

The Correlation Between Vitamin D and Colorectal Cancer in Admitted Patients in Oncology Teaching Hospital

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Abstract

Objectives: This study aimed to investigate the correlation between vitamin D and Colorectal Cancer.

Methods: In this prospective study, data from 100 patients with newly diagnosed colon cancer were taken non-randomly and data from 100 other control cases were taken from December 2019 to December 2020 in Rizgary Oncology Center in Erbil to find out the relation between vitamin D and colorectal cancer.

Results: The current study revealed that, mean of vitamin D level of patients were 6.833 (SD = 2.940), while mean of vitamin D level were 14.435 (SD = 4.356) in control group. Concerning the level of vitamin D level based on stage IV cases have lower vitamin D level compared to other earlier stages, the stage of disease, in stage I-III cases vitamin D level was 8.456 (SD = 6.696), while the mean of vitamin D in stage IV colon cancer cases were 6.723 (SD = 3.191).

Conclusion: This study found out that vitamin D deficiency is common in colon cancer cases with more than 95 percent of cases having vitamin D deficiency. Another finding of this study is that when the mean vitamin D level within the deficit group is compared to the control group within the same group. The colorectal cancer cases have lower mean vitamin D level.

Keywords: Vitamin D, colorectal neoplasms, oncology, Iraq

Introduction

Vitamin D is a fat-soluble vitamin that can be obtained from multiple sources. It can be synthesized in the skin after exposure to ultraviolet (UV)-B radiation from sunlight and dietary sources, or obtained from vitamin D supplements directly. Vitamin D from these sources is in the form of vitamin D₃ and undergoes enzymatic hydroxylation by 25-hydroxylase (CYP2R1) in the liver to form 25-hydroxyvitamin D (25[OH]D), the main circulating form of vitamin D and the best indicator of vitamin D status. 25(OH)D undergoes a second hydroxylation step in the kidney by 1 α -hydroxylase (CYP27B1) to yield its active form 1,25-dihydroxyvitamin D (1,25[OH]2D) or calcitriol, which binds to the vitamin D receptor (VDR) in the cell nucleus. Bound VDR forms a heterodimer with the retinoic-acid receptor (RXR) and this complex binds to vitamin D response elements to regulate target gene expression.^{1,2} The study of vitamin D has focused predominantly on its role in bone health as a regulator of calcium and phosphate metabolism. Adding to that, some studies showing Vitamin D can play a role in cancer prevention and cell growth regulation.³ Moreover, Vitamin D has a broad anti-inflammatory effect by inhibiting cyclooxygenase (COX) expression and downregulating nuclear factor (NF)- κ B,⁴ and is a proliferation inhibitor,⁵ reduces angiogenesis³ and decreases metastatic process.⁶ New studies highlight that Vitamin D has been shown to upregulate the expression of the calcium-sensing receptor (CaSR), which plays an important role in cell proliferation and has been suggested as a mediator of vitamin D's anti-cancer impact.⁷ The activity of vitamin D in the laboratory is largely compatible with epidemiological evidence in CRC. Several ecological and prospective observational studies have consistently revealed an inverse association between plasma 25(OH)D levels and the risk of developing CRC.⁸ Conversely, the results of randomized, placebo-controlled trials of vitamin D supplementation have

been conflicting. The Women's Health Initiative (WHI) trial, a study in healthy, postmenopausal women from Nebraska, and a trial among elderly men and women at risk for fractures in the United Kingdom (UK) revealed contrasting results using vitamin D₃ 400 IU day⁻¹, 1100 IU day⁻¹, and 100,000 IU every four months, respectively.⁹ The Nebraska study found a significant 60% decrease in all-cancer risk among participants in the vitamin D supplementation arm. Conversely, the WHI and UK studies obtained largely null results; nevertheless, it was revealed that women with the highest baseline 25(OH)D levels in the WHI study showed a substantial 60% reduction in CRC risk (P -trend = 0.02).^{10,11} A trial with the involvement of 2259 patients after removing colorectal adenomas, daily supplementation with vitamin D₃ (1000 IU), calcium (1200 mg), or both did not significantly reduce the risk of recurrent colorectal adenomas over a 3- to 5-year period.^{12,13} An ongoing trial, the vitamin D and Omega-3 Trial (VITAL) phase III randomized controlled trial is using vitamin D₃ 2000 IU/day for the primary prevention of cardiovascular disease and different cancer types, including CRC, as primary endpoints. An important methodological difference between these trials is the dose of vitamin D used in the study.¹⁴ The wealth of experimental and epidemiological evidence supporting a protective effect of vitamin D against the development of CRC has motivated observational studies and clinical trials to assess whether the antineoplastic effects of vitamin D translate into improved recurrence and survival outcomes among CRC survivors.¹⁵ Based on the above raised points this study is conducted. The aim of the study is to look for relation between vitamin D and colorectal cancer.

Patients and Methods

This prospective, non-randomized observational study is conducted at Rizgary Teaching Hospital-Oncology

Center-Erbil- Kurdistan region- Iraq, from December 2019 to December 2020. In this study, data from 100 patients with newly diagnosed colon cancer were taken non-randomly on one hand; on the other hand, 100 other control cases were taken. The study participants were those visiting Rizgary Teaching Hospital-Oncology Center consultation unit. The included cases were newly diagnosed colorectal cases either early, advanced or metastatic cases, while the colorectal cases were diagnosed for more than 6 months before, recurrent colorectal cases and other gastrointestinal cancer cases were excluded. Adding to that, patient's age, sex, body mass index and stage of disease were taken. Concerning the patient's profile, all of them were asked if they agreed to participate in the study or not; then their files and related information were recorded. The control cases were those persons visiting Rizgary teaching hospital for administrative purposes, accompanying patients rather than cancer cases, medical staffs and administrative staffs. All the control participants were asked if they agreed to participate in the study as well. A sample of blood was taken from all the participants after taking informed consents, patients and controls, and then serum Vitamin D was measured at Laboratory unit of Rizgary Teaching Hospital-Oncology center. Based on the previous international and local studies,¹⁶⁻¹⁸ a level of vitamin D less than 20 ng/ml regarded as deficient, a level of vitamin D between 20–29 ng/ml regarded as insufficient and a level of vitamin D of 30 ng/ml and above regarded as a safe range (Table 1). All the data were analyzed using Statistical Package for the Social Sciences (SPSS version 21.0 for windows 10 pro).

Results

The study showed that 53% of the participant patients were male while 47% of the patients were female. Besides, 44% of the control participants were male whereas 56% of the control cases were female (Figure 1).

With regard to the patient's age, 16% of the patients were at 40 years of age or younger, 23% of them were between in 4 decay, 19% of them in 5 decay, 27% of them in 6 decay, 11% in 70 decay and 5% in eightieth or older years of age since, 21%

Table 1. Mean of vitamin D level in both patients and control group

Measurement of vitamin D	Mean \pm SD of CVD (ng/dl)	Mean \pm SD of PVD (ng/dl)	P-value
Deficiency <20	14.435 \pm 4.356	6.833 \pm 2.940	<0.0001
Insufficiency 20–29	24.930 \pm 2.517	None	ns
Safe range \geq 30	52.350 \pm 21.640	34.0 \pm 2.707	0.0310

CVD, Control Vitamin D; PVD, Patient Vitamin D.

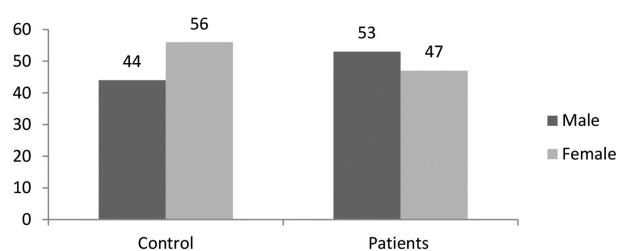


Fig. 1 Gender of both patients and control group.

of the control participants were at 40 years of age or younger, 33% of them in 40th, 17% of them in 50th, 18% of them in 60th, 9% of them in 70th and 2% of them in their eightieth or older years of age (Figure 2).

Concerning of Patient's stage of the disease, 49% of the patients had stage III colorectal cancer, 36% of them had stage IV of disease while only 15% of them had stage I and II disease (Figure 3). When we looked at the pathology reports, all of the 100 patient's histopathological disease was adenocarcinoma and nearly 2/3 of the patients had grade II adenocarcinoma as 1/3 of the remaining case had grade I and III adenocarcinomas (Figure 3).

By comparing Vitamin D level in both patients and control groups, 96% of the patient's vitamin D (PVD) level was in deficient level while 75% of the control group's. Only 3% of the patient's vitamin D level was in safe range, while 15% of control group's vitamin D level was in safe range. Furthermore, only 1% of the patient's vitamin D level was in insufficiency range since, 10% of the control group's vitamin D level in insufficiency range (Figure 4).

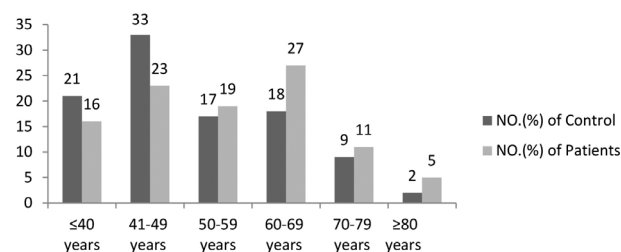


Fig. 2 Age distribution in both patients and control group.

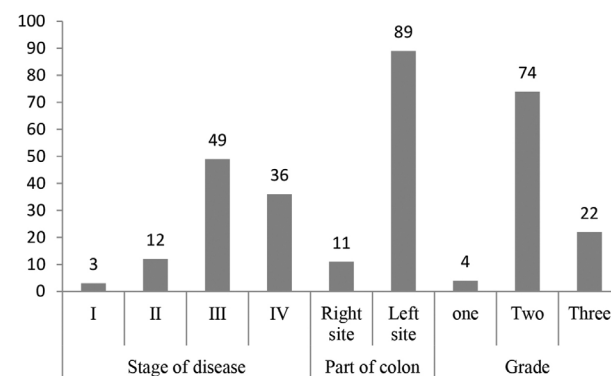
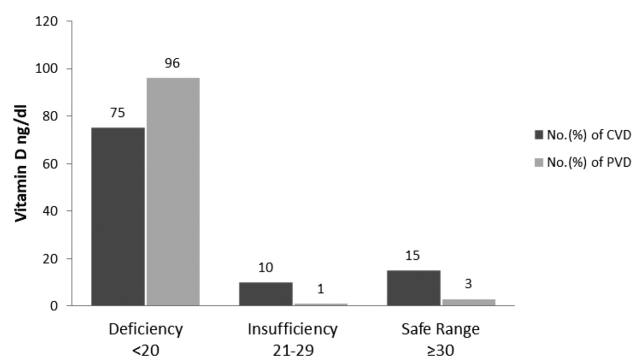


Fig. 3 Percentage of stage, grade and disease sidedness in patient group.



No = Number, CVD = Control vitamin D, PVD = Patient vitamin D

Fig. 4 Percentage of vitamin D level in both patients and control group.

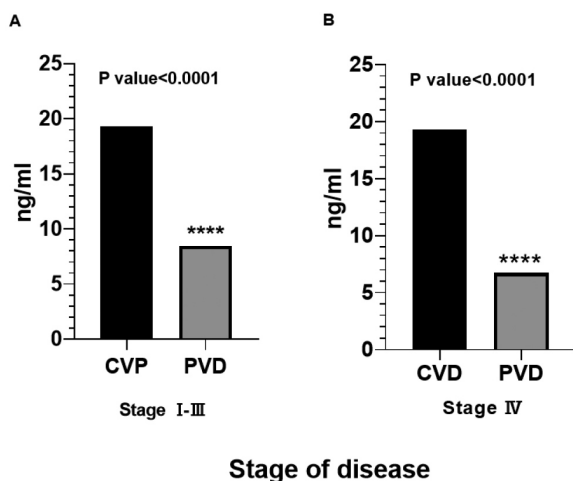


Fig. 5 Mean of vitamin D level in correlation with stage of disease.

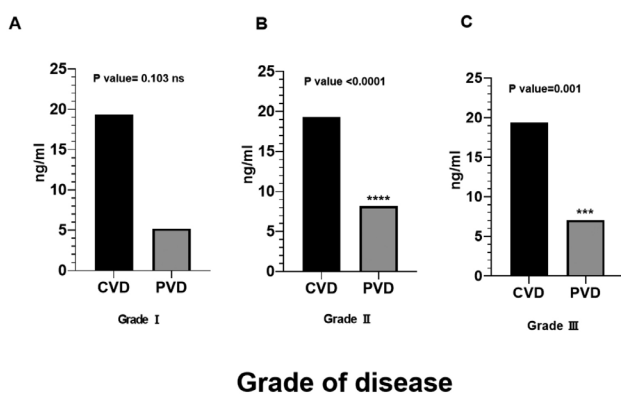


Fig. 6 Mean of Vitamin D level in correlation with grade of disease.

When mean of vitamin D level were taken in the deficit subgroups, mean of vitamin D level of patients were 6.833 (SD = 2.940), while mean of vitamin D level were 14.435 (SD = 4.356) in control group. In safe range group, vitamin D level was also lower in the Patient group while it was 34.0 (SD = 2.707) while in control group it was 52.350 (SD = 21.640).

Concerning Mean of vitamin D level based on stage of disease, in stage I-III cases vitamin D level was 8.456 (SD = 6.696), while the mean of vitamin D in stage IV colon cancer cases were 6.723 (SD = 3.191).

By looking at the level of vitamin D based on the grade of the tumor, mean of vitamin D were 5.200 (SD = 1.349), 8.199 (SD = 6.421) and 7.077 (SD = 2.967) in grade I, II and III tumors respectively.

Discussion

Colorectal cancer is the third most common newly diagnosed and leading cause of cancer death in the United States.¹⁹ Age impacts CRC incidence greater than any other demographic factor.²⁰ Ingestion of red meat,²¹ Obesity,²² High Caloric-diet,²³ physical inactivity²⁴ and prolonged cigarette smoking²⁵ are independent risk factors for colon cancer. Vitamin D level is also investigated in the pathogenesis of colorectal cancer.²⁶ According to studies, there is an inverse relationship between serum vitamin D levels and the occurrence of polyps and adenomas in the colon.^{26,27} Furthermore, the inverse relationship between dietary vitamin D3 intake or sunlight exposure and human colorectal cancer is supported by other researches.^{28,29} Although other local studies³⁰ and our study showed vitamin D deficiency is prevalent in our locality, our study revealed that vitamin D deficiency is more prevalent and common within diagnosed cases of colorectal cancer cases. By looking at our data, 21% more of the CRC patients have a deficiency in vitamin D compared to the control group. Moreover, when the mean vitamin D level was taken, in both patients and the control group, the level of vitamin D was more deficient in colorectal cancer patients than in the control group. These results take our attention to a point that there may be a link between vitamin D deficiency and colorectal cancer. Furthermore, within the patient's group, we analyzed the level of vitamin D based on the stage of cancer, we found that vitamin D level was lower in stage IV CRC cases in comparison to earlier stages. vitamin D deficiency did not show any relationship with pathological grade. Here, we come to a point that, our study is concurrent with other studies³¹ that have been published in international journals that have shown that vitamin D level deficiency is prevalent in colorectal cancer cases. Meanwhile, studies showing that, the level of 25OHD in the blood is more deficient in advanced stage,³² we should think about how to deal with this low level of Vitamin D in both our control group and patients. In the end, we should wait for further studies with large sample size to tell us that how much vitamin D supplement administration is beneficial to be given to reduce incidence and mortality of colorectal cancer cases.

Conclusion

This study is found out that Vitamin D deficiency is prevalent within colorectal cancer cases while more than Ninety five percent of the cases have deficiency in vitamin D level. Another point which was highlighted in this study is that when mean of vitamin D level was taken within the deficit group, mean of vitamin D level is lower in the CRC cases compared to control group within the same group. In addition this study showed that vitamin D level was revealed to be lower in stage IV CRC cases compared to early stage CRC cases. ■

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