

## A Study of Serum Vitamin D Levels in Newly Diagnosed Breast Cancer

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**Abstract:** Vitamin D is found to have anti neoplastic properties in Breast carcinoma and proven to have improved survival rate as evidenced by literature. Serum levels of Vitamin D in patients with breast carcinoma is found to have a significant impact on its incidence worldwide as evidenced by various laboratory and epidemiological studies. It is postulated that breast cells have Vitamin D receptor in their nuclei and polymorphism of genes for these Vitamin D receptor results in increased risk of breast cancer.

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### I. Introduction

Globally breast carcinoma is the most common carcinoma among all females. In India there is a rising trend in the incidence of Breast carcinoma across all population overtaking the incidence of cervical carcinoma. Several factors like age, menstrual status, nulliparity, lactation, family history, serum estrogen levels, body mass index etc., have a significant role on its incidence. Recently, Vitamin D is found to have anti neoplastic properties in Breast carcinoma and proven to have improved survival rate as evidenced by literature<sup>3, 4, 5</sup>. Serum levels of Vitamin D in patients with breast carcinoma is found to have a significant impact on its incidence worldwide as evidenced by various laboratory and epidemiological studies<sup>3,4,5</sup>.

Vitamin D is available as cholecalciferol (D3) from animal source, from sunlight exposure and as ergocalciferol (D2) from plant sources<sup>6</sup>. Majority of vitamin D is synthesized from exposure to sunlight. Vitamin D is hydroxylated in the liver by 25 hydroxylase to 25(OH) Vitamin D and further it is hydroxylated in the kidneys by 1 alpha hydroxylase into 1,25, Di Hydroxy vitamin D - Biologically active form. The concentration of 25 Hydroxy Vitamin D depends on dietary sources and sunlight exposure and hence it is a good indicator of Vitamin D stores. The activation of vitamin D can also occur in other tissues like Breast, Colon and Prostate which expresses 1 alpha hydroxylase and vitamin D receptor (VDR) to regulate cell turn over<sup>6, 8, 8</sup>. Vitamin D exhibits anti neoplastic effects by binding with VDR to form a nuclear receptor ligand complex. This in turn expresses target genes like *p 21*, *p 27*, *c-fos* and *c-myc*<sup>9</sup>.

Two different mechanisms are attributed to these anti carcinogenic effects of vitamin D. 'The Endocrine pathway' involves 1,25 (OH)<sub>2</sub> D which reaches breast tissue and binds with VDR and to specific DNA sequences to inhibit the cellular proliferation, neo angiogenesis and induces cell differentiation along with apoptosis<sup>6</sup>.

'The Autocrine pathway' involves circulating 25(OH) D which is catalysed to 1, 25 (OH)<sub>2</sub> D by the 1 alpha hydroxylase present in breast epithelium. 1, 25 (OH)<sub>2</sub> D in turn binds to VDR and regulates the cell proliferation, differentiation and apoptosis<sup>6</sup>.

Numerous research works has been undertaken to find out this association between the levels of vitamin D and breast cancer risk.

Various studies have also suggested that the genetic VDR polymorphisms is also linked to breast cancer due to its altered effects on the VDR gene expressions like *FOK1*, *BSM1*, *Apa1*, *Taq1* and Poly (A)<sup>10</sup>.

But for unknown reasons there are many inconsistencies in literature and needs to be understood better<sup>7</sup>. There are few studies being conducted in India and native population as well. Hence this study has been proposed to reveal the uncertainties in literature and to establish a significant association of the serum levels of Vitamin D in cases diagnosed with carcinoma breast in our institution.

### II. Aim & Objectives

TO EVALUATE THE PREVALENCE OF SERUM VITAMIN D LEVELS IN CARCINOMA BREAST.

METHODOLOGY: Observational study.

SOURCE OF DATA:

Our study is an observational study on serum vitamin D levels in newly diagnosed patients with carcinoma breast. A total of 90 patients were selected for our study during at Government Rajaji Hospital in the Department of General Surgery, Madurai.

**ELIGIBILITY CRITERIA:**

**INCLUSION CRITERIA:**

- Newly diagnosed patients with histologically proven Breast Carcinoma.
- All Patients who had consented to be included in the study as per the designed proforma.
- Age criteria <45 years.

**EXCLUSION CRITERIA:**

- Patients not consented to be included in the study.
- Patients with deranged hepatic and renal parameters.
- Patients who underwent chemo or radio therapy.
- Patients on Vitamin D and Calcium supplements.

**SELECTION OF STUDY SUBJECTS:**

Patients who full fill the inclusion criteria and who were admitted for treatment in the department of General Surgery, Madurai medical college Hospital.

**METHOD OF COLLECTION OF DATA:**

- All the patients who had fulfilled our study criteria were selected.
- A complete data regarding the clinical history, clinical examination, menstrual status, BMI was collected.
- A detailed biochemical investigation (Serum vitamin D, Serum Calcium, Blood urea, Serum creatinine) was done.
- Radiograph of long bones and spine were also analysed to rule out osteopenia.
- Histological typing and Clinical staging were also done as per standard protocol.

**III. Results And Discussion**

In our study about 90 cases of newly diagnosed breast carcinoma were analysed by measuring serum Vitamin D levels and other relevant investigations.

Hence our study mainly focuses on the Prevalence of low serum Vitamin D levels in newly diagnosed patients with Carcinoma Breast in our population.

Serum vitamin D levels were estimated by Chemiluminescence method.

Our study in 90 cases of newly diagnosed carcinoma breast, the levels of Vitamin D was analysed against the following variables.

- Age.
- Parity.
- BMI.
- Menstrual status.
- Clinical staging

**AGE:**

- The mean age of our study group was 40.58 years.
- From table no.1: 74% i.e 67 out of 90 cases were found to have low levels of Serum Vitamin D.
- From figure no.1: It is evident that, 80% i.e. 36 out of 45 cases who were above 40 years had i.e 36 out of 45 had low levels of Vitamin D.

AGE	VIT D LEVEL(mg/ml)		
	Deficiency(<20)	Sub Optimal(20-39)	Optimal(>40)
<35(8)	2	4	2
36 - 40(37)	12	13	12
41 - 45(44)	24	11	9
<45(1)	0	1	0
Total	38	29	23

Table 1: Age and serum vitamin D level.

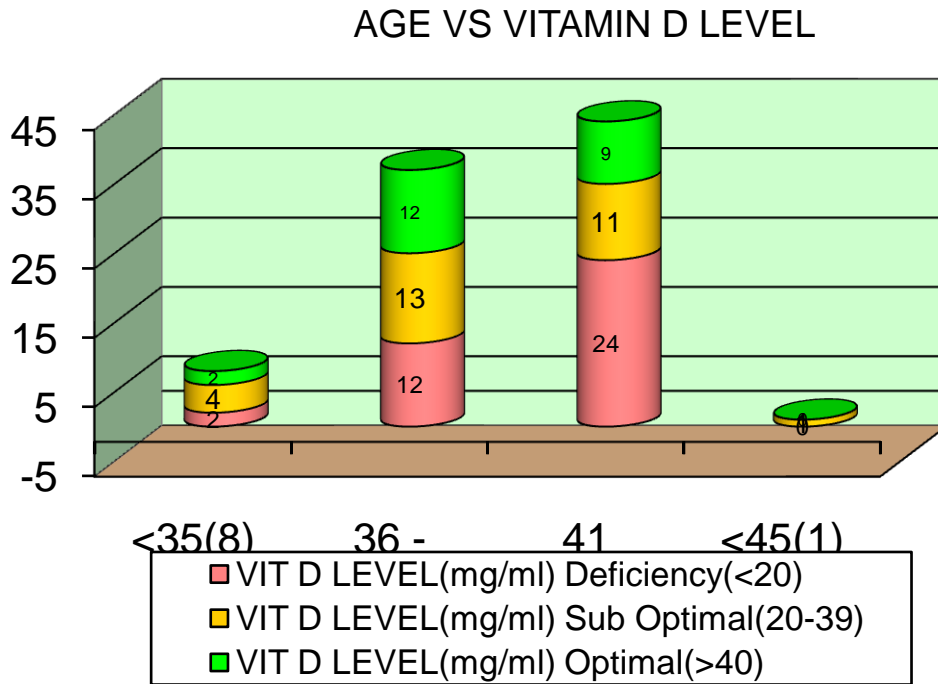


Fig.1 – Age vs Vitamin D level

**PARITY:**

- In our study multiparous women constituted the majority of the group.
- From the table no. 2: Among them 76% i.e 52 out of 68 cases had low levels of vitamin D.
- From the figure no. 2: In nulliparous women only 68% i.e 15 out of 22 cases had low levels of serum Vitamin D.

PARITY	VIT D LEVEL(mg/ml)		
	Deficiency(<20)	Sub Optimal(20-39)	Optimal(>40)
Multipara(68)	28	24	16
Nullipara(22)	10	5	7
Total	38	29	23

Table 2: Parity and Vitamin D level.

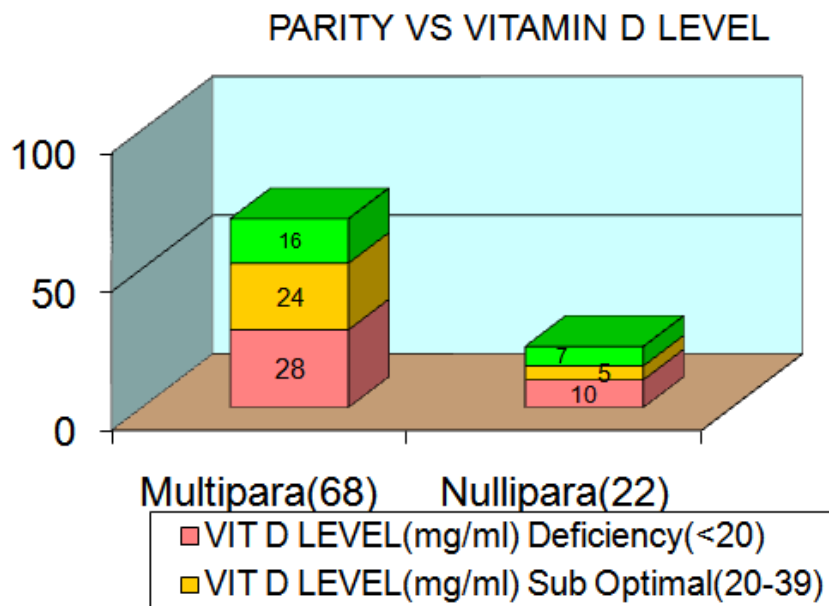


Fig. 2 : Parity vs Vitamin D levels.

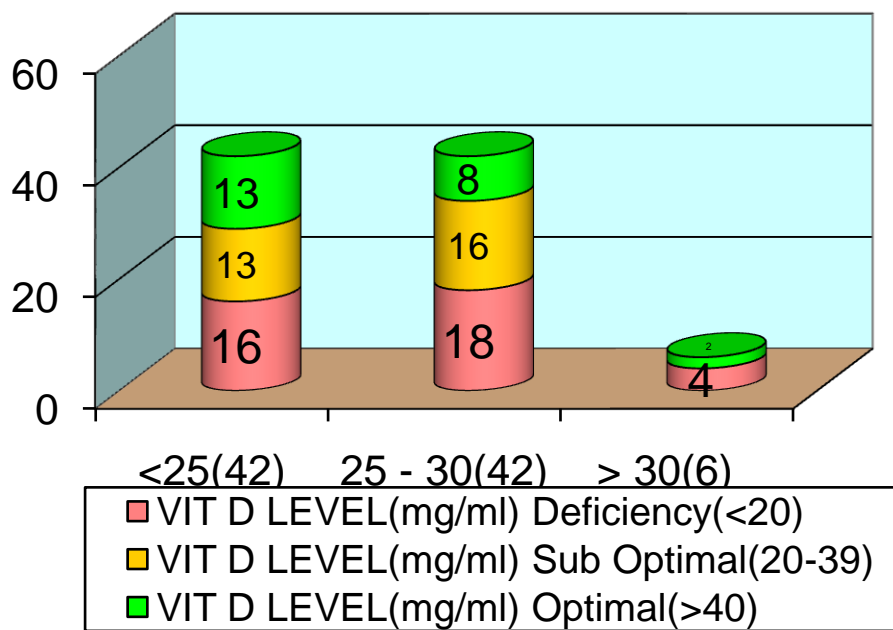
**BODY MASS INDEX:**

- BMI was high in majority of our subjects i.e 48 out of 90 cases were overweight.
- From table no.3 : In our study group 80% i.e 38 out of 48 cases had BMI more than 25.
- From figure no.3 : 80% i.e 38 out of 48 individuals who were over weight had low level of serum vitamin D.

BMI	VIT D LEVEL(mg/ml)		
	Deficiency(<20)	Sub Optimal(20-39)	Optimal(≥40)
<25(42)	16	13	13
25 - 30(42)	18	16	8
> 30(6)	4	0	2

**Table.3:** Body mass index and Serum vitamin D levels.

**BMI VS VITAMIN LEVEL**



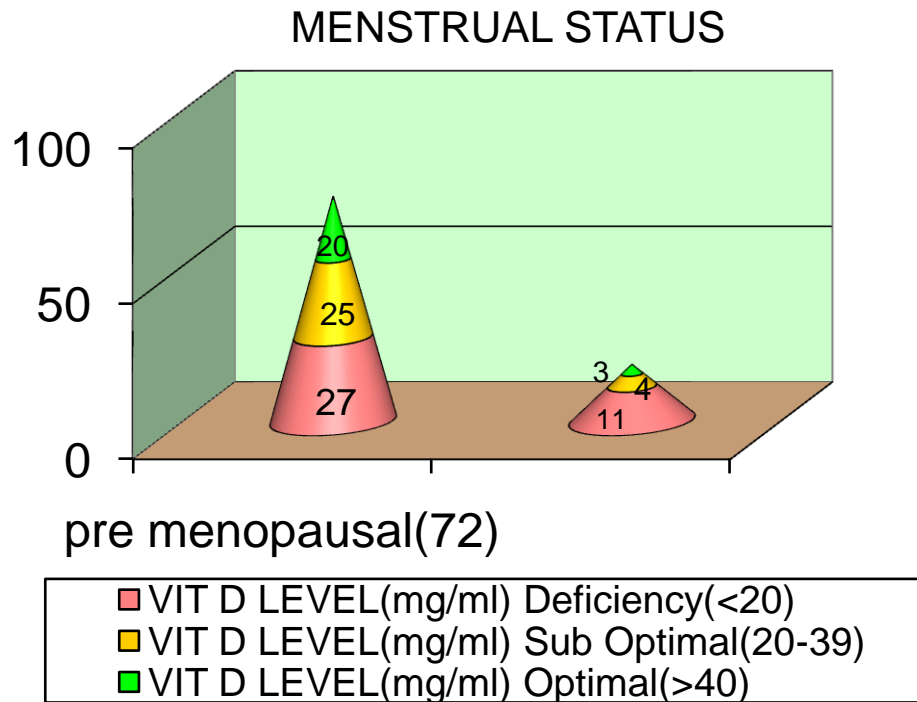
**Fig.3:** BMI vs Serum Vitamin D levels.

**MENSTRUAL STATUS:**

- From table no.4: 80% of our study group i.e 72 out of 90 cases belonged to premenopausal status.
- Among the remaining 20% i.e 18 out of 90 case also had low levels of vitamin D.
- From figure no.4: among the premenopausal women with carcinoma breast 72% i.e 52 out of 72 cases have low serum vitamin D levels.

MENSTRUAL STATUS	VIT D LEVEL(mg/ml)		
	Deficiency(<20)	Sub Optimal(20-39)	Optimal(≥40)
pre menopausal(72)	27	25	20
post menopausal(18)	11	4	3
Total	38	29	23

**Table. 4:** Menstrual status vs Serum Vitamin D levels.



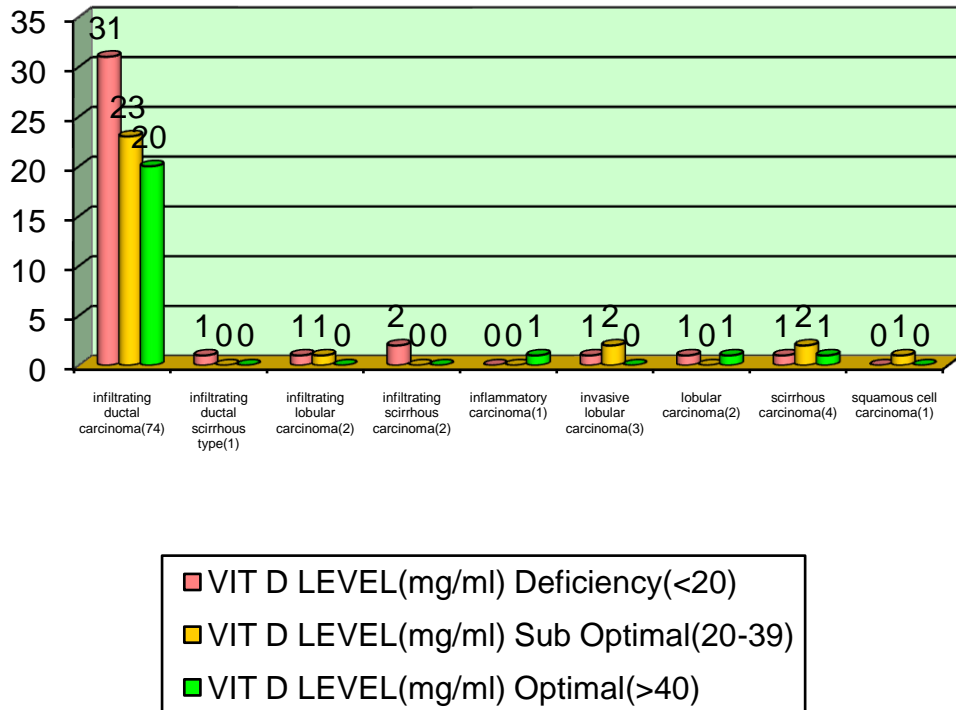
**Fig.4:** Menstrual status vs Serum Vitamin D levels.

**HISTOLOGICAL TYPE:**

- From table no.5: Infiltrating ductal carcinoma was the commonest type of breast carcinoma detected in our study population.
- From table no.5: 74% i.e 67 out of 90 cases had low levels of serum Vitamin D.
- From figure no.5: 72% i.e 54 out of 74 cases of infiltrating ductal carcinoma had low levels of serum vitamin D.

BIOPSY	VIT D LEVEL(mg/ml)		
	Deficiency(<20)	Sub Optimal(20-39)	Optimal(≥40)
infiltrating ductal carcinoma(74)	31	23	20
infiltrating ductal scirrhus type(1)	1	0	0
infiltrating lobular carcinoma(2)	1	1	0
infiltrating scirrhus carcinoma(2)	2	0	0
inflammatory carcinoma(1)	0	0	1
invasive lobular carcinoma(3)	1	2	0
lobular carcinoma(2)	1	0	1
scirrhus carcinoma(4)	1	2	1
squamous cell carcinoma(1)	0	1	0

### Histological type VS Vitamin D level



**Table & Fig.5:** Histological typing and Vitamin D levels.

**CLINICAL STAGING:**

- In our study group of 90 cases 30 were diagnosed at stage II, 54 cases were diagnosed at stage III and 6 cases were diagnosed at stage IV.
- From figure no.6: 100% i.e 6 out of 6 cases in stage IV were found to have low levels of serum Vitamin D.
- From figure no.6: 80% i.e 43 out of 54 cases in stage III were found to have low levels of serum Vitamin D.
- From figure no.6: 60% i.e 18 out of 30 cases in stage II were found to have low levels of serum Vitamin D.
- Hence the prevalence of Vitamin D deficiency is high as the disease advances.

STAGE	VIT D LEVEL(mg/ml)		
	Deficiency(<20)	Sub Optimal(20-39)	Optimal(≥40)
II(30)	9	9	12
III(54)	25	18	11
IV(6)	4	2	0
Total	38	29	23

**Table.6:** Clinical stage vs Vitamin D level.

## CLINICAL STAGE VS VITAMIN D LEVEL

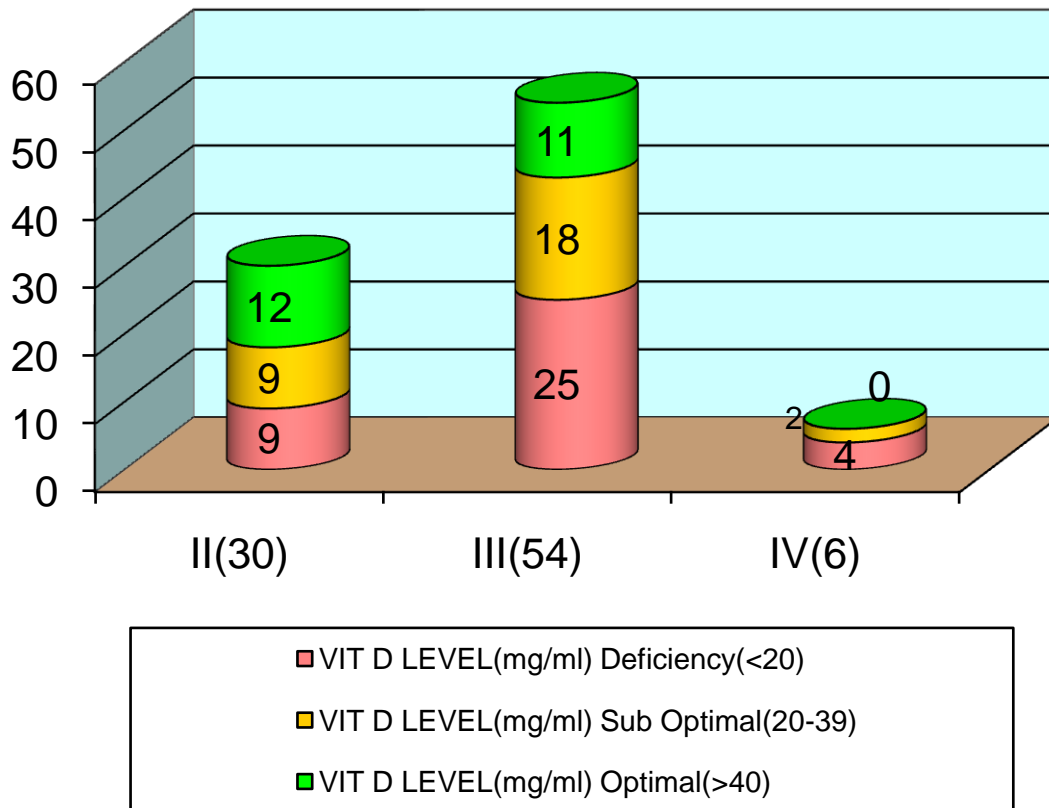


Fig.6: Clinical Stage vs Vitamin D level.

### IV. Conclusion

- From the Study on 90 cases of newly diagnosed breast carcinoma, we conclude the following based on our observation.
- Low levels of serum Vitamin D was found in 75% of all cases i.e in every 3 out of 4 cases.
- A low level of Vitamin D was found to be more prevalent in women more than 40 years of age.
- A low level of Vitamin D was also apparent in women with BMI >25.
- In our population Vitamin D levels were found to be low in premenopausal women.
- Strikingly in our study the prevalence of Vitamin D deficiency is high as the disease advances.

This study was conducted after various literatures stating the relationship between serum vitamin D levels and breast carcinoma. In a study conducted by Yao et al in 2001, it has been found that the relationship between vitamin D levels and the risk of breast cancer was stronger among premenopausal women. Other studies by Linn et al and colleagues also found the association between low serum vitamin D levels and breast carcinoma in premenopausal women. Our study group was restricted to women less than 45 years and 80% of them are premenopausal and were detected with low vitamin D levels which correlate with the literature.

As per the study published by Peppone et al in the Journal Of Clinical Oncology, patients with suboptimal levels of vitamin D levels were affected with more aggressive profile. Another study by Thanasitthichai et al and Rainville et al in 2009 noted that vitamin D deficiency is common in all breast cancer patients and is particularly prevalent in those with triple negative or basal like tumours the most aggressive form. Our study also showed patients who presented with stage III disease had low serum vitamin D levels as compared to patients with stage II disease.

This observational study suggests that vitamin D deficiency is common in breast cancer patients and low vitamin D status enhances the risk for disease development or progression. Even though there is no rigorous proof of benefits of supplemental vitamin D, correction of vitamin D deficiency can be done by giving prophylaxis especially for women with high risk for breast cancer.

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