



CORRELATION OF VITAMIN D LEVELS WITH HIP FRACTURES IN PATIENTS ABOVE THE AGE OF SIXTY YEARS – A CLINICAL STUDY

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ABSTRACT Hip fractures are common in elderly population and pose great social and economic burden on the society. The role of low levels of Vitamin D, factors responsible for hypovitaminosis D, alteration in the levels of biochemical parameters and their correlation with hip fractures in 50 patients above 60 years was evaluated. Serum vitamin D₂, Bone Mineral Density (BMD) and related biochemical parameters were evaluated. Mean age for hip fractures was 69.36 ± 5.13 years. Females (62.00%) outnumbered males (38.00%) with fall at home being the commonest mode of injury (62.00%). Malnutrition (36.00%), Alcoholism (24.00%), Drug intake (14.00%), Smoking (12.00%), Diabetes Mellitus (38.00%), deranged liver function (22.00%) and renal function (12.00%) were the risk factors associated with hypovitaminosis D. Secondary hyperparathyroidism (64.00%) also came out to be an important marker for geriatric hip fractures. Osteopenia (38.00%) and Osteoporosis (28.00%) as measured by BMD was another important association. Higher age group, urban living, inactive lifestyle, various risk factors and comorbidities contribute to hypovitaminosis D.

KEYWORDS : Hypovitaminosis D, Hip Fractures, Parathyroid Hormone, Bone Mineral Density

INTRODUCTION

Hip fractures are quite common, especially in elderly population. Hip fractures have a bimodal distribution with high energy trauma in the young and low energy trauma in the elderly of which proximal femoral fractures have a high incidence in patients older than 60 years. The incidence of hip fracture is estimated to rise from 1.66 million in 1990 to 6.26 million in 2050 throughout Asia.¹ Hip fractures are seen more in females due to low BMI, early menopause or amenorrhoea. About 90% of these fractures are due to trivial falls. Elderly people are at a greater risk of hypovitaminosis D due to impaired intestinal absorption and impaired hydroxylation in the liver and kidneys.² Further, the ability to synthesize Vitamin D from sunlight³ and also to be activated to 1,25(OH)₂D in the kidney decreases with age.² Vitamin D is mainly synthesized from skin, dietary sources being less significant and a minimum level of 30ng/ml serum Vitamin D is necessary in older adults to minimize the risk of fractures due to falls.

Osteoporosis is characterized by low bone mass and micro-architectural deterioration of bone with an increase in bone fragility and susceptibility to fractures. According to the WHO criteria, osteoporosis is defined as a BMD that lies 2.5 standard deviations or more below the average value for young healthy women (a T-score of <-2.5 SD).⁴

Vitamin D from diet is transported as D₂/D₃ by incorporation into chylomicrons and 7-dehydrocholesterol from the skin is converted by solar radiation to pre-vitamin D₃; both of which are then metabolized to 25-hydroxyvitamin D [25(OH)D] in the liver; thereafter in the kidneys, 25(OH)D is metabolized by the enzyme 25(OH)D-1 α -hydroxylase (CYP27B1) to its active form 1,25-dihydroxyvitamin D [1,25(OH)₂D]. The renal production of 1,25(OH)₂D is regulated tightly by plasma parathyroid hormone levels as well as serum calcium and phosphorus levels.⁵

Vitamin D deficiency also leads to low or low-normal serum calcium levels which in turn leads to secondary stimulation of Parathyroid Hormone that leads to high bone turnover with increased bone resorption and in due course, it leads to bone loss or fracture. Hence, severe Vitamin D deficiency causes a mineralization problem and

osteomalacia, while on the other end it causes increased PTH leading to increased bone conversion, bone resorption and fractures.

Women wearing the traditional veil with face and hands uncovered (hijab) or covered (niqab) have poor Vitamin D status and more prevalent Vitamin D deficiency (or insufficiency) than those with Western style clothing. Skin pigmentation, sunscreen use, latitude, season, time of day and ageing affect the cutaneous synthesis of Vitamin D. Malabsorption due to Cystic Fibrosis, Coeliac Disease, Whipple's disease, bypass surgery; increased catabolism of Vitamin D due to anti-retroviral therapy or glucocorticoids and steroids; chronic kidney disease, liver failure and nephrotic syndrome may also lead to hypovitaminosis D.

Vitamin D deficiency is also associated with increased muscle weakness and pain leading to reduced strength, balance, function; increased bone turnover and increased risk of falls and hip fractures.⁶ Elderly may develop sarcopenia, a condition characterized by a combination of the reduction in muscle mass plus either muscle strength or performance.⁷

VITAMIN D LEVELS:

US Endocrine Society Classification
 Vitamin D Deficiency: <20 ng/ml
 Vitamin D Insufficiency: $21-29$ ng/ml
 Vitamin D Sufficiency: >30 ng/ml
 Vitamin D Toxicity: >150 ng/ml

The purpose of this study was to find out Vitamin D levels in patients admitted in our institution with different types of hip fractures over the age of sixty years; to assess the correlation between them if any and to study the factors responsible for Vitamin D deficiency in these patients.

METHODS

This study was conducted on 50 patients of hip fractures with low energy falls presenting to the Orthopedics Department of a tertiary care hospital in North India. All cases were evaluated for Vitamin D₂ levels using immunoassay technique. Related biochemical markers like Calcium, Phosphorus, Alkaline Phosphatase were also assessed. BMD

was estimated using Ultrasound technology. Ethical Committee clearance and patient's valid consent was taken. Patients of either sex, above 60 years were included; the exclusion criteria being high impact trauma, old nonunion or malunion, pathological fracture, bisphosphonate use in the past year, previous operation on proximal femur, primary hyperparathyroidism, multiple myeloma, malignant bone disease, metastatic bone disease, osteogenesis imperfecta and Paget's disease. Data on co-morbidities, demographic profile, functional status and serum Vitamin D₂ level was noted.

RESULTS

In the present study, commonest age group for hip fractures was 71-75 years (52.00%) followed by 61-65 years (30.00%). Neck of Femur fracture was most common in the age group of 61-65 years while Intertrochanteric Femur fracture was more common in the 70 plus age group signifying gradual shift towards occurrence of I/T Femur fractures with advancing age. Mean age was 71.42±3.91 years for Intertrochanteric Femur Fracture and 67.13±5.13 years for Neck of Femur Fracture. Overall, the mean age was 69.36±5.13 years.

Table 1: Age-wise Distribution Of Hip Fractures

Age Groups	I/T Femur	Neck of Femur Fracture	Total
61-65	3 (6.00%)	12 (24.00%)	15 (30.00%)
66-70	2 (4.00%)	5 (10.00%)	7 (14.00%)
71-75	20 (40.00%)	6 (12.00%)	26 (52.00%)
>75	1 (2.00%)	1 (2.00%)	2 (4.00%)

Hip fractures were common in females (62.00%) than males (38.00%). However, Intertrochanteric Femur fracture was seen in 15 (30.00%) males while Neck of Femur fracture was seen in 20 (40.00%) females. 66.00% of the patients belonged to urban/semi-urban areas whereas 34.00% were from rural area.

Hindus and Sikhs constituted majority of the population (90.00%) followed by Muslims (8.00%) and Christians (2.00%) 62.00% patients had inactive lifestyle before injury while 38.00% were active.

Trivial trauma was the mode of injury with fall at home occurring in majority of the patients (62.00%) while outdoor fall was seen in 38.00%.

Malnutrition/Malabsorption (36.00%) was the commonest risk factor followed by Alcoholism (24.00%), Medication (14.00%) and Smoking (12.00%).

The commonest comorbidity was Type II Diabetes Mellitus followed by deranged Liver function (due to Alcoholism or drug intake) and deranged renal function due to Type II DM, etc.

Table 2: Vitamin D Levels In Different Age Groups

Age Groups	Vitamin D		
	Deficiency (<20 ng/ml)	Insufficiency (21-29 ng/ml)	Optimal (>30 ng/ml)
61-65	12 (24.00%)	2 (4.00%)	1 (2.00%)
66-70	6 (12.00%)	1 (2.00%)	0 (0.00%)
71-75	19 (38.00%)	3 (6.00%)	4 (8.00%)
>75	2 (4.00%)	0 (0.00%)	0 (0.00%)
Total	39 (78.00%)	6 (12.00%)	5 (10.00%)

78.00% had deficient Vitamin D levels (<20 ng/ml) with 71-75 years being the commonest deficient age group (38.00%). Vitamin D level less than 20 was most commonly associated with hip fractures in 78.00%.

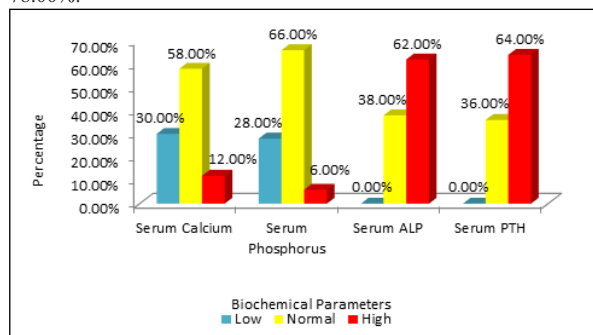


Fig.1: Levels Of Biochemical Markers In Hip Fracture Patients

An important observation made was a secondary rise in Parathyroid Hormone level due to negative feedback leading onto secondary hyperparathyroidism in 64.00% of the patients. Subsequent to this, probably normal to high serum calcium level was seen in 70.00% of the patients and normal to high serum phosphorus level was seen in 72.00%.

Reduced Bone Mineral Density using Ultrasound technology and T-score as a criterion was an important association in majority of the hip fractures. Osteoporosis was seen in 28.00% of the patients while Osteopenia was seen in 38.00%.

DISCUSSION

Most of the hip fractures encountered in our study were in the age group of 71-75 years (n=26, 52.00%) followed by 61-65 years (n=15, 30.00%) with a mean age of 69.36 ± 5.13 years which is in accordance with studies done by Sakuma M et al. in 2006 (70 years and above)⁸, Dhanwal DK et al in 2013 (65.9 ± 12.6 years)⁹, Pederson MA et al. in 2014 (65 plus age group)¹⁰, Guerra MT et al. in 2016 (60 plus age group)¹¹ and Ahuja K et al. in 2017 (60-69 years)¹². Neck of Femur (NOF) fractures were seen in 61-65 year age group (50.00%) while Intertrochanteric (I/T) Femur fractures predominated in the higher age group i.e. 71-75 years (77.00%). This is probably due to decreased cutaneous synthesis of Vitamin D³, less dietary intake as well as absorption¹³ and impaired hydroxylation² with advancing age.

In the present study, females clearly outnumbered males. The male: female ratio was 38.00% (n=19): 62.00% (n=31). This is in line with a study by Dhanwal DK et al. in 2013 [32.70% (n=20): 77.70% (n=70)]⁹ and Khadgawat R et al. in 2010 [20.90% (n=9): 79.00% (n=34)]¹⁴. This is probably due to the fact that males tend to be more active and go outdoors even with advancing age with more chances of a fall. In females, post-menopausal loss of protective estrogen effect on bone mineralization makes them more susceptible to osteoporosis and fractures as explained in a study done by Ahuja K et al. in 2017.¹² I/T Femur fracture seems to be slightly more in males with a higher age group and NOF fracture was seen more in females as compared to I/T Femur fracture which is in line with studies done by Fox K et al. in 1999 (I/T - 53.74%, NOF - 46.26%)¹⁵ and Krishna H et al. in 2015 (I/T - 49.00%, NOF - 51.00%)¹⁶.

64.00% (n=32) of the patients were from urban/semi-urban population. Residential area was an important association with hip fractures because of congested lanes, confinement to small closed houses with less outdoor mobility and exposure to sunlight which is in accordance with a study done by Guerra MT et al. in 2016¹¹ and Ramason R et al. in 2014 who outlined hypovitaminosis D in the housebound¹⁷.

Similarly, customs and traditions were probably responsible for hypovitaminosis D as majority of the patients were Hindus and Sikhs (90.00%) who wore full sleeved clothes, head covered with dupatta especially by village females; hijab worn by Muslim females made them vulnerable to hypovitaminosis due to reduced sunlight exposure. This is in accordance with an earlier study done by Ramason R et al. who reported hypovitaminosis with less sunlight exposure¹⁷, Pederson MA et al. who reported hypovitaminosis D in patients with sheltered housings¹⁰ and Holvik K et al. with similar findings¹⁸.

Inactive lifestyle had a direct relationship with hip fractures due to defective mineralization and poor bone quality. Also, physical inactivity speeds the aging process in many people¹⁹ and loss of muscle mass, strength & function (sarcopenia) and loss of bone mass with advancing age when left untreated may increase the risk of falls and subsequent fractures.⁶

The commonest mode of injury was a fall at home (62.00%) which is in correlation with studies done by Ahuja K et al.¹² and Khadgawat R et al.¹⁴

Various risk factors involved were Malnutrition (36.00%), Alcoholism (24.00%), Pharmacological agents (14.00%) and Smoking (12.00%). These factors affected Vitamin D through different pathways ultimately leading to low serum Vitamin D which is in accordance with a study done by Ahuja K et al. in 2017¹² and Brot C et al. in 1999.²⁰

Diabetes Mellitus (Type II) was the most common co-morbidity followed by deranged Liver Function and Renal Function which is in line with a study carried out by Wei J et al. in 2019.²¹ Impaired hydroxylation of Vitamin D and chemical disturbances in the bone

increase the risk of falls and thus subsequent hip fractures.²²

Vitamin D (<20 ng/ml) was observed as a significant biochemical parameter with 78.00% of the patients having deficient while 12.00% having insufficient levels which is in line with various studies conducted by Dhanwal DK et al. (76.70% had deficient Vitamin D levels)⁹, Sakuma M et al. (62.00% had levels <20ng/ml)⁸, Guerra MT et al. (54.50% had deficient Vitamin D₂ levels while 27.20% had insufficient levels)¹¹, Phruetthiphat OA et al. (Vitamin D inadequacy in 70.50% and Vitamin D deficiency in 37.70%)²³, Ramason R et al. (57.50% had hypovitaminosis D)¹⁷, Krishna H et al. (22.00% had Vitamin D deficiency while 36.00% had insufficient levels)¹⁶ and LeBoff MS et al. (50.00% patients had low Vitamin D).²⁴

Another highlighting point was a secondary rise in the level of Parathyroid Hormone (SPTH) [66.00% (n=33)] in response to hypovitaminosis D to maintain the normal serum calcium homeostasis. Hypovitaminosis D tends to lead on to a lower serum calcium level which in turn stimulates serum parathyroid hormone so as to maintain normal serum calcium further reducing the bone mass with susceptibility to fractures. This eventually leads to an increase in the bone turnover rate causing a significant rise in the serum level of Alkaline Phosphatase leading to further osteopenia and osteoporosis. This is in line with studies carried out by Dhanwal K et al. (68.90% patients had secondary hyperparathyroidism)⁹, Shinkov A et al.²⁵ and Sakuma M et al.⁸

Serum calcium deficiency was seen in 30.00% while in 70.00% patients it was normal to high; serum phosphorus was low in 28.00% while in 72.00% of the patients, it was normal to high; Alkaline phosphatase was elevated in 62.00% patients; which is in accordance with studies done by Riaz S et al. in 2006.²⁶

Another highlighting point was reduced Bone Mineral Density (BMD) in 66.00% of the patients using T-score as a criterion. Osteoporosis was seen in 28.00% patients while Osteopenia was seen in 38.00% patients which is in line with a study done by Farouk O et al. in 2016 where they showed the association of reduced BMD with Hypovitaminosis D.²⁷

From the above study, it can be seen that various factors like age, physical inactivity, drug intake, alcoholism, smoking; comorbidities like deranged LFT's, RFT's, DM Type II play an important role in lowering the Vitamin D level. Another major factor seen was a secondary increase in Parathyroid Hormone level further reducing the BMD to maintain serum calcium homeostasis, hence contributing to hip fractures in elderly patients. Vitamin D and PTH level are thus good predictors for geriatric hip fractures. Hence, probably it needs more general awareness among the masses and health workers to timely diagnose this condition, overcome the deficiency with probable correction of serum Vitamin D and subsequent correction of PTH levels in geriatric population leading to a probable decrease in the incidence of hip fractures.

Another important point of investigation could be an analysis of post-operative outcome in such patients after supplementation of Vitamin D and thereby normalizing the level of Vitamin D and subsequently Parathyroid Hormone. However, a much larger multi-centric study is required to reach the final conclusion.

CONCLUSION

Hypovitaminosis D is a major risk factor for hip fractures in elderly patients above the age of sixty years and can be a useful marker for identifying geriatric population at risk for hip fracture.

Increased Parathyroid Hormone level secondary to hypovitaminosis D in order to maintain normal serum calcium homeostasis leading onto further osteopenia and osteoporosis is another useful predictor of hip fracture in elderly.

Higher age group, urban living, inactive lifestyle, risk factors like smoking, alcoholism, drug intake, malnutrition; comorbidities like diabetes mellitus (Type II), deranged liver and renal function are major contributors to hypovitaminosis D and all these factors should be taken into account while correcting the deficiency.

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