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Original Article

The relationship of beck depression inventory with vitamin D levels and visceral fat mass in cancer patients

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Abstract: Purpose: The aim of this study is to determine the relationship between Beck Depression Inventory (BDI) and vitamin D levels, total and visceral fat mass in cancer patients. Methods: A total of 219 patients participated in this study. Patients' blood tests including prealbumin, vitamin D levels, BMI values and total and visceral fat masses were measured. Also, all subjects completed a self-administered BDI questionnaire. Obtained data were analyzed by using NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA). Results: A total of 219 patients consisted of 53.9% (n=118) females and 46.1% (n=101) males with median age 52.41±13.66 (range, 19-84) years. Mean BMI value was 24.70±3.75 kg/m^2; mean BDI score was 13.02±8.72; and mean prealbumin level was 0.21 ± 0.07 g/L. BMI was negatively correlated with BDI in all study groups (P=0.002). Also prealbumin levels, vitamin D levels and hemoglobin levels were negatively correlated with BDI (P<0.05 for all). But no significant correlation was determined between total fat mass, visceral fat mass levels and BDI (P>0.05). Depression status had a significant relationship with BMI, vitamin D levels, prealbumin levels and malnutrition status in patients (P = 0.008, 0.001, 0.001, and 0.001, respectively). Conclusions: We have determined a significant correlation between vitamin D levels and BDI scores in cancer patients. Also prealbumin and hemoglobin levels may indicate BDI scores in cancer patients. There was no correlation between BDI score and visceral fat mass. There was a negative correlation between BDI score and BMI levels but no correlation was found between BDI score and total or visceral fat mass in cancer patients. Thus vitamin D levels could be used to determine the depression and nutritional status in cancer patients which may help to improve the clinical outcomes in those patients.

Keywords: Beck depression inventory, vitamin D, cancer, depression, prealbumin, body-mass index

Introduction

Obesity and cancer have been linked to impaired vitamin D status [1]. Recently, many of new studies demonstrated that low vitamin D status has been associated with increased risk of several cancers, obesity, Type 2 Diabetes Mellitus, autoimmune disease. Immune cells in tumor can convert 25-hydroxyvitamin D [25(OH) D] to active form 1α,25-dihydroxyvitamin D3. This active form acts as an autocrine and paracrine factor on neoplastic and immune cells [2, 3]. Body mass index (BMI) and serum 25-hydroxy vitamin D3 (25OHD) concentrations are inversely related [4]. As BMI contains only limited information regarding body fat distribution, sometimes evaluation of body fat mass and visceral fat mass could be valuable markers. Some experimental and clinical data determined that parathyroid hormone (PTH) and vitamin D may affect cerebral function. This affect may be due to PTH and 1,25-dihydroxyvitamin D3 receptors in the brain. Also 1,25(OH)2 vitamin D3 has an anti-cancer feature because of its anti-proliferative and pro-differentiating effect. Also this active form of vitamin D induces apoptosis in cancer cells and slows their proliferation [2-5]. More over mortality rates and vitamin D levels inversely related. The Third National Health and Nutrition Examination Survey determined an association between plasma levels of vitamin D and reduced colorectal

Table 1. Demographic and clinic parameters of patients

		Min-Max	Mean ± SD
Age (year)		19-84	52.41±13.66
BMI (kg/m^2)		16.7-38.7	24.70±3.75
		n	%
Gender	Female	118	53.9
	Male	101	46.1
BMI	Underweight	2	0.9
	Normal	117	53.4
	Overweight	81	37.0
	Obese	19	8.7
Comorbidity	Absent	126	57.5
	Present	93	42.5

Table 2. Distribution of cancer types of patients

Cancer Type	n	%
Breast	74	33.8
Colorectal	52	23.7
Urogenital	22	10.0
Gastric and Esophageal	20	9.1
Gynecologic	15	6.8
Lung	13	5.9
Pancreas and Biliary tract	7	3.2
Head and Neck	6	2.7
Skin	4	1.8
Others	6	2.7

cancer mortality. Subjects with higher vitamin D blood levels (≥80 nmol/L) had a 72% lower risk of colorectal cancer death than those with lower vitamin D blood levels (<50 nmol/L) [6].

Vitamin D deficiency is now a global public health problem affecting more than half billion people worldwide [5]. The mechanisms of action of Vitamin D are now recognized to be endocrine, paracrine and autocrine via Vitamin D receptors (VDRs) affecting most physiological systems, including the brain [7]. Epidemiological evidence shows that Vitamin D deficiency is associated with an 8%-14% increase in depression and a 50% increase in suicide; however, causality and efficacy of supplementation remain controversial [8, 9].

Among the available self-assessment instruments, the 21-item Beck Depression Inventory (BDI) is one of the most popular measures of depressive symptoms worldwide. First proposed by Beck et al., this instrument has been used in more than 7,000 studies so far. The theoretical assumption of the original BDI relied upon the belief that negativistic distorted cognitions would be the core characteristic of depression. Based on available psychometric evidence, the BDI-II can be viewed as a cost-effective questionnaire for measuring the severity of depression, with broad applicability for research and clinical practice worldwide [10].

Cancer patients tend to have the highest prevalence of co-occurring psychiatric disorders such as depression, anxiety, adjustment disorders, and substance dependence or abuse [11]. They are also at an elevated risk for suicide [12]. Distress is an important symptom to address in all patients affected by cancer, especially patients with advanced disease, who experience longer and more aggressive treatments, are particularly susceptible to long-term effects.

Malnutrition is an important factor for the surveillance of cancer patients. Some studies showed that malnutrition affects 88% of patients [13]. Early signs of malnutrition include body weight loss and fatigue that may possibly be controlled and even eliminated by early detection and treatment. Failure to provide nutrition support may result in more severe malnutrition, especially when compounded by side effects of chemotherapy and radiotherapy such as mucositis, xerostomia, and nausea and vomiting [14]. Prealbumin, BMI, and hemoglobin levels could be used to assess nutritional status [15].

Depression and malnutrition have important effects (e.g. mortality) on the treatment of cancer patients. At the time of diagnosis, determining nutritional state and depression in such patients could provide additional benefits. Thus, in this study we tried to evaluate the relationship of vitamin D levels between visceral fat tissue and BDI in cancer patients.

Materials and methods

This prospective study was conducted between 2014 and 2015 at Bakirkoy Dr. Sadi Konuk Education and Research Hospital after obtained our hospital's ethical committee. Informed consent was received from all patients. A total of 219 cancer patients with ECOG performance status score of <3 were included in the study. All assessments and tests were completed before initiating chemotherapy in order

Table 3. Distribution of beck depression inventory and visceral fat mass in patients

		Min-Max (Median)	Mean ± SD
BECK depression Inventory Score		1-44 (10)	13.02±8.72
Visceral Fat Mass		1-17 (7)	7.56±2.57
		n	%
Depression (BDI score)	Absent/Minimal (<10)	104	47.5
	Mild (10-18)	51	23.3
	Moderate (19-29)	50	22.8
	Severe (>30)	14	6.4

Table 4. Prealbumin levels and malnutrition status in patients

		Min-Max (Median)	Mean ± SD
Prealbumin g/L		0.1-0.43 (0.21)	0.21±0.07
		n	%
Malnutrition (Prealbumin ≥ or <0.17 g/L)	Absent (≥0.17)	161	73.5
	Present (<0.17)	58	26.5

to avoid the effect of chemotherapy on patients' moods or laboratory values.

At the time of their first visits in oncology clinics, all patients underwent blood tests including prealbumin, vitamin D. Blood samples were collected in tubes containing 3.8% sodium citrate or K3EDTA as an anticoagulant and serum separator. Samples were centrifuged at 3,000 rpm for 10 min to obtain plasma and serum supernatants. The plasma and serum samples were then stored at -80°C until biochemical analyses. Serum 25OH vitamin D levels were measured by high-performance liquid chromatography (HPLC). Nutritional status was determined by measuring serum concentrations of prealbumin (turbidimetric immunoassay).

Also patients' BMI values were calculated as weight in kilograms divided by square of height in meters. Additionally, total and visceral fat masses of all patients were measured by bioimpedance analyzer (TANITA SC-330; Tanita Corporation).

Lastly, all subjects completed a self-administered questionnaire. These questionnaires measured subjects' symptoms of depression using the previously validated BDI questionnaire which was designed to assess the intensity of 21 depressive symptoms and attitudes. When the test is scored, a value of 0 to 3 is assigned for each answer and then the total score is compared to a key to determine the depression's severity. The standard cut-off scores are as follows: 0-9: indicates minimal depression 10-18: indicates mild depression 19-29: indicates moderate depression 30-63: indicates severe depression.

Statistical analysis

Obtained data were analyzed by using NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA). During the evaluation of study variables, categorical and continuous variables were summarized using the descriptive statistics (e.g., median, range, frequency, and percentage) and compared with Kruskal Wallis test, Mann-Whitney-U test, and Spearman's correlation analysis as appropriate. A value of $P<0.05$ and <0.01 were considered as statistically significant.

Results

A total of 219 patients consisted of 53.9% (n=118) female and 46.1% (n=101) male patients with median age 52.41±13.66 (range, 19-84) years. Mean BMI value was 24.70±3.75 kg/m^2 (range, 16.7-38.7) and of the patients 0.9% (n=2) were underweight, 53.4% (n=117) were normal, 37.0% (n=81) were overweight, and 8.7% (n=19) were obese (**Table 1**). Distribution of cancer types in study population was shown in **Table 2**.

Mean BDI score was 13.02±8.72 (range, 1-44) and mean visceral fat mass 7.56±2.57 and of

Table 5. Correlation analysis between beck depression inventory and body-mass index, prealbumin, vitamin D, hemoglobin, total fat mass and visceral fat mass levels

Beck Depression Inventory Score VS		r	*P*
BMI (kg/m^2)	Female	-0.110	*0.237*
	Male	-0.251	*0.011**
	Total	-0.207	*0.002***
Prealbumin		-0.597	*0.001***
Vitamin D		-0.714	*0.001***
Total Fat Mass (%)		-0.071	*0.299*
Hemoglobin		-0.399	*0.001***
Visceral Fat Mass		-0.028	*0.681*

*P≤0.05, **P≤0.001.

Table 6. Correlation analysis of BMI, total fat mass, visceral fat mass and prealbumin levels

		r	*P*
BMI (kg/m^2)-Total Fat Mass (%)	Female	0.672	*0.001***
	Male	0.547	*0.001***
	Total	0.709	*0.001***
BMI (kg/m^2)-Visceral Fat Mass	Female	0.479	*0.001***
	Male	0.425	*0.001***
	Total	0.424	*0.001***
Prealbumin-Visceral Fat Mass		0.182	*0.007***
Total Fat Mass (%)-Visceral Fat Mass		0.343	*0.001***

*P≤0.05, **P≤0.001.

the patients 47.5% (n=104) had BDI <10, 23.3% (n=51) had BDI 10-18, 22.8% (n=50) had BDI 19-29, and 6.4% (n=14) had BDI >30 (**Table 3**).

Mean prealbumin level was 0.21±0.07 g/L and of the patients 26.5% (n=58) had malnutrition (prealbumin levels <0.17 g/L) (**Table 4**).

BMI was negatively correlated with BDI in all study group (*P*=0.002) and in male patients (*P*=0.011) whereas there was no correlation in female patients between BMI and BDI (*P*= 0.237). Also prealbumin levels, vitamin D levels and hemoglobin levels were negatively correlated with BDI (*P*<0.05 for all). But no significant correlation was determined between total fat mass, visceral fat mass levels and BDI (*P*>0.05) (**Table 5**).

BMI value was positively correlated with total fat mass and visceral fat mass (*P*=0.001 for all). Also visceral fat mass was positively correlated with prealbumin levels and total fat mass (*P*=0.007 and 0.001, respectively) (**Table 6**).

Depression status had a significant relationship with BMI, vitamin D levels, prealbumin levels and malnutrition status in patients (*P*=0.008, 0.001, 0.001, and 0.001, respectively) (**Table 7**).

Discussion

Monitoring nutritional and depression status in cancer patients, even in early stages of disease, increase compliance to treatment and improve mortality rates. Maintaining their own weight, and some blood parameters, such as vitamin D, hemoglobin, albumin levels, near normal levels impact positively on clinical outcome.

In the literature, there are several studies regarding low vitamin D levels in cancer patients. For example, recent Czech study, in which serum 25(OH)D3 concentrations were measured in 215 healthy individuals and in 170 patients with colorectal, lung, prostate and pre- and postmenopausal breast cancers, showed that vitamin D levels were significantly lower in cancer patients when compared to the control group [16]. But the impact of vitamin D replacement on survival in cancer patients is contradictive. Suggestions are offered to maintain serum vitamin D levels higher than its insufficient or deficient levels [2]. Furthermore, a study by Lauter et al. has shown that vitamin D replacement increased serum hemoglobin levels in patients with multiple myeloma [17]. Also, several meta-analyses showed that low serum levels of 25(OH)D was associated with colorectal cancer and overall mortality, while the association with cancer mortality was less consistent. Vitamin D supplementation was found to be associated with a reduced risk of overall mortality, reviewing all published trials on healthy subjects, whereas the evidence of an effect on cancer risk and mortality is less clear. Furthermore, long-term health effects of high doses of vitamin D, extended duration of supplementation, and the association with different baseline vitamin D levels remain to be investigated. Epidemiological and preclinical studies support the development of vitamin D as preventative and therapeutic anticancer agents, with significant associations especially found for low vitamin D status with overall mortality and cancer outcome, more than cancer incidence. However, a definitive conclusion can-

Table 7. Determining of the relationship between depression status and BMI, vitamin D levels, prealbumin levels and malnutrition status

		Depression Status				
		Absent/Minimal (n=104)	Mild (n=51)	Moderate (n=50)	Severe (n=14)	*P*
		Mean ± SD (Median)	Mean ± SD (Median)	Mean ± SD (Median)	Mean ± SD (Median)	
BMI (kg/m^2)		25.32±3.50 (25.1)	24.75±3.17 (24.8)	23.67±4.48 (22.7)	23.55±4.00 (22.5)	[a]*0.008***
Vitamin D		24.89±10.50 (23.3)	14.21±6.10 (12.2)	10.51±4.67 (9.2)	9.04±5.07 (6.6)	[a]*0.001***
Prealbumin		0.25±0.07 (0.24)	0.20±0.05 (0.20)	0.17±0.05 (0.15)	0.14±0.05 (0.12)	[a]*0.001***
		n (%)	n (%)	n (%)	n (%)	
Malnutrition	Absent	95 (91.3)	40 (78.4)	23 (46.0)	3 (21.4)	[b]*0.001***
	Present	9 (8.7)	11 (21.6)	27 (54.0)	11 (78.6)	

[a]Kruskal Wallis Test, [b]Pearson Ki-kare Test, ***P*<0.01.

not be drawn and only large randomized clinical trials, both in healthy subjects and in cancer patients, will allow drawing definitive conclusions on the effect of vitamin D supplementation on cancer risk, prognosis, and mortality [18].

Malnutrition contributes to distress independently of other psychosocial problems. The problems most frequently endorsed by patients as contributing to psychological distress were depression (49%) and anxiety (42%), which commonly co-occur in cancer patients [11]. Other problems included changing appearance, boredom, sleep problems, and pain. Patients with reduced food intake or with more pain reported greater distress. Swallowing difficulties, low appetite, and mouth sores accompanied by pain were commonly endorsed by the 36% of patients with decreased food intake. In facing a diagnosis of cancer, most patients have brief periods of mood swings, fear, anger, hopelessness, worries about uncertain outcomes, and other psychosocial concerns such as employment and financial worries [19]. Deficiencies in nutrition may occur before diagnosis and are often unrecognized and untreated. Without early detection and treatment, nutrition deficiencies can worsen leading to cachexia [20]. Thus, malnutrition not only contributes to and compounds the impact of distress; it also contributes to poor prognosis [21]. The mechanisms mediating the relationship between malnutrition and distress still have to be elucidated and will likely vary from patient to patient. Those mechanisms might involve biologic processes such as systemic inflammation in addition to psychological factors such as the perception by the patient of disease severity and any concomitant change in behavior. Although further research is needed to understand these processes, the accumulating evidence highlights the importance of routine screening for malnutrition in cancer care as well as screening for distress to improve clinical outcomes.

In our study, the negative correlation between vitamin D levels and BDI indicates worsening depression status, which causes diminished nutrition, reduces vitamin D levels. We also determined a correlation between BMI levels and BDI scores in male patients, but not in female patients. Also in all study population (regardless of gender) a correlation between BMI levels and BDI scores still existed. Interestingly, there was no correlation between BDI and total fat mass and visceral fat mass. Worsening depression status in cancer patients causes lower prealbumin, BMI, total fat mass, and visceral fat mass levels. As expected, this result could be caused from the fact that worse depression status could lead to worse nutritional status.

In conclusion, we have determined a significant correlation between vitamin D levels and BDI scores that indicates depression status in cancer patients. Also prealbumin and hemoglobin levels can indicate BDI scores in cancer patients. There was no correlation between BDI and visceral fat mass. There was a negative correlation between BDI score and BMI levels but this was not associated with total or visceral fat mass in cancer patients. Thus vitamin D levels could be used to determine the depres-

sion and nutritional status which might help to improve the clinical outcomes in cancer patients.

Disclosure of conflict of interest

None.

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