Original Research Article

ANTIDIABETIC TREATMENT AND CANCER PREVALENCE IN DIABETIC PATIENTS

Mehmet Yamak*, İbrahim Halil Boyacı, Süleyman Ahbab, Emre Hoca, Hayriye Esra Ataoğlu

MD, Internal Medicine Clinic, Haseki Health Training and Research Hospital, University of Health Sciences, İstanbul, Turkey

Abstract

Background: There can be a possible relationship between diabetes mellitus and cancer development, according to the literature. The aim of the present study was to investigate the relationship between diabetes and prevalence of cancer.

Method: This study consisted of 306 patients with diabetes who referred to Haseki Training and Research Hospital Diabetes outpatient clinic between 2000–2002. Patients were followed up until October 2011 and medical records were evaluated. The prevalence of cancer was investigated retrospectively in these patients. Findings were evaluated statistically.

Results: The prevalence of was cancer was established to be 3.3% in the present study. The relation between the ages and HDL-cholesterol values of patients and cancer prevalence was found to be statistically significant, respectively p 0.024 and 0.037.

Conclusion: Cancer prevalence was found to be higher than that in the normal population. However, the number of cases was low, which may be the reason why results in other studies are not similar. There is agreement that cancer prevalence increases in diabetic patients.

Keywords: diabetes mellitus, metformin, insulin treatment, cancer, prevalence.

1. Introduction:

Diabetes mellitus (DM), also predisposes to various diseases in addition to having many complications. DM and obesity which is an important health problem in developing and developed countries at present have been reported to increase the risk of colon, rectum, esophagus, pancreas, breast, and endometrium cancer (1). There is a significant relation between many cancers such as breast, endometrium, kidney, prostate and gastrointestinal (esophagus, gastric, colon) cancers and obesity (2,3). There can be a relationship between insulin resistance, diabetes, hyperlipidemia, hypertension, and coronary artery disease and visceral fat increase (4).

In western countries, insulin resistance syndrome is considered as a risk factor for many cancers including

hepatocellular cancer (HCC) (5). According to epidemiological evidence, a relation has been reported between colorectal cancer (CRC) and insulin resistance (IR). IR, which is also termed as syndrome X or metabolic syndrome, is defined as an impaired biological response to insulin effect (6). In cohort studies, it has been demonstrated that CRC risk increases in those with IR, metabolic syndrome and type II Diabetes. It is thought that adipocytokines play part in the pathogenesis of insulin resistance. High TNF-α, IL-6 and IL-1β and low adiponectin levels lead to detrimental effects on glucose balance, resulting in type II DM and chronic hyperinsulinemia. It has been suggested that the Insulin-like growth factor system may mediate the effect of hyperinsulinemia. Insulin and IGF system contributes to cellular proliferation, differentiation, and apoptosis and has been implicated for tumor development. Data obtained from studies indicate that IGF binding protein-1 (IGFBP-1) and IGF binding protein-2 (IGFBP-2) are in inversely proportional l to body fat and insulin levels (7). In in vitro studies, the expression of IGF-1 receptors has been demonstrated on CRC cells (8). Increased IGF-1 levels in circulation are associated with many cancers including squamous cell cancer and CRC. Correlation has been found between IGF-1 level and pathological stage of the tumor and poor prognosis (9).

Adiponectin is the most commonly released adipocytokine and is mostly released in visceral fat tissue. Adiponectin level is inversely proportional to BMI and it is an insulin-sensitizing, anti-angiogenic, an anti-inflammatory hormone which contributes to the organization of inflammation (10). Its mean circulatory level is higher in men than in women (11). It may prevent tumor growth in animals. Its levels have a negative correlation with stomach cancer. Although this protein is not insulin inducer, it protects from the effect of insulin by increasing the beta-oxidation of free fatty acids in skeletal muscle. It has been seen that Adiponectin level decreases in insulin-resistant states such as Type-2 DM, obesity and dyslipidemia (12). Plasma adiponectin level is inversely proportional to BMI and decreases in abdominal obesity. Adinopectin has two forms as low molecular weight and high molecular weight forms and the latter is more closely associated with cancer (13). The findings of the study support the idea that adinopectin may prevent carcinogenesis by inhibiting neovascularization. It is known that an increase in BMI and a decrease in adiponectin levels increase the risk of cancer six-fold. Although cancer varies according to its type, geographical regions, age, and gender of the patient, its incidence ranges between 85 and 350 per 100.000 in the community (14). The aim of the present study was to determine the relationship between diabetes mellitus and cancer development.

2. Methods:

This study consisted of 306 patients (183 female, 123 male) with DM, who referred to Haseki Traning and Research Hospital Diabetes Outpatient clinic between 2000-2002. Patients were followed up until October 2011 and medical records were evaluated. The study aimed to investigate the prevalence of cancer in diabetic individuals retrospectively. Information about patients history was collected from patient files. For statistical analyses, SPSS 16.0 (Statistical Packages for the Social Sciences) program was used. Continuous variables were expressed with mean and standard deviation and results were compared using Student's t-test. Categorical variables were expressed with percentage and in their comparison, Chi-square test was used. $P<0.05a$ was considered statistically significant.

3. Results:

The mean age of the patients was 62.7±10.7 and that of the patients with malignancy was 70.2±9.4 years, with a statistically significant difference (p:0.029). %93 of the patients was diagnosed with Type-2 DM, 6.2% with Type -1 DM and 0.3% with Gestational DM. The most common malignity was prostate cancer (1%). The rate of smokers was 17.3% and that of alcohol users was 14.9%. No relation was found between smoking, alcohol use and malignity. Antidiabetic c drug treatment was evaluated statistically. Accordingly, the rate of those who use sulfonylurea was 81.7%, metformin 89.9%, acarbose 87.3%, and insulin 71.9%. There was a significant relationship between malignancy and age (p:0.024) and HDL-cholesterol levels (p:0.037) as shown in Table-1. No significant relation was found between the highest HbA1c values and development of malignancy (Table-2). No significant relation was found between gender and type of diabetes and malignancy risk.

Table-1: The relation between various parameters and malignancy in diabetic patients

Parameters	Malignancy	n	Mean	S. deviation	P value
Age	Absent	296	62.5	10.7	**0.024**
	Present	10	70.2	9.4	**0.029**
Duration of Diabetes (Year)	Absent	296	16.7	6.3	0.601
	Present	10	15.6	5.1	0.537
Sulfonylurea treatment (Years)	Absent	277	4.7	3.9	0.668
	Present	10	4.2	2.2	0.479
Metformin treatment (Years)	Absent	289	7.6	3.8	0.840
	Prsesent	10	7.4	3.3	0.824
Body Mass Index	Absent	296	29.89	5.51	0.446
	Present	10	28.55	3.76	0.301

Table-2: The relation between laboratory values and malignancy in diabetic patients

	Malignancy	n	Mean	S. deviation	P value
Glucose	Absent	296	195.7	80.3	0.483
	Present	10	213.7	59.9	0.377
HbA1c	Absent	289	7.67	2.2	0.624
	Present	10	8.01	1.7	0.551
Urea	Absent	296	26.9	9.6	0.384
	Present	10	29.6	7.8	0.316
Creatinin	Absent	296	0.9	0.3	0.999
	Present	10	0.9	0.2	0.999
Total Cholesterol	Absent	296	202.8	41.4	0.272

	Present	10	188.2	40.6	0.290
LDL-Cholesterol	Absent	296	125.6	36.2	0.687
	Present	10	120.9	34.4	0.682
HDL-Cholesterol	Absent	296	47	22.8	**0.037**
	Present	10	31.8	11.8	**0.003**
VLDL-Cholesterol	Absent	296	31.1	16.8	0.415
	Present	10 an	35.5	15.6	0.404

4.   Discussion:

In the present study, the prevalence of cancer was found to be 3.3%. In the world,   this rate was reported to be 300 per hundred thousand in males and 225 per hundred thousand in women in developed countries, while in developing countries it was 160 per hundred thousand in men and 138 per hundred thousand in women. (15). Although prevalence rates seem to increase significantly in the present study. It is known that all types of cancer increase with age. Similarly, in the present study, a significant relation was found between cancer prevalence and age (p:0.024). It is estimated that 25-30% of all cancers in developed countries is associated with smoking. According to studies performed in Europe, Japan, and North America, 87% to 91% of lung cancer cases in males and 57-86% of all lung cancer cases in females seem to be attributable to smoking (16). In the present study, no significant relation was found between smoking and the prevalence of malignancy. In the present study, the common cancer was a prostate cancer in 2 cases. The prevalence of hepatocellular carcinoma has been reported to be 8 per hundred thousand all over the world. In the present study, HCC developed only in one case (0.3%). A significant proportion of HCC (30-80%) develop from cryptogenic cirrhosis and it may be considered the most concerning complication of non-alcoholic steatohepatitis. The relation between diabetes treatments and the risk of cancer is one of the investigated issues. In the present study, no relation has been found between treatments in diabetic patients and cancer development. Metformin is the drug used most commonly in the treatment of patients with type-2 DM and is frequently prescribed as starting or combination treatment (17,18). Patients with type 2 diabetes have increased cancer risk and cancer-related mortality, which can be reduced by metformin treatment. However, it is unclear whether metformin can also modulate clinical outcomes in patients with cancer and concurrent type 2 diabetes (19). The findings of observational studies carried out in humans suggest that metformin treatment is associated with a decrease in cancer risk. Additional observational studies suggest that metformin may improve cancer prognosis (20-23). Pioglitazone is widely used for glycemic control in patients with type 2 diabetes mellitus but evidence regarding the association between pioglitazone and bladder cancer risk is confusing (24). In a small number of observational studies, it has been reported that in cases treated with sulfonylureas (e.g. gliburid, glipizide, glimepiride) the risk of cancer or cancer mortality is higher than those treated with metformin or other diabetes drugs (25,26). In the present study, there was no any relation between insulin treatment and cancer development. According to recent studies, long-acting insulin therapy was not associated with an increased risk of cancer. (27-29).

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