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Osteoporosis in Diabetics- A observational study in Kashmiri population

Faisal Naseer Mir*, [1] Rahi Akhter Rasool, [2] and Naseer Ahmed Mir[3]

[1]Government Medical College Srinagar
[2]Government Medical College Srinagar
[3]SKIMS Medical College, Bemina, Srinagar

Corresponding Author
Faisal Naseer Mir
Government Medical College Srinagar
E-mail: mirfais@gmail.com

Abstract

Introduction- Diabetes mellitus (DM) is a very common disorder with distressing effects on metabolism causing various complications including bone disorders. The aim of the study was to assess the occurrence of osteoporosis in diabetics along with other factors, to closely observe the relation of diabetes with risk of fractures & osteoporosis. **Material and method-** DM patients visiting outpatient clinic of GMC (Government medical college), Srinagar, J&K (Jammu & Kashmir) were recruited in the study along with healthy volunteers as control. Lumbar spine (LS) and femoral neck (FN) T-score was assessed by DXA (dual x-ray absorptiometry) scan and then WHO interpretation of T-score was done to evaluate risk of osteoporosis. Data was analyzed and "$P \leq 0.05$ was considered as statistically significant." **Result-** Mean difference in age (between diabetics and control group) and association of gender with diabetes was found non-significant. The BMI (body mass index), FBS (fasting blood sugar) and HbA1c (glycosylated hemoglobin) levels were significantly higher in diabetics than non-diabetics. Mean LS T-score was significantly lower and FN T-score was non-significantly lower in diabetics than non-diabetics. LS and FN T-score of diabetic males was significantly more than diabetic females. Risk of osteoporosis was found significantly more in diabetic females than diabetic males. **Conclusion-** The Study recommends screening of DM population for bone health regardless of age and sex. Further for prevention and better management of osteoporosis in DM patients, clinicians must counsel them regarding adequate nutrient intake for good glycaemic control and bone health.

Keywords- DM, Diabetics, Osteoporosis, FN, LS, T-score etc.

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Introduction-

Diabetes Mellitus (DM) is a metabolic disorder which increases global burden day by day. As per the data by IDF "(International Diabetes Federation)", the DM had worldwide incidence of 9.3 percent in 2019, which is anticipated to raise up to 10.2 percent by 2030 and then to 10.9 percent by the year 2045.[(1)] According to a study in 2017, the WHO (World Health Organization) estimated a total of 422 million inhabitants globally to be diabetics[(2)] DM alters the metabolism of biomolecules of our body leading to a sequence of complications. It also affects the regulation of minerals like calcium (Ca), phosphorus (P), and magnesium (Mg) consequently causing metabolic bone diseases i.e osteomalacia, parathyroidism and osteoporosis.[(3-5)] Among these disorders, osteoporosis is a clinically quiet disease with higher occurrence as around 125 million inhabitants in US (United States), Europe, Japan and India were affected.[(6)] Osteoporosis and DM have many factors in common like both are affected by modifications in lifestyle, gender and age so high chances prevail for their coexistence, mainly in elderly, although actual prevalence is not fully elucidated.

Osteoporosis is a common metabolic skeletal disease having largely preventable though devastating effects. Various risk factors for osteoporosis are known and few of them involve complex multiple mechanisms like DM. However, deteriorating skeletal complications induced by type 1 and type 2 DM differ noticeably in magnitude probably due to involved cellular and molecular mechanisms behind them. Further, Asian origin and type 2 DM (T2DM) favors osteoporosis to be a public health issue in Asian people than other ethnicities.[(7)] Few previous studies reported higher and some reported reduced risk of fractures in diabetics suggesting low osteoporosis risk in them. Conversely, new clinical researches have reported increased risk of osteoporosis in diabetics regardless of bone mineral density (BMD) status.[(8-12)] Though skeletal disorders in diabetics have been documented but due to inconsistent results found in prior studies, the clinical significance & osteoporosis risk in diabetics is still debatable. Hence, there is a demand for additional research to closely observe the relation of diabetes with risk of fractures & osteoporosis. So our study aimed to see the occurrence of osteoporosis in diabetics.

Osteoporosis is a disorder having definite combination of tainted bone quality, decreased bone mass with micro-architectural changes, leading to low bone strength causing upraised risk of fractures. Till now, the best predictor of osteoporosis is the standard tool used for bone mass

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assessment i.e BMD (bone mineral density) assessed by DXA (dual x-ray absorptiometry). The primary advantage of DXA scans are that their results can be evaluated considering T-score (peak bone mass) definition of osteoporosis by the WHO (World Health Organization). Decreased BMD, fairly well predicts risk of osteoporotic fracture and according to WHO, *T*-score of ≤−2.5 signifies osteoporosis.[13] Although this interpretation is widely followed but the main constraint is that, the considerable BMD overlap happens among patients with and without consequent fractures as numerous micro-architectural bone properties are not evident by DXA. Therefore, while assessing diabetics complete risk evaluation for osteoporosis must be done. So in our study we aimed to observe the association of osteoporosis in diabetics along with consideration of demographic characteristics and other related risk factors.

Material and Method-

Our study was an observational hospital oriented research, based on cross-sectional study design. 180 DM patients with age above 18 years of both sex, visiting outpatient clinic of GMC (Government medical college), Srinagar, J&K (Jammu & Kashmir) from October 2020 to September 2022 were recruited in study group using convenient sampling method. The age and sex matched 180 healthy volunteers without diabetes were recruited in control group. The approval for the research was given by the Institutional ethical committee and the consent was taken from all the subjects fulfilling inclusion criteria. The subjects having any metabolic syndrome, any condition affecting metabolism like pregnancy and on drugs affecting our results were excluded from the study. The patients were diagnosed as diabetics after clinical examination and investigating their glucose status. To check glucose status of the subjects, HbA1c (glycosylated hemoglobin) was analyzed and 8-12 hours fasting was suggested to assess fasting blood sugar (FBS). The diagnosis of diabetes was grounded on WHO criteria of FBS ≥ 126mg/dl[14] and HbA1c > 6%. Further to confirm osteoporosis in participants, DXA scan was done to assess BMD at femoral neck (FN) and lumbar spine (LS) based on T-score. The results were interpreted according to WHO i.e T-Score >-1 indicates normal BMD, ≤-2.5 SD signifies osteoporosis and -2.5 < T-Score ≤-1 indicates osteopenia.[15] The data along with other demographic variables like age, sex, calculated BMI (body mass index) was tabulated and analyzed using SPSS 20 statistical software and "P≤ 0.05 was considered as statistically significant."

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Result-

In our study 180 diabetic patients and 180 non-diabetic healthy controls were enrolled. As visible in table 1, the mean age of diabetics and non-diabetics was almost similar i.e. 55.1 ± 12.70 and 53.8 ± 11.80years with statistically non-significant difference between them. In diabetic group males 94 (52.22%) were more than females 86 (47.77%) and in non-diabetics, the distribution of males and females was almost similar i.e. 89 (49.44%) and 91 (50.55%). The association of diabetes with the gender was non-significant. The BMI was found to be more in diabetics (28.8 ± 4.30kg/m^2) than non diabetics 26.8 ± 4.40kg/m^2). The FBS and HbA1c levels were high in diabetics i.e. 178 ± 21.01mg/dl and 7.28 ± 1.19% when compared to non diabetics i.e. 87 ± 14.02mg/dl and 4.2 ± 1.01% respectively. The difference in mean BMI, FBS and HbA1c was calculated to be significant. Further to check BMD status of the subjects, T- score by DXA scan was assessed of LS and FN. Table 1 clearly shows that T score of both, LS and FN was higher in non diabetics (-0.39 ± 1.59 and -0.93 ± 1.48) than diabetics (-1.71 ± 1.66 and -1.75 ± 1.18). The difference in mean of LS T-score between diabetics and non-diabetics was statistically significant although difference in FN T-score was assessed to be non-significant. According to WHO, the T-score of both the groups was interpreted into three classes i.e normal, osteopenia and osteoporosis. If any T-score disconcordance was observed at the two sites (LS and FN) then the major class was considered. As visible from figure 1, higher number of non-diabetics 125 (69.44%) were having normal BMD than diabetics 92 (51.11%). Osteopenia and osteoporosis was found to be more in diabetics i.e. 20 (11.11%) and 68 (37.77%) when compared to non-diabetics i.e. 14 (7.77%) and 41 (22.77%) respectively. Our study documented significant association of diabetes with the classes based on WHO interpretation of T-score.

Table 1- Profile of diabetic and non-diabetic group.

Parameter		Diabetics	Non-Diabetics	p-value
Age (years)		55.1 ± 12.70	53.8 ± 11.80	0.3151
Gender	Males	94 (52.22%)	89 (49.44%)	0.5980
	Females	86 (47.77%)	91 (50.55%)	
BMI (kg/m^2)		28.8 ± 4.30	26.8 ± 4.40	< **0.0001**
FBS (mg/dl)		178 ± 21.01	87 ± 14.02	< **0.0001**
HbA1c (%)		7.28 ± 1.19	4.2 ± 1.01	< **0.0001**
T-score	LS	-1.71 ± 1.66	-0.39 ± 1.59	0.0626
	FN	-1.75 ± 1.18	-0.93 ± 1.48	< **0.0001**
WHO T-score	Normal	92 (51.11%)	125 (69.44%)	**0.0016**

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interpretation	Osteopenia	20 (11.11%)	14 (7.77%)	
	Osteoporosis	68 (37.77%)	41 (22.77%)	

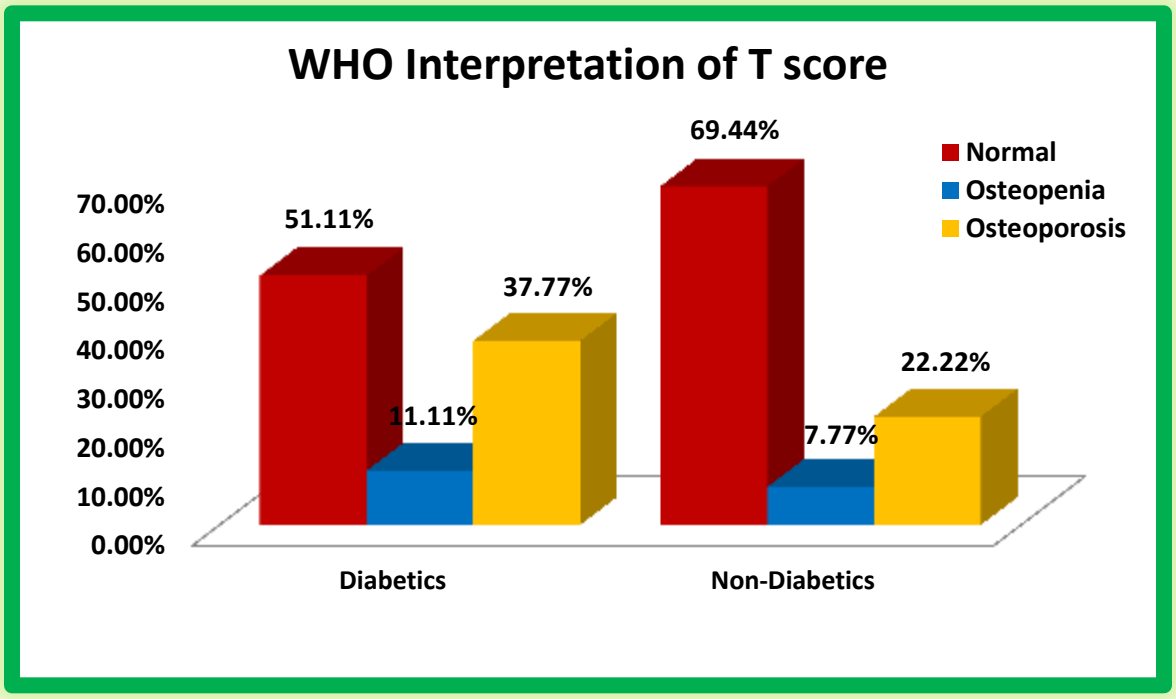

Figure 1- WHO Interpretation and classes based on T score of diabetics and non-diabetics.

Table 2 shows T- Score and its WHO interpretation among males and females of both groups. LS and FN T-score of diabetic males i.e. -0.77 ± 1.77 and -1.54 ± 1.23 was higher than females i.e. -1.66 ± 1.54 and -1.97 ± 1.14 respectively. Our study observed the difference in mean of T score of both sites between diabetic males and females to be statistically significant. Similarly LS and FN T-score of non-diabetic males i.e. -0.30 ± 1.60 and -0.90 ± 1.37 was also assessed to be higher than females i.e. -0.47 ± 1.57 and -0.96 ± 1.58 respectively. Although our study did not observe any significant difference in mean of T score of both sites between non- diabetic males and females.

As visible from table 2, the current study reported higher number of diabetic males i.e. 57 (60.63%) to have normal BMD than diabetic females i.e. 35 (40.69%). Osteopenia and osteoporosis was seen to be more in diabetic females i.e. 13 (15.11%) and 38 (44.19%) than

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diabetic males i.e. 7 (7.44%) and 30 (31.91%) respectively. Our study observed significant association of gender with the classes based on WHO interpretation of T-score in diabetics. Similarly our study observed higher number of non-diabetic males i.e. 65 (73.03%) to have normal BMD than non-diabetic females i.e. 60 (65.93%). Osteopenia and osteoporosis was reported to be upraised in non-diabetic females i.e. 8 (8.79%) and 23 (25.27%) when compared to non-diabetic males i.e. 6 (6.74%) and 18 (20.22%) correspondingly. However, association of gender with the classes based on WHO interpretation of T-score in non-diabetics was analyzed to be non-significant.

Table 2--T- Score and it's WHO interpretation among males and females of both groups.

T- Score and it's WHO interpretation		Males	Females	p-value
Diabetics	LS	-0.77 ± 1.77	-1.66 ± 1.54	**0.004**
	FN	-1.54 ± 1.23	-1.97 ± 1.14	**0.0163**
Non-Diabetics	LS	-0.30 ± 1.60	-0.47 ± 1.57	0.4728
	FN	-0.90 ± 1.37	-0.96 ± 1.58	0.7860
Diabetics	Normal	57 (60.63%)	35 (40.69%)	**0.0216**
	Osteopenia	7 (7.44%)	13 (15.11%)	
	Osteoporosis	30 (31.91%)	38 (44.19%)	
Non-Diabetics	Normal	65 (73.03%)	60 (65.93%)	0.5847
	Osteopenia	6 (6.74%)	8 (8.79%)	
	Osteoporosis	18 (20.22%)	23 (25.27%)	

Discussion-

DM is one of the widespread disorders and its numerous complications including bone involvement affect many tissues and can badly influence quality of life. The current study was done among DM patients visiting outpatient department of GMC, Srinagar, J&K to see association of diabetes with osteoporosis. In our study, the mean age and gender distribution among diabetics and non-diabetics was almost comparable although males were bit more in diabetics. The mean difference in age (between diabetics and control group) and association of gender with diabetes was found non-significant. A report by Yingke Xu & Qing Wu[16] is in agreement with our findings of mean age and sex distribution as they also observed more males in diabetic and females in non-diabetic group. Another study by Lin H-H et al.[17] also supported our findings although they observed significant mean age difference among the groups. However mean age found by Kirkizlar TA et al.[18] was bit upraised (60.07±6.99years) than our study. The

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mean BMI, FBS and HbA1c levels in present study were significantly higher in diabetics when compared to non-diabetics. These findings are strongly in agreement with study by Lin H-H et al.[17] as they also observed significant findings. Further to check risk of osteoporosis, LS and FN T- score was assessed by DXA scan. According to WHO, for healthy bones T-score should be >-1. The current study assessed significantly lower mean LS and non-significantly lower FN T-score in diabetics (< -1) than non-diabetics (>-1), which signifies that diabetics are more at risk of bone disorders. A study by Mohammad Ali Bayan et al.[19] also observed similar findings of higher T-score in non-diabetics although T-score was <-1 in both the groups. In contrast to these findings Kirkizlar TA et al.[18] reported disconcordance in mean LS (>-1) and FN T-score (<-1) indicating healthy bones and bone involvement respectively in diabetics. The present study observed significantly higher osteoporosis in diabetics. This finding is in well harmony with the outcomes of study by Lin H-H et al.[17] as they suggested a significantly higher osteoporosis risk among diabetics. However this is in disagreement with study by Mohammad Ali Bayan etal.[19] The possible reason behind our result might be prolonged diabetes as hyperglycemia through several means like raised AGEs (advanced glycation end products), obesity, angiopathies, neuropathies, hypercalciuria, decreased kidney function, inflammation etc encourage impairment in bone micro-architecture and bone metabolism.[3,20] Hyperglycemia and related hyperosmolarity also hold back the gene expression of osteoblast maturation. Further it adds on to calcium homeostasis imbalance by suppressing formation of bone and increasing rate of resorption of bone.

The present study also compared of T-score and risk of osteoporosis among diabetic and non-diabetics males and females. In our study, LS and FN T-score of diabetic males was significantly raised than diabetic females. However it was non-significantly higher in non-diabetic males when compared to non-diabetic females. Our outcome is in concordance with the findings by Leidig-Bruckner et al.[21] As far as risk of osteoporosis is concerned based on WHO interpretation of T-score, risk of osteoporosis was found significantly more in diabetic females than diabetic males. This finding is in harmony with the study by Wen et al.[22] and Leidig-Bruckner et al.[21] However our study reported non-significantly upraised risk of osteoporosis in non-diabetic females when compared to non-diabetic males which is in contrast to findings of Wen et al.[22] as they observed significantly higher osteoporosis in non-diabetic females. The

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reason behind our outcome of diabetic or non-diabetic females being at higher risk of osteoporosis might be the mean age of our study. The mean age of our study for both the groups was near 50years which is the menopausal age for women and studies have already proven that risk of osteoporosis increases after menopause in women[18,23-25)] as their bone mass declines about 12 to 20 percent in initial 5years. Thus, reduced peak bone mass and estrogen insufficiency after menopause provokes elevated risk of fractures in women than men.

Conclusion-

DM is a very common disorder with distressing effects on metabolism. T1DM or T2DM patients, both are at increased risk of osteoporosis. T-score assessment for BMD measurement by DXA scan is good tool to assess risk of osteoporosis along with consideration of other factors. Our study suggests vigorous screening of population at high risk for prevention and better management of osteoporosis. Our findings stress the call for clinicians to screen bone health in all DM patients regardless of age and sex and counsel them about sufficient intake of Ca, vitamin D and other nutrients related to bone health along with good glycaemic control.

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Conflict of interest- None

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