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To study Osteoporosis as risk factor in non alcoholic fatty liver disease (NAFLD) patients

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ABSTRACT

AIMS

To study the prevalence of Osteoporosis as risk factors associated with severity of NAFLD.

OBJECTIVES

Primary objective:

- To assess prevalence of osteoporosis in NAFLD patients.

Secondary objective:

- To assess association of osteoporosis as risk factors in NAFLD patients

METHODOLOGY

Present study was an observational prospective study between January 2023 to June 2024 in patients between age group 25-65 years attend OPD/IPD services at Department of Medicine, Mahatma Gandhi Hospital, Jaipur

RESULTS

The lower BMD values observed in our study population may be attributed to several factors associated with NAFLD, including insulin resistance, chronic inflammation, adipokine dysregulation, and vitamin D deficiency (Mitsuyoshi et al., 2015). Insulin resistance, a hallmark of NAFLD, has been implicated in the pathogenesis of osteoporosis by promoting bone resorption and impairing bone formation (Pacifico et al., 2016).Chronic inflammation, another feature of NAFLD, can lead to increased osteoclast activity and bone loss (Polyzos et al., 2016). Adipokine dysregulation, characterized by altered secretion of adipose tissue-derived hormones, may also contribute to bone metabolism abnormalities in NAFLD patients (Polyzos et al., 2015). Furthermore, vitamin D deficiency, prevalent in NAFLD patients due to limited sun exposure and hepatic dysfunction, can impair calcium absorption and skeletal mineralization, further predisposing individuals to osteoporosis (Eliades et al., 2013).

CONCLUSION-

The prevalence of osteoporosis in our study population was found to be 8.4%, highlighting the significance of this skeletal disorder as a comorbidity in individuals with NAFLD. This finding underscores the importance of screening for osteoporosis in patients with NAFLD to identify those at risk of fractures and implement appropriate preventive measures. Given the potential

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bidirectional relationship between NAFLD and osteoporosis, comprehensive management strategies targeting both liver and bone health are warranted to optimize clinical outcomes in affected individuals.

KEY WORDS- NAFLD, DEXA, NASH, FIB-4, APRI

KEY MESSAGE

The association between non-alcoholic fatty liver disease (NAFLD) and osteoporosis has garnered increasing attention due to the potential impact on both liver and bone health. In our study, Bone mineral density (BMD) analysis showed mean total femur BMD of 0.92 ± 0.2 gm/cm², femur neck BMD of 0.75 ± 0.1 gm/cm², and total lumbar spine BMD of 0.99 ± 0.1 gm/cm². Osteoporosis was present in 8.4% of the study population. Our study contributes to this body of knowledge by providing insights into the relationship between NAFLD and bone mineral density (BMD) at different anatomical sites..

1. INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is defined as a condition where more than 5% of the body's hepatic cells contain fatty deposits without a history of alcohol consumption. This deposition of fat can cause a variety of diseases ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), cirrhosis, liver failure, and hepatocellular carcinoma [1].

The frequency of non-alcoholic fatty liver disease (NAFLD) has increased significantly throughout the past periods, and it has become the prominent reason of liver disease worldwide with a global prevalence of one billion, which can be moderately recognized to the rising prevalence of obesity. The global prevalence of NAFLD is 24%, with the highest rates are reported from South America, the Middle East, and Asia.

As for osteoporosis, a skeletal condition caused by systemic low bone mass and microarchitectural damage, resulting in higher probability of fractures. Osteoporosis is linked to many physical disorder or health related behaviors such as estrogen deficiency, endocrine disorder, hypertension, and smoking. Interestingly, patients with NAFLD present comorbid clinical profiles similar to osteoporosis. For example, NAFLD is associated with hypertension, dyslipidemia, insulin resistance, and diabetes.[2] Patients with NAFLD were considered to have tumor necrosis factor-alpha (TNF-a) and interleukin-6 (IL-6) overexpression; impairment in Kupffer cell phagocytosis may also play an important role in NAFLD.[3] Although the exact role of IL-6 in the pathogenesis of NAFLD is still waiting to be determined, elevation of IL-6 levels was also observed in patients with NAFLD.[4-7] An increased production of TNF-a produced by hepatocytes and nonparenchymal cells in patients with NAFLD was noted in several studies.[8-10] Osteopontin, a T-helper 1 cytokine, exacerbates inflammation in several chronic inflammatory diseases including NAFLD.[11] Many risk factors such as systematic inflammation have been identified for abnormal bone turnover and osteoporosis. Chronic inflammation results in the systemic bone loss, one of the mechanisms of osteoporosis. The inflammatory cytokines, especially TNF-a and IL-1, have been implicated in osteoporosis [12]. These inflammatory cytokines may play a crucial role in the development of osteoporosis. Thus, inflammation may be related both to NAFLD and to osteoporosis. Similar to the clinical manifestations observed in patients with NAFLD, patients with osteoporosis often show no remarkable clinical signs and symptoms until fractures occur. Therefore, the diagnosis of

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osteoporosis is easily under-recognized, and the prevalence of the disease is often underestimated in NAFLD patients.

2. MATERIAL AND METHODS:

Type of Study: Hospital based Observational Prospective study.
Study population: All patients age between 25 to 65 years attended OPD/IPD services at Department of Medicine, Mahatma Gandhi Hospital, Jaipur from January 2023 to June 2024.
Place of Study: Department of General Medicine, Mahatma Gandhi Medical College & Hospital, Jaipur

Duration of Study: 18 months from approval of IEC [January 2023 to June 2024]
Detailed history and necessary investigations will be undertaken. The purpose of the study will be explained to the patient and informed consent obtained.
Patients are selected for study that satisfy all inclusion and exclusion criteria.
Institute Ethics Committee approval will be taken before undertaking the study.
Written and inform consent will be taken from all participants before enrolment into the study.

Inclusion criteria;

- The diagnosis of NAFLD will be based on meeting the following criteria: non-alcoholic, fatty degeneration detected by imaging or histological examination with other liver diseases excluded, non invasive assessment for significant fibrosis which is FIB-4 grading
- Grading: FIB-4
- 0.00 – 1.29 low risk for advanced liver fibrosis
- 1.30-2.67 intermediate risk
- >2.67 high risk

- Age = 25 years and < 65 years of both genders will be studied

Exclusion subjects:

- Alcoholics
- Patients with renal disease
- Patients on Drugs modifying CIMT (ACE inhibitors, statins, aspirin & ARB)
- Those not willing to give informed consent

Sample size: All patients age 25- 65 years OPD/IPD services at Department of Medicine, Mahatma Gandhi Hospital, Jaipur from January 2023 to June 2024

Osteoporosis: the standard criterion for defining and diagnosing osteoporosis and applying the ICD-9 code 733.0 is the finding of a T-score of ≤ −2.5 at the lumbar spine, femur neck, or total hip by bone mineral density (BMD) testing.

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DEXA Diagnostic Criteria

T-score	Category
>-1.0	Normal
-1.0 through -2.5	Osteopenia
≤-2.5	Osteoporosis

- Z Score < -2.0 Considered Osteoporosis in Pts <50
- Incorrect Positioning and Osteophytes can cause false positives
- Fragility Fracture = Osteoporosis
- Primary Hyperparathyroidism Wrist DEXA

Aim of study-
To study the prevalence of osteoporosis as risk factors associated with severity of NAFLD.

Objective
Primary objective:
- To assess prevalence of osteoporosis in NAFLD patients.

Secondary objective:
- To assess association of osteoporosis as risk factors in NAFLD patients.

3. RESULT-

Table 11: Bone mineral density in study population

BMD (gm/cm2)	Mean	SD
Total femur BMD	0.92	0.2
Femur neck BMD	0.75	0.1
Total Lumber spine BMD	0.99	0.1

Table 12: prevalence osteoporosis in study population

Osteoporosis [N (%)]	Frequency	Percentage
	27	8.4

In the examined population, the incidence of osteoporosis was found to be 8.4%, with 27 individuals diagnosed with the condition. This finding underscores the significance of osteoporosis as a prevalent health concern within the studied cohort.

Bone mineral density	**Non-NAFLD N=160**	**NAFLD N=160**	**p-Value**
Total femur BMD (gm/cm^2)	0.87 ± 0.1	0.97 ± 0.6	<0.0001
Femur neck BMD (gm/cm^2)	0.72 ± 0.1	0.78 ± 0.3	<0.017O

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Total Lumber spine BMD (gm/cm2)	0.96 ± 0.0	1.05 ± 0.2	<0.0001

In this comparative analysis of bone mineral density (BMD) between individuals with and without non-alcoholic fatty liver disease (NAFLD), significant differences were observed across multiple skeletal sites. Among the 160 participants without NAFLD, the mean BMD at the total femur was 0.87 gm/cm² with a standard deviation of 0.1 gm/cm², while among the 160 participants diagnosed with NAFLD, the mean total femur BMD was notably higher at 0.97 gm/cm² with a standard deviation of 0.6 gm/cm². Statistical analysis revealed a highly significant p-value of less than 0.0001 for total femur BMD between the two groups, indicating a strong association between BMD levels and the presence of NAFLD.
Similarly, significant differences were observed in BMD at the femur neck and total lumbar spine between individuals with and without NAFLD. Among individuals without NAFLD, the mean femur neck BMD was 0.72 gm/cm² with a standard deviation of 0.1 gm/cm², whereas among those with NAFLD, the mean femur neck BMD was slightly higher at 0.78 gm/cm² with a standard deviation of 0.3 gm/cm². Statistical analysis revealed a significant p-value of 0.017 for femur neck BMD between the two groups. Moreover, for total lumbar spine BMD, individuals without NAFLD exhibited a mean of 0.96 gm/cm² with no standard deviation reported, while those with NAFLD had a higher mean of 1.05 gm/cm² with a standard deviation of 0.2 gm/cm². Statistical analysis also revealed a highly significant p-value of less than 0.0001 for total lumbar spine BMD between the two groups.

Finally, bone mineral density (BMD) parameters, such as total femur BMD (OR: 0.070, 95% CI: 0.060-0.080), femur neck BMD (OR: 0.050, 95% CI: 0.040-0.070), and total spine BMD (OR: 0.012, 95% CI: 0.010-0.013), exhibited negative associations with NAFLD, indicating that lower BMD levels were associated with increased odds of NAFLD.

4. DISCUSSION-

The association between non-alcoholic fatty liver disease (NAFLD) and osteoporosis has garnered increasing attention due to the potential impact on both liver and bone health. In our study, Bone mineral density (BMD) analysis showed mean total femur BMD of 0.92 ± 0.2 gm/cm², femur neck BMD of 0.75 ± 0.1 gm/cm², and total lumbar spine BMD of 0.99 ± 0.1 gm/cm². Osteoporosis was present in 8.4% of the study population. Our study contributes to this body of knowledge by providing insights into the relationship between NAFLD and bone mineral density (BMD) at different anatomical sites.
The observed lower BMD values in the femur neck and lumbar spine among individuals with NAFLD suggest a possible association between hepatic steatosis and skeletal fragility. This finding is consistent with previous studies indicating a link between NAFLD and bone metabolism disturbances. For instance, a study by Li et al. demonstrated that patients with NAFLD had lower BMD at the femoral neck and lumbar spine compared to controls, suggesting an increased risk of osteoporosis in this population (Li et al., 2018).[13] Similarly, a meta-analysis by Verdelho Machado et al. found that NAFLD was associated with lower BMD at the lumbar spine, femoral neck, and total hip, indicating a systemic effect on bone density (Verdelho Machado et al., 2016).[14]
The lower BMD values observed in our study population may be attributed to several factors associated with NAFLD, including insulin resistance, chronic inflammation, adipokine dysregulation, and vitamin D deficiency (Mitsuyoshi et al., 2015).[14] Insulin resistance, a hallmark of NAFLD, has been implicated in the pathogenesis of osteoporosis by promoting

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bone resorption and impairing bone formation (Pacifico et al., 2016).[15] Chronic inflammation, another feature of NAFLD, can lead to increased osteoclast activity and bone loss (Polyzos et al., 2016). [16] Adipokine dysregulation, characterized by altered secretion of adipose tissue-derived hormones, may also contribute to bone metabolism abnormalities in NAFLD patients (Polyzos et al., 2015). [17] Furthermore, vitamin D deficiency, prevalent in NAFLD patients due to limited sun exposure and hepatic dysfunction, can impair calcium absorption and skeletal mineralization, further predisposing individuals to osteoporosis (Eliades et al., 2013).[18]

5. CONCLUSION-

The prevalence of osteoporosis in our study population was found to be 8.4%, highlighting the significance of this skeletal disorder as a comorbidity in individuals with NAFLD. This finding underscores the importance of screening for osteoporosis in patients with NAFLD to identify those at risk of fractures and implement appropriate preventive measures. Given the potential bidirectional relationship between NAFLD and osteoporosis, comprehensive management strategies targeting both liver and bone health are warranted to optimize clinical outcomes in affected individuals.

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