Osteoporosis and associated factors among patients with chronic obstructive pulmonary disease

By:

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Abstract

***Background*:** Osteoporosis is one of the systemic features of chronic obstructive pulmonary disease, and its prevalence is assumed to be two -to five -folds higher than in age and sex matched healthy subjects.

***Objective*:** This study was designed to assess the prevalence of osteoporosis and associated factors among patients with chronic obstructive pulmonary disease attending in chest clinic of Jimma University Specialized Hospital, South West Ethiopia

***Methods*:** In this cross-sectional study, we conducted dual-energy X-ray absorptiometry bone mineral density scan of the lumbar spine (2—4) for three repetitive measurements and collected data from patient's medical chart (doses and frequency of corticosteroid therapy), and other potential factors via structured questionnaires. Data was processed and analyzed using statistical package for social sciences (SPSS) version 21. Binary logistic regression was used to control the confounders, and the strength of the association was expressed in adjusted odds ratio (AOR**)** with 95% confidence interval (CI). Finally, an association with p-value < 0.05 was considered as statistically significant.

***Results*:** Among 80 -patients with chronic obstructive pulmonary disease evaluated; the prevalence of osteoporosis was found to be 33 (41.3%). Further, two variables such as; smoking cigarette [AOR= 4.949; 95% CI: 1.323, 18.508] and doses of corticosteroid therapy [AOR= 4.768; 95% CI: 1.258, 18.065] were found to be significantly associated with osteoporosis (p-value < 0.05).

***Conclusion*:** This study comes with high prevalence of osteoporosis among patients with chronic obstructive pulmonary disease in Jimma University Specialized Hospital. Factors such as smoking cigarette and doses of corticosteroid therapy were found to be significantly associated with osteoporosis.

Key words: Prevalence, DEXA, BMD, T- score, osteoporosis, COPD, Ethiopia

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I would like to give my heartfelt thanks to my respectful advisors Dr. Elsah Tegene and Mr. Samuel Tadesse for their professional, compassionate comments, valuable supports throughout my study and without their support this thesis would not have come to completion. Finally, I would like also to express my appreciation to chest clinic and radiology department staffs of JUSH, for their cooperation and assistance in giving relevant information.

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Abbreviation/Acronomy

BMI: Body Mass Index

BMC: Bone Mineral Content

BMD: Bone Mineral Density

COPD: Chronic Obstructive Pulmonary Disease

DEXA: Dual Energy X-ray Absorptiometry

FEV1: Forced Expiratory Volume in 1 second

FVC: Forced Vital Capacity

GOLD: Global initiative for chronic Obstructive Lung Disease

JUSH: Jimma University Specialized Hospital

NIH: National Institute of Health

OPG: Osteoprotegerin

PDXA: Peripheral Dual Energy X-ray Absorptiometry

PQCT: Peripheral Quantitative Computed Tomography

QCT: Quantitative Computed Tomography

QUS: Quantitative Ultrasound

RA: Radiographic Absorptiometry

RANK: Receptor Activator of Nuclear Factor-Kappa B

RANKL: Receptor Activator of Nuclear Factor-Kappa B Ligand

SXA: Single Energy X-ray Absorptiometry

WHO: World Health Organization

WNT: Wingless tail signaling pathway

1. INTRODUCTION

1.1. Background of the study

World Health Organization (WHO) defined osteoporosis as "a state of disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and consequent increase in fracture risk". Fractures of the hip, vertebrae and forearm are the most common fractures in patients with osteoporosis, although fractures of other body parts can also be the result of osteoporosis [1].

Osteoporosis should not be confused with osteomalacia. In osteomalacia, there is a decrease in the amount of Ca^{2+} per unit of bone matrix or characterized by deficient calcification of recently formed bone and partial decalcification of already calcified matrix. However, in osteoporosis, frequently found in immobilized patients and in postmenopausal women, is an imbalance in skeletal turnover so that bone resorption exceeds bone formation [2].

Bone mineral density (BMD) is the standard tool used to diagnose osteoporosis. Several methods of imaging have been developed to measure BMD, including dual energy X-ray absorptiometry (DEXA), quantitative computed tomography (QCT), peripheral dual energy X-ray absorptiometry (pDXA), single energy X-ray absorptiometry (SXA), peripheral quantitative computed tomography (pQCT), radiographic absorptiometry (RA) and quantitative ultrasound (QUS). However, DEXA- scan is considered as the gold standard methods used to diagnose osteoporosis [3]. The WHO guidelines for the diagnosis of osteoporosis are based on DEXA measurements of the hip or spine [4]. This test is capable of measuring bone mineral content (BMC) at any site in the body, but usually is used at central sites (the lumbar spine and the proximal femur) and peripheral sites including the distal forearm [5]. This is accomplished by passing two -beams of different energies through the site of bone being measured. The major advantage of DEXA is that it exposes the patient to radiation levels approximately 90 % less than a standard chest radiograph [6]. The unit of measurement for BMD with the use of DEXA is areal density (g/cm^2); however, it is reported as T-score on the basis of this measurement. Peripheral DEXA techniques analyze BMD at the distal radius and calcaneus with high precision and low radiation exposure. But, these measurements are less useful in predicting the risk of fractures of the spine and proximal femur than spinal and hip of central sites. A low BMD value obtained by peripheral techniques is not

sufficient for a diagnosis or for making treatment decisions, but it does warrant further assessment. In addition, peripheral sites are less likely than central sites to show an increase in BMD in response to treatment [7].

Chronic obstructive pulmonary disease (COPD) has been defined by the Global initiative for chronic Obstructive Lung Disease (GOLD), as "a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by a progressive airflow limitation that is not fully reversible and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases" [8].

Smoking cigarette, indoor and outdoor air pollutants, occupational dusts and chemicals, genetic factors, respiratory infections and others are possible risk factors of COPD; however, cigarette smoking is the primary cause of COPD. Therefore, health education can play a role in improving skills, ability to cope with illness, and health status. It is effective in accomplishing certain goals, including smoking cessation [9].

Chronic obstructive pulmonary disease includes: emphysema, an anatomically defined condition characterized by destruction and enlargement of the lungs alveoli; chronic bronchitis, a clinically defined condition with chronic productive cough and phlegm; and asthma is "a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variably, airflow obstruction within the lungs that is often reversible either spontaneously or with treatment" [10,11].

A medical history and physical examination may suggest COPD, but they are not reliable predictors of airflow obstruction; the diagnosis must be confirmed with the use of spirometry. Airflow obstruction as measured by spirometry is defined as a ratio of the forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) of less than 0.70 [12].

According to the GOLD, the cut –off values of the stages and severity of COPD can be stratified as; stage I — mild COPD: FEV1/FVC < 0.70, FEV1 ≥ 80% of predicted value; stage II — moderate COPD: FEV1/FVC < 0.70, 50% ≤ FEV1 < 80 % of predicted value; stage III — severe

COPD: FEV1/FVC < 0.70, 30 % ≤ FEV1 < 50 % of predicted value; stage IV— very severe COPD: FEV1/FVC < 0.70, FEV1 < 30% of predicted or FEV1 < 50% of predicted value plus chronic respiratory failure. I.e. respiratory failure: arterial partial pressure of oxygen less than 60 mm Hg with or without arterial partial pressure of CO_2 greater than 50 mm Hg while breathing air at sea level [13].

Forced vital capacity (also known as the forced expiratory volume) is the maximal volume of air exhaled with a maximally forced effort from a position of full inspiration and is expressed in liters. FEV1 is the maximal volume of air exhaled in the first second of a forced exhalation that follows a full inspiration, expressed in liters. The FEV1 reflects the average flow rate during the first second of the FVC maneuver. The FEV1 is the most important spirometric variable for assessment of the severity of airflow obstruction. The FEV1/FVC ratio is the fraction of the FVC that can be exhaled in the first second. It is the most important parameter for detecting airflow limitation in diseases like asthma and COPD. However, once it has been determined that a patient has airways obstruction, the FEV1/FVC ratio is not useful for gauging severity of disease, since the FVC also tends to decrease with increasing obstruction. The FEV1, not the FEV1/FVC ratio, should be used to monitor patients with asthma or COPD [14].

Chronic obstructive pulmonary disease patients benefit from exercise training programs, improving with respect to both exercise tolerance and symptoms of dyspnea and fatigue. Bronchodilator medications (β_2-agonists, anticholinergics, theophylline, and a combination of these drugs) are central to the symptomatic management of COPD. They are given on an as-needed basis or on a regular basis to prevent or reduce symptoms. Combining bronchodilators may improve efficacy and decrease the risk of side effects compared to increasing the dose of a single bronchodilator. Inhaled corticosteroids combined with a long-acting β_2-agonist are more effective than the individual components. Chronic treatment with systemic glucocorticosteroids should be avoided because of an unfavorable benefit-to-risk ratio of osteoporosis [15—23].

Some of the factors for osteoporosis in COPD patients are; life style, sex, advanced age, low body weight, smoking cigarette, nutritional deficiencies, chronic corticosteroid therapy and endocrinological disorders like hyperthyroidism and primary hyperparathyroidism [24,25].

In COPD patients, the prevalence of osteoporosis is assumed to be two -to five -folds higher than in age and sex matched healthy subjects [26,27]. Further, in a recently developed screening tool for factors of osteoporosis, the presence of COPD is one of the parameters increasing the risk almost four times [28].

The treatment of osteoporosis aims at fracture prevention and, according to the WHO, should consist of lifestyle modification (such as smoking cessation, weight-bearing physical exercise and adequate calcium intake) and anti-osteoporotic therapy. The latter should consist of bisphosphonates, calcium supplementation (in the case of low dietary intake) and vitamin D supplementation (in the case of vitamin D deficiency). Especially in COPD patients it is important to prevent vertebral fractures since they might result in a decreased forced vital capacity [29].

1.2. Statement of the problem

Osteoporosis is one of the most common public health problems in adults and older people worldwide [30]. It is a common silent disease affecting both women and men over the age of 50 years. A significant number of clinical symptoms associated with osteoporosis become evident only after the occurrence of hip, vertebral, or wrist fractures. These fractures lead to many problems such as mortality, morbidity, and economic problems to individuals and the society [31].

Chronic obstructive pulmonary disease is the most prevalent and major causes for morbidity and mortality throughout the world, and results a socioeconomic burden [32]. In 2005 WHO estimated that, 5% of all deaths worldwide were caused by COPD. This equates to 3- million people [33]. Currently, it is the fourth leading cause of death in the world and projected to be the third leading cause of death by 2030 [34] and its global prevalence is from 9 ─10% in adults of 40 years and older [35].

One of the main causes for COPD is tobacco consumption. The prevalence of tobacco use in Africa is 8─ 43% for men and 5─30% for women and there are intensive efforts by the tobacco industry to expand African markets, consequently the rate of COPD is rising in Africa [36]. But, there is no documented number in Africa including Ethiopia.

Chronic obstructive pulmonary disease is a progressive disease of adulthood and older age. While the initial treatment is focused on relieving the symptoms due to the impairment of the lung function, a variety of systemic effects become obvious as the disease progresses [37]. One of the systemic effects of COPD is osteoporosis, but debates continue on the precise mechanisms involved and on the options for treatment [38]. The etiology of osteoporosis in COPD is probably complex and various factors may contribute to its pathogenesis. Some of these are the consequences of the chronic inflammatory lung disease and lung damage (reduced physical activity due to dyspnea, reduced skeletal muscle mass and changes in body composition, systemic inflammation), of the therapy used during the disease (corticosteroid treatment), and of the natural changes due to ageing (hypogonadism, reduced muscle mass, inactivity). Environmental factors and habits from earlier in life also contribute to the pathogenesis of osteoporosis. When fractures

occur as a complication of osteoporosis the quality of life of such patients, who are already restricted because of the lung disease, is further reduced [39].

So far there are no published studies in Ethiopia on the burden of osteoporosis, although factors predisposing to the condition are prevalent (nutritional deficiency, coffee consumption.) As studies conducted throughout different countries suggest that, prolonged daily overdose of corticosteroid therapy and COPD itself in these patients also contribute for osteoporosis. Therefore, the overall objective of this cross-sectional study aims to assess the prevalence of osteoporosis and associated factors among patients with COPD attending in chest clinic of JUSH, South West Ethiopia.

2. LITERATURE REVIEW

2.1. Prevalence of osteoporosis among patients with COPD

A recent systematic review reported that, the prevalence of osteoporosis and osteopenia can vary from 9–69% and 27–67% respectively, and the overall mean prevalence of osteoporosis and osteopenia, was 35.1% and 38.4%, in COPD patients respectively [40].

A cross-sectional study conducted in Brazil, 2011 reports that, out of 95 –COPD patients the prevalence of osteoporosis, osteopenia and normal bone mass, were 42%, 42% and 16%, respectively. A similar study done in Denmark, 2007 states that, out of 58 –patients, the prevalence of osteoporosis were 44.8% and osteopenia were 22.3% in severe COPD patients and 25.9% had normal bone mass [41, 42].

A cross-sectional study done in Netherland, 2011 shows that, out of 255 –COPD patients the prevalence of osteoporosis based on DEXA was 23.6%. Different study design, but the same country, in 2009 revealed that, from 554 –COPD patients, the prevalence of osteoporosis was 21% and osteopenia was 41% in COPD patients [43, 44].

A case –control study done in Iran, 2004 shows that, the frequency of osteoporosis in COPD patients and control groups were 52% and 8%, respectively [45].

2.2. Factors associated with osteoporosis among patients with COPD

Several studies done in different parts of the world demonstrated that sex and advanced age, treatments with prolonged daily overdoses of corticosteroid for COPD exacerbations, predisposing life style conditions and nutritional factors were associated with osteoporosis.

2.2.1. Socio-demographic factors

In women, accelerated bone loss usually begins after monthly menstrual periods stop, when a woman's production of estrogen slows down (usually between the ages of 45 and 55). In men, gradual bone thinning typically starts at about 45 to 50 years of age, when a man's production of testosterone slows down. Women are usually affected at an earlier age than men, because they start out with lower bone mass [46].

2.2.2. Lifestyle factors

Physical inactivity is an important modifiable risk factor for osteoporosis, and several studies have suggested that exercise can prevent bone loss. Studies done in UK, 2003 and Australia, 2000 have shown that doing any physical exercise, such as lifting weights two or three times a week was associated with the development of osteoporosis [47,48].

A cross-sectional study done in Austria, 2009 have shown that, chronic heavy alcohol use, especially during adolescence and young adult years by interfering calcium absorption, can dramatically affect bone health and increase the risk of osteoporosis later in life [49].

A meta-analysis, 2001 demonstrated that tobacco smoking had a cumulative, dose-dependent independent effect on bone mass. Smokers had significantly reduced bone mass compared with non-smokers at several major sites of osteoporosis-related fractures, including the hip, lumbar spine, and forearm [50].

A study done in UK, 2005 was shown that, cigarette smoking is a risk factor for the development of osteoporosis [51]. However, other studies from Brazil, 2011 and Iraq, 2004 were revealed that, the amount of cigarette smoking is not associated with osteoporosis [41,45].

A study done in UK, 2005 was implied that caffeine increases urinary calcium output and has been implicated as a risk factor for osteoporosis that leads to hip fracture, while other research in California, 2002 have indicated that the effect of caffeine on bone mineral density is because of the interaction between cigarette and alcohol abuse [51,52].

2.2.3. Anthropometric factors

Studies conducted in USA, 2000; 2004 and Korea, 2004 have reported that high BMI (above 30 kg/m^2) has a protective effect for both men and women; in contrast low BMI less than 19 kg/m^2 can lead to osteoporosis [53—55].

2.2.4. Drug related factors

Research conducted in UK, 2000 have showed that, patients using daily dose of oral corticosteroids were strongly related to BMD. The risk of both hip and vertebral fractures was approximately doubled in patients using high daily doses ($\geq$ 7.5 mg corticosteroid) compared with those using low dose (< 2.5 mg corticosteroid) [56].

2.2.5. Nutritional factors

A study done in USA, 2007 indicate that higher fruit intake was found to be significantly associated with higher BMD in both sexes, however higher vegetable consumption has no positive impact on BMD [57]. Other studies conducted in UK, 2004 and USA, 2005 have revealed that consumption of more fresh fruits and vegetables are unlikely to be detrimental to bone health and may be beneficial [58,59].

Studies conducted in Iran, 2000; India, 2010; UK, 2001; and USA, 2003 have reported that the positive associations between earlier milk consumption or calcium intake and BMD. The milk's main selling point is calcium, and milk-drinking is touted for building strong bones in children and preventing osteoporosis in older persons [60—63].

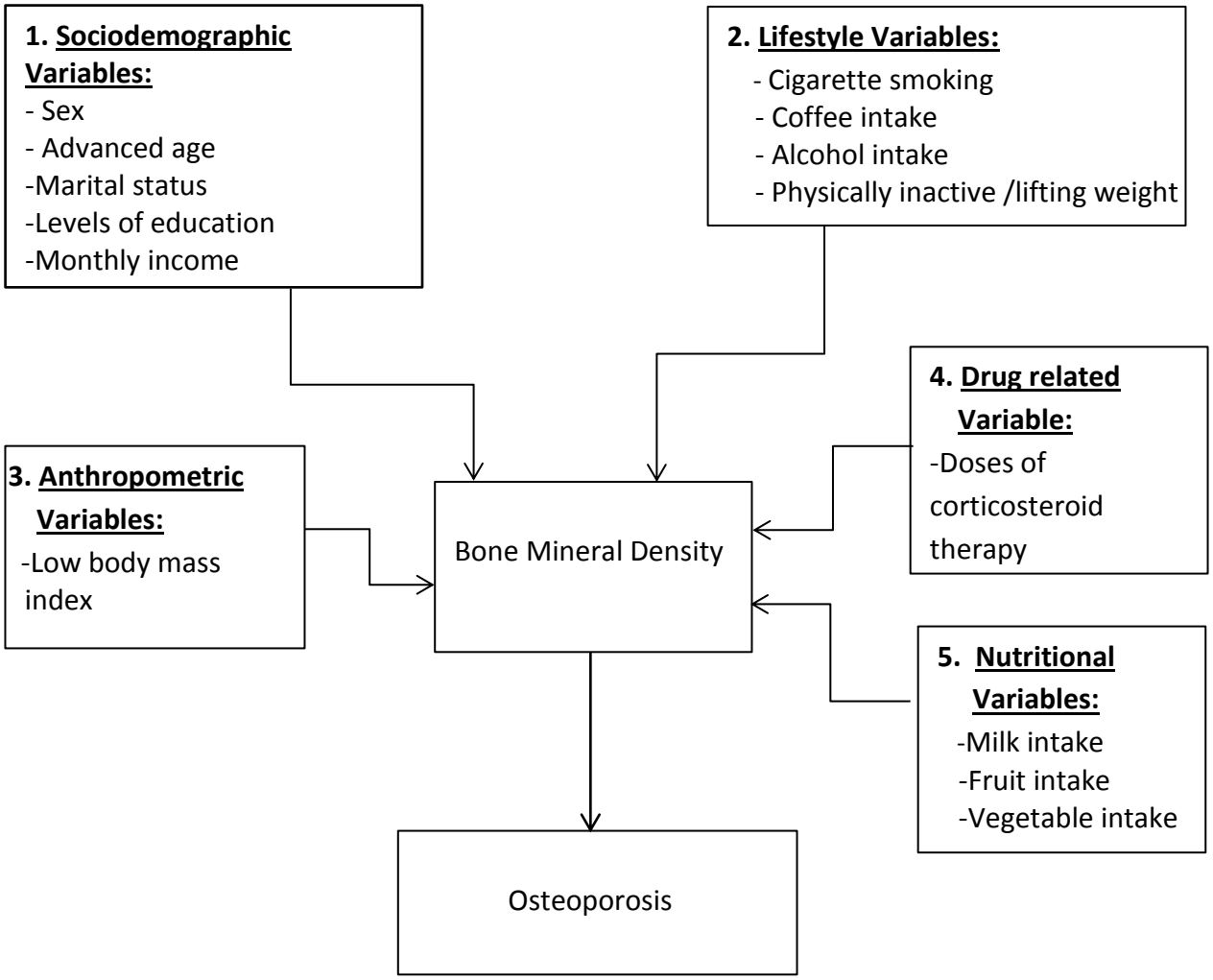

Figure 1: Conceptual framework of osteoporosis and associated factors among patients with chronic obstructive pulmonary disease

2.3. Significance of the study

This study was aimed to assess the prevalence of osteoporosis and associated factors among patients with COPD. So, the implication of information obtained from this study may guide health policy makers to intervene in a way to decrease factors related to osteoporosis and help for practice improvement especially on the area of prescription of drugs and its effect. To create public awareness on factors associated with osteoporosis and help programmers to give attention and work in this area. As well help researchers as benchmark to do further in this area.

3. OBJECTIVES

3.1. General objective

To assess the prevalence of osteoporosis and associated factors among patients with chronic obstructive pulmonary disease attending in chest clinic of JUSH, South West Ethiopia from March 15─ May 15, 2015

3.2. Specific objectives

- To determine the prevalence of osteoporosis among patients with COPD attending in chest clinic of JUSH, South West Ethiopia
- To identify factors associated with osteoporosis among patients with COPD attending in chest clinic of JUSH, South West Ethiopia

4. METHODS AND MATERIALS

4.1. Study area and period

Study was conducted from March 15 ─ May 15, 2015 in chest clinic of JUSH. Jimma is located 357 km far from Addis Ababa. Currently, JUSH is the only teaching and referral hospital in southwestern part of the country. It provide services for approximately 9,000 inpatient and 80,000 outpatient attendances a year coming to our hospital from the catchment populations of about 15 million people. Chest clinic is one of the many chronic follow-up clinics of the hospital, which gives service once weekly on Thursday. The service is given by internists, medical residents, medical interns, and general nurses [64].

4.2. Study design

A cross-sectional study was designed to assess the prevalence of osteoporosis and associated factors among patients with COPD attending in chest clinic of JUSH, South West Ethiopia from March 15─ May 15, 2015

4.3. Population

4.3.1. *Source population*

All patients with restrictive and obstructive lung disease attending chest clinic of JUSH

4.3.2. *Study population*

Patients with COPD who were attending in chest clinic during data collection period and fulfill the inclusion criteria

4.4. Inclusion and exclusion criteria

4.4.1. *Inclusion criteria*

Patients were included in the study if they

- have a ratio of [FEV1] to [FVC] < 0.7 and adequate medical records
- were attending in the previous one-year

4.4.2. *Exclusion criteria*

Patients were excluded from the study if they

- have no adequate medical records
- are menopausal women
- are people with endocrine disorders
- are ovarian and testicular problems

- are taking anti-inflammatory medications other than corticosteroids
- are taking anti-allergy medications
- are taking immunosuppressant drugs

4.5. Sample size determination and sampling technique

4.5.1. *Sample size determination*

In this study, the sample size was determined based on the total number of target population attending chest clinic, in JUSH in the year 2013/14 G.C. According to the existing data available, the hospital had a total of 100 -COPD patients in one -year. By considering this number as a target population, the total sample size of the study was determined by using *Yamane Taro*, 1967 equation.

$$n = \frac{N}{1 + N e^2}$$

Therefore, the required sample size at 95% confidence interval with 5% degree of precision was;

$$\boldsymbol{n} = \frac{100}{1+100\ (0.05)^2} = 80$$ + 5% non-response rate => 84

Where: -**N**= target population

n = sample size

e= level of precision (sampling error)

Five percent of the calculated sample size was considered for non-response rate and the total sample size adjusted to 84 -COPD patients.

4.5.2. *Sampling technique*

Simple random sampling technique was used to select the study participants through computer generated random number methods. First a complete listing of all COPD patients was done from 1—100, and then applying a computer generated random number method to select 84- study population without replacement. So, all COPD patients included in the sample have equal chances of being selected in the sample.

4.6. Data collection procedure and personnel's

4.6.1. *Data collection procedures*

After identifying the study participants and obtaining verbal consents, face to face interview was started by using pre-tested structured questionnaires to assess associated factors like; socio-demographic, lifestyle, nutritional intake and anthropometric variables. Anthropometric variables were calculated by weight of the subject in kilogram divided by the height of the subject in meter square. Moreover, patient's drug related factors; dose and frequencies were collected from their medical card.

The gold standard dual energy X-ray absorptiometry scanner (DEXA, QDR 4500A, Hologic, Bedford, MA, Spain) was used to measure the amount of BMCs, expressed in gram and divided by the area of the bone being scanned, expressed in centimeter square. After three- repetitive measurements, the average BMD values of each lumbar spine were calculated to acquire a definite BMD. First patients lie on DEXA -scan and the scanner passes over lumbar spine. The mean BMD value of the patient's 2^{nd}, 3^{rd} and 4^{th} lumbar spine was collected. For categorization, the WHO standard was applied. T-score > −1 was considered as normal BMD, T-score between −1 and −2.5 was considered as osteopenia and T- score ≤ −2.5 was osteoporosis [4].

$$\text{BMD} = \frac{\text{Amount of bone mineral contents (g)}}{\text{Area of the bone being measured (cm}^2\text{)}}$$

$$\text{T –score} = \frac{\text{Patient's measured BMD — Age and sex matched healthy young adult mean BMD}}{\text{Age and sex matched healthy young adult standard deviation}}$$

4.6.2. *Data collection personnel's*

Data from structured questionnaires were collected by trained nurses, who were working at chest follow-up clinic. BMD results were collected by trained radiographers selected from radiology clinic of JUSH. Training was given for 2-days before starting data collection for data collectors. The training was focused on the objectives of the study, data collection instruments and procedures, and also confidentiality of the information. In addition the principal investigator was supervised the overall activities during data collection.

4.7. Data quality assurance

The quality of the data was assured by using validated pre-tested questionnaires, and calibrated DEXA -scan machine. First data collection tool developed by English and translated to Amharic and Afan-Oromo and back translated to English to see its consistence, then pre-testing was done on **10**% of the total study population at radiology and chest clinic of JUSH. Data collectors were intensively trained for 2 -days on the data collection instruments and procedures. They were also acquainted about the relevance and objectives of the study, and confidentiality of the information. To ensure adherence, to correct data collection procedures and completeness of data, the investigator reviewed the collected data every week.

4.8. Study variables

4.8.1. *Dependent variables*

- Osteoporosis
- Osteopenia

4.8.2. *Independent variables*

- Sex
- Advanced age
- Marital status
- Educational status
- Monthly income
- Physically inactive
- Low body mass index
- Milk intake
- Fruit intake
- Vegetable intake
- Cigarette smoking
- Coffee intake
- Alcohol intake
- Doses of corticosteroid therapy

4.9. Operational definitions

Advanced age: In this study, patient's ≥ 50 years of age is considered as advanced age, on the other hand < 50 years of age is normal.

Osteomalacia: A state of disease characterized by deficient calcification of recently formed bone and partial decalcification of already calcified matrix or decrease in the amount of Ca^{2+} per unit of bone matrix [2].

Bone mineral content: Is defined as the amount of bone mineral contained within the skeletal mass, measured in gram [4].

Bone mineral density: Is defined as the amount of bone mineral content divided by the area of the bone being scanned, measured in g/cm^2 [4].

Normal bone mineral density: T-score is: > -1.0 [4].

Osteopenia: A condition in which, bone mineral density is lower than normal. It is considered as the preclinical stage of osteoporosis. T-score is: between –1.0 and –2.5 [4].

Osteoporosis: T-score is: ≤ -2.5 [4].

Chronic obstructive pulmonary disease (COPD): A chronic lung disease of which, a lung volume ratio of forced expiratory volume in 1 -second to forced vital capacity is considered as < 0.7 [8].

According to the GOLD, the cut –off values of the stages and severity of COPD can be stratified as;

Stage –I: Mild –COPD ----------FEV1 ≥ 80% of predicted values.

Stage –II: Moderate –COPD ----------50 ≥ FEV1 < 80% of predicted values.

Stage –III: Severe –COPD ----------30 ≥ FEV1 < 50% of predicted values.

Stage –IV: Very severe –COPD ----------EV1 < 30% of predicted values [13].

Forced expiratory volume in one second (FEV1): Is the maximal volume of air exhaled in the first second of a forced exhalation that follows a full inspiration, expressed in liters [14].

Forced vital capacity (FVC) (also known as the forced expiratory volume): Is the maximal volume of air exhaled with a maximally forced effort from a position of full inspiration, expressed in liters [14].

Physically inactive/ lifting weight: Patients who engaged in any physical exercise for < 3 hours/week are considered as physically inactive, in contrast ≥ 3 hours/week are physically active [47].

Alcohol intake: In this study, excess alcohol consumption is defined as an intake of any liquor (one bottle of beer, a glass of wine, spirits, fermented cider, Tella or Tej (Local beer)) >2 drinks/ day, in contrast ≤ 2 drinks/day is considered as normal [49].

Cigarette smoking: High cigarette smoking is defined as consumption of >20 packs of cigarette/ year, on the other hand ≤ 20 packs of cigarette/year are considered as normal [50].

$$\text{Pks of cigarette/}year = \frac{\text{average № of packs of cigarette smoked}}{\text{day}} \times \text{total № of years of smoked}$$

Coffee intake: Excess coffee consumption is defined as an intake of > 2 cups/day (70 ml), however ≤ 2 cups/day is normal [52].

Body Mass Index (BMI): The cut offs for BMI is based on the WHO criteria, where underweight is defined as a BMI < 18.5 kg/m^2, normal weight BMI between 18.5—24.9 kg/m^2, BMI between 25—29.9 kg/m^2 is over-weight, and obesity is defined as BMI ≥ 30 kg/m^2 [53].

Doses of corticosteroid therapy: High doses of corticosteroid is defined as an intake of > 7.5 mg/day, however ≤ 7.5 mg/day is normal [56].

Fruit intake: Less fruit intake is defined as ingestion of fruits like; orange, banana, etc. ≤ 4 times/ week, though > 4 times/week is normal [58].

Vegetable intake: Less vegetable intake is defined as ingestion of vegetables like; cabbage, spinach etc. ≤ 4 times/week, whereas > 4 times/week is normal [59].

Milk intake: Less milk intake is defined as consumption of milk ≤ 4 glasses/week, however > 4 glasses/week is normal [63].

4.10. Data analysis and interpretation

Data were entered in to Epi info version 3.5.3, checked, edited and then exported to statistical package for social sciences (SPSS) version 21 for analysis. Descriptive statistics including frequencies, percentages, mean and standard deviations were used to describe findings. In bi-variate analysis; simple-crosstab and chi –square test was conducted to see the existence of association between the dependent and independent variables. Those variables with **p-value < 0.25** were considered as a candidate for the final model. In multi-variate analysis; binary logistic regression analysis was used to control confounders, and the strength of the association was expressed in adjusted odds ratio **(AOR)** with **95**% confidence interval (CI). Finally, an association with **p-value < 0.05** was considered as statistically significant.

4.11. Ethical consideration

Ethical clearance was obtained from Ethical Committee of Jimma University College of Health Sciences. The willingness and verbal informed consent were obtained from all study participants before inclusion into the study.

4.12. Dissemination plan

The findings of the study will be submitted to Jimma University postgraduate studies office and Department of Biomedical Sciences, the Hospital Medical Director and Health Providers. Further it will be published on national or international reputable journals.

5. RESULTS

5.1. Socio-demographic variables of respondents

Out of the total 84 -sampled COPD patients attending in chest clinic of JUSH, four -patients had no a complete medical records. Hence 80 -COPD patients were included in the analysis and making a response rate of 95%. Majority of the study participants were male 54 (67.5%), within the age group of (≥ 60 years) 51 (63.8%), married 70 (87.5%), illiterate 40 (50%), merchant 36 (45%), orthodox in religion 35 (43.8%), Oromo in ethnicity 50 (62.5%), and monthly income within range of (< 1000 Eth. birr) 45 (56.3%). [**Table- 1**]

The (mean±SD) of patient's age, monthly income, height and weight were 52.56 ±11.058, 998.25 ±46.32, 1.6266 ±0.03965 and 52.99 ±4.632, respectively. The (mean±SD) of patient's BMD results of lumbar spine-2, lumbar spine-3, and lumbar spine-4 were 1.8748 ±0.75563, 1.8754 ±0.75504 and 1.8774 ±0.75457, respectively. Further, their (mean ±SD) of average BMD results of lumbar spine and T-scores of lumbar spine (L2—L4) were 1.8756 ±0.75532 and −1.82 ±1.90, respectively. [**Table- 2**]

As of lifestyle, anthropometric, nutritional and doses of drug related variables**;** majority of the patients 49 (61.3%) smoked greater than 20 -packs of cigarette per year**,** 54 (67.5%) consumed greater than 2 -cups of coffee per day**,** 47 (58.8%) took greater than 2 -drinks of alcohol per day, 53 (66.3%) took greater than 7.5 mg of corticosteroid per day**,** 50 (62.5%) consumed less than or equal to 4 –times of fruits per week**,** 57 (71.3%) eaten less than or equal to 4 –times of vegetables per week**,** 51 (63.8%) took less than or equal to 4 –glasses of milk per week**,** 34 (42.5%) were underweight in BMI, 62 (77.5%) engaged in any physical exercise for less than 3 -hours per week and, 23 (28.8%) had moderate and severe COPD. [**Table- 3**]

Table1: Socio-demographic variables of patients with COPD attending in chest clinic of JUSH, South West Ethiopia from March 15 ─ May 15, 2015, n= 80

Variables	Categories	n (%)
Sex	Male	54 (67.5)
	Female	26 (32.5)
Age (year**)**	< 50	22 (27.5)
	50 – 59	28 (35)
	≥ 60	30 (37.5)
Marital status	Married	70 (87.5)
	Divorced	6 (7.5)
	Widowed	4 (5)
Levels of education	Illiterate	40 (50)
	Primary [1–8]	33 (41.3)
	Secondary [9–12]	7 (8.8)
Occupation status	Unemployed	11 (13.8)
	Merchant	36 (45)
	Farmer	33 (41.3)
Religion	Orthodox	35 (43.8)
	Muslim	31 (38.8)
	Protestant	11 (13.8)
	Others**	3 (3.8)
Ethnicity	Oromo	50 (62.5)
	Amhara	9 (11.3)
	Kefa	12 (15)
	Dawro	4 (5)
	Others*	5(6.3)
Monthly income (ETB**)**	< 1000	45 (56.3)
	1001 –2000	28 (35)
	> 2000	7 (8.8)

* – indicates *Tigre, Wolayta*; * * – indicates *Catholic, Jehovah witness*;

ETB = *Ethiopian Birr*

Table 2: Socio-demographic, anthropometric and bone mineral density results of COPD patients attending in chest clinic of JUSH, South West Ethiopia from March 15 ─ May 15, 2015, n= 80

Variables	**Mean ±SD**
Age (years)	52.56 ±11.058
Monthly income (ETB)	998.25 ±46.32
Height (m)	1.6266 ± 0.04
Weight (kg)	52.99 ± 4.6
Patient's bone mineral density result	
Lumbar spine −2 (g/cm^2)	1.8748 ±0.75563
Lumbar spine −3 (g/cm^2)	1.8754 ±0.75504
Lumbar spine −4 (g/cm^2)	1.8774 ±0.75457
Average Lumbar spine (L-2, L-3, L-4) (g/cm^2)	1.8756 ±0.75532
T-scores of lumbar spine	−1.82 ±1.90

SD= *standard deviation* ETB= *Ethiopian Birr*

Table 3: Lifestyle, anthropometric, nutrition and drug related variables of COPD patients attending in chest clinic of JUSH, South West Ethiopia from March 15 ─ May 15, 2015, n=80

Variables	Categories	n (%)
Body mass index	Under weight	34 (42.5)
	Normal weight	33 (41.3)
	Over weight	9 (11.3)
	Obese	4 (5)
Severity of COPD	Mild	22 (27.5)
	Moderate	23 (28.8)
	Severe	23 (28.8)
	Very severe	12 (15)
Physically inactive	< 3 hrs/wk	62 (77.5)
	≥ 3 hrs/wk	18 (22.5)
Smoking cigarette	> 20 pks/yr	49 (61.3)
	≤ 20 pks/yr	31 (38.8)
Alcohol intake	> 2 drinks/day	47 (58.8)
	≤ 2 drinks/day	33 (41.3)
Coffee intake	> 2 cups/day	54 (67.5)
	≤ 2 cups/day	26 (32.5)
Milk intake	≤ 4 glasses/wk	51 (63.8)
	> 4 glasses/wk	29 (36.3)
Fruit intake	≤ 4 times/wk	50 (62.5)
	> 4 times/wk	30 (37.5)
Vegetable intake	≤ 4 times/wk	57 (71.3)
	> 4 times/wk	23 (28.8)
Doses of corticosteroid therapy	> 7.5 mg/day	53 (66.3)
	≤ 7.5 mg/day	27 (33.8)

5.2. Prevalence of osteoporosis among patients with COPD

Among 80 -patients with chronic obstructive pulmonary disease evaluated; the prevalence of osteoporosis, osteopenia and normal bone mineral density were found to be 33 (41.3%), 21 (26.3%) and 26 (32.5%), respectively. [**Figure -2]**

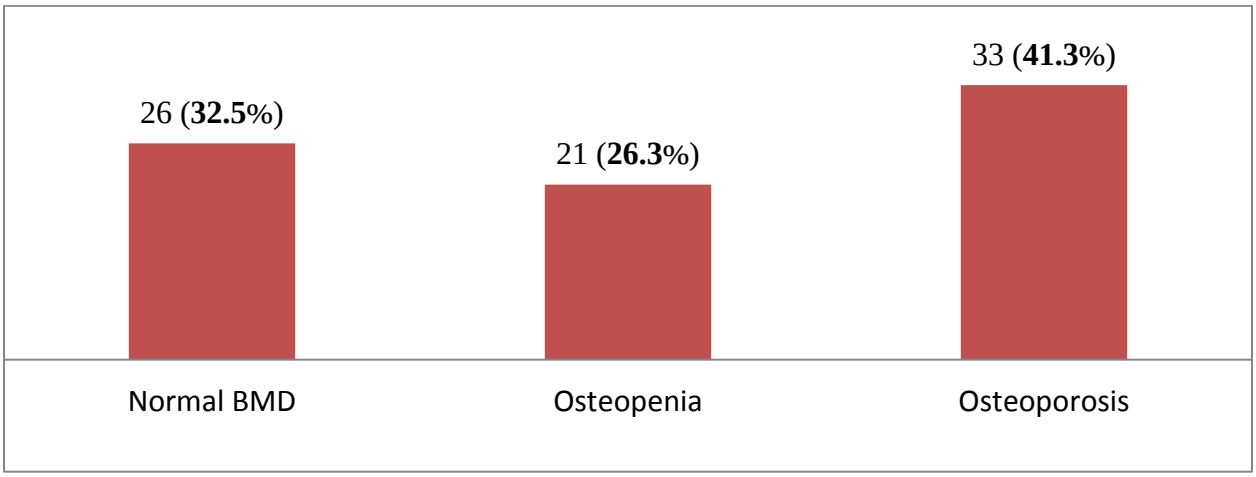

Figure 2: Prevalence of osteoporosis among patients with chronic obstructive pulmonary disease attending in chest clinic of JUSH from March 15 ─ May 15, 2015, n= 80

Concerning patient's osteoporotic status; 21 (38.9%) male, 12 (46.2%) female, with in the age group of (< 50 years) 3 (33.3%), (50—59 years) 5 (25%), (≥ 60 years) 25 (49%), married 26 (37.1%), illiterate 18 (45%), underweight 18 (52.9%), and monthly income within range of (< 1000 Eth. birr) 17 (37.8%) had osteoporosis. **[Table- 4]**

Similarly; 27 (55.1%) had osteoporosis from patients who smoked greater than 20 -packs of cigarette per year, 17 (36.2%) had osteoporosis from patients who took greater than 2 -drinks of alcohol per day, 25 (46.3%) had osteoporosis from patients who consumed greater than 2 -cups of coffee per day, 27 (43.5%) had osteoporosis from patients who engaged in any physical exercise for less than 3 -hours per week, 23 (45.1%) had osteoporosis from patients who took less than or equal to 4 –glasses of milk per week, 22 (44%) had osteoporosis from patients who consumed less than or equal to 4 –times of fruits per week, 20 (35.1%) had osteoporosis from patients who eaten less than or equal to 4 –times of vegetables per week, 29 (54.7%) had osteoporosis from patients who took greater than 7.5 mg of corticosteroid per day. Further 5 (21.7%), 9 (39.1%), 12 (54.5%), and 7 (58.3%) patients had osteoporosis from patients with mild, moderate, severe and very severe COPD, respectively. **[Table- 5]**

Table 4: Socio-demographic and anthropometric related variables of patients with COPD by their osteoporosis status.

Variables	Categories	Osteoporosis	
		Yes (%)	**No (%)**
Sex	Female	12 (46.2)	14 (53.8)
	Male	21 (38.9)	33 (61.1)
Age (year**)**	< 50	3 (33.3)	6 (66.7)
	50 –59	5 (25)	15 (75)
	≥ 60	25 (49)	26 (51)
Marital status	Married	26 (37.1)	44 (62.9)
	Divorced	4 (66.7)	2 (33.3)
	Widowed	3 (75)	1 (25)
Levels of education	Illiterate	18 (45)	22 (55)
	Primary [1-8]	11 (33.3)	22 (66.7)
	Secondary [9-12]	4 (57.1)	3 (42.9)
Monthly income (ETB**)**	< 1000	17 (37.8)	28 (62.2)
	1001– 2000	14 (50)	14 (50)
	> 2000	2 (28.6)	5 (71.4)
Body mass index	Under weight	18 (52.9)	16 (47.1)
	Normal weight	9 (27.3)	24 (72.7)
	Over weight	4 (44.4)	5 (55.6)
	Obese	2 (50)	2 (50)

ETB= *Ethiopian Birr*

Table 5: Lifestyle, nutrition and drug related variables of patients with COPD by their osteoporosis status.

Variables	Categories	Osteoporosis	
		Yes (%)	**No** (%)
Physically inactive	< 3 hrs/wk	27 (43.5)	35 (56.5)
	≥ 3 hrs/wk	6 (33.3)	12 (66.7)
Smoking cigarette	> 20 pks/yr	27 (55.1)	22 (44.9)
	≤ 20 pks/yr	6 (19.4)	25 (80.6)
Alcohol intake	> 2 drinks/day	17 (36.2)	30(63.8)
	≤ 2 drinks/day	16 (48.5)	17 (51.5)
Coffee intake	> 2 cups/day	25 (46.3)	29 (53.7)
	≤ 2 cups/day	8 (30.8)	18 (69.2)
Milk intake	≤ 4 glases/wk	23 (45.1)	28 (54.9)
	> 4 glases/wk	10 (34.5)	19 (65.5)
Fruit intake	≤ 4 times/wk	22 (44.0)	28 (56.0)
	> 4 times/wk	11 (36.7)	19 (63.3)
Vegetable intake	≤ 4 times/wk	20 (35.1)	37 (64.9)
	> 4 times/wk	13 (56.5)	10 (43.5)
Doses of corticosteroid therapy	> 7.5 mg/day	29 (54.7)	24 (45.3)
	≤ 7.5 mg/day	4 (14.8)	23 (85.2)
Severity of COPD	Mild	12 (54.5)	10 (45.5)
	Moderate	9 (39.1)	14 (60.9)
	Severe	5 (21.7)	18 (78.3)
	Very severe	7 (58.3)	5 (41.7)

5.3. Factors associated with osteoporosis among patients with COPD

In the bi-variate analysis candidate variables such as; advanced age, marital status, level of education, low body mass index, smoking cigarette, coffee intake, vegetable intake and doses of corticosteroid therapy were selected for the final model with **p-value < 0.25**. **[Table- 6]**

Further, multi-variate analysis (binary logistic regression methods) were used to identify the main predictor variables by controlling the confounders, and showed two variables such as; smoking cigarette **[AOR**= 4.949; 95% CI: 1.323, 18.508**]** and doses of corticosteroid therapy **[AOR**= 4.768; 95% CI: 1.258, 18.065**]** were found to be significantly associated with osteoporosis at **p-value < 0.05**. **[Table- 7]**

Table 6: Bivariate analysis to select candidate variables for the final model in relation to osteoporosis among patients with COPD attending in JUSH, South West Ethiopia from March 15 — May 15, 2015, n= 80

Variable	Category	Osteoporosis		X^2-test	COR(95%CI)	p-value
		Yes (%)	No (%)			
Sex	Female	12 (46.2)	14 (53.8)	0.382	0.742 (0.288 ─ 1.911)	0.536
	Male	21 (38.9)	33 (61.1)		1	
Age (year**)**	< 50	7 (25)	21 (75)	3.505	0.396 (0.148 ─ 1.058)	0.061*
	50 –59	5 (16.7)	25 (83.3)	8.823	0.206 (0.148 ─ 1.058)	0.028*
	≥ 60	21 (95.5)	1 (4.5)		1	
Marital status	Married	26 (37.1)	44 (62.9)	1.893	1	0.169*
	Divorced	4 (66.7)	2 (33.3)		0.197 (0.019 ─ 1.993)	
	Widowed	3 (75)	1 (25)	0.079	0.667 (0.039 ─ 8.285)	0.779
Level of educaton	Illiterate	18 (45)	22 (55)	1.337	1	0.248*
	Primary [1-8]	11 (33.3)	22 (66.7)		0.375 (0.071─ 1.978)	
	Secondary [9-12]	4 (57.1)	3 (42.9)	0.348	0.614 (0.121─ 3.105)	0.555
Monthly income (ETB**)**	< 1000	17 (37.8)	28 (62.2)		1	
	1001–2000	14 (50)	14 (50)	0.512	0.721 (0.294 ─ 1.769)	0.474
	≥ 2000	2 (28.6)	5 (71.4)	3.510	3.565 (1.403 ─ 6.102)	0.297
Body mass index	Under weight	18 (52.9)	16 (47.1)	3.335	1	
	Normal weight	9 (27.3)	24 (72.7)		0.430 (0.173 ─ 1.072)	0.068*
	Over weight	4 (44.4)	5 (55.6)	0.034	0.800 (0.076 ─ 8.474)	0.850
	Obese	2 (50)	2 (50)	0.835	0.375 (0.046 ─ 3.076)	0.361
Severity of COPD	Mild	12 (54.5)	10 (45.5)		1	
	Moderate	9 (39.1)	14 (60.9)	4.372	0.198 (0.044─0.904)	0.337
	Severe	5 (21.7)	18 (78.3)	1.153	0.459 (0.111─1.901)	0.283
	Very severe	7 (58.3)	5 (41.7)	0.045	0.857 (0.207─3.552)	0.832
Physically inactive	< 3 hrs/wk	27 (43.5)	35 (56.5)	0.601	0.648 (0.216 ─ 1.949)	0.438
	≥ 3 hrs/wk	6 (33.3)	12 (66.7)		1	
Smoking cigarette	> 20 pks/yr	27 (55.1)	22 (44.9)	10.012	0.196 (0.068 ─ 0.561)	0.002*
	≤ 20 pks/yr	6 (19.4)	25 (80.6)		1	
Alcohol intake	>2 drinks/day	17 (36.2)	30 (63.8)	1.213	1.661 (0.672 ─ 4.108)	0.271
	≤2 drinks/day	16 (48.5)	17 (51.5)		1	

Variable	Categories	Osteoporosis		X^2-test	COR(95%CI)	p-value
		Yes (%)	No (%)			
Coffee intake	> 2 cups/day	25 (46.3)	29 (53.7)	1.746	0.516 (0.192 ─ 1.387)	0.186*
	≤ 2 cups/day	8 (30.8)	18 (69.2)		1	
Milk intake	≤ 4 glases/wk	23 (45.1)	28 (54.9)	0.860	0.641 (0.249 ─ 1.646)	0.354
	> 4 glases/wk	10 (34.5)	19 (65.5)		1	
Fruit intake	≤ 4 times/wk	22 (44.0)	28 (56.0)	0.416	0.737 (0.291 ─ 1.866)	0.519
	> 4 times/wk	11 (36.7)	19 (63.3)		1	
Vegtable intake	≤ 4 times/wk	20 (35.1)	37 (64.9)	3.107	2.405 (0.896—6.458)	0.078*
	> 4 times/wk	13 (56.5)	10 (43.5)		1	
Doses of corticosteroid therapy	> 7.5 mg/day	29 (54.7)	24 (45.3)	11.752	0.144 (0.044—0.474)	0.001*
	≤ 7.5 mg/day	4 (14.8)	23 (85.2)		1	

*****Candidate variables for the final model at **p-value < 0.25**; CI= *confidence interval***; COR**= *crude odds ratio*

Table 7: Multivariate analysis of selected variables in relation to osteoporosis among patients with COPD attending in JUSH, South West Ethiopia from March 15 ─ May 15, 2015, n= 80

Variables	Categories	Osteoporosis		AOR(95%CI)	p-value
		Yes (%)	No (%)		
Age (year)	< 50	7 (25)	21 (75)	1.197 (0.354 ─ 4.056)	0.772
	50─59	5 (16.7)	25 (83.3)	0.435 (0.001─ 2.204)	0.231
	≥ 60	21 (95.5)	1 (4.5)	1	
Marital status	Married	26 (37.1)	44 (62.9)	1	
	Divorced	4 (66.7)	2 (33.3)	0.531 (0.912 ─ 3.108)	0.482
	Widowed	3 (75)	1 (25)	2.032 (1.013 ─ 6.635)	0.167
Level of education	Illiterate	18 (45)	22 (55)	1	
	Primary [1-8]	11 (33.3)	22 (66.7)	1.592 (0.507 ─ 4.998)	0.425
	Secondary [9-12]	4 (57.1)	3 (42.9)	0.314 (1.124 ─ 7.001)	0.721
Body mass index	Under weight	18 (52.9)	16 (47.1)	1	
	Normal weight	9 (27.3)	24 (72.7)	2.699 (0.848 ─ 8.594)	0.093
	Over weight	4 (44.4)	5 (55.6)	0.249 (1.561─ 3.528)	0.561
	Obese	2 (50)	2 (50)	7.121 (0.781─ 1.134)	0.055
Smoking cigarette	> 20 pks/yr	27 (55.1)	22 (44.9)	4.949 (1.323 ─ 18.508)	0.017▲
	≤ 20 pks/yr	6 (19.4)	25 (80.6)	1	
Coffee intake	> 2 cups/day	25 (46.3)	29 (53.7)	1.433 (0.429 ─ 4.782)	0.559
	≤ 2 cups/day	8 (30.8)	18 (69.2)	1	
Vegetable intake	≤ 4 times/wk	20 (35.1)	37 (64.9)	0.300 (0.077 ─ 1.167)	0.082
	> 4 times/wk	13 (56.5)	10 (43.5)	1	
Doses of corticosteroid therapy	> 7.5 mg/day	29 (54.7)	24 (45.3)	4.768 (1.258 ─ 18.065)	0.022▲
	≤ 7.5 mg/day	4(14.8)	23 (85.2)	1	

▲Variables statistically significant at **p- value < 0.05**; AOR= *adjusted odds ratio***; CI**= *confidence interval*

6. DISCUSSION

This cross sectional study is the first of its kind to assess the prevalence of osteoporosis and associated factors among patients with chronic obstructive pulmonary disease attending in chest clinic of JUSH in the Ethiopian context.

According to the current study, the prevalence of osteoporosis was 41.3% among patients with COPD, which might be related with majority of the patients, are using daily high doses of corticosteroid for COPD exacerbations, and smoking cigarette. This finding is inline with the previous two cross-sectional studies done in Brazil 42% [41] and Denmark 44.8% [42] on the prevalence of osteoporosis. However, this prevalence is higher from other two studies done in Netherland 23.6% [43] and 21% [44]. But, lower than a study conducted in Iran 52% [45]. The main explanation for such discrepancy might be different in life style and economic status of other study areas to the current study.

This study identified factors of osteoporosis such as smoking cigarette and doses of corticosteroid therapy were found to be significantly associated. However, other variables such as sex, advanced age, marital status, educational status, income, physically inactive, low BMI, alcohol intake, coffee intake and nutritional variables were not significantly associated with osteoporosis.

In women, accelerated bone loss usually begins after monthly menstrual periods stop, when a woman's production of estrogen slows down (usually between the ages of 45 and 55). In men, gradual bone thinning typically starts at about 45 to 50 years of age, when a man's production of testosterone slows down. Women are usually affected at an earlier age than men, because they start out with lower bone mass. Estrogen receptors have been demonstrated on cell lines of both osteoblasts and osteoclasts. However, estrogen does not appear to act directly at these sites but appears to be mediated through locally produced cytokines, mainly through changes in interleukin -1, interleukin -6, tumor necrosis factor -alpha and granulocyte /macrophage colony stimulating factor. It appears that estrogen deficiency allows greater expression of these cytokines, all of which are associated with increased stimulation of bone resorption which then leads to increased bone loss and a reduction in BMD. Androgens can directly affect and modulate bone cell function. Androgen receptors are found on osteoblasts cell lines and they can cause osteoblasts proliferation. Hypogonadal men, in common with postmenopausal women, have decreased Ca^{2+} absorption and low vitamin D levels. The replacement of androgens with testosterone can correct

these abnormalities, suggesting again that sex hormones are required for the maintenance of bone health [46]. But the current study didn't find association between being a female and osteoporosis.

Evidence from USA and Australia showed that exercise may help to build and maintain bone density at any age. Studies have shown bone density increase by doing regular resistance exercises, such as lifting weights two or three times a week. This type of weight-bearing exercise appears to stimulate bone formation and retain Ca^{2+} in the bones that are bearing the load. The force of muscles pulling against bones stimulates this bone-building process. So any exercise that places force on a bone will strengthen that bone [47, 48]. But, the result of our study showed that exercise has no significant association with the development of osteoporosis.

Moderate alcohol consumption is not harmful to bone health, but heavy drinking is negatively impacts bone health for several reasons; excessive alcohol interferes with the balance of calcium, an essential nutrient for healthy bones, it also increases parathyroid hormone levels, which in turn reduce the body's calcium reserves. Ca^{2+} balances are further disrupted by alcohol's ability to interfere with the production of vitamin D, a vitamin essential for Ca^{2+} absorption. A study from Austria have demonstrated that chronic heavy alcohol use, especially during adolescence and young adult years by interfering Ca^{2+} absorption, can dramatically affect bone health and increase the risk of osteoporosis later in life [49]. However, this study observed that greater than 2-drinks of alcohol per day had no significant association with the development of osteoporosis.

Smoking is an important synergistic risk factor for both COPD and osteoporosis. A meta-analysis demonstrated that tobacco smoking had a cumulative, dose-dependent independent effect on bone mass. Smokers had significantly reduced bone mass compared with nonsmokers at several major sites of osteoporosis-related fractures, including the hip, lumbar spine, and forearm [50]. Smoking induces osteoporosis by several potential mechanisms: altering metabolism of calciotropic hormone; dysregulation in the production, metabolism, and binding of estradiol; changing metabolism of adrenal cortical hormone; effects on the Receptor Activator of Nuclear Factor-Kappa B (RANK) –Receptor Activator of Nuclear Factor-Kappa B Ligand (RANKL) –Osteoprotegerin (OPG) system; and effects on collagen metabolism and bone angiogenesis [51].

Literatures from Iran, Brazil and UK indicated that smoking greater than 20-packs of cigarette per year have a risk for the development of osteoporosis; the reason is that cigarette smoke generates huge amounts of free radical molecules that attack and overwhelm the body's natural defenses. The result is a chain-reaction of damage throughout the body, including cells, organs, and hormones involved in keeping bones healthy [45, 48, 51]. This study also found that smoking greater than 20-packs of cigarette per year have 5- times risk to develop osteoporosis with the [AOR= 4.949; 95% CI: 1.323, 18.508]. Moreover, in the current study majority of the patients 49 (61.3%) are smoking > 20-packs of cigarette per year.

A study done in UK implied that coffee contains high amounts of caffeine, which increases urinary Ca^{2+} output and decreases absorption of Ca^{2+} in the gastrointestinal tracts, and has been implicated as a risk factor for osteoporosis that leads to fracture, [51] while other research in California indicate that the effect of caffeine on BMD is because of the interaction between cigarette and alcohol abuse [52]. In this study, consumption of greater than 2-cups of coffee per day didn't show a significant association with osteoporosis.

Studies from USA and Korea confirms that a high BMI (greater than 30 kg/m^2) has a protective effect for both men and women, in contrast low BMI less than 19 kg/m^2 can lead to osteoporosis [53—55]. Our study, however, did not show the association between low BMI and osteoporosis.

Systemic corticosteroid treatment is recommended in international guidelines for the treatment of COPD exacerbations; however prolonged treatment with systemic corticosteroids is associated with a reduction in BMD, osteoporosis, and a risk of fractures. But, the effect of corticosteroid therapy appears to be dose-dependent. Among several adverse effects of corticosteroid on BMD are; direct inhibition of osteoblast function, direct enhancement of bone resorption, inhibition of gastrointestinal Ca^{2+} absorption, increase in urinary Ca^{2+} loss, and inhibition of gonadal hormones. A study from UK reported that, patients using daily dose of oral corticosteroid were strongly associated with reduction in BMD. The risk of both hip and vertebral fractures was approximately doubled in COPD patients using doses of $\geq$ 7.5 mg per day [56]. Similarly, this study revealed that using greater than 7.5 mg of corticosteroids per day have more than four -times risk to develop osteoporosis with the [AOR= 4.768; 95% CI: 1.258, 18.065]. As the present study indicates, almost more than a half of patients 53 (66.3%) are using greater than 7.5 mg of corticosteroid per day.

A study conducted in USA has linked higher intakes of fruits and vegetables with better bone health. Though it is not clear why fruits and vegetables promote healthy bones, many scientists believe that fruits and vegetables contain certain nutrients such as Ca^{2+}, magnesium, potassium, vitamin C, vitamin K or a combination of these vitamins that are beneficial for bones. Some studies indicate that the higher fruit intake was found to be significantly associated with higher BMD in both sexes. High vegetable consumption, however, did not positively impact BMD [57]. Further UK and USA studies also indicate consumption of more fresh fruits and vegetables are unlikely to be detrimental to bone health and may be beneficial [58,59]. However, the current study did not show association between consuming less than or equal to 4-times of fruits and vegetables per week, and osteoporosis. Similarly, this might be because of methodological difference.

Several studies from Iran, India, UK and USA reported that the positive associations between earlier reported milk consumption or Ca^{2+} intake and BMD. The milk's main selling point is Ca^{2+}, and milk-drinking is touted for building strong bones in children and preventing osteoporosis in older persons [60—63]. But, our study indicated that low milk consumption did not significantly associate with osteoporosis.

7. STRENGTHS AND LIMITATION OF THE STUDY

7.1. Strengths of the Study

Calibrated DEXA -scan machine was used.

7.2. Limitation of the Study

In this cross-sectional study, the sample sizes were not very large, so a large prospective study will be required. On the other hand, this study is the first of its kind in the study area to assess the prevalence of osteoporosis and associated factors among patients with COPD, while many of the published studies in the literature come from American, European and Asian countries.

8. CONCLUSION

This study comes with high prevalence of osteoporosis among patients with COPD in JUSH Indeed, factors such as smoking cigarette and doses of corticosteroid therapy were found to be significantly associated with osteoporosis. In contrast, didn't find any association between osteoporosis and sex, advanced age, marital status, educational status, income, low BMI, physically inactive, alcohol intake, coffee intake or nutritional variables.

9. RECOMMENDATIONS

Most countries have guidelines concerning long-term corticosteroid treatment and prevention of secondary osteoporosis. As of this study is the first of its kind in Ethiopian context, there is no guideline concerning osteoporosis among COPD patients with long-term corticosteroid treatment (oral and inhaled). On the basis of the findings in this study it is recommended that Health Policy Makers and Programmers should give attention to improve, especially on the area of prescription of long-term corticosteroid and its dose. The Hospital Medical Director and Health Providers should create awareness on factors associated with osteoporosis among COPD patients, particularly on cessation of smoking cigarette. Further studies are needed to determine the severity of osteoporosis in relation with degree of COPD.

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ANNEXES

Annex-1: Study Information Sheet (English version)

Greetings:

My name is_____

I am a Postgraduate student in Medical Physiology specialization in Department of Biomedical Sciences (Physiology), College of Health Sciences, Jimma University. I am now conducting a research on the following title **"**Osteoporosis and associated factors among patients with COPD**"**.

The information that you give using this questionnaire used only for research purpose and all information you provide will be kept confidential. The study has no risk to you and your family members. I believe that the study findings will help you to create awareness about the determinants, and preventive measures and management controls for decreasing bone mineral density in COPD patients.

If you have any question you can contact the principal investigator at any time convenient for you using the following address:

Name: Tariku Anjamo **Phone number**: 09 10 13 26 38

Address: Jimma, Ethiopia **E-mail**: tarikuanjamo@gmail.com

Annex-2: የመረጃ እና የመግባቢያ ፎርም (የአማርኛ ትርጉም)

ሰላምታ፡

ስሜ_____ይባላል፡፡

እኔ በባዮሜድካል ትምህርት ክፍል በጤና ሳይንስ ኮሌጅ በጅማ ዩኒቨርሲቲ የሜድካል ፊዚዮሎጅ ድህረ ምረቃ ተማሪ ነኝ፡፡ የመመረቂያ ፅሑፍ ጥናቴንም የማከናውንበት ርዕስ እንደሚከተለዉ ይሆናል፡- “ከመጋቢት **15** እስከ ግንቦት **15**, 2015 እ.ኤ.አ በደቡብ ምዕራብ ኢትዮጵያ በጅማ ዩኒቨርሲቲ ስፔሻላይዝድ ሆስፒታል በተመላላሽ የክሮኒክ ሳምባ በሽተኞች ላይ ስለአጥንታቸዉ ጥንካሬ እና በአጥንታቸዉ ላይ ልያስከትሉ ስለምችሉ ተጓዳኝ ችግሮችን ለመዳሰስ፡፡”

እርሶ የምሰጡት መረጃ ለምርምር/ ጥናት ዓላማ ብቻ ስለሆነ የምሰጡትንም መረጃ ምስጥር በመጠበቅ ጥናቱ ይከናወናል፡፡ እንድሁም ጥናቱ በእርሶና በቤተሴቦ ላይ ምንም ዓይነት ችግር አያደርስም፡፡ በአጥንት ጥንካሬ ላይ ልያስከትሉ ስለምችሉ ተጓዳኝ ችግሮች እንድሁም ሊወሰዱ ስለሚገባቸዉ ጥንቃቄና መፍትሔዎቻቸዉ ከጥናቱ ግኝት የተሻለ ግንዛቤም ያገኛሉ፡፡

ጥናቱን በሚመለከት ምንም ዓይነት ጥያቄ ቢኖርዎ ጥናቱን የሚያጠናውን ግለሰብ በፈለጉት ሰዓት በሚከተሉት አድራሻ ማግኘት ይችላሉ፡፡

ስም፡ ታሪኩ አንጃሞ **ሞባይል፡** 09 10 13 26 38

አድራሻ፡ ጅማ, ኢትዮጵያ **ኢ-ሜይል**: tarikuanjamo@gmail.com

Annex-3: Afan-Oromo version

Maqaan_____jedhama

Ani barata digirii lamaffaa jimma yunivarsitii kolleeji fayyaa dipaartimanti fiziyooloji dha. Matadureen qorronnoo barreffama ebbaa koos kan armaan gadi ta'a. Bitooteesa 15 haga caamsaa 15, 2015 A.L.A dedebi'a dhukuubsatoota kironikii sombaa hospiitala speeshiyaayzdi jimma kibba dhihaa Itiyoopiyaa irratti waayee jabina lafee isaa fi lafee isaanii irratti wantoota rakkoo fidan qorachuu ta'a .

Oduu isiin nuf kennitana qorannof qoofa waaan ta'ef icitti oduu isiin nuf kennitan eguudhaan kan gaggeffamu ta'a. Akkasuumaas qoorannon kuun isiin fi maati kessan irratti rakkooo tokko hin fidu. Wantoota Jabina lafee irratti rakkoo fidan akkasummaas of eganno godhamuu qaban fi furmaata isaani qoranno kana irraa bu'aa guddaa argachuu dandessu.

Qorannoo kana irratti gaafi kamiyyuu qorataaf gaafi qabdan armaan gadiin argachuu dandessuu

Maqaa: Taariku Anjaamo **Mobaayili:** 09 10 13 26 38

Adressi: Jimaa, Itiiyoopiyaa **Email:** tarikuanjamo@gmail.com

Annex-4: Consent Form (English version)

Informed consent agreement

Dear study participants,

Greetings:

My name is_____

This study is proposed to assess the prevalence of osteoporosis and associated factors among patients with COPD here in chest clinic of JUSH. If you are agreed to take part in the research work, it will not take more than **20** minutes. Moreover, each page will be filled by data collectors according to your response, medication card and radiology assessment results. Therefore, I kindly request your cooperation to respond to all questions according to the questions.

For participation as a volunteer in research undertaking

Code №: _____

I have been informed about. It is, therefore, with full understanding of the informed consent and voluntarily allows the researcher to the questions. Moreover, I have had the opportunity to ask questions about it and received clarification to my satisfaction. I have also been informed that the nature of the questionnaire is private. So, willingly to participate in the study I will assure with my signature.

Signature/ thumbprint of participant: _____

Interviewer's name: _____Signature: _____Date of interview_____

Supervisor's name: _____ Signature: _____Date of checking_____

Annex-5: የመግባቢያ ፎርም (የአማርኛ ትርጉም)

ውድ የጥናቱ ተሳታፊዎች,

ስሜ _____ይባላል፡፡

ይህ ቃለ-መጠይቅ ዓላማዉ በጅማ ዩኒቨርሲቲ ስፔሻላይዝድ ሆስፒታል በተመላላሽ የክሮኒክ ሳምባ በሽተኞች ላይ ስለአጥንታቸዉ ጥንካሬ እና በአጥንታቸዉ ላይ ልያስከትሉ ስለምችሉ ተጓዳኝ ችግሮች ለመዳሰስ የተዘጋጀ ነዉ፡፡ እርሶ በጥናቱ ላይ ለመሳተፍ ፍቃደኛ ከሆኑ ቃለ- መጠይቁ ከ **20** ደቂቃ በላይ አይፈጅም፡፡ እንድሁም እያንዳንዱ ገጽ የሚሞላዉ በመረጃ ሰብሳቢዎች (በጤና ባለሙያዎች) ሲሆን ይህም ከእርሶ/ከተሳታፍዉ/ ቃለ-መጠይቅ፣ ከሜድካል ካርድ (ስለ መድሐኒት አጠቃቀም) እና ከኤክስሬይ /ራጂ ዉጤት በመዉሰድ ይሆናል፡፡ ሲለዚህ መረጃ ሰብሳቢዎች ለምጠይቁት ቃለ-መጠይቅ ሙሉ መረጃ በመስጠት እንድተባበሩ በትህትና እጠይቃለሁ፡፡

<u>የጥናቱ ተሳታፊ</u>

መለያ ቁጥር፡_____

ከላይ ስለ ጥናቱ የተጠቀሱትን ሐሳቦች እና አንዳንድ ጥያቄ የሆኑብኝን ነገሮች ከሚያጠናዉ ግለሰብ በመቅረብና በመጠየቅ ስለ ጥናቱ አጥጋብ መልስ አግኝቻለሁኝ እንድሁም የመጠይቁም ባህሪ ግለሰባዊ መሆኑንም ጭምር በሚገባ ተረድቻለሁኝ፡፡ ስለዚህ በጥናቱ ላይ ለመሳተፍ ፍቃደኛነቴን በፊርማዬ አረጋግጣለሁኝ፡፡

የተሳታፊዉ ፊርማ/ የጣት አሻራ፡ _____

የጠያቂዉ (ነርስ) ስም፡_____ፊርማ፡_____ቃለ-መጠይቅ የተደረገበት ቀን፡_____

የሱፐርቫይዘሩ ስም፡_____ፊርማ፡_____ቼክ የተደረገበት ቀን፡_____

Annex-6: Waligaltee (Afan-Oromo version)

Kabajamtoota hirmaatoota qorannoo

Maqaa _____jedhama

Kaayyon gaafi kanaa dedebi'a dhukuubsatoota kironikii sombaa hospiitala speeshiyaayzdi jimma kibba dhihaa Itiyoopiyaa irratti waayee jabina lafee isaa fi lafee isaanii irratti wantoota rakkoo fidan qorachuuf kan qoophaaye dha. Isiin gaafi fi debii kanaaf hirmaachuuf fedhii yoo qabaatan daqiiqaa 20 hin caalu. Akkasuumas formin kun kan gutamu oggeyyoota fayyaa dhaan yoo ta'u kunis hirmaatoota irraa kaardi fayyaa (akkaata qoricha fudhatan) fi qabxii eksreeyi (raaji) irraa argamen ta'a. kanaafu gaafi oggayyoota gaafatan oduu gutuu kennuun akka hirmaatan kabajaan isiin gaafadha.

Hirmaatota qorannoo

Kodi iccittii_____

Akka yaada qorannoo kanaa akka armaan olii hubadhetti fi wantoota gaafi natti ta'an qorataa gafachuudhan debii gahaa waan argadheefi akkasuumas qorannoon iccitidhaan waan gaggeefamuuf hubdheera. Kanaaf qorannoo irratti hirmaachuf mallatto kootin ragaasiseera.

Mallattoo hirmaataa_____

Maqaa gaafataa/narsii/ _____Mallatto_____Guyyaa_____

Maqaa qorataa_____Mallattoo_____Guyyaa raagafame_____

Annex-7: Questionnaire Form (English version)

Structured questionnaires contained **4-** sections and **47-** questions, and it will be intended to assess the prevalence of osteoporosis and associated factors among patients with COPD. Each page will be filled by data collectors according to the patient's response, medication card and radiology assessments.

SECTION-ONE

Socio-demographic variables

101. Card number _____

102. Age (in completed years) _____

103. Height (m) _____

104. Weight (kg) _____

105. Sex

A. Male B. Female

106. Current marital status

A. Single C. Divorced

B. Married D. Widowed

107. Level of education

A. Illiterate C. Secondary school [9-12]

B. Primary school [1-8] D. College/University

108. Occupation/ Employment

A. Employed C. Merchant E. Others_____

B. Unemployment D. Farmer

109. Monthly income

A. < 1000 C. 2001−3000

B. 1001−2000 D. > 3000

110. Religion status

A. Orthodox C. Protestant

B. Muslim D. Others_____

111. Ethnicity status

A. Oromo C. Kefa E. Others_____

B. Amhara D. Dawro

SECTION- TWO

The following questions assess the patient's lifestyle and nutritional status

201. Do you have a habit of doing any physical exercise?

A. Yes B. No

202. If "**Yes**" for Q.201, in the last- six months have you done any physical exercise?

A. Yes B. No

203. Currently are you doing any physical exercise?

A. Yes B. No

204. within a week how many days do you exercise? _____

205. For how many minutes or hours do you exercise per day? _____

206. Do you have a habit of smoking cigarrate?

A. Yes B. No

207. If "**Yes**" for Q.206, in the last – one year did you smoke cigarette?

A. Yes B. No

208. Currently do you smoking cigarette?

A. Yes B. No

209. How many № of packs of cigarette do you smoke per day? _____

210. For how many years did you smoke cigarette? _____

211. Do you have a habit of consuming coffee?

A. Yes B. No

212. If "**Yes**" for Q.211, in the last- six months did you consume coffee?

A. Yes B. No

213. Currently do you consuming coffee?

A. Yes B. No

214. How much cups of coffee do you consume per day? _____

215. Do you have a habit of drinking alcohol? **I.e**. any type of alcohol

A. Yes B. No

216. If "**Yes**" for Q.215, in the last- six months did you drink alcohol?

A. Yes B. No

217. Currently do you drinking alcohol?

A. Yes B. No

218. How much units (frequency) of alcohol do you drink per day? _____

219. Do you have a habit of consuming milk?

A. Yes B. No

220. If "**Yes**" for Q.219, in the last- six months did you consume milk?

A. Yes B. No

221. Currently do you consuming milk?

A. Yes B. No

222. How much glasses of milk do you consume per week? _____

223. Do you have a habit of consuming fruits like; orange, banana, etc…?

A. yes B. No

224. If "**Yes**" for Q.223, in the last- six months did you consume fruits?

A. yes B. No

225. Currently do you consuming fruits?

A. Yes B. No

226. How many times (frequency) do you consume fruits per week? _____

227. Do you have a habit of consuming vegetables like; cabbage, spinach, etc…?

A. yes B. No

228. If "**Yes**" for Q.227, in the last- six months did you consume vegetables?

A. yes B. No

229. Currently do you consuming vegetables?

A. Yes B. No

230. How many times (frequency) do you consume vegetables per week? _____

SECTION- THREE

The following question assess the patient's medication use status

301. How much doses (frequency) of corticosteroids you are using?

_____mg/day

SECTION- FOUR

Radiology assessments of the patient's bone mineral density result

401. Lumbar spine -2 _____ g/cm^2

402. Lumbar spine -3 _____ g/cm^2

403. Lumbar spine -4 _____ g/cm^2

404. Average values of lumbar spine _____ g/cm^2

405. T-scores of lumbar spine _____

Thank you for your cooperation!!!

Annex-8: የመጠየቂያ ፎርም (የአማርኛ ትርጉም)

የመጠይቅ ፎርሙ በዉስጡ **አራት** ክፍል እና **አርባ-ሰባት** ጥያቄዎች አሉት፡፡ ይህም ቃለ-መጠይቅ ዓላማዉ "በጅማ ዩኒቨርሲቲ ስፔሻላይዝድ ሆስፒታል በተመላላሽ የክሮኒክ ሳምባ በሽተኞች ላይ ስለአጥንታቸዉ ጥንካሬ እና በአጥንታቸዉ ላይ ልያስከትሉ ስለምችሉ ተጓዳኝ ችግሮችን ለመዳሰስ ነዉ፡፡" እያንዳንዱ ገጽ የሚሞላዉ በመረጃ ሰብሳቢዎች ሲሆን ይህም ከበሽተኛዉ ቃለ-መጠይቅ፣ ከሜድካል ካርድ (ስለ መድሐኒት አጠቃቀም) እና ከኤክስሬይ /ራጂ ዉጤት በመዉሰድ ይሆናል፡፡

ክፍል አንድ

<u>ማህበራዊ ፤ ዴሞግራፊያዊ እና እኮኖሚያዊ ሁኔታ</u>

101. የካርድ ቁጥር፡ _____

102. ዕድሜ (በዚህ በተጠናቀቀዉ ዓመት) _____

103. ቁመት (ሜትር)፡ _____

104. ክብደት (ኪሎ ግራም)፡ _____

105. ፆታ፡

ሀ. ወንድ ለ. ሴት

106. የጋብቻ ሁኔታ፡

ሀ. ያላገባ ለ. ያገባ ሐ. የተለያየ መ. የሞተበት/ባት

107. የትምህርት ሁኔታ፡

ሀ. ያልተማረ ለ. አንደኛ ደረጃ (1—8ኛ ክፍል)

ሐ. ሁለተኛ ደረጃ (9—12ኛ ክፍል) መ. ኮሌጅ/ ዩኒቨርሲቲ

108. የስራ ሁኔታ፡

ሀ. የቅጥር ሰራተኛ ለ. የቤት እመቤት ሐ. ነጋዴ

መ. አርሶ አደር ሠ. ሌላ ከሆነ ይግለፁ፡ _____

109. የወር ገቢ (በኢትዮጵያ ብር)

ሀ. ከ 1000.00 ብር በታች ለ. ከ 1001.00 እስከ 2000.00 ብር

ሐ. ከ 2001.00 እስከ 3000.00 ብር መ. ከ 3000.00 ብር በላይ

110. ሀይማኖት፡

ሀ. ኦርቶዶክስ ለ. ሙስሊም. ሐ. ፕሮቴስታንት

መ. ሌላ ካለ ይግለፁ_____

111. ብሔረሰብ፡

ሀ. ኦሮሞ ለ. አማራ ሐ. ወላይታ መ. ከፋ

ሠ. ዳውሮ ረ. ሌላ ካለ ይግለፁ _____

ክፍል ሁለት

ከዚህ በታች የተዘረዘሩት ጥያቄዎች ስለበሽተኛው የህይወት ተግባራት ሁኔታ የምጠይቅ ቃለ መጠይቅ ነው፡፡

201. የአካል ብቃት እንቅስቃሴ የማድረግ ልምዱ አሎት? (ማንኛዉንም ዓይንት እንቅስቃሴ)

ሀ. አዎ ለ. የለኝም

202. መልሶ "**አዎ**" ከሆነ፡ ባለፉት 6- ወር ዉስጥ የአካል ብቃት እንቅስቃሴ ያደረጉ ነበር?

ሀ.አዎ ለ. አላደርግም

203. በአሁኑ ሰዓት የአካል ብቃት እንቅስቃሴ ያደርጋሉ?

ሀ.አዎ ለ. አላደርግም

204. በሣምንት ለምን ያህል ቀን የአካል ብቃት እንቅስቃሴ ያደረጋሉ? _____

205. በቀን ለምን ያህል ደቂቃ/ሠዓት የአካል ብቃት እንቅስቃሴ ያደረጋሉ? _____

206. ስጋራ የማጨስ ልምዱ አሎት?

ሀ. አዎ ለ. የለኝም

207. መልሶ "**አዎ**" ከሆነ፡ ባለፈዉ አንድ-ዓመት ዉስጥ ስጋራ ያጨሱ ነበር?

ሀ. አዎ ለ. አላጨስም

208. በአሁኑ ሰዓት ስጋራ ያጨሳሉ?

ሀ. አዎ ለ. አላጨስም

209. በቀን ምን ያህል ፓከት ስጋራ ያጨሳሉ? _____

210. ለስንት ዓመት ያህል ስጋራ አጭሰዋል? _____

211. ቡና የመጠጣት ልምዱ አለ/ት?

ሀ. አዎ ለ. የለኝም

212. መልሶ "**አዎ**" ከሆነ፡ ባለፉት 6- ወር ዉስጥ ቡና ይጠጡ ነበር?

ሀ. አዎ ለ. አልጠጣም

213. በአሁኑ ሰዓት ቡና ይጠጣሉ?

ሀ. አዎ ለ. አልጠጣም

214. በቀን ምን ያህል ሲኒ ቡና ይጠጣሉ? _____

215. አልኮል የመጠጣት ልምዱ አለ/ት? ማንኛዉንም ዓይነት

ሀ. አዎ ለ. የለኝም

216. መልሶ **አዎ** ከሆነ፡ ባለፉት 6- ወር ዉስጥ አልኮል ይጠጡ ነበር?

ሀ. አዎ ለ. አልጠጣም

217. በአሁኑ ሰዓት አልኮል ይጠጣሉ?

ሀ. አዎ ለ. አልጠጣም

218. በቀን ምን ያህል አልኮል ይጠጣሉ? _____

219. ወተት የመጠጣት ልምዱ አለ/ት?

ሀ. አዎ ለ. የለኝም

220. መልሶ "**አዎ**" ከሆነ፡ ባለፉት 6- ወር ዉስጥ ወተት ይጠጡ ነበር?

ሀ. አዎ ለ. አልጠጣም

221. በአሁኑ ሰዓት ወተት ይጠጣሉ?

ሀ. አዎ ለ. አልጠጣም

222. በሣምንት ምን ያህል ብርጭቆ ወተት ይጠጣሉ?_____

223. ፍራፍሬ የመመገብ ልምዱ አሎት? **ለምሳሌ፡**- ብርትካን, ሙዝ,…..

ሀ. አዎ ለ. የለኝም

224. መልሶ "**አዎ**" ከሆነ፡ ባለፉት 6- ወር ዉስጥ ፍራፍሬ ይመገቡ/ይጠቀሙ ነበር?

ሀ. አዎ ለ. አልመገብም/አልጠቀምም

225. በአሁኑ ሰዓት ፍራፍሬ ይመገባሉ/ይጠቀማሉ?

ሀ. አዎ ለ. አልመገብም/አልጠቀምም

226. በሣምንት ዉስጥ ምን ያህል ጊዜ ፍራፍሬዎችን ይመገባሉ/ይጠቀማሉ? _____

227. አትክልት የመመገብ ልምዱ አሎት? **ለምሳሌ፡**- ጎመን, ዱባ,…..

ሀ. አዎ ለ. የለኝም

228. መልሶ "**አዎ**" ከሆነ፡ ባለፉት 6- ወር ዉስጥ አትክልት ይመገቡ/ይጠቀሙ ነበር?

ሀ. አዎ ለ. አልመገብም/አልጠቀምም

229. በአሁኑ ሰዓት አትክልት ይመገባሉ/ይጠቀማሉ?

ሀ. አዎ ለ. አልመገብም/አልጠቀምም

230. በሣምንት ዉስጥ ምን ያህል ጊዜ አትክልት ይመገባሉ/ይጠቀማሉ? _____

ክፍል ሦስት

<u>ከዚህ በታች ያለዉ ጥያቄ ስለበሽተኛዉ የመድሐኒት አጠቃቀም ሁኔታ የምጠይቅ ይሆናል፡፡</u>

301. በቀን ምን ያህል ምል ግራም ኮርቲኮስቴሮይድ (መድሐኒት) ይዉጣሉ?

_____ምልግራም/ቀን

ክፍል አራት

<u>የበሸተኛዉ የአጥንት ንጥሬ ነገር ይዘት ኤክስሬይ (ራጅ) ዉጤት፡፡</u>

401. ሉምባር ስፓይን -2_____ግራም ሴንት ሜትር ስኩዌር

402. ሉምባር ስፓይን -3_____ግራም ሴንት ሜትር ስኩዌር

403. ሉምባር ስፓይን -4_____ግራም ሴንት ሜትር ስኩዌር

404. በአማካይ የሉምባር ስፓይን ዉጤት _____ግራም ሴንት ሜትር ስኩዌር

405. የ "**T**"—ዉጤት _____

<u>ለትብብሮ አመሰግናለሁ!!!</u>

Annex-9: Afan-Oromo version

Formiin gaafi kanaa kutaa afuur (4) fi gaafilee afuurtani torba (47) qaba. Kaayyon gaafi kanaa dedebi'a dhukuubsatoota kironikii sombaa hospiitala speeshiyaayzdi jimma kibba dhihaa Itiyoopiyaa irratti waayee jabina lafee isaa fi lafee isaanii irratti wantoota rakkoo fidan qorachuuf kan qoophaaye dha. Akkasuumas formin kun kan gutamu oggeyyoota fayyaa dhaan yoo ta'u kunis hirmaatoota irraa kaardi fayyaa(akkaata qoricha fudhatan) fi qabxii eksreeyi (raaji) irraa argamaniin ta'a.

Kutaa tokko

Waayee haawasa, dimoograafi fi qabeeyna

101. Lakkoofasa kaardi_____

102. Umrii (dhuma waggaa kanaa) _____

103. Hojaa(dheerina) (m) _____

104. Hanga (kg) _____

105. Saala:

A. dhira B. dhalaa

106. Fuudhaa fi heruuma

A. hin fune B. fudhe C. hikee D. Du'e/dute

107. Sadarkaa baruumsaa

A. hin barannee B. sadarkaa 1^{ffaa} (kutaa $1\text{-}8^{ffaa}$)

C. sadarka 2^{ffaa} (kutaa $9\text{-}12^{ffaa}$) D. kolleeji/yunivarsitii

108. Hojii:

A. hojataa motuummaa B. hadha manaa C. daldalaa

D. qotee bulaa E. hojii biraa yoo ta'e ibsaa_____

109. Galii guyyaa (birrii Itoopiyaaatin):

A. birrii 1000.00 gadi B. birrii 1001.00 haga birrii 2000.00

C. birrii 2001.00 haga 3000.00 D. birrii 3000.00 oli

110. Amantii:

A. Ortoodoksii B. Musliima C. Proteestaanti

D. kan biraa yoo ta'e ibsaa_____

111. Saba:

A. Oroomo B. Amaaraa C. Walaaytaa

D. Kafaa E. Daawroo F. Kan biraa yoo ta'e ibsaa_____

Kutaa lamaffaa

Gaafilee armaan gadittii tarreefaman wantoota dhukubstaa si'essan fi sirna nyaataa dhukkubstaa ittiin gaafadhuu ta'a.

201. Dandeettii sochii qaamaa gotuu? (sochii qaamaa kamiyyuu).

A. Eyyee B. hin godhuu

202. Deebin kessan "**Eyyee**" yoo ta'e ji'ota darban 6 kessattii sochii qaamaa gotani beektu?

A. Eyyee B. hin gone

203. Yeroo ammaa sochii qaamaa gotuu?

A. Eyyee B. hin godhuu

204. Torbettii guyyaa meqaaf sochii qaamaa gotuu? _____

205. Guyyatti daqiiqaa/ sa'aati meqaaf sochii qaaamaa gotuu? _____

206. Sigaraa/tanboo ni arsituu?

A. Eyyee B. hin arsuu

207. Deebin kessan "**Eyyee**" yoo ta'e waggaa tokkoo darbee kana kessaa arsitanii beektu?

A. Eyyee B. hin arsuu

208. Yeroo ammaa kessattii ni arsituu?

A. Eyyee B. hin arsuu

209. Guyyaatii sigaaraa paaketi meeqa arsituu? _____

210. Waggaa meqaaf sigaaraa arsitan? _____

211. Buna dhugduu?

A. Eyyee B. hin dhugu

212. Deebin kessan "**Eyyee**" yoo ta'e ji'ota darban 6 kana kessatii buna dhugdu?

A. Eyyee B. hin dhugu

213. Yeroo ammaa kessattii buna dhugdu?

A. Eyyee B. hin dhugu

214. Guyyaatii buna sinii meeqa dhugdu? _____

215. Alkooli dhugduu?

A. Eyyee B. hin dhugu

216. Deebin kessan "**Eyyee**" yoo ta'e ji'ota darban 6 kana kessatii alkooli dhugdu?

A. Eyyee B. hin dhugu

217. Yeroo ammaa kessattii alkooli dhugdu?

A. Eyyee B. hin dhugu

218. Guyyaatii alkooli meeqa dhugdu? _____

219. Annan dhugduu?

A. Eyyee B. hin dhugu

220. Deebin kessan "**Eyyee**" yoo ta'e ji'ota darban 6 kana kessatii annan dhugdu?

A. Eyyee B. hin dhugu

221. Yeroo ammaa kessattii annan dhugdu?

A. Eyyee B. hin dhugu

222. Torbetti bircuuqqoo alkooli meeqa dhugdu? _____

223. Amala kuduraa nyaachuu qabdu? (burtukaani, muza..)

A. Eyyee B. hin qabu

224. Deebin kessan "**Eyyee**" yoo ta'e ji'ota darban 6 kana kessatii kuduraa ni fayyadamtu?

A. Eyyee B. hin fayyadamu

225. Yeroo ammaa kessattii kuduraa fayyadamtu?

A. Eyyee B. hin fayyadamu

226. Torbetti yeroo meeqaaf kuduraa fayyadamtu? _____

227. Amala muduraa nyaachuu qabdu? (raafuu, Dabaaqula...)

A. Eyyee B. hin qabu

228. Deebin kessan "**Eyyee**" yoo ta'e ji'ota darban 6 kana kessatii muduraa ni fayyadamtu?

A. Eyyee B. hin fayyadamu

229. Yeroo ammaa kessattii muduraa fayyadamtu?

A. Eyyee B. hin Fayyadamu

230. Torbetti yeroo meeqaaf muduraa fayyadamtu? _____

Kutaa sadaffaa

Gaafileen armaan gadii haalaa dhukustaan qoricha ittin fayyadamuu gaafachuu ta'a.

301. Guyyaati qooricha koortikosterooydi miligiraamii meeqa liqimsituu?

_____ miligrami/guyyaatti.

Kutaa Afuraffaa

Qabxii eksireeyi/raaji jabina albuuda lafee

401. Lumbbaar Spaayin -2 _____sentimetiri skuuweri graami

402. Lumbbaar Spaayin -3 _____sentimetiri skuuweri graami

403. Lumbbaar Spaayin -4 _____sentimetiri skuuweri graami

404. Avirajii lumbbaar Spaayin gatii_____sentimetiri skuuweri graami

405. Gatiin **"T"** _____

Hirmaannaa keessaniif galatomaa!!!

Annex-10: Dummy table

10.1. Socio-demographic variables

Variables	**Category**	**n (%)**
Sex	Male	
	Female	
Age (year)	< 50	
	50—59	
	≥ 60	
Marital status	Single	
	Married	
	Divorced	
	Widowed	
Religion status	Orthodox	
	Muslim	
	Protestant	
	Others	
Level of education	Illiterate	
	Primary [1–8]	
	Secondary [9–12]	
	College /University	
Ethnicity status	Oromo	
	Amhara	
	Kefa	
	Dawro	
	Others	
Occupation / Employment status	Employed	
	Unemployed	
	Merchant	
	Farmer	

Monthly income (Ethiopian Birr)	< 1000	
	1001—2000	
	> 2000	

10.2. Anthropometric variables

Variables	**Mean ± SD**	
Height (m)		
Weight (kg)		
Variables	**Category**	**n (%)**
Low body mass index	≤ 18.5 kg/m^2	
	> 18.5 kg/m^2	

10.3. Lifestyle related variables

Variables	**Category**	**n (%)**
Smoking cigarette	≤ 20 packs/year	
	> 20 packs/year	
Coffee intake	≤ 2 cups/day	
	> 2 cups/day	
Alcohol intake	≤ 2 drinks/day	
	> 2 drinks/day	
Physically inactive	< 3 hours/week	
	≥ 3 hours/week	

10.4. Nutrition related variables

Variables	**Category**	**n (%)**
Milk intake	≤ 4 glasses/week	
	> 4 glasses/week	
Fruit intake	≤ 4 times/week	
	> 4 times/week	
Vegetable intake	≤ 4 times/week	
	> 4 times/week	

10.5. Drug related variables

Variables	**Category**	**n (%)**
Doses of corticosteroid therapy	≤ 7.5mg/day	
	> 7.5mg/day	

10.6. Bone mineral density result

Variables	**Values of BMD (g/cm^2)**
Lumbar spine—2	
Lumbar spine—3	
Lumbar spine—4	
Average lumbar spine:	

T- scores of lumbar spine	

10.7. Categorization of bone mineral density based on T- scores (WHO criteria)

Variables	**Category**	**n (%)**
Normal BMD	T- scores; > −1.0	
Osteopenia	T- scores; b/n −1.0 and −2.5	
Osteoporosis	T- scores; ≤ −2.5	

DECLARATION

I, the undersigned declare that this research thesis is my original work in partial fulfillment of the requirements for the Degree of Master of Science (Msc) in Medical Physiology. I also declare that it has never been presented in this or any other University and all people who gave support for this work are fully acknowledged.

Student: _____

Signature: _____

Name of the institution: Jimma University

Date of submission: _____

This research thesis has been submitted for examination with my approval as University advisor.

Principal advisor;

Name: _____

Signature: _____

Co -advisor;

Name: _____

Signature: _____

Examiner;

Name: _____

Signature: _____