ASSOCIATION OF SERUM VITAMIN -D AND CALCIUM LEVELS WITH THE SEVERITY OF HIP FRAGILITY FRACTURES IN THE ELDERLY: A PROSPECTIVE STUDY

By

Dr. ANMOL HUBLIKAR

Dissertation submitted to

BLDE (Deemed to be University) Vijayapura, Karnataka

In partial fulfillment of the requirements for the degree of

MASTER OF SURGERY

In

ORTHOPAEDICS

Under the guidance of

Dr.ASHOK.NAYAK

PROFESSOR

DEPARTMENT OF ORTHOPAEDICS

BLDE (Deemed to be University)

SHRI B.M.PATIL MEDICAL COLLEGE

HOSPITAL & RESEARCH CENTRE, VIJAYAPUR KARNATAKA

"ASSOCIATION OF SERUM VITAMIN-D AND CALCIUM LEVELS WITH THE

SEVERITY OF HIP FRAGILITY FRACTURES IN THE ELDERLY:

A PROSPECTIVE STUDY"

MASTER OF SURGERY

in

ORTHOPAEDICS

CONTENTS

LIST OF ABBREVIATIONS

OPERATIONAL DEFINITIONS

Elderly patient: a patient who is older than 50

Fragility fracture: A fragility fracture may be defined as **a pathological fracture that results from minimal trauma (e.g. a fall from a standing height) or no identifiable trauma at all**. The fracture is both a sign and a symptom of osteoporosis.

Type of hip fracture: Neck of femur fractures, intertrochanteric femur fractures and subtrochanteric femurfractures.

Sub classifications:

- 1. Neck of femur fracture = $[$ Garden Classification type 1, 2, 3, 4 $]$
- 2. Intertrochanteric femur fracture = [Boyd and Griffin Classification type 1 , 2 , 3 , 4]
- 3. Subtrochanteric femur fracture = $[$ Russell-Taylor Classification type 1, 2 $]$

Selected patient characteristics: Age and Gender

LIST OF FIGURES

- Figure 1: Hip fracture per 100000 person years in different continents:
- Figure 2: Hip fracture pattern
- Figure 3: Anatomy of the trochanteric region
- Figure 4 : Classification of Intertrochanteric Femur Fracture
- Figure 5 : Classification of Neck of Femur Fracture
- Figure 6 : Classification of Subtrochanteric Femur Fracture
- Figure 7: Overview of Vitamin D synthesis, intake and activation
- Figure 8: Total serum calcium reference ranges in males and females by age group
- Figure 9: Study flow chart
- Figure 8: Conceptual framework
- Figure 9: Serum vitamin D levels
- Figure 10: Hip fracture patterns

LIST OF TABLES

- Table 1: Gender vs No. of Patients in Percentage
- Table 2: Age vs No. of patients in Percentage
- Table 3: No. of Patients in percentage vs type of hip fracture
- Table 4: No. of Patients in percentage vs type of Intertrochanteric femur fracture
- Table 5: No. of Patients in percentage vs type of Neck of femur fracture
- Table 6: No. of Patients in percentage vs type of Subtrochanteric femur fracture
- Table 7: Serum calcium levels among Hip fractures
- Table 8: Serum phosphorous levels among Hip fractures
- Table 9: Serum Vitamin-D levels among Hip fractures
- Table.10: Association of serum calcium levels with the types of IT fracture
- Table.11: Association of serum phosphorous levels with the types of IT fracture
- Table.12: Association of serum vitamin-D levels with the types of IT fracture
- Table.13: Association of serum calcium levels with the types of NOF fracture
- Table.14: Association of serum phosphorous levels with the types of NOF fracture
- Table.15: Association of serum vitamin-D levels with the types of NOF fracture.
- Table.16: Association of serum calcium levels with the types of ST fracture.
- Table.17: Association of serum phosphorous levels with the types of ST fracture.
- Table.18: Association of serum vitamin-D levels with the types of ST fracture.
- Table 19: Correlation of serum calcium levels with different age groups.
- Table 20: Correlation of serum vit-d levels with different age groups.
- Table 21: Correlation of serum calcium levels with different sex.
- Table 22: Correlation of serum vit-d levels with different sex.
- Table 23: Correlation of serum vit-d levels with diagnosis.
- Table 24: Correlation of serum calcium levels with diagnosis.
- Table 25 : Correlation of serum calcium levels with severity of all Hip fractures
- Table 26 : Correlation of serum Vitamin-D levels with severity of all Hip fractures

LIST OF CHART

- Chart 1: Gender vs No. of Patients in Percentage
- Chart 2: Age vs No. of patients in Percentage
- Chart 3: No. of Patients in percentage vs type of hip fracture
- Chart 4: No. of Patients in percentage vs type of Intertrochanteric femur fracture
- Chart 5: No. of Patients in percentage vs type of Neck of femur fracture
- Chart 6: No. of Patients in percentage vs type of Subtrochanteric femur fracture
- Chart 7: Serum calcium levels among Hip fractures
- Chart 8: Serum phosphorous levels among Hip fractures
- Chart 9: Serum Vitamin-D levels among Hip fractures
- Chart 10: Association of serum calcium levels with the types of IT fracture
- Chart.11: Association of serum phosphorous levels with the types of IT fracture
- Chart.12: Association of serum vitamin-D levels with the types of IT fracture
- Chart.13: Association of serum calcium levels with the types of NOF fracture
- Chart.14: Association of serum phosphorous levels with the types of NOF fracture
- Chart.15: Association of serum vitamin-D levels with the types of NOF fracture.
- Chart.16: Association of serum calcium levels with the types of ST fracture.
- Chart.17: Association of serum phosphorous levels with the types of ST fracture.
- Chart.18: Association of serum vitamin-D levels with the types of ST fracture.
- Chart 19: Correlation of serum calcium levels with different age groups.
- Chart 20: Correlation of serum vit-d levels with different age groups.
- Chart 21: Correlation of serum calcium levels with different sex.
- Chart 22: Correlation of serum vit-d levels with different sex.
- Chart 23: Correlation of serum vit-d levels with diagnosis.
- Chart 24: Correlation of serum calcium levels with diagnosis.
- Chart 25: Comparing serum calcium levels with the types of IT fracture

Chart 26: Comparing serum calcium levels with the types of NOF fracture Chart 27: Comparing serum calcium levels with the types of ST fracture Chart 28: Comparing serum vit-d levels with the types of IT fracture Chart 29: Comparing serum vit-d levels with the types of NOF fracture Chart 30: Comparing serum vit-d levels with the types of ST fracture

ABSTRACT

BACKGROUND

Due to changes in bone mass, architecture, and material properties, older people with fragility fractures have markedly lower bone strength. They result from low energy injuries in elderly people. Hip fragility fractures have been linked to vitamin D insufficiency as a separate risk factor. It is linked to poor muscle function and muscle weakness in the elderly, an increased risk of falling, inadequate post-injury rehabilitation, and a higher chance of refracture in these patients. Understanding the relationships between Vitamin-D, Serum Calcium, and severity of fractures can help in personalizing preventive measures, improving prognosis, planning treatment, and providing differentially targeted interventions , there are no any studies done to see for association of serum calcium and vitamin-D with severity of fragility hip fractures. This study aims to analyze baseline differences between patients with different types of hip fracture and their severity

OBJECTIVE: To study the association of serum vitamin-D and calcium levels with the severity of hip fractures in the elderly patients presenting to BLDE Hospital , Vijayapura .

METHODOLOGY: This was a hospital based descriptive prospective Study carried out among elderly patients (>50yrs) presenting with hip fragility fractures at the B.L.D.E. (deemed to be university) Shri B. M. Patil Medical College, Hospital & research centre, Vijayapura, Karnataka. , Accident and emergency and Orthopedic wards. The study duration was $1st$ January 2021- $1st$ June 2022. Consecutive sampling was done until the desired sample of 120 was achieved. The patient's biodata, date and type of injury was documented. Upon admission, the serum calcium , serum phosphorous and serum Vitamin-D levels were assayed and recorded.

DATA MANAGEMENT: Data was entered, coded and analyzed using Statistical Package for Social Sciences (SPSS)version 23. The serum levels of calcium and 25-hydroxycholecalciferol were the main findings. The distribution of serum levels of 25-hydroxycholecalciferol and calcium was summarized using means with standard deviations and the median with interquartile range (IQR). To determine if serum calcium and vitamin D levels correlate with particular patient features, the Kruskal-Wallis and Mann-Whitney tests were conducted. The connection between serum calcium and vitamin D levels and gender groups, different types of fractures, and the severity of fractures was examined using the Chi square test.

RESULTS:

Out of 120 enrolled patients for the study, 37.5% of patients with hip hip fractures were of age group 60-69 years with a predominance of males (56.7%). More men as compared to women had a deficient vitamin D level . . This study showed that hypovitaminosis D is prevalent among elderly patients with hip fragility fractures. Among the study population, 43.3% had vitamin D deficiency 44.2% had vitamin D insufficiency while only 12.5% had normal serum vitamin D levels. The albumin adjusted calcium levels were normal in 45.8% of the study participants and low in 42.5% of them . The most common type of hip fractures was Intertrochanteric femur fracture at 59.2%, followed by Neck of femur fracture at 29.2% then Sub-trochanteric femur fracture at 11.7%. Among intertrochanteric femur fractures , 25.8% belonged to Boyd and griffin type-4 and 6.7% belonged to type-1 . Among Neck of femur fractures , 16.7% belonged to Gardens type-4 and 2.5% belonged to type-1 . Among Subtrochanteric femur fractures , 8.3% belonged to Russell-taylors type-1 and 3.3% belonged to type-2 . Thus maximum percentage of

patients with different hip fractures presented to us belonged to more severe type of their respective fractures . there was a statistically significant differences observed for the Intertrochanteric femur fracture , Neck of femur fracture and Subtrochanteric femur fracture for the varying levels of serum Calcium and vitamin D. 45.1% of Intertrochanteric femur fracture and 54.3% of Neck of femur fracture patients had Hypocalcemia and 46.5% of Intertrochanteric femur fracture and 57.1% of Neck of femur fracture had Vitamin D deficiency .There was significant association of serum calcium and Vitamin D levels with severity of hip fractures , Among Intertrochanteric femur fractures all type-4 fractures had hypocalcemia (100%) & Vitamin D Insufficiency (100%) , Among Neck of femur fractures almost all type-4 fractures had hypocalcemia (95%) & vitamin D deficiency (100%).

CONCLUSION:

In conclusion, the prevalence of vitamin D deficiency and insuffiency as well as Hypocalcemia was high in this study. Especially when evaluated among different types of hip fractures and their severity. We could conclude that more deficient the serum calcium levels and more deficint / insufficient the serum Vitamin-D levels more sever the type of fractures , There was a statistically significant, though weak, association between serum calcium and vitamin D levels with age and sex.

CHAPTER ONE

INTRODUCTION

Fragility fractures are fractures that develop in the absence of an evident trauma or as a result of mild trauma, such as a fall from standing height or less. Age increases the likelihood of sustaining a fragility fracture. The ability of bone to fracture is referred to as bone fragility. Strength, brittleness, and work to failure are the minimum number of components required by the biomechanical definition (1).

A reduction in bone formation combined with ongoing bone resorption in each basic multicellular unit (BMU) that remodels bone on its endosteal surface, an increase in remodeling rate, and a decrease in periosteal bone formation are the four changes in the cellular machinery responsible for reaching peak bone strength during growth and maintaining it during adulthood that lead to bone fragility (2).

Hip fragility fractures are of great interest worldwide because they are linked to increased morbidity and death. Due to the high cost of post-injury care, they are the most often operated-on fracture type, have the highest postoperative death rate among surgically treated fractures, and are now a significant health resource issue. A third of elderly patients with hip fractures die within the first year after the injury, and many of them are unable to return to their pre-fracture functional state (3).

According to several research, vitamin D deficiency prevalence ranges from 55% to 92% in patients with hip fractures and is reported to be higher in aged individuals in western nations with seasonal fluctuations. The risk of vitamin D deficiency is higher in elderly people due to risk factors include inadequate sun exposure, decreased cutaneous vitamin D production, reduced

food intake, and impaired intestinal function. poor hydroxylation in the liver and kidneys, as well as absorption . A lack of vitamin D is linked to increased muscle weakness and discomfort, which reduces muscle strength, balance, and function. It is also linked to faster bone turnover and an increased risk of falls and hip fractures in older persons. According to some writers, patients with hip fractures who are vitamin D deficient repair their fractures more slowly and have a greater death rate $(4–6)$.

The levels of calcium and vitamin D in patients with hip fragility fractures have not been studied locally. The study's findings will help orthopedic surgeons treat patients who arrive with fragility hip fractures and have varied levels of vitamin D and calcium.

CHAPTER TWO

LITERATURE REVIEW

2.1 Fragility hip fracture epidemiology

Because they are linked to significant healthcare costs, morbidity, and mortality, hip fractures are among the most frequent fractures among the elderly worldwide. For senior Caucasian women over 50, the lifetime risk of hip fractures is around 15%. (7). They are linked to major effects in western nations, including significant survival impairment, a high prevalence of persistent disability, and a higher risk of institutionalization (4,8).

Fragility fractures are fractures that develop in the absence of an evident trauma or as a result of a minor trauma, such as a fall from standing height or less. Each year, 200 million people worldwide are at risk of fragility fractures. Comparing the USA and Scandinavia to Great Britain and central Europe, the prevalence is higher in the USA and Scandinavia (9). The lifetime chance of a hip fragility fracture in an American woman after the age of 50 is 33%, compared to 20% for a male. After age 65, the incidence grows exponentially (10). According to projections, there would be 6.26 million hip fractures worldwide year by 2050, up from 1.66 million in 1990. (11). The likelihood of hip fractures is highest in Sweden and North America, with rates in Southern European nations roughly seven times lower (3). In the US, there are about 330,000 fragility hip fractures per year, and by 2040, that number is expected to rise to 550,000. (10). The majority of these fractures are consequently well documented as osteoporosis-related fragility injuries in Europe, America, and Asia (11).

In a study carried out in Cameroon, Zabezi et al. discovered an incidence of 52.1/100,000 in women and 43.7/100,000 in men over the age of 35. (12). These fractures were more prevalent in men than in women, and they mostly occurred in men before the age of 50 while they were more prevalent in women after the age of 50. After 50 years, fragility fractures linked to falls accounted for 90% of fractures in women and 83.3% in males (12). No evidence of an agerelated rise in the frequencies of hip fractures in women was discovered by Adebajo et al. in their study in Nigeria (13).

In Kenya, there were 243 post-menopausal hip fractures per 100,000 people on average (14). In Kenya, the prevalence of osteopenia is 32% as opposed to 20.5%, and that of osteoporosis is around 24.3% as opposed to 0.9% in premenopausal women (15).

2.2 Causes of hip fragility fractures

Minimal trauma results in hip fragility fractures. Low energy axial trauma with some rotation following falls is known to induce these fractures in the elderly. Falls may be brought on by slick surfaces or uneven terrain, while others may occur as a result of unrelated medical disorders. The persistence of fractures brought on by falls points to skeletal fragility. The exponential rise in hip fracture incidence among the elderly cannot be fully explained by age-related osteoporosis or the rising frequency of falls (16). Low body mass index, environmental risk, a history of fragility fractures, early menopause, a lack of vitamin D, endocrine disorders such diabetes mellitus, excessive alcohol consumption, and immobility are the most prevalent risk factors for fragility fractures (17).

2.3 Type of hip fractures

According to the figure below, there are three subtypes of hip fractures (10,18):

Figure 2: Patterns for hip fractures taken from Parker M. and Johansen A. (2006) in the BMJ

2.3.1 Intertrochanteric fractures

The extra-capsular femoral neck and the area just distal to the lesser trochanter are referred to as the femur's "intertrochanteric area" (18,19). Over 9 out of 10 of these fractures affect individuals older than 65, with nearly 3/4 of them affecting women (19).

The term "pertrochanteric fractures" refers to injuries that happen in the area between the extracapsular basilar neck and the lesser trochanter close to the medullary canal development. Per trochanteric fractures are referred to as intertrochanteric and peritrochanteric fractures respectively. In this proximal metaphyseal region of bone, trauma causes a variety of fractures, including damage to the thin cortical bone and the intersecting cancellous compression and tensile lamellar networks. This results in displacement of the fracture fragments and attached muscle groups.

Boyd and Griffin established the first classification of treatment recommendations in 1949, indicating how challenging it would be to reduce each of the four categories of fractures:

1. Stable (two-part)

2. Stable with posteromedial disintegration

3. Subtrochanteric extension with the fracture's lateral shaft extending distally at or just below the lesser trochanter (Wright refers to this as a "reverse obliquity").

4. Subtrochanteric with intertrochanteric extension with fracture in at least two planes of the fracture

FIGURE 50-1 Boyd and Griffin classification. Type 1, stable (two-part); Type 2, unstable comminuted; Type 3, unstable reverse obliquity; Type 4, intertrochanteric-subtrochanteric with two planes of fracture.

Figure 3 : Classification of Intertrochanteric femur fracture

2.3.2 Neck of femur fractures

For over 50% of all hip fractures, the intra-capsular femoral neck is the site of the fracture (20). They are more prevalent in females and their frequency rises age-wise significantly. Although they are mostly identified from the AP pelvis due to the difficulty getting the lateral radiograph due to pain, these fractures are detected from the AP pelvis and lateral radiography (18,20).

In 1961, the Garden classification was introduced. Four groups of femoral neck fractures are identified (Fig. 49-3). According to the relationship between the trabecular lines in the femoral head and those in the acetabulum, which can be seen on the AP radiograph, the divisions are made based on the degree of displacement.

The trabecular lines in the femoral head of the nonfractured hip are oriented similarly to those in the acetabulum.

A valgus-impacted subcapital fracture is the Garden I fracture. The medial cortex is not breached by the lateral fracture line, indicating an incomplete fracture. As a result, the trabecular lines in the femoral head and acetabulum are at an angle.

The trabecular lines in the head are colinear with those in the acetabulum and the femoral neck distal to the fracture, and the Garden II fracture is complete but undisplaced.

Garden III subcapital fractures are fractures with incomplete displacement. Although the femoral head and neck are still in touch, the head is stretched and varus, which angles the trabecular lines. In contrast to the angulation mentioned for Garden I fractures, this fracture has the opposite angulation.

The femoral head recovers to a neutral position within the acetabulum as the Garden IV fracture is entirely displaced and the trabecular line up. The trabecular lines in the neck are not colinear with those in the head because the femoral neck separates from the head and externally rotates.

Figure 4 : Classification of Neck of femur fracture

2.3.3 Sub-trochanteric fractures.

The proximal femur suffers from these fractures between the lesser trochanter's inferior side and roughly 5 cm below it. They are the result of low energy falls in the elderly osteopenic population. They account for 10–30% of hip fractures and are less common than intertrochanteric and neck of femur fractures (18,21).

The Russell-Taylor categorization system places special emphasis on the proximal segment's involvement of the lesser trochanter and fracture extension into the piriformis fossa.

FIGURE 51-2 The Russell-Taylor classification system, which focuses on two distinctive features of the proximal segment: Fracture extension into the piriformis fossa (I versus II) and involvement of the lesser trochanter (A versus B).

Figure 5 : Classification of Neck of femur fracture

2.3.4 Distribution in fragility fractures

There is evidence that around half of all hip fractures in people with fragility are intertrochanteric fractures (22). Studies from Asia and India have reported this finding (23). In their study of fragility fractures in patients aged 50 and older in Tanzania, Tsabasvi et al. discovered that the majority of fractures were intertrochanteric, accounting for 55.8% ($n = 96$), followed by neck of femur fractures at 28.5% ($n = 49$), sub trochanteric fractures at 9.9% ($n =$ 17), and mixed intertrochanteric and sub trochanteric fractures at 5.8%. (24).

2.4 Diagnosis of hip fractures

AP pelvis radiography and clinical symptoms are used to diagnose hip fractures. To more clearly define the displacement of the fracture, a lateral view radiograph of the hip might be taken. The ideal image of the femoral neck is obtained with the hip internally rotated by 15-20 degrees on an AP radiograph (7)

2.5 Anatomy of the Hip

The per-trochanteric area and the neck of the femur are included in the hip. The majority of the bone in this region is cancellous bone. There are both tension and compression groups of trabecular in the neck area (Figure 2). The trabecular pattern in this area encloses the Wards triangle. In the posteromedial aspect of the junction between the neck and the lesser trochanter, there is a thick bone ridge called the calcar femorale (Figure 3). The ridge of the calcar projects laterally toward the greater trochanter and has a vertical position.

The inside of the femur's neck and trochanteric area has a spongy structure, which is a sign of cancellous (spongy) bone. It is made up of a tangle of interconnected marrow compartments and numerous interconnecting bony trabeculae (25). The three-dimensional orientation of bone trabeculae, which is not random, is related to the size and directionality of hip joint loads (forces acting on the hip joint and transmitted on the head of the femur). The bone's exterior is robustly constructed and serves as an illustration of compact (dense) bone (25).

Figure 6: Illustrating the trochanteric region's anatomy. The arrow in picture A depicts the Adams Arch or the calcar femorale. Stable fractures are those that cause this section to fall apart.

2.6 Bone strength and peak bone mass

Bone mass, shape, and composition, as well as material characteristics and microstructure, all affect bone strength. 50% to 70% of the bone's strength is determined by bone mass. It relies on the size, volume, and mineral density of the bone. Because strength rises by the radius of the affected bone raised to the power of 4, larger bones are often stronger than smaller ones. Bone strength is also influenced by material characteristics such as mineral content and protein content and quality. The amount of bone tissue present at the conclusion of skeletal development is known as peak bone mass (PBM). It plays a significant independent role in determining bone fragility . According to conventional wisdom, a 1 SD increase in PBM reduces the incidence of fracture by 50%. The difference in PBM between males and females is due to variations in the rate of bone growth during puberty (26,27).

From infancy through post-puberty, bone mineral mass formation is a complex process involving genetic, endocrine, mechanical, and dietary components. By the end of the second decade, PBM is reached in the axial skeleton and the proximal femur, and from that point on, a gain in mass and strength is mostly caused by a growth in bone size. The peak bone mass reached by ages 18 to 25 less the quantity of bone that was subsequently lost affects bone mass in older persons (28). Skeletal failure due to normal or non-traumatic conditions is caused by ageing and various skeletal illnesses including osteoporosis and osteogenesis imperfecta that impair bone strength. It has been demonstrated that bone loading affects bone strength and remodelling. Bone tissue is mechanosensitive, and the cells that make up bone react to mechanical stimuli by changing turnover to either produce more or less tissue, which changes both the structure and the characteristics of the material. The integration of the loading history a person has undergone over the course of a lifetime is represented by the bone structure (2).

Bone mass and density, microarchitecture, or the geometrical and spatial distribution and connection of trabeculae, and tissue material qualities lastly determine how bones behave structurally. Any of these elements could change, compromising the strength of the bone structure and its capacity to support loads. This change can be brought on by ageing, sex, and sickness (2).

2.7 Bone modeling and remodeling

Deposition of new bone without previous bone resorption is referred to as bone modelling. On the other hand, bone remodelling is marked by the emergence of focally and transiently discrete zones of resorption followed by bone production in the basic multicellular units (BMUs) (29).

Osteoclastic bone resorption and osteoblastic bone synthesis take place in a highly controlled sequence during the process of bone remodelling. The basic multicellular unit (BMU) in cortical bone and the bone structural unit in trabecular bone are the spatial units where this interaction takes place. Age-related bone loss is caused by an imbalance between these mechanisms(29).

There is ongoing debate concerning the cellular process causing the reduced bone growth. Lower collagen synthesis capacity, a shorter life expectancy, and decreased osteoblast recruitment have all been put out as potential causes by certain authors. Additionally, age-related bone loss is linked to a rise in the amount of bone absorption (30,31). The unbalanced remodelling results in disorganised skeletal architecture, which raises the risk of fracture (28).

A rapid remodelling rate shortens the window of opportunity for secondary mineralization, which makes bones more brittle. The material stiffness of the bone is decreased by replacing the excised bone with fresh, less heavily mineralized bone. By impairing isomerization, maturation, and crosslinking, high bone remodelling itself also changes the composition of collagen (29).

2.8 Factors affecting bone remodeling

Environmental influences, systemic and local factors, as well as both, have an impact on bone remodelling. The hormone levels that influence the activity and propensity for survival of osteoclasts are detected by osteoclasts. Oestrogens and glucocorticoids are a couple of these hormones. Blood capillaries carry systemic hormones to the BMU, and cells release local hormones in an autocrine/paracrine manner. This can affect the balance of cells inside each BMU as well as the activation frequency, which is dictated by the number of BMUs present at any particular time (31).

Additionally, prostaglandins, cytokines, and local growth factors influence or suppress osteoclast development and activity. IL-1, IL-3, IL-6, and IL-11 stimulate osteoclast activity. among others, granulocyte macrophage colony stimulating factor and tumour necrosis factor. On the other side, the growth of osteoclasts is inhibited by IL-4, IL-10, IL-18, and interferon. Different stages of osteoblastogenesis are also modulated by members of the BMP family, Wnt family, hedgehog family, and growth hormones such insulin-like growth factor. Additionally, prostaglandins target both osteoblasts and osteoclasts in the process of bone remodelling and repair (31).

Hormones play a major role in bone remodelling and are the main systemic factors:

Parathyroid hormone : The 84-amino acid peptide known as parathyroid hormone controls the calcium homeostasis in the short term. Its secretion from the parathyroid gland is regulated by the calcium levels outside of cells. It increases the amount of calcium absorbed by the renal tubules and promotes 1,25-dihydroxyvitamin D3 production in the kidneys (31).

1, 25-Dihydroxyvitamin D3: The bone, kidneys, and intestine are its main target tissues. It is secreted in reaction to low calcium levels. It increases bone resorption by promoting osteoclast activity in bone. By promoting calbindin production, it improves calcium absorption in the gut. Then, these proteins bind to calcium and move it against the gradient of its concentration. In the renal calcium reabsorption, a comparable mechanism is also present (31).

Sex steroidsLoss of trabecular bone structure is gradual and correlated with oestrogen decline. Bone formation cannot keep up with the accelerated bone resorption in oestrogen deprivation. Through a longer osteoclast lifespan and a shorter osteoblast lifespan, oestrogen shortage is linked to an increase in the intensity of bone remodelling (29).

Bone remodelling has been demonstrated to be influenced by mechanical elements as well. According to Wolf's law, osteocytes serve as mechanosensors that alert bone to the need for remodelling in response to functional loads. They are believed to be able to detect variations in the interstitial flow rate within the canaliculi system that happen when the bone is loaded functionally. They communicate the need to create a new BMU to the bone surface since they are related to osteoblasts and bone lining cells (31). Bone is negatively impacted by inactivity, sleep, and weightlessness. Trabeculae frequently line up with the highest stresses. As new bone is created, mechanical stress also affects collagen orientation (26).

2.9 Effect of aging on bone fragility

The ability of bone to fracture is a general definition of bone fragility. Strength, brittleness, and work to failure are at least three of the biomechanical components that define bone fragility (1). A decrease in bone mass and density leads to bone fragility. Therefore, abnormalities in collagen, the composition and distribution of minerals, and abnormalities in bone remodelling might cause bone fragility (29).

Bone density, structure, and material qualities are all impacted by ageing. After reaching its peak in both men and women, bone mass declines with age. Men's BMD declines by 13-18% and women's BMD declines by 15-54% by the age of 80. Recent research shows that the mineral to matrix ratio is much higher in femoral heads of hip fracture patients undergoing THR than it is in femoral heads of individuals without fractures, indicating that compositional failures may have occurred before to the fracture (32).

A reduction in bone formation coupled with ongoing bone resorption in each basic multicellular unit (BMU) that remodels bone on its endosteal surface, an increase in remodelling rate, and a decrease in periosteal bone formation can all have an impact on bone fragility. Changes in the cellular machinery responsible for reaching peak bone strength during growth and maintaining it during adulthood can also have this effect (1).

2.10 Pathophysiology of fragility

Bone's capacity to support heavy loads is determined by its stiffness (resistance to deformation) and strength (maximum stress before failure), while its toughness, or ductility, determines its capacity to absorb the energy from impact loads. The amount of minerals in bones affects their strength. A change in the cross-linking profile of collagen, which not only stiffens the organic matrix but also influences the morphology of the mineral component, may potentially contribute to increased

brittleness. Age-related sex-related changes in the distribution's geometry and morphology become more obvious, and it is thought that these variances are a factor in the extremely senior population's higher fracture incidence.

Increases in cortical porosity, non-enzymatic collagen cross-links, and absolute collagen content were linked to age-dependent alterations. Repetitive stress causes cracks to form in the bone, initially at the sub-micron level. Eventually, these fractures become visible, and if the bone remodelling process does not fill them in, they might cause failure. It has been suggested that the initial source of the cracks is either rupture of collagen fibrils, interference with bonding at the mineral organic interface, or some combination of all three. Alterations to the mineral-embedded bone cells' structural integrity may also be to blame. As objects get older, the degree of this microdamage grows exponentially along with the densities and lengths of the micro-cracks. The inability to fix the cracks and their growth with time are probably the main causes of both cortical and trabecular bone's decreased toughness(35).

Fragility is also impacted by aging-related changes in bone shape. Bones change in order to better perform their mechanical roles, which include withstanding powerful forces while being simplified to reduce energy requirements. Long bones' cross-sectional geometry changes during the early stages of life due to a process called cortical drift, which starts with a more uniform outer wall thickness and eventually leads to an ellipsoidal shape. This happens when bone is deposited on the periosteal surface but formation is reduced and resorption is accelerated on the endosteal surface. When endosteal resorption exceeds production, it causes cortical thinning and an increase in bone diameter. Cortical drift picks up speed during pre-pubertal development and slows down after the epiphyseal plate closes. In the elderly, it rises once more, frequently leading to weaker bone that has a wider diameter and significantly thinner cortice(33).

With ageing, bone cells also undergo changes. Within 200 days, apoptosis kills 60–80% of osteoblasts recruited to a resorption pit. Some develop into tiny, dormant bone lining cells on inactive surfaces. The remaining osteoblasts have lengthy, mineralized processes (dendrites) that extend from their bodies and allow signalling and nutrient transport between cells via canaliculi. 90% of the cells in bone are what are known as osteocytes. They serve as mechanoreceptors and have a lifespan of 1 to 50 years. Osteoclasts are multinucleated large cells with haematological origins that remove bone (resorb) in response to signals from osteoblasts and osteocytes.

The longevity of osteoblasts, osteoclasts, and osteocytes is constrained and is influenced by both internal and external influences. The development of an incapacity to react to forces is linked to ageing. As a result, the body becomes more vulnerable to mechanical damage, experiences more apoptosis, changes in intracellular signalling, and has trouble controlling gene expression. With each remodelling cycle, less bone is added as you become older. This is most likely caused by a decrease in osteoblast cell precursors, a decrease in stem cells from which these precursors are derived, or a decrease in osteoblast lifespan. Additionally, it has been observed that osteocytic apoptosis rises with tissue ageing and leads to bone thinning independently of BMD (33). As people age, changes in bone protein also take place. The bone matrix is made up of primarily

type I collagen and 5% non-collagenous proteins. Collagen gives the bone structure flexibility (toughness), which resists impact loads and acts as a template for the directed deposition of mineral crystals. With age, protein synthesis decreases (33).

2.11 Hormonal changes with aging.

Hormones that regulate bone metabolism, such as estrogens, androgens, growth hormones, and vitamin D, as well as other hormones, are known to drop as we age. In postmenopausal women, oestrogen insufficiency is linked to rapid bone loss, with women losing 1/3 to 1/2 of their bone mass within the first 10 years following menopause. With advancing age, both spontaneous and induced growth hormone secretion as well as insulin-like growth factor 1 diminish. Vitamin D deficiency in elderly people is common. Lack of sun exposure, a poor diet, drugs that may interfere with vitamin D metabolism, and underlying medical issues are all blamed for the insufficiency. A lack of vitamin D can cause secondary hyperparathyroidism, which can result in increased bone turnover and bone loss, weak muscles, and discomfort (31).

2.12 Sex and Disease

Women typically experience more fragility fractures than men do. Human cancellous bone's volume fraction and density gradually decrease over time in both sexes (32). Studies on histophometry have indicated that sex has little effect on this decline. Trabeculae in men gradually thin despite preserving the trabeculae network, resulting in decreased bone volume. Contrarily, in women, the loss of trabeculae (which causes an increase in trabeculae separation) is the primary cause of bone volume decline, while the thickness of the remaining trabeculae is maintained $(1,32,34)$.

Osteoporosis and other diseases that disrupt bone metabolism can affect the structural integrity and load-bearing capacity of the bone. Reduced bone density and impaired bone architecture, which lower bone strength and increase the risk of fractures, are symptoms of osteoporosis. A hip, forearm, or spine fracture caused by osteoporosis has been linked to white women's lifetime risk of 40% and white men's lifetime risk of 13% at age 50. (32,34)
2.13 Vitamin D

Early in the 20th century, vitamin D was originally recognised as a vitamin; today, it is understood to be a pro-hormone. A class of fat-soluble seco-sterols is contained in vitamin D, sometimes referred to as calciferol. Vitamin D2 and vitamin D3 are the two main types. While vitamin D3 (cholecalciferol) is produced in the human skin from 7-dehydrocholesterol and is also taken in the diet through the consumption of animal-based foods, vitamin D2 (ergocalciferol) is primarily created by humans and added to foods (35).

There are a few naturally occurring vitamin D dietary sources. These include egg yolk, fatty fish, and fish liver oil. However, some foods are vitamin D-fortified. Some nations, like Canada, require the addition of vitamin D to foods like milk and margarine (36). The active form of vitamin D, calcitriol (1,25 dihydroxyvitamin D3), has a half-life of approximately 15 hours, whereas calcidiol (25 hydroxyvitamin) has a half-life of around 15 days (6,35).

Vitamin D production in the skin is reduced by more than 95% when using sunscreen with a UV protection factor of 30. People with darker skin tones have built-in sun protection and need to be exposed to the sun for at least three to five times as long as those with lighter skin tones need in order to produce the same quantity of vitamin D. (37).

Figure 4: Overview of the production, absorption, and activation of vitamin D

2.14 Mechanism of action of Vitamin D

The VDR, a member of the nuclear receptor superfamily that includes receptors for thyroid hormone, retinoids, and steroid hormones (androgen, progesterone, glucocorticoid, and oestrogen), mediates the effects of 1, 25-VD. 1,25-VD attaches to VDR in the cell membrane or nucleus of different cell types, passively diffuses into target cells, and activates target genes that have one or more vitamin D response elements (VDREs) in their promoters. Target genes include p21, calbindin, 24-hydroxylase, osteocalcin, osteopontin, and osteopontin (6).

The retinoic receptor and the active VDR form heterodimers when the VDR is activated at the nuclear level(RXR).

This results in the "genomic consequences" of vitamin D being activated by the vitamin D response element (VDRE), a group of genes (5,38). This controls the expression of more than 900 genes, which has an impact on numerous bodily signalling cascades (38).

2.15 Effects of vitamin D in muscles

The VDR is expressed in muscles as well, and the effects of vitamin D on muscles are mediated by two different receptors: nuclear receptors that mediate so-called genomic effects and nonnuclear receptors that mediate non-genomic actions.

The genomic effects of VDR include an increase in calcium handling through enhanced calcium binding protein (calbindin-D9K) activities in cell sarcoplasm, muscle cell differentiation and proliferation through impacts on insulin growth factor production, and skeletal muscle hypertrophy as a result.

It is unclear how non-genomic activities work. MAP kinase (MAPK) and phospholipase C (PLC) pathways are activated by 1,25 vitamin D, and they in turn provide a transduction signal that causes a rapid influx of calcium into the cell (5).

The connection between vitamin D levels and muscle strength and function has been studied by numerous writers. With the exception of very old people, the majority of observational studies show a substantial correlation between hypovitaminosis D and muscular dysfunction across all age groups. On the other hand, muscular dysfunction is least likely when vitamin D levels are larger than 50 nmol/L. (5).

Fast twitch muscles, which are the first to react after a fall, have vitamin D receptors as well. Seniors who have low vitamin D concentrations experience more falls (37).

Muscle weakness that is frequently accompanied by a slower reflex response raises the risk of falling. Low muscle strength has been demonstrated to have a long-term detrimental effect on bone density, which raises the risk of fragility fracture. It has been demonstrated that a lack of muscle mass and strength can affect the development of hip fractures after a fall because there is insufficient shock absorption (3,39).

2.16 Vitamin D Deficiency and Hip Fracture risk

Increased bone turnover and a higher risk of falls and hip fractures in older persons are linked to vitamin D insufficiency, which is related with increased muscular weakness and pain. These effects also result in a reduction in muscle strength, balance, and function (4,8). Due to risk factors such inadequate sun exposure, decreased cutaneous vitamin D production, decreased food intake, poor intestinal absorption, and impaired hydroxylation in the liver and kidneys, elderly persons are more likely to experience vitamin D deficiency (4,40).

According to studies conducted in the west, elderly people frequently suffer from vitamin D deficiency, especially in the springtime when cutaneous production is at its lowest. In their investigation, Cauley et al. discovered that the adjusted odds ratio for a hip fracture was 1.3 times higher for every 10ng/ml drop in serum 25 vitamin D. Similar studies that measured BMD showed that the risk of fracture in vitamin D insufficiency was unrelated to bone density (4,41). In a Singaporean research of 412 patients with acute hip fractures, vitamin D deficiency was discovered in 57.5% of the patients, insufficiency in 34%, and sufficiency in 8%. (41). According to Todd et al., post-menopausal women with vitamin D insufficiency had a high mortality rate (42).

In a case-control research in the Chinese population, Fu et al. in 2015 found a link between postmenopausal women's hip fractures and low serum levels of 25-hydroxycholecalciferol (43). Additionally, persons with acute hip fractures in the Japanese community have been shown to have overall hypovitaminosis D.

In a study conducted by Larrosa M et al. (2012), they concluded that although serum vitamin D levels are not different between patients with intracapsular and extracapsular hip fractures, the more the severity of vitamin D deficiency, the more seems to be the association with the severe osteoporotic fractures of the hip. A prior vitamin D supplementation could avoid a higher severity of these fractures. (79)

In a study conducted by Hwang et al. (2020), they concluded that Low vitamin D and calcium levels are associated with an unstable intertrochanteric fracture in elderly patients. Maintaining adequate vitamin D and calcium levels could avoid an increase in the severity of intertrochanteric fractures. (80)

In a study conducted by Maheshwar Lakkireddy et al. (2019), they concluded that: There was a significant association between hypovitaminosis D, osteoporosis, and fracture site comminution. The fracture site comminution and high prevalence of hypovitaminosis D in patients presenting with hip fractures implicate the necessity for an effective supplementation and proper evaluation of vitamin D in older patients along with anti-osteoporotic regimens for the appropriate management and effective prevention of osteoporotic hip fractures.(81)

In a study conducted by Peng-Fei Li et al. (2016), they concluded that The capability of restoration and reservation of serum calcium in patients who are diagnosed with femoral neck fracture is better than that in patients with femoral intertrochanteric fracture. A low serum calcium level may be susceptible to femoral intertrochanteric fracture . (82)

According to earlier research, vitamin D insufficiency is prevalent in patients with fragility fractures at a rate of between 55% and 91.6%. (8,11,41,44,45).

In osteoporosis, the fracture risk at varying vitamin D levels has previously been studied. However, there has been debate among writers over the ideal serum 25(OH)D levels linked to a higher risk of fracture.

Melhus et al. discovered in 2010 that a blood 25(OH)D level below 40nmol/l implied a higher fracture risk. According to a 2008 study by Cauley et al, the lowest risk of fracture was associated with 25(OH) D levels between 60 and 70 nmol/l. In 2008, Van Schoolar discovered that the highest risk of fracture was associated with serum 25 (OH) D levels less than or equal to 30 nmol/l $(4,46,47)$.

Previous research of a similar nature has revealed regional, seasonal, and gender differences in calcium and vitamin D levels among older patients with hip fractures. Hypovitaminosis D was found in 50% of older patients with hip fractures in the US, compared to 34% in India and just 21.6% in Italy (11,43). Independent of the number of falls, physical function, frailty, and sex steroid hormone levels, patients with lower vitamin D levels have been shown to have a higher risk of hip fracture (4). A range of writers have shown that levels below 50 nmol/l of serum vitamin D are predictive of fracture development while levels over 75 nmol/l are sufficient to maintain bone metabolism. However, there is still disagreement over the usefulness of vitamin D in predicting the development of fractures (43). The effectiveness of vitamin D and calcium supplements in reducing hip fractures has been examined in other research. According to research by Lips et al, taking 800 IU of vitamin D daily decreased the incidence of hip fracture by 26% to 29%. (40,48). Daily doses of less than 400 IU were discovered to have no beneficial effects on lowering the risk of fracture (37).

If dietary consumption and solar exposure are insufficient, the current recommended for vitamin D supplementation in persons with osteoporosis or significant risk of developing the condition is 800 to 1200 IU of vitamin D3 (10). Age, comorbid illnesses, nutritional state, and ambulation status among the elderly are all known to differ. Muscle weakness is now understood to result from vitamin D insufficiency. According to studies, patients with vitamin D insufficiency can considerably benefit from vitamin D treatment in terms of performance speed and muscle strength (40,48).

There are publications, though, that do not link hypovitaminosis D to hip fractures (49,50).

2.17 Assessment of Vitamin D levels

The measurement of plasma 25-hydroxyvitamin D concentration is the most accurate method of determining vitamin D status. Because the half-life of 25(OH) D is approximately 3 weeks, quantitation of serum 25(OH) D offers a therapeutically meaningful evaluation of a person's vitamin D status.

This acts as a far more accurate indication for vitamin D received over extended periods of time from food sources and UV irradiation (51–53). Second, the liver's ability to produce 25(OH) D is only weakly controlled and mostly reliant on the amount of substrate present. Therefore, serum 25(OH)D measurement offers the most accurate assessment of the patient's vitamin D status $(51, 54, 55)$.

Depending on the manufacturer, different techniques are used to measure vitamin D levels. The methods for evaluating vitamin D have increased recently, however depending on the machine and type of analysis, this has been accompanied by a significant level of inter- and intra-user variability. Liquid chromatography isotope dilution tandem mass spectrometry (LC-IDMS/MS) is the industry standard (54,56–58). The amount of total vitamin D and its various metabolites can be detected using a variety of immunoassays.

Because they rely on antibodies that may differ in their detection of both the vitamin D2 and D3 metabolites, these immunoassays are more unpredictable than the LC-MS/MS. Through a twostep process, DiaSorin LIASON's CLIA technique evaluates total 25-hydroxyvitamin D and other metabolites in human serum. After being released from its binding protein, 25(OH)D2 first binds to the particular solid phase antibody. The chemiluminiscent process is then started by the addition of a vitamin D isoluminal tracer. A photomultiplier then detects the light signal, and this value is inversely proportional to the amount of 25-hydroxyvitamin D present (58,59).

2.17.1 Suggested vitamin D levels

A 25(OH)D level below 20 ng/ml (50 nmol/l) is considered to be a vitamin D insufficiency. A 25(OH)D level below 21 ng/ml (52.5-72.5 nmol/l) is considered insufficient, whereas a level above 30 ng/ml (75 nmol/l) is considered sufficient (35,40,54).

2.18 Calcium in hip fractures

Based on its crucial structural role in bone and metabolic equilibrium, calcium is protective of the bones (60,61). In the form of calcium hydroxyapatite, bones and teeth contain 99% of the calcium in the body. The remaining one percent is found in the extracellular fluid, where fifty percent of it is free, forty percent is tightly bound to proteins (eighty percent to albumin and twenty percent to globulins), and ten percent is present as diffusible inorganic and organic anions, such as bicarbonates and citrates (62). Calcium is mostly obtained from diet and supplements. Dairy products including milk, cheese, and yoghurt are the main dietary sources. Fortified foods and medical supplements are both types of supplements (63). Both parathyroid hormone and vitamin D control its metabolism. Through the intestinal mucosa, calcium is absorbed both actively (transcellularly) and passively (paracellularly). Calcitriol and the intestinal vitamin D receptor work together to facilitate the active transport of calcium (VDR). At low and moderate consumption levels, the majority of the absorption of calcium is accounted for by this transcellular pathway, which is stimulated by calcitriol. In the duodenum, where the VDR is expressed most abundantly, transcellular transport predominates.

After age 40, it has been observed that fractional calcium absorption decreases on average by 0.21 percent annually due to ageing and menopause. Age-related declines in absorption have also been documented by other writers (62,64).

The foundation of the calcium homeostatic mechanism in animals is the vitamin D metabolic pathway. The range of the serum's total calcium concentration, which must stay between 8.5 and 10.5 mg/dL (2.12 and 2.62 mmol/L), is strictly controlled.

The release of PTH is signalled by a little deviation in this level by the parathyroid gland's calcium detecting receptor. Then, PTH works to raise calcium levels by causing the kidneys to secrete more 1, 25 vitamin D, which increases absorption in the intestines and reabsorption in the kidneys (64,65).

2.18.1 Reference ranges for serum calcium

High physiologic variation in the serum calcium levels (both free and total), which varies with age, sex, physiologic state, and even season. As a result, distinct reference ranges based on both sex and age have been established, as shown below:

Figure 5: Male and female age-specific reference ranges for total serum calcium.

Pseudo-hypocalcemia is frequently brought on by hypoalbuminemia. In order to adjust calcium levels for albumin levels, the following equations (60, 62, and 66) are used:

Normal range for the corrected total calcium concentration is 8.5 to 10.2 mg/dl.

Between 8.5 and 10.5 mg/dl (4.3–5.3 mEq/L or 2.2–2.7 mmol/L), calcium is kept within a relatively small range. There may be up to a 0.5 mg/dl difference in normal readings and reference ranges between laboratories (62).

Low calcium levels have been linked to osteoporosis, which has led to the recommendation of calcium supplementation as a way to prevent fragility fractures (67,68). There is debate regarding whether calcium supplementation can stop fragility fractures, though. Long-term calcium supplementation prevents fractures, according to some studies (69,70). While previous research hasn't shown that taking calcium supplements reduces the incidence of hip fracture significantly (71) .

However, low serum calcium concentrations have been linked to low bone mineral density and a higher risk of trochanteric fractures (61,72). Li et alstudy .'s concentrated on people in vegetative states who had low BMD and discovered that these people also had low serum calcium levels (72). None of the studies examined the calcium levels of a healthy patient population who had trochanteric fractures. Therefore, it would be interesting to measure and study the serum calcium levels in otherwise healthy patients soon following hip fractures.

2.19 Conclusion of literature review

The most typical osteoporotic fracture is a fragility hip fracture. They are linked to high rates of morbidity and mortality as well as extremely high treatment costs. Patients with fragility hip fractures are known to have high vitamin D insufficiency levels, and low vitamin D has been linked to an increased risk of developing these fractures. Secondary osteoporosis has been linked to low calcium levels in research studies. If dietary consumption and sun exposure are insufficient, it is currently advised that those with osteoporosis or a significant risk of developing the condition take calcium and vitamin D supplements.

2.20 Justification

Globally, people are living longer, and there are more old people. The strength of a person's bones and muscles affects their chance of suffering a fragility fracture. This risk is influenced by a variety of physiological, mechanical, and pathological conditions. In addition to calcium playing a crucial structural function in bone and metabolic balance, serum vitamin D and PTH are important regulators of bone remodelling.

Due to decreased sun exposure, low cutaneous production, lower dietary intake, impaired intestinal absorption, and hydroxylation in the liver and kidneys, elderly persons are more likely to have vitamin D and calcium deficiencies. Observational studies have shown a strong correlation between muscular dysfunction and hypovitaminosis D in people of all ages. Muscle dysfunction is least likely to occur in people with adequate serum vitamin D levels (>50 mmol/l). High dose vitamin D and calcium supplementation in elderly adults improves bone density while also improving balance and decreasing the risk of falls.

Previous research has revealed regional, seasonal, and gender differences in calcium and vitamin D levels in older patients with hip fractures. There hasn't been any research on the relationship between vitamin D and calcium levels in people with hip fragility fractures and the severity of those fractures. Therefore, the goal of this study was to fill in the knowledge gap about calcium and vitamin D level patterns in our environment. The information will be helpful in managing older individuals who have or are at risk for hip fragility fractures.

2.21 Problem statement

Age-related deficiencies in calcium and vitamin D are widespread. The sustenance of fragility fractures has also been linked to vitamin D insufficiency as a separate risk factor. Patients with hip fragility fractures have not been investigated locally for calcium and vitamin D levels. Therefore, the purpose of this study was to measure the serum calcium and vitamin D levels in elderly patients who were presenting at BLDE Hospital in Vijayapura with fragility hip fractures and to correlate these levels with the patients' chosen characteristics, such as the type of hip fracture, the severity of the fracture, age, and gender.

2.22 Research question

What are the levels of serum calcium and vitamin D level among elderly patients with hip fragility fractures and does it vary with severity of hip fractures presenting to BLDE Hospital ,

Vijayapura?

2.23 Objectives

2.23.1 Broad objective

the severity of hip fragility fractures in patients admitted to Shri B M Patil Medical college and Hospital (BLDE Hospital), Vijayapura, and the relationship between serum calcium, phosphorus, and vitamin D levels.

2.23.2 Specific objectives

- 1. To determine the serum calcium, serum phosphorous and vitamin D levels among elderly patients with hip fragility fractures at BLDE.
- 2. To describe the type of hip fractures and further subclassify them based on their severity
- 3. To correlate the serum calcium, serum phosphorous and vitamin D levels among elderly patients with severity of hip fractures, subclassified fracture severity, age and gender

CHAPTER 3:

METHODOLOGY

1.1 Study design

This was a hospital based prospective study.

3.1 Study site

Patients admitted in Department of Orthopedics in B.L.D.E. (DEEMED TO BE UNIVERSITY) Shri B.M.Patil Medical College, Hospital and Research Centre, Vijayapura with the diagnosis of Hip fracture and age 50 years and older

3.2 Study period

This study was conducted between the month of $1st$ January 2021- $1st$ June 2022.

3.3 Study population

The participants comprised of elderly (50 and more years) patients with hip fragility fractures admitted in Department of Orthopedics in B.L.D.E. (DEEMED TO BE UNIVERSITY) Shri B.M.Patil Medical College, Hospital and Research Centre, Vijayapura.

3.3.2 Case definition for hip fracture

Hip fractures that occur as a result of little trauma, such as a fall from standing height or less, or in the lack of a visible trauma were referred to as hip fragility fractures.

Femoral neck fractures, intertrochanteric femur fractures, and subtrochanteric femur fractures were all categorized as hip fracture types..

3.3.3 Inclusion criteria

- Patients aged ≥ 50 years with a hip fracture and seen at BLDE within the study period.
- Patients who give written informed consent.
- **Intertrochanteric fracture of femur**
- Subtrochanteric fracture of femur
- Neck of femur fracture

3.3.4 Exclusion Criteria

- Patients aged less than 50 years with a hip fracture
- A hip fracture due to metastatic bone disease.
- \blacksquare Hip fractures resulting from high energy.
- Patients with metabolic disorders
- Patients currently taking anti-osteoporotic drugs
- Patients are currently taking Vit-D and/or Calcium.

3.4 Sample size calculation

With anticipated Proportion of Deficiency of vitamin D level among with severity of Hip fractures in the elderly patients $58\%^{(2)}$, the study would require a sample size of 65 patients with 95% level of confidence and 12% absolute precision.

Formula used

 $n=$ $z^2 p^*q$ **d 2** Where $Z = Z$ statistic at α level of significance

> d^2 = Absolute error P = Proportion rate $q= 100-p$

3.5 Sampling method and recruitment

Patients were enrolled in the trial using the consecutive sampling approach up until the target sample size was reached. In order to identify all eligible patients seen or admitted on each day, the lead investigator and one research assistant went through the daily admission/patient register at the A&E and orthopaedic wards. In order to identify patients with hip fragility fractures, the patient's file and radiographs were retrieved. Patients who met the inclusion criteria were informed about the study's nature and objectives, and those who agreed to participate were asked for written informed consent. Ineligible patients were those who refused to consent.

3.6 Data collection procedure

Study flow chart

Patient admission register Review of patients' files and radiographs t **Exclude patients with any of the exclusion criteriaStudy purpose explained to eligible participants Informed consent obtained Socio-demographic data obtained and recordedBlood samples drawn for analysis**

Figure 6: Study flow chart.

3.7.1 Clinical methods

The subject was asked for consent to access clinical data from their records, and the principal investigator (PI) then determined that the individual had a hip fragility fracture based on the mechanism of injury. The primary investigator and an orthopaedics consultant identified the type of hip fracture on the radiograph and recorded their findings in a study proforma. On the study proforma, information on the mechanism of injury as well as participant demographics like age, sex, marital status, history of smoking, and alcohol consumption were also noted.

To maintain secrecy, each study proforma was given a special study serial number; no participant identifiers were used. Only the appropriate staff members had access to the securely kept data. Password-protected access systems were used to protect all databases.

3.7.2 Laboratory methods

Using the aseptic method Following the insertion of a tourniquet to the arm, each study participant had 5 millilitres of blood collected from the ante-cubital fossa. The blood was drawn into a standard vacutainer with a red cap and used to measure the levels of phosphorous, vitamin D, and calcium in the serum. To protect patient confidentiality and privacy, the samples were marked with particular serial numbers that were allocated to each patient. After that, they were taken to the BLDE lab for processing. The LIAISON® 25-OH Vitamin D assay method was used to measure the levels of vitamin D in the serum. This is a quick, accurate, and precise automated chemiluminescent immunoassay (CLIA) technique.

In accordance with NCCLS (National Committee for Clinical Laboratory Standards) guidelines, this technique has a strong level of validation (74). The automated biochemistry analyzer COBAS INTEGRA 400/800 was used to assess the levels of calcium and albumin. When this wasn't possible, the samples were kept in the refrigerator or held on ice for up to 48 hours. All samples were evaluated within 30 minutes of collection (62,67). All used samples were disposed of in accordance with the Lancet's standard operating procedures for the disposal of biological waste.

3.7.3 Definition of variables

– Serum Vitamin D levels

- Gender male or female
- Age in years

–

- Type of hip fractures: Hip fractures were subdivided into; Neck of femur fractures, intertrochanteric fractures and sub-trochanteric fractures.
	- = Each fractures were further subclassified
- Neck of femur fracture = $[$ Garden Classification type 1, 2, 3, 4 $]$
- Intertrochanteric femur fracture $=$ [Boyd and Griffin Classification type 1, 2, 3, 4]
- Subtrochanteric femur fracture = $[$ Russell-Taylor Classification type 1, 2 $]$

3.7.4 Conceptual Framework

Due to the related decline in bone density and resulting increase in muscular weakness, which increases the risk of falling, low serum levels of vitamin D and calcium are linked to an increased risk of hip fragility fractures. Due to a number of variables, including decreased cutaneous synthesis, decreased exposure to sunshine, decreased intestinal absorption, and impaired kidney and liver metabolism, vitamin D insufficiency is more prevalent in the elderly. The patients' features, such as age and gender, are other noteworthy causes of hip fractures that are supported by the literature.

Figure 7: Conceptual Framework

3.7.5 Quality control

To reduce pre-analytical mistakes, the Standard Operating Procedures for specimen collection, labelling, storage, and transport were rigorously followed. The analysis equipment was correctly calibrated using industry-accepted calibration techniques and supplies, and the tests were compared to controls. Both internal and external quality control were performed at the Lancet laboratory.

3.8 Data management and analysis

A password-protected computer's Microsoft Excel 2021 was used to enter data. Version 23 of the Statistical Package for Social Sciences was used for data cleaning, coding, and analysis. To find and fix discrepancies (missing data or excessive values) in the data, data cleaning was conducted. The data and variables were compiled using a univariate analysis. The serum levels of calcium and 25-hydroxycholecalciferol were the main findings. The distribution of serum levels of 25 hydroxycholecalciferol and calcium was summarised using means with standard deviations and the median with interquartile range (IQR). To determine if serum calcium and vitamin D levels correlate with particular patient features, the Kruskal-Wallis and Mann-Whitney tests were conducted. The connection between serum calcium and vitamin D levels and gender groups, different types of fractures, and the severity of fractures was examined using the Chi square test. At a significance level of 0.05, the study was conducted.

3.9 Ethical considerations

The Department of Orthopedics and the BLDE Scientific and Ethical Review Committee approved the study before it was started. Eligible participants were given a thorough explanation of the study's goals in a language they could understand. After signing the consent form, only patients who provided informed consent were enrolled in the trial. The patients were given the assurance that participation in the study was voluntary and that if they chose not to participate, they would still get medical care.

At any time, patients had the option to leave the study without penalty. By keeping the study proformas in a safe place and removing the patients' identities from the electronic data sheets, confidentiality was preserved. Only the blood needed for the study was drawn, and when it was examined, it was discarded. To help with patient care, a copy of the laboratory findings was distributed to the healthcare professionals and put in the patient's file.

CHAPTER 4

RESULTS

Patient characteristics

A total of 120 patients were enrolled into the study after meeting the inclusion criteria.

- The study participants were mostly male (56.7%) [table 1]

Gender	No. of patients	Percentage
Female	52	43.3
Male	68	56.7
Total	120	100.0

Table 1: Gender vs No. of Patients in Percentage

Chart 1: Gender vs No. of Patients in Percentage

- 37.5% of patients with hip fractures were of age group 60-69 years
- 2.5% of patients with hip fractures were of age group 90+ years

Age(Years)	No. of patients	Percentage
< 60	22	18.3
$60 - 69$	45	37.5
$70 - 79$	30	25.0
$80 - 89$	20	16.7
$90+$	3	2.5
Total	120	100.0

Table 2: Age vs No. of patients in Percentage

Chart 2: Age vs No. of patients in Percentage

59.2% of patients had Intertrochanteric femur fracture , 29.2% had Neck of femur fracture and

11.7% had Subtrochanteric femur fracture

Types of Fractures	Frequency	Percentage
Intertrochanteric femur fracture	71	59.2
Neck of femur fracture	35	29.2
Subtrochanteric femur fracture	14	11.7
Total	120	100

Table 3: No. of Patients in percentage vs type of hip fracture

Intertrochanteric femur fractures were further classified according to fragmentation and displacement of the fracture [**Boyd and Griffin Classification]**

- 25.8% of patients belonged to type-4, 6.7% to type-1

Intertrochanteric femur fracture	Frequency	Percent
Boyd and griffin type-1	8	6.7
Boyd and griffin type-2	14	11.7
Boyd and griffin type-3	18	15
Boyd and griffin type-4	31	25.8

Table 4: No. of Patients in percentage vs type of Intertrochanteric femur fracture

Chart 4: No. of Patients in percentage vs type of Intertrochanteric femur fracture

Neck of femur fractures according to the degree of displacement of the femoral head in relation to

the femoral neck [**Garden classification**]

- 16.7% of patients belonged to type-4, 2.5% to type-1

Chart 5: No. of Patients in percentage vs type of Neck of femur fracture

Subtrochanteric femur fractures will be classified based on the presence or absence of fracture involvement of the lesser trochanter (medial calcar) and the greater trochanter (piriformis fossa)

[**Russell and Taylor classification**]

- 8.3% of patients belonged to type-1, 3.3% to type-2

Serum calcium levels among the hip fractures were evaluated , Mean calcium levels in Intertrochanteric femur fractures was 8.83 mg\dl (n=71) with standard deviation of 0.956 ,Neck of femur fractures was 8.71 mg/dl with standard deviation of 0.926 (n=35) , Subtrochanteric femur fractures was 10.14 mg/dl (n=14) with standard deviation of 0.949.

Table 7: Serum calcium levels among Hip fractures

Chart 7: Serum calcium levels among Hip fractures

Serum phosphorous levels among the hip fractures were evaluated , Mean phosphorous levels in Intertrochanteric femur fractures was 3.11 mg\dl (n=71) with standard deviation of 0.5578, Neck of femur fractures was 3.00 mg/dl (n=35) with standard deviation of 0.5247 , Subtrochanteric femur fractures was 3.886 mg/dl (n=14) with standard deviation of 0.5895.

Table 8: Serum phosphorous levels among Hip fractures

Chart 8: Serum phosphorous levels among Hip fractures

Serum Vitamin-D levels among the hip fractures were evaluated , Mean Vit-D levels in Intertrochanteric femur fractures was 21.85 ng\dl (n=71) with standard deviation of 4.662, Neck of femur fractures was 21.03 ng/dl (n=35) with standard deviation of 4.402 , Subtrochanteric femur fractures was 28.00 ng/dl (n=14) with standard deviation of 3.595 .

Table 9: Serum Vitamin-D levels among Hip fractures

Chart 9: Serum Vitamin-D levels among Hip fractures
Serum calcium level evaluated with the types of IT fractures based on Boyd and griffin classification , where type-1 had mean serum calcium of 10.38(n=8) with S.D of 0.518, type-2 had mean serum calcium of 9.86(n=14) with S.D of 0.535, type-3 had mean serum calcium of 8.78(n=18) with S.D of 0.428, type-4 had mean serum calcium of $8.00(n=31)$ with the S.D of 0.000. The Kruskal-Wallis test was 59.697 and p-value was 0.001. Serum calcium levels associated with the types of IT fracture were found to be statistically significant.

BOYD AND	NUMBER	SERUM CALCIUM		Kruskal-Wallis Test	\mathbf{P}
GRIFFIN'S	OF	(mg/dl)			VALUE
CLASSIFICATION	PATIENTS	Mean	Std.		
OF IT FRACTURE			Deviation		
OF HIP					
TYPE-I	8	10.38	.518	59.697	0.001
TYPE-II	14	9.86	.535		
TYPE-III	18	8.78	.428		
TYPE-IV	31	8.00	.000		
Statistically significant					

Table.10: Association of serum calcium levels with the types of IT fracture

Chart 10: Association of serum calcium levels with the types of IT fracture

Serum phosphorous level evaluated with the types of IT fractures were evaluated based on Boyd and griffin classification where type-1 had mean serum phosphorous of 4.00(n=8) with S.D of 0.000, type-2 had mean serum phosphorous of $3.71(n=14)$ with S.D of 0.469, type-3 had mean serum phosphorous of 3.06(n=18) with S.D of 0.236, type-4 had mean serum phosphorous of 2.81(n=31) with the S.D of 0.402. The Kruskal-Wallis test was 45.856 and p-value was 0.001. Serum phosphorous levels associated with the types of IT fracture were found to be statistically significant.

BOYD AND	NUMBER	SERUM PHOSPHOROUS		Kruskal-Wallis Test	\mathbf{P}
GRIFFIN'S	OF	(mg/dl)			VALUE
CLASSIFICATION	PATIENTS	Std. Mean			
OF IT FRACTURE		Deviation			
OF HIP					
TYPE-I	8	4.00	.000		
TYPE-II	14	3.71	.469		0.001
TYPE-III	18	3.06	.236	45.856	
TYPE-IV	31	2.81	.402		

Table.11: Association of serum phosphorous levels with the types of IT fracture

Serum vitamin-D level evaluated with the types of IT fractures were evaluated based on Boyd and griffin classification where type-1 had mean serum vitamin-D of 30.50(n=8) with S.D of 1.309, type-2 had mean serum vitamin-D of 25.29(n=14) with S.D of 3.099, type-3 had mean serum vitamin-D of $22.17(n=18)$ with S.D of 1.295, type-4 had mean serum vitamin-D of $17.87(n=31)$ with the S.D of 1.821. The Kruskal-Wallis test was 55.854 and p-value was 0.001. Serum vitamin-D levels associated with the types of IT fracture were found to be statistically significant.

BOYD AND	NUMBER	SERUM VITAMIN-D		Kruskal-Wallis Test	\mathbf{P}
GRIFFIN'S	OF	TOTAL(ng/dl)			VALUE
CLASSIFICATION	PATIENTS	Mean Std.			
OF IT FRACTURE			Deviation		
OF HIP					
TYPE-I	8	30.50	1.309		
TYPE-II	14	25.29	3.099		0.001
TYPE-III	18	22.17	1.295	55.854	
TYPE-IV	31	17.87	1.821		

Table.12: Association of serum vitamin-D levels with the types of IT fracture

Chart.12: Association of serum vitamin-D levels with the types of IT fracture

Serum calcium level evaluated with the types of NOF fractures were evaluated based on garden's classification where type-1 had mean serum calcium of $10.67(n=3)$ with S.D of 0.577, type-2 had mean serum calcium of 10.00(n=4) with S.D of 0.000, type-3 had mean serum calcium of 9.00(n=8) with S.D of 0.000, type-4 had mean serum calcium of 8.05(n=20) with the S.D of 0.224. The Kruskal-Wallis test was 31.744 and p-value was 0.001. Serum calcium levels associated with the types of NOF fracture were found to be statistically significant.

GARDENS	NUMBER	SERUM CALCIUM (mg/dl)		Kruskal-Wallis Test	\mathbf{P}
CLASSIFICATION	OF	Mean	Std.		VALUE
OF NOF	PATIENTS	Deviation			
FRACTURE					
TYPE-I	3	10.67	.577		
TYPE-II	4	10.00	.000		0.001
TYPE-III	8	9.00	.000	31.744	
TYPE-IV	20	8.05	.224		

Table.13: Association of serum calcium levels with the types of NOF fracture

Chart.13: Association of serum calcium levels with the types of NOF fracture

Serum phosphorous level evaluated with the types of NOF fractures were evaluated based on Garden's classification where type-1 had mean serum phosphorous of 4.00(n=3) with S.D of 0.000, type-2 had mean serum phosphorous of $3.75(n=4)$ with S.D of 0.500, type-3 had mean serum phosphorous of 3.00(n=8) with S.D of 0.000, type-4 had mean serum phosphorous of 2.85(n=20) with the S.D of 0.489. The Kruskal-Wallis test was 18.012 and p-value was 0.001. Serum phosphorous levels associated with the types of NOF fracture were found to be statistically significant.

GARDENS	NUMBER	SERUM PHOSPHOROUS		Kruskal-Wallis Test	\mathbf{P}
CLASSIFICATION	OF	(mg/dl)			VALUE
OF NOF	PATIENTS	Std. Mean			
FRACTURE			Deviation		
TYPE-I	3	4.00	.000		
TYPE-II	$\overline{4}$	3.75	.500		0.001
TYPE-III	8	3.00	.000	18.012	
TYPE-IV	20	2.85	.489		

Table.14: Association of serum phosphorous levels with the types of NOF fracture

Chart.14: Association of serum phosphorous levels with the types of NOF fracture

Serum vitamin-D level evaluated with the types of NOF fractures were evaluated based on garden's classification where type-1 had mean serum vitamin-D of 30.00(n=3) with S.D of 0.000, type-2 had mean serum vitamin-D of 26.25(n=4) with S.D of 1.500, type-3 had mean serum vitamin-D of 23.00(n=8) with S.D of 0.756, type-4 had mean serum vitamin-D of 17.85(n=20) with the S.D of 1.821. The Kruskal-Wallis test was 27.431 and p-value was 0.001. Serum vitamin-D levels associated with the types of NOF fracture were found to be statistically significant.

GARDENS	NUMBER	SERUM VITAMIN-D		Kruskal-Wallis Test	P
CLASSIFICATION	OF	(Ng/dl)			VALUE
OF NOF	PATIENTS	Std. Mean			
FRACTURE			Deviation		
TYPE-I	3	30.00	.000		
TYPE-II	4	26.25	1.500		0.001
TYPE-III	8	23.00	.756	27.431	
TYPE-IV	20	17.85	1.843		

Table.15: Association of serum vitamin-D levels with the types of NOF fracture.

Chart.15: Association of serum vitamin-D levels with the types of NOF fracture.

Serum calcium level evaluated with the types of ST fractures were evaluated based on Russell and Taylor's classification where type-1 had mean serum calcium of 10.60(n=10) with S.D of 0.516, type-2 had mean serum calcium of 9.00(n=4) with S.D of 0.0.816.The Mann-Whitney test was 2.000 and p-value was 0.001. Serum calcium levels associated with the types of ST fracture were found to be statistically significant.

RUSSELL AND	NUMBER	SERUM CALCIUM (mg/dl)		Mann-Whitney Test	P
TAYLOR	OF	Mean	Std.		VALU
CLASSIFICATIO	PATIENT	Deviatio			E
N OF	S		n		
SUBTROCHANT					
ERIC FRACTURE					
TYPE-I	10	10.60	.516		
TYPE-II	$\overline{4}$	9.00	.816	2.000	0.001

Table.16: Association of serum calcium levels with the types of ST fracture.

Chart.16: Association of serum calcium levels with the types of ST fracture.

Serum phosphorous level evaluated with the types of ST fractures were evaluated based on Russell and Taylor's classification where type-1 had mean serum phosphorous of $4.00(n=10)$ with S.D of 0.000, type-2 had mean serum phosphorous of 3.25(n=4) with S.D of 0.500.The Mann-Whitney test was 5.000 and p-value was 0.001. Serum phosphorous levels associated with the types of ST fracture were found to be statistically significant.

RUSSELL AND TAYLOR	NUMBER OF	SERUM PHOSPHOROUS(mg/dl)		Mann-Whitney Test	P VALU
CLASSIFICATIO N OF	PATIENT S	Mean Std. Deviatio			E
SUBTROCHANT ERIC FRACTURE			n		
TYPE-I	10	4.00	.000		
TYPE-II	4	3.25	.500	5.000	0.001

Table.17: Association of serum phosphorous levels with the types of ST fracture.

Chart.17: Association of serum phosphorous levels with the types of ST fracture.

Serum vitamin-D level evaluated with the types of ST fractures were evaluated based on Russell and Taylor's classification where type-1 had mean serum vitamin-D of 29.80(n=10) with S.D of 2.348, type-2 had mean serum vitamin-D of 23.50(n=4) with S.D of 1.291.The Mann-Whitney test was 0.500 and p-value was 0.001. Serum vitamin-D levels associated with the types of ST fracture were found to be statistically significant.

RUSSELL AND TAYLOR	NUMBER OF	SERUM VITAMIN- D(ng/dl)		Mann-Whitney Test	\mathbf{P} VALUE
CLASSIFICATIO N OF	PATIENT S	Std. Mean Deviatio n			
SUBTROCHANT ERIC FRACTURE					
TYPE-I	10	29.80	2.348		
TYPE-II	$\overline{4}$	23.50	1.291	.500	0.001

Table.18: Association of serum vitamin-D levels with the types of ST fracture.

Chart.18: Association of serum vitamin-D levels with the types of ST fracture.

Serum calcium level evaluated with different age groups where it was found that <60 age (n=22), 50% had normal serum calcium level, 31.8% had hypocalcemia,18.2% had hypercalcemia. Among 60-69 age(n=45), 46.7% had normal serum calcium level, 44.4% had hypocalcemia and 8.9% had hypercalcemia. Among 70-79 age(n=30), 36.7% had normal serum calcium levels, 56.7% had hypocalcemia and 6.7% had hypercalcemia. Among 80-89 age(n=20), 55% had normal serum calcium levels,30.0% had hypocalcemia, 15.0% had hypercalcemia. Among 90+ age(n=3) 33.3% had normal serum calcium levels,33.3% had hypocalcemia,33.3% had hypercalcemia. The Chi-square test was 7.090 and P-value was 0.527. Serum calcium level evaluated with different age groups were found to be statistically insignificant.

Table 19: Correlation of serum calcium levels with different age groups.

Serum vit-D level evaluated with different age groups where it was found that <60 age (n=22), 40.9% had normal serum vit-d level, 36.4% had low serum vit-d,22.7% had high vit-d. Among 60- 69 age(n=45), 44.4% had normal vit-d level, 44.4% had low vit-d and 11.1% had high vit-d. Among 70-79 age(n=30), 36.7% had normal vit-d levels, 56.7% had low vit-d and 6.7% had high vit-d. Among 80-89 age(n=20), 50% had normal vit-d levels, 35.0% had low vit-d, 15.0% had high vit-d. Among 90+ age(n=3) 66.7% had normal serum vit-dlevels, 33.3% had low serum vit-d, 0% had hypercalcemia. The Chi-square test was 7.090 and P-value was 0.527. Serum Vitamin-d level evaluated with different age groups were found to be statistically insignificant**.**

Table 20: Correlation of serum vit-d levels with different age groups.

Serum calcium level evaluated with different sex where it was found that among females(n=52), 44.2% had normal serum calcium level, 48.1% had hypocalcemia, 7.7% had hypercalcemia. Among males(n=68), 47.1% had normal serum calcium levels, 38.2% had hypocalcemia, 14.7% had hypercalcemia. The Chi-square test was 1.965 and P-value was 0.374. Serum calcium level evaluated with different sex were found to be statistically insignificant.

Table 21: Correlation of serum calcium levels with different sex.

Serum vit-d level evaluated with different sex where it was found that among females(n=52), 44.2% had normal serum vit-d level, 50.0% had low vit-d, 5.8% had high vit-d. Among males(n=68), 42.6% had normal serum vit-d levels, 39.7% had low serum vit-d, 17.6% had high serum vit-d. The Chi-square test was 4.050 and P-value was 0.132. Serum vit-d level evaluated with different sex were found to be statistically insignificant**.**

Table 22: Correlation of serum vit-d levels with different sex.

Serum vit-d level correlated with diagnosis where it was found that among IT femur fractures(n=71), 46.5% had normal serum vit-d level, 46.5% had low vit-d, 7.0% had high vit-d. Among NOF fracture(n=35), 34.3% had normal serum vit-d levels, 57.1% had low serum vit-d, 8.6% had high serum vit-d. Among ST fractures(n=14), 50.0% had normal vit-d level, 0% had low vit-d, 7% had high vit-d. The Chi-square test was 26.445 and P-value was 0.000. Serum vit-d level evaluated with diagnosis were found to be statistically significant.

Table 23: Correlation of serum vit-d levels with diagnosis.

Serum calcium level correlated with diagnosis where it was found that among IT femur fractures(n=71), 47.9% had normal serum calcium level, 45.1% had hypocalcemia, 7.0% had hypercalcemia. Among NOF fracture(n=35), 40.0% had normal serum calcium levels, 54.3% had hypocalcemia, 5.7% had hypercalcemia. Among ST fractures(n=14), 50.0% had normal calcium level, 0% had hypocalcemia, 7% had hypercalcemia. The Chi-square test was 27.580 and P-value was 0.000. Serum calcium level evaluated with diagnosis were found to be statistically significant.

Table 24: Correlation of serum calcium levels with diagnosis.

Grades	Serum calcium(mg/dl)				Chi square test	P value
	< 8.5	$8.5 -$	$10.3+$	Total		
		10.2				
Boyd and griffin $type-1$	$\boldsymbol{0}$	3	5	$8\,$		
$\%$	0.0%	37.5%	62.5%	100.0%		
Boyd and griffin $type-2$	$\mathbf{1}$	13	$\boldsymbol{0}$	14		
$\frac{0}{0}$	7.1%	92.9%	0.0%	100.0%		
Boyd and griffin $type-3$	$\boldsymbol{0}$	18	$\boldsymbol{0}$	18		
$\%$	0.0%	100.0%	0.0%	100.0%		
Boyd and griffin $type-4$	31	$\overline{0}$	$\boldsymbol{0}$	31		
$\frac{0}{0}$	100.0%	0.0%	0.0%	100.0%		
Garden's type-1	θ	$\mathbf{1}$	$\overline{2}$	$\overline{3}$		
$\frac{0}{0}$	0.0%	33.3%	66.7%	100.0%		
Garden's type-2	$\mathbf{0}$	$\overline{4}$	$\mathbf{0}$	$\overline{4}$	181.568	0.000
$\frac{0}{0}$	0.0%	100.0%	0.0%	100.0%		
Garden's type-3	$\overline{0}$	8	$\overline{0}$	8		
$\%$	0.0%	100.0%	0.0%	100.0%		
Garden's type-4	19	$\mathbf{1}$	$\overline{0}$	20		
$\frac{0}{0}$	95.0%	5.0%	0.0%	100.0%		
Russell-Taylor's $type-1$	$\overline{0}$	3	τ	10		
$\%$	0.0%	30.0%	70.0%	100.0%		
Russell-Taylor's $type-2$	$\boldsymbol{0}$	$\overline{4}$	$\boldsymbol{0}$	$\overline{4}$		
$\%$	0.0%	100.0%	0.0%	100.0%		
Total	51	55	14	120		
$\%$	42.5%	45.8%	11.7%	100.0%		

Table 25 : Correlation of serum calcium levels with severity of all Hip fractures

Chart 25: Comparing serum calcium levels with the types of IT fracture shows that Boyd and griffin type-4 has 100.00% correlation with low calcium level .

Chart 26: Comparing serum calcium levels with the types of NOF fracture shows that

Chart 27 :Comparing serum calcium levels with the types of ST fracture shows that Russell-

Table 26 : Correlation of serum Vitamin-D levels with severity of all Hip fractures

Chart 28: Comparing serum vit-d levels with the types of IT fracture shows that <u>Boyd and</u> griffin type-4 has 100.00% correlation with low vit-d levels (vit D deficient).

Chart 29: Comparing serum vit-d levels with the types of NOF fracture shows that Garden's

Chart 30: Comparing serum vit-d levels with the types of ST fracture shows that Russell-

CHAPTER 5

DISCUSSION

Elderly patients frequently suffer from hip fragility fractures, which are brought on by minor trauma such falling from standing height or less. Some of the risk factors influencing the onset of osteoporosis include calcium and vitamin D deficiency (75). Osteoporosis is linked to a higher risk of fragility fractures, which mostly affect the wrist, hip, and spine. According to reports, the lifetime risk of fragility fracture varies between 33% and 44% for females and 20% to 27% for males (10,75,76).

Serum Vitamin D and calcium levels

Out of the 120 patients who were enrolled in the study, 37.5% had hip fractures, and the majority of these men (56.7%) were in the 60-69 age range. Though there was no statistically significant difference, more men than women had low vitamin D levels. Our results diverged from those of studies conducted in Western and Asian regions. A Chinese study by Fu et al. found a link between postmenopausal women's hip fractures and low levels of blood 25 hydroxycholecalciferol (43). This study demonstrated that older patients with hip fragility fractures frequently have hypovitaminosis D. 43.3% of the people in the study were vitamin D deficient. Only 12.5% of people had normal serum vitamin D levels, whereas 44.2% were vitamin D deficient. Similar findings were made by Ramason et al (41) in Singapore, where vitamin D deficiency rates were 57.5%, insufficiency rates were 34.5 percent, and normal serum vitamin D levels were 8%. The frequency of vitamin D deficiency among individuals with fragility fractures has been found to be quite high, ranging from 55% to 91.6% in other investigations. In contrast to Ramason et al. and other research in Western nations, this study, however, revealed lower prevalence of Vitamin D deficiency and insufficiency (41,45,77).

The levels of vitamin D and calcium in the elderly have been found to vary geographically and seasonally in previous research of a similar nature, with a higher frequency of vitamin D deficiency during periods of spring due to lower cutaneous production in the winter months (77,78). It's conceivable that the slightly lower prevalence of hypovitaminosis in this study is due to the fact that the participants were selected from Nairobi and its surroundings, where the climate is primarily sunny with few seasonal fluctuations. Additionally, it is possible to hypothesise that the discrepancies seen can be explained by the small sample size, slightly lower mean population age, and smaller percentage of women.

45.8% of research participants had normal albumin-adjusted calcium levels, while 42.5% had low levels. The findings are not surprising because calcium is tightly regulated by parathyroid hormone and vitamin D, in spite of the fact that it is predicted that calcium absorption declines with age. The scope of this study did not allow for evaluation of other contributing factors, such as kidney illness, liver disease, hypoparathyroidism, and diet, which may have caused calcium shortage in 42.5% of the study group (62,67,69).

Hip fracture pattern and Severity

Intertrochanteric femur fractures made up 59.2% of all hip fractures, followed by neck of femur fractures at 29.2% and sub-trochanteric femur fractures at 11.7%. According to studies, the likelihood of developing an intertrochanteric fracture increases dramatically with age and is most frequently found in women (18,19,21). Intertrochanteric fractures are more frequent than other fracture patterns, according to studies conducted in different areas (22). In a retrospective study conducted in Tanzania, Tsabasvi et al. revealed that intertrochanteric fractures were the most prevalent type of fracture, accounting for 55.8% of cases, followed by neck of femur fractures, which were shown to be 28.5% more common (24).

Despite the fact that there were more women with fractures in this category, this study found no significant differences. Fox et alearlier .'s study, which was similar, similarly found no variation in gender distribution (23). 25.8% of intertrochanteric femur fractures were Boyd and griffin type-4, while 6.7% were type-1. 16.7% of neck of femur fractures were of Gardens type-4, while 2.5% were of type-1. 8.3% of subtrochanteric femur fractures were Russell-Taylor type-1, while 3.3% were type-2. Thus, a majority of the patients who came to us with various hip fractures belonged to the more severe variety of those fractures.

Correlation between Vitamin D and calcium levels and selected patient characteristics

There was no statistically significant correlation between age groups and serum calcium and vitamin D levels. It was shown that there was no statistically significant relationship between sex and the serum levels of calcium and vitamin D. Notably, statistically significant differences were found for the different levels of serum calcium and vitamin D for the Intertrochanteric femur fracture, Neck of femur fracture, and Subtrochanteric femur fracture. Hypocalcemia was seen in 46.5% of Intertrochanteric femur fracture patients and Vitamin D deficiency was present in 45.1% of Intertrochanteric femur fracture patients and 54.3% of Neck of femur fracture patients. In the past, research on osteoporosis and vitamin D levels examined the overall fracture risk. However, there has been debate among writers over the ideal serum 25(OH)D levels linked to an increased risk of fracture. Melhus et al. discovered in 2010 that a blood 25(OH)D level below 40nmol/l predicted an elevated fracture risk (47). According to a 2008 study by Cauley et al, the lowest risk of fracture was related with 25(OH) D levels between 60 and 70 nmol/l (4). In 2008, Van Schoolar discovered that the highest risk of fracture was associated with serum 25 (OH) D levels less than or equal to 30 nmol/l (46). The levels of vitamin D or serum calcium did not show a statistically significant correlation with patient age or gender.

There was significant association of serum calcium and Vitamin D levels with severity of hip fractures , Among Intertrochanteric femur fractures all type-4 fractures had hypocalcemia (100%) & Vitamin D Insufficiency (100%) , Among Neck of femur fractures almost all type-4 fractures had hypocalcemia (95%) & vitamin D deficiency (100%).

100

Conclusion

In conclusion, the prevalence of vitamin D deficiency and insuffiency as well as Hypocalcemia was high in this study. Especially when evaluated among different types of hip fractures and their severity. We could conclude that more deficient the serum calcium levels and more deficint / insufficient the serum Vitamin-D levels more sever the type of fractures , There was a statistically significant, though weak, association between serum calcium and vitamin D levels with age and sex.

Strengths and limitations

In India's Karnataka state, this is the first study of its kind. The tiny sample size precluded extrapolating the findings to the entire population. Recall bias existed with regard to calcium and vitamin D supplementation. Osteoporosis cannot be accurately diagnosed because DEXA scans are expensive and not widely available to measure bone mineral density. It was impossible to standardise the exposure of X-rays because radiographs were obtained on various equipment and at various locations.

Recommendations

Due to the high frequency of calcium and vitamin D insufficiency / deficiency revealed in this study, it should be advised that older patients with fragility hip fractures undergo screening for vitamin D deficiency and replacement when appropriate.

It is advised to begin taking calcium and vitamin D supplements if you are over 50. It is suggested that a bigger prospective case control research be conducted to evaluate calcium and

vitamin D levels in elderly people with and without hip fragility fractures.

a similar study that used a DEXA scan to accurately identify osteoporosis in fractures prone to fragility.

101

REFERENCES

1. Turner CH. Biomechanics of Bone: Determinants of Skeletal Fragility and Bone Quality. Osteoporos Int. 2002 Feb 1; 13(2):97–104.

2. Adler R. Osteoporosis: Pathophysiology and Clinical Management, Humana Press; 2010 8: 183-89.

3. Marks R. Hip fracture epidemiological trends, outcomes, and risk factors, 1970–2009. Int J Gen Med. 2010 Apr 8; 3:1–17.

4. Cauley JA, Lacroix AZ, Wu L, Horwitz M, Danielson ME, Bauer DC, et al. Serum 25 hydroxyvitamin D concentrations and risk for hip fractures. Ann Intern Med. 2008 Aug 19; 149(4):242–50.

5. Halfon M, Phan O, Teta D. Vitamin D: A Review on Its Effects on Muscle Strength, the Risk of fall, and Frailty. BioMed Research International. 2015

6. Jones G, Strugnell SA, DeLUCA HF. Current Understanding of the Molecular Actions of Vitamin D. Physiol Rev. 1998 Oct 1; 78(4):1193–231.

7. Zuckerman JD. Hip Fracture. N Engl J Med. 1996 Jun 6 [cited 2017 Aug 28]; 334(23):1519–25.

8. Nurmi I, Kaukonen J-P, Lüthje P, Naboulsi H, Tanninen S, Kataja M, et al. half of the patients with an acute hip fracture suffer from hypovitaminosis D: a prospective study in southeastern Finland. Osteoporos Int J Dec; 16(12):2018–24.

9. Pietri M, Lucarini S. The orthopaedic treatment of fragility fractures. Clin Cases Miner Bone Metab. 2007; 4(2):108–16.

10. Bukata SV, DiGiovanni BF, Friedman SM, Hoyen H, Kates A, Kates SL, et al. A Guide to Improving the Care of Patients with Fragility Fractures. Geriatr Orthop Surg Rehabil. 2011 Jan; $2(1):5-37.$

11. Dhanwal DK, Dennison EM, Harvey NC, Cooper C. Epidemiology of hip fracture: Worldwide geographic variation. Indian J Orthop. 2011 Jan; 45(1):15–22.

12. Zebaze RMD, Seeman E. Epidemiology of hip and wrist fractures in Cameroon, Africa. Osteoporos Int. 2003 Jun 1; 14(4):301–5.

13. Adebajo AO, Cooper C, Evans JG. Fractures of the hip and distal forearm in West Africa and the United Kingdom. Age Ageing. 1991 Nov; 20(6):435–8.

14. Hilliard CB. High osteoporosis risk among East Africans linked to lactase persistence genotype. BoneKEy Rep. 2016 Jun 29; 5.

15. Oyoo G, G Kariuki J. Osteoporosis - From hormonal replacement therapy to bisphosphonates and beyond: A review. Vol. 84. 2007. 534.

16. Cummings SR, Nevitt MC. A hypothesis: the causes of hip fractures. J Gerontol. 1989 Jul; 44(4):M107-111.

17. Pisani P, Renna MD, Conversano F, Casciaro E, Di Paola M, Quarta E, et al. Major osteoporotic fragility fractures: Risk factor updates and societal impact. World J Orthop. 2016 Mar 18; 7(3):171–81.

18. Parker M, Johansen A. Hip fracture. BMJ. 2006 Jun 29; 333(7557):27–30.

19. Browner BD. Skeletal Trauma: Basic Science, Management, and Reconstruction. Elsevier Health Sciences; 2009. 1747.

20. Rockwood and Green's fractures in adults. $7th$ edition; Lippincott William & Wikins: Bucholz, Charles M et al, 2010; 492-99.

103

21. MittalR, Banerjee S. Proximal femoral fractures: Principles of management and review of literature. J Clin Orthop Trauma. 2012 Jun; 3(1):15–23.

22. Ahn J, Bernstein J. In Brief: Fractures in Brief: Intertrochanteric Hip Fractures. Clin Orthop Relat Res. 2010 May 1; 468(5):1450–2.

23. Fox KM, Magaziner J, Hebel JR, Kenzora JE, Kashnei TM. Intertrochanteric Versus Femoral Neck Hip Fractures: Differential Characteristics, Treatment, and Sequelae. J Gerontol Ser A. 1999 Dec 1; 54(12):M635–40.

24. Tsabasvi M, Davey S, Temu R. Hip fracture pattern at a major Tanzanian referral hospital: focus on fragility hip fractures. Arch Osteoporos. 2017 Dec; 12(1):47.

25. Wojciech P, Ross M. Histology: A Text and Atlas. Lippincott Wilkins & Wilkins 2011 8; 218- 53.

26. Bonjour JP, Theintz G, Law F, Slosman D, Rizzoli R. Peak bone mass. Osteoporos Int J Establ Result Coop Eur Found Osteoporos Natl Osteoporos Found USA. 1994; 4 Suppl 1:7–13.

27. Bonjour J-P, Chevalley T, Ferrari S, Rizzoli R. The importance and relevance of peak bone mass in the prevalence of osteoporosis. Salud Publica Mex. 2009; 51 Suppl 1:S5-17.

28. Cosman F, Beur SJ de et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int. 2014:25(10):2359.

29. Tranquilli Leali P, Doria C, et al. Bone fragility: current reviews and clinical features. Clin Cases Miner Bone Metab. 2009; 6(2):109–13.

30. Vernejoul MC. Bone remodelling in osteoporosis. Clin Rheumatol. 1989 Jun; 8 Suppl $2:13-5.$

31. Jergas M. Radiology of Osteoporosis. In bone densitometry and osteoporosis. Springer 1998. 11. p193-225.

104

32. Robert A. Adler in; Osteoporosis - Pathophysiology and Clinical Management | Hamana press. 2010.

33. Boskey AL, Coleman R. Aging and Bone. J Dent Res. 2010 Dec; 89(12):1333–48.

34. Fonseca H, Moreira-Gonçalves D, Coriolano H-JA, Duarte JA. Bone Quality: The Determinants of Bone Strength and Fragility. Sports Med. 2014 Jan 1; 44(1):37–53.

35. Ross AC, Manson JE et al. The 2011 Report on Dietary Reference Intakes for Calcium and Vitamin D from the Institute of Medicine: What Clinicians Need to Know. J Clin Endocrinol Metab. 2011 Jan 1; 96(1):53–8.

36. Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, et al. Vitamin D3 and Calcium to Prevent Hip Fractures in Elderly Women. N Engl J Med. 1992 Dec 3; 327(23):1637– 42.

37. Nair R, Maseeh A. Vitamin D: The "sunshine" vitamin. J Pharmacol Pharmacother. 2012; 3(2):118–26.

38. Norval M, Coussens AK, Wilkinson RJ, Bornman L, Lucas RM, Wright CY. Vitamin D Status and Its Consequences for Health in South Africa. Int J Environ Res Public Health. 2016 Oct; 13(10) 1019.

39. Nielson CM, Bouxsein ML, et al. Trochanteric Soft Tissue Thickness and Hip Fracture in Older Men. J Clin Endocrinol Metab. 2009 Feb; 94(2):491–6.

40. Holick MF. Vitamin D Deficiency. N Engl J Med. 2007 Jul 19; 357(3):266–81.

41. Ramason R, Selvaganapathi N et al. Prevalence of Vitamin D Deficiency in Patients With Hip Fracture Seen in an Orthogeriatric Service in Sunny Singapore. Geriatr Orthop Surg Rehabil. 2014 Jun; 5(2):82–6.

42. Todd CJ, Freeman CJ et al. Differences in mortality after fracture of hip: the east Anglian audit. BMJ. 1995 Apr 8; 310(6984):904–8.

43. Fu X-M, Fan S-G, Li S-L et al. Low 25(OH) D serum levels are related with hip fracture in postmenopausal women: a matched case–control study. J Transl Med. 2015 Dec 23; 13.

44. Gallacher SJ, McQuillian C et al. Prevalence of vitamin D inadequacy in Scottish adults with non-vertebral fragility fractures. Curr Med Res Opin. 2005 Sep 1; 21(9):1355–61.

45. LeBoff MS, Kohlmeier L, et al. Occult Vitamin D Deficiency in Postmenopausal US Women With Acute Hip Fracture. JAMA. 1999 Apr 28; 281(16):1505–11.

46. Schoor NM van, Visser M et al. Vitamin D deficiency as a risk factor for osteoporotic fractures. Bone. 2008 Feb 1; 42(2):260–6.

47. Melhus H, Snellman G, et al. Plasma 25-hydroxyvitamin D levels and fracture risk in a community-based cohort of elderly men in Sweden. J Clin Endocrinol Metab. 2010 Jun; 95(6):2637–45.

48. Bischoff-Ferrari HA, Giovannucci E, et al. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr]. 2006 Jul 1; 84(1):18–28.

49. Isaia G, Giorgino R, et al. Prevalence of hypovitaminosis D in elderly women in Italy: clinical consequences and risk factors. Osteoporos Int. 2003 Jul 1; 14(7):577–82.

50. Looker AC, Mussolino ME. Serum 25-Hydroxyvitamin D and Hip Fracture Risk in Older U.S. White Adults. J Bone Miner Res. 2008 Jan 1; 23(1):143–50.

51. Zerwekh JE. Blood biomarkers of vitamin D status. Am J Clin Nutr. 2008 Apr 1; 87(4):1087S-1091S.

52. Barragry JM, France MW, Corless D, Gupta SP, Switala S, Boucher BJ, et al. Intestinal cholecalciferol absorption in the elderly and in younger adults. Clin Sci Mol Med. 1978 Aug; 55(2):213–20.

53. Clemens TL, ZHOUf X-Y, et al. Serum Vitamin D2 and Vitamin D3 Metabolite Concentrations and Absorption of Vitamin D2 in Elderly Subjects. J Clin Endocrinol Metab. 1986 Sep 1; 63(3):656–60.

54. Holick MF, Binkley NC, Bischoff-Ferrari HA et al. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2011 Jul 1; 96(7):1911–30.

55. Ryan CS, Petkov VI, Adler RA. Osteoporosis in men: the value of laboratory testing. Osteoporos Int. 2011 Jun 1; 22(6):1845–53.

56. Hollis BW. Measuring 25-hydroxyvitamin D in a clinical environment: challenges and needs. Am J Clin Nutr. 2008 Aug 1; 88(2):507S-510S.

57. Roth HJ, Schmidt-Gayk H, Weber H, Niederau C. Accuracy and clinical implications of seven 25-hydroxyvitamin D methods compared with liquid chromatography–tandem mass spectrometry as a reference. Ann Clin Biochem. 2008 Mar 1; 45(2):153–9.

58. Malmstroem S, Rejnmark L, Imboden JB, Shoback DM, Bikle DD. Current Assays to Determine Free 25-Hydroxyvitamin D in Serum. J AOAC Int. 2017 Sep 1; 100(5):1323–7.

59. Arneson WL, Arneson DL. Current Methods for Routine Clinical Laboratory Testing of Vitamin D Levels. Lab Med . 2013 Feb 1; 44(1):e38–42.

60. Reid IR, Bolland MJ, Grey A. Effect of calcium supplementation on hip fractures. Osteoporos Int J Establ Result Coop Eur Found Osteoporos Natl Osteoporos Found USA. 2008 Aug; 19(8):1119–23.

107
61. OpplB, Michitsch G, MisofB, Kudlacek S, Donis J, Klaushofer K, et al. Low bone mineral density and fragility fractures in permanent vegetative state patients. J Bone Miner Res Off J Am Soc Bone Miner Res. 2014; 29(5):1096–100.

62. Goldstein DA. Serum Calcium. Clinical Methods: The History, Physical, and Laboratory Examinations. Butterworths Publishers, 3rd ed.; 1990; 143: 1-5.

63. Omidvar N, Neyestani T-R, et al. Calcium Intake, Major Dietary Sources and Bone Health Indicators in Iranian Primary School Children. Iran J Pediatr. 2015 Feb; 25(1).

64. Eastell R, Yergey AL, Vieira NE, Cedel SL, Kumar R, Riggs BL. Interrelationship among vitamin D metabolism, true calcium absorption, parathyroid function, and age in women: Evidence of an age-related intestinal resistance to 1, 25-dihydroxyvitamin D action. J Bone Miner Res. 1991; $6(2):125-32.$

65. Martins JS, Palhares M de O, Teixeira OCM, Gontijo Ramos M. Vitamin D Status and Its Association with Parathyroid Hormone Concentration in Brazilians. J Nutr Metab. 2017.

66. Goltzman D. Approach to Hypercalcemia. 2019 Oct 29 In: Feingold KR, Anawalt B, et al., editors. Endotext. MDText.com, Inc.; 2000: 11; 1-19.

67. Cooper C, Mclaren M, Wood PJ, Coulton L, Kanis JA. Indices of calcium metabolism in women with hip fractures. Bone Miner. 1989 Jan; 5(2):193–200.

68. Raisz LG. Pathogenesis of osteoporosis: concepts, conflicts, and prospects. J Clin Invest. 2005 Dec 1; 115(12):3318–25.

69. Warensjö E, Byberg L, et al. Dietary calcium intake and risk of fracture and osteoporosis: prospective longitudinal cohort study. BMJ. 2011 May 24; 342: d1473.

70. Boonen S, Lips P, Bouillon R, et al. Need for Additional Calcium to Reduce the Risk of Hip Fracture with Vitamin D Supplementation: Evidence from a Comparative Metaanalysis of Randomized Controlled Trials. J Clin Endocrinol Metab. 2007 Apr 1; 92(4):1415–23.

71. Bischoff-Ferrari HA, Dawson-Hughes B, et al. Calcium intake and hip fracture risk in men and women: a meta-analysis of prospective cohort studies and randomized controlled trials. Am J Clin Nutr 2007 Dec 1 86(6):1780–90.

72. Li P-F, Lin Z-L, Pang Z-H, Zeng Y-R. Does serum calcium relate to different types of hip fracture? A retrospective study. Chin J Traumatol. 2016 Oct 13; 19(5):275–7.

73. Charan J, Biswas T. How to Calculate Sample Size for Different Study Designs in Medical Research? Indian J Psychol Med [Internet]. 2013; 35(2):121–6.

74. Ersfeld DL, Rao DS, Body J-J, Sackrison JL, Miller AB, Parikh N, et al. Analytical and clinical validation of the 25 OH vitamin D assay for the LIAISON automated analyzer. Clin Biochem. 2004 Oct; 37(10):867–74.

75. Fischer V, Haffner-Luntzer M, Amling M, Ignatius A. Calcium and vitamin D in bone fracture healing and post-traumatic bone turnover. Eur Cell Mater. 2018 22; 35:365–85.

76. Cooley H, Jones G. A Population-Based Study of Fracture Incidence in Southern Tasmania: Lifetime Fracture Risk and Evidence for Geographic Variations within the Same Country. Osteoporos Int [Internet]. 2001 Feb 1; 12(2):124–30.

77. Dhanwal DK, Sahoo S, Gautam VK, Saha R. Hip fracture patients in India have vitamin D deficiency and secondary hyperparathyroidism. Osteoporos Int J Establ Result Coop Eur Found Osteoporos Natl Osteoporos Found USA. 2013 Feb; 24(2):553–7.

109

78. O'Connor MY, Thoreson CK, Ramsey NLM, et al. The Uncertain Significance of Low Vitamin D Levels in African Descent Populations: A Review of the Bone and Cardiometabolic Literature. Prog Cardiovasc Dis. 2013 Nov 1; 56(3):261–9.

- 79. Larrosa M, Gomez A, Casado E, Moreno M, Vázquez I, Orellana C, Berlanga E, Ramon J, Gratacos J. Hypovitaminosis D as a risk factor of hip fracture severity. Osteoporos Int. (2012) Feb;23(2):607-14. doi: 10.1007/s00198-011-1588-z. Epub 2011 Mar 11. PMID: 21394494
- 80. Hwang, Seok-Min & Hwang, Suk-Hyun & Kim, Yeon-Ho. (, 2020). Association of Serum Vitamin D and Calcium Levels With the Severity of Intertrochanteric Fractures in the Elderly: A Retrospective Study. 10.21203/rs.3.rs-34943/v1.
- 81. Lakkireddy, M.Vardhan Mudavath, S., Karra, M. L., & Arora, A. J. (2019). Hypovitaminosis D in patients with osteoporotic fractures of the hip. Journal of clinical orthopaedics and trauma, 10(4), 768-773.
- 82. Li, Peng-Fei, et al. "Does serum calcium relate to different types of hip fracture? A retrospective study." Chinese Journal of traumatology = Zhonghua Chuang Shang za Zhi vol. 19,5 (2016): 275-277. doi:10.1016/j.cjtee.2016.06.003

B.L.D.E. (DEEMED TO BE UNIVERSITY) SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTER, VIJAYAPURA-586103

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/RESEARCH

I, the undersigned, _____________, S/O D/O W/O _____________, aged years, ordinarily resident of do hereby state/declare that **Dr. Anmol Abhay Hublikar** of Shri. B. M. Patil Medical College Hospital and Research Centre has examined me thoroughly on at (place) and it has been explained to me in my own language that I am suffering from disease (condition) and this disease/condition mimic following diseases. Further **Dr. Anmol Hublikar** informed me that he/she is conducting dissertation/research titled ".**ASSOCIATION OF SERUM VITAMIN-D AND CALCIUM LEVELS WITH THE SEVERITY OF HIP FRAGILITY FRACTURES IN THE ELDERLY : A PROSPECTIVE STUDY**" under the guidance of Dr Ashok Nayak. requesting my participation in the study.

The doctor has informed me regarding the procedure of this study , which is investigation based and it requires blood investigations to evalute the deficiency.

Further Doctor has informed me that my participation in this study help in the evaluation of the results of the study, which is a useful reference to the treatment of other similar cases soon, and also I may be benefited in getting relieved of suffering or cure of the disease I am suffering.

The Doctor has also informed me that information given by me, observations made/ photographs/ video graphs taken upon me by the investigator will be kept secret and not assessed by the person other than my legal hirer or me except for academic purposes.

The Doctor did inform me that though my participation is purely voluntary, based on the information given by me, I can ask for any clarification during the course of treatment/study related to diagnosis, the procedure of treatment, result of treatment, or prognosis. I have been instructed that I can withdraw from my participation in this study at any time if I want, or the investigator can terminate me from the study at any time from the study but not the procedure of treatment and follow-up unless I request to be discharged.

After understanding the nature of dissertation or research, diagnosis made, mode of treatment, I the undersigned Shri/Smt under my full conscious state of mind agree to participate in the said research/dissertation.

Signature of the patient:

Signature of Doctor:

Witness: 1.

2.

Date:

Place

APPENDIX I: DATA COLLECTION SHEET

Radiographic (X- ray) Observations

Neck of femur fracture

Intertrochanteric fracture

Sub-trochanteric fracture

Serum level of:

- a) 25 hydroxycholecalciferol
- b) Albumin corrected serum calcium
- c) Phosphorous

DocuSign Envelope ID: 3B0A43C5-4390-4455-A5D9-974AF60F2562

