

Original article

## Vitamin D Deficiency as a Risk Factor for Colorectal Cancer

Angjel Stojanovski \*<sup>1</sup><sup>1</sup> City General Hospital "September 8th", Skopje, North Macedonia

\*Corresponding author: Angjel Stojanovski, angelostojanovski@yahoo.com

### Abstract

**Introduction:** Colorectal cancer is the third most common diagnosis and cause of death in both sexes in highly developed countries. It is assumed that environmental factors are involved in the development of the disease, with strong evidence favoring lifestyle as well as the influence of diet. There are also many studies that indicate that low vitamin D levels are a significant risk factor for the occurrence of colorectal cancer.

**Objective:** To evaluate and compare serum concentrations of 25-hydroxyvitamin D (25(OH)D) between people diagnosed with colorectal cancer and a control group of healthy subjects.

**Materials and methods:** A total of 30 people with colorectal cancer and a control group of 30 healthy subjects were analyzed in the study.

**Results:** The comparison of the colorectal cancer group and control group in terms of serum vitamin D concentration showed that lower values were measured in the group with colorectal cancer. The mean vitamin D concentration in the colorectal cancer group was  $16.6 \pm 7.8$ , while in the control group it was  $28.7 \pm 10.3$ ; the difference of 12.1 was statistically significant, for  $p=0.001$ .

**Conclusion:** The results of the presented study indicate significantly lower serum concentrations of 25(OH)D in individuals with colorectal cancer compared to the control group.

(Stojanovski A. Vitamin D Deficiency as a Risk Factor for Colorectal Cancer. SEEMEDJ 2024; 8(2); 56-61)

---

Received: Jan 17, 2025; revised version accepted: Feb 11, 2025; published: Feb 14, 2025

KEYWORDS: colorectal cancer, cancer, vitamin D

## Introduction

Colorectal cancer (CRC) is the third most common diagnosis and cause of death in both genders in highly developed countries (1). The incidence rate is decreasing in Western countries, mainly due to endoscopic screening, but the incidence in the population younger than 50 years is increasing (2). Environmental factors are assumed to be involved in the development of the disease, with strong evidence favoring lifestyle as well as the influence of nutrition (3). A nutrition rich in red meat and calories, and low in fiber, fruits and vegetables, as well as physical inactivity, increase the risk of CRC. There are also many studies that indicate that low levels of vitamin D<sub>3</sub> are a significant risk factor for the occurrence of CRC (4). Hypovitaminosis of this vitamin is very widespread worldwide and is associated with several chronic diseases, including malignant diseases. Vitamin D<sub>3</sub> is a fat-soluble vitamin, the main function of which is to regulate the metabolism of calcium, magnesium and phosphate along with numerous other biological functions (5). As anti-inflammatory, immunomodulatory, pro-apoptotic and anti-angiogenic functions (6). Many studies suggest that it also acts as an inhibitor of carcinogenesis slowing tumor progression by promoting cell differentiation and inhibiting the proliferation of cancer cells (4). This vitamin also affects the activity of the systemic and mucosal immune system, generally with its regulatory and anti-inflammatory properties (6).

25-hydroxyvitamin D (25(OH)D) is a metabolite of vitamin D in the human body and is indicative of the total level of vitamin D. Measuring the serum concentration of (25(OH)D) is a common test performed to determine vitamin D status and to indicate vitamin D deficiency or sufficiency. Laboratories generally report (25(OH)D) levels in ng/mL. Normal values of serum vitamin D concentrations are those above 30 ng/mL, insufficient or reduced from 20-30 ng/mL and deficient or low values below 20 ng/mL (7,8).

The purpose of this study is to evaluate and compare serum 25(OH)D concentrations

between patients with diagnosed colorectal cancer (CRC) and a control group of healthy subjects (CG)(9).

## Material and methods

The study analyzed a total of 30 subjects with CRC and a CG of 30 healthy subjects. The study was conducted in the period from June 2022 to January 2024 in Skopje - North Macedonia.

Inclusion criteria for the study were: age 40-80 years, positive medical history, elevated tumor markers CEA and CA 19-9, and pathohistologically detected colorectal cancer.

Serum concentrations of 25(OH)D in the subjects were determined with an Access 2 BeckmanCoulter immunoassay analyzer using the CLIA (Chemiluminescence Immunoassay) method. Normal values of serum vitamin D concentrations were taken as those above 30 ng/mL, insufficient or reduced from 20-30 ng/mL and deficient or low values below 20 ng/mL.

Statistical analysis of data: The statistical analysis of the data obtained from the study was performed in the statistical programs Statistica for Windows 7.0 and SPSS 23.0. The obtained data are presented in tables and pictures.

Categorical (attributive) variables are presented with absolute and relative numbers. Numerical (quantitative) variables are presented with average, standard deviation, minimum and maximum values.

For comparison of the analyzed groups, in terms of gender, age, serum concentrations of vitamin D, non-parametric (Pearson Chi square test, Fischer exact test) and parametric tests for independent samples (Student t-test) were used.

Statistical significance was defined at the level of  $p < 0.05$ .

## Results

The gender structure of the subjects who participated in the study consisted of 26 (43 %) male and 34 (57%) female subjects. Female subjects were more frequently represented in

both the CRC group and the CG. The difference in the distribution of male and female subjects between the study and control groups was statistically insignificant ( $p=0.71$ ).

**Table 1. Gender of subjects with colorectal cancer and control group**

Variable	groups			p-value
	n	CRC n (%)	CG n (%)	
gender				
male	26	12 (40)	14 (47)	
female	34	18 (60)	16 (53)	$p=0.71$

CRC – colorectal cancer;  $\chi^2$  (Pearson Chi-square); CG - healthy subjects

Comparison of the CRC and CG groups in terms of serum vitamin D concentrations showed that lower values were measured in the group with diagnosed CRC. The mean vitamin D concentration in the CRC group was  $16.6 \pm 7.8$ ,

while in CG it was  $28.7 \pm 10.3$ ; the difference of 12.1 was statistically significant, for  $p=0.001$ .

The data are shown in Table 2.

**Table 2. Serum vitamin D concentrations in subjects with CRC and CG**

groups	Descriptive statistics vitamin D (ng/mL)		p-value
	mean SD	min-max	
CRC	$16.6 \pm 7.8$ ng/mL	5.4-34.1 ng/mL	
CG	$28.7 \pm 10.3$ ng/mL	12.5-47.7 ng/mL	$p=0.001^{**}$

CRC-colorectal cancer;  $t$ (Student  $t$ -test);  $**p$ ; CG- control group

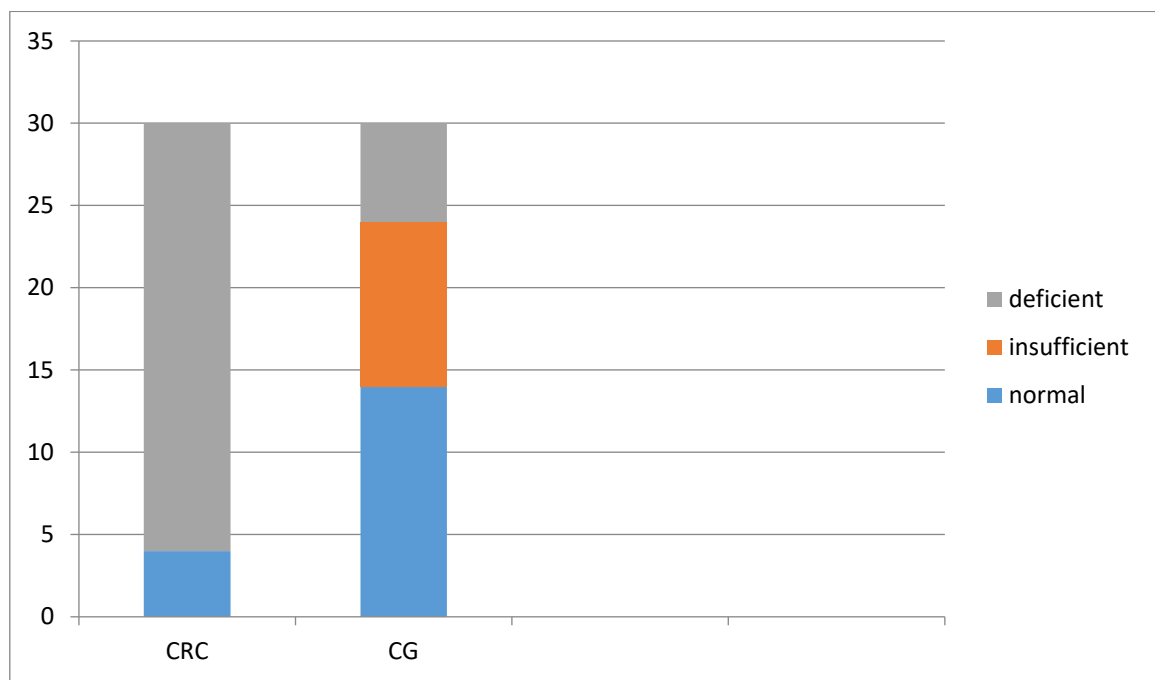
Normal vitamin D values were registered only in 4 (13%) subjects with CRC, and in 14 (47%) healthy subjects. Insufficient values were recorded in 10 (33%) subjects, all from the CG, while deficient vitamin D values were found in 26 (87%) subjects with CRC and 6 (20%) healthy subjects. For  $p <$

0.001, a statistically significant difference in the distribution of normal, insufficient and deficient vitamin D values between subjects from the CRC group and the CG of subjects was confirmed.

The data are shown in Table 3 and Figure 1.

**Table 3. Number (%) of cases with CRC and CG with normal, insufficient or deficient serum concentrations of vitamin D**

Vitamin D	group			p-value
	n	CRC n(%)	CG n(%)	
Normal values	18	4 (13)	14 (47)	Fisher exact p < 0,001
Insufficient values	10	0	10 (33)	
Deficiency values	32	26 (87)	6 (20)	

**Figure 1. Number (%) of CRC and CG cases with normal, insufficient or deficient serum vitamin D concentrations**

## Discussion

The results of our study indicate that patients with CRC have lower mean serum concentrations of vitamin D compared to the CG. There was a statistically significant difference in the distribution of normal, insufficient and deficient values of vitamin D between the CRC group and the CG. In the literature, there are conflicting views on the relationship between vitamin D deficiency and CRC. Our study identified vitamin D deficiency in 86.7% of patients with CRC. Our subjects have lower serum concentrations of vitamin D than reported

so far [11] for CRC, where Huncharek M et al. [11] reported that vitamin D deficiency was not associated with CRC, but another study [10] reported that there was a correlation. The results of our study indicate that serum concentrations of vitamin D are strongly associated with CRC.

**Acknowledgement.** None.

## Disclosure

**Funding.** No specific funding was received for this study.

**Competing interests.** None to declare.

## References

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA Cancer J Clin.* 2023 Jan;73(1):17-48. [PubMed]
2. Stoffel EM, Murphy CC. Epidemiology and Mechanisms of the Increasing Incidence of Colon and Rectal Cancers in Young Adults. *Gastroenterology.* 2020 Jan;158(2):341-353. [PMC free article] [PubMed]
3. Institute of Medicine Committee to Review Dietary Reference Intakes for Vitamin D and Calcium. *Dietary Reference Intakes for Calcium and Vitamin D.* Editors: AC Ross, CL Taylor, AL Yaktine, HB Del Valle. Washington, DC: National Academies Press; 2011.
4. National Institutes of Health, Office of Dietary Supplements (2021). Vitamin D Fact Sheet for Consumers. Retrieved May 4, 2022, from <https://ods.od.nih.gov/factsheets/VitaminD-Consumer/>
5. Herrick KA, Storandt RJ, Afful J, et al. Vitamin D status in the United States, 2011–2014. *American Journal of Clinical Nutrition* 2019; 110(1):150–157.  
[PubMed Abstract]
6. Heaney RP. Functional indices of vitamin D status and ramifications of vitamin D deficiency. *The American Journal of Clinical Nutrition.* 2004 Dec 1;80(6):1706S1709S.
7. Theodoratou E, Tzoulaki I, Zgaga L, Ioannidis JPA. Vitamin D and multiple health outcomes: umbrella review of systematic reviews and meta-analyses of observational studies and randomised trials. *BMJ.* 2014;348(apr01 2):g2035–5.
8. Holick MF. Vitamin D deficiency. *The New England journal of medicine.* 2007;357(3):266–81.
9. Deeb KK, Trump DL, Johnson CS. Vitamin D signalling pathways in cancer: Potential for anticancer therapeutics. *Nature Reviews Cancer* 2007; 7(9):684–700.  
[PubMed Abstract]
10. Deeb KK, Trump DL, Johnson CS. Vitamin D signalling pathways in cancer: Potential for anticancer therapeutics. *Nature Reviews Cancer* 2007; 7(9):684–700.[PubMed Abstract]
11. Huncharek M., Muscat J., Kupelnick B. Colorectal Cancer Risk and Dietary Intake of Calcium, Vitamin D, and Dairy Products: A Meta-Analysis of 26,335 Cases From 60 Observational Studies. *Nutr. Cancer.* 2008;61:47–69. doi: 10.1080/01635580802395733. [DOI] [PubMed] [Google Scholar] Ferrer-Mayorga G., Larriba M.J., Crespo P., Muñoz A. Mechanisms of action of vitamin D in colon cancer. *J. Steroid Biochem. Mol. Biol.* 2019;185:1–6. doi: 10.1016/j.jsbmb.2018.07.002. [DOI] [PubMed] [Google Scholar].

---

**Author contribution.** single author article

## Manjak vitamina D kao čimbenik rizika za kolorektalni karcinom

### Sažetak

**Uvod:** Kolorektalni karcinom treća je najčešća dijagnoza i uzrok smrtnosti kod oba spola u visoko razvijenim zemljama. Pretpostavlja se da su čimbenici okoliša uključeni u razvoj bolesti, pri čemu postoje snažni dokazi koji upućuju na utjecaj načina života i prehrane. Također, brojne studije ukazuju na to da su niske razine vitamina D značajan čimbenik rizika za nastanak kolorektalnog karcinoma.

**Cilj:** Procijeniti i usporediti serumske koncentracije 25-hidroksivitamina D (25(OH)D) kod osoba s dijagnosticiranim kolorektalnim karcinomom i kontrolne skupine zdravih ispitanika.

**Materijali i metode:** U studiji je analizirano ukupno 30 osoba s kolorektalnim karcinomom te kontrolna skupina od 30 zdravih ispitanika.

**Rezultati:** Usporedba skupine s kolorektalnim karcinomom i kontrolne skupine u pogledu serumske koncentracije vitamina D pokazala je da su niže vrijednosti izmjerene u skupini s kolorektalnim karcinomom. Prosječna koncentracija vitamina D u skupini s kolorektalnim karcinomom iznosila je  $16,6 \pm 7,8$ , dok je u kontrolnoj skupini bila  $28,7 \pm 10,3$ ; razlika od 12,1 bila je statistički značajna ( $p=0,001$ ).

**Zaključak:** Rezultati prikazane studije ukazuju na značajno niže serumske koncentracije 25(OH)D kod osoba s kolorektalnim karcinomom u usporedbi s kontrolnom skupinom.