

# Evaluating osteoporosis and its hormonal determinants in diabetic men: insights from a tertiary care setting in Pakistan

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## ABSTRACT

**Objectives:** To evaluate the frequency of osteoporosis in male population with diabetes mellitus and to determine the association of osteoporosis with body mass index (BMI), smoking status, and gonadal status.

**Methods:** This cross-sectional study was conducted at Lady Reading Hospital, Peshawar-Pakistan, from March 2023 to August 2023 with a sample size of 292 male diabetic participants. The sampling was done by non-probability convenient sampling. The inclusion criteria were diabetic male patients aged 25-80 years, whereas patients who were on corticosteroids and diagnosed cases of chronic heart failure, chronic kidney disease, respiratory failure, malignancy, connective tissue disorders, and fracture in the past 6 months were excluded from the study. Bone density and testosterone level were measured. The associations between descriptive data (age, gender, BMI, and gonadal status) and bone density were analyzed.

**Results:** Out of 292 male diabetic participants with a mean age of  $54.41 \pm 8.71$  years, 203 (69%) were smokers, 136 (47%) were overweight, 23 (7.8%) were obese, while 170 (58.2%) patients were having lower testosterone levels. Bone mineral density levels, measured with DEXA-Scan, demonstrated high frequency of osteoporosis in 120 (41.4 %) patients, and osteopenia in 106 (36.2 %) cases. Chi square statistics showed a significant association of osteoporosis with testosterone ( $p=0.001$ ) and FSH levels ( $p=0.01$ ) while such association was not significant with smoking status ( $p=0.2$ ), LH level ( $p=0.8$ ) and BMI ( $p=0.1$ ).

**Conclusion:** High frequency of osteoporosis is a concern among the diabetic male population which is positively associated with hypogonadism, warranting early hormonal screening and intervention.

**Keywords:** Osteoporosis (MeSH); Diabetes Mellitus (MeSH); Risk Factors (MeSH); Testosterone (MeSH); Luteinizing Hormone (MeSH); Follicle Stimulating Hormone (MeSH); Male (MeSH); Smoking (MeSH); Body Mass Index (MeSH).

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## INTRODUCTION

**O**steoporosis is a musculoskeletal disease resulting in reduced bone strength and an increased fracture risk.<sup>1</sup> According to the World Health Organization (WHO), bone mineral density (BMD) is classified as normal when the T-score is greater than -1, osteopenia between -1 and -2.5, and osteoporosis when the T-score is  $\leq -2.5$ .<sup>2,3</sup> Globally, over 200 million individuals are affected by osteoporosis, resulting in approximately 1.3 million fractures annually—primarily involving the vertebrae, hip, and wrist—at an

estimated cost of 10 billion USD.<sup>4,5</sup> Although osteoporosis is more prevalent in women, its incidence is rising among men, who experience an estimated annual bone mass loss of 1%.<sup>6,7</sup> Diabetes Mellitus (DM), a global epidemic affecting 347 million people according to WHO estimates,<sup>8</sup> has been implicated in altered bone metabolism. Obesity, often associated with DM, has been linked to an increased fracture risk in men compared to normal-weight individuals.<sup>9,10</sup>

A U.S.-based study on body composition in white and black men with DM reported elevated BMI scores,

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suggesting an overlap between DM and osteoporosis.<sup>11</sup> In Iran, the prevalence of osteoporosis in individuals aged  $>60$  years was 24.6% in men and 62.7% in women, with positive associations reported for age, smoking, and renal disease, and a negative association with BMI and diabetes in men.<sup>12</sup> Additionally, a study from Western USA indicated a positive correlation between metabolic syndrome and BMD ( $p=0.01$ ).<sup>13</sup>

Male osteoporosis remains an under-recognized public health issue, accounting for one-third of osteoporotic fractures in men over 50 years. Moreover, fracture-related morbidity and mortality are higher in men than in women.<sup>14</sup> Despite its significance, osteoporosis in men is underexplored due to fewer longitudinal studies and its relatively lower prevalence.

In this context, the present study was planned to evaluate the association of gonadotropins-follicle-stimulating hormone (FSH) and luteinizing hormone (LH)-with BMD and osteoporosis, considering age, BMI, and gonadal status. We hypothesize that elevated levels of FSH and LH are significantly correlated with the pathogenesis of osteoporosis, particularly among men with diabetes mellitus.

## METHODS

This descriptive cross-sectional study was conducted at the Department of Endocrinology, Lady Reading Hospital, Peshawar, following ethical approval from the Institutional Review Committee (Ref No: 04/LRH/MTI). The

study period spanned from March to August 2023.

A total of 292 male patients of diabetes mellitus, aged between 25 and 80 years were enrolled using non-probability convenience sampling. Patients on corticosteroid therapy, or those with chronic heart failure, chronic kidney disease, respiratory failure, malignancy, connective tissue disorders, or a history of fracture within the past six months were excluded.

Osteoporosis was defined as a bone mineral density (BMD) T-score  $\leq -2.5$  as measured by dual-energy X-ray absorptiometry (DEXA) using the Horizon® DXA System.<sup>15</sup> Diabetes mellitus was diagnosed based on the presence of symptoms (e.g., polyuria, polydipsia) along with either a random blood glucose level  $\geq 200$  mg/dL or an HbA1c  $\geq 6.5\%$ , according to the American Diabetes Association criteria.<sup>16</sup>

The estimated study population size was 1,200 patients, based on outpatient clinical records indicating an average of 40 osteoporosis patients examined daily over 30 working days across six months. The sample size of 292 was calculated using the Rao-soft sample size calculator, assuming a 95% confidence interval and 5% margin of error.

Data collected included age, height, weight, smoking status, and relevant clinical history. Body Mass Index (BMI) was calculated as weight (kg) divided by height squared ( $m^2$ ) and categorized as:  $< 18.5$  (underweight),  $18.5-24.9$  (normal),  $25.0-29.9$  (overweight),  $30.0-34.9$  (obese), and  $\geq 35.0$  (extremely obese).

Venous blood samples were analyzed for follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone, random blood sugar (RBS), and HbA1c. LH, FSH, and testosterone levels were measured using chemiluminescent immunoassay on a special chemistry analyzer, while HbA1c was assessed using a spectrophotometric assay. The reference ranges were: testosterone (2.5–8 ng/mL), LH (1.5–8.6 mIU/mL), and FSH (1.5–12.4 mIU/mL).

All data were analyzed using IBM SPSS Statistics version 23.0.

## RESULTS

A total of 292 male participants were enrolled in this study, with a mean age of  $54.41 \pm 8.71$  years. The mean HbA1c was  $9.3 \pm 1.4$ . A summary of frequency and percentages of different physiological variables is given in Table I.

Out of 292 male diabetic participants, 203 (69.5%) were smokers, 136 (46.6%) were overweight, 23 (7.9%) were obese, 07 (3.1%) were extremely obese while 170 (58.2%) patients were having lower testosterone levels. Moreover, the LH and FSH levels were higher than normal in 42 (14.4%) and 50 (17.1%) patients, respectively. The bone mineral density levels, measured with DEXA-Scan, demonstrated high frequency of osteoporosis in 120 (41.4%) patients, and osteopenia in 106 (36.2%) cases.

The stratification of osteoporosis for BMI, smoking status, and testosterone, LH and FSH levels is summarized in Table II. The stratification for BMI demonstrated that the majority of

osteoporosis (i.e.,  $n=59$ , 20.2%) and osteopenia (i.e.,  $n=54$ , 18.5%) prevailed for the overweight patients, followed by normal patients. However, these differences were not statistically significant ( $p = 0.10$ ). For the smokers, the osteoporosis prevailed in 89 (30.5%) while the osteopenia was in 72 (24.7%) patients. Likewise, the osteoporosis and osteopenia in patients with lower than normal testosterone levels were 48 (16.4%) and 85 (29.1%), respectively. These differences in osteoporosis in patients with testosterone concentrations below normal levels (hypogonadism) were significant at  $p = 0.001$ . Moreover, the osteoporosis was observed in 90 (30.8%) while the osteopenia was observed in 102 (34.9%) patients with normal LH levels. Finally, the differences in osteoporosis and osteopenia in patients with normal and above normal FSH levels were significant (92 vs. 11, and 91 vs. 30:  $p = 0.01$ , respectively).

## DISCUSSION

This cross-sectional study was

**Table I: Frequency and percentages of different physiological variables for patients enrolled in this study**

Variable	Category	Frequency (percentage)
Smoking status	Smoker	203 (69.5%)
	Non-smoker	89 (30.5%)
Body Mass Index (BMI)	Underweight	3 (1.0%)
	Normal	121 (41.4%)
	Overweight	136 (46.6%)
	Obese	23 (7.9%)
	Extremely obese	7 (3.1%)
Dexa scan	Normal	66 (23.3%)
	Osteopenia	106 (36.3%)
	Osteoporosis	120 (41.4%)
Testosterone level	Normal	122 (41.8%)
	Below normal	170 (58.2%)
Luteinizing hormone (LH) level	Normal	250 (86.6%)
	Above normal	42 (14.4%)
Follicle stimulating hormone (FSH) level	Normal	242 (82.9%)
	Above normal	50 (17.1%)

LH: Luteinizing hormone, FSH: Follicle stimulating hormone

**Table II: Stratification of osteoporosis for BMI, smoking status, testosterone LH and FSH levels**

Variable		Dexa-Scan			p value
		Normal	Osteopenia	Osteoporosis	
Body Mass Index (BMI)	Underweight	2 (0.7%)	1 (0.4%)	0 (0%)	0.10
	Normal	31 (10.6%)	39 (13.4%)	51 (17.5%)	
	Overweight	23 (7.9%)	54 (18.5%)	59 (20.2%)	
	Obese	10 (3.4%)	5 (1.4%)	8 (2.7%)	
	Extremely obese	2 (0.7%)	4 (1.4%)	3 (1.0%)	
Smoking	Smoker	42 (14.4%)	72 (24.7%)	89 (30.5%)	0.23
	Non-Smoker	26 (8.9%)	31 (10.6%)	32 (10.9%)	
Testosterone	Normal	31 (10.6%)	55 (18.8%)	36 (12.3%)	0.01
	Below normal	37 (12.7%)	48 (16.4%)	85 (29.1%)	
Luteinizing hormone (LH) level	Normal	58 (19.9%)	90 (30.8%)	102 (34.9%)	0.08
	Below normal	10 (3.4%)	13 (4.5%)	19 (6.5%)	
Follicle stimulating hormone (FSH) level	Normal	59 (20.2%)	92 (31.5%)	91 (31.2%)	0.01
	Below normal	9 (3.1%)	11 (3.8%)	30 (10.3%)	

Normal Dexa-scan: BMD > -0.1; Osteopenia Dexa-scan: BMD = -0.1 to -2.5; Osteoporosis Dexa-scan: BMD ≤ -2.5; BMD = bone mineral density; LH=Luteinizing Hormone; FSH=Follicle Stimulating Hormone

conducted to determine the prevalence of osteoporosis in the male population with diabetes mellitus. Our main findings showed that 120 participants (41.4 %) were found to have osteoporosis whereas 106 participants (36.2 %) reported being osteopenic. Regarding the association of bone mineral density, it was present for gonadal status whereas no association was noted with smoking status and BMI. The unexpectedly high prevalence of osteoporosis and testosterone deficiency in our cohort may be partly explained by the interplay of hormonal factors, as elevated FSH and LH levels have been implicated in bone resorption. Socioeconomic factors, including limited access to healthcare, variations in dietary calcium intake, and lower levels of physical activity compared to neighboring regions, might also contribute to these findings. Further investigation is warranted to confirm these hypotheses and identify targeted interventions.

The present findings align with previous studies highlighting the role of testosterone in maintaining bone density through osteoblast activation

and inhibition of osteoclast-mediated resorption.<sup>17</sup> For example, Mohamad NV, et al.,<sup>17</sup> demonstrated a direct relationship between testosterone deficiency and increased risk of osteoporosis, which supports the association observed in our cohort. Furthermore, we explored potential mediating factors such as hypogonadism, which may exacerbate this relationship, as suggested by Gold G, et al.,<sup>18</sup> The findings of the present study are consistent with these studies.

Testosterone deficiency in this cohort may be linked to the high prevalence of metabolic syndrome and diabetes, which are known to negatively impact testosterone production through inflammatory and endocrine dysregulation. These findings highlight the need for targeted interventions addressing metabolic health to mitigate hypogonadism. In addition, the high frequency of osteoporosis in diabetic men is likely multifactorial, involving both direct effects of hyperglycemia on bone quality and secondary effects related to diabetes complications. To comprehensively address these observations, we recommend

conducting future longitudinal studies to elucidate causal pathways and the role of targeted interventions, such as testosterone replacement therapy or diabetic bone disease management strategies.

El-Desouki MI, et al., determined the prevalence of osteoporosis in Saudi men (aged 30-90 years) with a Mean BMI of 28.56 (±5.4) and reported 21.4% and 35.7% osteoporosis and osteopenia, respectively, with an overall high prevalence of low bone mineral density.<sup>19</sup> In a similar study in Demark and the UK the prevalence was 17.7% and 6% among men (age >50 years) respectively.<sup>20, 21</sup> Our study reported high prevalence rates although the difference might be due to some genetic factors and a sedentary lifestyle. In another study, the osteoporosis prevalence was 49.6% and 38.3% in Saudi and American men aged above fifty years.<sup>20</sup> The high rates correspond with our study, which reported it to be an alarming concern in the male population as well.

Agrawal NK, et al., determined the levels of bone mineral density in men above 50 years with a mean age of 62.61 ± 7.64. The reports showed 8.5% osteoporosis, and 42% osteopenia while 49.5% were the population labeled as normal.<sup>22</sup> The results were more the less in equivalence with our study comparing the statistics. A study was conducted by Abbas SS, et al., in Pakistan to establish the influence of testosterone on osteoporosis in the population aged above 45 years. The results reported a positive association with p=0.00001.<sup>23</sup> The results of this study were in line with the present study as both of the studies were conducted in a similar cultural zone and age group.

Another study in Iran determined the prevalence of osteoporosis to be 24.6% and 62.7% in men and women (age >60), respectively. Osteoporosis was positively associated with age, smoking, and history of kidney disease while a negative association was reported with BMI and diabetes in men.<sup>24</sup> The results of our study showed some similar associations while some were different which might be reflected due to the different demographics of our population.

## Limitations of the study

This study has several limitations that warrant consideration. First, the sample was derived from a single center, which may restrict the generalizability of the findings to broader populations. Second, the cross-sectional design limits the ability to infer causal relationships between the observed associations and osteoporosis; longitudinal studies are needed to confirm these findings over time. Sampling bias may also be present, as individuals with known risk factors for osteoporosis might have been more likely to participate.

The study did not evaluate low gonadotropin levels (FSH and LH) in detail, and serum prolactin levels were not measured, which may have led to the under-recognition of underlying conditions such as pituitary dysfunction or hyperprolactinemia-potentially confounding the DEXA scan results. Furthermore, Vitamin D3 levels were only assessed in patients who could afford the test, due to its high cost. As a result, these data were excluded from statistical analyses to ensure consistency, which limits the completeness of the findings.

These limitations emphasize the need for future research involving larger, multicenter cohorts and prospective designs, along with more comprehensive hormonal and biochemical assessments.

## CONCLUSION

Osteoporosis is a prevalent and often underrecognized comorbidity in men with diabetes mellitus. This study demonstrates a significant association between hypogonadism and elevated FSH levels with reduced bone mineral density, while no meaningful relationship was observed with smoking status or body mass index. These findings suggest the need for early hormonal screening, particularly for testosterone and FSH, to facilitate timely diagnosis and management of osteoporosis. Public health strategies targeting hormonal health in men with MD may play a vital role in preventing osteoporosis-related complications. Further longitudinal studies are recommended to confirm these associations and inform interventional

approaches.

## RECOMMENDATION

Male patients with diabetes mellitus should be regularly screened for osteoporosis. Those having osteoporosis should have their testosterone and FSH levels measured as part of an early screening program to reduce the economic burden promoting a healthy lifestyle and prognosis. Routine hormonal assessments should be integrated into osteoporosis screening programs. Moreover, promoting awareness of lifestyle modifications, such as increased physical activity and dietary calcium intake, will help support bone health.

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### AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

**AS:** Conception, acquisition, analysis and interpretation of data, drafting the manuscript, critical review, approval of the final version to be published

**SK:** Acquisition, analysis and interpretation of data, drafting the manuscript, approval of the final version to be published

**IA:** Concept and study design, critical review, approval of the final version to be published

**MUR & IU:** Acquisition of data, drafting the manuscript, critical review, approval of the final version to be published

*Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.*

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### DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request



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