

# Vitamin D status among postmenopausal osteoporotic women: a hospital based cross-sectional study from Northern Sri Lanka.

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## Research article

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# Abstract

Background Vitamin D deficiency is common among post-menopausal women and it is important to treat vitamin D deficiency to prevent falls and fractures in patients with osteoporosis. Few studies examined the prevalence of vitamin D deficiency in general population of Sri Lanka but no studies to date done among post-menopausal women with osteoporosis. This is the first study of such kind conducted to evaluate the serum vitamin D levels and factors related to Vitamin D deficiency among postmenopausal women. Methodology Hospital based Cross-sectional study was conducted at the Endocrine Unit, Teaching Hospital from January to December 2018. During the study period 105 postmenopausal women registered for DEXA scan with Endocrine Unit were recruited to the study. Data collection was done by investigators and blood sample was taken from each participant by registered nursing officers and sample was analysed by using immunohistochemistry assays. Serum Vitamin D levels were categorized and data analysis was done using SPSS 26. Results Mean age of 105 postmenopausal women was 67.7 with minimum 33 and maximum 84 years. Mean Vitamin D levels were 27.5 (range 11.7-52.5 ng/ml). Vitamin D levels were adequate in only 36.2% (95%CI: 27.4-45.7) of women, 44% had insufficient levels and deficiency was present in 19% (95%CI: 12.4-27.4) of participants. Among the 105 women 20% were vegetarian and 53% of them consuming milk on average 3 days per week, 76.2% consuming fish on average 2 days per week, 64.8% consuming egg on average 1 day per week. Furthermore seventy five participants (71.4%) reported adequate level of sun exposure (>30 minutes). Commonly reported vitamin deficiency symptoms includes paraesthesia (57.1%), bone pain (55.2%), easy fatigability (54.3%), malaise (51.4%), muscle cramps (43.8%) and proximal myopathy (40.0%). Among 71 (66.7%) completed bone density assessment, 38% (27.3-49.7) of them showed osteoporosis range. Vertebral Z score showed a significant correlation with vitamin D level ( $r=0.252$ ,  $P=0.034$ ). Conclusion Prevalence of vitamin D deficiency is relatively high among the post-menopausal women with a provisional diagnosis of osteoporosis. It is essential to correct vitamin D deficiency with supplementation when initiating treatment for osteoporosis. So vitamin D testing is desirable in decision making to treat or not to treat.

## Background:

In recent years the prevalence and the awareness of osteoporosis are increasing and it has been estimated that 200 million of individuals suffer from osteoporosis worldwide (1). Nevertheless, about 75% of these people represent undiagnosed cases and do not receive appropriate treatment (1, 2). Bone is remodelled constantly throughout life. Peak bone mass is around the age of 30 years after which rate of bone-resorption is greater than the rate of bone formation. Approximately 3% of cortical bone is replaced each year and 25% of trabecular bone is resorbed and replaced each year (3). Osteoporosis is defined as bone mineral density less than 2.5 SD below the mean peak value in young adults of the same race and sex (t score of -2.5). Women of all ethnic groups show an additional accelerated phase of bone loss, which occurs for about 10 years after the cessation of ovarian function. Total bone loss in osteoporosis may exceed 30 to 40% (4). Vitamin D deficiency is a risk factor for fall and fracture among post-menopausal women with osteoporosis (5) and vitamin D deficiency is pandemic (6) health problem which

was attributed for several health problems and well documented in different parts of the world including Sri Lanka. Moderate level of sun exposure is the major source for Vitamin D as only limited dietary sources are rich in Vitamin D (7). But it is still debatable regarding the cut off level to be treated and most of the evidences for health related implications of Vitamin D deficiencies are through observational studies and with limited evidences from randomized control trials (8). Health problems varies with life cycle and it was well known to link with rickets in paediatric population and osteopenia osteoporosis and fractures in Adults (6, 9) .

Justification:

A study of Vitamin D Inadequacy among 200 postmenopausal women presenting to Orthopaedics and Gynaecology outpatient departments of Khyber Teaching Hospital in Pakistan, showed high prevalence (59%) vitamin Deficiency in postmenopausal women owing to their lack of knowledge, deficient diet, sedentary lifestyle and inadequate sun exposure(10). In Sri Lanka as far as to our knowledge, prevalence of Vitamin D status not estimated among postmenopausal women even though a general prevalence study indicated high prevalence of vitamin D deficiency (57.2%) (11). So this study conducted to evaluate serum vitamin D levels, symptoms related to vitamin D inadequacy and factors related to Vitamin D deficiency in postmenopausal women.

Methodology:

Study Design

Hospital based Cross-sectional study

Place and duration of Study

This study was conducted at the Endocrine Unit, Teaching Hospital Jaffna from January 2018 to December 2018.

## **Materials And Methods:**

During the study period (January 2018 to December 2018), 105 postmenopausal women registered for DEXA scan with Endocrine Unit, Teaching Hospital Jaffna were recruited to the study. Women on drugs, such as glucocorticoids and anticonvulsants popularly known to cause bone loss, individuals on hormone replacement therapy, those with conditions that affect bone metabolism and contributing to osteoporosis, such as multiple myeloma, diseases of the kidney or liver, mal absorption diseases, Paget's disease, primary hyperparathyroidism and uncontrolled hypo- or hyperthyroidism and who has been on vitamin D supplements were excluded from the study.

Data collection was done by investigators by using interviewer administered questionnaire and venepuncture was done in aseptic condition and blood sample (10 ml) was taken from each participant by registered nursing officers and sample was analysed by Chemical pathology laboratory at Teaching hospital Jaffna. To maintain uniformity, sample analysis was done by registered MLTs at Teaching hospital Jaffna and measured by immuno histochemistry assay which is said to be the gold standard

test. Serum Vitamin D levels were analysed and were categorized as sufficient (more than 30 ng/ml), insufficient (20–30 ng /ml) and deficient (less than 20 ng/ml).

Study variables collected by using interviewer administered questionnaire. Data analysis was done using SPSS 26 (statistical package for social sciences) .Descriptive statistics such as mean with SD calculated and in addition Chi-square test used significance between groups. P value less than 0.05 was considered as significant. Frequency presented as percentage with 95% CI.CI was calculated by using WIN PEPI epidemiological software version 11.65(12).Bone Mineral Density Assessment Categorized based on Hip bone mineral density based on the WHO and International Osteoporosis Foundation dual-energy x-ray absorptiometry assessment diagnostic categories. T-score is the number of standard deviations below the mean value of the young healthy population (13, 14).

## **Results:**

Background characteristics: This study included 105 postmenopausal women. Mean age was 67.7 with minimum 33 and maximum 84 years. Twenty one participants are vegetarian (20%), 24 women (22.9%) reported walking as their main mode of transport whereas 3.8% used cycling. Furthermore seventy five participants (71.4%) reported adequate level of sun exposure (> 30minutes) and only 2 women reported using sunscreen(1.9%).Mean Vitamin D levels were 27.5 ng /ml with a range of 11.7–52.5 ng/ml. Out of 105 participants 77 had calcium level measured, mean calcium level was 3.50 with SD of 2.74, among them 16.9% had low level of calcium and 18.2% had high level of calcium (Table 1).

Table 1  
Basic Statistics of Vitamin D level among Participants

Variable	Statistics	Value
Vitamin D Level (ng/ml)	Mean	27.75
	Median	27.5
	Mode	25.2
	SD	8.09
	Skewness	0.43
	Minimum	11.7
	Maximum	52.5
Age	Mean	61.77
	SD	12.16
	Minimum	33
	Maximum	84
Vegetarian	Number (%)	21(20%)
Walking	Number (%)	24(22.9%)
Cycling	Number (%)	4(3.8%)
Adequate level Sun exposure(> 30minutes)	Number (%)	75(71.4%)
Using Sub screen	Number (%)	2(1.9%)
Calcium level mmol/l (N-77)	Mean	3.50
	Median	2.34
	SD	2.74
	Minimum	1.16
	Maximum	10.20
Calcium level range	Normal (Number (%))	50(64.9%;53.8–75.0)
	Low (Number (%))	13(16.9%;9.7–26.5)
	High (Number (%))	14(18.2%;10.7–28.0)

Prevalence: Vitamin D levels were adequate only in 36.2% (95%CI: 27.4–45.7) of women. Forty four percent had insufficient levels. Vitamin D deficiency was present in 19% (95%CI: 12.4–27.4) of

postmenopausal women. Cumulative prevalence of insufficient and deficient level of Vitamin D level was 63.8% (95%CI: 54.3–72.6) (Table 2 and Fig. 1). A positive correlation was observed between age and Vitamin D level (Pearson co efficient:  $r=0.225$ ,  $P=0.021$ ) among study participants.

Table 2  
Vitamin D Status among postmenopausal women with suspected osteoporosis

Vitamin D level	Number	Percentage with (95% CI)	Mean	SD	ANOVA Statistics
Sufficient Level(N = 38)	38	36.2(27.4–45.7)	36.26	5.43	Sum of Squares-5286.86 Df-2 Mean Squares-2643.43 P < 0.001
Insufficient level (20–30 ng/ml )(N = 47)	47	44.8(35.5–54.4)	25.41	2.62	
Deficient Level (< 20 ng/ml)(N = 20)	20	19(12.4–27.4)	17.09	2.36	
Cumulative Prevalence of deficiency and insufficiency	67	63.8(54.3–72.6)	27.75	8.09	

#### Food habits related to vitamin D

Among the 105 participants only 20% were vegetarian and 53% percentage of them consuming milk on average 3 days per week, 76.2% consuming fish on average 2 days per week, 64.8% consuming egg on average 1 day per week (Fig. 2 and Table 3). Mean Vitamin D level among vegetarian group was 28.54 but among non-vegetarian group level was 27.55( $P=0.615$ ).

Table 3  
Vitamin D rich dietary intake among participants

Vitamin D rich food	Number	Percentage with 95%CI	Number of days in week(mean)
Egg	68	64.8(55.5–73.4)	1.32
Fish	80	76.2(67.4–83.6)	2.39
Milk	53	50.5(41.0–60.0)	3.28
Dairy products	82	78.1(69.4–85.2)	--

#### Symptoms

Commonly reported vitamin deficiency symptoms are summarised in Table 4. Fifty eight postmenopausal women reported bone pain paraesthesia (57.1%) followed by bone pain (55.2%), easy fatigability (54.3%), Malaise (51.4%), muscle cramps (43.8%) and proximal myopathy (40.0%). Further Comparison of musculoskeletal symptoms between group with sufficient level of vitamin D and group of insufficient and deficient level of vitamin D level showed statistically not significant results( $P > 0.05$ ) (Table 5).

Table 4  
Common musculoskeletal symptoms among  
postmenopausal symptoms

Symptoms	Number	Percentage with 95% CI
Bone pain	58	55.2(45.6–64.5)
Easy Fatigability	57	54.3(44.7–63.6)
Malaise	54	51.4(41.9–60.9)
Muscle cramps	46	43.8(34.6–53.4)
Paraesthesia	60	57.1(47.5–66.4)
Proximal Myopathy	42	40.0(31.0-49.6)

Table 5

Comparison of musculoskeletal symptoms between group with sufficient level of vitamin D and group of insufficient and deficient level of vitamin D level

Symptoms	Sufficient level of Vitamin D	Insufficient & deficient level of vitamin D	P Value
	No (percentage)	No (Percentage)	
Bone Pain	18(31%)	40(69.0%)	P = 0.222
Easy Fatigability	22(38.6%)	35(61.4%)	P = 0.576
Malaise	16(29.6%)	38(70.4%)	P = 0.150
Muscle cramps	16(34.8%)	30(65.2%)	P = 0.791
Paraesthesia	24(40.0%)	36(60.0%)	P = 0.348
Proximal Myopathy	19(45.2%)	23(54.8%)	P = 0.115

**Co-Morbid conditions**

Comorbid conditions hypertension (44.8%), osteoarthritis (41.9%), psychiatric conditions (30.5%), IHD (11.4%), rheumatoid arthritis (3.8%) and malignancy (2.9%) were observed among participants (Fig. 3) No one had Type 1 Diabetes Mellitus nor TB and further analysis showed no association with vitamin D and psychiatric conditions (P=0.081) nor with any other comorbid conditions studied(P > 0.05)(Table 7).

Table 7  
Comparison of Vitamin D level with selected factors

Factors		Number	Mean Vitamin D Level with SD	Statistics
Adequate sun exposure	Yes	75	28.55+_8.37	T = 1.61,P-0.110
	No	30	25.75+_7.26	
Walking	Yes	24	27.95+_9.40	T-0.135 P-0.893
	no	81	27.69_-7.72	
Vegetarian Status	Vegetarian	21	28.54+_9.45	T-0.5,P-0.615
	Non Vegetarian	84	27.55+_7.76	
Psychiatric Condition	Yes	32	25.63+_7.53	T-1.794,P-0.076
	No	73	28.68+_8.20	
Osteoporosis of Hip	Yes	27	29.83+_10.38	T-0.903,P-0.370
	No	44	27.92+_7.61	
Osteoarthritis	Yes	44	27.08+_8.67	T- -0.721,P-0.473
	No	61	28.23+_7.68	
Milk	Yes	53	26.92+_7.82	T- -1.059,P-0.292
	No	52	28.59+_8.35	
Egg	Yes	68	27.35+_7.35	T-0.678,P-0.49
	No	37	28.48+_9.36	
Fish	Yes	80	27.66+_7.72	T- -0/193,P-0.848
	No	25	28.02+_9.33	
Figure 1				

**Bone Density assessment**

Among 105 participants 71 completed DEXA scan for bone density assessment (66.7%) (Table 6).But postmenopausal women with a Vertebrae T score within osteoporosis range was high 46 (64.8%) and in the osteopenia range was 24 (33.8%).Also worth to note that 7 participants (6.7%) had a prosthesis in situ. Further bivariate analysis showed no significant association between vitamin D deficiency and different categories of bone mineral density (P > 0.05).Postmenopausal women with Vertebrae T score in osteoporosis range was high 46 (64.8%) and vertebral Z score showed a significant correlation with vitamin D level(r-0.252, P-0.034). Mean level of Vitamin D among women with osteoporosis range was 29.8 whereas mean level among non-osteoporosis range 27.92(P-0.370) (Table 7).

Table 6  
BONE MINERAL DENSITY ASSESSMENT RESULTS

Category Hip bone mineral density	Number	Percentage with 95% CI
Normal T-score of - 1 or higher	17	24%(15.1–34.9)
Low bone mass (osteopenia) T-score between - 1 and - 2.5	27	38%(27.3–49.7)
Osteoporosis T-score of - 2.5 or lower	27	38%(27.3–49.7)

## Discussion

Current study examined 25(OH)-D levels to determine the prevalence of vitamin D deficiency or insufficiency and also studied selected associated factors among post-menopausal women with suspected osteoporosis. Bone density assessment was carried out among 77 participants. To the best of our knowledge, this is the first study in our region examined vitamin D status among post-menopausal women even though several studies examined vitamin D level in general population. Gunawardane et.al found that Vitamin D deficiency was 57.2% (< 20 ng/ml), vitamin D insufficiency 31%(20–30 ng/ml) and the cumulative prevalence of deficiency & insufficiency was 88.2% (11) and high prevalence was found among young adults (age 18 – 14)(4). In the present study, the mean 25(OH)-D concentration was 27.5 ng /ml ± 8.09 ng/mL and 19% (95%CI: 12.4–27.4) had vitamin D deficiency (25(OH)-D concentration < 20 ng/mL). Overall, we have found that cumulative deficiency and insufficiency of vitamin D was common, 63.8% (95%CI: 54.3–72.6). But a study among 123 postmenopausal women evaluated in Romania reported 91.9% of them had 25OHD serum levels below 30 ng/ml (15) and likewise a study from Pakistan among 200 postmenopausal women presented to Orthopaedics and Gynaecology outpatient departments of Khyber Teaching Hospital showed that prevalence of vitamin D deficiency was 59% and 22% had insufficient levels (10). Almost similar findings revealed in a study from North India which showed vitamin D deficiency among 62% of subjects (16). Even though direct comparison among these studies is difficult, relatively low prevalence among our sample could be due to a good exposure of sunlight a natural source of vitamin D throughout the year as northern Sri Lanka is located in the middle of the tropical Indian subcontinent. Historically, most of the requirement of vitamin D is from sunlight-induced manufacture of cholecalciferol by skin (7). Seventy five of participants (71.4%) reported adequate level of sun exposure (> 30minutes). Authors of the study conducted in Pakistan reported that the use of sun protection, wearing purdah and in general women do not go out of their home were possible explanations for low vitamin D levels in their population(10) however in Sri Lankan culture there is neither observation of purdah nor any cultural restriction for women to go out from their homes to support our findings.

Many studies have showed an increasing level of vitamin D deficiency with age [17, 18]. The main reason would be that the elders would have decreased concentrations of precursor of vitamin D3 (7-dehydrocholesterol) that leads to decreased ability to make vitamin D by skin [7]. However, in the present study, vitamin D level showed positive correlation with advancing age (r=0.225, P=0.021). Again the

amount of sun exposure is a possible factor contributed to this findings. Young women tend to spend more time indoors with their occupation while a traditional house wife in Jaffna and the elderly could have spent more time outdoors. This finding was comparable to some previous studies (19, 20) and further a study in Thailand showed young people may use more sunscreen because of cosmetic reasons (19), however this practice was not observed in this study as only two participants (1.9%) reported to use sunscreen. In terms of dietary sources, common non-fortified food sources include breast milk, cod liver oil, Egg yolk, Fish such Mackerel (canned), Salmon (canned), Salmon (fresh, farmed), Salmon (fresh, wild), Sardines (canned) Tuna (canned) cat fish, yogurt, margarine, cereals and mushroom (1,21). Among 105 participants 53% percentage of them consuming milk on average 3 days per week, 76.2% consuming fish on average 2 days per week, 64.8% consuming egg on average 1 day per week. But no significant difference in vitamin d level is observed who consuming above vitamin D rich resources and not consuming. This indicates dietary source plays a pivotal role.

Vitamin D deficiency symptoms are rather nonspecific which include back pain (non-radiating), arthralgia, proximal muscle weakness, headache, fatigue, altered mood, insomnia and hair loss (22, 23). In our study 57.1% postmenopausal women reported bone pain paraesthesia followed by bone pain (55.2%), easy fatigability (54.3%), Malaise (51.4%), muscle cramps (43.8%) and proximal myopathy (40.0%). But there was no statistical significance observed at 5% level when comparing symptoms among groups with vitamin D deficiency and with adequate level of Vitamin D. This could be due to the fact that the symptoms are non-specific and are common in post-menopausal women even without vitamin D efficiency or might also be associated with other age related co morbid conditions such as osteoarthritis. For example among 105 participants 41.9% had osteoarthritis and 3.8% had rheumatoid arthritis. The study also investigated the relationship between vitamin D deficiency and menopausal symptoms and concluded that the data is not supportive of vitamin D status is associated with menopause related symptoms (24).

Vitamin D deficiency reported to be high in prevalence among inpatients with mental illness in previous studies (25,26). Thirty percent of sample had psychiatric conditions and mean vitamin D level (25.63 ng/ml) less among the participants with psychiatric conditions compare to who are not having psychiatric conditions (28.68 ng/ml). But this results not showed statistically significant (P=0.076).

It is well known fact that prevalence of osteoporosis is common among postmenopausal women and several risk factors implicated for this high prevalence including vitamin D deficiency. Falls and risk of fractures well associated with vitamin D deficiency among post-menopausal osteoporosis (5). Out of 105 post-menopausal women suspected with osteoporosis 71 (66.7%) completed bone density assessment and results revealed osteoporosis range was 38% (27.3–49.7) and same amount showed osteopenia range. But Vertebrae T score in osteoporosis range was high 46 (64.8%) and osteopenia range were 24 (33.8%). Present study failed to show association with different categories of t scores with vitamin D deficiency except Vertebral Z score showed a significant correlation with vitamin D level (r=0.252, P=0.034). This results could be due to a small size and this study not designed to show this association (not comparative study). But it is a well-known fact that vitamin D deficiency is more prevalent among post-

menopausal women and supplement of vitamin D might prevent of falls and fractures specially with people with osteoporosis(5,27,28).

But the appropriate cut off level to treat vitamin D deficiency or insufficiency is a dilemma (8). But to maintain of minimum required vitamin D level (30 to 32 ng /mL) requires 2,200 to 3,000 IU/d from all available resources including sun exposure, food and supplements(29,30,31).Further age specific recommendations suggest 200 IU of vitamin D daily from birth to age 50, 400 IU/d for age 51 to 70 years, and 600 IU/d for those age 70 years and above (32,33) This recommendation presume that usual sources of vitamin D such as sun exposure and food are not adequate (30,31).It is an observation that vitamin D supplements for all post-menopausal women may leads to hyper vitaminosis. But supplementation with vitamin D for post-menopausal women with vitamin deficiency is beneficial in preventing osteoporosis especially to prevent complications of fall and fracture (11, 15).Since high prevalence of vitamin D deficiency among post-menopausal women with suspected osteoporosis shown by this study, it emphasize the fact that early screening for suboptimal vitamin D level among the above group is crucial to prevent osteoporotic fractures and falls.

Limitations:

The strengths of this study are that this is the first study in Sri Lanka specifically examined the prevalence vitamin D deficiency among post-menopausal women with suspected osteoporosis and explored some protective factors like sun exposure. Vitamin D level measured by immuno histochemistry method which quoted as standard method. However, some limitations of the study includes that we did not obtain information about some anthropological measurements such as BMI; physical activity; socioeconomic status and the influence of seasonal effects and climatic changes on vitamin D deficiency. Also sample size estimated only with the aim of estimating prevalence but validity of the study would have been improved if we had an estimated sample size for sub analysis. Some participants (33.3%) did not complete bone density assessments which could be the reason for some factors not showed statistically significant association even though some relationship observed in psychiatric condition, sun exposure, z/t scores of vertebrae and vitamin D level.

## Conclusions

As this study demonstrated relatively high prevalence of vitamin D deficiency among post-menopausal women with suspected osteoporosis, treatment of vitamin D deficiency with supplementation is essential to prevent fractures in whom with vitamin D deficiency as contribution by dietary sources would not play a significant role. In addition, it is essential to correct vitamin D deficiency with supplementation when initiating treatment for osteoporosis in particular the bisphosphonate therapy. The authors recommend routine testing of vitamin D in postmenopausal women of this population in order to make concrete decisions to initiate Vitamin D supplements as a routine.

## Declarations

Ethics approval and consent to participate Ethical clearance was obtained from the Ethical Review Committee of the Faculty of Medicine, University of Jaffna. Permission to carry out this study was obtained from the Director, TH, Jaffna and written consent was obtained from the participants after explaining the purpose and the nature of the study

### **Consent to publish**

Not applicable as there is no individual data in any form

### **Availability of data and material**

Data can be provided on request from NR or NS

### **Competing interests**

The authors declare that none of the authors has competing interests.

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This study was self-funded study and Director Teaching Hospital allowed to use the chemical needed for vitamin D testing from teaching hospital Jaffna

### **Authors' contributions**

NS, VK, MA and TK conceived the study. NS, VK and KA involved in the data and sample collection. NR did analysis. NR, NS and TK wrote the manuscript. All authors read and approved the manuscript.

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## Abbreviations

DEXA -dual-energy x-ray absorptiometry, SPSS- Statistical Package for the Social Sciences, SD-Standard Deviation, CI-Confidence Interval, IHD-Ischaemic Heart Disease, TB-Tuberculosis

## Figures

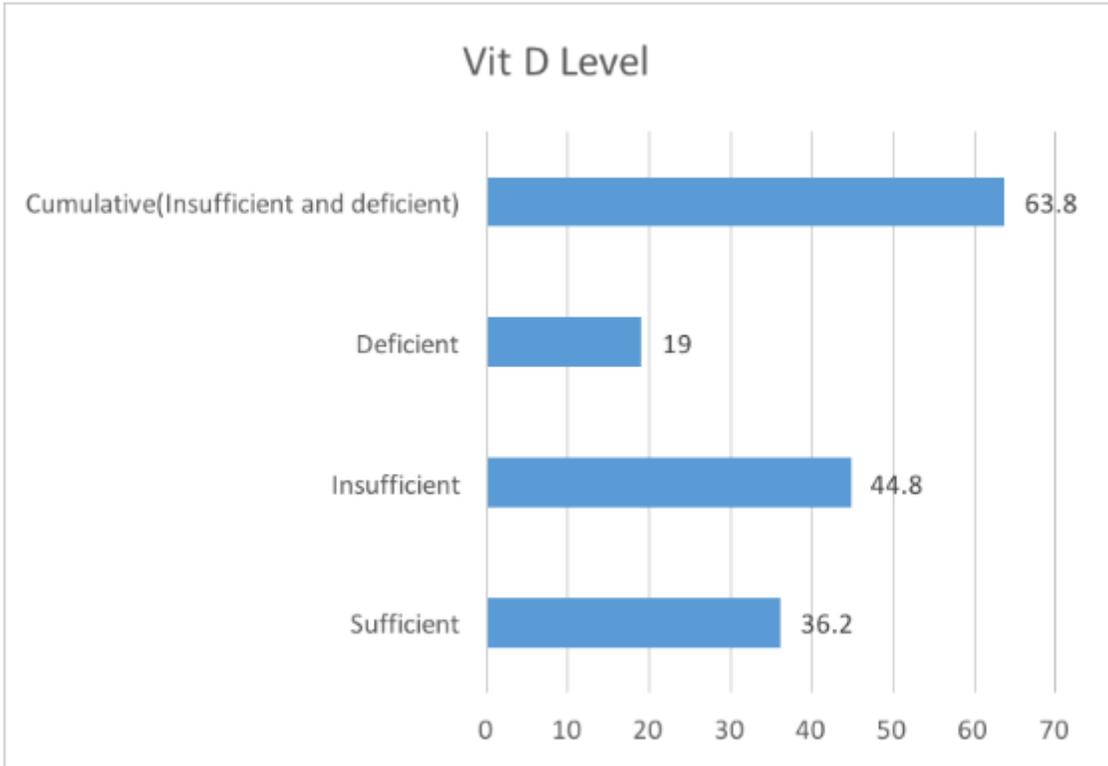


Figure 1

Prevalence of vitamin d status

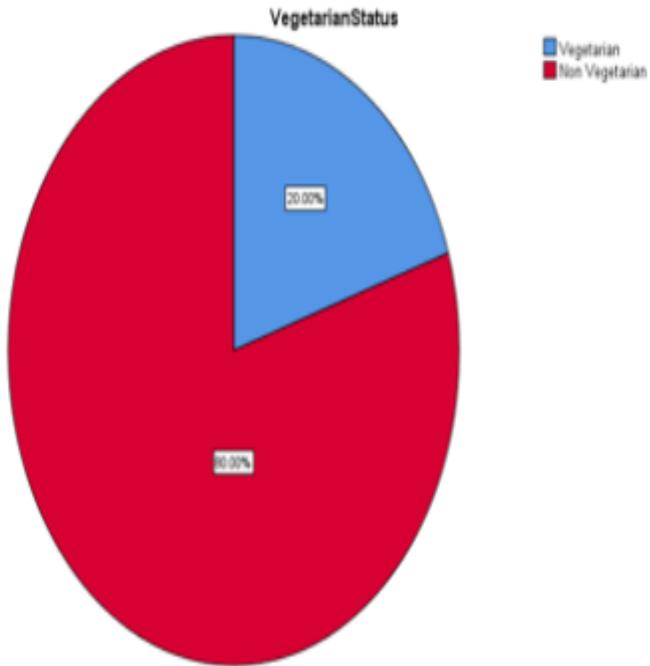
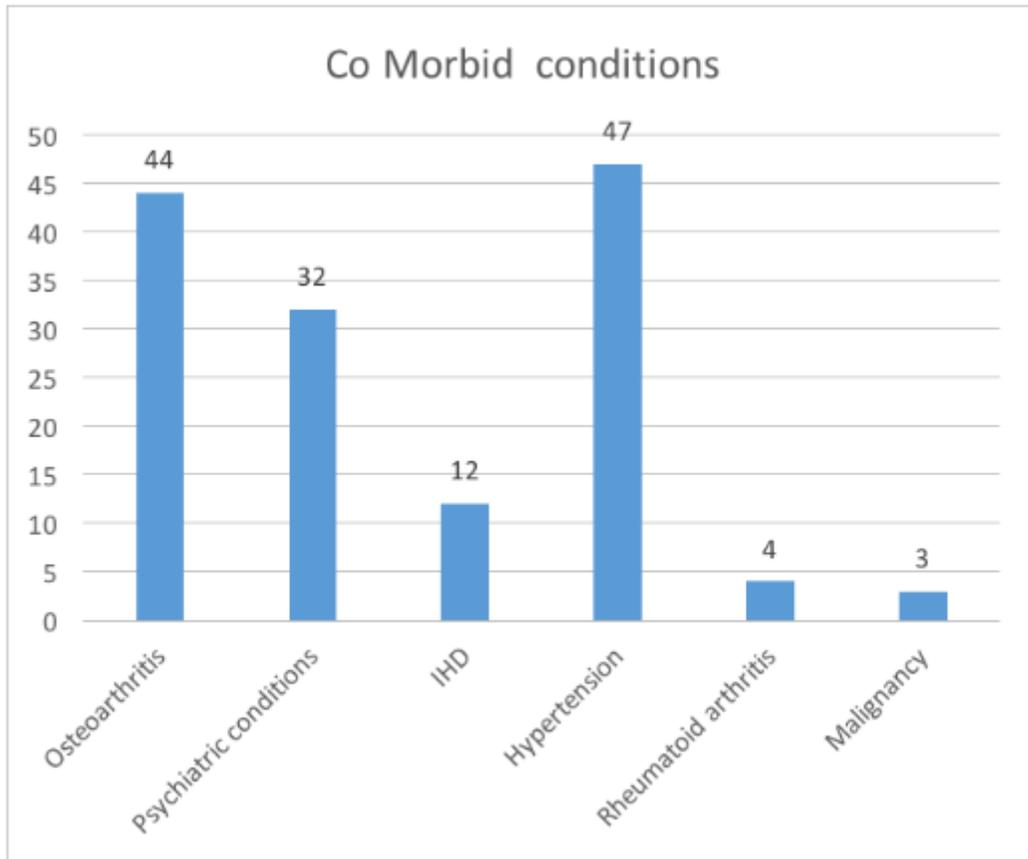


Figure 2

## Food Habit of participants



**Figure 3**

Co Morbid conditions among participants