Citation: Naseer, R., Cheema, N. H., & Ikram, Q. (2023). Multiple Malignancies in Relation to Vitamin D Levels Among Women of Reproductive Age. *Global Drug Design & Development Review, VIII*(IV), 34-45. https://doi.org/10.31703/gdddr.2023(VIII-IV).04

- **Pages:** 34–45
- **Vol.** VIII, **No.** IV (Fall 2023)
- **p- ISSN:** 2788-497X
- **e- ISSN:** 2788-4120

Corresponding Author: Rashida Naseer (Medical Officer in Charge (MOIC), Oncology Ward, Department of Oncology, Fauji Foundation Hospital Rawalpindi, Punjab, Pakistan.) Email: docrashidaffhgmail.com)

Cite Us

- **DOI:** 10.31703/gdddr.2023(VIII-IV).04
- **URL:** http://dx.doi.org/10.31703/gdddr.2023(VIII-IV).04

Multiple Malignancies in Relation to Vitamin D Levels Among Women of Reproductive Age

Rashida Naseer [a] Naseer Haider Cheema[b] Quratulain Ikram[c]

Abstract: *The global burden of cancer, with deaths projected to increase from 7.6 million to 13.1 million by 2030, calls for urgent research into potential mitigating factors, such as Vitamin D levels. This study specifically addresses the correlation between Vitamin D and cancer prevalence among women of reproductive age, scrutinizing variables like age, socioeconomic background, and geographic location. Conducted at Fauji Foundation Hospital's Oncology department through detailed questionnaires, the study analyzes Vitamin D levels in newly diagnosed female cancer patients. While a significant direct association with cancer occurrence was not established, an alarming rate of Vitamin D deficiency and high obesity risk were noted. Furthermore, the study indicates an inverse relation between Vitamin D levels, sun exposure, and certain patient demographics. These findings underscore the necessity of considering environmental and lifestyle factors in cancer prevention strategies.*

Key Words: Malignancy, Reproductive age, Vitamin D levels, Prevention, Apoptosis, Prognosis

Introduction

Vit-D, a vital nutrient, serves as a precursor to a potent steroid hormone that regulates a wide array of biological functions in the body. Beyond its traditional role in bone metabolism, recent research has elucidated Vit-D's significant involvement in the regulation of disease processes, particularly in the onset and progression of various chronic diseases, including cancer. The antitumor properties of Vit-D are increasingly recognized, influencing cancer development and progression. However, it has been observed that Vit-D metabolism is often altered in different types of cancer, affecting its tumor-suppressing abilities and consequently influencing cancer growth and spread. This alteration in Vit-D metabolism is a critical factor in cancer development, highlighting the potential for new Vit-D-based therapeutic strategies in cancer treatment (Jeon & Shin, 2018). Worldwide, Vit-D deficiency (VDD) and insufficiency (VDI) are on the rise, correlating with an increased risk of various diseases. According to data from the National Health and Nutrition Examination Survey (NHANES) from 2001-2010, the prevalence of VDD and VDI was reported at 28.9% and 41.4%, respectively. These deficiencies

[a] Medical Officer in Charge (MOIC), Oncology Ward, Department of Oncology, Fauji Foundation Hospital Rawalpindi, Punjab, Pakistan.
[b] Research Scholar, Information Systems, Riphah Institute of System Engineering, Islamabad, Pakistan.
[c] Medical Officer in Charge (MOIC), Gyne Ward, Citymed Hospital, Rawalpindi, Punjab, Pakistan.

were particularly prominent among underprivileged, less educated, overweight adults who had limited physical mobility and low milk consumption. A study in Pakistan among female university students showed that severe VDD was not prevalent, with Vit-D levels remaining above 18.0 ng/ml across different age groups. Vit-D deficiency, defined as serum 25-hydroxy Vit-D levels below 25 nmol/l, is a global issue, especially in regions like the Middle East, China, Mongolia, and India. Less than half of the global population maintains satisfactory Vit-D levels, particularly during winter. The deficiency of Vit-D is a contributing factor to several chronic diseases, including cancer. Addressing Vit-D deficiency is crucial in reducing the risk of cancer development and aiding recovery during cancer treatment. Preventing Vit-D deficiency can mitigate its adverse impact on cancer incidence, prognosis, and survival.

In this research, we tried to describe the relationship between multiple malignancies and Vit-D in females of reproductive age by utilizing proportions of occurrence and pervasiveness as per statistical attributes, such as age, sex, financial status, geographical area, and timeframe. We likewise examine the inconstancy of disease events in connection to changes in hazard aspects, such as decreases in Vit-D levels.

The research objectives are to assess the Vitamin D25 (OH) level in newly diagnosed cancer patients and to evaluate the relationship between vitamin D levels and different malignancies.

The rest of the paper is organized as follows: section 2 has the latest literature, section 3 has the methodology, section 4 has results and discussion, and the last section has the conclusion and future work.

Literature Review

In 1980, for the first-time sunlight based UVB –Vit-D malignancy speculation was assumed and thought that it was dependent on the biological environment. Nowadays, in the United States, cancer is one of the public health burdens, and 40% of the population at some point in their lives will suffer from cancer diagnosis along with morbidity association, and it affects the quality of life. In the United States outlay of cancer care is estimated to increase from $125 billion in 2010 to $156 billion in 2020. Worldwide, it is estimated that during the next 20 years (Ullah, Nadeem, Abrar, Amin, Salam, Alabrah, et al., 2023). The annual number of cancer diagnoses will increase from 14 million in 2012 to 22 million by 2032 (Nguyen et al., 2019).

Apoptosis plus decreasing angiogenesis are the two mechanisms in any disease control and cell development, and it has been found that Vit-D has a basic impact on cancer control by regulating these two mechanisms (Giammanco et al., 2015). North America published almost 80 years ago the relation between sun introduction and, in general, malignancy occurrence and mortality rate since, at that point, numerous epidemiological examinations have upheld an extensive UVB–Vit-D–disease theory in around 18 distinctive sorts of malignancies. The theory has been additionally bolstered by studies demonstrating the immediate relationship between nutrient D and malignancy chance. A few lines of populace-based investigations uncovered an opposite connection between serum (25(OH) Vit-D level and elevated danger of colon, breast, prostate, gastric, and different malignancies. Alongside this, there are sharp bits of proof exist which demonstrate the antitumorigenic impact of nutrient D from a few cellular and creature backgrounds (Jeon & Shin, 2018). 25-Dihydroxyvitamin D3 is the organically dynamic end product of Vit-D metabolism and appears to control the development of different cellular forms. The Vit-D 25-hydroxylase (25-OHase) and the 1α-hydroxylase (1α-OHase) are two essential chemicals engaged with the development of flowing, 1, 25(OH) 2D3 from Vit-D. The investigation aims to analyze the statement of Vit-D binding receptor (VDR) and these two fundamental chemicals associated with the blend and digestion of calcitriol in cancers of the female reproductive system and compare solid cellular structure. Verbalization of VDR, 25-OHase, 1α-OHase, and 24-OHase was dissected in breast cancer (BC), ca ovary (OC), and ca cervix (CC) and comparing sound tissues utilizing constant PCR

and explicit hybridization tests just as utilizing immunohistochemistry (IHC). RNA for VDR, 1α-OHase, 24-OHase, and 25-OHase was up managed and VDR immune reactivity was expanded in malignancies of breast ovary and cervical cancer when contrasted with comparing sound tissue. Our discoveries show that malignancies of the cervix, breast, and ovary might be measured as a probable focus for anticipation or management by means of the latest Vit-D analogs that apply practically zero calcemic reactions and digestion in these malignancies (Vitamin, 2008).

The worldwide leading cause of mobility and mortality among females of reproductive age groups are cancers of the ovaries, endometrial, cervical, vaginal, and vulva. In 2017, in the United States, 7% of newly diagnosed malignant patients among females were endometrial cancers. The 2nd most familiar malignancy in the females of the reproductive age group is the cervix, which is now a day's severe health problem among two-thirds of gynecological cancers. Even the most common cancer is ovarian cancer, which is becoming the eighth cause of death worldwide, with a high incidence rate in North America and Europe. It is usually diagnosed in advanced stages. Vulvae and vaginal disease are startling with a trivet degree of 3% and 2% or less in gynecological malignancies (Rickard et al., 2021; Stade et al., 2009). Many approachable studies have been done in recent years, which showed an association of vitamin – D with overall improved cancer survival, but somehow not all, although low Vit –D levels have been observed in disease individuals after diagnosis with cancer (Albanes1, 2018).

The biological and environmental studies recognized colorectal carcinoma primarily as UVB-sensitive. Ecologically research done in the U.S showed a converse association between sun exposure and colorectal carcinoma, it has been found that elevated levels of Vit-D and high UVB radiation exposures decrease the prevalence and enhance survival rate same was found that more daily sunlight exposure and Vit-D serum 25 (OH) D levels greatly decrease the risk and occurrence rate of breast malignancy (Ogawa et al., 2022). Several years ago, it was postulated that the decreased incidence and mortality of colorectal, breast, and several other cancers at lower latitudes are due to increased ambient sunlight exposure, which the Garlands postulated acts by producing Vit-D (Miller et al., 2017).

So, we came to know from the latest and previous research and met analysis that vitamin deficiency is one of the non-negligible factors in females' reproductive tumors and in other malignancies, A converse relationship exists among flowing Vit-D 25 (OH) D deficiency, colorectal and breast cancer which could be overcome by Vit-D supplementation, by changing our lifestyle pattern or could be overcome by improving sun exposure. Past randomized controlled trials (RCTS) on cancer occurrence and low administration of Vit-D unfortunately gave inconsistent results. However, high levels of Vit-D supplementation > 1100 IU/day reduce the mortality results.

Methodology

The methodology section explores the link between Vit-D levels and cancer in reproductive-age females at FFH Rawalpindi, Pakistan. Employing an analytical and observational approach, it involves study design and questionnaires to assess factors like dietary habits impacting cancer incidence.

Study Design

Analytical hospital-based observational study. The hypotheses are:

i. Null hypothesis: No relation exists between serum Vit-D (25 (OH) D) level and different malignancies.
ii. Alternative Hypothesis: Relation exists between serum Vit-D (25 (OH) D) and different malignancies.

Study Locale

The study took place in the oncology department of Fauji Foundation Hospital Rawalpindi, a well-

equipped 220-bed facility. It focused on examining Vit-D levels in female patients of reproductive age attending the hospital's oncology outpatient department.

Study Population

The research was done among newly diagnosed female cancer patients of the reproductive age group reported in the oncology department. Females belonging to different localities at the time of cancer diagnosis reported between July 2018 to April 2019 were studied.

Sample Size

To make the study more significant, 101 patients with different malignancies were taken. Samples were collected randomly among targeted females reporting in OPD on their regular visits. In this way, 101 samples were collected from 500 populations.

Sampling Technique

The purposive sampling technique, a non-random sampling technique, was applied to choose cancer patients. Focused on particular characteristics of a population and the objective of the study.

Inclusion Criteria

Females of the reproductive age group were focused on any type of malignancy.

Exclusion Criteria

i. Patients on chemotherapy and radiotherapy.
ii. Females of non-reproductive age groups.
iii. Male subjects.

Ethical Issues

The study was approved by the hospital's ethical committee. After obtaining consent, subjects were briefed about the study, and its purpose was explained.

Data Collection

Demographic and risk factor data, including name, sex, age, marital status, education, family history of cancer, chronic illness, physical activity, BMI, waist-to-hip ratio (WPR), Vit-D supplementation, and daily sun exposure, were collected using a structured questionnaire.

The questionnaire is comprised of the following parts.

i. Socio-Demographic Variables.
ii. Lifestyle data.
iii. Dietary intake.
iv. History of chronic illnesses.
v. Biochemical Data

Study Instruments

A customized, pretested questionnaire was used to collect data on various factors influencing disease rates, including age, socio-demographic profile, dietary intake, education, marital status, physical activity, sun exposure, family cancer history, chronic illnesses, and vitamin D and calcium supplementation. The researcher administered this questionnaire to randomly selected participants.

Body Mass Index (BMI)

Body index is specified as body mass index (BMI) and is one of the markers of body fat, and it is used to measure obesity. Obesity was classified into three different groups as per the Asian Pacific Corpulence Arrangement 2018, weight was characterized into three distinct gatherings as:

i. Normal weight (BMI) = 18.5-22.9kg/m^2
ii. Overweight (BMI) = 23-24.9 kg/m^2
iii. Obese (BMI > 25 kg/m^2)

Waist Pelvic Ratio

The waist-hip (WHR) or waist-pelvic ratio (WPR) ratio is the ratio of the circumference of the waist to that of the hips. Calculated as waist size divided by hip size in cm.

Waist Circumference

The waist circumference was recorded by the researcher with the help of a female worker in OPD. It was measured using measuring tape and was measured by placing the tape around the belly button or approximately just above the belly button.

Pelvic Circumference

Pelvic circumference was measured by placing the measuring tape at the level of the hip bone and wrapping the tape around the buttock, the widest part of the hip bone.

Dietary Intake

The questionnaire consists of food items that are good sources of vitamin D. Subjects were interviewed about their regular eating habits during the preceding year of the present-onset situation. FFQ was used to estimate the frequency (Days/weeks), frequency times/day, and amount /portion size of the selected food groups.

H/P Reports

Histopathology, defined by The National Cancer Institute as the microscopic examination of diseased cells and tissues, involves a pathologist assessing biopsy samples. These samples, obtained through biopsy or minor surgery, are prepared in a histopathology lab into thin slices and stained for detailed analysis under a microscope. This process helps in identifying specific tissue characteristics, which is crucial for determining the nature of a tumor and guiding cancer treatment.

Biochemical Evaluation of Vit-D Level (Immunoassay Kit)

The active form of Vit-D in the blood is measured using the Enzyme-Linked Immunosorbent Assay (ELISA) technique, a process taking around 1 hour and 30 minutes. The ELISA kit, used for quantifying both Vit-D3 and D2 in serum, is a standard tool in fields like immunology and cancer research. Vit-D levels are determined in nmol/l using this method and categorized according to Endocrine Society guidelines:

i. Deficient: < 20ng /ml and or <50nmol/l
ii. Insufficient: 21 – 29ng /ml or 52nmol/l - 73nmol/l
iii. Sufficient: > 30ng/ml or > 74nmol/l

Statistical Methods for Data Analysis

Data was coded and entered SPSS Version 22 for analysis. Chi-square tests examined the relationship between serum Vit-D and various malignancies, while ANOVA assessed the mean serum 25 (OH) Vit-D levels across different variables. Results were compared with standard outcomes, considering a p-value of < 0.050 as significant.

Results and Discussion

The research findings emphasize the importance of data analysis as a crucial step in research. The collected data was analyzed using SPSS-22. Descriptive statistics such as means, frequencies, and ratios were employed for data interpretation. After analysis and tabulation, critical examination led to clear conclusions. The Chi-square test was used to determine relationships between dependent and independent variables, while ANOVA was applied to assess significant differences, with a significance threshold set at $p < 0.05$.

Prevalence of Cancer in Females of Reproductive Age Group

The occurrence of malignancies in women of reproductive age group in the presence of the following characteristics, i.e. family history, parity and education status, sun exposure, physical activities, obesity, dietary habits, and chronic illnesses, were studied.

The rate of occurrence of different malignancies in females of reproductive age group, among 101 respondents, a maximum of 60% cases were of a breast, and only 1% case of RCC was documented.

Table *1*

Descriptive Analysis of Vitamin –D Levels in Cancer Patients

	Num	Minimum	Maximum	Mean	Std. Deviation
Vitamin- D Levels	101	7.50	141	39.0	21.96215

Table depicts the descriptive analysis of serum 25 (oH) Vit-D in cancer patients. Patients had a mean value of 39.0, the lowest value of 7.50, and the highest value of 141.

Table 1

Frequency Distribution of Vitamin –D Levels in Cancer Patients

less than 50nmol/l or < 20ng/ml very deficient	50 nmol/l - 73nmol/l or 21 - 29ng/ml insufficient	74-150 nmol/l or 30 -100 ng/ml sufficient
81(80.2%)	12(11.9%)	8(7.9%)

Table 1 depicts the overall frequency distribution of 25(OH) Vit-D levels in female cancer patients were found, where a maximum of 80.2% of Vit-D levels were lying at very deficient levels.

Table 2

Frequency distribution of Vit-D levels in multiple malignancies

VIT-D LEVELS	P-value: 0.80			
Clinical Diagnosis	less than 50nmol/l or < 20ng/ml very deficient	> 50 nmol/l - 73nmol/l or 21 - 29ng/ml insufficient	74-150 nmol/l or 30 -100 ng/ml sufficient	Total
CA BREAST	48	10	3	61
CA LUNG	1	0	0	1
H.L	1	0	0	1
SOL Brain	1	1	0	2
CA OVARY	9	0	1	10
CA CERVIX	4	0	1	5
CA ENDOMETRIUM	5	0	1	6
RECTUM	2	0	0	2
OESOPHAGUS	1	1	0	2
SARCOMA	4	0	1	5
NHL	6	0	0	6
TOTAL	81	12	7	101

Table 2 depicts the frequency distribution of Vit-D levels in multiple malignancies. In total, 81% of cases were at very deficient levels, 48% of which were cases of breast cancer. The significance of the non-significant P value is 0.80.

Table 3

Descriptive Statistics and Characteristics of Cancer Patients

Descriptive Statistics	Mean SD	
AGE	40.59 7.63	
BMI	2.72 0.82	
WPR	2.74 0.54	
Characteristics OF Patient		
Variables	Frequency	Percent Frequency
BMI	n	%
<18.5under-wt	9	8.9
18.5-24.9 healthy	25	24.8
25.0- 29.9 over-wt	52	51.5
> 30 obese	15	14.9
WPR		
0.80 or low risk	5	5.0
0.81- .84moderaste risk	16	15.8
0.85 or high risk	80	79.2
Family History		
Yes	10	9.9
No	80	79.2
Other than this	10	9.9
Marital Status		
Single	13	12.9
Married	83	82.2
Divorce	5	5.0
Parity Status		
Nulli	13	12.9
Primi	10	9.9
Multi	78	77.2
Type of Housing		
Indoor	25	24.8
Outdoor	76	75.2
Exposure to Sunlight		
Yes	80	79.2
No	21	20.8
Average Sun Exposure		
less than 5 min /day	4	4.0
5-15 min /day	13	12.9
15 30 min /day	31	30.7
>30 min /day	53	52.5
Use of Veil		
Yes	23	22.8
No	78	77.2
Exercise /Physical Activity		
Yes	21	20.8
No	80	79.2

Descriptive Statistics	Mean SD	
Chronic Illness		
Yes	21	20.7
No	80	79.2

Table 3 shows BMI and WPR in female cancer patients: 51.5% overweight, 14.9% obese, and 79.2% at high risk. Of breast cancer patients, 8% had a family history of cancer, with 11% overall. Sun exposure was daily for 79.2%, over 30 minutes for 52.5%, 77.2% didn't wear veils, 77.2% were multiparous, and 79.2% didn't exercise.

Table 4

Mean SD Serum Levels of Vit-D with respect to Lifestyle

Variables	Vit-D levels. (Mean SD)	P value
Body Mass Index		0.16*
>18.5 under-wt	57.4333 23.100	
18.5-24.9 healthy	38.5160 22.6	
25.0- 29.9 over-wt	36.17692 0.98	
< 30 obese	38.6067 20.22	
Waist pelvic ratio (WPR)		0.20*
0.80 or low low-risk	67.180 09.50	
.81-.84 moderate-risk	41.6438 25.7	
.85 or high high-risk	36.7238 20.5	
Average Sun Exposure/wk		0.26*
less than 5 min /day	38.0000 31.32	
5-15 min /day	39.0769 24.65	
15- 30 min /day	39.9516 19.47	
>30 min /day	38.5208 22.60	
USED VEIL		0.29*
Yes	38.6391 21.24	
No	39.1205 22.30	
Sun Screen		0.12*
Yes	70.2000	
No	38.6990 21.84	
Exercise		0.33*
Yes	49.9190 32.59	
No	36.1475 17.36	
Type of Housing		0.51*
Indoor	38.6520 22.03	
in and out the door both access	39.1289 22.08	
Vit-D with Ca		0.05**
yes/dose IU/day	41.5000 25.16	
No	38.9021 22.11	

**The p-value is not statistically significant **The p-value is statistically significant at p 0.05*

Table 4 depicts the association of different variables with serum vitamin D levels. Statistical non-significant values are found between BMI, WPR, average sun exposure, and daily physical drills. Between serum 25(OH) vitamin D level and serum 25(OH) vitamin D and calcium supplements, there is a statistically significant p-value of 0.05.

Table 5

Using One-Way ANOVA, while Percentages were compared using Chi-square

		ANOVA				
		Sum of Squares	Df	Mean Square	F	Sig
Body Mass Index	Between Groups	63.571	86	.739	2.218	.048
	Within Groups	4.667	14	.333		
	Total	68.238	100			
Waist Pelvic Ratio	Between Groups	27.307	86	.318	2.223	.048
	Within Groups	2.000	14	.143		
	Total	29.307	100			
Family History	Between Groups	14.823	86	.172	.391	.996
	Within Groups	6.167	14	.440		
	Total	20.990	100			
Average Sun Exposure/wk	Between Groups	64.861	86	.754	1.508	.196
	Within Groups	7.000	14	.500		
	Total	71.861	100			

**Means in two groups were compared using one-way ANOVA, while percentages were compared using chi-square as shown in Table 5.*

Table 6

Frequency Distribution of Intake of Meat in Cancer Patients

	Daily %	1-2/wkly %	Once/2wkly %	1/2Times/monthly%	Never %
Mutton		12.9	6.9	29.7	50.5
Beef		16.8	12.9	32.7	37.6
Chicken	1.0	45.5	21.8	17.8	13.9
Fish		5.9	5.0	49.5	36.6

Table 6 depicts the frequency of intake of four meat products: mutton, beef, chicken, and fish. The chicken weekly intake (45.5 %) is the most frequent, whereas the mutton intake is the least, at 29.7 % monthly.

Table 7

Frequency Distribution of Intake of Dairy Products in Cancer Patients

	Daily %	1-2/wkly %	Once/2wkly %	1-2 Times/Monthly %	Never %
Egg	16.8	32.7	7.8	13.9	18.8
Milk		42.6	14.9	6.9	32.7
Lassie		9.9	19.8	6.9	5.0
Yogurt		61.4	1.0	73.3	26.7

Table 7 depicts the frequency of intake of eggs, milk, lassie, and yogurt. The frequent intake of eggs is weekly (32.7%) and yogurt (73.3%) monthly, whereas the intake of milk is (42.6%) weekly and lassie (19.8%) 2wkly.

Table 8

Association (Chi-Square Asymp. Sig.2-sided) between Vit-D levels and Food Group Consumption in Cancer Patients

Vit-D Status	Meat Products				
	Mutton	Beef	Chicken	Fish	
	0.30*	0.47*	0.20*	0.17*	
Dairy /poultry products					
	Eggs	Milk	Lassie	Yogurt	Cheese
	0.39*	0.51*	0.31*	0.24*	0.17*
Fruits / Nuts					
	Nuts	Peach	Oranges	Apricots	Others
	0.71*	0.78*	0.16*	0.57*	0.20*

**The p-value is not statistically significant **The p-value is statistically significant at p 0.05*

Table 8 depicts the association between food groups and vitamin D levels. No statistically significant values are found between meat, dairy, poultry, and fruits and vitamin D levels.

Discussions

This research involved 101 female patients, with 60% having breast cancer, 10% ovarian, 6% endometrial and non-Hodgkin s lymphoma, 5% cervical and sarcoma, 2% rectal, esophageal and brain, and 1% each Hodgkin lymphoma, lung cancer, and renal cell carcinoma (RCC). Most cancers were reproductive system-related. Globally, breast cancer is the leading cause of female mortality. (Ullah, Nadeem, Abrar, Amin, Salam, & Khan, 2023). A Karachi study found that 24.9% of 402 female participants had breast cancer, with a majority being illiterate and from lower socioeconomic backgrounds (Saeed et al., 2019). In our study, Vit-D deficiency (<50 nmol/l) was common, affecting nearly half the population. At Aga Khan University Hospital, 75% of patients were Vit-D deficient, 16% insufficient, and 9% sufficient (Khan et al., 2015). Our study found an average serum Vit-D level of 39.0 nmol/l, with 80.2% deficient and 11.9% insufficient.

Table 2 shows Vit-D levels across various cancers in females of reproductive age: 48% with breast cancer, 9% with ovarian, and 5% with endometrial cancer were Vit-D deficient. Additionally, 4% with cervical cancer and 6 cases of non-Hodgkin's lymphoma showed deficiency. 81% of cancer cases were Vit-D deficient, 12% insufficient, and 7% sufficient, with a non-significant p-value of 0.80.

One of the studies showed that in a country like Pakistan, which is situated near the equator with plenty of sunlight, it is unforeseen to have

such an elevated incidence of Vit-D deficiency and cancer incidence, several sociodemographic and lifestyle factors have been reported to be linked with Vit-D deficiency (Safari et al., 2017).

Table 4 A study with participants averaging 44.4 years found no significant difference in vitamin D levels between those who exercised and those who didn't. (Heald, 2023) study on breast cancer patients, average age of 40, showed 64.8% had no family cancer history, and 99.2% were married at diagnosis, suggesting cancer occurrence might be influenced by environmental rather than familial factors. Despite sufficient sunlight, most of Pakistan's population is deficient in vitamin D. Table 4 indicates that 79.2% of female cancer patients are at high obesity risk, correlating obesity and Vit-D deficiency with cancer occurrence. Another study on breast cancer patients found varied BMI distributions, while a thyroid cancer study revealed a higher obesity rate in older women.

Table 4 Mean SD of Vit–D level with respect to lifestyle depicted in this, and only a significant p-value of 0.05 is seen in Vit– D with Ca.

One of the clinical randomized trials was done in the past on intake of Vit-D supplementation signal reduction in cancer death rather than in incidence. However, it was surprising to know that a greater reduction was seen among the participants who were average weight or lower weight.

In Table 5, a one-way ANOVA and chi-square tests analyzed the relationship between various variables and Vit-D. Table 7 shows that 45.5% of female cancer patients consume chicken weekly, and 49.5% eat fish monthly, indicating these as primary Vit-D sources. Red and processed meats are associated with higher breast cancer risks. Table 8 reveals limited dairy consumption among these patients, with 42.6% drinking milk daily. High dairy intake potentially reduces colorectal and breast cancer risks. Table 9 finds no significant correlation between Vit-D levels and food consumption. The study highlights the need for more research on VDD in diverse socio-economic groups in Pakistan, where low education and unhealthy lifestyles are prevalent. Despite limited data, the rising cancer prevalence in Pakistan and the lack of family cancer history in most cases suggest environmental factors' role in cancer development.

Conclusion and Future Work

The study confirms a link between Vit-D deficiency and multiple malignancies in reproductive-age females. While cancer isn't solely dependent on Vit-D levels, it's associated with lifestyle factors like obesity and environmental influences. High cancer risk in premenopausal females is attributed to obesity and lack of physical activity, with poor dietary habits and insufficient Vit-D intake as contributing factors. This necessitates national surveys to better understand this issue and emphasizes the need for lifestyle changes, including diet modifications and increased physical activity. Further research on environmental and genetic interactions is essential, particularly regarding the role of Vit-D in cancer prognosis and recurrence. Education about Vit-D-rich foods and supplementation is vital, as 80.2% of the study participants were Vit-D deficient. This research paves the way for further studies on the critical role of Vit-D in cancer among Pakistani females, especially considering their adequate sun exposure but high cancer incidence without a family history.

References

Giammanco, M., Di Majo, D., La Guardia, M., Aiello, S., Crescimannno, M., Flandina, C., Tumminello, F. M., & Leto, G. (2015). Vitamin D in cancer chemoprevention. *Pharmaceutical Biology*, *53*(10), 1399–1434. https://doi.org/10.3109/13880209.2014.988274

Heald, F. A. (2023). Promoting Cardiac Rehabilitation Use Across the Phases: Focus on Women.

Jeon, S., & Shin, E. (2018). Exploring vitamin D metabolism and function in cancer. *Experimental and Molecular Medicine/Experimental and Molecular Medicine*, *50*(4), 1–14. https://doi.org/10.1038/s12276-018-0038-9

Khan, I., Jawaid, A., Ahmad, K., & Noordin, S. (2015). Hip fragility fractures: Anaemia, calcium and vitamin D supplementation. *PubMed*, *65*(11 Suppl 3), S55-8. https://pubmed.ncbi.nlm.nih.gov/26878537

Miller, K. M., Hart, P., De Klerk, N., Davis, E. A., & Lucas, R. (2017). Are low sun exposure and/or vitamin D risk factors for type 1 diabetes? *Photochemical & Photobiological Sciences*, *16*(3), 381–398. https://doi.org/10.1039/c6pp00294c

Nguyen, S. M., Deppen, S. A., Nguyen, G. H., Pham, D. X., Bui, T. D., & Tran, T. A. (2019). Projecting cancer incidence for 2025 in the 2 largest populated cities in Vietnam. *Cancer Control*, *26*(1), 1073274819865274. https://doi.org/10.1177/1073274819865274

Ogawa, S., Sato, J., Tanaka, R., Sakakibara, T., & Shino, M. (2022). Hyponatremia timing, incidence, and associated risk factors in patients treated with cisplatin for lung cancer: a retrospective study. *Journal of Population Therapeutics and Clinical Pharmacology*, *29*(4). https://doi.org/10.47750/jptcp.2022.907

Rickard, B. P., Conrad, C., Sorrin, A. J., Ruhi, M. K., Reader, J., Huang, S., Franco, W., Scarcelli, G., Polacheck, W. J., Roque, D. M., Del Carmen, M. G., Huang, H., Demirci, U., & Rizvi, I. (2021). Malignant ascites in ovarian cancer: cellular, acellular, and biophysical determinants of molecular characteristics and therapy response. *Cancers*, *13*(17), 4318. https://doi.org/10.3390/cancers13174318

Saeed, S., Khan, J., Iqbal, N., Irfan, S., Shafique, A., & Awan, S. (2019). Cancer and how the patients see it; prevalence and perception of risk factors: a cross-sectional survey from a tertiary care centre of Karachi, Pakistan. *BMC Public Health*, *19*(1). https://doi.org/10.1186/s12889-019-6667-7

Safari, H., Eftekhari, M. H., Zadeh, J. H., & Dashtabi, A. (2017). Prevalence of vitamin D deficiency and its relationship with metabolic syndrome markers and lifestyle in the adult population in a sunny tropical region. *DOAJ (DOAJ: Directory of Open Access Journals)*. https://doaj.org/article/84f4a5ed323844f1f9abf1a8c1d70c013

Stade, B., Ali, A. I., Bennett, D., Campbell, D., Johnston, M., Lens, C., Tran, S., & Koren, G. (2009). The burden of prenatal exposure to alcohol: revised measurement of cost. *PubMed*, *16*(1), e91-102. https://pubmed.ncbi.nlm.nih.gov/19168935

Ullah, F., Nadeem, M., Abrar, M., Amin, F., Salam, A., Alabrah, A., & AlSalman, H. (2023). Evolutionary Model for Brain Cancer-Grading and Classification. *IEEE Access*, *11*, 126182–126194. https://doi.org/10.1109/access.2023.3330919

Ullah, F., Nadeem, M., Abrar, M., Amin, F., Salam, A., & Khan, S. (2023). Enhancing Brain Tumor Segmentation Accuracy through Scalable Federated Learning with Advanced Data Privacy and Security Measures. *Mathematics*, *11*(19), 4189. https://doi.org/10.3390/math11194189

VITAMIN, D. (2008). Eighth European Congress on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis – ECCEO 8. (2008b). *Osteoporosis International*, *19*(S1), 1–4. https://doi.org/10.1007/s00198-008-0567-