Original Article

High Prevalence of Vitamin D Deficiency in Asian-Indian Patients with Fragility Hip Fracture: A Pilot Study

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Abstract

Objective: To assess vitamin D nutrition status in Asian-Indian patients with fragility hip fracture.

Methods: The study subjects included patients with non-traumatic hip fracture with age more than 50 years. Any patient who sustained fracture after road side accident of any severity was excluded. The other exclusion criteria were history of previous non-traumatic fracture or history of intake of systemic steroids, anti-osteoporotic medication, anti-tubercular or antiepileptic drugs. Routine biochemistry, serum 25-hydroxy vitamin D [25(OH)D] and BMD (DXA) were measured in all patients. Diagnosis of vitamin D deficiency (VDD) was considered when serum 25(OH)D levels were <20 ng/ml. Age and sex matched apparently healthy subjects (without history of fracture at any site) were selected from general population. All controls under went BMD measurement at spine.

Result: Final analysis included 43 patients, 9 men (20.9%) and 34 women (79.0%, all postmenopausal). The mean age of patients was 62.2 ± 12.3 years (range 50.5 to 74.2 years, men - 62 ± 13.4 years; women - 62.3 ± 12.4 years; *p* 0.73). History of adequate sun exposure was obtained in 34.8% cases only. Fracture occurred while patients were outside home in 10/43 (23.25%) while 33/43 (76.7%) patients sustained fracture at home. Of all fractures occurring at home, 51.5% patients sustained fracture consequent to fall/slip in the bathroom. The mean serum 25(OH)D level was 9.9 ± 4.8 ng/ml (range 5 - 21.5 ng/ml). All patients except one (96.7%) had VDD. No significant difference in serum 25(OH)D levels was observed between patients with and without adequate sun exposure. BMD of patients with fragility fractures were significantly low in comparison to BMD of healthy controls. (cases - 0.790 ± 0.1 gm/sq cm vs controls 0.924 ± 0.1 gm/sq cm; *p* 0.000). The mean Z-score of spine BMD of cases was -1.13 ± 1.4. No significant difference was observed in the BMD of patients with or without adequate sun exposure and with or without calcium and vitamin D supplementation at the time of fracture. Similarly, no significant difference was noted in BMD of patients with severe VDD and patients with mild to moderate VDD. All patients were contacted by telephone one year after the surgery (mean 12.3 months, range 9 to 13 months). Out of total 43 patients, 26 patients/families could be contacted, 11 (42.3%) died within one year of surgery, of which 8 patients died within first 6 months after surgery. Two patients died within 72 hours after discharge from hospital. Of 15 patients alive one year after surgery, two were able to walk without any support while 13 were able to walk with some support (stick or walker).

Conclusion: Our study shows very high prevalence (96.7%) of vitamin D deficiency in Asian-Indian patients with fragility hip fracture. The BMD of these patients is significantly low in comparison to age and sex matched healthy controls. More fractures occurred at home than outside, with a majority of fall being in the bathroom.

Osteoporosis is a major public health problem around the world, largely due to the morbidity and mortality associated with osteoporotic fractures. Although spine fractures are more common, hip fractures are the major cause of morbidity and mortality. Calcium and vitamin D nutrition plays an important role in determining bone health. Vitamin D deficiency in adults can precipitate or exacerbate osteopenia and osteoporosis, cause osteomalacia and muscle weakness, and increase the risk of fracture.[1] Vitamin D deficiency (VDD) is one of the important risk factor for an osteoporotic fracture in all age groups especially among elderly population. It has been estimated that 1 billion people worldwide have vitamin D deficiency or insufficiency.[1]

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According to several studies, 40 to 100% of U.S. and European elderly men and women living in the community (not in nursing homes) are deficient in vitamin D.[1] Prevalence of VDD in elderly hip fracture patients varies in different population. In the United States, a serum 25-hydroxy vitamin D [25(OH)D] level lower than 12 ng/ml was observed in 50% of women with osteoporotic hip fractures[2] and in Italy this value was found to be 13.5%, with 21.6% of patients having a 25(OH)D level less than 20 ng/ml[3] In a study from Japan, 62% of hip fracture patients had vitamin D insufficiency (<20 ng/ml).[4] Recently, Leboff et al reported Vitamin D insufficiency (≤32 ng/ml) in 96% of the women with hip fractures including 38% who had extremely low levels ≤9 ng/ml.[5] In another recently published study, all but two of the 78 patients (97.4%) had 25(OH)D <30 ng/ml and the majority (81%) of the patients had 25(OH)D <20 ng/ml.[6]

Despite adequate availability of sunshine in India, VDD is widely prevalent among Asian Indians. VDD has been reported in almost all age groups in healthy Indian subjects.[7] Recent data have shown a high prevalence of VDD in different subgroups of healthy Indian population. This includes both urban and

Table 1 : Clinical and biochemical parameters of study population

Parameters	Total	Male	Female	*p*
Study subjects	43	9 (20.9%)	34 (79.0%),	-
Age in yrs (mean ± SD)	62.2 ± 12.3	62 ± 13.4	62.3 ± 12.4	0.73
Corrected S Calcium (mean ± SD) (Normal range 8.5-10.5 mg%)	9.8 ± 0.8	10.1 + 0.7	9.6 + 0.5	0.53
S. Alkaline Phosphatase (mean ± SD) (Normal range 80-240 IU/L)	187.5 ± 60.9 range 83-276	157 ± 57.1	227 + 50	0.08
Serum creatinine (mean ± SD) (Normal range 0.5-1.8 mg%)	1.21 ± 0.43	1.39 ± 0.7	1.12 ± 0.5	0.72

semi-urban Indians, postmenopausal women, pregnant women, school children and newborns.[8-12] High prevalence of vitamin D deficiency has been reported in elderly Asians, living in Britain.[13] There is no information available on prevalence of VDD in Indian patients with fragility hip fracture.

We planned a study to assess vitamin D nutrition status in Asian-Indian patients with fragility hip fracture.

Material and Methods

This prospective observational study was carried out from July 2006 to March 2008, in the Department of Endocrinology, in collaboration with Department of Orthopedics, All India Institute of Medical Sciences. Study population consisted of all those patients who were referred to our institute for management of hip fracture. The study was approved by Ethics Committee, All India Institute of Medical Sciences.

Study subjects

Patients with non-traumatic hip fracture (including fracture of neck of femur and inter-trochanteric fracture) and age more than 50 years, were included in this study. Any patient who sustained fracture after road side accident of any severity was excluded. Similarly, patients with history of fall with major impact were also excluded. The other exclusion criteria were history of intake of systemic steroid for more than one year, history of treatment with any anti-osteoporotic medication except calcium and vitamin D, history of previous non-traumatic hip fracture or fracture of forearm (Colles' fracture), use of anti-tubercular or antiepileptic treatment in past one year, presence of any systemic disease (chronic liver failure, chronic renal failure, inflammatory bowel disease, and chronic pulmonary disease), or presence of any active malignant disease or treatment with anti-malignant drug in last one year. Age and sex matched apparently healthy controls (without history of fracture at any site) were selected from general population. All controls underwent BMD measurement at spine. The exclusion criteria for patients were also applied in the selection of controls.

After obtaining informed consent, detailed history (including history of sun exposure, detailed history of cause of fracture) and tailored physical examination, blood samples were collected in fasting state for routine tests and S. 25(OH)D. Exposure of both hands and face to direct sunlight, without any clothing, for 15-20 minutes daily for five days a week (total 2 hours per week) was considered as 'sufficient sun light exposure'.[14] All routine biochemical tests were performed with auto-analyzer (Hitachi Auto Analyzer; Hitachi, Tokyo, Japan) on the day of sample collection except for 25(OH)D. Samples for 25(OH)D were stored at -20 degree centigrade till analysis. 25(OH)D was measured by radioimmunoassay (RIA, DiaSorin, USA). BMD was measured at spine with DXA (Hologic QDR 4500, Hologic, Inc., USA).

Vitamin D deficiency

Diagnosis of VDD was considered when 25(OH)D levels were <20 ng/ml.[1] Diagnosis of severe VDD was made with 25(OH)D levels were <5 ng/ml while that of mild to moderate VDD with 25(OH)D levels between 5-20 ng/ml.

Statistical analysis

Statistical analysis was performed using SPSS 10.0 (SPSS Inc, USA). Results are expressed as mean ± SD.

Results

Total 50 patients consented for the study, of which 7 were excluded. The reasons for exclusion were: BMD measurement could not be done in 5 patients because of associated pain and inconvenience. One patient was excluded from analysis as she was diagnosed to have breast carcinoma with multiple bony metastases during the admission for management of hip fracture. One patient had vertebral fractures involving all lumbar vertebras so interpretation of BMD was not possible. Hence, final analysis included 43 patients, 9 men (20.9%) and 34 women (79.0%, all postmenopausal, Table 1).

History of adequate sun exposure was obtained in 34.8% cases only. Five out of 43 (11.62%) patients were on regular calcium and vitamin D supplementation at the time of fracture. Twenty eight (65.1%) patients had fracture on left side while 15 (35.8%) patients had on right side. Neck of femur was the commonest site of fracture in 40 (93.1%) while inter-trochanteric fracture was seen in 3 (6.9%) patients. Fracture occurred while patients were outside home in 10/43 (23.25%) while 33/43 (76.7%) patients sustained fracture at home. Of all fractures that occurred at home, 51.5% patients sustained fracture consequent to fall/slip in the bathroom.

Vitamin D Level

The mean 25(OH)D level was 9.9 ± 4.8 ng/ml (range 5 - 21.5 ng/ml). All patients except one (96.7%) had VDD. 10/43 (23.25%) patients had severe VDD while 33/43 (74.4%) had 25(OH)D less than 10 ng/ml. 9/43 (23.25%) patients had 25(OH)D level between 10-20 ng/ml. No significance difference in 25(OH)D levels was observed between patients who had history of adequate sun exposure and who did not have and in between patients taking calcium and vitamin D supplementation and those who did not.

BMD Results

BMD of patients with fragility fractures were significantly low in comparison to BMD of healthy controls (Table 2). No significant difference was observed in the BMD of patients with or without adequate sun exposure and with or without calcium and vitamin D supplementation at the time of fracture. Similarly, no significant difference was noted in BMD of patients with severe vitamin deficiency and patients with mild to moderate VDD.

Follow-up After One Year

All patients were contacted by telephone one year after the surgery (12.3 months, range 9 to 13 months). Out of total 43 patients, only 26 patients/families could be contacted by phone. Seventeen patients or families could not be contacted as they moved out of city or their phone numbers were changed. Of these 26 patients/families contacted, 11 (42.3%) died within one year of surgery, of which 8 patients died within first 6 months after surgery. Two patients died within 72 hours after discharge from hospital. It was not possible to ascertain cause of death as most

Table 2 : Comparison of BMD in controls and cases

Parameters	Cases	Controls	*p*
Age in years	62.24 ± 12.3	61.64 ± 11.5	0.86
Ht in cms	155.7 ± 10.1	155.5 ± 6.5	0.93
Wt in kgs	63.3 ± 10.6	59.8 ± 8.3	0.35
Spine BMD in gm/sq cm	0.790 ± 0.1	0.924 ± 0.1	0.000

of the deaths occurred at home and postmortem examinations were not carried and affected families were not willing to provide further details. Of 15 patients alive one year after surgery, two were able to walk without any support while 13 were able to walk with some support (stick or walker).

Discussion

To the best of our knowledge, this is the first study to evaluate vitamin D status in Asian-Indian population with fragility hip fracture and reveals very high prevalence of VDD. This study also shows high mortality one year after fragility hip fracture.

Calcium and vitamin D nutrition plays an important role in determining bone health. 25(OH)D estimation is the most practical and widely used parameter to assess vitamin D nutrition status of an individual. Although there is no consensus on optimal levels of 25(OH)D, VDD is defined as 25(OH)D level of <20 ng/ml (50 nmol per liter). The level of 25(OH)D of 21 to 29 ng/ml (52 to 72 nmol per liter) is considered as a state of relative insufficiency of vitamin D, and a level of 30 ng/ml or greater can be considered to indicate sufficient vitamin D.[1] There is no study of the prevalence of VDD in fragility hip fracture in the Indian population. Using a cutoff of 20 ng / ml to diagnose VDD, we found 96.7% patients had VDD, which would rise to 100% if we increased the cutoff to 30 ng / ml.

Although reliable epidemiological data are lacking, hospital data suggest that hip fractures are common in India. Data also suggest that men are probably more commonly affected than women, although this may be because the likelihood of men seeking hospital attention is greater than that for women.[7] Nordin reviewed 119 hip fractures from India and found that they occurred at all ages, with two peaks at 30-39 yr and again at 50-70 yr. There was no attempt to distinguish traumatic from fragility fractures.[15] Gupta et al[16] studied 425 patients of hip fractures and reported that 63 per cent were men with average age at fracture of 55 years (49 yr for men and 57 yr in women). Although there are no reports of vitamin D status of patients with hip fracture, a couple of studies have tried to address this issue by looking at osteomalacia in bone biopsy.

Vaishnava and Rizvi[17] found osteomalacia and osteoporosis based on iliac crest biopsies in 141 out of 421 hip fracture patients, and again more than half their patients were men. Tucker et al studied incidence of osteomalacia (by iliac crest biopsy) in fractures of the proximal end of femur in 26 patients and found osteomalacia in 65% cases.[18]

Another important finding from our study is younger mean age of patients at the time of fracture, in comparison to reports from western countries.[19] Moniz et al reported mean age at the time of fracture was 73.4 years while 100% were aged 60 years or over and 41% were aged 75 years or over.[20] Similar to our findings, early age of hip fracture have been reported from older studies of hip fracture from India.[14-16] More recent data from Sankaran, involving 1393 patients of hip fracture from three large Delhi hospitals, showed that the peak age at which these fracture occurred was 60-70 years.[21] Indians living in Singapore were also found to have hip fracture at an early age of 58 years.[22] Similarly, early age at the time of hip fracture has also been reported from Pakistan (average age of 61 years).[23] The important factor which might have affected the age at fracture in our study was careful exclusion of all those cases who had prior fragility fracture or who had been treated with anti-osteoporotic drugs. This finding of younger age at the time of fracture has many important implications.

Only 11.6% of our patients were taking regular calcium and vitamin D supplementation at the time of fracture. Similar results have also been shown by Moniz et al in a study of 103 patients with hip fracture.[20] They found that around 20% of the patients were receiving supplementation with calcium and/or vitamin D at the time of fracture.

High mortality after hip fracture is a well described phenomenon. It varies from as low as 6.9% in low risk group to 80% in high risk group one year after fracture. Most studies report mortality of 20-40% one year after hip fracture in elderly population.[23-25] There are many factors which can affect mortality like age, post surgery prophylaxis for thrombo-embolism, staying out of house after surgery (in care homes) and social rehabilitation. Our study showed mortality of 42.3% one year after surgery. This is more important when mean age of our population was less in comparison to reports from western countries. This may be biased as we could get follow-up in only 60% patients.

More fractures were seen on left than right side. This may be because of dominance of right handed people in the population. Fall on right side might have been prevented by use of dominant hand to hold some object during fall which may prevent or lessen the impact of fall. Another important finding from our study is that more fractured at home than outside home and out of all patients who fractured at home, ~40% fractures was associated with fall in bathroom.

The main limitation of our study is that it involves a small number of subjects reporting to urban tertiary care hospital for surgery and so may not reflect the population at large. Absence of PTH measurement and incomplete follow-up information are additional limitations.

Conclusion

Our study shows very high prevalence of vitamin D deficiency in elderly Asian-Indian patients with fragility hip fracture. The BMD of these patients is significantly low in comparison to age and sex matched health controls. More fractures occurred at home than outside, with a majority of falls being in the bathroom.

References

1. Holick MF. Vitamin D deficiency. *N Engl J Med* 2007;357:266-81.
2. LeBoff MS, Kohlmeier L, Hurwitz S, Franklin J, Wright J, Glowacki J. Occult vitamin D deficiency in postmenopausal US women with acute hip fracture. *JAMA* 1999;281:1505–1511.
3. Nuti R, Martini G, Valenti R, Gambera D, Gennari L, Salvadori S, Avanzati A. Vitamin D status and bone turnover in women with acute hip fracture. *Clin Orthop Relat Res* 2004;422:208–213.
4. Sakuma M, Endo N, Oinuma T, Hayami T, Endo E, Yazawa T, Watanabe K, Watanabe S. Vitamin D and intact PTH status in patients with hip fracture. *Osteoporos Int* 2006;17:1608–1614.
5. Leboff MS, Hawkes WG, Glowacki J, Yu-Yahiro J, Hurwitz S, Magaziner J. Vitamin D-deficiency and post-fracture changes in lower extremity function and falls in women with hip fractures. *Osteoporos Int* 2008;19:1283-90. Epub 2008 Mar 29.
6. Simonelli C, Weiss TW, Morancey J, Swanson L, Chen YT. Prevalence

of vitamin D inadequacy in a minimal trauma fracture population. *Curr Med Res Opin* 2005;21:1069-74.

7. Malhotra N, Mithal A. Osteoporosis in Indians. *Indian J Med Res* 2008;127:263-268.
8. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. *Am J Clin Nutr* 2005;81:1060-4.
9. Marwaha R, Tandon N, Reddy DR, Aggarwal R, Sawhney RC, Saluja B, et al. Vitamin D and bone mineral density status of healthy schoolchildren in northern India. *Am J Clin Nutr* 2005;82:477-82.
10. Harinarayan CV. Prevalence of vitamin D insufficiency in postmenopausal south Indian women. *Osteoporosis Int* 2005;16:397-402.
11. Harinarayan CV, Ramalakshmi T, Prasad UV, Sudhakar D, Srinivasarao P, Sarma KVS, et al. High prevalence of low dietary calcium, high phytate consumption, and vitamin D deficiency in healthy south Indians. *Am J Clin Nutr* 2007;85:1062-7.
12. Goswami R, Gupta N, Goswami D, Marwaha RK, Tandon N, Kochupillai N. Prevalence and significance of low 25 hydroxyvitamin D concentrations in healthy subjects in Delhi. *Am J Clin Nutr* 2000;72:472-5.
13. Solanki T, Hyatt RH, Kemm JR, Hughes EA, Cowan RA. Are elderly Asians in Britain at a high risk of vitamin D deficiency and osteomalacia? *Age Ageing* 1995;24:103-7.
14. Bouillon R. Vitamin D: From Photosynthesis, Metabolism, and action to clinical applications. *In* Endocrinology, DeGroot LJ, Jameson JL (Eds) 5th Edition 2006, Elsevier Saunders, Philadelphia PA, pp1435-1463.
15. Nordin BEC. International patterns of osteoporosis. *Clin Orthop* 1966;45:17-30.
16. Gupta AK, Samuel KC, Kurian PM, Rallan RC. Preliminary study of the incidence and aetiology of femoral neck fracture in Indians. *Indian J Med Res* 1967;55:1341-8.
17. Vaishnava H, Rizvi SNA. Frequency of osteomalacia and osteoporosis in fractures of proximal femur. *Lancet* 1974;1:676-7.
18. Tucker GS, Middha VP, Sural A, Sagreiya K. Incidence of osteomalacia in fractures of the proximal end of femur. *Injury* 1988;19:89-92.
19. Becker C. Crow S, Toman J, Lipton C, McMahon DJ, Macaulay W, Siris E. Characteristics of elderly patients admitted to an urban tertiary care hospital with osteoporotic fractures: correlations with risk factors, fracture type, gender and ethnicity. *Osteoporos Int* 2006;17:410-6. Epub 2005 Nov 8. PubMed
20. Moniz C, Dew T, Dixon T. Prevalence of vitamin D inadequacy in osteoporotic hip fracture patients in London. *Curr Med Res Opin* 2005;21:1891-4.
21. Sankaran B. Clinical studies: Incidence of fracture neck of femur and intertrochanteric fractures in three Delhi hospitals. In: Sankaran B, editor. *Osteoporosis*. New Delhi: South East Asia Regional Office, World Health Organization 2000;9-18.
22. Wong PC. Femoral neck fractures among the major racial groups in Singapore. incidence patterns compared with non-Asian communities. *Singapore Med J* 1964;39:150-7.
23. Riaz S, Alam M, Umer M. Frequency of osteomalacia in elderly patients with hip fractures. *J Pak Med Assoc* 2006;56:273-6.
24. Beringer TR, Clarke J, Elliott JR, Marsh DR, Heyburn G, Steele IC. Outcome following proximal femoral fracture in Northern Ireland. *Ulster Med J* 2006;75:200-6.
25. Pioli G, Barone A, Giusti A, Oliveri M, Pizzonia M, Razzano M, Palummeri E. Predictors of mortality after hip fracture: results from 1-year follow-up. *Aging Clin Exp Res* 2006;18:381-7.