Journal of Current Science and Technology, September-December 2024 Vol. 14 No. 3, Article 56

ISSN 2630-0656 (Online)

Cite this article: Sabah, Y. H., & Hassan, F. (2024). Comparison of serum vitamins C, D, and E in Iraqi colorectal cancer patients with and without non-alcoholic fatty liver disease to healthy individuals. *Journal of Current Science and Technology*, *14*(3), Article 56. https://doi.org/10.59796/jcst.V14N3.2024.56

Journal of Current Science and Technology

Journal homepage: https://jcst.rsu.ac.th

Comparison of Serum Vitamins C, D, and E in Iraqi Colorectal Cancer Patients with and without Non-Alcoholic Fatty Liver Disease to Healthy Individuals

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Received 1 March, 2024; Revised 9 April, 2024; Accepted 17 April, 2024
Published online 1 September, 2024

Abstract

Depending on their protective properties against different cases of Colorectal Cancer (CRC), vitamins C, D, and E are the main focus of this research. CRC is one of the global public health concerns. 30 healthy individuals provided serum samples, whereas the group of CRC patients was divided into three, totaling 90 individuals. Group I consisted of 30 newly diagnosed cases of CRC. Group II 30 consisted of consisted of 30 CRC patients who were administered three cycles of chemotherapy. Group III consisted of 30 diagnosed CRC patients who also have non-alcoholic fatty liver disease (NAFLD). The concentrations and groups of vitamins C, D, and E were evaluated using ELISA. The levels of Vitamin C were significantly lower ($p < 0.0001$) in individuals newly diagnosed with CRC, as compared to the control group. Patients who were recently diagnosed and treated for CRC and NAFLD exhibited comparable amounts of vitamin C. The level of vitamin E in control, newly diagnosed CRC and treated CRC patients displayed no significant differences, however comparing with newly diagnosed patients that suffered NAFLD, a significant decrease ($p = 0.0014$) in the level of vitamin E in CRC with NAFLD group was. The levels of Vitamin D in all groups of patients with colorectal cancer were significantly lower than those in the control group ($p < 0.0001$). Colon cancer patients exhibited significantly decreased levels of vitamin C and D compared to healthy individuals. Vitamins showed potential as diagnostic markers for distinguishing between groups. It is necessary to analyze these findings as the level of serum vitamins may have potential use in the prognosis of the CRC in patients.

Keywords**:** *Vitamin D; vitamin C; vitamin E; CRC; NAFLD*

1. Introduction

Three distinct factors form the foundation of Cases of Colorectal Cancer (CRC). The premise that Colon Cancer (CC) and Rectal Cancer (RC) develop in the large intestine, which is regarded as a single organ, is the first component. The colonic and rectal walls share a similar anatomical structure, including a muscular layer, mucosa, and partially serosa. Their histology is also similar. The colorectal tract's roles in stool concentration, fluid resorption, transit, and excretion make up the third factor (Alzahrani et al., 2021). CRC originates in the mucosal lining of the colon or rectum due to the uncontrolled growth of epithelial cells. This genetically diverse cancer often involves V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (KRAS) and V-raf murine sarcoma viral oncogene homolog B1 (BRAF) oncogenic mutations. Globally, CRC ranks third in frequency and fourth in cancer-related mortality. In Iraq, it is the fourth most common cancer (El Halabi et al., 2018; Mhaidat et al., 2021; Khalil et al., 2021; Sung et al., 2021).

Cancer and metabolic disorders have significant global health and economic impacts, often co-occurring and influencing disease severity (Liu et al., 2024; Saelee et al., 2022). Non-alcoholic fatty liver disease (NAFLD), a prevalent gastrointestinal metabolic disorder, affects approximately 25% of the world's

population. Factors like obesity, poor nutrition, a sedentary lifestyle, and hyperlipidemia contribute to NAFLD, which can lead to metabolic disorders such as hyperlipidemia and type 2 diabetes if left undiagnosed and untreated (Younossi et al., 2019b; Koenig et al., 2019; Younossi et al., 2019a). Additionally, untreated NAFLD can progress to NASH/fibrosis, cirrhosis, and Hepatocellular Carcinoma (HCC) and is associated with gastrointestinal malignancies, including CRC (Rastogi & Kapil, 2020; Muhidin et al., 2012).

Vitamin C, a crucial water-soluble micronutrient, is an antioxidant and cofactor in human enzymatic processes. It exists in two molecular forms with distinct stability and transport mechanisms. Studies suggest that physiological Vitamin C may possess anticancer properties, involving the transportation of hydrogen peroxide and oxygen free radicals to destroy tumor cells through metabolic pathways. Although the exact mechanism of action remains unknown, therapeutic concentrations of ascorbic acid have shown cytotoxic, antiproliferative, and genotoxic effects in colon cancer cell lines (Pires et al., 2018; Vissers, & Das, 2019; Roa et al., 2020; Chen et al., 2020).

Sunlight and ultraviolet-B (UVB) rays cause keratinocytes in the skin to produce more vitamin D. Vitamin D is important for many bodily functions, such as keeping calcium and phosphorus levels stable (Wacker, & Holick, 2013). Recent research has focused on vitamin D's potential anticancer effects, particularly in CRC, affecting pathways such as Wnt/β-catenin signaling, inflammation, and apoptosis to slow carcinogenesis (Boughanem et al., 2021; Javed et al., 2020).

Vitamin E plays a crucial role in maintaining good health and preventing illnesses (Pateiro et al., 2020). Its composition includes tocopherol and tocotrienol homologs, primarily sourced from nuts and vegetable oils (Panpraneecharoen, & Chumanee, 2022; Meganathan, & Fu, 2016). Interestingly, alpha-tocopherol is the least metabolized form of vitamin E, owing to alpha-tocopherol transfer protein (TTP) in the liver (Viola et al., 2012; Niki, 2015). Additionally, it has been discovered that the eight lipophilic antioxidants found in vitamin E are the most abundant lipid-soluble antioxidants present in human plasma, according to recent research (Jiang, 2014; Abraham et al., 2019).

In one of the studies in Iraq they also investigated the levels of vitamin C and D which they have found a significant differences between the levels of CRC patients and healthy individuals (Mustafa et al., 2022). In another study by Abdulrahman et al., (2021) found the following chemotherapy, vitamin D levels significantly increased from their baseline, which was lower than normal. However, the vitamin D level stayed below normal (21.11 ± 7.21 vs. 26.55 ± 15.22) (Abdulrahman et al., 2021).

The study by Sadeq et al., (2021) in Erbil, Kurdistan, Iraq, showed that over 95% of colon cancer cases have vitamin D deficiency. This suggests that vitamin D deficiency is common in these cases. Another finding of this study is that the mean vitamin D level is lower in the deficit group compared to the control group (Sadeq et al., 2021).

Researchers have found that compared to healthy individuals, cancer patients had noticeably more DNA damage (Oh, & Jun, 2023; Ketkomol et al, 2024; Najeeb et al., 2020). Remarkably, Najeeb et al. (2020) have discovered a strong negative association between vitamin D plasma levels and DNA damage in both cancer patients and healthy individuals ($p < 0.001$) in Iraq. By inducing apoptosis and cell cycle arrest, vitamin E has an inhibitory effect on cell proliferation. Two different pathways lead to apoptosis: the intrinsic pathway, which is affected by mitochondrial rupture releasing cytochrome c into the cytosol, and the extrinsic pathway, which is mediated by death receptor signaling. Ultimately, these pathways come together to cause the activation of caspases during execution, specifically caspase-3, which causes poly-ADP-ribose-polymerase (PARP) to fragment (Aggarwal et al., 2010). Angiogenesis, which involves the fast proliferation and migration of endothelial cells, is essential for the development and dissemination of tumors (Reiter et al., 2020). Research carried out in both in vitro (laboratory settings) and in vivo (living organisms) environments has demonstrated that specific forms of vitamin E, particularly tocotrienols, can impede the angiogenesis process. Furthermore, it has been discovered that tocotrienols can reduce VEGF receptor expression (Samant, & Sylvester, 2006).

2. Objectives

To compare the serum levels of vitamins C, D, and E in Iraqi CRC patients with and without NAFLD to those of healthy persons.

3. Materials and methods

3.1 Study design

The study was conducted on 120 individuals (64 males and 56 females) from February 2022 to August 2022. Blood samples were collected from

patients who were diagnosed with colon cancer from Al-Amal Hospital for Radiation and Nuclear Medicine and Oncology Teaching Hospital at Baghdad Medical City. Human blood specimens were obtained from patients attending these hospitals. Inclusion criteria involved newly diagnosed patients and patients who had received three doses of chemotherapy. A comprehensive set of clinic pathological parameters, including age, gender, tumor site, grade, and stage, were collected with the patient's medical reports. The necessary permissions were acquired from Al-Amal Hospital for Radiation and Nuclear Medicine and Oncology Teaching Hospital and were accepted by the institutional Ethics Council of Al-Nahrain University/College of Science (Reference Number COS 592/2021). The subjects provided informed consent and/or agreement. Studied individuals were categorized into three groups as described in Table 1: Group I: 30 newly diagnosed patients with colorectal cancer (CRC) (13 males and 17 females). Group II: 30 CRC diagnosed patients who received 3 doses of chemotherapy (16 males and 14 females). Group III: 30 newly diagnosed CRC patients with nonalcoholic fatty liver diseases (NAFLD) (18 males and 12 females). Thirty healthy individuals participated in this study as controls (15 male and 15 female) with age range of 30 – 40 years as Group IV.

3.2 Estimation of serum vitamins C, D and E levels

Each participant, including both patients and healthy control subjects, provided a 5-millilitre blood sample. The sample was allowed to clot for one hour at room temperature before being centrifuged at 5,000 RPM for 10 minutes. After separation into smaller portions, all sera were frozen at -80^{o}C until ready for use. The concentrations of vitamins C, D, and E were determined using the Human Vitamins C, D, and E ELISA® Kits from SunLong Biotech (China).

3.3 Statistical analysis

The statistical analysis was performed using GraphPad Prism version 9.2 (GraphPad Software Inc., LaJolla, CA). Student's t-test and Two-way ANOVA (Tukey's Test) were used to determine whether group variance was significant or not. Receiver operating characteristic (ROC) curve analysis was performed to determine the area under curve (AUC) and the optimum cut-off value of serum markers. Quantitative parametric data were subjected to the Shapiro-Wilk test to confirm the normal distribution and were expressed as mean ± SD. Statistical differences were defined as * $p < 0.05$ and ** $p < 0.01$. For new methods and protocols, please provide a comprehensive description. Well-established methods can be briefly summarized and appropriately referenced.

4. Results and discussion

4.1 Evaluation of vitamin C

The level of vitamin C in the serum of different study groups was investigated. Results in Table 2 and Figure 1A showed that the level of vitamin C was significantly ($p < 0.001$) decreased in newly diagnosed (0.4507 ±0.1566 mg/dL), treated CRC (0.4880±0.1591 mg/dL), and NAFLD patients (0.5067±0.2738 mg/dL) compared with the control group (1.847± 0.5139 mg/dL). Newly diagnosed CRC, treated CRC, and NAFLD patients almost shared the same level of vitamin C with no significant differences.

Table 1 Group of CRC patients categorized by age and gender, with the group of healthy persons as the control

No. of Patients (%)	Type	Group	Age Range and percentage			Sex	
			Age	N.	%	Nale	Female
I	Newly Diagnosed CRC	30 (25%)	< 40	4	13.3%	17 (56.7%)	13 (43.3%)
			40-60	14	46.7%		
			> 60	12	40%		
II	Treated CRC	30 (25%)	23.3%	7	< 40	14 (46.7%)	16 (53.3%)
			50%	15	40-60		
			26.7%	8	> 60		
III	Newly Diagnosed CRC with NAFLD	30 (25%)	< 40	30%	9	12 (40%)	18 (60%)
			40-60	36.7%	11		
			> 60	33.3%	10		
IV	Control	30 (25%)	Age between 30 -40			15 (50%)	15 (50%)
Total			**120 (100%)**				

Table 2 Mean ± SD serum levels of vitamins C, D and E in different study groups

Vitamin	Control	Newly Diagnosed CRC	Treated CRC	Newly Diagnosed CRC with NAFLD
Vitamin C (mg/dL)	1.847± 0.5139[a]	0.4507 ±0.1566[b]	0.4880±0.1591[b]	0.5067±0.2738[b]
Vitamin D (ng/ml)	32.33±8.9[a]	16.7±5.9[b]	22.5±7.0[b]	21.0±5.7[b]
Vitamin E (ug/mL)	13.3±3.34[a]	12.02±3.1[a]	12.2±2.6[a]	9.3±1.9[b]

Normal ranges of vitamins: vitamin C (0.6-2 mg/dL), vitamin D (> 30 ng/mL), and vitamin E (5.5-17 µg/mL)
Indicates statistical significance at p-value of < 0.01.

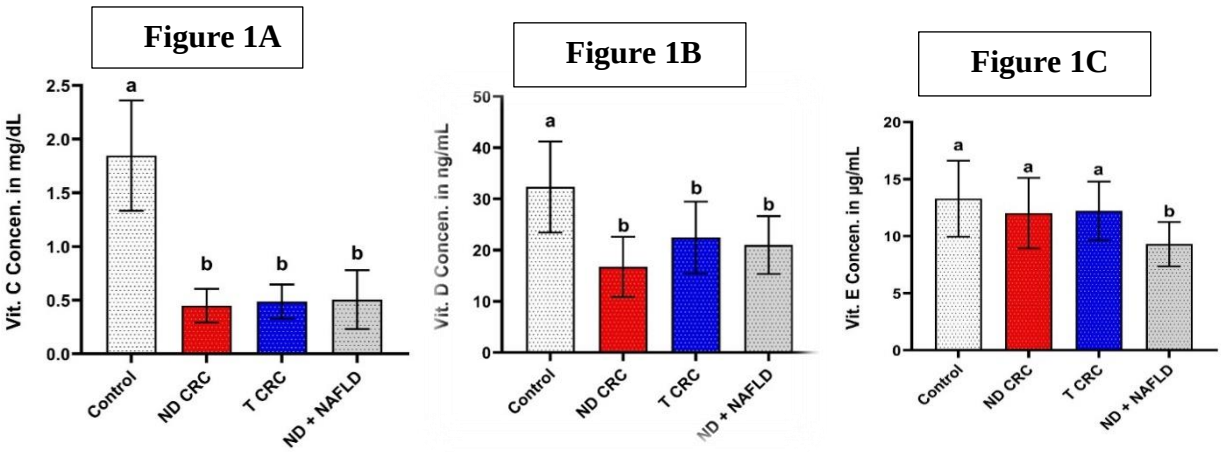

Figure 1 Serum levels of vitamin C (1A), vitamin D (1B), and vitamin E (1C) in various groups: newly diagnosed colorectal cancer (CRC) patients (ND CRC), cisplatin-treated CRC patients (T CRC), newly diagnosed CRC patients with non-alcoholic fatty liver disease (NAFLD) (ND + NAFLD), and healthy individuals as the control group (Control)

Several studies analyzing vitamin C status in newly diagnosed CRC patients have observed significantly lowered blood plasma vitamin C levels compared to healthy controls. A meta-analysis compiling data across ten case-control studies found that newly diagnosed CRC patients had an average plasma vitamin C concentration of around 38 µmol/L, nearly 30% lower than healthy individuals without cancer. Plasma vitamin C levels in participants with CRC are in accordance with those reported in the literature, which ranged between 1.8 and 4.8 mg/L for cancers of the gastrointestinal tract (Temraz et al., 2023).

Furthermore, higher stage III and IV CRC tumors correlated with greater deficiencies in circulating vitamin C (Temraz et al., 2023). These findings are in agreement with the results obtained in which more than 33% of vitamin C level was dropped in newly diagnosed CRC patients (Leenders et al., 2014) reported a significant decrease in vitamin C level in CRC compared with control, while Saygili et al., (2003) confirmed that the level of vitamin C in healthy control was double that of CRC patients. These findings can be attributed to increased oxidative stress and inflammation associated with rapidly proliferating malignant cancer cells in newly diagnosed patients. Vitamin C is an essential antioxidant and enzymatic cofactor that becomes excessively depleted by reactive oxygen species generated during oncogenic transformations. Additionally, dysfunctional metabolic pathways in tumor tissue can also reduce vitamin C transport and absorption from diet or supplementation (Linowiecka et al., 2020). The considerably lower vitamin C reserves observed in newly diagnosed CRC patients underline its insufficient availability during the critical pre-clinical phases of tumorigenesis and early cancer progression. Boosting vitamin C status through increased supplementation shows promise as a safe, low-cost intervention that may improve prognostic outcomes. Further research should analyze longitudinal fluctuations in vitamin C levels across all CRC stages while accounting for confounding lifestyle factors like diet, smoking status, and alcohol intake between cases and controls (Shi et al., 2023). The vitamin C status of colorectal cancer patients can be significantly impacted by ongoing anticancer

treatments. The plasma vitamin C levels in patients currently undergoing surgical, chemotherapeutic, radiotherapeutics, or combined treatment regimens for colorectal malignancies have been observed with reduction compared to control. This appears primarily attributable to increased inflammation and oxidative stress provoked by aggressive cancer therapies coupled with decreased oral intake and intestinal absorption of vitamin C (El Halabi et al., 2018). The CRC patients with NAFLD were reported to have decreased level of vitamin C. Results showed that the level of vitamin C in newly diagnosed CRC with NAFLD was not significantly different from that of newly diagnosed CRC and treated groups. This means that NAFLD condition does not markedly affect the level of vitamin C in CRC patients. Low vitamin C levels are thought to be mostly caused by oxidative stress. Ascorbate's capacity to donate electrons, either as an antioxidant or a cofactor for enzymes that contain metals, allows it to have physiological effects. Ascorbate is a necessary cofactor for the 2-oxoglutarate dependent dioxygenases, a class of enzymes that are particularly relevant to cancer. In addition, this superfamily contains hydroxylases that control the hypoxic response through transcription factor activation, influencing the development of cancer, as well as DNA and histone demethylases that alter the phenotype of cancer cells (White et al., 2023).

Patients diagnosed with CRC showed lower plasma vitamin C concentrations compared to individuals without any health conditions. This study conducted a prospective statistical analysis to evaluate the ability of plasma vitamin C levels at the time of diagnosis to predict survival and progression of people with colorectal cancer (CRC) by comparing these levels to a control group without disease. The results indicated that plasma levels were consistent with values published of (Temraz et al., 2023). In addition, it was noted that colorectal cancer (CRC) was an important factor in predicting low plasma vitamin C levels due to malabsorption, independent of other variables.

4.2 Evaluation of vitamin D

The level of vitamin D in all studied groups was evaluated. According to Table 2 and Figure 1B, the level of vitamin D in three different CRC patient groups was significantly reduced compared with the control group ($p < 0.001$ with newly diagnosed CRC, 0.0016 for treated CRC patients and 0.0002 for newly diagnosed CRC patients with NAFLD).

Numerous studies measuring and comparing vitamin D status between CRC patients and healthy controls consistently demonstrate significantly reduced plasma 25-hydroxyvitamin D [25(OH)D] levels among CRC cases. A meta-analysis of 21 case-control studies found that newly diagnosed CRC patients had mean plasma 25(OH)D levels of just over 35% lower than those of disease-free controls. Furthermore, inverse associations are repeatedly observed between circulating 25(OH)D concentrations and advancing stages of CRC tumors (Fukui et al., 2015). These trends underline how adequate vitamin D reserves likely play a protective role against the onset and progression of colorectal malignancy. The anti-carcinogenic effects of vitamin D are multifaceted, modulating transcription of genes involved in regulating inflammation, apoptosis, angiogenesis, differentiation, and proliferation/ metabolism of colon tissue. Consequently, depressed plasma 25(OH)D levels prevalent among CRC patients signify loss of these tumor-suppressive benefits during pathogenesis of the disease (Meeker et al., 2016). The considerably insufficient vitamin D status characterizing CRC may stem from inadequate dietary intake, reduced solar UVB exposure, dysregulated metabolism by diseased bowel tissue, inflammation-induced sequestration, and rapid utilization by aggressively proliferating tumors. Genetic factors influencing vitamin D transport and binding proteins may also disproportionately affect status in CRC patients (Emmanouilidou et al., 2016). Regardless of the exact mechanisms, the overt deficiencies observed underscore the necessity of screening and boosting vitamin D availability as an adjuvant supportive strategy alongside conventional CRC treatment (Engelsen, 2010). The levels of both total vitamin D in the blood of CRC patients were found to be significantly lower than in healthy controls. The small intestine is the site of numerous significant homeostatic functions of calcitriol. vitamin D2 is derived from plants, whereas vitamin D3 is nearly entirely created after exposure to sunlight. The four forms of vitamin D are vitamin D3, vitamin D2, ergocalciferol, and calcidiol. They are carried to the liver, where they are transformed into calcidiol, the body's active form of vitamin D. The kidney is where calcitriol is mostly produced from calcidiol. CYP27A1, CYP27B1, and CYP24B1 are the three cytochrome P450s (CYPs) involved in the metabolism of vitamin D. CYP27A1 hydroxylates vitamin D in the liver to produce 25(OH)D. Next, in the kidney, CYP27B1 catalyzes the conversion of 25 (OH)D to

calcitriol, which is the active form that affects human biology. CYP24A1 changes calcitriol into calcitroic acid, an inactive, water-soluble form, as calcitriol levels rise. Cancerous cells abundantly express CYP24A1, which neutralizes vitamin D, potentially having antitumor effects, thereby promoting the progression of cancer. Cancer cells may benefit from CYP24A1 and calcitriol knockdown as possible therapeutics (Wang et al., 2018).

Patients diagnosed with colorectal cancer (CRC) frequently exhibit heightened infiltration of immune cells, which in turn plays a significant role in the progression of CRC. Immunotherapy is widely acknowledged as a successful approach for enhancing the prognosis of patients with colorectal cancer (CRC). The correlation between the 25-OHD level and the survival of patients with colorectal cancer (CRC) is more pronounced in cases where there is a decreased presence of lymphocytes surrounding the tumor. Vitamin D insufficiency is linked to substantial fluctuations in peripheral immune cells. Regulatory T (Treg) cells and T-helper type 17 (Th17) cells play a role in the immune response. Presently, there is a dispute over the involvement of Th17 in the CRC. The prevailing perspective is that Th17 cells have a role in the development of CRC. Th17-mediated pro-inflammatory reactions contribute to the development of tumors, while Treg has varying functions at different stages of colorectal cancer (CRC) (Marques et al., 2021)

4.3 Evaluation of vitamin E

The serum level of vitamin E in all tested groups was determined. The level of vitamin E in control, newly diagnosed CRC, and treated CRC patients displayed no significant differences, however comparing with newly diagnosed patients suffering from NAFLD, a significant decrease in the level of vitamin E in CRC with NAFLD group was detected ($p = 0.0014$ with control, 0.0468 with newly diagnosed and 0.0295 with treated CRC patients), as illustrated in Table 2 and Figure 1C.

While vitamin C status is frequently found to be compromised in newly diagnosed colorectal cancer (CRC) patients, emerging research indicates that circulating vitamin E levels exhibit little significant difference compared to healthy controls. A meta-analysis of 17 case-control studies measured and compared plasma α-tocopherol (the main form of vitamin E) concentrations between newly diagnosed CRC subjects and colonoscopy-cleared controls. No considerable distinctions in plasma α-tocopherol were found between the groups across most studies examining vitamin E status - mean values differed by less than 5% among cases and controls (Xu et al., 2013). These findings signify that despite increased inflammation and oxidative stress characterizing malignant CRC tumors, the vitamin E reserves of newly diagnosed patients remain mostly preserved to a degree similar to healthy individuals without cancer. This contrasts with the frequent vitamin C deficiencies observed and suggests distinct antioxidant mechanisms at play during early CRC onset compared to other micronutrients. The lipid solubility of vitamin E may provide buffering protection and retention in plasma carriers (Myara et al., 2003). Furthermore, interfaces between CRC pathogenesis pathways and vitamin E-dependent enzymatic activity may uniquely preserve its availability. While vitamin E status seems to remain mostly unaffected among newly diagnosed colorectal cancer (CRC) patients without comorbidities, emerging evidence indicates that CRC patients additionally suffering from nonalcoholic fatty liver disease (NAFLD) exhibit considerable depletion of circulating vitamin E reserves (Myara et al., 2003). Numerous studies have analyzed and cross-compared plasma vitamin E (specifically α-tocopherol) levels between healthy controls, newly diagnosed CRC subjects, and cohorts diagnosed with both simultaneous NAFLD-CRC. Across multiple analyses, patients with the NAFLD-CRC comorbidity consistently displayed significantly lowered plasma α-tocopherol concentrations-up to a 60% reduction compared to newly presenting CRC patients without liver disease. The declines in the dual diagnosis group appeared most stark in those with advanced histopathological NAFLD severity and higher stage CRC tumors. Declining plasma vitamin E strongly correlated with worsening prognostic indicators (Sato et al., 2015). These findings highlight NAFLD as a negative modifier of micronutrient status in CRC patients, substantially decreasing vitamin E bioavailability through mechanisms of chronic systemic inflammation, impaired E absorption and transport from the steatotic liver, and depleted hepatic vitamin E storage innate to worsening NAFLD. Furthermore, aggressive tumor-driven oxidative stress likely rapidly consumes any available vitamin E in advanced malignancies (Dong et al., 2017).

Recent research supports findings suggesting that vitamin E has the potential to offer protection against cancer, possibly due to its demonstrated properties. The chemical has antioxidant properties

and boosts the immune system. The interaction between the two phenomena is characterized by a distinct cause-and-effect pattern. The correlation between cancer and vitamin E has not been conclusively proven, and it is probable that extensive intervention trials will be necessary to ascertain this. Vitamin E, along with other vitamins, whether taken alone or in combination, is unlikely to be associated with protection against the development of cancer at any site in the body. However, there is a growing belief that the use of vitamins, together with other micronutrients, may be highly advantageous in preventing cancer during chemotherapy (Baharuddin et al., 2019). Tocotrienol, a form of vitamin E, has been demonstrated to not only impede the proliferation of cancer cells but also induce apoptosis in these cells. Tocotrienols exert an anticancer effect on cancer cells by limiting the formation of new blood vessels (angiogenesis) and by slowing the development of tumor cells. A laboratory study was conducted to investigate the impact of delta-tocotrienol on HCT-116 and SW-620 cells, which are human colon cancer cells and metastatic colon cancer cells, respectively. The results demonstrated that delta-tocotrienol effectively suppressed the proliferation of cancer cells and triggered apoptosis (Husain, 2017).

4.4 Receiver Operating Characteristic (ROC) analysis for vitamins

The diagnostic significance of vitamins C, D, and E detection between control and patient groups was determined using ROC analysis. The decreased serum level of vitamin C in patient groups occupied a significant area under the curve (AUC), which was 0.8570 ($p < 0.0001$). At a cut-off value of 1.74 mg/dL, the sensitivity and specificity of vitamin C were 69 and 80%, respectively as shown in Figure 2. The AUC of vitamin D was also considered between control and patient groups of CRC. The decrease of vitamin D in CRC patients showed a high significant prognostic power with an AUC of 0.8867 ($p < 0.0001$) and the best sensitivity of 87% and specificity of 73% were achieved at a cut-off value of 36.5 ng/mL. ROC analysis of vitamin E indicated a non-significant value for CRC with an AUC of 0.7096 ($p = 0.0157$). The cut-off value that exhibited 73% sensitivity and 60% specificity was 13.0 µg/mL.

5. Conclusion

Low levels of vitamins C, D, and E in the blood are correlated with CRC. Decreased amounts of these vitamins can be quite dangerous in Iraq. The lowered level of vitamin C and D in blood may have potential use in prognosing CRC in patients and can benefit and help CRC patient by their mechanism against cancer or against oxidative stress. Thus, vitamins C, D, and E should increase the rate of 5-year survival in CRC patients. The risk of developing NAFLD is also influenced by vitamin C levels. In cancer patients, vitamin C may function as a protective barrier against oxidation, while vitamin E reduces oxidation. Controlling the amount of fat and fruit consumed in the diet can help prevent colon cancer. Dietary factors can have a substantial impact on the development of colon cancer.

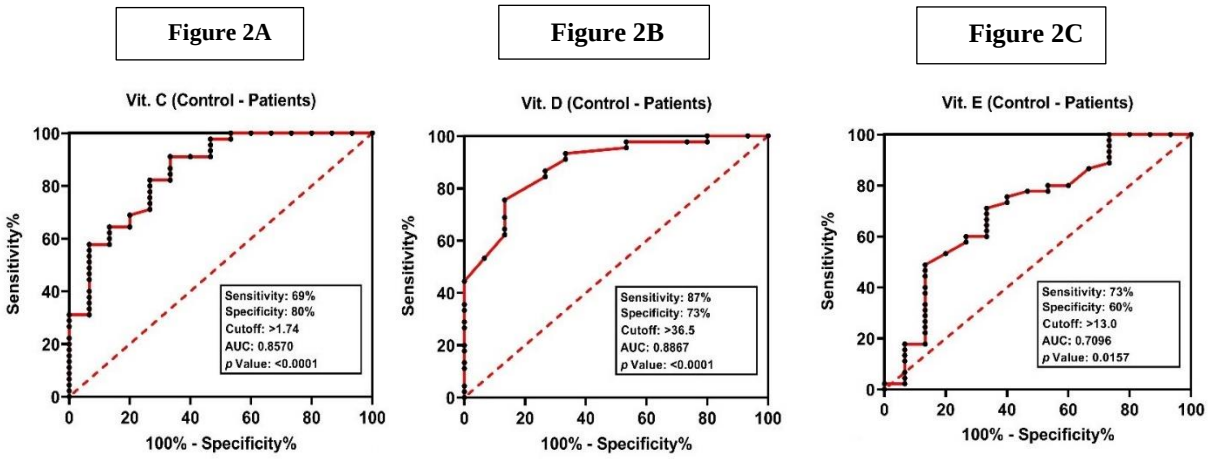

Figure 2 Receiver operating characteristic (ROC) analysis of vitamin C(2A), vitamin D(2B) and vitamin E(2C) level among CRC patients showing area under curve (AUC), p-value, sensitivity, specificity, and cut-off value

6. Acknowledgements

We are sincerely grateful to the staff, healthcare professionals, and administration at the Al-Amal Hospital for Radiation and Nuclear Medicine and Oncology Teaching Hospital at Baghdad Medical City for their unwavering dedication and exceptional care provided to patients, as well as for their assistance in providing and collecting the necessary samples for our research.

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