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RESEARCH ARTICLE

Relationship between Bone Mineral Density and Serum Vitamin D with Low Energy Hip and Distal Radius Fractures: A Case-Control Study

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Abstract

Background: The main purpose of this study was to determine the relationship between serum vitamin D and the status of bone mineral density in patients with low-energy hip and distal radius fracture.

Methods: This retrospective case-control study was performed between January 2013 and January 2014. Participants aged 55 years or older were divided to case group including 85 patients with low-energy hip fracture and 83 patients with low-energy distal radius fractures, and 82 subjects as a matched control group. Bone mineral density was measured with dual energy X-ray absorptiometry and serum sample was obtained to check vitamin D, calcium, phosphorus, alkaline phosphatase, and protein.

Results: Study subjects for final evaluation consisted of 78 in hip and distal radius fracture groups and 80 in control group. There were no significant differences in the mean serum levels of calcium, phosphorus and alkaline phosphatase between the three groups. The overall mean serum level of vitamin D3 was significantly different among the three groups. Similar results were observed with hip and spine t-score between the groups.

Conclusion: There is not only a direct relation between serum vitamin D and the risk of low energy hip and distal radius fractures, but also a significant relation between low bone density in hip and spine area with low serum calcium was observed.

Keywords: Bone mineral density, Distal radius fracture and hip fracture, Low energy fracture, Vitamin D

Introduction

Osteoporosis is a major public health concern that is characterized by low bone mass and abnormal bone structure, which leads to increased bone fragility and fractures (1,2). Dual X-ray absorptiometry (DXA) is the preferred clinical tool for the diagnosis of osteoporosis and determination of its severity (3, 4). This equipment is widely available and a major number of clinicians currently employ the hip and spine scan as the gold standard. Low bone mineral density (BMD) is an important risk factor for osteoporosis and its related fractures (3, 5).

Vitamin D status affects the rate of bone turnover, bone mineralization and occurrence of fractures. Epidemiological studies revealed low BMD is related to vitamin D deficiency. The important consequences can be considered as muscle weakness, increased risk of falling and also low energy fractures (6-9). The prevalence of vitamin D deficiency does not follow the same pattern in different parts of the world (10). The major factors , which may play a role on osteoporosis and bone mass density are differences in lifestyle and living conditions, race, nutritional status, and physical activity (2).

Although, distal radius fractures occur about 15 years earlier than hip fractures on average, both are among the most common fractures associated with osteoporosis and vitamin D deficiency (11-13). Hip fracture is a major cause of hospital admission in osteoporotic patients. It is associated with a significant cost for both the health care systems and patients with a remarkable morbidity and mortality rate (14).

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According to Cooper et al. its incidence in developing Asian countries is increasing rapidly (15).

The estimated prevalence of osteoporosis among Iranian men and women population, who are in the sixth decade of their age, is 147 and 358 per 10000, respectively. This prevalence increases more dramatically in patients who are in their seventh to ninth decades of age (1). However, serum vitamin D status and BMD among patients with hip and distal radius fractures have not been compared to subjects without fractures.

The main purpose of this study was to determine the relationship between serum vitamin D and BMD status in patients with low-energy hip and distal radius fracture.

Materials and Methods

1. Study design and participants:

After obtaining institutional approval from the university ethic committee and review board, this retrospective case-control study was performed between January 2013 and January 2014 in Kashani Hospital, a tertiary referral center for trauma, affiliated with Isfahan University of Medical Sciences located in Isfahan, Iran. Each participant signed an informed consent form.

We recruited all patients aged 55 years or older with a low-energy hip and distal radius fracture. All enrolled patients were from Isfahan. In this study, initial subjects were divided to three groups. Two case groups were included 85 patients with low energy hip fracture (hip fracture group), 83 patients with low energy distal radius fractures (distal radius fracture group). 82 subjects were enrolled as a matched control group.

Participants in control group were matched on place of residence, body weight, age (±2 years), gender, history of smoking and diabetes mellitus..

A low-energy fracture was defined as a fracture following a minor trauma, equivalent to falling from standing height or less (16).

Our exclusion criteria consisted of participants who had been taking glucocorticoids, vitamin D or osteoporosis medications, and the patients with medical factors, which are capable of affecting vitamin D levels, such as gastrointestinal diseases, previous gastrointestinal surgery and renal diseases. We also excluded subjects with previous fractures in hip or distal radius and subjects with bilateral hip fractures, which might affect bone densitometry of hip region. All hip and distal radius fractures were radiologically confirmed.

2. Observations and measurements:

Weight and height were measured with standard apparatus in light clothing without shoes at our clinic. Weight was measured with an accuracy of ±0.1 kg using a calibrated beam scale. Height was measured with an accuracy of ±0.5 cm using a measuring tape. We calculated BMI employing the ratio of weight (kg) to height squared (m^2).

Bone mineral density (BMD) was measured with dual energy X-ray absorptiometry (DXA) (Lunar Prodigy, GE Madison, WI, USA) for all patients for the groups with hip fracture (HF) and distal radius fracture (DRF) within 3 weeks of fracture at the femoral neck, total hip and lumbar spine (L2–L4). The results were reported based on measurements of femoral neck BMD as a standard (17). To control for possible baseline drift, the scanner was calibrated daily against the standard calibration block supplied by the manufacturer. In the control group BMD was done after their enrollment.

Diagnosis of osteoporosis/osteopenia was done according to t-scores as follows: normal if t-score ≥ −1.0, osteopenia if −2.5 < t-score < −1.0, and osteoporosis if t-score ≤−2.5 (18). Data were collected according to recommendations of the International Society for Clinical Densitometry (19).

For all groups including hip fracture group (HFG), distal radius fracture group (DRFG), and control group, serum samples were obtained to check calcium, phosphorus, alkaline phosphatase, and protein. All serum samples were analyzed at the Hormone Laboratory of the university hospital. Serum 25 (OH) D level was measured using a radioimmunoassay.

The HFG and DRFG were sampled within 48 hours of trauma, while for the control group the sampling process was performed during outpatient clinic visit after enrolment.

3. Statistical methods:

Differences in Vitamin D level among HFG, DRFG and the control group were compared using Student's t-test. Analysis of variance (ANOVA) was performed to analyze differences in vitamin D levels with respect to group age. The statistical analysis utilized the Kruskal-Wallisto test to compare the three categories. Correlation analysis was performed to determine association between vitamin D levels and various variables, such as age and BMDs. Statistical analysis was performed using SPSS software (Ver. 20; Chicago, IL, USA). A value of $P<0.05$ was considered statistically significant.

Results

1. Characteristics of patients and controls:

At the end of the study, 78 patients in HFG and DRFG and 80 patients in control group underwent a complete evaluation. The mean age of patients in HFG, DRFG, and control group was 70.5±5.1, 68.1±6.9, and 68.7±6.3 years, respectively ($P=0.1$). The ratio of female to male was 71.8% to 28.2% in HFG, 61.5% to 38.5% in DRFG and 69.2% to 30.8% in the control group. Chi-square tests showed there was no statistically significant difference between the groups in the ratio of female to male ($P=0.603$). The mean BMI in HFG, DRFG, and control group was 27.55, 26.93, and 27.13, respectively.

2. Serum markers and bone mineral density:

Results from one-way ANOVA tests revealed that there was no significant difference in the mean serum levels of calcium ($P=0.54$), phosphorus ($P=0.49$) and

Table 1. Comparison of serum levels of calcium, phosphorus and alkaline phosphatase in different groups

		Mean ± SD	Min	Max	*P- value*
Ca	HFG	0.52 8.7±	7.7	10.1	0.54
	DRFG	0.49 8.8±	8	10.1	
	Control	8.7±0.38	7.9	9.6	
P	HFG	0.37 3.5±	2.9	4.4	0.49
	DRFG	0.36 3.6±	2.4	4.2	
	Control	0.28 3.5±	3.2	4.5	
Alk- P	HFG	41 206.8±	108	295	0.13
	DRFG	37 189.6±	83	259	
	Control	40 192.2±	158	268	

Data are presented as mean ± standard deviation.
* *P-value* lesser than 0.05 ($P < 0.05$) is significant

alkaline phosphatase ($P=0.13$) among the three groups [Table 1].

According to ANOVA tests, the overall mean serum level of vitamin D3 was significantly different among the three groups ($P=0.035$). Moreover, an LSD post-hoc test revealed that there was no significant difference between the serum vitamin D3 in HFG (range: 8-77 ng/ml), and DRFG (range: 10-68 ng/ml) ($P=0.64$). The same findings also revealed no significant difference between spine and hip t-score in HFG and DRFG ($P=0.1$ and $P=0.09$, respectively). However, the serum vitamin D3 in control group (range: 17-91 ng/ml) was significantly more than HFG ($P=0.01$), and DRFG ($P=0.03$) [Table2].

As illustrated in Figures 1 and 2, the distribution of osteopenia and osteoporosis according to spine and hip t-scores was slightly different. According to spine t-score, most of the patients with hip fractures were in osteoporotic category whilst patients with distal radius fractures were mostly categorized as

Table 2. Difference between mean of vitamin D, spine and hip t-score between groups

	HFG (mean ± SD)	DRFG (mean ± SD)	Control (mean ± SD)	*P value*	*P1**	*P2**	*P3**
Vit. D	25.9 ±17.1	27.6 ±14.1	34.2 ±14.2	0.035	0.64	0.01	0.03
Spine t-score	-2.43 ±0.85	-2.15 ±0.72	-1.71 ±0.64	<0.001	0.1	<0.001	<0.001
Hip t-score	-2.91 ±0.63	-2.61 ±0.57	-1.95 ±0.62	<0.001	0.09	<0.001	<0.001

* *P-value* in *P1* (between HFG and DRFG), *P2* (between HFG and control), *P3* (between DRFG and control)
Data are presented as mean ± standard deviation.
* *P-value* lesser than 0.05 ($P < 0.05$) is significant.

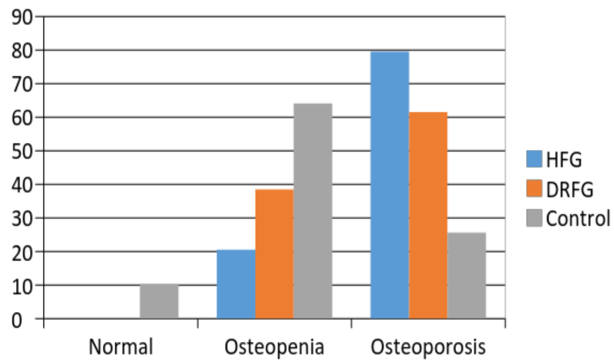

Figure 1. Distribution of bone density according to Hip t-score.

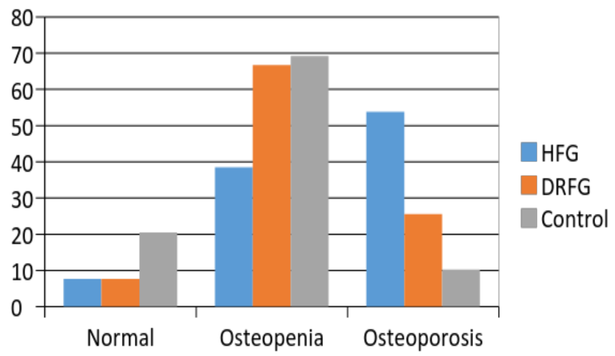

Figure 2. Distribution of bone density according to Spine t-score.

Table 3. Pearson correlation coefficient between serum Vitamin D3 with T- score of hip and spine

Group	*Spine t-score*		*Hip t-score*	
	r	*P-value*	*r*	*P-value*
HFG	0.57	<0.001	0.49	<0.001
DRFG	0.31	0.015	0.27	0.03
Control	0.56	<0.001	0.46	<0.001

Data are presented as mean ± standard deviation.
* *P-value* lesser than 0.05 ($P < 0.05$) is significant.

osteopenia [Figure 1].

Pearson correlation revealed that there was a significant direct correlation between serum vitamin D3 and hip and spine t-score in all three groups [Table 3].

Discussion

The main finding of this study was that low amount of serum vitamin D can be associated with low energy hip and distal radius fractures. According to previous studies, smoking and Diabetic Mellitus can affect bone density (20, 21). Smoking can affect different aspects of bone metabolism including decreased peak bone mass, increased rate of bone loss, and osteoporosis (20).

Vitamin D deficiency is present in all over the world, but it has been reported to be higher in South Asia and the Middle East (22). The link between vitamin D and BMD is under investigation and there is no consensus on it. Several studies have suggested that there is a direct relationship between low levels of serum vitamin D and low BMD (23-25). Vitamin D is extremely important for bone metabolism. When vitamin D is deficient, serum PTH levels rise, which will consequently lead to osteoclast activation and decrease in bone density (9). Bischoff-Ferrari et al. found a positive relation between vitamin D levels and bone mineral density in young Caucasians and elderly men (26).

In this case-control study, we compared serum vitamin D levels and BMD in low energy hip and distal radius fracture patients of over 55 years of age with their matched controls. Our control subjects were matched on age, body weight, gender, and place of residence. Unlike most of previous studies, male patients were included as well. This study revealed a lower mean serum vitamin D in patients with hip and distal radius fracture compared to controls in both women and men, and there was a direct relationship between vitamin D status and BMD. Our results were comparable with those of Jang et al. and Lee et al., which report not only lower serum vitamin D and BMD in Korean women with distal radius fractures than in their control group. Also, their results showed a significant relation between vitamin D and BMD (10,27).

However, there are studies that do not support this conclusion (28,29). Oyen et al. in their case–control study, emphasized that although vitamin D shortage is associated with distal radius fractures, but differences in vitamin D levels are independent of BMDs. Their study was done on Western sample populations and the age and BMI were not well matched between the case and control groups (8). Garnero et al. (30) and Allali et al. (31) were also unable to find a significant correlation between vitamin D levels and bone mineral density.

In the present study, although the levels of BMD and serum vitamin D were not statistically significant between HFG and DRFG, but the mean serum vitamin D and t-score in both hip and spine in HFG was less than DRFG [Table 2]. This might indicate that if our sample size were larger, the difference between these variables would be statistically significant. Moreover, we found a statistically significant difference between hip and spine t-score within HFG and DRFG, but not in the control group. This might indicate that in fracture conditions, bone mineral density is affected more in hip than spine. To confirm this finding, more studies with larger sample size are recommended. Furthermore, comparing Figures 1 and 2, in which the mean t-score is smaller in femoral neck area than lumbar spine area, this finding might suggest a higher sensitivity of hip t-score than spine in identifying osteoporotic patients. This conclusion is antithetic with the results of Rassouli et al. (32) who found a correlation with the bone mineral density of the spine. Ethnic differences in the patient populations and various age groups, as well as the fact that the studies have focused on different regions of the human body can explain the heterogeneity of results.

The study has several strengths. First, it compares BMD and serum vitamin D levels of patients with hip and distal radius fractures with the BMD and serum vitamin D levels of the control patients with respect to their age and BMI. Second, the recruitment of subjects within 48 hours of their low energy hip and/or distal radius fractures allowed for measurement within the time frame before the musculoskeletal changes could affect our biochemical analyses. Third, the participation rate in all three groups was more than 90 percent.

The present study had also some limitations. First, the subjects were ethnic Iranians; therefore, our results may not be representative of all ethnicities. Second, all patients were selected from a tertiary referral university hospital; hence the subjects may not represent general population with hip and/or distal radius fractures. Third, the controls were not recruited from a healthy population, and it is not known to what extent their conditions altered vitamin D levels. Fourth, although vitamin D levels fluctuate according to circadian rhythm, sampling times were not standardized. However, all sampling was performed between 8am and 10am, which according to Rejnmark et al. (33) study, might not affect the results. Fifth, our determination of serum vitamin D relied on single measurement, which may not necessarily reflect long-term exposure. Nevertheless, this potential bias was the same for all of our subjects.

Sixth, information about some variables such as dietary habits, socioeconomic status, level of exposure to sunlight, physical activity, and muscle power, which can affect vitamin D levels, was not obtained.

The present study indicates that there is a direct relation between serum vitamin D and risk of low energy hip and distal radius fractures. In addition, a significant relation between low bone density in hip and spine area with low serum calcium was observed.

The authors declare that there is no conflict of interests regarding the publication of this paper.

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