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Estimation of the Levels of UDP Glucuronosyltransferase 2 Activity and some Vitamins (B12, B17, C and D) for Patients with Colon Cancer

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ABSTRACT

One of the most prevalent types of cancer in humans and a well-known cause of mortality is colon cancer. This study aimed to measure the serum levels of UDP glucuronosyltransferase vitamins (B12, B17, C and D) in patients with colon cancer and to determine how these levels affect the course of the disease. The participants in the current study include 45 healthy people (mean age = 62.03±12.3 yrs.) who serve as a comparison group and 65 subjects with subjectively diagnosed colon cancer (mean age = 64.03±12.2 yrs.). The serum UDP glucuronosyltransferase 2B17, Vitamin B12, Vitamin D, and Vitamin C levels were among the determined biochemical markers**.** When colon cancer patients were compared to the control group, UDP glucuronosyltransferase 2B17 levels were significantly higher ($P < 0.0001$). In comparison to the control group, the serum Vitamin B12, Vitamin D, and Vitamin C levels in colon cancer patients were all considerably lower ($P < 0.0001$), $P < 0.001$, and $P< 0.05$, respectively). In our investigation, a marker for colon cancer was shown to be an increase in blood UDP glucuronosyltransferase 2B17 and a decrease in vitamin B12, vitamin D, and vitamin C levels.

Keywords: Colon Cancer, (UDP -2B17), Vitamin B12, Vitamin C, Vitamin D.

INTRODUCTION

The susceptibility to this and other configurations of cancer may be significantly influenced by enzymes involved in the therapeutic elimination of mutagenic substances to the synthesis of genetic material (DNA) (Guillemette, 2003; Nagar and Remmel, 2006). Therefore, it would be valuable to shed light on the relationship between a person's changeability in the genes that code for these enzymes and changed risk health for carcinoma vulnerability. In humans, different endogenous and exogenous species are detoxified by uridine diphosphate-glucuronosyltransferases (UGTs), which are fundamental enzymes of phase II metabolism (Haakensen *et al.*,2010; He *et al.*, 2009; Hirata *et al.*,2010). In phase II processes of metabolic pathways, UGTs are in charge of transporting the glucuronosyl group from the uridine diphosphate-glucuronic acid to a variety of hydrophobic molecules, including bile salts, bilirubin, steroid compounds, medicines, and environmental oncogenes (Hum,1999; Park *et al.*,2006). UGTs also play a role in converting endogenous and exogenous steroid hormones like estrogens and androgens into less potent substances through glucuronidation (Yong *et al.*,2010). The glucuronide molecules produced are more hydrophilic, less toxic, and more effectively excreted from the body through bile and urine (Turgeon He *et al.*, 2003; Zheng *et al.*,2002). Vitamin D (1,25-Dihydroxycholecalciferol) deficiency has been reported to be associated with several carcinomas, including breast, colorectal, prostate, and plasma cell myeloma. While some studies have viewed vitamin D (1,25-Dihydroxycholecalciferol) as a potential health danger, others have found an inverse link between vitamin D concentrations and cancer death rates. It is necessary to assess vitamin D (1,25-Dihydroxycholecalciferol) levels in cancer since 1,25-Dihydroxycholecalciferol is thought to affect the currency, risk, and continuity of cancer (Gupta *et al.*,2011).

the significant molecular and genetic findings encourage 1,25-Dihydroxycholecalciferol's protective function against colon cancer. Numerous epidemiological studies have also examined the connection between a vitamin D deficiency and a higher risk of developing this malignancy. Numerous studies have shown a connection between 1,25-Dihydroxycholecalciferol deficiency and colon cancer (Kim, 2000; Haghighi *et al.*,2009; Selhub, 2000). Despite the link between 1,25-hydroxy vitamin D status and colon cancer risk, there is not enough information about the relationship between vitamin D and colon cancer progression from stages I to IV. According to a study, colorectal cancer cases had greater 1,25-Dihydroxycholecalciferol concentrations than healthy people. While vitamin D (1,25-Dihydroxycholecalciferol) levels decreased with increasing cancer stages, 1,25-Dihydroxycholecalciferol levels showed homogeneity throughout the various grades of colon carcinoma (Niv *et al.*,1999).

As coenzymes in the metabolic route of a one-carbon molecule necessary for DNA methylation and nucleotide production, vitamin B12 plays a crucial function. Defects in this metabolic system may lead to changes in DNA precursors, disturbed DNA methylation, and insufficient DNA repair, all of which may contribute to oncogenesis, particularly in colon cancer (Selhub *et al.*, 2000). The current study aimed to measure the serum levels of the UDP glucuronosyltransferase 2 vitamins (B12, B17, C and D) in patients with colon cancer.

MATERIALS AND METHODS

Study Subjects

This study involved 65 subjects, aged 29–67 years, who have been admitted the Nanakaly Hospital in Erbil City. These Patients' serum was diagnosed to have colon cancer. A total of 45 healthy individuals from the outpatient were involved in this study as a control group.

Blood sample collection

A Blood sample (Six mL of venous blood) was collected before taking any treatment. To separate serum, blood was allowed in red top collection tubes ("Vacutainer") to clot at room temperature, undisturbed for a minimum of 30 to 60 minutes. The clot was removed by centrifugation at 1,000-1,500 x g for 10 minutes using a centrifuge. Following centrifugation,

immediately the serum was transferred into sterile polypropylene tubes (preferably 1.5 ml Eppendorf tubes). Aliquot serum in 100 µl portions were stored at –80°C until they were analyzed.

METHODS

Measurement of serum (UDP glucuronosyltransferase 2B17 and Vitamin D and Vitamin 12)

The concentration of (UDP 2B17, Vitamin D and Vitamin 12) in serum samples was measured by competitive enzyme-linked immunosorbent assay (ELISA) technique using the kit manufactured by BioVision company.

Measurement of serum Vitamin C:

Serum Vitamin C was measured photometrically using a kit from Biovision laboratories USA.

Statistical analysis:

The study's data were statistically analyzed using ANOVA test and paired t-test. Statistical comparisons were performed A P-value of <0.05 was regarded as satisfactory and remarkable.

RESULTS AND DISCUSSION

(UDP glucuronosyltransferase 2 B17) Serum's level

The results in (Table 1) and Fig. (1) demonstrated a remarkable elevation at [p<0.0001] in the concentration of (UDP-2 B17) in colon cancer patients compared to the healthy control group.

Table 1: Mean values of serum Interleukins (B12, B17, C and D) levels in control and colon cancer patients

Parameters	Control group	Patients group	P-Value
(UDP glucuronosyltransferase 2 B17) **(IU/L)**	456±32.01	612±320.1	<0.0001
Vitamin B12(pg/mL)	257±29.2	234±17.2	<0. 001
Vitamin C (mg/dL)	1.46± 0.15	1.03±0.13	P< 0.05
Vtamin D (ng/mL)	19.06±1.85	5.78±1.30	<0.001

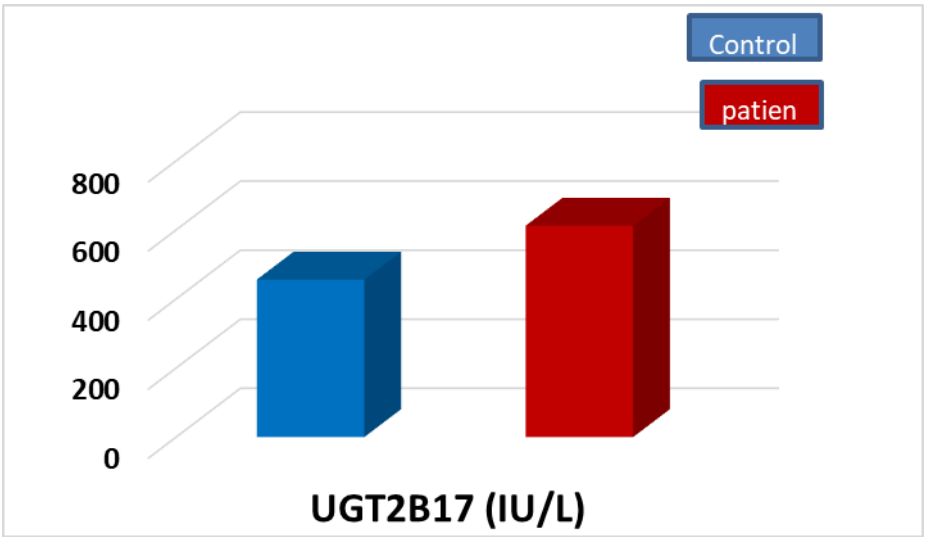

Fig. 1: Mean values of serum (UDP glucuronosyltransferase 2 B17) levels in control and colon cancer patients

The current result is in agreement with the fact that diminishing the function of UDP glucuronosyltransferase may possibly elevate susceptibility to colon carcinoma. UDP glucuronosyltransferase 2 B17 plays a vital role in the medicinal removing of oncogene

(Pande *et al.*, 2008). Various researches have determined the impact of UDP glucuronosyltransferase 2 B17deletion polymorphism on the risk of various carcinomas. Gallagher *et al.*, (2008). recorded a positive association between UDP glucuronosyltransferase 2 B17deletion polymorphism and elevated risk for lung cancer. Park *et al*. revealed that deletion polymorphism of the UDP glucuronosyltransferase 2 B17 gene increases prostate carcinoma risk (Park *et al.*, 2006). However, (Setlur *et al.*, 2010) and (Olsson *et al.*, 2008) found no correlation between UDP glucuronosyltransferase 2 B17 deletion polymorphism and capability to prostate carcinoma. Various studies have determined the role of UGTs comprising UGT1A1, UGT2B15, and UGT2B7 in breast oncogenesis (De Almagro *et al.*, 2011; Justenhoven *et al.*, 2010; Starlard-Davenport *et al.*, 2008)

Serum level of Vitamin B12

Table (1) and Fig. (2) showed that the mean circulating concentration of vitamin B12 among colon cancer patients was remarkably lower (P<0. 001) than in the healthy individual groups.

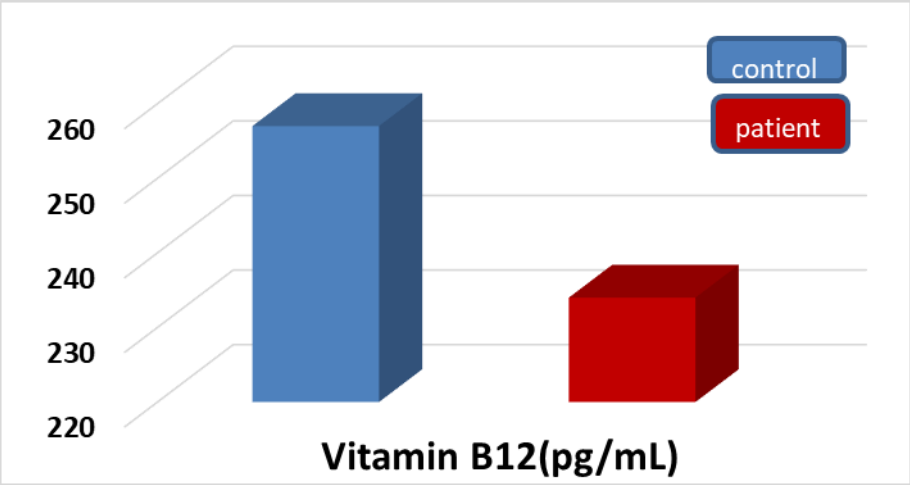

Fig. 2: Mean values of serum vitamin B12 levels in control and colon cancer patients

Nutritional deficiencies of vitamin B12 among patient with colon cancer patients attribute to low consumption of vitamin B12, as shown by its low circulating concentration, in comparison to the controls. The finding of current research is in concurrence with the western researches that have recorded a remarkable relationship between decrease intake of vitamin B12 with elevated risk of colon carcinoma (MacLennan *et al*.,1995*;* de Vogel *et al.*, 2008). In addition, various studies have proposed low capacity of methylation in human cells with a sequential decrease in methylation of DNA, hypomethylation of DNA attribute to that decrease dietary intake of vitamin B12 (Tsai *et al.*, 2011; Haghighi *et al.*, 2009; Kim, 2000).

Vitamin B12, play a vital role as cofactor of enzyme in the form of coenzymes in metabolism of biochemical compound with one-carbon atom which is necessary for formation of nucleotide and methylation process of DNA. Disruption of this metabolic pathway can cause abnormality in methylation of DNA, disturbance in DNA precursors and defect in DNA repair which each may contribute to the oncogenesis of colon carcinoma (Selhub *et al.*, 2000)

Level of vitamin D (1,25-Dihydroxycholecalciferol)

The results in (Table1) and Fig. (3) revealed a remarkable decline (p<0.0001) in the level of 1,25 (OH)2D in colon cancer patients compared to the healthy control group.

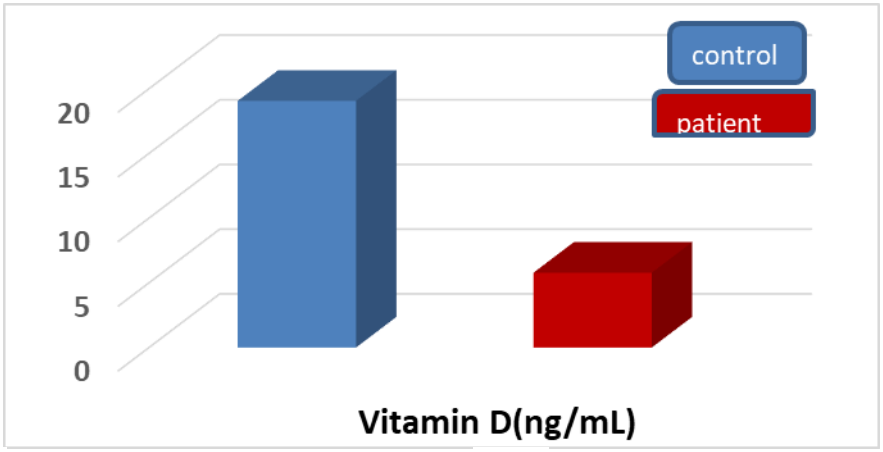

Fig. 3: Mean values of serum vitamin D levels in control and colon cancer patients

Experimental studies embroil vitamin D (1,25-Dihydroxycholecalciferol) insufficiency in the etiology of various common cancers. Several confirmations propose an Inverse relationship between Ergocalciferol level and colon carcinoma` risk. (Theodoratou *et al.*, 2014; Vaughan-Shaw *et al.*, 2017; Maalmi *et al.*, 2017; McCullough *et al.*, 2019) However, a causal association remains to be determinatively created (Manson *et al.*, 2019)

Elevated risk health of colorectal carcinoma has been linked with a decrease concentration of serum Ergocalciferol (1-5). A believable explanation for this association is the insufficient local colonic interconversion of inactive circulating 25hydroxy vitamin D into active 1,25dihydroxy vitamin D.

Assessment of, 25(OH)2D with several health outcomes comprising cancer have been identified principally in the context of circulating concentration of 1,25(OH)2D metabolites. Laboratory studies suggest that 1,25(OH)2D and its analogues may block colon cancer progression and growth through controlling of cellular differentiation and proliferation (Lamprecht *et al.*, 2001) and blocking the angiogenesis process. Epidemiology studies of vitamin D (1,25-Dihydroxycholecalciferol) intake and predicted 1,25-Dihydroxycholecalciferol concentration status have been completely agreement in proposing an relationship between higher 1,25(OH)2D and declined colon cancer risk (Institute of Medicine (US) (Committee, 2011; Giovannucci, 2008)

Serum level of Vitamin C

Table (1) and Fig. (4) revealed that the mean serum concentrations of ascorbic acid among colon cancer patients were remarkably lower (P= 0.02) than in the healthy individual groups.

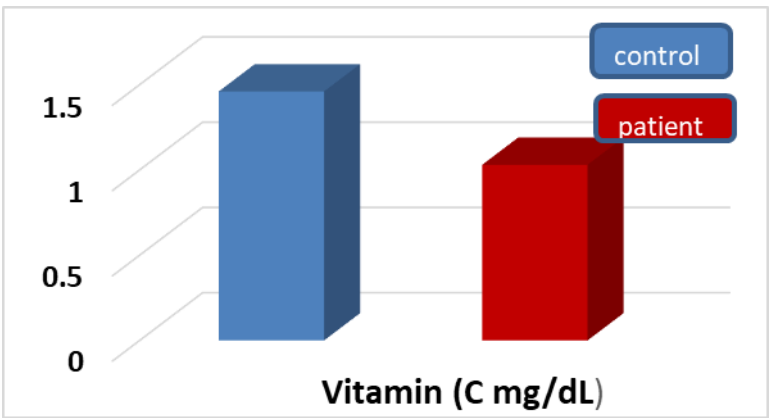

Fig. 4: Mean values of serum vitamin concentrations in control and colon cancer patients

The current results are in line with earlier reports (Szwed ***et al.***, 2005), where similar finding on low ascorbic acid level in colon cancer patients were reported. Low ascorbic acid concentration may be attributed to declined absorption via the digestive tract due to decreased production of the ciliary wall. It has been investigated that ascorbic acid plays a vital role in the formation of Collagen which the most abundant protein in the body. Its fiber-like structure is used to make connective tissue., and insufficiency of it, hence influence the probity of intracellular matrix and has a privilege impact on sarcoma growth. Insufficiency of ascorbic acid could disable sarcoma encapsulation. Therefore, there is a low concentration of circulating ascorbic acid from the present study because such nonenzymatic antioxidants cannot inhibit oxidative damages of cell constituents. Their concentrations declined cautiously with the development of colon carcinoma (Skrzydlewska ***et al.***, 2005).

Jocobs *et al*. (2001) reported that augmentation intake of ascorbic acid involved in blocking colon carcinoma in animal models and diminished *Mutagenicity* of *fecal* in human. Antioxidants properties of ascorbic acid contribute in the process of defense mechanism that scavenger free radical from body. Diminished concentration of antioxidant capability might attribute to its usage for repeal the effect of oxygen radical species.

CONCLUSION

Our results propose that elevated concentration of UGT2B17 and declined concentration of vitamin D, vitamin B12, and vitamin C may play a key role in the development and pathogenesis of colon carcinoma.

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تقدير مستويات يوريدين ثنائي الفوسفات الجلوكورونوسيل ترانسفيراز وبعض الفيتامينات (بى12، بي 17، سي، د) لمرضى سرطان القولون

پشتيوان عبدالله يوسف پروين عبدالصمد إسماعيل لطفية محمد حسن
قسم الكيمياء/ كلية التربية/ جامعة صلاح الدين/ أربيل

الملخص

يعد سرطان القولون أحد أكثر أنواع السرطانات انتشارًا بين البشر وسببًا معروفًا للوفاة. هدفت هذه الدراسة إلى قياس مستويات المصل من يوريدين ثنائي الفوسفات الجلوكورونوسيل ترانسفيراز وبعض الفيتامينات (بي 12، بي 17، سي، د) لمرضى سرطان القولون وتحديد كيفية تأثير هذه المستويات على مسار المرض. شمل المشاركون في الدراسة الحالية 45 شخصًا سليما كعينات سيطرة (متوسط العمر = 12,3±62,03 سنة) و65 شخصًا مشخصا بسرطان القولون (متوسط العمر = 12,2± 64,03سنة). كانت مستويات يوريدين ثنائي الفوسفات الجلوكورونوسيل ترانسفيراز، فيتامين بي 12، فيتامين بي 17، وفيتامين د، وفيتامين سي في الدم من بين المؤشرات الكيميائية الحيوية المحددة. عندما تمت مقارنة مرضى سرطان القولون بالمجموعة السيطرة، كانت مستويات يوريدين ثنائي الفوسفات الناقل لكورونوسيل وفيتامين بي 17 أعلى بشكل ملحوظ بالمقارنة مع مجموعة السيطرة، كانت مستويات فيتامين بي 12 وفيتامين د وفيتامين سي في مصل الدم في مرضى سرطان القولون أقل بكثير بالمقارنة مع مجموعة السيطرة. في التحقيق الذي أجريناه، تبين أن من مؤشرات سرطان القولون هي زيادة في يوريدين ثنائي الفوسفات الجلوكورونوسيل ترانسفيراز وفيتامين بى 17 في الدم وانخفاض في مستويات فيتامين ب 12 وفيتامين د وفيتامين سي.

الكلمات الدالة: سرطان القولون، يوريدين ثنائي الفوسفات الجلوكورونوسيل ترانسفيراز، فيتامين بي 12، فيتامين بي 17، فيتامين سي، فيتامين د.