis or lung cancer.

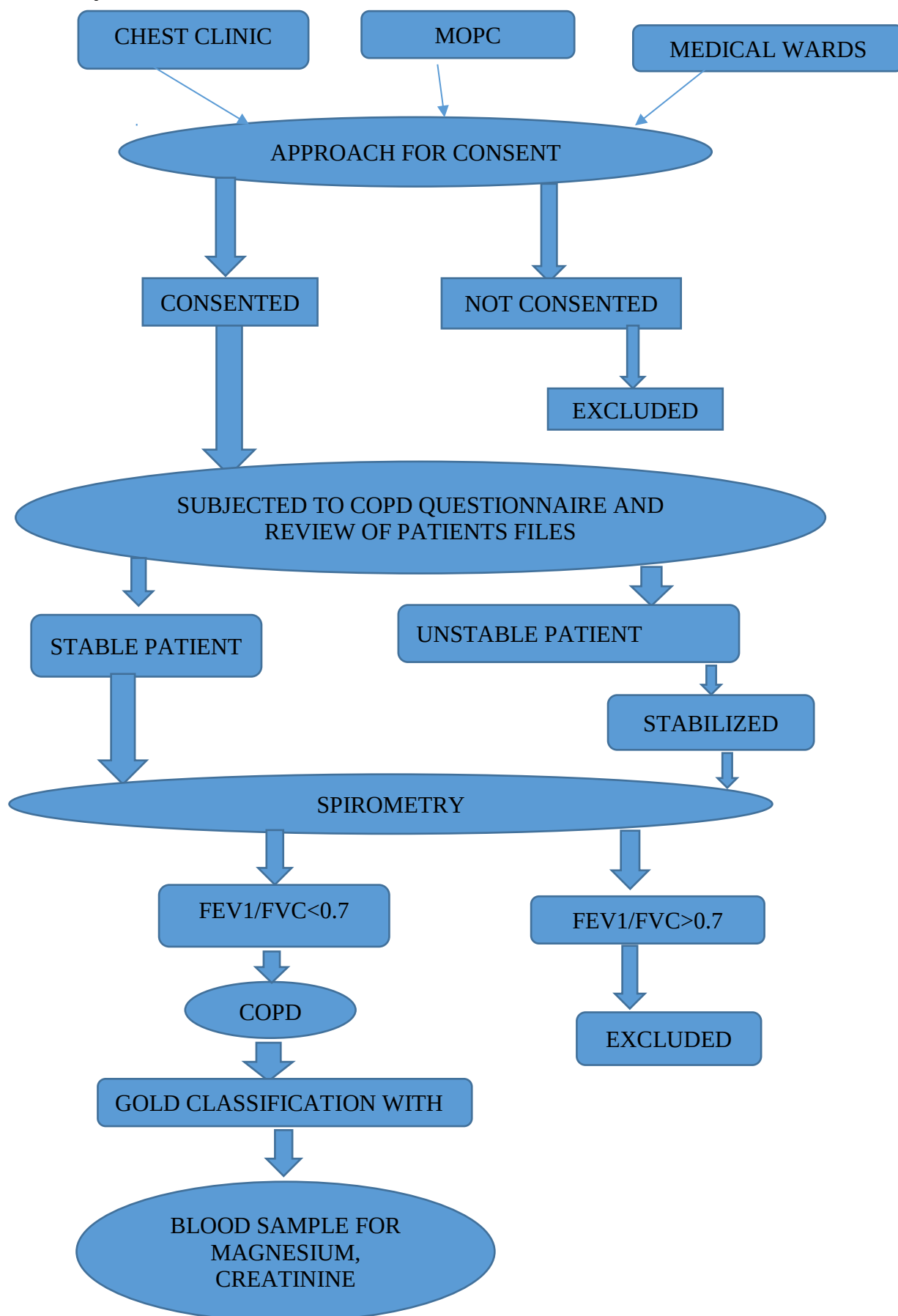
### **3.6 Sampling Technique**

For this study, we utilized consecutive sampling, a non-random sampling method in which all eligible participants who met the inclusion criteria and consented to participate were recruited consecutively throughout the data collection period. This approach involved enrolling COPD patients who presented to the chest clinic, the Medical Outpatient Clinic (MOPC), and the medical wards at Moi Teaching and Referral Hospital (MTRH) during the six-month study period.

Each patient who visited these departments and was identified as potentially eligible for the study was assessed to determine whether they met the inclusion criteria outlined in the study protocol, which were based on GOLD 2024 guidelines and previous studies on COPD patient selection (Singh et al., 2012). Once eligibility was confirmed, patients were approached and invited to participate in the study. Participants who agreed to join the study provided informed consent, ensuring that they were fully aware of the study's purpose, procedures, and any potential risks involved.

This systematic approach allowed us to capture a comprehensive sample of COPD patients attending these key hospital departments, ensuring that the study's findings were representative of this population during the specified time frame. The use of consecutive sampling, although not random, was appropriate given the target population and the goal of obtaining a manageable yet sufficient sample size for the study's analyses.

### 3.7 Study Procedure



### **3.8 Study Procedure**

Participants for this study were recruited by the principal investigator in collaboration with a trained research assistant. Recruitment took place at Moi Teaching and Referral Hospital (MTRH), specifically targeting individuals seen at the chest clinic, the medical outpatient clinic, and those admitted to the medical wards. Eligible patients were approached and informed about the study's objectives and procedures. Those who agreed to participate provided written informed consent before enrollment.

Once consent was obtained, participants were taken through a structured COPD questionnaire administered by the research team. The questionnaire collected detailed information including the participants' sociodemographic data, history of COPD-related symptoms and signs, risk factor exposure (such as smoking history or environmental pollutants), current medications, and history of comorbidities. Medical records were also reviewed to supplement and confirm self-reported information.

Following this, spirometry was performed to assess lung function and confirm the diagnosis and severity of COPD. The test was only conducted on participants who were clinically stable at the time of evaluation; for those experiencing acute exacerbations, spirometry was deferred until clinical stabilization was achieved. Spirometry was carried out by a trained respiratory technician at the MTRH Lung Function Laboratory using a pre-calibrated Contec SP10 spirometer. Both the principal investigator and the research assistants received comprehensive training in spirometry procedures and quality control from the Duke Lung Laboratory team as well as the MTRH Chest Clinic team. This dual training ensured standardized, accurate, and reliable performance of spirometry measurements throughout the study.

The procedure followed standard international guidelines. Initially, baseline (pre-bronchodilator) values were recorded. Participants were then administered 400 micrograms ( $\mu\text{g}$ ) of inhaled albuterol (salbutamol) via a metered-dose inhaler (MDI) with a spacer. After a waiting period of 15 minutes, post-bronchodilator spirometry was repeated. The main spirometric parameters recorded included the Forced Expiratory Volume in one second ( $\text{FEV}_1$ ), Forced Vital Capacity (FVC), and the  $\text{FEV}_1/\text{FVC}$  ratio. Both the post-bronchodilator  $\text{FEV}_1/\text{FVC}$  ratio and the  $\text{FEV}_1$  % predicted were used in determining the presence and severity of airflow obstruction.

Only patients with a post-bronchodilator  $\text{FEV}_1/\text{FVC}$  ratio of less than 0.70 were considered to have COPD and were included in the study. Patients who did not meet this diagnostic threshold were excluded. For those with confirmed COPD, disease severity was classified using the  $\text{FEV}_1$  % predicted, in line with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines:

- GOLD 1 (Mild):  $\text{FEV}_1 \geq 80\%$  predicted
- GOLD 2 (Moderate):  $\text{FEV}_1$  50–79% predicted
- GOLD 3 (Severe):  $\text{FEV}_1$  30–49% predicted
- GOLD 4 (Very Severe):  $\text{FEV}_1 < 30\%$  predicted

In addition to spirometry, a venous blood sample was collected from the antecubital vein of each participant. The blood was drawn into red-top vacutainer tubes and sent to the main laboratory for analysis of serum magnesium ( $\text{Mg}^{2+}$ ) and creatinine levels. All biochemical analyses were performed using the Cobas c 501 analyzer by Roche Diagnostics. The MTRH laboratory is certified as a Biosafety Level 2 (BSL-II) facility, ensuring adherence to internationally accepted standards for the handling of biological samples.

Serum magnesium levels were categorized based on standard laboratory reference ranges as follows:

- Normomagnesemia: Serum magnesium between 0.70 and 1.05 mmol/L (1.7–2.6 mg/dL)
- Hypomagnesemia: Serum magnesium less than 0.70 mmol/L (<1.7 mg/dL)
- Hypermagnesemia: Serum magnesium greater than 1.05 mmol/L (>2.6 mg/dL).

### **3.9 Data Variables**

#### **3.9.1 Independent Variables**

- Age
- Sex
- Body Mass Index (BMI)
- Smoking status (Ex-smoker, Current smoker and Non-smoker)
- Indoor pollution-Biomass smoke exposure
- Comorbidities (Diabetes Mellitus, Heart Failure, Chronic Kidney Disease).
- Medications (Diuretics, PPIs, Prednisolone, LABA/ICS).
- Serum magnesium levels: In three categories: Hypomagnesemia, Normomagnesemia and Hypermagnesemia.

#### **3.9.2 Dependent Variable**

- COPD severity (GOLD 1-mild, GOLD 2 –moderate, GOLD 3-severe and GOLD 4-very severe)

### **3.10 Data Collection and Management**

#### **3.10.1 Data Collection**

Data for this study was collected using interviewer-administered questionnaires, conducted by the principal investigator in collaboration with a trained research

assistant. The questionnaires were available in both English and Kiswahili to ensure participants could comfortably understand and respond, regardless of their language preference. The structured tool was designed to gather detailed information relevant to the study's objectives.

The questionnaire captured a wide range of variables, including patient sociodemographic details (such as age, sex, education level, and occupation), the duration since the diagnosis of COPD, history of tobacco use and exposure to biomass smoke (such as firewood or charcoal), and anthropometric measurements including weight, height, and body mass index (BMI). Additional information collected included the length of time the patient had been receiving COPD-related care at Moi Teaching and Referral Hospital (MTRH), signs and symptoms experienced, history of medications used for COPD management, as well as any known comorbid conditions such as hypertension, diabetes, or chronic kidney disease (CKD). Heart failure was assessed and recorded in accordance with the European Society of Cardiology (ESC) diagnostic guidelines to ensure standardized and clinically accurate identification of the condition.

A physical examination was conducted for each participant to assess their general health status. Patients were clinically evaluated and classified into two categories based on their condition at the time of assessment either as stable or experiencing an acute exacerbation. Acute exacerbation of COPD (AECOPD) was determined using the Anthonisen criteria, which define an exacerbation as the presence of at least two of the following: increased dyspnea, increased sputum volume, and increased sputum purulence. These criteria were incorporated into the questionnaire and clinical assessment to ensure standardized identification of exacerbations. Patients identified

with AECOPD were deferred from spirometry until clinical stabilization, in line with recommended practice. This classification helped determine the appropriate timing for performing spirometry, as those in exacerbation were tested only after stabilization.

In addition to primary data from interviews and physical assessments, secondary data was extracted from participants' medical records. This included previously recorded clinical information and laboratory test results. All relevant data, such as age, gender, weight, height, BMI, co-existing medical conditions, current medications, and education level, were reviewed and entered into a structured case report form.

Laboratory and diagnostic test results were also recorded for each participant. These included spirometry results, as well as serum levels of magnesium, and creatinine. Spirometry was carried out following standardized procedures to ensure consistency and reliability of results. Initially, pre-bronchodilator spirometry was performed to establish baseline lung function. Afterward, a bronchodilator was administered—specifically, 400 micrograms ( $\mu\text{g}$ ) of albuterol delivered via a metered-dose inhaler (MDI) with a spacer, or alternatively, 2.5 milligrams (mg) via nebulization. Fifteen minutes following bronchodilator administration, post-bronchodilator spirometry was conducted to assess the reversibility of airflow limitation. Special focus was placed on the forced expiratory volume in one second ( $\text{FEV}_1$ ), which is a key marker in the diagnosis and classification of COPD severity.

### **3.10.2 Data Management**

For the purpose of efficient and secure data collection and management, a structured questionnaire was designed and deployed using Research Electronic Data Capture (REDCap), a secure, web-based application specifically tailored for managing online databases and research surveys. REDCap allowed for real-time data entry during

participant interviews, minimizing the risk of data loss and transcription errors associated with manual entry. All participant responses were input directly into the REDCap system by the research team.

After data collection, the information was extracted from REDCap and initially organized using Microsoft Excel for preliminary review, tabulation, and sorting. This step allowed the research team to check for obvious inconsistencies, incomplete records, and formatting issues. Once the dataset was verified for completeness, it was exported into Statistical Package for the Social Sciences (SPSS) for detailed cleaning, validation, and comprehensive statistical analysis.

SPSS was used to conduct the main analytical procedures. This included univariate analysis to describe the distribution of individual variables, bivariate analysis to explore associations between two variables, and multivariate analysis to examine the relationships between multiple independent variables and the dependent variable in a statistically significant manner.

To further support analysis, certain statistical procedures were also carried out using STATA version 16, particularly when specialized commands or cross-verification of SPSS outputs were required. This multi-software approach allowed for robust and cross-validated data analysis.

To ensure data confidentiality and security, all identifying information was removed from the dataset before analysis. The REDCap database was encrypted and protected by a password, accessible only to the principal investigator. The physical copies of the questionnaires were securely stored in a locked cabinet and were only accessible by the

principal investigator. Electronic data was routinely backed up to an external hard drive stored in a separate, secure location to mitigate the risk of data loss.

Regular data quality checks were conducted throughout the study to assess consistency, completeness, and accuracy. Any inconsistencies identified were addressed promptly through verification with the original records. All data stored in REDCap, including backups and duplicates, will be permanently deleted seven years after publication of the study results, in accordance with institutional data retention policies.

### **3.10.3 Data Analysis**

The data collected for this study were initially entered into Research Electronic Data Capture (REDCap), a secure web-based application used for managing online surveys and databases. All patient data, including sociodemographic details, clinical measures, and laboratory results, were systematically entered and stored in REDCap. The collected data was then exported to Microsoft Excel for preliminary organization, categorization, and cleaning, ensuring accuracy and completeness.

Following this, the cleaned data were imported into Statistical Package for the Social Sciences (SPSS) for further validation and statistical analysis. The statistical analysis included univariate, bivariate, and multivariate techniques to assess the relationships and associations between the dependent and independent variables, ensuring all findings were statistically significant and interpretable.

After the analysis in SPSS, the results were cross-validated and additional analyses were conducted using STATA version 16 to provide a comprehensive understanding of the data, particularly focusing on multivariate modeling.

### **3.10.3.1 Univariate Analysis**

In this study, univariate analysis was performed as the initial step in understanding and summarizing the basic features of the data collected. This form of analysis involves examining each variable individually in order to describe and present its distribution, central tendency, and overall pattern within the sample population. Univariate methods are essential for gaining foundational insight into the characteristics of the dataset before exploring relationships between variables through more complex analytical approaches.

For categorical variables, such as sex, smoking status, presence of comorbidities, and other relevant clinical indicators, the data were summarized using frequencies (the number of times a value appears) and percentages to provide a clear picture of how common each category was within the study population. This approach allowed for the identification of dominant categories and patterns among the participants, which helped to frame the analysis of associated risk factors.

Additionally, some categorical variables were derived from continuous variables by applying pre-defined cutoff points grounded in clinical evidence and literature. For example, COPD severity was categorized based on forced expiratory volume in one second (FEV<sub>1</sub>) predicted percentage, and age was grouped into clinically meaningful bands to facilitate comparison across age strata.

For continuous variables, such as age, Body Mass Index (BMI), and mean serum magnesium level, measures of central tendency and dispersion were employed. Specifically, the mean and standard deviation (SD) were used to summarize the data when the variable followed a normal distribution (also known as a Gaussian

distribution). These statistics provided an estimate of the average value of the variable and how much variability existed around the mean.

However, in cases where the distribution of continuous variables was skewed—meaning the data did not conform to the assumptions of normality—alternative measures were applied. These included the median, which represents the central value of the dataset, and the interquartile range (IQR), which captures the spread of the middle 50% of values. This approach ensured that the summary statistics were robust and accurately reflected the data distribution, regardless of the shape of the distribution.

- **Objective 1:** One of the key objectives of this study was to stratify patients with Chronic Obstructive Pulmonary Disease (COPD) based on the severity of their condition. To achieve this, the study utilized the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, which categorizes COPD severity into four distinct groups: mild (GOLD 1), moderate (GOLD 2), severe (GOLD 3), and very severe (GOLD 4). The classification is based on post-bronchodilator  $FEV_1$  as a percentage of the predicted value. For each of these categories, the frequency and proportion of patients were calculated to provide a detailed understanding of how disease severity was distributed within the study population.
- **Objective 2:** Another important objective was to assess the distribution of serum magnesium levels among COPD patients. To facilitate this, serum magnesium concentrations were classified into three clinically relevant categories: hypomagnesemia (magnesium levels below 0.70 mmol/L), normomagnesemia (magnesium levels between 0.70–1.05 mmol/L), and hypermagnesemia (levels above 1.05 mmol/L). These thresholds were derived

from internationally accepted laboratory reference values. The study reported the number and percentage of patients falling into each category, allowing for an evaluation of how common magnesium imbalances were in the study sample.

This univariate analysis served as a foundation for the subsequent bivariate and multivariate analyses by providing essential descriptive statistics that helped characterize the study population and guided the selection of appropriate statistical methods for further investigation.

#### **3.10.3.2 Bivariate Analysis**

Bivariate analysis was employed as the second phase of statistical exploration to investigate the association between pairs of variables—specifically between the outcome variable (serum magnesium levels) and key independent variables such as demographic, clinical, and anthropometric characteristics. This level of analysis is essential for identifying potential relationships between variables and informing further, more complex multivariate models.

To assess the association between two categorical variables, such as gender and serum magnesium levels, the Pearson's Chi-square test was utilized. This non-parametric test is widely used to determine whether there is a statistically significant relationship between two categorical variables by comparing observed frequencies with expected frequencies under the assumption of independence. It provided insight into whether the distribution of serum magnesium levels varied significantly between male and female participants.

For associations between a categorical variable and a continuous variable, such as serum magnesium levels and age or Body Mass Index (BMI), different statistical tests were selected based on the distribution of the continuous variable:

- If the continuous variable was found to be normally distributed (i.e., following a Gaussian distribution), a two-sample independent t-test was applied to compare the means across the two categories. This test helped determine whether there were statistically significant differences in mean age or BMI between patients with different serum magnesium classifications (e.g., hypomagnesemia vs. normomagnesemia).
- However, in instances where the continuous variable did not meet normality assumptions, the Wilcoxon rank-sum test (also known as the Mann-Whitney U test) was employed as a non-parametric alternative to the t-test. This test compares the distributions of the continuous variable across two groups without assuming a normal distribution, providing a more robust method when data are skewed or have outliers.

When the categorical independent variable had more than two levels, such as COPD severity, which includes four categories (GOLD 1 to GOLD 4), the Kruskal-Wallis test was used. This test is a non-parametric equivalent of the one-way ANOVA and is suitable for comparing medians across more than two independent groups. It allowed for the assessment of whether serum magnesium levels significantly differed across the various stages of COPD severity.

Before conducting these tests, normality assumptions of continuous variables were evaluated using the Shapiro-Wilk and Shapiro-Francia tests. These statistical tests

assess whether the data are normally distributed, guiding the selection of appropriate parametric or non-parametric statistical techniques.

**Objective 3:** Association between COPD Severity and Serum Magnesium Levels

The third objective of the study was to examine the association between the severity of Chronic Obstructive Pulmonary Disease (COPD) and serum magnesium levels among patients attending Moi Teaching and Referral Hospital (MTRH). To analyze this, a Chi-square test of independence was used to assess whether there was a significant relationship between the level of COPD severity (categorized as GOLD 1 through GOLD 4) and the serum magnesium classification (hypomagnesemia, normomagnesemia, hypermagnesemia). This analysis provided critical insight into whether the degree of airway obstruction as measured by spirometry was associated with magnesium status in this patient population.

This bivariate analysis formed the basis for more comprehensive multivariate modeling, allowing for further investigation into whether any observed associations remained significant after adjusting for potential confounding factors.

**3.10.3.3 Multivariate Analysis**

In the final stage of data analysis, multivariate logistic regression was employed to evaluate the association between serum magnesium levels (the primary response variable) and a broad range of independent variables. This advanced statistical approach allowed for the simultaneous adjustment of multiple covariates, thereby controlling for potential confounding factors and providing a more accurate assessment of the independent effects of each variable on serum magnesium status among patients with Chronic Obstructive Pulmonary Disease (COPD).

The regression model included a combination of clinical, non-clinical, comorbid, and pharmacological variables that were both statistically significant in the univariate and bivariate analyses or were considered clinically relevant based on existing literature and expert judgment. Among the key clinical variables included were age, gender, Body Mass Index (BMI), and COPD severity with severity stratified according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, based on post-bronchodilator FEV<sub>1</sub> predicted values. These factors are well-documented influencers of disease progression and may play a role in electrolyte imbalances, including disturbances in magnesium levels.

In addition to clinical variables, non-clinical risk factors were also incorporated into the model. This included cigarette smoking status categorized as current smokers, former smokers, and never smokers and exposure to indoor air pollution, particularly from the use of biomass fuels. Both smoking and indoor pollution are known contributors to chronic airway inflammation and systemic oxidative stress, conditions which may have downstream effects on serum electrolyte profiles.

Crucially, the model also examined the impact of pharmacological therapies that are commonly prescribed in COPD management, and which may independently influence magnesium homeostasis. These medications included:

- Diuretics (loop and thiazide classes), which are well known for causing renal magnesium wasting.
- Inhaled corticosteroids (ICS) and long-acting beta-agonists (LABA), often used in combination as maintenance inhalers for COPD symptom control.
- Systemic corticosteroids, particularly prednisolone, which can affect renal electrolyte handling when used chronically.

- Proton Pump Inhibitors (PPIs), which have been associated with impaired magnesium absorption, especially during long-term therapy for gastroesophageal reflux and peptic ulcer disease—conditions frequently coexisting in COPD patients.

The regression model further controlled for common comorbid conditions that could confound the relationship between COPD and serum magnesium levels. These included:

- Chronic Kidney Disease (CKD), which disrupts normal magnesium clearance due to impaired renal function.
- Diabetes Mellitus (DM), where osmotic diuresis and metabolic dysregulation may lead to altered serum magnesium levels.
- Heart Failure, a frequent comorbidity in COPD patients, in which both the disease process and its pharmacologic treatment can lead to electrolyte imbalances, including hypomagnesemia.

To measure the strength and direction of these associations, both unadjusted (crude) and adjusted odds ratios (ORs) were computed, each with 95% confidence intervals (CIs). The adjusted ORs provided a clearer and more isolated view of each variable's contribution to serum magnesium levels after accounting for the influence of other covariates in the model. This allowed for a detailed and robust understanding of which factors were significantly and independently associated with hypomagnesemia, normomagnesemia, or hypermagnesemia in the COPD population.

The dataset underpinning this analysis was securely collected and managed using REDCap (Research Electronic Data Capture), a HIPAA-compliant electronic tool that

facilitated real-time and structured data input. Once data collection was complete, it underwent thorough cleaning and validation, initially organized using Microsoft Excel. The refined dataset was subsequently analyzed using a combination of SPSS and STATA version 16, enabling sophisticated statistical modeling and verification across multiple platforms. This multilayered data processing approach helped ensure integrity, reproducibility, and internal consistency of the analytical results.

In conclusion, this multivariate logistic regression analysis provided a nuanced and evidence-based assessment of the various clinical, environmental, pharmacologic, and comorbid factors associated with serum magnesium levels in COPD patients at Moi Teaching and Referral Hospital (MTRH). The findings from this comprehensive approach can offer valuable insights for targeted interventions, risk stratification, and improved management strategies for this patient population.

### **3.11 Ethical Considerations**

Prior to initiating the study, all necessary ethical and institutional approvals were obtained to ensure compliance with national and institutional research guidelines. Formal authorization was secured from Moi Teaching and Referral Hospital (MTRH) and the Moi University Institutional Research and Ethics Committee (IREC) under approval number IREC/187/2022, with approval FAN: 0004197. Additional clearance was granted by the National Commission for Science, Technology and Innovation (NACOSTI), through license number NACOSTI/P/22/19183, as well as from the management of MTRH. These approvals were obtained to confirm that the study met established ethical standards for research involving human subjects.

All individuals approached to participate in the study were first fully informed about the nature, purpose, and procedures of the research. The study team ensured that

potential participants received a thorough explanation using clear, non-technical language to promote understanding. Participation was entirely voluntary, and no form of coercion, undue influence, or pressure was applied. Informed consent was obtained in writing from each participant prior to enrollment. They were assured that they retained the right to withdraw from the study at any stage without facing any form of discrimination or negative consequence in their ongoing or future medical care.

The research instruments and data collection processes were carefully designed to align with the study's objectives while ensuring the protection of participants' privacy and dignity. All responses and medical information gathered were treated with strict confidentiality. Identifiable data were de-identified before entry into electronic databases to maintain anonymity. Data were securely stored in locked filing cabinets for physical documents, and password-protected digital databases for electronic records. All consent and interviews were conducted in private consultation rooms to maintain discretion and ensure participant comfort.

Importantly, no monetary compensation or financial incentives were provided to encourage participation, thereby avoiding any risk of coercion or bias. The ethical framework applied throughout the study adhered to international standards for the protection of human research participants and demonstrated a commitment to integrity, transparency, and respect for human rights.

## **CHAPTER FOUR**

### **4.0 RESULTS**

#### **4.1 Introduction**

This chapter presents the findings of the study on the severity of Chronic Obstructive Pulmonary Disease (COPD) and its association with serum magnesium levels at Moi Teaching and Referral Hospital (MTRH). The results are structured according to the study objectives and include a visual recruitment schema summarizing participant flow. Descriptive statistics such as means, percentages, and interquartile ranges summarize key characteristics of the participants, including age, gender, smoking history, BMI, comorbidities, and medication use. Bivariate analyses explore associations between serum magnesium levels and clinical or demographic variables using chi-square and other appropriate statistical tests based on data distribution. Finally, multivariate logistic regression identifies independent predictors of COPD severity while adjusting for potential confounders such as medication use and comorbidities.

These results form the foundation for the discussion and recommendations in the next chapter.

## 4.2 Recruitment schema

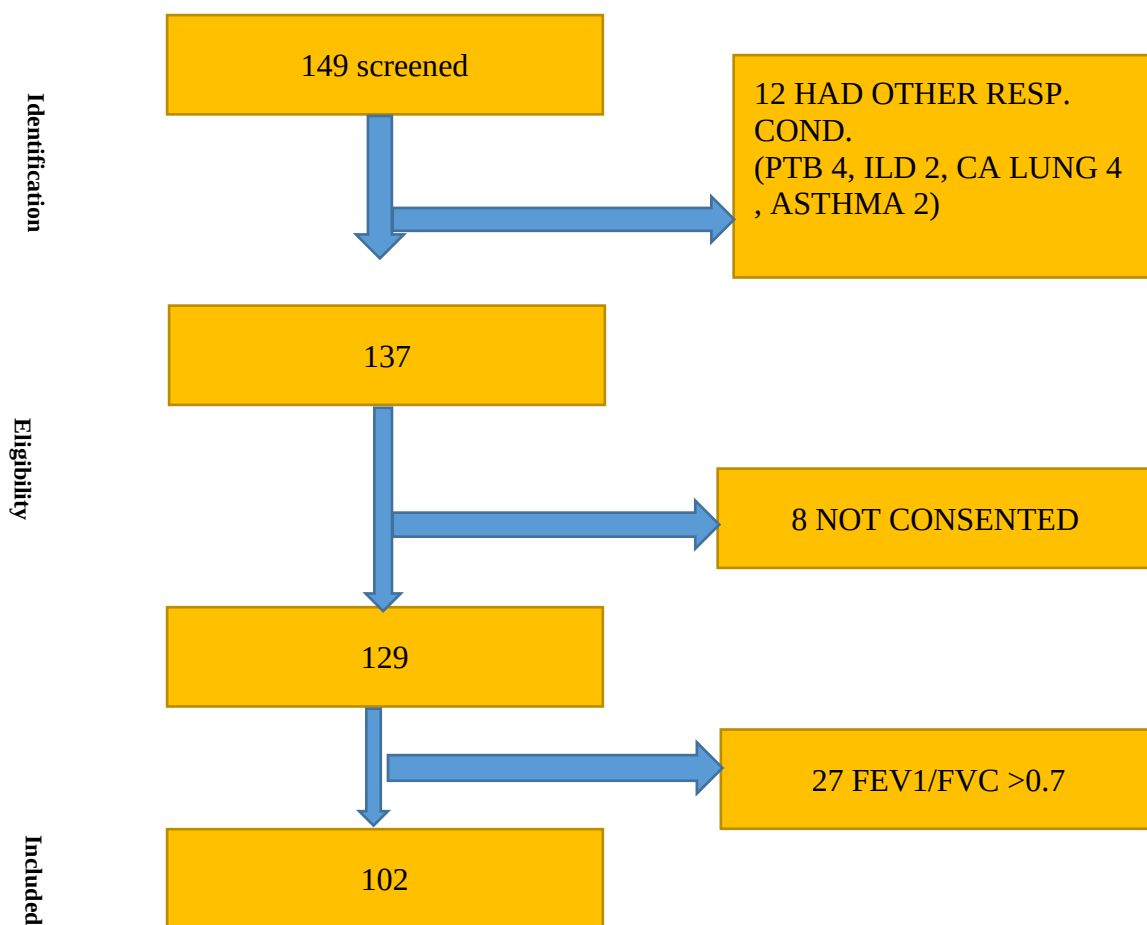


**Figure 4.1** Recruitment schema

### **4. 3 Sociodemographic characteristics**

The mean age of participants was 71.3 years (SD = 14.8), with ages ranging from 40 to 94 years. The majority were female (60.78%), while males accounted for 39.22% of the study population. Most participants were recruited from the chest clinic (64.71%), with fewer from the medical ward (22.55%) and medical outpatient clinic (12.75%), reflecting the distribution of COPD patient care settings during the study period.

Over half of the participants (52.9%) had no formal education. About one-third (33.3%) had completed primary education, while 10.8% had attained secondary education. Only a small proportion (2.9%) had pursued post-secondary (tertiary) education. The majority of participants (72.5%) were unemployed. A smaller proportion (22.5%) were self-employed, while only 4.9% were in formal employment. The average duration of COPD among participants was 8.75 years (SD = 6.07), with durations ranging from 1 to 40 years.

A majority of participants (58.86%) were non-smokers, while 30.39% were former smokers. Current smokers accounted for 12.75% of the population. The mean number of cigarette pack-years among participants was 1.44 (SD = 2.72), with values ranging from 0 to 13. The average duration of cigarette exposure was 5.73 years (SD = 9.9), with a range of 0 to 50 years. A vast majority of participants (99.0%) reported a history of exposure to biomass or firewood smoke, while only 1.0% had no such exposure.

**Table 4.1: Sociodemographic characteristics**

|                                                    |            | <b>Total<br/>N=102</b> |
|----------------------------------------------------|------------|------------------------|
| <hr/>                                              |            |                        |
| Age                                                |            |                        |
| Mean (SD)                                          |            | 71.3 (14.8)            |
| Range                                              |            | 40 – 94                |
| <hr/>                                              |            |                        |
| Gender                                             |            |                        |
| Female                                             |            | 62 (60.78%)            |
| Male                                               |            | 40 (39.22%)            |
| <hr/>                                              |            |                        |
| BMI                                                |            |                        |
| Underweight                                        | 15(14.71%) |                        |
| Normal                                             | 41(40.2%)  |                        |
| Overweight                                         | 24(23.53%) |                        |
| Obese                                              | 22(21.57%) |                        |
| <hr/>                                              |            |                        |
| Point of recruitment                               |            |                        |
| Medical Ward                                       |            | 23 (22.55%)            |
| Chest Clinic                                       |            | 66 (64.71%)            |
| MOPC                                               |            | 13 (12.75%)            |
| <hr/>                                              |            |                        |
| Educational level                                  |            |                        |
| Primary                                            |            | 34 (33.3%)             |
| Secondary                                          |            | 11 (10.8%)             |
| Tertiary                                           |            | 3 (2.9%)               |
| None                                               |            | 54 (52.9%)             |
| <hr/>                                              |            |                        |
| Occupation                                         |            |                        |
| Employed                                           |            | 5 (4.9%)               |
| Self employed                                      |            | 23 (22.5%)             |
| Unemployed                                         |            | 74 (72.5%)             |
| <hr/>                                              |            |                        |
| Duration of COPD                                   |            |                        |
| Mean (SD)                                          |            | 8.75 (6.07)            |
| Range                                              |            | 1 – 40                 |
| <hr/>                                              |            |                        |
| History of Smoking                                 |            |                        |
| Current smoker                                     |            | 13 (12.75%)            |
| Ex-smoker                                          |            | 31 (30.39%)            |
| Non-smoker                                         |            | 58 (58.86%)            |
| <hr/>                                              |            |                        |
| Cigarette pack years                               |            |                        |
| Mean (SD)                                          |            | 1.44 (2.72)            |
| Range                                              |            | 0 – 13                 |
| <hr/>                                              |            |                        |
| History of use of biomass/ firewood smoke exposure |            |                        |
| No                                                 |            | 1 (1.0%)               |
| Yes                                                |            | 101 (99.0%)            |

Source: Data Analysis, 2025

### 4.3.1 County of origin

Patients were drawn from a total of 15 counties. The majority were from Uasin Gishu County (46.1%), followed by Nandi (17.6%), Elgeyo Marakwet (10.8%), and Trans Nzoia (6.9%). Smaller proportions came from Kakamega (3.9%), Siaya (2.9%), and a group of counties each contributing 2.0% or less, including Kisii, Bomet, Nakuru, Turkana, Kisumu, Kericho, Baringo, West Pokot, and a group of counties each contributing 2.0% or less, including Kisii, Bomet, Nakuru, Turkana, Kisumu, Kericho, Baringo, and West Pokot.

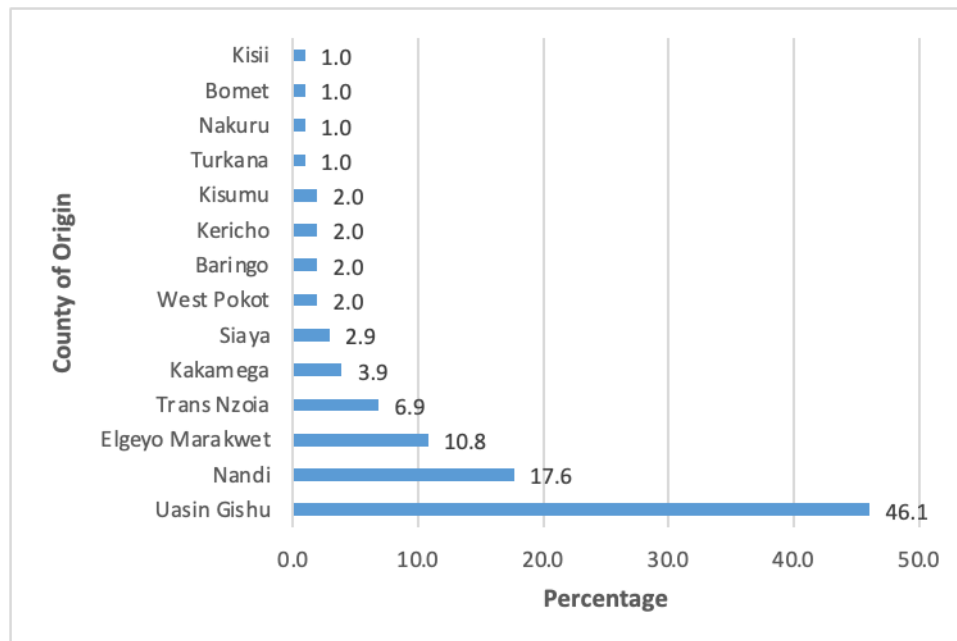


**Figure 4.2: County of origin**

### 4.4 COPD Clinical Characteristics

At the time of recruitment, the majority of participants (77.45%) were in a stable clinical state, while 22.55% were experiencing an exacerbation of COPD. The most commonly reported symptoms were dyspnea (86.3%) and cough (78.4%). Additional symptoms included sputum purulence (60.8%) and wheezing (28.4%).

Among those with exacerbation, the most frequently reported worsening symptoms were increased cough (82.4%), increased dyspnea (80.4%), and increased sputum production (33.3%). A smaller proportion reported increased sputum purulence (5.9%) and increased wheezing (11.8%).

On clinical examination, crepitations were observed in 39.2% of participants, while wheezing was noted in 28.4%. A small number had reduced air entry (2.0%). Additionally, tachycardia was present in 22.5%, and tachypnea in 13.7% of participants.

Heart failure (44.12%) and hypertension (39.22%) were the most prevalent comorbidities, underscoring the robust cardiovascular-COPD connection. Furthermore, 11.76% of the participants had chronic kidney disease (CKD), and 12.7% had atrial fibrillation.

**Table 4.2: COPD Clinical characteristics**

| <b>Characteristics</b>            | <b>N (%)</b> |
|-----------------------------------|--------------|
| <b>Patient status</b>             |              |
| Stable                            | 79 (77.45%)  |
| Unstable (in exacerbation)        | 23 (22.55%)  |
| <b>COPD symptoms</b>              |              |
| Cough                             | 80 (78.4%)   |
| Dyspnea                           | 88 (86.3%)   |
| Sputum purulence                  | 62 (60.8%)   |
| Wheeze                            | 29 (28.4%)   |
| <b>COPD exacerbation symptoms</b> |              |
| Increased Cough                   | 84 (82.4%)   |
| Increased dyspnea                 | 82 (80.4%)   |
| Increased Sputum production       | 34 (33.3%)   |
| Increased sputum purulence        | 6 (5.9%)     |
| Increased wheezing                | 12 (11.8%)   |
| <b>COPD Exam Findings</b>         |              |
| Crepitations                      | 40 (39.2%)   |
| Wheeze                            | 29 (28.4%)   |
| Reduced air entry                 | 2 (2.0%)     |
| Tachypnea                         | 14 (13.7%)   |
| Tachycardia                       | 23 (22.5%)   |

#### 4.4.1 Comorbidities

The most common comorbidities among participants were heart failure (44.1%) and hypertension (39.2%), highlighting the significant overlap between cardiovascular conditions and COPD. Other comorbid conditions included chronic kidney disease (11.8%), atrial fibrillation (11.8%), and diabetes mellitus (6.9%). Less frequent comorbidities included venous thromboembolism (2.9%), right ventricular dysfunction (2.0%), post-tuberculosis lung fibrosis (2.0%), hypothyroidism (1.0%), gout (1.0%), and rheumatoid arthritis (1.0%).

Among participants with heart failure, right heart failure (RHF) was observed in 38.2%, while heart failure with reduced ejection fraction (HFrEF) was present in 5.9%

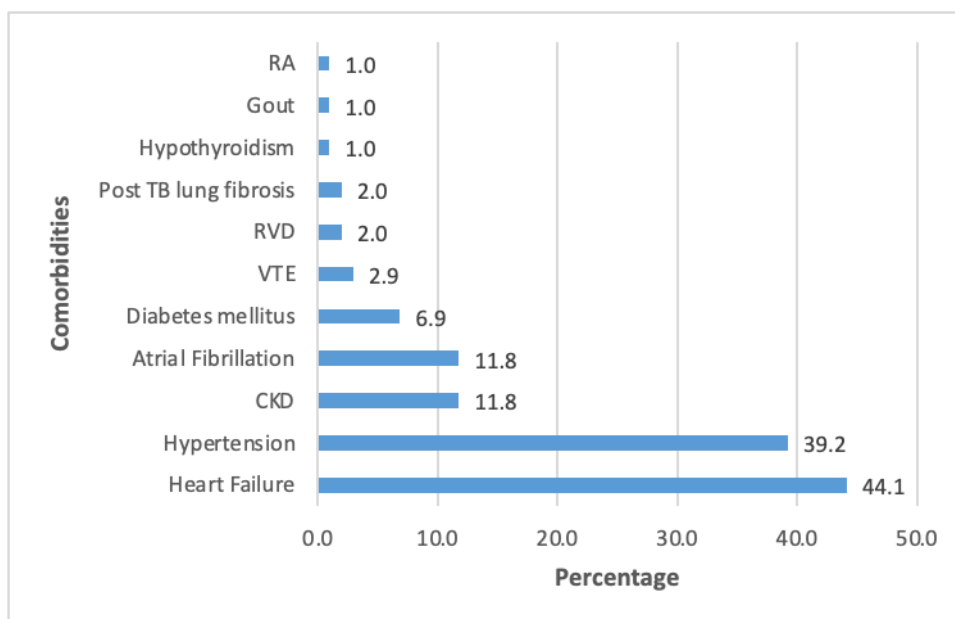


**Figure 4.3: Comorbidities**

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Heart Failure Phenotypes

|       |             |
|-------|-------------|
| RHF   | 39 (38.24%) |
| HFrEF | 6 (5.88%)   |

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#### 4.5 Medications

##### 4.5.1 COPD Medications

The majority of participants (72.5%) were using a combination of long-acting beta-agonists and inhaled corticosteroids (LABA/ICS). A smaller proportion were prescribed leukotriene antagonist (10.8%), systemic corticosteroids (8.8%) and short-acting beta-agonists (SABA, 3.9%). Notably, none of the participants were on Short – acting muscarinic antagonist or long-acting muscarinic antagonists (LAMA).

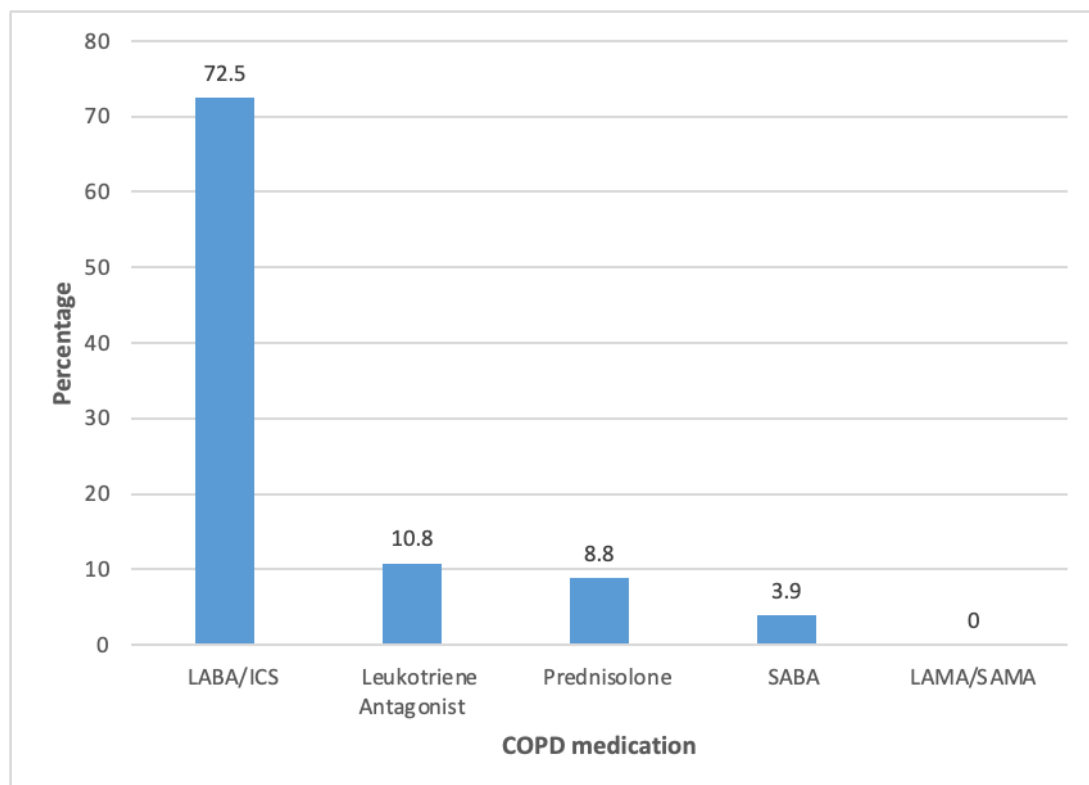


**Figure 4.4: COPD medication**

#### 4.5.2 Other Medications

The prescribed medications among the study participants revealed a diverse pharmacological profile. Diuretics were the most frequently prescribed, with 52.0% of participants receiving them, including furosemide for 44.12%. Calcium channel blockers (CCBs) were prescribed to 24.5% of patients, followed by proton pump inhibitors (PPIs) at 17.6%. Anticoagulants were used by 14.7%, and angiotensin receptor blockers (ARBs) by 8.8%. Beta-blockers (BBs) were prescribed to 9.8%, oral hypoglycemic agents (OHAs) to 6.9%, metformin to 5.9% and enalapril (an ACE inhibitor) to 4.9%. Gabapentin and digoxin were each prescribed to 2.9% of participants, while SGLT2 inhibitors, atorvastatin, HAART, and celecoxib were prescribed to 2.0%. Insulin, colchicine, levothyroxine, JASA, and Neurobione were each prescribed to 1.0% of participants.

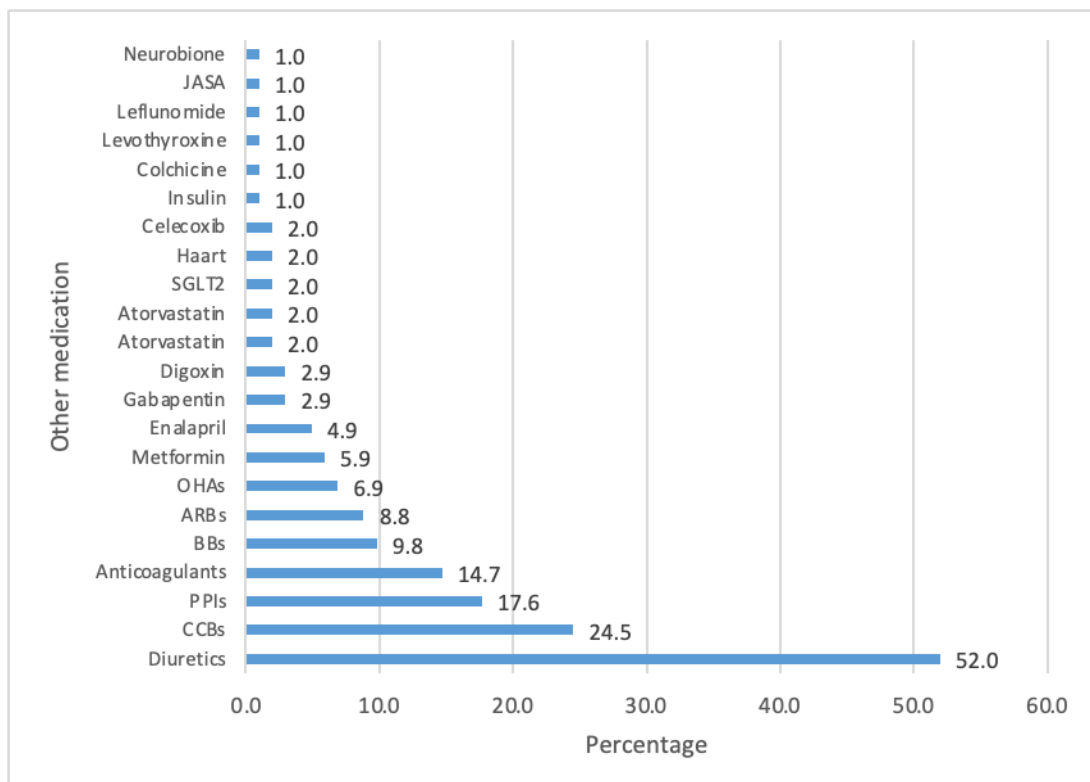


**Figure 4.5: Other medications**

#### 4.6 COPD Severity

Among the 102 participants, COPD severity was stratified using GOLD criteria based on post-bronchodilator FEV<sub>1</sub> % predicted values. As illustrated in Figure 4.6. The distribution showed that 40 participants (39.22%) were classified as GOLD III (severe; FEV<sub>1</sub> <50%), while 23 participants (22.55%) had GOLD IV (very severe; FEV<sub>1</sub> <30%). Collectively, these advanced stages accounted for 63 participants (61.77%) of the cohort. Moderate COPD (GOLD II; FEV<sub>1</sub> <80%) was observed in 20 participants (19.61%), and mild COPD (GOLD I; FEV<sub>1</sub> ≥80%) was the least prevalent, affecting 19 participants (18.63%).

The proportion of severe cases (GOLD III; 39.22%) was approximately twice that of moderate cases (GOLD II; 19.61%), while very severe cases (GOLD IV; 22.55%) slightly outnumbered mild cases (GOLD I; 18.63%).

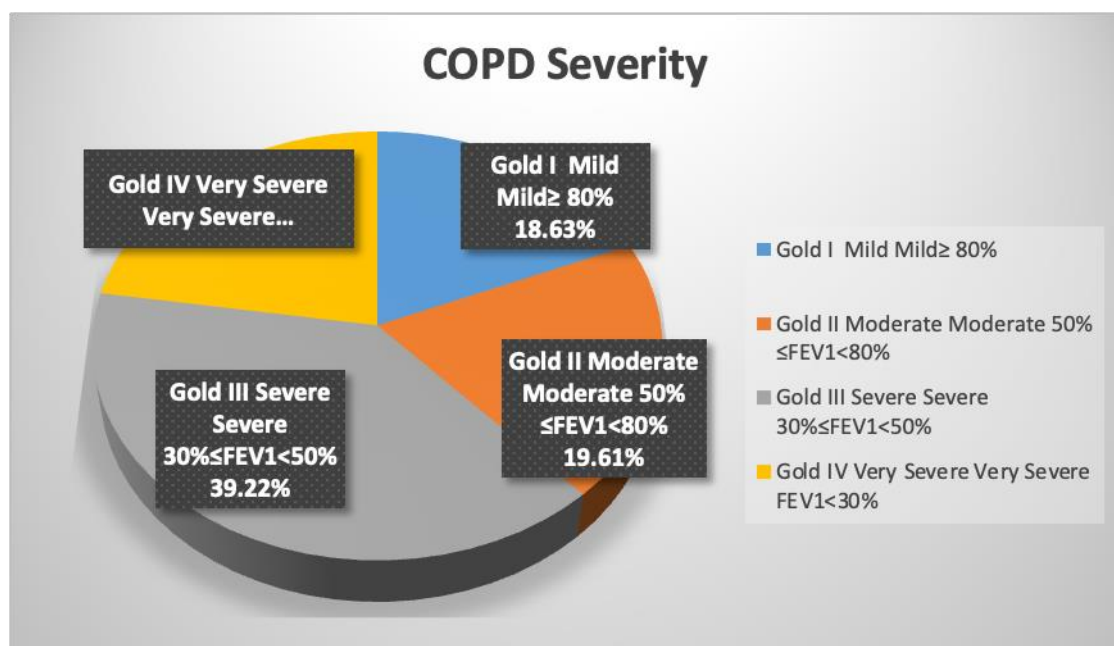


**Figure 4.6: COPD Severity**

#### 4.7 Serum Magnesium Levels

The mean serum magnesium level among the 102 participants was  $0.77 \pm 0.12$  mmol/L, with values ranging from 0.47 to 1.14 mmol/L. Participants with mild to moderate COPD (GOLD I–II) had a slightly higher mean magnesium level of  $0.82 \pm 0.09$  mmol/L, compared to  $0.74 \pm 0.12$  mmol/L among those with severe to very severe disease (GOLD III–IV). Hypomagnesemia was observed in 31 participants (30.4%), the vast majority of whom (93.5%) were classified under GOLD stages III and IV. Further classification of magnesium status showed that out of the total participants, 31 (30.4%) had hypomagnesemia, 69 (67.7%) had normomagnesemia, and 2 (2.0%) had hypermagnesemia. These findings indicate that nearly one-third of the study population had magnesium levels below the normal range, with a significant concentration among patients with advanced COPD.

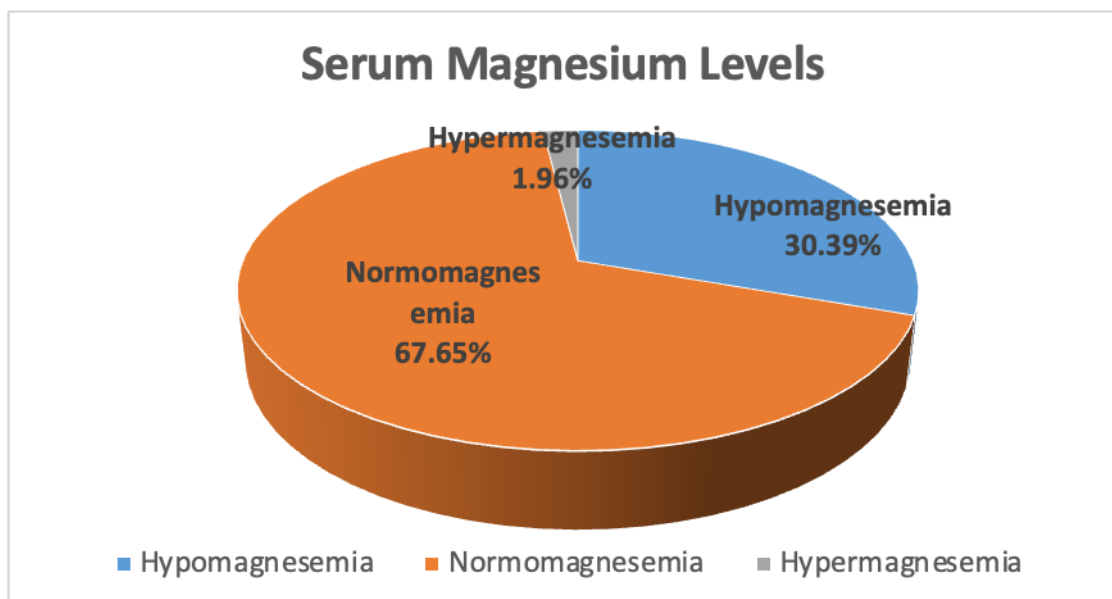


**Figure 4.7: Serum Magnesium Levels**

#### 4.7.1 Bivariate Analysis of COPD Severity and Serum Magnesium Levels.

A bivariate analysis was conducted to assess the association between serum magnesium levels and COPD severity among 102 participants. Serum magnesium was categorized into hypomagnesemia, normomagnesemia, and hypermagnesemia, while COPD severity was grouped into mild/moderate (GOLD I–II) and severe/very severe (GOLD III–IV) classifications.

Among participants with hypomagnesemia (n=31), 93.55% had severe/very severe COPD, while only 6.45% had mild/moderate disease. Conversely, normomagnesemia (n=69) was more frequently observed in milder COPD cases (52.17%), with 47.83% in the severe categories. Hypermagnesemia was rare (n=2), with an even distribution across severity levels. A chi-square test confirmed a statistically significant association between serum magnesium levels and COPD severity ( $p=0.001$ ).

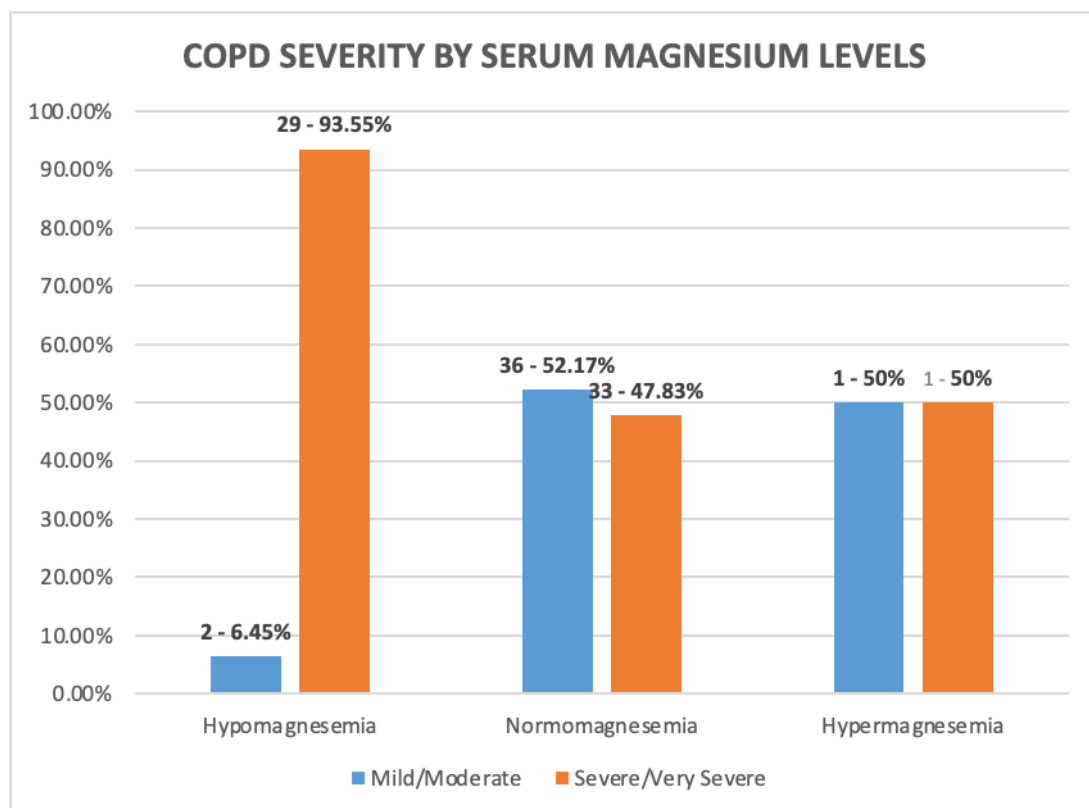


**Figure 4.8: COPD Severity and Serum Magnesium Levels**

#### **4.8 Multivariate Logistic Regression on COPD Severity**

A multivariate logistic regression analysis was conducted to assess the association between serum magnesium levels and COPD severity among 102 participants, alongside selected demographic and clinical variables. COPD severity was categorized into mild/moderate (GOLD I–II) and severe/very severe (GOLD III–IV) for binary logistic regression.

The model produced both unadjusted odds ratios (UOR) and adjusted odds ratios (AOR), each with corresponding 95% confidence intervals and p-values.

Hypomagnesemia was significantly associated with higher odds of severe/very severe COPD. Participants with hypomagnesemia had 15.82 times higher odds of severe COPD compared to those with normomagnesemia in the unadjusted model (UOR: 15.82; 95% CI: 3.50–71.51;  $p < 0.001$ ). This association remained statistically significant and stronger after adjusting for potential confounders (AOR: 27.30; 95% CI: 4.38–170.19;  $p < 0.001$ ).

Age and male sex were statistically significant in the unadjusted model (UOR: 0.97; 95% CI: 0.94–0.99;  $p = 0.045$  and UOR: 4.00; 95% CI: 1.59–10.05;  $p = 0.003$ , respectively), but both lost statistical significance after adjustment.

In the adjusted multivariable logistic regression model (Table 4.3), other variables including BMI category, diabetes mellitus, heart failure, chronic kidney disease (CKD), and the use of medications such as diuretics and proton pump inhibitors (PPIs) did not show statistically significant associations with COPD severity.

Table 4.3 summarizes the multivariate logistic regression results.

**Table 4.3: Multivariate logistic regression on Factors associated with COPD severity**

|                        | UOR          | 95% CI      | P-value | AOR          | 95% CI       | P-value          |
|------------------------|--------------|-------------|---------|--------------|--------------|------------------|
| Serum magnesium levels |              |             |         |              |              |                  |
| Normomagnesemia        | 1            |             |         | 1            |              |                  |
| Hypomagnesemia         | <b>15.82</b> | 3.50, 71.51 | <0.001  | <b>27.30</b> | 4.38, 170.19 | <b>&lt;0.001</b> |
| Age                    | 0.97         | 0.94, 0.99  | 0.045   | 0.99         | 0.94, 1.05   | 0.743            |
| Sex                    |              |             |         |              |              |                  |
| Female                 | 1            |             |         | 1            |              |                  |
| Male                   | 4.00         | 1.59, 10.05 | 0.003   | 2.31         | 0.56, 9.43   | 0.245            |
| BMI                    |              |             |         |              |              |                  |
| Underweight            | 1            |             |         | 1            |              |                  |
| Normal                 | 1.36         | 0.38, 4.89  | 0.634   | 2.06         | 0.40, 10.49  | 0.386            |
| Overweight             | 0.50         | 0.13, 1.91  | 0.310   | 0.37         | 0.06, 2.50   | 0.310            |
| Obese                  | 0.50         | 0.13, 1.95  | 0.318   | 1.25         | 0.20, 7.67   | 0.811            |
| DM                     |              |             |         |              |              |                  |
| No                     | 1            |             |         | 1            |              |                  |
| Yes                    | 0.81         | 0.17, 3.85  | 0.795   | 1.72         | 0.10, 29.25  | 0.707            |
| Heart failure          |              |             |         |              |              |                  |
| Absent                 | 1            |             |         | 1            |              |                  |
| Present                | 0.74         | 0.33, 1.65  | 0.462   | 2.00         | 0.52, 7.68   | 0.312            |
| CKD                    |              |             |         |              |              |                  |
| No CKD                 | 1            |             |         | 1            |              |                  |
| CKD                    | <b>2.00</b>  | 0.51, 7.89  | 0.322   | <b>4.86</b>  | 0.80, 29.55  | 0.086            |
| Diuretics              |              |             |         |              |              |                  |
| No                     | 1            |             |         | 1            |              |                  |
| Yes                    | 0.39         | 0.17, 0.90  | 0.027   | 0.38         | 0.07, 1.91   | 0.239            |
| PPIs                   |              |             |         |              |              |                  |
| No                     | 1            |             |         | 1            |              |                  |
| Yes                    | 0.56         | 0.20, 1.55  | 0.262   | 0.38         | 0.07, 1.91   | 0.239            |

## CHAPTER FIVE

### 5. 0 DISCUSSIONS, STUDY STRENGTHS AND LIMITATIONS

#### 5.1 DISCUSSIONS

##### 5.1.1 Age

The mean age of COPD patients in our study was  $71.3 \pm 14.8$  years, which aligns with findings from high-income countries. For instance, Aziz et al. reported a similar mean age of 70.4 years among COPD patients in the United States (Aziz et al., 2005) and Gumus et al. also reported a comparable mean age of  $70.4 \pm 7.8$  years among hospitalized COPD patients in Turkey (Gumus et al., 2014). In contrast, regional studies from South Asia report younger COPD populations; Shah et al., found a mean age of 62.5 years in Kashmir, India (Shah et al., 2010). The age discrepancy is more pronounced in low-income countries like Uganda, where van Gemer et al. observed COPD in a much younger population, with a mean age of approximately 46.6 years. Notably, their study included participants aged 30 years and above, which partially explains the lower average age (van Gemer et al., 2016). These comparisons suggest that age-related differences in COPD populations may reflect variations in study design, population structure, and exposure to environmental or occupational risk factors.

The mean age of participants in this study was 71.3 years, which is relatively high compared to findings from other regional and global studies. Several key factors may explain this age difference. First, the study was conducted at Moi Teaching and Referral Hospital (MTRH), a tertiary care facility that typically manages patients with advanced disease. As such, older patients with more severe or long-standing COPD are more likely to be captured in this hospital-based setting. This contrasts with community-

based studies such as the FRESH AIR Uganda study by van Gerner et al.(van Gerner et al., 2016).

Environmental exposures may also differ across settings. While biomass fuel exposure remains a key COPD risk factor in both Uganda and Kenya, early and chronic exposure in rural settings can lead to earlier disease onset. However, the higher average age in our study may indicate that only those who survive into older age with chronic exposure and persistent symptoms present at tertiary centers for diagnosis and management. Additionally, differences in healthcare-seeking behavior, access to diagnostic services, and awareness of respiratory diseases may delay diagnosis until later stages in Kenya, particularly among rural or lower socio-economic populations. Lastly, a form of survival bias may be present, where older patients living longer with COPD are more likely to be included in the hospital population, unlike in some LMIC community studies where younger individuals may still be underdiagnosed. These contextual factors help explain the relatively higher mean age in our study and emphasize the importance of healthcare access and disease awareness in shaping COPD demographics in low- and middle-income countries.

### **5.1.2 Gender, Biomass exposure and smoking status**

In our study at Moi Teaching and Referral Hospital (MTRH), the majority of COPD patients were female (60.78%), with a striking 99% reporting exposure to biomass fuel. Additionally, the prevalence of current smokers was relatively low (12.75%), while 30.39% were former smokers. These findings reflect trends commonly observed in other low- and middle-income countries (LMICs), where biomass smoke is a leading contributor to COPD, particularly among women, who are often responsible for household cooking. For example, the FRESH AIR Uganda study (van Gerner et al.,

2016) reported that 93% of participants were exposed to biomass smoke, with women comprising 51% of the sample. Notably, only 8% of women with COPD in that study were current smokers, compared to 44% of men, highlighting the disproportionate role of biomass exposure in female COPD prevalence in regions where tobacco use among women is relatively uncommon (van Gerner et al., 2016).

Similarly, a systematic review and meta-analysis by Hu et al., demonstrated that women exposed to biomass smoke were 1.38 times more likely to develop COPD than those using cleaner fuels, underscoring the gender-specific vulnerability linked to household air pollution (Hu et al., 2010). Supporting this, a study from the BOLD trial (Buist et al., 2007) initiative conducted in Morocco reported a significant association between biomass exposure and COPD in women, independent of smoking status. Women with high levels of cooking-related biomass exposure had an adjusted odds ratio of 7.2 for developing COPD (Harch et al., 2024). These studies collectively reinforce the finding that in LMICs, women are disproportionately affected by COPD due to intensive and prolonged exposure to biomass fuels, often in the absence of significant tobacco use. These results underscore the urgent need for public health policies that promote cleaner household energy sources and improved ventilation systems, particularly in rural and underserved areas.

The predominance of females (60.78%) among COPD patients in this study, coupled with the extremely high prevalence of biomass fuel exposure (99%) and relatively low rates of smoking (12.75% current smokers, 30.39% ex-smokers), can be attributed to cultural, environmental, and socio-economic factors unique to the study setting in Eldoret, Kenya. In many rural and peri-urban regions of Kenya, women are primarily responsible for cooking, often using biomass fuels such as wood, charcoal, or dung in

poorly ventilated indoor environments. This routine exposure to household air pollution significantly elevates their risk of developing COPD, even in the absence of tobacco use. Supporting this, a systematic review and meta-analysis by Sana et al. (Sana et al., 2018) found that women exposed to biomass smoke were 1.38 times more likely to develop COPD compared to those not exposed, and the association was significant across both rural and urban settings. The study also noted a strong association between biomass exposure and chronic bronchitis (OR 2.11), reinforcing the contribution of indoor air pollution to respiratory morbidity among women. Additionally, low smoking prevalence among Kenyan women, shaped by cultural norms and social stigma, further supports the notion that non-smoking-related risk factors like biomass exposure disproportionately affect women. These findings collectively suggest that the high burden of COPD among women in this study is driven by gender-specific exposure patterns, highlighting the need for targeted interventions promoting cleaner fuel alternatives and improved indoor ventilation.

### **5.1.3 County of origin, Educational status, and Occupational History in COPD**

#### **Patients**

Participants in this study were drawn from multiple municipalities, with the largest proportion coming from Uasin Gishu County (46.1%), and followed by Nandi (17.6%), Elgeyo Marakwet (10.8%), and Trans Nzoia (6.9%). This distribution underscores the role of MTRH as a referral center serving a vast geographical region, highlighting the widespread impact of chronic obstructive pulmonary disease (COPD) beyond urban centers.

A significant finding in our study was the low educational attainment among participants, with 52.9% lacking formal education and only 33.3% having completed

primary school. This limited educational background potentially affects health literacy, influencing disease awareness, treatment adherence, and healthcare-seeking behaviors. Delayed diagnoses and inadequate symptom management may be exacerbated by low literacy levels, increasing the risk of severe COPD and accelerating disease progression. These findings align with a study conducted in Jiangsu Province, China by, (Fang et al., 2018) which reported that lower educational attainment was associated with a higher prevalence of COPD. Specifically, individuals with  $\leq 9$  years of education had a COPD prevalence of 12.7%, compared to 5.7% among those with  $\geq 13$  years of education.

The socioeconomic burden of COPD was further reflected in the occupational history of our participants. A majority (72.5%) were unemployed, 22.5% were self-employed, and only 4.9% were formally employed. The advanced age and deteriorating health status of many participants may contribute to this high unemployment rate. Limited financial resources can restrict access to healthcare, medications, and necessary lifestyle modifications, complicating the management of COPD. This observation is consistent with findings from a multicenter study in China by Zhang et.al, which reported that blue-collar workers had a higher risk of developing COPD compared to white-collar workers (OR: 0.60, 95% CI: 0.43–0.83) (Zhang et al., 2021).

Globally, the association between socioeconomic status (SES) and COPD has been well-documented. A systematic review found consistent significant inverse associations between SES and COPD outcomes, indicating that individuals of lower socioeconomic strata were at least twice as likely to have poor outcomes as those of higher strata. Furthermore, a study analyzing data from multiple low- and middle-income countries (LMICs) reported that lower education and household income were

associated with higher COPD prevalence. Specifically, completing secondary school was associated with a lower odds ratio (OR = 0.73, 95% CI: 0.55–0.98) for COPD (Hua et al., 2024). In the present study, socioeconomic indicators such as education level and occupation did not show statistically significant associations with COPD severity after adjustment. This differs from findings in broader LMIC settings and may reflect the relatively homogeneous socioeconomic characteristics of the study population, the clinical context in which all patients were already diagnosed with COPD, or limited variability in SES categories within the sampled group. Nevertheless, the direction of association in our unadjusted analysis still suggested that participants with lower educational attainment tended to have more severe disease, aligning with the pattern reported in literature, although these differences were not statistically significant.

These findings collectively emphasize the critical role of socioeconomic factors, including education and occupation, in the prevalence and management of COPD. Addressing these disparities through targeted public health interventions, such as improving access to education and healthcare services, is essential in mitigating the burden of COPD, particularly in LMICs like Kenya.

#### **5.1.4 COPD Symptom Profile and Exacerbation Status**

In this study conducted at Moi Teaching and Referral Hospital (MTRH) in Eldoret, Kenya, COPD patients exhibited a high burden of respiratory symptoms and a considerable rate of exacerbations. At the time of recruitment, 77.45% of participants were in a stable phase, while 22.55% were experiencing exacerbations. This distribution underscores the chronic and episodic nature of COPD, where periods of relative stability are punctuated by acute worsening of symptoms.

To ensure accurate assessment of pulmonary function, spirometry was conducted only after patients had returned to their baseline health status, typically after a minimum of two weeks post-exacerbation. This approach aligns with current clinical guidelines, which recommend performing spirometry when patients are clinically stable to avoid underestimating lung function due to the transient effects of exacerbations(GOLD, 2024).

The symptomatology observed in this cohort is consistent with the characteristic features of COPD. Dyspnea was reported by 86.3% of participants, and increased wheezing was noted in 82.4%. Additionally, 33.3% of patients experienced increased sputum production, and 5.9% had purulent sputum, indicating possible airway infections or heightened inflammation. These findings are in line with global studies, such as the ECLIPSE study (Hurst et al., 2010), which identified breathlessness as the most prevalent symptom among COPD patients.

Physical examination findings further corroborate the severity of the disease in this population. Crepitations were present in 39.2% of patients, wheezing in 28.4%, tachypnea in 13.7%, and tachycardia in 22.5%. These signs are indicative of airflow limitation and respiratory distress, common in advanced stages of COPD. The presence of such clinical signs necessitates prompt and effective management to prevent further deterioration.

Comparatively, studies conducted in other regions have reported similar clinical presentations. For instance, a multicenter study in China by Zeng et al., observed that dyspnea and chronic cough were the most common symptoms among COPD patients, with exacerbations leading to significant declines in lung function(Zeng et al., 2020).

These parallels highlight the universal challenges in managing COPD across different healthcare settings.

The decision to perform spirometry after a period of clinical stability is further supported by evidence from the WISDOM trial by Watz et al., 2018, which demonstrated that lung function, as measured by FEV<sub>1</sub>, begins to decline approximately two weeks before the onset of an exacerbation and does not return to baseline levels even eight weeks post-exacerbation (Watz et al., 2018). This underscores the importance of timing in spirometric assessments to obtain accurate measurements of pulmonary function.

In conclusion, the clinical status and symptom profile of COPD patients at MTRH reflect the complex nature of the disease, characterized by chronic symptoms and acute exacerbations. The alignment of these findings with international studies emphasizes the need for standardized management protocols and highlights the importance of conducting spirometry during periods of clinical stability to guide appropriate treatment strategies.

#### **5.1.5 Comorbidities**

In this study, a significant proportion of COPD patients exhibited comorbid conditions, with heart failure (44.12%) and hypertension (39.22%) being the most prevalent. These findings are consistent with global trends, where cardiovascular comorbidities are commonly associated with COPD. For instance, a multicenter study in China by Fang et al., reported hypertension as the most frequent comorbidity among COPD patients, with a prevalence of 42.4% (Fang et al., 2018). The high prevalence of heart failure in our cohort may be attributed to shared risk factors such as aging, systemic

inflammation, and chronic hypoxia inherent in COPD pathophysiology (Smith & Wrobel, 2014).

Mollica et al., highlighted the strong association between COPD and cardiovascular diseases in elderly populations, noting that 10% of people over 75 years of age in the US suffer from COPD, often complicated by conditions such as heart failure, lung cancer, obstructive sleep apnea, and malnutrition. Similarly, in our study, the presence of comorbidities like heart failure and hypertension underscores the systemic consequences of COPD, particularly in the elderly. These findings align with the broader literature emphasizing the increased risk of comorbid cardiovascular diseases in COPD patients, especially as they age (Mollica et al., 2021).

Diabetes mellitus was present in 6.86% of our patients, which is lower than the global prevalence reported in COPD populations, ranging from 10% to 25% (Mollica et al., 2021). This discrepancy may be due to differences in lifestyle, genetic predisposition, or underdiagnosis in our setting. Chronic kidney disease (CKD) was observed in 11.76% of patients, aligning with studies that report a CKD prevalence between 1.5% and 43% among COPD patients (Smith & Wrobel, 2014). The association between COPD and CKD may be explained by common risk factors such as smoking, systemic inflammation, and comorbid conditions like hypertension and diabetes (Gaddam et al., 2016).

Atrial fibrillation (AF) was identified in 11.76% of our cohort. AF is a recognized comorbidity in COPD patients, with studies indicating a prevalence of approximately 13% (Romiti et al., 2021). The coexistence of AF and COPD can exacerbate symptoms and complicate management, necessitating careful monitoring and tailored therapeutic strategies.

Regarding venous thromboembolism (VTE), 2.94% of patients experienced events, including deep vein thrombosis (0.98%) and pulmonary embolism (1.96%). While this prevalence is lower than some reports, which indicate VTE occurrences up to 24.5% in hospitalized COPD patients (Liu et al., 2023). It underscores the importance of vigilance for thromboembolic complications, especially during acute exacerbations.

Other comorbidities observed included hypothyroidism (0.98%), gout (0.98%), rheumatoid arthritis (0.98%), right ventricular dysfunction (1.96%), and post-tuberculosis lung fibrosis (1.96%). These conditions, though less prevalent, can significantly impact the clinical course and quality of life in COPD patients. The presence of post-tuberculosis lung fibrosis is particularly relevant in our setting, given the high burden of tuberculosis in Kenya.

The distribution of heart failure phenotypes revealed that right heart failure (RHF) was predominant (38.24%), with a smaller proportion exhibiting heart failure with reduced ejection fraction (HFrEF) at 5.88%. The high incidence of RHF may be attributed to chronic hypoxic pulmonary vasoconstriction leading to pulmonary hypertension, a common complication in advanced COPD (Smith & Wrobel, 2014).

In conclusion, the high prevalence of comorbidities among COPD patients in our study highlights the need for comprehensive assessment and integrated management approaches. Addressing these comorbid conditions is crucial for improving patient outcomes and reducing healthcare burdens associated with COPD.

### **5.1.6 Medications**

#### **5.1.6.1 COPD Medication Use**

In this study, the majority of COPD patients (72.5%) reported using a combination of long-acting beta-agonists and inhaled corticosteroids (LABA/ICS), while 27.5% were not on any form of COPD medication. Medication data were obtained from patient self-reports during structured interviews and verified, where possible, with available clinic records. Notably, no patients reported using short-acting muscarinic antagonists (SAMA) or long-acting muscarinic antagonists (LAMA), despite their central role in COPD management according to current treatment guidelines. Use of short-acting beta-agonists (SABA) was similarly low at 3.92%, and only 10.78% of patients reported using leukotriene receptor antagonists (LTRA). The limited reporting of SABA and bronchodilator use may reflect constraints inherent to self-reported medication histories and possible discrepancies between prescribed and actual medication use, rather than true absence of therapy. It may also indicate variations in prescribing patterns at the facility, particularly if bronchodilators are less frequently stocked or prescribed for COPD compared to asthma.

Globally, SABA is often over-prescribed in both asthma and COPD populations, sometimes leading to poor disease control and increased exacerbation risk (Chakaya et al., 2023)(SABINA III Study Group, 2023). The underreporting in this cohort contrasts with findings from Kenya in the SABINA III study by Chakaya et al., where SABA was widely used but linked to negative outcomes when over-relied upon (Chakaya et al., 2023). This suggests that the patients in the present study may not have been accurately recalling their medication use or may have been under-prescribed due to limited symptom recognition or inadequate follow-up care.

The complete absence of SAMA and LAMA in the treatment regimens is significant, as both are recommended by GOLD. Guidelines for maintenance therapy, especially in moderate to severe COPD (GOLD, 2024). Their exclusion could be due to limited availability or affordability in the public sector, lack of clinician familiarity, or systemic constraints within the healthcare infrastructure. A Nigerian nationwide survey reported similar challenges, noting that LAMA availability was as low as 0–2% in public facilities, while cost remained a major barrier (Ozoh et al., 2021).

The fact that 27.5% of patients were not on any COPD medication is especially concerning and may reflect missed diagnosis, financial barriers, poor follow-up, or inadequate understanding of disease management among patients and providers. This aligns with previous studies in LMICs that highlight gaps in continuity of care and medication adherence due to economic and systemic challenges (Alupo et.al, 2025).

In conclusion, while LABA/ICS combination therapy appears to be the dominant treatment among those receiving care, the complete absence of SAMA and LAMA, underreporting or underuse of SABA, and a high proportion of patients not on any treatment indicate significant gaps in COPD pharmacological management. These findings highlight the urgent need to improve medication access, enhance clinician training, and implement patient education strategies to promote optimal COPD care in resource-limited settings.

#### **5.1.6.2 Other Medications and Comorbidities**

In our study, a significant proportion of patients were prescribed medications addressing comorbid conditions commonly associated with chronic obstructive pulmonary disease (COPD), such as cardiovascular diseases, metabolic disorders, and gastrointestinal issues. This pattern reflects the multifaceted nature of COPD

management, where addressing comorbidities is crucial for improving patient outcomes.

Diuretics were prescribed to 51.96% of patients, with furosemide (44.12%) and spironolactone (40.20%) being the most commonly used. While diuretics are essential for managing conditions like heart failure and hypertension, their use in COPD patients requires careful consideration. A study indicated that incident use of diuretics, particularly loop diuretics, was associated with increased respiratory-related morbidity and mortality in older adults with COPD. This underscores the importance of monitoring for potential adverse respiratory effects when prescribing diuretics to COPD patients (vozoris, 2018).

Beta-blockers were used by 9.80% of patients, with metoprolol (6.86%) and carvedilol (2.94%) being the primary agents. Historically, there has been hesitancy in prescribing beta-blockers to COPD patients due to concerns about bronchoconstriction. However, recent evidence suggests that cardioselective beta-blockers are generally safe and may even reduce the risk of COPD exacerbations. Therefore, in COPD patients with compelling indications such as heart failure or post-myocardial infarction, beta-blockers should not be withheld (Lipworth & Devereux, 2025).

CCBs were prescribed to 24.51% of patients, with amlodipine (17.65%) being the most common. ARBs, including losartan (7.84%) and telmisartan (0.98%), were used by 8.82% of patients. These medications are standard treatments for hypertension and other cardiovascular conditions. Their use in COPD patients is appropriate, especially when managing comorbid cardiovascular diseases (Chandy et al., 2013).

Anticoagulant therapy was administered to 14.71% of patients, predominantly with rivaroxaban (13.73%). COPD patients are at an increased risk for thromboembolic events, particularly during acute exacerbations. Anticoagulant therapy can reduce mortality and prevent recurrent embolic events in COPD patients with conditions like pulmonary hypertension or a history of pulmonary embolism. However, the decision to initiate anticoagulation should be individualized, considering the patient's bleeding risk and comorbidities (Lai et al., 2022).

OHAs were used by 6.86% of patients, with metformin (5.88%) being the most prevalent. Insulin therapy was reported in 0.98% of patients. The presence of diabetes mellitus in COPD patients necessitates careful glycemic control, as poor glucose management can exacerbate COPD symptoms and increase the risk of infections.

Atorvastatin was prescribed to 1.96% of patients. Beyond lipid-lowering effects, statins have anti-inflammatory properties that may benefit COPD patients by reducing systemic inflammation. However, the evidence is mixed, and routine use of statins solely for COPD management is not currently recommended.

Dapagliflozin and empagliflozin were each used by 0.98% of patients. These agents are primarily used for glycemic control in type 2 diabetes and have shown cardiovascular benefits. Their role in COPD management is not well-established, and their use in this cohort likely reflects treatment for comorbid diabetes.

Proton pump inhibitors (PPIs) were prescribed to 17.65% of patients, with esomeprazole (9.8%) being the most common. PPIs are used to manage gastroesophageal reflux disease (GERD), which is prevalent in COPD patients and can

contribute to exacerbations. Managing GERD symptoms may help reduce COPD exacerbation frequency.

Other medications reported include colchicine (0.98%), gabapentin (2.94%), digoxin (2.94%), and levothyroxine (0.98%). These medications address various comorbid conditions such as gout, neuropathic pain, atrial fibrillation, and hypothyroidism, respectively. Their presence in the medication profiles of COPD patients highlights the complexity of managing multiple chronic conditions concurrently.

In summary, the diverse range of medications prescribed to COPD patients in this study underscores the importance of a comprehensive approach to management that addresses both pulmonary and extrapulmonary conditions. Clinicians should remain vigilant for potential drug interactions and side effects, ensuring that treatment regimens are optimized for each patient's unique clinical profile.

#### **5.1.7 COPD Severity Based on GOLD Criteria**

The severity distribution of COPD in the current study reveals a substantial disease burden, with 61.77% of patients falling into the severe (GOLD III) and very severe (GOLD IV) categories. Only a minority presented with mild (GOLD I) or moderate (GOLD II) disease, representing 18.63% and 19.61%, respectively. This pattern underscores the late presentation and underdiagnosis of COPD in this population, which is consistent with trends observed in similar low- and middle-income settings.

The low prevalence of early-stage COPD likely reflects a combination of limited disease awareness, low health-seeking behavior, and restricted access to diagnostic services such as spirometry particularly in rural or underserved areas. In Kenya and other parts of sub-Saharan Africa, limited healthcare infrastructure and poor health

literacy contribute to delayed diagnosis and treatment of chronic diseases, including COPD (Zhou et al., 2009).

Comparative studies highlight similar trends. A multicenter observational study in China reported a high proportion of patients in GOLD stages III and IV, attributing this to late diagnosis and poor awareness of early symptoms (Zhou et al., 2009). Similarly, the ECLIPSE study found that a significant proportion of patients with GOLD III and IV had frequent exacerbations, worse quality of life scores, and a greater need for hospital-based care (Agustí et al., 2012). These findings parallel the current study, where advanced-stage COPD is dominant, suggesting the need for public health interventions to improve early detection and chronic disease management.

Moreover, the predominance of severe COPD among participants may also be linked to biomass exposure, smoking, comorbidities, and low socioeconomic status, which are established risk factors for disease progression (Sana et al., 2018). In the current study, most participants were unemployed and had low educational levels, which further supports the interplay between poverty and chronic disease severity. Patients with lower socioeconomic status are less likely to engage with healthcare systems early or adhere to long-term therapies.

The implications of severe and very severe COPD are substantial. These stages are associated with increased mortality, frequent exacerbations, poor exercise tolerance, and reduced quality of life (GOLD, 2024). Advanced-stage patients require complex and costly interventions, including inhaled therapies, pulmonary rehabilitation, and in some cases, long-term oxygen therapy.

To address these challenges, there is a need for community-level screening, targeted education campaigns, and capacity-building for primary healthcare providers in spirometry use and early COPD recognition. Additionally, integrating COPD into chronic disease programs that already exist for conditions like HIV and hypertension may facilitate earlier interventions.

#### **5.1.8 Discussion on Serum Magnesium Levels**

Magnesium is indispensable for maintaining respiratory muscle function, modulating immune responses, and regulating airway tone. This study investigated the association between serum magnesium levels and the severity of Chronic Obstructive Pulmonary Disease (COPD), aiming to elucidate the prevalence and clinical implications of magnesium abnormalities in this patient population.

The study revealed that a majority of patients (67.65%) exhibited normomagnesemia. However, a significant proportion (30.39%) presented with hypomagnesemia, while a minority (1.96%) had hypermagnesemia. This distribution underscores the potential link between magnesium imbalance and COPD pathogenesis, particularly in patients experiencing frequent exacerbations or advanced disease stages.

These findings are consistent with prior research. For instance, a study by Youssef et al. (2022) reported that patients with acute exacerbations of COPD had significantly lower serum magnesium levels compared to stable patients, suggesting a role for magnesium deficiency in disease exacerbation (Youssef et al., 2022). Similarly, Kshirsagar et al. (2005) found that serum magnesium levels were significantly lower in patients undergoing exacerbations than in stable COPD patients (Kshirsagar & Patil, 2021e).

Hypomagnesemia has been associated with increased airway hyperresponsiveness, impaired bronchodilation, and reduced respiratory muscle function. In patients hospitalized for acute exacerbations of Chronic Obstructive Pulmonary Disease (COPD), low serum magnesium levels were significantly more common compared with stable COPD, and were linked to longer hospital stays (Makwana et al., 2022). A prospective study also demonstrated that COPD patients during exacerbations had lower mean serum magnesium levels compared to their stable counterparts (Abou Youssef et al., 2022). Earlier research from Kashmir similarly found that mean serum magnesium was significantly lower among exacerbation cases than controls, and that hypomagnesemia was more frequent in more advanced COPD stages (Shah et al., 2010). These findings reinforce the view that magnesium deficiency may exacerbate COPD symptoms, contribute to disease progression, and worsen clinical outcomes.

Supporting this, a study by Shah et al. (2010) observed that hypomagnesemia was present in 33.8% of patients during acute exacerbations, compared to 4% in stable patients, indicating a significant association between low magnesium levels and disease exacerbation (Shah et al., 2010b). Additionally, Gumus et al. (2014) found that serum magnesium levels were independent predictors of the number of COPD exacerbations, further emphasizing the clinical importance of maintaining adequate magnesium levels (Gumus et al., 2014b).

Several factors were identified as potential contributors to low magnesium levels in COPD patients. Diuretic use (51.96%), particularly loop diuretics like furosemide (44.12%), increases urinary magnesium excretion, leading to depletion. Long-term corticosteroid therapy (8.82%), commonly used to manage COPD inflammation, may also alter electrolyte balance and promote magnesium loss. Additionally, chronic

kidney disease (11.76%) and diabetes mellitus (6.86%) were present in some patients, conditions that further disrupt magnesium homeostasis.

These findings are corroborated by previous studies. For example, a study by Makwana et al. (2022) reported that hypomagnesemia was common in patients with acute exacerbations of COPD and was associated with longer hospital stays (Makwana et al., 2022c). Furthermore, a study by Khan et al. (2005) highlighted the significant association between low serum magnesium levels and acute exacerbations, suggesting that monitoring and managing magnesium levels could be beneficial in COPD management (Aziz et al., 2005c).

The correlation between COPD severity and magnesium deficiency suggests that routine screening of serum magnesium levels may be beneficial in patients with frequent exacerbations or advanced disease stages. Addressing hypomagnesemia through magnesium supplementation, dietary interventions, or medication adjustments could potentially improve respiratory function, reduce exacerbations, and enhance overall disease management.

#### **5.1.9 Association between COPD Severity and Serum Magnesium Levels**

The third objective of this study was to evaluate the association between the severity of Chronic Obstructive Pulmonary Disease (COPD) and serum magnesium levels among patients attending Moi Teaching and Referral Hospital (MTRH). The findings demonstrated a statistically significant inverse relationship between COPD severity and serum magnesium levels ( $p = 0.001$ ), indicating that magnesium deficiency becomes more common as the disease progresses.

Hypomagnesemia was observed in 30.39% of the total study population, with a notably higher prevalence in patients classified as GOLD III (severe) and GOLD IV (very severe). Specifically, 45.0% of those with severe COPD and 47.83% of those with very severe COPD had hypomagnesemia. In contrast, 94.74% of patients with mild COPD (GOLD I) and 90.0% with moderate COPD (GOLD II) had normal magnesium levels. These findings highlight a trend in which magnesium depletion is more pronounced in advanced disease stages.

This observation is consistent with findings from other studies. For instance, Settu et al. (2023) reported hypomagnesemia in 48.3% of GOLD III and 66.7% of GOLD IV patients (Settu et al., 2023), reinforcing the association between COPD severity and magnesium deficiency. Similarly, Gumus et al. (2014) demonstrated that lower serum magnesium levels were significantly linked to the frequency of acute exacerbations. These comparisons support the internal validity and external consistency of your study findings (Gumus et al., 2014b).

The clinical relevance of hypomagnesemia in COPD is significant. Magnesium plays a vital role in bronchodilation, respiratory muscle function, and modulation of airway inflammation. In your study, patients with lower magnesium levels were more likely to experience frequent exacerbations and hospitalizations, a trend mirrored in literature by Kumar et al. (2025), who found that hypomagnesemia was associated with prolonged hospital stays and increased severity of acute exacerbations (Kumar et al., 2025).

From a clinical standpoint, these findings suggest that routine monitoring of serum magnesium levels may be beneficial, especially in patients with moderate to severe COPD. Early identification and correction of hypomagnesemia through dietary

measures, supplementation, or medication review may help reduce exacerbation rates, improve respiratory function, and enhance overall disease control.

In conclusion, the study provides compelling evidence of a strong association between COPD severity and serum magnesium levels, emphasizing the need to incorporate magnesium assessment into routine COPD management protocols. Magnesium could potentially serve as a biomarker to identify patients at higher risk of poor outcomes, guiding targeted interventions for improved clinical care.

#### **5.1.10 Multivariate Logistic Regression Analysis of Factors Associated with COPD Severity**

Multivariate logistic regression analysis revealed a strong and statistically significant association between hypomagnesemia and increased severity of Chronic Obstructive Pulmonary Disease (COPD). Patients with hypomagnesemia had markedly higher odds of severe or very severe COPD (GOLD III–IV) compared to those with normal magnesium levels, with an adjusted odds ratio (AOR) of 27.30 (95% CI: 4.38–170.19;  $p < 0.001$ ). This suggests that hypomagnesemia may be a significant independent predictor of advanced COPD, even after adjusting for other clinical and demographic factors.

These findings are consistent with previous literature. Gumus et al. (2014) reported that serum magnesium levels were significantly associated with the frequency of acute COPD exacerbations (Gumus et al., 2014b), indicating that lower magnesium levels may exacerbate disease progression. Similarly, Aziz et al. (2005) found significantly lower serum magnesium concentrations among patients experiencing acute exacerbations of COPD ( $0.77 \pm 0.10$  mmol/L) compared to stable patients ( $0.91 \pm 0.10$  mmol/L), with a highly significant  $p$ -value ( $< 0.0001$ ), reinforcing the connection

between hypomagnesemia and disease severity (Aziz et al., 2005d). Additionally, Settu et al. (2022) demonstrated a comparable pattern, reporting that 48.3% of GOLD III and 66.7% of GOLD IV patients exhibited hypomagnesemia, further corroborating the observed trend that magnesium deficiency becomes more prevalent as COPD severity increases (Settu et al., 2023).

While the majority of studies point to an inverse relationship between serum magnesium and COPD severity, some findings have suggested more complex dynamics. For example, Gumus et al. (2014) noted that higher magnesium levels were unexpectedly associated with increased frequency of exacerbations. Such discrepancies may reflect differences in study design, population characteristics, or the timing of magnesium measurement (e.g., during exacerbation vs. stable phases), underscoring the need for further investigation.

Clinically, the strong association observed between hypomagnesemia and severe COPD stages highlights the potential role of magnesium as a biomarker for identifying high-risk patients. Routine screening and correction of magnesium deficiency in patients with advanced COPD could improve respiratory function, reduce exacerbation rates, and enhance overall disease management strategies.

## **5.2 Study Strengths**

This study has several notable strengths. It is the first at Moi Teaching and Referral Hospital (MTRH) to assess COPD severity using post-bronchodilator spirometry in line with GOLD guidelines. This represents a shift from previous reliance on clinical diagnosis alone, improving diagnostic accuracy and enabling objective classification of disease severity.

A key strength of this study is its focus on the association between hypomagnesemia and COPD severity, an area with limited research, particularly in sub-Saharan Africa. By generating local data on this relationship, the study adds valuable evidence suggesting hypomagnesemia may be linked to more severe stages of COPD.

The application of both bivariate and multivariate logistic regression allowed for a more accurate assessment of the relationship between hypomagnesemia and COPD severity. By adjusting for confounding variables such as age, sex, comorbid conditions, and medication use, the analysis strengthened the reliability of the observed association.

Conducted in a real-world hospital setting, the study reflects practical clinical realities and demonstrates the feasibility of integrating spirometry and serum magnesium testing into routine care. This provides practical insights for improving COPD management, especially in resource-limited settings.

Lastly, the findings offer a foundation for future research and may inform clinical guidelines, particularly regarding the potential role of magnesium monitoring in COPD care in low- and middle-income countries.

### **5.3 Study Limitations**

While this study offers important insights into the association between serum magnesium levels and COPD severity, several limitations should be considered when interpreting the findings:

1. **Cross-Sectional Design:** The study's cross-sectional nature limits the ability to infer causality. While an association between hypomagnesemia and severe COPD was observed, the direction or mechanism of this relationship cannot be determined.

2. **Single-Center Setting:** Conducted solely at Moi Teaching and Referral Hospital, the findings may not be generalizable to other populations or healthcare settings with different environmental, demographic, or clinical characteristics.
3. **Sample Size:** Although sufficient for analysis, the relatively small sample may limit statistical power and the ability to detect subtle associations. A larger and more diverse cohort could improve external validity.
4. **Unmeasured Confounders:** Despite multivariate adjustment, certain factors such as dietary magnesium intake, genetic factors, or undetected comorbidities may have influenced magnesium levels and COPD severity but were not assessed.
5. **Single-Time Magnesium Measurement:** Serum magnesium was measured at a single time point, which may not reflect long-term magnesium status. Serial measurements would provide a more reliable assessment.
6. **Medication and Comorbidity Effects:** Although common comorbidities and medications (e.g., diuretics, PPIs) were considered, their variable use and intensity may have influenced magnesium levels in ways not fully captured in the analysis.
7. **Selection Bias:** Participants were recruited from hospital-based clinics and wards, which may have led to overrepresentation of individuals with more advanced disease, limiting insights into earlier stages of COPD.
8. **Serum magnesium levels were not corrected for hypoalbuminemia,** which may have led to misclassification of true magnesium status in some participants.

## CHAPTER SIX

### 6.0 CONCLUSIONS AND RECOMMENDATIONS

#### 6.1 Conclusion

This study demonstrated a strong association between hypomagnesemia and advanced COPD severity, with all patients presenting with hypomagnesemia falling within GOLD stages III and IV. These findings suggest that hypomagnesemia may be linked to disease progression and could serve as a useful clinical marker of COPD severity.

A significant proportion of participants were also exposed to biomass smoke (99%), reinforcing its role as a major risk factor for COPD in low-resource settings. While tobacco smoking remains a recognized contributor, this study highlights the pressing need to address indoor air pollution from biomass fuels.

Although causality cannot be established, the results underscore the potential value of routine serum magnesium assessment in the clinical management of COPD. Early identification of hypomagnesemia may aid in risk stratification and guide more targeted care in affected populations.

#### 6.2 Recommendations

Based on this study's findings on the association between serum magnesium levels and COPD severity, the following recommendations are made:

1. Routine assessment of serum magnesium levels should be incorporated into the clinical evaluation of COPD patients, particularly those with severe disease, to enhance early identification of hypomagnesemia and support more comprehensive clinical decision making. Increased clinical vigilance for

magnesium deficiency may improve overall patient assessment, even though magnesium targeted therapeutic interventions were not evaluated in this study.

2. Public Education on Biomass Exposure: Given widespread biomass smoke exposure among participants, community programs should promote cleaner cooking methods, improved ventilation, and access to alternative fuels.
3. Further Research: Prospective studies, particularly randomized trials, are needed to determine whether magnesium correction improves COPD outcomes and should be integrated into treatment protocols.
4. At the policy level, the Ministry of Health should strengthen COPD prevention and diagnosis by mitigating key risk factors such as biomass fuel exposure and tobacco use, expanding access to diagnostic tools like spirometry, and enhancing healthcare worker training on updated COPD guidelines.

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## APPENDICES

### **Appendix 1: Consent (English)**

**Study Title: COPD SEVERITY AND ITS ASSOCIATION WITH SERUM MAGNESIUM LEVELS AMONG PATIENTS AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET.**

**Name of Principal Investigator(s): Dr. Qhalib Ali Abdi**

**Co-investigator(s): Prof. Lameck Diero**

**Name of Organization: MOI UNIVERSITY**

**Address: PO BOX 4606 – 30100 ELDORET    Telephone Number: 0790617151**

**Name of Sponsor/Funding Agency: Self-funded by the principal investigator**

#### **Informed Consent Form for:**

Patients with COPD Severity and Its Association with serum magnesium levels

#### **This Informed Consent Form has two parts:**

- Part I: Information Sheet [to share information about the study with you]
- Part II: Certificate of Consent [for signatures if you choose to participate]

### **PART I: INFORMATION SHEET**

#### **Introduction:**

You are being asked to take part in a research study. This information is provided to tell you about the study. Please read this form carefully. You will be given a chance to ask questions.

Taking part in this research study is voluntary. Saying no will not affect your rights to health care or any other services. Your treatment/payment or enrollment in any health plans or eligibility for benefits will not be affected if you decide not to take part. You are also free to withdraw from this study at any time. If after data collection you choose to quit, you can request that information provided by you be destroyed under

supervision. This would be before data is de-identified and aggregated. You will be notified if new information becomes available about the risks or benefits of this research. You will receive a copy of this form after it is signed

**Purpose of the study:** To determine COPD severity and its association with serum magnesium levels among patients at MTRH.

**Study site:** The study will be carried out at the medical wards (male and female), chest clinic and the medical outpatient clinic (MOPC) of Moi Teaching and Referral Hospital (MTRH).

**Study population:** All adult patients aged 40 years and above documented with history of COPD.

**Study procedures:** The principal investigator and the research assistant will recruit participants for the study from the chest clinic, medical outpatient clinic and the medical wards. The patients will then be approached for consent to participate in the study. Once the participants have consented, they will be taken through a structured COPD questionnaire and their files reviewed after which a spirometry test will be done.

On the other hand, the participants' files will be reviewed and a standardized questionnaire will be filled with their demographic information, history of COPD symptoms and signs, risk factors of COPD, medications the patient is on and history of comorbidities. Additionally, participants who are stable will be subjected to spirometry test while those who are unstable in acute exacerbation, spirometry will be done when they stabilize.

Spirometry test will be performed to all patients; those with previous spirometry diagnosis, those on follow up for possible COPD based on clinical presentation and new patients presenting with COPD symptoms. Spirometry will be conducted by a trained technician at MTRH lung function lab. The forced expiratory volume at 1

second (FEV<sub>1</sub>%), forced vital capacity (FVC) and FEV<sub>1</sub>/FVC ratio will be determined using a precalibrated Contec Sp10 spirometer machine. However, the patients who are not able to fulfill postbronchodilator FEV<sub>1</sub>/FVC ratio < 0.70 are excluded (Not COPD). Patients are then stratified based on FEV<sub>1</sub> into four categories (mild-GOLD 1, moderate-GOLD 2, severe-GOLD 3 and very severe-GOLD 4). Patient with confirmed COPD diagnosis based on postbronchodilator FEV<sub>1</sub>/FVC ratio < 0.70.

A sterile 10cc capacity syringe and an 18gauge needle will be used to draw sample from a cleaned and sterilized anterior cubital vein on your body. A tourniquet will be used to facilitate the collection of blood samples, and this may be associated with some feeling of pain. You may also experience some pain when your skin is punctured, and blood samples are drawn; which we do not expect to last for long. Approximately 4 cc of whole blood will be drawn and put in a red vacutainer bottle for magnesium, and Creatinine. Magnesium levels and creatinine levels will be analyzed by Cobas c 501 analyzer by Roche diagnostics.

**If you agree you will do the following:**

You will be required to answer some structured questions in form of questionnaires that will ask personal and sometimes emotional questions that you will be required to answer, should you wish not to answer some of the questions you can skip a particular section, and you may or may not provide a reason. No sample will be taken from you, no procedures will be done on you.

**Benefits:** This is a research project, and the findings may be used by the MTRH management, Government's policy makers and health providers to design appropriate policies and plans to provide better health services for COPD management. Your participation will help us to gain a better understanding of COPD severity and the effect of serum magnesium levels on COPD.

**Risks/Discomforts:** I am aware of the fact that some of the questions regarding research participation are not convenient to you. Everything you will tell me will be kept confidential. Under no circumstance will we link your name to the data during analysis and dissemination of the study findings.

**Payments and Reimbursements:**

There is no payment or reimbursement for participating in the study

**Confidentiality:** All reasonable efforts will be made to keep your protected information (private and confidential). Using or sharing (“disclosure”) of such information will follow National privacy guidelines. By signing the consent document for this study, you are giving permission (“authorization”) for the use and disclosure of your study information. We may need to share your protected information with the community advisory board, MTRH//MU-IREC, NACOSTI or the healthcare team. We will retain your research records for at least six years after the study is completed. At that time, the research information is destroyed [Inform the participant how the records will be destroyed]. If you decide to withdraw your permission for use of your personal data, contact the [PI] in writing and let them know your decision. At that time, we will stop further collection of any information about you. However, the health information collected before this withdrawal may continue to be used for the purposes of reporting and research quality.

**Compensation for injury:** In the event of an injury resulting from participating in this study, medical expenses will be covered for treatment of that injury.

## PART II: CONSENT OF PATICIPANT:

I have read or have had someone read to me the description of the research study. The investigator or his/her representative has explained the study to me and has answered all the questions I have at this time. I have been told of the potential risks, discomfort, and possible benefits (if any) of the study. I freely volunteer to take part in this study.

[This section must be written in the first person. If the participant is illiterate, or for some reason is unable to write, they should provide a thumbprint, and a competent witness must be engaged during the consent process]

|                                      |                                     |            |
|--------------------------------------|-------------------------------------|------------|
| _____                                | _____                               | _____      |
| Name of Participant                  | Signature of participant/Thumbprint |            |
| Date & Time                          |                                     |            |
| _____                                | _____                               | _____      |
| Name of Witness [Optional]           | Signature                           | of Witness |
|                                      | Date & Time                         |            |
| _____                                | _____                               | _____      |
| Name of the person obtaining consent | Signature of person                 |            |
|                                      | Date & Time                         |            |
|                                      | obtaining consent                   |            |
| _____                                | _____                               | _____      |
| Printed name of the investigator     | Signature of Investigator           |            |
|                                      | Date                                |            |

### **Contacts for questions about the study**

Questions about the study: I Contact Information

[Dr. Qhalib Ali Abdi 0790 617 151, qhalibaliabdi@outlook.com]

Questions about your rights as a participant: You may contact the Institutional Ethics and Research Committee (MTRH//MU-IREC) 0787723677 or email [irec@mtrh.go.ke](mailto:irec@mtrh.go.ke) or [irecoffice@gmail.com](mailto:irecoffice@gmail.com). The MTRH//MU-IREC is a group of people that review studies for safety and to protect the rights of participants.

## **Appendix 2: Consent (Swahili)**

### **Survey – Hati ya ridhaa**

*Lazima kusoma salamu hii kwa mshiriki wa utafiti, na kuendelea na mahojiano tu baada ya yeye kupeana ridhaa.*

Habari ya leo, madam/bwana. Jina langu ni Dr. Qhalib Ali Abdi. Mimi ni mwanafunzi wa shahada ya juu katika Chuo kikuu cha Moi, Eldoret; na leo ningependa kukusanya habari zaidi kuhusu utafiti unaoangazia Ugonjwa wa mapafu wa kudumu na uhusioano wake na madini ya magnesiamu. Pia tutapima damu kuangalia kiwango cha magnesiamu na kretini mwilini.

Nitakuuliza maswali kuhusu umri wako, makao yako, na kiwango cha elimu ya shule uliyotimisha; pamoja na hayo nitakusanya habari inayohusika na hali yako ya afya, na hali ya ugonjwa wako wa mapafu ya kudumu. Pia baadaye, tutafanya kipimo cha spirometry ambalo utaonyesha ugonjwa wa mapafu ya kudumu, pia kuweza kuwaainisha katika vitego tofauti na kufanya kipimo cha maabara. Ili kuwezesha kipimo cha maabara kuweza kutendeka, damu itatolewa kotoka kwa mishipa wa damu ambao unaonekana kwa rahisi. Mara nyingi mshipa wa damu ambao hutumika kutolea damu ni mshipa unaopatikana sehemu ya ungu wa kikukuu. Sindano yenye ukubwa wa kipimo cha 18, na yenye uwezo wa kubeba damu kiwango cha 4mls ndio itakayo tumika wakati wakutoa damu kwa ajili ya vipimo vya maabara. Nina tarajia yakuwa huenda uka hisi maumivu kiwango ndogo, ambayo sidhanii itakaa kwa muda mrefu, pindi damu itakapotolewa kwenye mshipa wa damu. Kifaa cha kusahilisha utowaji wa damu pia itatumika, na hii huenda itakufanya kuhisi mbano kwenye sehemu ya mwili ambayo kifaa hichi kilitumika. Huenda ukahisi maumivu pindi kifaa hichi kitatumika, lakini natumai maumivu haitaendelea kwa muda mrefu.

Mimi mpango wangu nikusajili wanaugua ugonjwa wa mapafu ya kudumu katika utafiti huu, kwa kipindi cha miezi 6. Taarifa zote zitakazokusanywa zitawekwa kwa hali ya siri.

### **Faida**

Huu ni mradi wa utafiti; na matokeo yanaweza kutumika na wasimamizi wa MTRH na watunga sera serikalini kwa mipango ya kutoa huduma bora, na kubuni sera mwafaka wa ajili ya matibabu wa ugonjwa wa mapafu ya kudumu. Ushiriki wako itatusaidia kupata uelewa vizuri wa uhusiano kati ya kiwango cha madini ya magnesiamu kwa mwili na ugonjwa wa mapafu ya kudumu.

### **Hatari**

Mimi nina fahamu yakuwa baadhi ya maswali kuhusu ushiriki katika utafiti huu si rahisi kwako. Kila utakachonieleza itakuwa siri. Hakuna wakati yeyote ambayo jina lako litambatanishwa pamoja na takwimu wa utafiti, iwe ni wakati wa uchambuzi au usambazaji wa matokeo ya utafiti huu. Kama utachagua kutoshiriki katika utafiti huu, haitakuathiri wewe kwa njia yeyote. Kama utakuwa na wasiwasi katika mwendo wowote wa utafiti huu, unaweza kuondoka wakati wowote. Pia hakuna malipo yoyote utapewa ili kushiriki katika utafiti huu. Lau utakubali kushiriki, itachukua dakika 15 kukamilisha mahojiano haya. Kama una maswali yoyote zaidi katika kipindi cha utafiti huu na katika siku zijazo, tafadhali usisite kuwasiliana na timu ya utafiti kwa kutumia namba za simu hapo chini.

**Tuendelee?** Ridhaa: Ndio.....Signature .....Date.....

La..... Signature .....Date .....

**Asante kwa kushirikiana nasi.**

Wasiliano wa timu ya utafiti,

Dr. Qhalib Ali Abdi,

Moi University, Eldoret

P.O Box 4606 -30100 Eldoret, Kenya

**Simu;** 0790617151; **Barua pepe:** qhalibaliabdi@outlook.com

**Appendix 3: Data Collection Form****DATA COLLECTION FORM****COPD QUESTIONNAIRE****Section A: Demographic Information and questions on COPD**

Patient no: \_\_\_\_\_ Age: \_\_\_\_\_ Gender: \_\_\_\_\_

County of Origin: \_\_\_\_\_

Educational level: \_\_\_\_\_

Occupation: \_\_\_\_\_

Mobile number of patient: \_\_\_\_\_

Mobile number of patients caretaker: \_\_\_\_\_

***Questions on COPD***

Duration of COPD: - \_\_\_\_\_

History of Smoking: -

-Current smoker/Ex-smoker \_\_\_\_\_ Non-smoker \_\_\_\_\_

-Amount of cigarette consumed per/day \_\_\_\_\_ Pack years \_\_\_\_\_

-Duration of cigarette exposure \_\_\_\_\_

History of use of biomass/ firewood smoke exposure: \_\_\_\_\_

Patient status: stable \_\_\_\_\_ Unstable (in exacerbation) \_\_\_\_\_

COPD symptoms: Increased Cough \_\_\_\_\_

Cough : \_\_\_\_\_

Shortness of breath : \_\_\_\_\_

Sputum purulence : \_\_\_\_\_

Wheeze : \_\_\_\_\_

**AECOPD symptoms & Signs**

Increased dyspnea : \_\_\_\_\_

Increased Sputum production : \_\_\_\_\_

Increased sputum purulence : \_\_\_\_\_

Increased wheezing : \_\_\_\_\_

Tachypnea : \_\_\_\_\_

Tachycardia : \_\_\_\_\_

Sign: Cyanosis : \_\_\_\_\_

Crepitations : \_\_\_\_\_

Reduced air entry : \_\_\_\_\_

Comorbidities: -Hypertension \_\_\_\_\_

-Diabetes mellitus \_\_\_\_\_

-Chronic Kidney Disease (CKD) \_\_\_\_\_

Current Medications: -

- LAMA \_\_\_\_\_

- LABA \_\_\_\_\_

- ICS \_\_\_\_\_

- Theophylline \_\_\_\_\_

- Thiazide diuretics/loop diuretics use \_\_\_\_\_

- Systemic steroids \_\_\_\_\_

- Others \_\_\_\_\_

**Section B: Anthropometric measures, Spirometry and Lab Results**

Patients number: - \_\_\_\_\_

Weight: \_\_\_\_\_ Height: \_\_\_\_\_ BMI: \_\_\_\_\_

Blood pressure: \_\_\_\_\_

Pulse: \_\_\_\_\_

Respiratory Rate: \_\_\_\_\_

SpO<sub>2</sub>: \_\_\_\_\_**Spirometry: pre-bronchodilator**FEV<sub>1</sub>: \_\_\_\_\_ FVC: \_\_\_\_\_

\_\_\_\_\_

FEV<sub>1</sub>/FVC RATIO: \_\_\_\_\_**Spirometry: post-bronchodilator (Albuterol 400ug)**FEV<sub>1</sub>/FVC RATIO: \_\_\_\_\_COPD GOLD class/severity based on FEV<sub>1</sub>: \_\_\_\_\_**Lab results:**

Creatinine: \_\_\_\_\_

Magnesium: \_\_\_\_\_

Patient's signature : \_\_\_\_\_

Health care worker signature : \_\_\_\_\_

#### Appendix 4: Budget

| No | Study Items                                           | Quantity                 | Cost per Unit in Kshs | Total cost     |
|----|-------------------------------------------------------|--------------------------|-----------------------|----------------|
| A  | Stationery and Equipment                              |                          |                       |                |
| 1  | Printing papers                                       | 7 reams                  | @ 400                 | 2,800          |
| 2  | Stapler and staples                                   | 1 and 1 Pkt respectively | @ 300 & 300           | 600            |
| 3  | Ball points                                           | 1 packet                 | @ 450                 | 450            |
| 4  | Pencils                                               | 5                        | @ 30                  | 150            |
| 5  | Erasers                                               | 5                        | @ 12                  | 60             |
| 6  | Notebooks                                             | 5                        | @ 50                  | 250            |
| B  | Development of Proposal                               |                          |                       |                |
| 7  | Printing of drafts                                    | 40 pages (x 8 copies)    | 10/page               | 3,200          |
| 8  | Printing & binding final                              | 3 copies                 | 600/copy              | 1,800          |
| C  | Fieldwork                                             |                          |                       |                |
| 9  | Phone and internet                                    | -                        |                       | 5,000          |
| 10 | Biostatistician consultations (statistician/Analysis) | -                        | -                     | 30,000         |
| 11 | Spirometry, test and Lab                              |                          |                       | 200,000        |
| 12 | Questionnaire printing, copies                        | 7 pages (x 200 copies)   | 2/copy                | 2,800          |
| 13 | Printing of draft thesis                              | 60 pages (x 10 copies)   | 10/page               | 6,000          |
| 14 | Final printing & binding (hard)                       | 7 copies                 | 800/ copy             | 5,600          |
| 15 | Contingencies (10%)                                   | -                        | @10%                  | 30,000         |
|    | <b>Grand Total</b>                                    |                          |                       | <b>288,710</b> |

## Appendix 5: Hospital Approval (MTRH)



### MOI TEACHING AND REFERRAL HOSPITAL

Telephone: (+254)-0532033471/2/3/4  
 Fax: 0532061749  
 Email: [ceo@mtrh.go.ke](mailto:ceo@mtrh.go.ke)/[ceosoffice@mtrh.go.ke](mailto:ceosoffice@mtrh.go.ke)

NANDI ROAD  
 P.O. BOX 3-30100  
 ELDORET, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

15<sup>th</sup> July, 2022

Dr. Qhalib Ali Abdi,  
 Moi University,  
 School of Medicine,  
 P.O. Box 4606-30100,  
 ELDORET-KENYA.

#### COPD SEVERITY AND ITS CORRELATION WITH SERUM MAGNESIUM LEVELS AMONGST PATIENTS IN MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA

You have been authorised to conduct research within the jurisdiction of Moi Teaching and Referral Hospital (MTRH) and its satellites sites. You are required to strictly adhere to the regulations stated below in order to safeguard the safety and well-being of staff, patients and study participants seen at MTRH.

- 1 The study shall be under Moi Teaching and Referral Hospital regulation.
- 2 A copy of MTRH/MU-IREC approval shall be a prerequisite to conducting the study.
- 3 Studies intending to export human bio-specimens must provide a permit from MOH at the recommendation of NACOSTI for each shipment.
- 4 No data collection will be allowed without an approved consent form(s) to participants unless waiver of written consent has been granted by MTRH/MU-IREC.
- 5 Take note that data collected must be treated with due confidentiality and anonymity.

The continued permission to conduct research shall only be sustained subject to fulfilling all the requirements stated above.

The approval period is 15<sup>th</sup> July, 2022 – 14<sup>th</sup> July, 2023.

*DR. WILSON K. ARUASA, MBS, EBS*  
 CHIEF EXECUTIVE OFFICER  
 MOI TEACHING AND REFERRAL HOSPITAL

c.c. - Senior Director, Clinical Services  
 - Director, Nursing Services  
 - HOD, HRISM



*All correspondence should be addressed to the Chief Executive Officer*

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## Appendix 6: IREC Approval



**MTRH/MU-INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)**  
MOI TEACHING AND REFERRAL HOSPITAL  
P.O. BOX 3  
ELDORET  
Tel: 33471/1/2/3

Reference: IREC/187/2022  
**Approval Number: 0004197**



MOI UNIVERSITY  
COLLEGE OF HEALTH SCIENCES  
P.O. BOX 4606  
ELDORET  
Tel: 33471/2/3  
14<sup>th</sup> July, 2022

Dr. Qhalib Ali Abdi,  
Moi University,  
School of Medicine,  
P.O. Box 4606-30100,  
**ELDORET-KENYA.**

Dear Dr. Qhalibi,

**COPD SEVERITY AND ITS CORRELATION WITH SERUM MAGNESIUM LEVELS AMONGST PATIENTS IN MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA**

This is to inform you that **MTRH/MU-IREC** has reviewed and approved the above referenced research proposal. Your application approval number is **FAN: 0004197**. The approval period is **14<sup>th</sup> July, 2022- 13<sup>th</sup> July, 2023**.

This approval is subject to compliance with the following requirements;

- i. Only approved documents including (informed consents, study instruments, Material Transfer Agreements (MTA) will be used.
- ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by **MTRH/MU-IREC**.
- iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to **MTRH/MU-IREC** within 72 hours of notification.
- iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to **MTRH/MU-IREC** within 72 hours.
- v. Clearance for export of biological specimens must be obtained from **MOH at the recommendation of NACOSTI** for each batch of shipment.
- vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
- vii. Submission of an executive summary report within 90 days upon completion of the study to **MTRH/ MU-IREC**.

Prior to commencing your study; you will be required to obtain a research license from the National Commission for Science, Technology and Innovation (NACOSTI) <https://oris.nacosti.go.ke> and other relevant clearances from study sites including a written approval from the CEO-MTRH which is mandatory for studies to be undertaken within the jurisdiction of Moi Teaching & Referral Hospital (MTRH) and its satellites sites.

Sincerely,

PROF. E. WERE  
CHAIRMAN



**INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE**

|    |           |   |      |      |   |     |      |   |     |
|----|-----------|---|------|------|---|-----|------|---|-----|
| cc | CEO       | - | MTRH | Dean | - | SOP | Dean | - | SOM |
|    | Principal | - | CHS  | Dean | - | SON | Dean | - | SOD |

## Appendix 7: NACOSTI Approval

|                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  <p>REPUBLIC OF KENYA</p> <p><b>Ref No: 556426</b></p>                                                                                                                                                                                |  <p><b>NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY &amp; INNOVATION</b></p> <p><b>RESEARCH LICENSE</b></p> <p><b>Date of Issue: 28/07/2022</b></p> |
| <p><b>This is to Certify that Dr. CHALIB ABU of Moi University, has been licensed to conduct research in Uasin-Gishu on the topic: COPD SEVERITY AND ITS CORRELATION WITH SERUM MAGNESIUM LEVELS AMONGST PATIENTS IN MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA, for the period ending : 28/July/2023.</b></p> |                                                                                                                                                                                                                                       |
| <p><b>License No: NACOSTI/P/22/19183</b></p>                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                       |
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| <p><b>Verification QR Code</b></p>                                                                                                                                                                                                |                                                                                                                                                                                                                                       |
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THE SCIENCE, TECHNOLOGY AND INNOVATION ACT, 2013

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### CONDITIONS

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3. The Licensee shall inform the relevant County Director of Education, County Commissioner and County Governor before commencement of the research
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