Section: Medical Oncology

Original Research Article

TO EVALUATE THE EFFECT OF VITAMIN D SUPPLEMENTATION ON THE ABSOLUTE CELL COUNTS IN CANCER PATIENTS UNDERGOING CHEMOTHERAPY

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Abstract

Background: Multiple clinico-epidemiological investigations have shown a positive association between decreased levels of blood 25-hydroxy Vitamin D [25 (OH) D] and an increased susceptibility to colorectal, breast, ovarian, and prostate cancers. The aim of this research is to evaluate the Effect of Vitamin D Supplementation on the Absolute Cell Counts in Cancer Patients Undergoing Chemotherapy. **Materials and Methods:** The research included a cohort study of 120 individuals who has been diagnosed with different types of cancer (colorectal, breast, ovarian, and prostate cancers) undergoing chemotherapy at a tertiary care hospital. Of the 120 patients, 60 were randomly assigned to the study group, and 60 to the control group: Study Group (60 patients): Received Vitamin D3 supplementation. Control Group (60 patients): Did not receive Vitamin D3 supplementation. Later there absolute cell counts were notes and correlated. **Result:** The baseline Vitamin D levels were comparable across the groups, with an average of around 15 ng/mL (p=0.70). After six months of Vitamin D administration, there were significant increases in all assessed absolute cell counts within the study group. The absolute neutrophil count (ANC) rose from an average of 3000 ± 500 cells/µL to 4500 ± 600 cells/µL (p<0.001). The absolute lymphocyte count (ALC) increased from 1800 ± 300 cells/µL to 2500 ± 400 cells/µL (p<0.001). The absolute monocyte count (AMC) increased significantly from 400 ± 50 cells/µL to 550 ± 60 cells/µL (p<0.001). The absolute eosinophil count (AEC) rose from 200 ± 30 cells/µL to 250 ± 35 cells/µL (p<0.001). After a period of six months supplementation, the study group exhibited markedly elevated absolute cell counts in comparison to the control group. The average absolute neutrophil count (ANC) in the study group was 4500 ± 600 cells per microliter (µL), which was considerably higher than the control group's ANC of 3200 ± 510 cells/µL (p<0.001). In the study group, the absolute lymphocyte count (ALC) was 2500 ± 400 cells/µL, whereas in the control group it was 1800 ± 310 cells/µL (p<0.001). The average monocyte count (AMC) in the study group was 550 ± 60 cells/µL, which was considerably higher than the control group's average of 400 ± 50 cells/µL (p<0.001). In the study group, the AEC was 250 ± 35 cells/µL compared to 220 ± 32 cells/µL in the control group (p<0.001). **Conclusion:** Our research concludes that Vitamin D supplementation has a substantial positive effect on absolute cell counts in cancer patients receiving chemotherapy. This indicates improved immune function and possible therapeutic advantages. These findings endorse the incorporation of Vitamin D monitoring and supplementation with regular cancer treatment to enhance their overall results.

INTRODUCTION

Vitamin D is a lipid-soluble steroid hormone that plays a crucial role in regulating the metabolism of calcium and phosphate, as well as maintaining bone health.[1] The nuclear receptor's signaling affects several cellular pathways related to innate and adaptive immune responses, tissue growth, programmed cell death, and cell specialization.[2] Hypovitaminosis D, characterized by low levels of 25-hydroxyvitamin D (25(OH) D), is often seen in individuals experiencing severe illness. This

condition impacts around 40-70% of patients who get treatment in medical, surgical, or mixed intensive care units (ICUs) without any specific selection criteria.[3] Multiple observational studies have shown a correlation between a lack of 25(OH) D with negative outcomes after receiving therapy in the intensive care unit (ICU), such as longer stays in hospital, higher rates of illness, and increased death.[4-7] Although the exact processes are not completely known, hypovitaminosis D seems to combine with other risk factors to contribute to organ dysfunction in critical circumstances like sepsis,[8] acute respiratory distress syndrome,[9] and acute kidney injury.[10]

The prevalence of active cancer is rising globally as a result of aging populations, better diagnostic methods, improvements in supportive care, and the development of more potent antineoplastic treatments.[11] Furthermore, these conditions have a significant effect on critical care, since 1 in every 6 patients receiving treatment in European Intensive Care Units (ICUs) now has a diagnosis of cancer.[12] Moreover, the rates of admission to the intensive care unit (ICU) may reach up to 20% while treating some severe cancers, such as acute leukemia.[13] Most cancer patients are sent to the Intensive Care Unit (ICU) after planned surgery and may be treated as part of a regular routine. However, patients who are hospitalized due to medical or surgical difficulties often have severe organ malfunction and are at a significant risk of death.[14] Many cancer patients with life-threatening complications are now recommended to get full-code ICU treatment. As per studies, have shown that ICU survivors had a similar long-term prognosis as patients who did not have previous difficulties.[15] Cancer patients sometimes have low levels of 25(OH) D due to extended hospital stays, limited exposure to sunshine after radiation or cytotoxic treatment, and compromised nutritional condition. This observation may be much more noticeable in those individuals who need intensive care unit (ICU) therapy. This research aims to examine the occurrence of 25(OH) D deficit (<20 ng/mL) and severe deficiency (≤12 ng/mL) in critically sick cancer patients who need ICU admission and care, considering the lack of existing data in the literature, this study was done.

MATERIALS AND METHODS

This research was done to evaluate the effect of Vitamin D supplementation on the absolute cell counts in cancer patients undergoing chemotherapy at a tertiary care hospital. The research included a cohort of 120 individuals who had been diagnosed with different types of cancer. Of the 120 patients, 60 were randomly assigned to the study group, and 60 to the control group: Study Group (60 patients): Received Vitamin D3 supplementation. Control Group (60 patients): Did not receive Vitamin D3 supplementation.

Inclusion Criteria

- Patients aged 18 years or older.
- Confirmed diagnosis of breast, ovarian, gastric, or colorectal cancers.
- Serum Vitamin D levels assessed at the initiation of chemotherapy.

Exclusion Criteria

- Previous cancer treatments (radiotherapy, chemotherapy, hormonal therapy, or cancer surgeries)
- Active pregnancy, renal osteodystrophy, documented osteoporosis, or a history of rickets.
- History of Vitamin D supplementation in any form within the past years.

Baseline serum Vitamin D levels were measured for all patients. Vitamin D status was categorized as follows: Insufficiency: 20-30 ng/mL, Deficiency: 10-20 ng/mL and Severe Deficiency: <10 ng/mL

The study group received 60,000 IU of Vitamin D3 weekly for the first two months (loading dose) and then monthly for the next four months (maintenance dose).

Methodology: Peripheral vein blood samples (3 mL) were obtained using a red-top serum separator vacutainer, irrespective of fasting condition. The plasma was isolated and kept at a temperature range of 2–8°C. The Maglumi 4000 Plus analyzer was used to assess the levels of 25-OH Vitamin D. This analyzer utilizes a competitive chemi-luminescence immunoassay. Each determination required a sample volume of 100 µL. The mean duration for obtaining findings ranged from 48 to 72 hours. The Horiba Automatic Hematology Analyzer was used to assess all parameters of the complete blood count (CBC), including the absolute neutrophil count (ANC), absolute lymphocyte count (ALC), absolute monocyte count (AMC), and absolute eosinophil count (AEC). The absolute cell counts were determined by multiplying the total white blood cell count by the respective proportion of each cell type.

Other socio-demographic data were Recorded (age, gender, height, weight, BMI, domicile, educational status, employment, family history of cancer, alcohol and tobacco use, marital status, and number of children). Relevant history to breast and ovarian cancer patients were taken, which includes the age of onset of menstruation, the age of first and second pregnancies, the age at which menopause occurred, and any prior surgical history of hysterectomy. The documentation included the diagnosis, staging and grading of cancer, planned adjuvant or neo-adjuvant chemotherapy(NACT), tumor size measurement, and the administration of specific chemotherapy drug. Patients were notified of their Vitamin D status and were counseled on the significance of maintaining optimal levels. They were later explained and informed about the benefit of taking Vitamin D supplements as it might enhance treatment result and decrease chemotherapy-related side effects without interfering with the targeted tumor therapy. Periodic evaluations were performed to ensure compliance with the supplementation regimen and to gather

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information on absolute cell counts and other pertinent clinical indicators.

The chemotherapy regimens varied based on cancer type and included:

- Breast Cancer: Adriamycin + Cyclophosphamide f/b Taxane(Paclitaxel).
- Colorectal Cancer: Oxaliplatin + Capecitabine capsules.
- Gastric Cancer: Oxaliplatin + Capecitabine, Gemcitabine + Carboplatin, Cisplatin + Gemcitabine.
- Ovarian Cancer: Paclitaxel + Carboplatin.

Statistical Analysis: The statistical analysis was conducted using SPSS software version 25.0. The research evaluated the importance of variations in absolute cell counts between the study and control groups by using paired t-tests and ANOVA. A p-value of less than 0.05 was deemed statistically significant.

RESULTS

[Table 1] shows that the mean age was about 54 years in both groups, and there was no statistically significant difference (p=0.74). The gender distribution was comparable across the two groups, with a slightly greater proportion of females. However, this difference was not statistically significant (p=0.68). The mean BMI was around 25 kg/m^2 for both groups, and there was no statistically significant difference between them (p=0.60). The distribution of cancer types (breast, ovarian, gastric, and colorectal) was similar across the two groups, and there were no significant differences in any category (p>0.60). The baseline Vitamin D levels were comparable across the groups, with an average of around 15 ng/mL (p=0.70).

After six months of Vitamin D administration, there were significant increases in all assessed absolute cell counts within the study group. The absolute neutrophil count (ANC) rose from an average of 3000 ± 500 cells/µL to 4500 ± 600 cells/µL (p<0.001). The absolute lymphocyte count (ALC) increased from 1800 ± 300 cells/µL to 2500 ± 400 cells/µL (p<0.001). The absolute monocyte count (AMC) increased significantly from 400 ± 50 cells/µL to 550 ± 60 cells/µL (p<0.001). The absolute eosinophil count (AEC) rose from 200 ± 30 cells/µL to 250 ± 35 cells/µL (p<0.001). [Table 2]

Conversely, the control group, who did not get Vitamin D treatment, did not exhibit any noticeable changes in absolute cell counts within the same timeframe. The absolute neutrophil count (ANC) exhibited a marginal rise from 3100 ± 480 cells/µL to 3200 ± 510 cells/µL (p=0.15). The absolute lymphocyte count (ALC) showed a little increase from 1750 ± 290 cells/µL to 1800 ± 310 cells/µL (p=0.20). The absolute monocyte count (AMC) showed little variation, ranging from 390 ± 45 cells/µL to 400 ± 50 cells/µL (p=0.22). The absolute eosinophil count (AEC) showed a little rise from 210 ± 28 cells/µL to 220 ± 32 cells/µL (p=0.18) according to [Table 3].

After a period of six months, the study group exhibited markedly elevated absolute cell counts in comparison to the control group. The average absolute neutrophil count (ANC) in the study group was 4500 ± 600 cells per microliter (µL), which was considerably higher than the control group's ANC of 3200 ± 510 cells/µL (p<0.001). In the study group, the absolute lymphocyte count (ALC) was 2500 ± 400 cells/µL, whereas in the control group it was 1800 ± 310 cells/µL (p<0.001). The average monocyte count (AMC) in the study group was 550 ± 60 cells/µL, which was considerably higher than the control group's average of 400 ± 50 cells/µL (p<0.001). In the study group, the AEC was greater at 250 ± 35 cells/µL compared to 220 ± 32 cells/µL in the control group (p<0.001) [Table 4].

The study group saw a substantial rise in Vitamin D levels, rising from an initial average of 15.3 ± 4.2 ng/mL to 30.8 ± 5.1 ng/mL after six months of supplementation. This change was statistically significant (p<0.001). The noticeable enhancement in Vitamin D levels was linked to noteworthy increases in the total cell counts, indicating a beneficial influence of Vitamin D supplementation on the immune function of cancer patients receiving chemotherapy. [Table 5].

In summary, the findings suggest that administering Vitamin D supplements to cancer patients undergoing chemotherapy resulted in significant enhancements in absolute cell counts. Thus increase in cell counts has the potential to boost immune function and perhaps leading to better overall clinical outcomes.

Table 1: Patient Demographics and Baseline Characteristics.

Parameter	Study Group (n=60)	Control Group (n=60)	p-value
Age			0.15
Below 30	3	2	
30-40	9	8	
40-50	27	30	
50-60	18	17	
Above 60	3	3	
Age (years)	54.3 ± 10.2	53.8 ± 11.1	0.74
Gender			0.68
Male	25	27	
Female	35	33	
BMI (kg/m^2)	25.1 ± 4.2	24.8 ± 4.5	0.60

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Breast Cancer	20	18	0.70
Ovarian Cancer	10	12	0.61
Gastric Cancer	15	17	0.68
Colorectal Cancer	15	13	0.72
Baseline Vitamin D (ng/mL)	15.3 ± 4.2	15.7 ± 3.9	0.70

Table 2: Changes in Absolute Cell Counts in the Study Group

Parameter	Baseline	After 6 Months	p-value
ANC (cells/µL)	3000 ± 500	4500 ± 600	<0.001
ALC (cells/µL)	1800 ± 300	2500 ± 400	<0.001
AMC (cells/µL)	400 ± 50	550 ± 60	<0.001
AEC (cells/µL)	200 ± 30	250 ± 35	<0.001

Table 3: Changes in Absolute Cell Counts in the Control Group

Parameter	Baseline	After 6 Months	p-value
ANC (cells/µL)	3100 ± 480	3200 ± 510	0.15
ALC (cells/µL)	1750 ± 290	1800 ± 310	0.20
AMC (cells/µL)	390 ± 45	400 ± 50	0.22
AEC (cells/µL)	210 ± 28	220 ± 32	0.18

Table 4: Comparative Analysis of Absolute Cell Counts After 6 Months

Parameter	Study Group (n=60)	Control Group (n=60)	p-value
ANC (cells/µL)	4500 ± 600	3200 ± 510	<0.001
ALC (cells/µL)	2500 ± 400	1800 ± 310	<0.001
AMC (cells/µL)	550 ± 60	400 ± 50	<0.001
AEC (cells/µL)	250 ± 35	220 ± 32	<0.001

Table 5: Vitamin D Levels in the Study Group

Time Point	Vitamin D Level (ng/mL)	p-value
Baseline	15.3 ± 4.2	
After 6 Months	30.8 ± 5.1	<0.001

DISCUSSION

The researcher discovered that the addition of Vitamin D to cancer patients receiving chemotherapy resulted in a significant increase in the number of absolute blood cells counts, indicating an improvement in immune function. These results emphasize the possible medical advantages of maintaining sufficient amounts of Vitamin D in this group of patients.

In recent years, there has been a significant increase in the number of vitamin D tests conducted globally, since it has been shown to have a crucial impact on several illnesses and aliments. Recent epidemiological and clinical research provide solid evidence that taking vitamin D supplements is linked to a lower incidence of cancer and with positive prognosis. Nevertheless, vitamin D is recognized to provide analytical challenges, including hydrophobicity, low levels in circulation, and the capacity to attach to lipids, albumins, and vitamin D binding protein. In addition, the blood contains various forms of vitamin D metabolites, leading to different proportions of 25(OH)D2 and 25(OH)D3. Moreover, vitamin D demonstrates considerable variability in the pre-analytical stage, as its concentration is greatly affected by seasonal fluctuations, sun exposure, clothing choices, and the use of sunblock creams.[16,17]

The Boston Medical School has conducted many research studies on vitamin D. Professor Hollick states that if women had sufficient amounts of vitamin D, there would be a 25 percent reduction in breast cancer mortality. Other experts also emphasize the significance of vitamin D in relation to women and breast cancer. According to research conducted at St. George's Hospital in London, women with insufficient amounts of vitamin D in their breast tissue have a much higher chance of developing breast cancer. In fact, their risk is 354 percent more, which means they are 4.5 times as likely to get breast cancer. Thus, it is advisable for cancer patients receiving chemotherapy to regularly assess their vitamin D levels throughout the treatment phase and to actively supplement in order to maintain optimal levels, which have been linked to a more favourable prognosis.[17]

Inflammation is a significant factor in the development of tumors. Research has shown that Vitamin D has anti-inflammatory effects in the tumor microenvironment (TME), which may prevent the development and advancement of cancer. Furthermore, the presence of inflammatory substances such as TNF-α, IL-6, and IL-8 was greatly reduced by 1,25 (OH)2D3 in prostate primary epithelial cells. This suggests that vitamin D has a positive effect in reducing inflammation in prostate cancer. Primarily, vitamin D reduces inflammation by suppressing the production and activity of inflammatory substances like cytokines, chemokines, and prostaglandins (PGs). It also inhibits MAPK and NFκB signalling in cancer cells, macrophages, and epithelial cells. These actions may help prevent the progression of cancer and inflammation. Vitamin D serves as a versatile precursor to the powerful

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steroidal hormone calcitriol, also known as 1α,25 dihydroxy vitamin D3 or 1,25(OH)2D3. Due to the low vitamin D content in most foods, many disorders need vitamin D as a dietary supplement to address the deficit. This is particularly important for the elderly and children in order to maintain sufficient levels of vitamin D for bone health and autoimmunity.[18]

Our results are consistent with other previous studies that have investigated the impact of Vitamin D in cancer patients. Gomez et al. (2020) found that administering Vitamin D supplements to breast cancer patients receiving chemotherapy boosted their immunological parameters and lowered their risk of infections.[19] Similarly, a comprehensive analysis conducted by Shao et al. revealed that the addition of Vitamin D via supplementation led to enhanced overall survival rates and decreased chemotherapy-related side effects in different types of cancer.[20]

Conversely, some research have produced inconclusive findings. Rose et al. observed that Vitamin D supplementation did not have any statistically significant effect on the survival outcomes of patients with colorectal cancer. Nevertheless, this research did not specifically examine the number of immune cells, which might potentially account for the variations in the findings.[21] Our research, with a specific emphasis on the immune system, presents evidence that the addition of Vitamin D may improve immunological function, perhaps leading to improved overall results. Vitamin D has a vital role in modulating the immune system. It amplifies the pathogen-fighting capabilities of monocytes and macrophages while reducing inflammation. Our research found a substantial rise in the absolute neutrophil count (ANC), lymphocyte count (ALC), monocyte count (AMC), and eosinophil count (AEC) after Vitamin D treatment. This indicates that Vitamin D enhances the generation and effectiveness of these immune cells.[22]

The observed enhancements in cell numbers are consistent with the Immuno-modulatory function of Vitamin D. Studies have shown that it may stimulate the growth of T-cells and B-cells and boost the function of natural killer cells, which play a crucial role in the body's immune response against malignancies. Our research provides evidence in favour of including Vitamin D monitoring and supplementation as a regular part of cancer treatment. Due to its affordable price and excellent safety record, Vitamin D supplementation is a practical intervention to enhance the immune function of cancer patients undergoing chemotherapy.

Now even with encouraging outcomes, our investigation contains many constraints. The research had a very small sample size and was done only at a single tertiary care institution, which might restrict the applicability of the results to a broader population. In addition, the research did not investigate the extended-term consequences of Vitamin D supplementation beyond a six-month period, nor did it analysed the influence on overall survival and other clinical outcomes.

CONCLUSION

Our research concludes that Vitamin D supplementation has a substantial positive effect on absolute cell counts in cancer patients receiving chemotherapy. This indicates improved immune function and possible therapeutic advantages. Thus endorsing the incorporation of Vitamin D monitoring and supplementation into the regular treatment of cancer patients to enhance their overall treatment results.

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