**Addis Ababa University College of Health Sciences**

**School of Medicine**

**Department of Internal Medicine**

# Assessment of the risk and associated factors of Osteoporosis in IBD patients followed at the Gastroenterology clinic of Tikur Anbessa Specialized Hospital.

A hospital-based cross-sectional Study

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**Advisor and Mentor** –Abate Bane, Professor of Internal medicine and consultant Gastroenterologist

A thesis proposal submitted to Addis Ababa University, College of Health Sciences, School of Medicine, Department of Internal Medicine in preparation for partial fulfillment of the requirement for a Specialty certificate in Internal Medicine

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|---|---|
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| The full title of the research project | Assessment of the risk and associated factors of Osteoporosis in IBD patients followed at the Gastroenterology clinic of TASH. |
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# Approval Sheet

**ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, SCHOOL OF MEDICINE, DEPARTMENT OF INTERNAL MEDICINE, POSTGRADUATE PROGRAM**

I, Dr. Yared Getachew, hereby declare that this thesis entitled "Assessment of the risk and associated factors of Osteoporosis in IBD patients followed at the Gastroenterology clinic of Tikur Anbessa Specialized Hospital" in line with the requirement of graduate studies was fully undertaken by me under the guidance of my advisor and that I have, to the best of my knowledge and effort, avoided plagiarism or duplication of materials unless and otherwise cited and/or acknowledged and that it has not been so far submitted for any form of publication or consideration before the final approval.

_____ _____ _____

Principal investigator Signature Date

We hereby certify that we have read and evaluated this research thesis relating to "Assessment of the risk and associated factors of Osteoporosis in IBD patients followed at the Gastroenterology clinic of Tikur Anbessa Specialized Hospital" under our guidance from its inception up to in its current format and that it can be submitted for final approval in partial fulfillment to the Certificate of Specialty in Internal Medicine.

_____ _____ _____

Advisor Signature Date

As a member of the MSc research open defense examination, I certify that I have read and evaluated the thesis prepared by Yared Getachew (MD), and examined the candidate. I recommend that the thesis be accepted as fulfilling the thesis requirements for the Certificate of Specialty in Internal Medicine.

_____ _____ _____ Examiner

Signature Date

## Acknowledgment

First and foremost, I will give all glory to God, who has been and will always be alongside me throughout my journey in life.

I am also thankful to the **Department** of **Internal Medicine** at Tikur Anbessa Specialized Hospital (**TASH**) for allowing me to undertake this study. I am grateful to my advisor, **Professor Abate**, for his constant guidance and to the staff of TASH for their unlimited assistance during data collection.

# List of Abbreviations

| | |
|---|---|
| AAU | **Addis Ababa University** |
| AGA | **American Gastroenterology Association** |
| BMD | **Bone Mineral density** |
| CD | **Chron's disease** |
| CDAI | **Chron's disease activity index** |
| DXA | **Dual x-ray absorptiometry** |
| EMR | **Electronic medical record** |
| FRAX | **Fracture risk assessment tool** |
| GI | **Gastrointestinal** |
| IBD | **Inflammatory bowel disease** |
| OP | **Osteoporosis** |
| OPD | **Outpatient department** |
| PTH | **Parathyroid hormone** |
| RANKL | **Receptor activator for the nuclear factor–kappa B ligand** |
| SPSS | **Statistical Package for Social Sciences** |
| TASH | **Tikur Anbessa Specialized Hospital** |
| UC | **Ulcerative Colitis** |
| WHO | **World Health Organization** |

# Abstract

## Background:

Inflammatory Bowel Disease (IBD) represents a group of long-term inflammatory conditions affecting the digestive tract, encompassing both Crohn's disease and ulcerative colitis. Although these diseases display distinct pathological and clinical features, they share considerable similarities in their underlying mechanisms, which are not fully understood. Osteoporosis, a prevalent condition marked by decreased bone density, structural deterioration of bone tissue, and increased vulnerability to fractures, is frequently diagnosed in individuals with IBD, such as those with Crohn's disease and ulcerative colitis. It is thought that the heightened risk of osteoporosis and subsequent fractures in IBD patients can be attributed to various factors, including the use of corticosteroids, dietary limitations, and issues with nutrient absorption.

## Objective:

To analyze the risk and associated factors of Osteoporosis in IBD patients who are followed at the GI clinic of TASH.

## Methods:

Cross-sectional study conducted on IBD patients followed at the GI clinic in TASH between June 2023 and November 2023. Data was collected from eligible individuals using a structured questionnaire on sociodemographic characteristics, GI symptoms, factors associated with Osteoporosis, and IBD-related factors. Data entered into SPSS version 26 and analyzed using descriptive statistics, Pearson correlation, binary logistic and multivariable regression for association between variables at a statistical significance set at p value <0.05.

## Results:

A total of 117 patients with Inflammatory Bowel Disease (CD and UC), were included in the study. There were 81 women and 36 men (F:M= 2.25:1). The mean and SD of the age of the participants were 34.8 ± 11.73 years respectively. The mean and SD value of 10-year Major Osteoporosis fracture risk and 10-year Hip fracture risk in percent were [3.94 ± 3.98] and [0.84 ± 1.01 %] respectively. From these, 19.6% of the participants had an increased osteoporosis and fracture risk. Multivariate logistic regression revealed four factors to be significantly correlated with increased osteoporosis risk in IBD patients; UC type IBD (p= 0.024), personal history of osteoporosis (p= 0.001), alcohol consumption history (p=0.005) and glucocorticoid use > 1 year. Pearson correlation also revealed increasing age (r= 0.234) (p= 0.011) and prolonged duration of IBD (r=0.272) (p= 0.003) with increased osteoporosis and fracture risks.

# Conclusion:

The study has revealed increasing age, having UC type of IBD, duration of IBD, personal history of osteoporosis, alcohol consumption history and glucocorticoid use duration of > 1 year were independent risk factors for increased risk of osteoporosis while increased disease activity for both CD and UC had a positive correlation to increased osteoporosis risk. Meanwhile sex, BMI, small bowel resection history and Glucocorticoid dose did not have significant association with increased risk of osteoporosis.

However, further large-scale, prospective studies are needed to draw firm conclusions on this subject and develop targeted prevention and treatment strategies for osteoporosis in the IBD population.

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# Introduction

## Background of the study

Inflammatory bowel disease (IBD) consists of two primary conditions: Crohn's disease and ulcerative colitis. Crohn's disease has the potential to impact any segment of the digestive tract., ranging from the mouth to the area around the anus, ulcerative colitis is specifically targeted at the colon. The onset of both conditions is thought to result from a mix of genetic predispositions, environmental influences, and immune system responses [1].

The prevalence of IBD has been increasing globally with variations by geographic region, and the number of individuals affected by IBD across the globe rose from 3.7 million in 1990 to 6.8 million by the year 2017 [2,3]. Rates of Crohn's disease and ulcerative colitis seem to be notably lower in regions such as Asia and the Middle East. Yet, emerging industrial nations across Africa, Asia, and South America have seen an uptick in inflammatory bowel disease cases[4–6].

While inflammatory bowel disease (IBD) has been well characterized in the West and other parts of the world, there is little data from sub-Saharan Africa (SSA)[7]. A descriptive study done at TASH in 2020 found a total of 102 IBD patients where there was a female predominance and the mean of diagnosis was three and four decades of life[8]. However, the risk of Osteoporosis or associated OP risk factors was not studied.

There is a paucity of documented cases of IBD in SSA, possibly reflecting under-diagnosis and under-reporting; suffice it to say, better effort must be put forth to combat the scarcity of data. [7]

Osteoporosis is increasingly recognized as a critical health and economic issue, marked by a widespread decrease in bone density, strength, and structural integrity. This condition significantly raises the risk of fractures from minor injuries. The World Health Organization (WHO) has set forth a specific definition for osteoporosis based on bone mineral density (BMD) measurements. According to this definition, osteoporosis occurs when a person's BMD is more than 2.5 standard deviations below the mean value for a young, healthy female population, equating to a T-score of less than -2.5 SD[9].

In a comprehensive review of 70 studies published in 2021, it was found that globally, 23.1% of women (with a 95% confidence interval (CI) of 19.8–26.9) and 11.7% of men (95% CI 9.6–14.1) suffer from Osteoporosis. This analysis included data from 453,964 men across 40 studies. Among various regions, Africa recorded the highest occurrence rate of Osteoporosis at 39.5% (95% CI 22.3–59.7)[10].

So far, there are no published studies in Ethiopia on the burden of Osteoporosis despite prevalent predisposing factors to the condition (nutritional deficiency and comorbid conditions like HIV).

A retrospective study from Ethiopia in all fracture subjects found that 9.3% of all fractures were secondary to Osteoporosis, and the sex-specific prevalence rate was 9.5 and 8.9% for men and women, respectively[11].

Individuals diagnosed with inflammatory bowel disease (IBD) have an elevated risk of developing osteoporosis. This condition increases the likelihood of fractures, which can lead to substantial financial and phycological strain.

## 2.2 Statement of the problem

As bone density loss often goes undetected without any noticeable symptoms until a fracture occurs, effective screening techniques must be utilized to identify cases in which preventive strategies can be implemented. And hence, the development of osteoporotic fractures as a consequence makes Osteoporosis associated with significant economic and psychological burden[12,13].

Research indicates that individuals suffering from inflammatory bowel disease possess a greater likelihood of being diagnosed with osteoporosis and osteopenia than the general population, with a relative risk of fracture 40% higher in patients with inflammatory bowel disease[14].

Identifying individuals with the highest risk of osteoporosis accurately continues to be a challenge. However, glucocorticoid therapy and hypogonadism are likely important contributory factors, and the increase in risk may be tremendous in patients with Crohn's disease[15].

This is the rationale for the AGA's recommendation for screening DXA in those "at risk" IBD patients with a history of vertebral fractures, postmenopausal women, men 50 years of age and above, chronic corticosteroid therapy, or hypogonadism[16].

Because of the lack of readily available DXA scans in resource-limited areas and other BMD-independent risk factors, other strategies should be utilized in caring for these patients.

Clinical fracture risk assessment tools such as the WHO Fracture Risk Assessment (FRAX) have been developed, which utilize clinical factors and (optionally) femoral neck bone mineral density to estimate the 10-year probability of developing a significant osteoporosis fracture or a 10-year probability of a hip fracture, which can then be used to guide decisions on instituting fracture-prevention therapies[17].

FRAX serves as a tool to estimate the likelihood of fractures without the need for direct bone mineral density (BMD) measurements, and it can pinpoint individuals with inflammatory bowel disease (IBD) for whom BMD information might not alter therapeutic strategies[18].

So, this study aims to assess the risk and associated factors of Osteoporosis in IBD patients using this clinical risk assessment tool.

## 2.3 Significance of the study

There is limited research done in Ethiopia[8,19,20] that assessed the prevalence and characteristics of IBD. Moreover, no study at Tikur Anbessa Hospital assessed the risk and variables associated with Osteoporosis among IBD patients. This study aims to fill this gap.

Research employing dual-energy X-ray absorptiometry indicates a significant occurrence of osteoporosis in individuals with inflammatory bowel disease. However, data from population studies on fracture rates only show a slight elevation in the risk of fractures in patients with IBD when compared to the broader population [21].

Hence, identifying patients with inflammatory bowel disease who are at a particularly high risk for fractures using clinical risk evaluation tools would be beneficial.

This approach enables medical practitioners to more accurately evaluate osteoporosis risk in individuals with IBD, allowing for personalized interventions aimed at minimizing fracture risk and enhancing their overall well-being. Furthermore, early diagnosis and treatment of Osteoporosis can prevent the progression of this condition and minimize its complications, such as fractures and disability.

# Literature review

## Epidemiology

Osteoporosis is common in patients with IBD such as Crohn's disease (CD) or ulcerative colitis (UC), and there have been varying reports concerning its prevalence in IBD patients.

In various population-based studies, the prevalence of Osteoporosis among IBD patients ranged from 2% to 15%, with a range of 2% to 9% in UC patients and 7% to 15% in CD patients. This was in contrast to the 3-10% prevalence of Osteoporosis among healthy controls[22].

A comprehensive analysis of 12 research papers, encompassing 3,661 patients with inflammatory bowel disease (IBD) and 12,789 individuals without the condition, revealed that the occurrence of osteoporosis ranged from 4% to 9% in research involving patients with both Crohn's disease (CD) and Ulcerative Colitis (UC), 2% to 9% in research focused solely on UC patients, and 7% to 15% in studies examining patients with CD. Among healthy controls, the prevalence of Osteoporosis was 3% and 10% in two studies[22].

In a different meta-analysis, it was found that patients with IBD had a considerably increased risk of fractures compared to the general population, with a relative risk of 1.38 (95% Confidence Intervals [CIs], 1.11–1.73) for all types of fractures and a relative risk of 2.26 (95% CIs, 1.04–4.90) specifically for vertebral fractures[23].

Therefore, individuals suffering from Inflammatory Bowel Disease (IBD) are more susceptible to fractures, particularly in the vertebrae. This increased risk is observed uniformly in both men and women and is largely equivalent between Crohn's Disease (CD) and Ulcerative Colitis (UC)[24].

## Risk factors

The risk factors for Osteoporosis can be seen as general or disease-specific risk factors of inflammatory bowel disease. The general risk factors can further be classified into modifiable and nonmodifiable risk factors, which include advancing age, female sex, personal and family history of fracture[25,26].

Modifiable risk factors encompass insufficient dietary intake of calcium and vitamin D or problems with their absorption, possessing a low body mass index (BMI), and the use of medications that might inhibit new bone formation, expedite bone degradation, or affect both processes[27,28].

Various clinical syndromes, including rheumatoid arthritis, celiac disease, chronic liver disease, chronic renal insufficiency, hyperthyroidism, and conditions that lead to prolonged immobility or decreased opportunities for weight-bearing exercise, are associated with higher rates of Osteoporosis[29–31].

In addition, it has demonstrated that a previous low-trauma fracture, prolonged glucocorticoid use, parental history of hip fracture, smoking, and high alcohol intake are known to increase the risk of fracture independent of their effects on BMD [32,33].

Several factors have been identified as contributing to the increased susceptibility to bone weakness in individuals with inflammatory bowel disease (IBD). These include genetic predispositions, nutritional deficiencies or malabsorption issues, lack of sufficient calcium and vitamin D, deficits in sex hormones, an imbalanced gut microbiome, and the impact of certain medications, especially long-term use of glucocorticoids. These elements should be taken into account when managing patients with IBD [27,34,35].

Evidence shows that increased systemic inflammatory activity increases bone resorption and decreases new bone formation [36]. The maturation and activation of osteoclasts are mainly driven by the nuclear factor kappa B, whose production is in turn regulated by the binding of receptor-activated nuclear factor kappa B ligand (RANK-L) to receptors found on the surface of osteoclast progenitor cells [37].

It is established that cytokines such as tumor necrosis factor (TNF) alpha, interleukin 1 and 6, and interferon-gamma, which are elaborated in the setting of IBD and other chronic inflammatory states, are known to increase production of RANK-L, thereby promoting increased bone turnover [37].

In support of a direct role for inflammation as detrimental to bone health, nonglucocorticoid-based treatment of intestinal inflammation with agents that inhibit TNF-alpha activity has been shown to improve BMD [38].

Many individuals with inflammatory bowel disease (IBD) frequently experience a deficiency in Vitamin D, attributed to various factors such as impaired absorption in the intestines, reduced dietary intake, and limited exposure to sunlight. This deficiency can adversely affect calcium equilibrium, resulting in secondary hyperparathyroidism[39].

Malnutrition also leads to a low BMI, commonly associated with osteopenia and decreased muscle strength. It might also contribute to sarcopenia, commonly observed in patients suffering from IBD. Sarcopenia has been strongly associated with osteopenia and Osteoporosis in patients suffering from IBD. Lower weight and lower BMI were predictors of Osteoporosis or low BMD in IBD patients in a recent systematic review [40].

Glucocorticoid exposure is very common in patients with IBD, with over 50% of persons exposed to systemic glucocorticoids within five years of diagnosis and 20% having used at least 3 g of prednisone in any one year [41].

Glucocorticoids are known to enhance the longevity of osteoclasts while strongly suppressing the formation of osteoblasts and elevating the rate of osteoblast cell death. Consequently, they are considered one of the most harmful substances affecting bone health [33]. The most significant

effect is usually seen in the initial months of treatment and with high dosages, especially in areas of trabecular bone, such as the vertebrae [42].

Studies on people suffering from inflammatory bowel disease (IBD) have consistently shown that taking systemic glucocorticoids poses a risk for developing osteoporosis and a gradual decrease in bone mineral density. Additionally, this use has been linked to an increased risk of fractures in those with IBD [42,43].

Even very low doses of corticosteroids (prednisolone 2.5-7.5 mg/day) are associated with increased fracture rates, although the risk increases with higher doses [43].

On the other hand, using anti-TNF-α agents has neutral or even positive effects on maintaining bone mass and preventing fracture in IBD due to its anti-inflammatory effects and possibly its direct effects on bone metabolism [44].

Tools like FRAX for predicting fractures can assist in identifying individuals who need treatment. Additionally, searching for signs of low bone mineral density (BMD) or utilizing CT scans can offer another means to evaluate the risk of fractures in individuals with inflammatory bowel disease (IBD) [45].

# Objectives of the study

## General objectives

To analyze the risk and associated factors of Osteoporosis in IBD patients who are followed at the GI clinic of TASH.

## Specific objectives

To quantify osteoporosis risk via FRAX in patients with IBD
To describe associated factors of Osteoporosis in patients with IBD
To analyze common risk factors of Osteoporosis in patients with IBD

# Research Methods and Materials

## Study area

The study was done at the GI clinic of Tikur Anbessa Specialized Hospital (TASH) in Addis Ababa, the capital city of Ethiopia. TASH is the largest tertiary hospital in Ethiopia, offering diagnosis and treatment for approximately 370,000–400,000 patients annually.

There are 16 outpatient clinics located within the hospital. The GI clinic has over 600 visits per month, of which are 100-150 IBD patients. The TASH GI unit was established in 1978 GC and has eight senior staff members.

The department offers outpatient and inpatient endoscopy and colonoscopy, diagnostic and therapeutic services, and teaching opportunities for undergraduate, postgraduate residency, and GI fellowship teaching activities.

## Study period

- The study was conducted from 1 June to 30 November 2023, GC

## Study design

- A hospital-based cross-sectional study was conducted

# Population

## Source population

- All adult registered IBD patients who visited the GI clinic of TASH

## Study population

- All eligible IBD patients who provided informed consent

## Sample size

- The sample size was determined using the formula for a single population proportion, considering a prevalence of 50% due to the lack of local data.
- The sample was calculated by assuming a Confidence interval of 95%, 5% margin of error, and 10% non-response rate.

$$n = \frac{Z^2 x\ (p)\ (1-p)}{d^2}$$

  - Z - z-score -1.96
  - d - margin of error- 0.05
  - p - population proportion—50% (0.5)
  - n - Sample size- 384.16% ≈ 384
  -
- Since the source population is <10,000
  - n= 384
  - N=200
  - Sample size=$\frac{n}{1+n/N}$ =$\frac{384}{1+384/200}$=131.4 ~ 131

Adjusting for non-response

- n*= Final sample size
- Response rate= 0.95
- n* = n /response rate= 131/0.95= 137.8~ 138

## Sampling procedures

A random sampling method was used after a list of patients with IBD is obtained from the clinics, and participants were selected randomly from the list.

## Study variables

### Dependent variables

- Risk of Osteoporosis and fracture

### Independent variables

- Age
- Sex
- BMI
- Disease activity
- Glucocorticoid dose
- Glucocorticoid duration
- Type of inflammatory bowel disease
- Small bowel resection history
- Vitamin D and calcium levels

## Inclusion and Criteria

### Inclusion criteria

- Adults aged 18 and above with a diagnosis of IBD who have been on follow-up at study areas for at least one month

### Exclusion criteria

- Patients who do not provide informed consent
- Age less than 18 years
- Patients with malignancy
- Patients with CKD (stage 3-5)
- Patients with untreated hyperthyroidism/hyperparathyroidism
- Patients with connective diseases
- Patients on the following medications
    - Anticoagulants, antiepileptics, hormonal replacement therapy

## Operational definitions

- Risk of Osteoporosis is defined as: **Very high, Intermediate/High risk of major osteoporotic fracture** or **high-risk hip fracture**

    - 10-year probability of hip fracture
        - High risk $\geq$ 3%
        - Low risk < 3%
    - 10-year probability combined major osteoporotic fracture
        - Very high risk ≥20%
        - Intermediate/high risk 10-19%
        - Low risk < 10%

- Fragility fracture: Fractures occurring spontaneously or from minor trauma, (eg. fracture from a fall of standing height or less)

- Associated factors: Variables that have a statistically significant association with the risk of Osteoporosis in patients with inflammatory bowel disease, as determined through multivariate logistic regression analysis

- Type of IBD: Crohn's disease, ulcerative colitis, and indeterminate IBD, as confirmed by histology from colonoscopies or endoscopies.

- Glucocorticoid use: Use of prednisolone (or equivalent dose steroid) ≥5 mg for ≥3 months

- Disease activity:
    - Will be assessed using “CDAI” for patients with CD as remission
    - Will be assessed using “The Montreal classification” for patients with UC as mild, moderate and severe
- Small bowel resection history: History of operation on the small intestine whereby partial or total removal was done

- Smoking: Self-reported history of cigarette smoking, including current or former smoking status and pack-years of smoking

## Data collection and procedures

The principal investigator prepared a data collection tool, and data was gathered from patients in GI clinic. If patients had recorded laboratory values of serum Ca, Vitamin D, and DXA results, these were collected from EMR and patients' medical charts.

## Data processing and analysis

After checking for completeness and internal consistency, data was entered into SPSS version 26 manually. Measured variables were expressed in terms of mean and Standard deviation. To assess the connection between outcome measures and predictive factors, the Pearson correlation was applied to continuous variables, while multivariable logistic regression was utilized for categorical variables. An association will be deemed significant if the p-value is less than 0.05.

## Ethical consideration

The proposal was submitted to department of internal medicine and ethical clearance was issued by the department of internal medicine and college of medicine and health sciences.

## Dissemination plan

The study findings will be submitted and be available on the AAU research repository. It will also be submitted for presentations and publications.

## Results

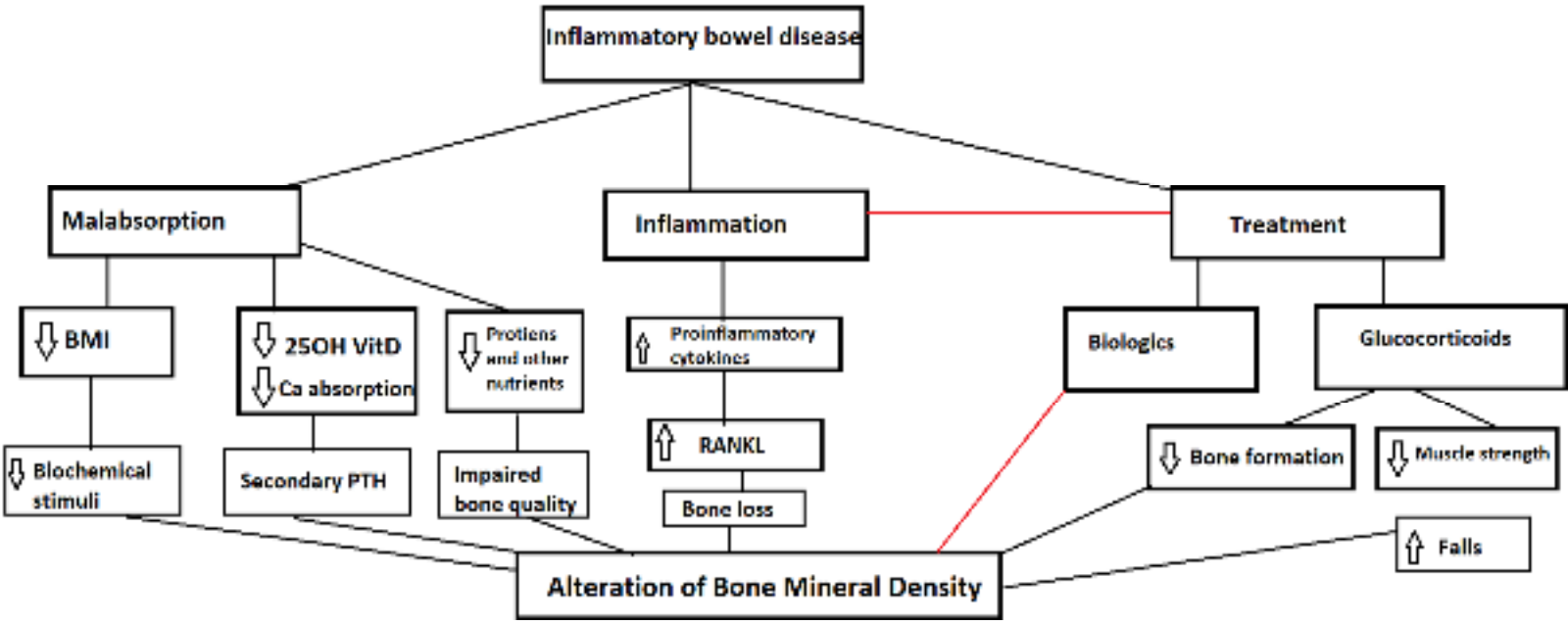
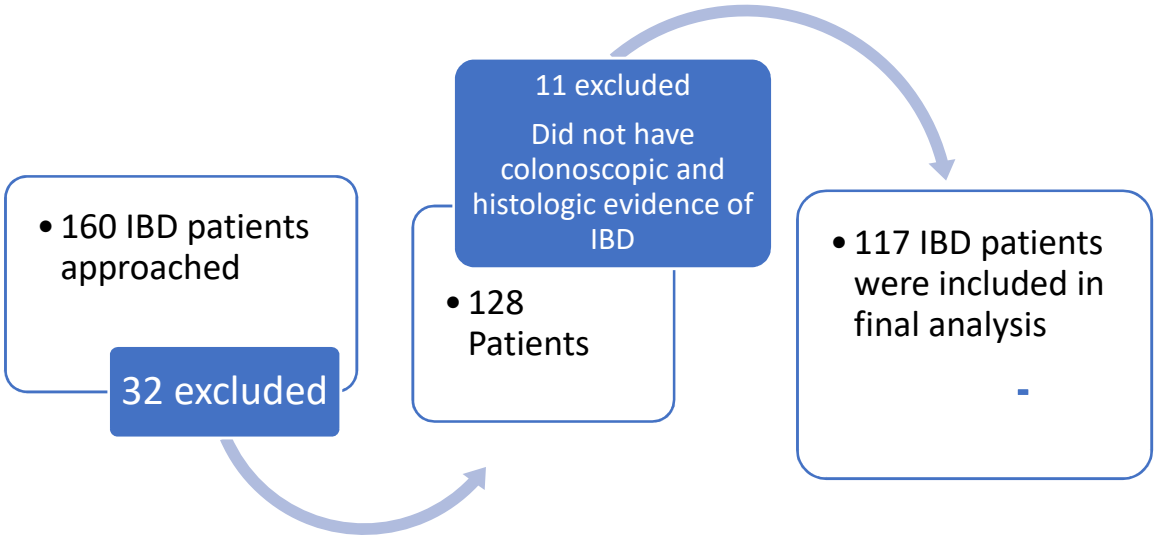



Figure 1 Pathophysiology and risk factors for Osteoporosis in Inflammatory bowel patients

## Flow chart




## Results

### Sociodemographic characteristics of the study participants

In this study, 117 study participants were involved, making a response rate of 89.3%. More than two-thirds of the study participants were female, and around 80% of the study participants were in the age range of 18-40 years, with a mean and SD of 34.8 ± 11.73 years, respectively. Most (84.6%) of the study participants were from urban areas, and 53% were married. Forty percent of the study participants had an education level of college and above, and 45.4% were employed.

Table 1. Sociodemographic characteristics of the study IBD patients followed at the Gastroenterology clinic of TASH, 2023.

| Variable | Frequency | Percent |
|---|---|---|
| **Sex of the participants** | | |
| **Male** | 36 | 30.8 |
| **Female** | 81 | 69.2 |
| **Age in years** | | |
| **18-30** | 47 | 40.2 |
| **31-40** | 46 | 39.2 |
| **41-50** | 11 | 9.4 |
| **>50** | 13 | 11.1 |
| **Residence** | | |
| **Urban** | 99 | 84.6 |
| **Rural** | 18 | 15.4 |
| **Marital status** | | |
| **Single** | 49 | 41.9 |

| | | |
|---|---|---|
| **Married** | 62 | 53 |
| **Divorced** | 5 | 4.3 |
| **Widowed** | 1 | 0.9 |
| **Education level** | | |
| **No formal educational** | 14 | 12 |
| **Primary school** | 26 | 22.2 |
| **Secondary school** | 30 | 25.6 |
| **Higher education** | 47 | 40.2 |
| **Occupation** | | |
| **Governmental employee** | 18 | 15.4 |
| **Private** | 23 | 19.7 |
| **Self-employed** | 12 | 10.3 |
| **Unemployed** | 55 | 47 |
| **Student** | 9 | 7.7 |

## Medical history-related characteristics of the study participants

Three forth of the study participants had Chron's type of Inflammatory bowel disease, and 62.4% of the participants had 1-5 years duration of IBD disease. Almost all (96.6%) of the study participants were using IBD treatment, and from those, Azathioprine was used by 83.2%. Ten percent of the study participants had comorbid diseases, Hypertension accounting for 50%, followed by Diabetes and HIV/AIDS infection.

Table 2. Medical history-related characteristics of the study participants

| Variable | Frequency | Percent |
|---|---|---|
| **Types of IBD** | | |
| **Chron's disease** | 90 | 76.9 |
| **Ulcerative colitis** | 27 | 23.1 |
| **Duration of IBD in years** | | |
| **<1** | 18 | 15.4 |
| **1-5** | 73 | 62.4 |
| **>5** | 26 | 22.2 |
| **Use treatment for IBD** | | |
| **Yes** | 113 | 96.6 |
| **No** | 4 | 3.4 |
| **Medication for IBD (n=11-3)** | | |
| **Azathioprine** | 94 | 83.2 |
| **Mesalamine** | 10 | 8.8 |
| **Sulfasalazine** | 1 | 0.9 |
| **Weekly methotrexate** | 8 | 7.1 |
| **Comorbidity** | | |
| **Yes** | 12 | 10.3 |
| **No** | 105 | 89.7 |

| | | |
|---|---|---|
| **Comorbidities (n=12)** | | |
| **Diabetes** | 2 | 16.7 |
| **Hypertension** | 6 | 50 |
| **Hyperlipidemia** | 1 | 8.3 |
| **Cardiovascular disease** | 1 | 8.3 |
| **HIV/AIDS infection** | 2 | 16.7 |

## Risk Factors for Osteoporosis related characteristics of the study participants

Thirteen patients had a history of osteoporosis, and from these, only eight were treated, taking calcium and vitamin D tablets. Twenty-four percent of the study participants were either former or current drinkers, and only one patient had a smoking history. 38.5% of the study participants, on average, exercised 3-5 times per week, but 37.6% never or hardly exercised. Only one participant had a personal history of hip fracture, while 2 of the participants had a family history of hip fracture. Calcium and Vitamin D supplement usage was 15.4% and 12% respectively among participants.

Table 3. Risk Factors for Osteoporosis related characteristics of the study participants

| Variable | Frequency | Percent |
|---|---|---|
| **History of osteoporosis** | | |
| **Yes** | 13 | 11.1 |
| **No** | 104 | 88.9 |
| **Bone mineral density done** | | |
| **Yes** | 2 | 1.7 |
| **No** | 115 | 98.3 |
| **Was osteoporosis treated (n=13)** | | |
| **Yes** | 8 | 61.5 |
| **No** | 5 | 38.5 |
| **Type of osteoporosis medication (n=8)** | | |
| **Calcium/Vitamin D** | 8 | 100 |
| **Alcohol consumption** | | |
| **Yes** | 28 | 23.9 |
| **No** | 89 | 76.1 |
| **Status of alcohol consumption (n=28)** | | |
| **Former** | 14 | 50 |
| **Current** | 14 | 50 |
| **Smoking history** | | |
| **Yes** | 1 | 0.9 |
| **No** | 116 | 99.1 |
| **Smoking pack years** | | |
| **1-5 pack years** | 1 | 100 |
| **Average weekly exercise** | | |
| **Never or hardly** | 44 | 37.6 |

| | | |
|---|---|---|
| **1-2times** | 20 | 17.1 |
| **3-5 times** | 45 | 38.5 |
| **6-7 times** | 8 | 6.8 |
| **History of hip fracture** | | |
| **Yes** | 1 | 0.9 |
| **No** | 116 | 99.1 |
| **Family history of hip fracture** | | |
| **Yes** | 2 | 1.7 |
| **No** | 115 | 98.3 |
| **Calcium supplement** | | |
| **Yes** | 18 | 15.4 |
| **No** | 99 | 84.6 |
| **Vitamin D supplement** | | |
| **Yes** | 14 | 12 |
| **No** | 103 | 88 |

## Inflammatory bowel disease-related management characteristics of the participants

In this study, 43.6% of the study participants took glucocorticoid ≤3 months, while 9% had usage for more than a year. 32.5% of the participants had a history of bowel surgery, where, in 60% of patients, the indication for surgery was fistulizing complications. Forty one percent of the study participants had weight loss after IBD treatment, and from those, 45.8% lost 5-10kgs. More than fifty-seven percent of the participants had normal body mass index, 44.6% had remission CDAI, while 16% of UC patients had severe disease activity.

Table 4. Inflammatory bowel disease-related management characteristics of the participants

| Variable | Frequency | Percent |
|---|---|---|
| **Glucocorticoid use duration in month** | | |
| **≤3** | 51 | 43.6 |
| **4-6** | 37 | 31.6 |
| **7-12** | 18 | 15.4 |
| **>12** | 11 | 9.4 |
| **Stable dose of glucocorticoids in mg (mean ±SD) =** | 26.07 ± 20.0 mg | |
| **History of bowel surgery** | | |
| **Yes** | 38 | 32.5 |
| **No** | 79 | 67.5 |
| **Indication for surgery (n=38)** | | |
| **Intestinal stricture** | 15 | 39.5 |
| **Fistulizing complication/abdominal abscess** | 23 | 60.5 |
| **Weight loss since IBD treatment** | | |
| **No** | 69 | 59 |
| **Yes** | 48 | 41 |

| | | |
|---|---|---|
| **Loss of weight in kg (n=48)** | | |
| **1-5kg** | 15 | 31.3 |
| **5-10kg** | 22 | 45.8 |
| **>10kg** | 11 | 22.9 |
| **BMI** | | |
| **<18.5** | 35 | 29.9 |
| **18.5-24.9** | 67 | 57.3 |
| **25-29.9** | 14 | 12 |
| **30-34.9** | 1 | 0.9 |
| **CDAI** | | |
| **Remission** | 41 | 44.6 |
| **Mild to moderate CD** | 29 | 31.5 |
| **Moderate to severely active CD** | 21 | 22.8 |
| **Severely active to fulminant disease** | 1 | 1.1 |
| **Montreal** | | |
| **Remission** | 1 | 4 |
| **Mild UC** | 14 | 56 |
| **Moderate UC** | 6 | 24 |
| **Severe UC** | 4 | 16 |

## The level of risk of osteoporosis characteristics of the study participants

In this study, 6%, 13.7 and 80.3% of the participants had very high, Intermediate-to-high, and low risk of osteoporosis, respectively. The mean and SD value of 10-year Major Osteoporosis fracture risk in percent had 3.94 ± 3.98, as shown in the table below.

Table 2. The level of risk of osteoporosis characteristics of the study participants

| Variable | Frequency | Percentage |
|---|---|---|
| **Osteoporosis risk** | | |
| **Low** | 94 | 80.3 |
| **Intermediate/High** | 16 | 13.7 |
| **Very high** | 7 | 6 |
| **10-year Major Osteoporosis fracture risk in percent mean ± SD** | 3.94 ± 3.98 % | |
| **10-year Hip fracture risk in percent mean ± SD** | 0.84 ± 1.01 % | |

## The risk of osteoporosis of the study participants

In this study, close to 20% of the study participants had a risk of osteoporosis, while 80% had a low risk of osteoporosis, as shown in the figure below.

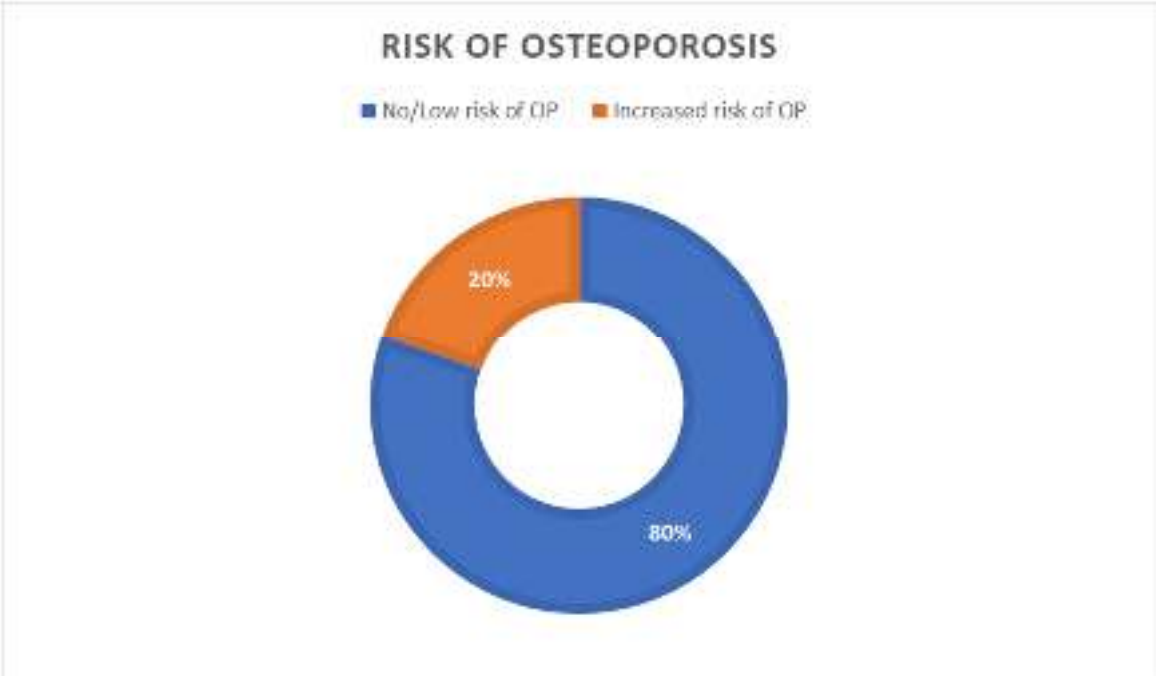



Figure 2. The prevalence of osteoporosis risk among inflammatory bowel disease patients in TASH and Adara Medical Center.

## The association of Pearson correlation function test

The Pearson correlation test showed that the "Duration of IBD" and "Glucocorticoid use duration" were in a positive and statistically significant correlation with 10-year Major Osteoporosis fracture and 10-year Hip fracture risks. On the other hand, daily dose of IBD medication did not demonstrate a significant correlation with either major osteoporosis fracture risk (r = 0.045, p = 0.636) or hip fracture risk (r = -0.007, p = 0.937).

Table 6. The association of the Pearson correlation function test between independent variable and dependent variable

| **Correlations** | | **10-year Major Osteoporosis fracture risk in percent** | **10-year Hip fracture risk in percent** |
|---|---|---|---|
| Age | Pearson Correlation | .158 | .234* |
| | Sig. (2-tailed) | .089 | **.011** |
| | N | 117 | 117 |
| Duration of IBD in years | Pearson Correlation | .185* | .272** |
| | Sig. (2-tailed) | **.046** | **.003** |
| | N | 117 | 117 |
| Daily dose of glucocorticoid in mgs | Pearson Correlation | .045 | -.007 |
| | Sig. (2-tailed) | .636 | .937 |
| | N | 113 | 113 |
| | Pearson Correlation | .205* | .188* |

| | | | |
|---|---|---|---|
| Glucocorticoid use duration in months | Sig. (2-tailed) | **.027** | **.043** |
| | N | 117 | 117 |
| **. Correlation is significant at the 0.01 level (2-tailed). | | | |
| *. Correlation is significant at the 0.05 level (2-tailed). | | | |

## The determinant factor of osteoporosis risk among study participants

The strength of association was measured using an odd ratio and a 95% Confidence interval. Accordingly, education level, types of inflammatory bowel disease, duration of inflammatory bowel disease, history of osteoporosis, history of alcohol consumption, and duration of glucocorticoid use had an association with osteoporosis risk by bivariate logistic regression.

The multivariate logistic regression revealed that study participants having ulcerative colitis had 9.7 folds increase in the risk of osteoporosis compared to patients with Chron's disease (AOR=9.7, 95% CI=1.35, 70.57) and personal history of osteoporosis increased osteoporosis risk 7.7 folds compared to having no history of osteoporosis (AOR=7.7, 95% CI=6.61, 47.47). Study participants who are current or former alcohol consumers had a 20-fold likelihood of osteoporosis compared to patients who had never drunk (AOR=20.2, 95% CI=2.53, 60.96). Study participants who took glucocorticoids for more than 12 months had a 9.5 times risk of osteoporosis compared to those who took them for < 3 months (AOR=9.5, 95%CI=1.52, 17.27).

Table 7. The bivariate and multivariate logistic regression of association between the independent variable and osteoporosis risk among IBD patients.

| Variable | Risk of osteoporosis | | p-value | COR with 95%CI | p-value | AOR with 95%CI |
|---|---|---|---|---|---|---|
| | Yes | No | | | | |
| **Sex** | | | | | | |
| **Male** | 4 | 32 | 1 | | 1 | |
| **Female** | 19 | 62 | 0.130 | 2.5(0.77, 7.82) | 0.156 | 4.6 (0.55, 38.12) |
| **Education level** | | | | | | |
| **Illiterate** | 6 | 8 | 1 | | 1 | |
| **Primary** | 8 | 18 | 0.446 | 0.59(0.15, 2.28) | 0.857 | 0.79 (0.06, 10.80) |
| **Secondary** | 5 | 25 | 0.70 | 0.27(0.06, 1.11) | 0.462 | 1.5 (0.09, 23.51) |
| **Collage and above** | 4 | 43 | 0.005 | 0.12(0.03, 0.54) | 0.130 | 0.09 (0.004, 2.01) |
| **Types of IBD** | | | | | | |
| **Chron's disease** | 12 | 78 | 1 | | 1 | |
| **Ulcerative colitis** | 11 | 16 | 0.003 | 4.5(1.68, 11.89) | 0.024 | **9.7 (1.35, 70.57)** |
| **Duration of IBD** | | | | | | |
| **<1** | 2 | 16 | 1 | | 1 | |
| **1-5** | 9 | 64 | 0.887 | 1.1(0.22, 5.73) | 0.913 | 1.2(0.09, 15.19) |
| **>5** | 12 | 14 | 0.023 | 6.9(1.30, 36.06) | 0.077 | 13.4(0.76, 23.59) |
| **Personal history of osteoporosis** | | | | | | |

| Level of Osteoporosis risk * BMI Crosstabulation | | | | | | |
|---|---|---|---|---|---|---|
| | | | BMI | | | Total |
| | | | < 18.5 | 18.5-24.9 | 25-29.9 | 30-34.9 | |
| Level of OP risk | Low | Count | 28 | 55 | 10 | 1 | 94 |
| | | % within BMI | 80.0% | 82.1% | 71.4% | 100.0% | 80.3% |
| | Intermediate/high | Count | 4 | 8 | 4 | 0 | 16 |
| | | % within BMI | 11.4% | 11.9% | 28.6% | 0.0% | 13.7% |
| | Very high | Count | **3** | **4** | 0 | 0 | 7 |
| | | % within BMI | 8.6% | 6.0% | 0.0% | 0.0% | 6.0% |
| Total | | Count | 35 | 67 | 14 | 1 | 117 |
| | | % within BMI | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |

| | | | | | | |
|---|---|---|---|---|---|---|
| **No** | 14 | 90 | 1 | | 1 | |
| **Yes** | 9 | 4 | 0.000 | 14.5(3.92, 53.37) | 0.001 | **7.7 (6.61, 47.47)** |
| **Alcohol consumption** | | | | | | |
| **Yes** | 12 | 16 | 0.000 | 5.3(1.99, 14.16) | 0.005 | **20.2 (2.53, 60.96)** |
| **No** | 11 | 78 | 1 | | 1 | |
| **Average weekly exercise** | | | | | | |
| **Never or hardly** | 8 | 36 | 0.698 | 1.6(0.17, 14.48) | 0.222 | 0.08(0.001, 4.54) |
| **1-2 times** | 8 | 12 | 0.185 | 0.48, 45.55) | 0.670 | 0.43(0.01, 20.49) |
| **3-5 times** | 6 | 39 | 0.949 | 1.1(0.11, 10.37) | 0.547 | 0.34(0.01, 11.11) |
| **6-7 times** | 1 | 7 | 1 | | 1 | |
| **Duration of glucocorticoid use in months** | | | | | | |
| **<3** | 6 | 45 | 1 | | 1 | |
| **4-6** | 4 | 33 | 0.889 | 0.91(0.24, 3.48) | 0.984 | 1.0(0.12, 8.42) |
| **7-12** | 5 | 13 | 0.121 | 2.9(0.76, 10.99) | 0.397 | 3.2(0.22, 46.22) |
| **>12** | 8 | 3 | 0.000 | 20.0(4.13, 96.78) | 0.029 | **9.5 (1.52, 17.27)** |

Table 8. Crosstabulation of association between BMI and levels of osteoporosis risk

The majority of participants in each BMI category are at low risk of developing osteoporosis, with percentages ranging from 71.4% to 100% across categories. The percentage of individuals at low risk of osteoporosis is highest among those in the obese class I category (100%), followed closely by those in the normal weight and underweight categories. A very high risk of osteoporosis is observed in the underweight and normal weight categories (8.6% and 6%, respectively) but not in the overweight and obese class I categories.

| Correlations | | | | |
|---|---|---|---|---|
| | | | RISK of OP | BMI |
| Kendall's tau_b | Risk of Osteoporosis | Correlation Coefficient | 1.000 | .014 |
| | | Sig. (2-tailed) | . | .874 |
| | | N | 117 | 117 |
| | BMI | Correlation Coefficient | .014 | 1.000 |
| | | Sig. (2-tailed) | .874 | . |
| | | N | 117 | 117 |

Table 9. Kendall's tau_b correlation between risk of osteoporosis and BMI

The correlation coefficient (0.14) indicates a very weak, practically negligible, positive correlation between these two variables, while the p-value (0.874) indicates that the observed correlation between the risk of osteoporosis and BMI is not statistically significant.

| Level of Osteoporosis risk * CDAI Crosstabulation | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | CDAI | | | | Total |
| | | | Remission | Mildly to moderately active CD | Moderately to severely active CD | Severely active to fulminant disease | |
| Level of OP risk | Low | Count | 40 | 27 | 12 | 0 | 79 |
| | | % within CDAI | 97.6% | 93.1% | 57.1% | 0.0% | 85.9% |
| | Intermediate /high | Count | 1 | 1 | 7 | 0 | 9 |
| | | % within CDAI | 2.4% | 3.4% | 33.3% | 0.0% | 9.8% |
| | Very High | Count | 0 | 1 | 2 | 1 | 4 |
| | | % within CDAI | 0.0% | 3.4% | 9.5% | 100.0% | 4.3% |
| Total | | Count | 41 | 29 | 21 | 1 | 92 |
| | | % within CDAI | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |

Table 10. Crosstabulation of association between CDAI and levels of osteoporosis risk

The majority (97.6%) of patients in remission were in the low OP risk category. As disease activity increases, the proportion of patients in the low OP risk category decreases, with no patients in the Severely Active to Fulminant Disease category falling into the low OP risk group. Conversely, the

percentage of patients in the intermediate and high OP risk categories increases with higher CDAI scores. This trend suggests a potential correlation between increased IBD activity and higher OP risk, highlighting the importance of managing IBD activity to mitigate OP risk.

**Correlations**

| | | | RISK_OSTEOPROSIS | CDAI |
|---|---|---|---|---|
| Kendall's tau_b | RISK_OSTEOPROSIS | Correlation Coefficient | 1.000 | .421** |
| | | Sig. (2-tailed) | . | .000 |
| | | N | 117 | 92 |
| | CDAI | Correlation Coefficient | **.421**** | 1.000 |
| | | Sig. (2-tailed) | **.000** | . |
| | | N | 92 | 92 |

**. Correlation is significant at the 0.01 level (2-tailed).

Table 11. Kendall's tau_b correlation between CDAI and risk of osteoporosis

The moderate positive and statistically significant (p-value 0.000) correlation (0.421) between osteoporosis risk and CDAI scores suggests that as the activity of Crohn's disease increases, there may be an associated increase in the risk of developing osteoporosis.

**Level of osteoporosis risk * Montreal Crosstabulation**

| | | | Montreal | | | | Total |
|---|---|---|---|---|---|---|---|
| | | | Remission | Mild UC | Moderate UC | Severe UC | |
| Level of OP risk | Low | Count | 1 | 13 | 1 | 0 | 15 |
| | | % within Montreal | **100.0%** | **92.9%** | **16.7%** | 0.0% | 60.0% |
| | Intermediate | Count | 0 | 1 | 3 | 3 | 7 |
| | | % within Montreal | 0.0% | 7.1% | 50.0% | 75.0% | 28.0% |
| | Very high | Count | 0 | 0 | 2 | 1 | 3 |
| | | % within Montreal | 0.0% | 0.0% | 33.3% | 25.0% | 12.0% |
| Total | | Count | 1 | 14 | 6 | 4 | 25 |
| | | % within Montreal | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |

Table 12. Crosstabulation of the association between Montreal UC disease activity and levels of osteoporosis risk

As UC severity increases from remission to severe, the percentage of individuals classified as having a low risk of OP decreases, while the percentage of those at intermediate or very high risk increases. Majority of patients with UC had mild disease and of those, 93% had low risk of osteoporosis.

| Correlations | | | | |
|---|---|---|---|---|
| | | | RISK_OSTEOPROSIS | Montreal |
| Kendall's tau_b | Risk of Osteoporosis | Correlation Coefficient | 1.000 | .753** |
| | | Sig. (2-tailed) | . | .000 |
| | | N | 117 | 25 |
| | Montreal | Correlation Coefficient | **.753**** | 1.000 |
| | | Sig. (2-tailed) | **.000** | . |
| | | N | 25 | 25 |
| **. Correlation is significant at the 0.01 level (2-tailed). | | | | |

Table 13. Kendall's tau_b correlation between UC disease activity and risk of osteoporosis

The correlation coefficient (0.753) and p-value (0.000) suggest a strong correlation between the Montreal disease activity scale and the risk of osteoporosis.

| Level of Osteoporosis risk *History of bowel surgery Crosstabulation | | | | | |
|---|---|---|---|---|---|
| | | | History of bowel surgery | | Total |
| | | | No | Yes | |
| **Level of OP risk** | **Low** | Count | 61 | 33 | 94 |
| | | % within history of bowel surgery | **77.2%** | **86.8%** | 80.3% |
| | **Intermediate/ high** | Count | 12 | 4 | 16 |
| | | % within history of bowel surgery | 15.2% | 10.5% | 13.7% |
| | **Very high** | Count | 6 | 1 | 7 |
| | | % within history of bowel surgery | 7.6% | 2.6% | 6.0% |
| **Total** | | Count | 79 | 38 | 117 |
| | | % within history of bowel surgery | 100.0% | 100.0% | 100.0% |

Table 14. Crosstabulation of the association between history of bowel surgery and levels of osteoporosis risk

The majority of individuals, both with and without a history of bowel surgery, fall into the low-risk category for osteoporosis. However, a slightly higher percentage of those with a history of surgery

(86.8%) are at low risk compared to those without (77.2%). A smaller portion of the study population is at intermediate/high risk of OP, with those having no history of bowel surgery being slightly more likely to fall into this category compared to those with a history. Very few participants are at a very high risk of osteoporosis, with those without a history of bowel surgery (7.6%) being somewhat more likely to be in this category than those with a bowel surgery history (2.6%).

**Correlations**

| | | | RISK_OSTEOPROSIS | History of bowel surgery |
|---|---|---|---|---|
| Kendall's tau_b | Risk of Osteoporosis | Correlation Coefficient | 1.000 | -.118 |
| | | Sig. (2-tailed) | . | .200 |
| | | N | 117 | 117 |
| | History of bowel surgery | Correlation Coefficient | -.118 | 1.000 |
| | | Sig. (2-tailed) | **.200** | . |
| | | N | 117 | 117 |

Table 15. Kendall's tau_b correlation between the risk of osteoporosis and history of bowel surgery

The table shows a slight but not statistically significant correlation (p-value 0.2) and a negative correlation (Correlation coefficient - 0.118) between having a history of bowel surgery and the risk of developing osteoporosis.

# Discussion

In this hospital-based cross-sectional study, the primary objective was to provide an evaluation of osteoporosis risk in patients with Inflammatory Bowel Disease (IBD). Utilizing the clinical tool (FRAX), it aimed not only to quantify the osteoporosis risk but also to meticulously describe and analyze the prevalent risk factors within this specific patient cohort. This discussion delves into the nuanced findings of the investigation, shedding light on the multifaceted landscape of osteoporosis risk factors among individuals with IBD under the care of the Gastroenterology clinic at TASH.

Based on the operational definition, 19.6% of the participants had a risk of osteoporosis, of whom seven patients (6%) and 16 patients (13.6%) had very high risk and intermediate-high risk, respectively. The mean 10-year Major Osteoporosis fracture and 10-year Hip fracture risks were 3.94 ± 3.98 % and 0.84 ± 1.01 %, respectively, and can be explained in large part due to the majority of the participants (80.4%) having a low risk of osteoporosis. This finding is congruent with the data reported from population-based studies suggesting an osteoporosis prevalence of 2-15% among IBD patients[22].

In the subjects with increased osteoporosis risk, the duration of IBD and glucocorticoid use were in a positively and statistically significant correlation with both 10-year Major Osteoporosis fracture and 10-year Hip fracture risks, indicating longer duration of IBD and

glucocorticoid use are associated with increased risk of both types of fractures. This corroborates numerous studies indicating that prolonged exposure to glucocorticoids[43] and chronic inflammation[46] are well-established risk factors for osteoporosis.

In addition, the correlation between increasing age and 10-year Hip fracture risk is statistically significant, and this finding aligns with existing literature, where advancing age is consistently recognized as a significant predictor of osteoporotic fractures[47]. The increased fracture risk observed with age could be attributed to the natural decline in bone density and mineral content, emphasizing the importance of age as a critical factor in assessing osteoporosis susceptibility.

Noteworthy associations from determinant risk factors, based on multivariate logistic regression, with an increased risk of osteoporosis on multivariate analysis were having UC type of IBD, personal history of osteoporosis, alcohol consumption history, and glucocorticoid use duration of > 1 year.

Divergence from the existing literature is evident in our findings related to the type of IBD. In this research, Ulcerative colitis (UC) participants displayed a 9.7 times increased risk of osteoporosis compared to Crohn's disease. This observation contrasts with studies that often report higher risk of osteoporosis in CD patients than UC[22]. In this study, 11 out of 16 (68%) of UC patients had an increased risk of osteoporosis in contrast to 15% in CD patients. Since baseline characteristics between subjects did not match the UC and CD groups, the relatively increased risk of osteoporosis in patients with UC can't conclusively be made, leaving a gap for future research.

The finding of strong associations between a personal history of osteoporosis and an increased risk of osteoporosis aligns with established knowledge. It is well-known that a prior occurrence of osteoporosis raises the likelihood of recurrence[32]. Furthermore, the association between alcohol consumption and increased osteoporosis risk found in this study is supported by existing literature, emphasizing the importance of addressing modifiable lifestyle factors in osteoporosis prevention strategies for IBD patients[48].

The study's findings also underscore the significant association between longer durations, particularly beyond 12 months, of glucocorticoid use and heightened osteoporosis risk. This is also consistent with prior literature that emphasizes the detrimental effect of extended exposure to glucocorticoids on bone density[42]. However, the observed magnitude of the association and specific duration thresholds may differ across studies due to variations in treatment regimens and patient populations.

Surprisingly, the daily dose of IBD medication did not demonstrate a significant correlation with either major osteoporosis fracture risk ($r = 0.045$, $p = 0.636$) or hip fracture risk ($r = -0.007$, $p = 0.937$). This contrasts with some previous studies suggesting a potential role of glucocorticoid doses (even as low as 2.5-7.5 mg) in increasing the risk of osteoporosis[43]. The analysis of a potential connection between osteoporosis risk and cumulative glucocorticoid dosage in

patients could have been influenced by the challenge of accurately assessing the total amount of glucocorticoids received (cumulative glucocorticoid dose), due to memory bias. Further exploration into specific medications, their dosage, and their impact on bone metabolism within the context of IBD is warranted to unravel the intricacies of this relationship.

The demonstrated significant correlation coefficient of 0.753 indicates a strong association between higher levels of UC activity (based on Montreal grading) and an increased risk of osteoporosis among the studied population. This finding is pivotal, as it aligns with previous research that has suggested a link between chronic inflammation, characteristic of IBD, and bone density loss, leading to osteoporosis[16]. In congruent with these findings, this study also indicated that as activity of Crohn's disease increases, there may be an associated increase in the risk of developing osteoporosis, supporting the notion that increased systemic inflammatory activity increases bone resorption, leading to accelerated osteoporosis and fracture risk[36].

Contrary to existing data[40], in this sample, BMI does not appear to be a predictor of osteoporosis, given the very weak positive correlation coefficient combined with the non-significant p-value. Although a history of bowel surgery might be associated with a lower probability of being at intermediate/high or very high risk for osteoporosis, the majority of participants, irrespective of their surgery history, are at low risk of developing osteoporosis. This finding could indicate potential protective factors or differences in the populations that underwent surgery versus those that did not, which warrants further investigation.

The low utilization of calcium and vitamin D supplementation (15.4% and 12%, respectively) observed in this study also underscores a potential area for intervention. Despite established guidelines recommending these supplements for osteoporosis prevention in IBD patients[49], adherence remains suboptimal. This gap highlights the need for enhanced patient education and healthcare provider awareness.

# Conclusion

The study has revealed increasing age, having UC type of IBD, duration of IBD, personal history of osteoporosis, alcohol consumption history, and glucocorticoid use duration of > 1 year were independent risk factors for increased risk of osteoporosis, while increased disease activity for both CD and UC had a positive correlation to increased osteoporosis risk. Meanwhile, sex, BMI, small bowel resection history, and Glucocorticoid dose did not have a significant association with increased risk of osteoporosis.

However, further large-scale, prospective studies are needed to draw firm conclusions on this subject and develop targeted prevention and treatment strategies for osteoporosis in the IBD population.

# Limitations of the study

The study's design, being cross-sectional, limits its ability to monitor changes over time and establish a cause-effect relationship between exposure and outcome. A second limitation stems from the absence of laboratory data on vitamin D and calcium levels for the majority of the eligible patients with IBD. Moreover, Bone Mineral Density (BMD) measurements, crucial for predicting the risk of osteoporosis-related fractures, were not conducted due to budgetary restrictions associated with the cost of Dual-Energy X-ray Absorptiometry (DXA) scans. Additionally, challenges in accurately determining the total glucocorticoid dosage received by patients, owing to memory bias, could have impacted the analysis of a potential link between the risk of osteoporosis and the cumulative dosage of glucocorticoids used in these patients.

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# Annex

## Consent form

### Please initial box:

1. I confirm that I have read/listened to and understood the information sheet for the above study and have had the opportunity to ask questions……

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected

3. I understand that a section of any of my medical notes may be looked at by responsible individuals from the research team where it is relevant to my taking part in research. I permitted for these individuals to have access to my records……..

4. I agree to take part in the above study ……..

| Name of patient | data | signature |
|---|---|---|
| …….. | …… | ……. |
| Name of person taking consent | date | signature |
| ……. | …….. | ……. |
| Researcher | date | signature |

## Structured questionnaire

**Title of the study**: Assessment of the risk and associated factors of Osteoporosis in IBD patients

### PART I: Sociodemographic Data

1. **Age in years**: 1.18-30 2. 31-50 3.51-70 5. >70
2. **Sex**: 1. Male 2. Female
3. **District of residence**: 1. Urban 2. Rural
4. **Marital status**: 1. Single 2. Married 3. Divorced 4. Widowed
5. **Educational level**:
   1. No formal education 2. Primary school 3. Secondary school 4. Higher education Student
6. **Occupation**: 1. Governmental 2. private 3. Self-employed 4. Unemployed

7. **Monthly income** (in Ethiopian Birr): 1, low (<3100 birr), 2. low moderate (3100-12100 birr), 3. moderate (12101-37600 birr), 4. high (>37600 birr)

## Part II: Past medical history

1. Type of IBD diagnosis: (Crohn's disease, ulcerative colitis, indeterminate colitis)

2. Date of IBD diagnosis (Disease duration in months/years):

3. Were you started on IBD medications? Yes No
   If yes, a. What medications?
   b. For how long?
4. Was medication changed during the course of treatment?
   If yes, why?
   b. What is the new medication?
5. Have you ever been diagnosed with Osteoporosis? Yes or No
   If yes, a. Was Bone mineral density measurement done? If yes, the most recent result
6. Have you ever been treated for Osteoporosis?
   If yes, what were the treatments? ……..
7. Comorbidities
   - Diabetes
   - Hypertension
   - Hyperlipidemia
   - Other CVD (IHD, PAD)

### Part III: General Risk Factors for Osteoporosis

1. **Alcohol abuse:** Do you consume alcohol regularly?
   a. Never
   b. Former
   c. Current…… If yes, how many drinks per day……
   If yes, what type of alcohol?
   a. beer
   b. wine
   c. whiskey (or other hard liquor)
2. **Smoking:** Do you smoke? If yes, pack years?

3**. Inadequate physical activity:** On average, how many times in a week did you exercise ((a time means
a minimum of 1-hour moderate-intensity or 30-minute vigorous-intensity exercise)?

a. never or hardly
b. 1–2 times/week
c. 3–5 times/week
d. 6–7 times/week

4. **Parental history of hip fracture?**
5. **Personal history of fragility fracture?**
6. **Weight**, **Height** and **BMI**

a. <18.5
b. 18.5-24.9
c. 25-29.9
d. 30-34.9
e. 35-39.9
f. >40

**7. Medication use:**

- Do you take calcium supplements? Yes / No
  - If yes, what type of calcium supplement(s) do you take?
- Do you take vitamin D supplements? Yes / No
  - If yes, what type of vitamin D supplement(s) do you take?

**<u>Part IV: IBD-related risk factors</u>**

1. **Glucocorticoid use**? Yes or No

If yes, a Dose
b. Duration

2. **Disease activity**

For **CD**, <u>CDAI</u> a. Asymptomatic remission
b. Mildly to moderately active Crohn's disease
c. Moderately to severely active Crohn's disease
d. Severely active to fulminant disease
e. Steroid dependent

For **UC**, <u>Montreal classification</u> a. mild
b. moderate
c. severe

3. **History of small bowel resection**? Yes or No

If yes, a. When was it done?

b. Complete or partial resection?

c. Indication for surgery (Fistula/Obstruction)?

4. **Are Serum Vitamin D or Calcium levels determined at any point during follow-up**?

If yes, a. 25(OH)D?

b. Ca (ionized or total)?

5. **Hypogonadism?????**

**a.** Have you experienced a decrease in sex drive? Yes or No

b. Have you experienced difficulty achieving or maintaining an erection? Yes or No

6**. Diet?** **a**. Do you consume milk regularly? If yes**,** how many glasses of milk do you consume per week?

b. Do you have a habit of consuming fruits like oranges, bananas.....? If yes, How many times (frequency) do you consume fruits per week?

c. Do you have a habit of consuming vegetables like cabbage and spinach.....? If yes, how many times (frequency) do you consume vegetables per week?

7**. Weight loss:** Have you experienced weight loss since diagnosis of IBD?

If yes, a. by how much?

## Part V Frax Score

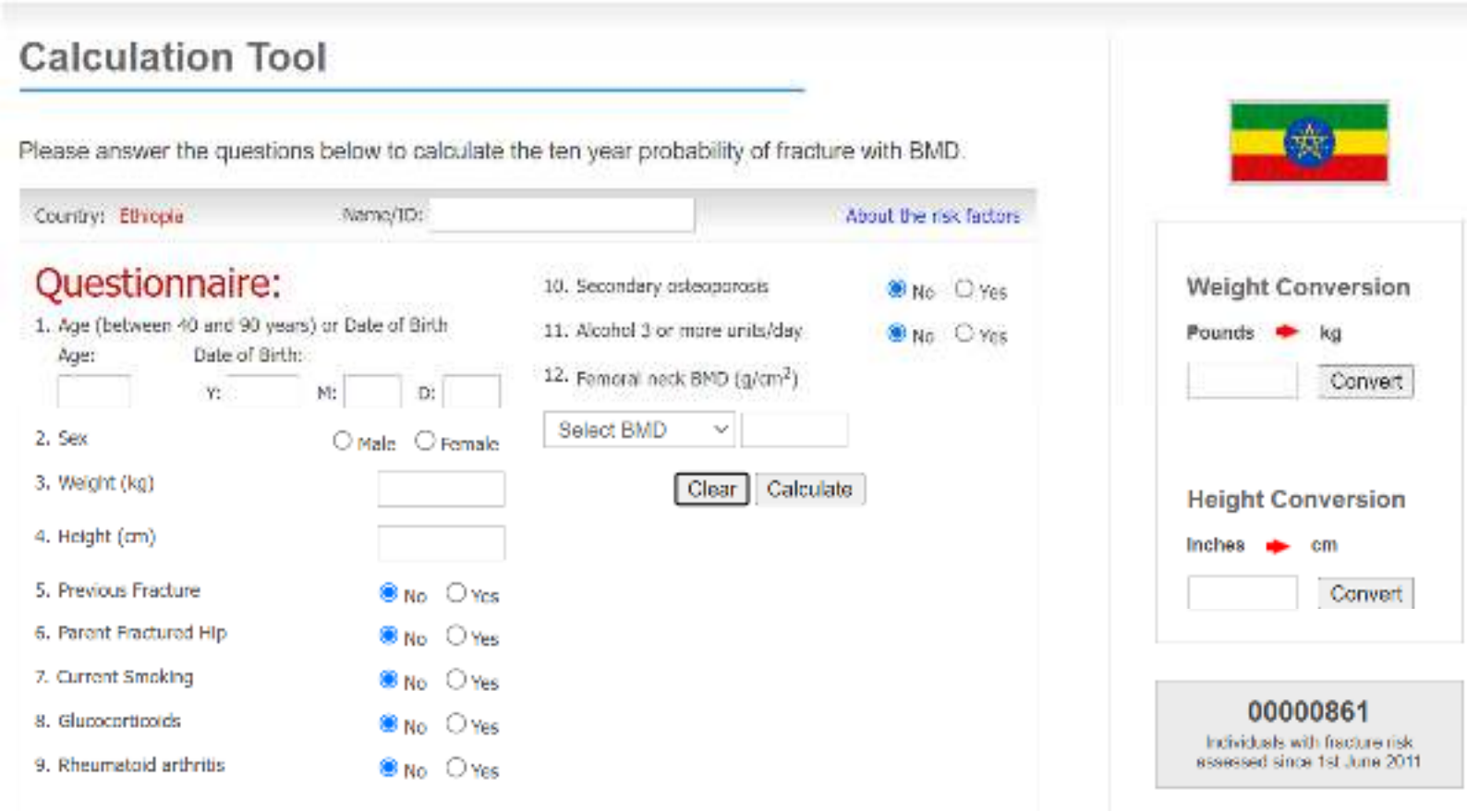


Figure 3: Frax calculation tool