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Association of Diabetes and Cancer: An Analysis on the Prevalence of Diabetes among Cancer Patients.

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ABSTRACT

Cancer and diabetes are the two major diseases growing at an alarming rate in many countries including India. The efforts in understanding the association between these two diseases intensified in recent years after identifying many common pathways between them. Most of these studies were carried out among the western population and the reports suggests a good correlation between diabetes and cancer. Since many causative factors of cancer are different for Indian population, we initiated a study to find out whether there is any association between these two diseases among Indian population. Glucose (FBS and PPBS) and whole glycated hemoglobin (HbA1C) levels of 138 patients undergoing cancer treatment was analyzed. Albeit the small number, the data indicated that patients with multiple myeloma, tongue, lung, and breast cancer have higher incidence of diabetes. Patients who were taking cisplatin were found to have marginally higher diabetes. Among the different age groups, maximum diabetes cases was observed among the patients in the 50-59 years age group. Alcoholic patients were found to have substantially higher incidence of diabetes as compared to non-alcoholic patients. In conclusion, we found that the prevalence of prediabetes (21-28 %) and diabetes (12-14 %) marginally higher among cancer patients as compared to that of the general population.

Keywords : Cancer, Diabetes, FBS, PPBS, HbA1C

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INTRODUCTION

Cancer is a leading cause of death worldwide accounting for more than 8 Million deaths and about 14 million new cases every year (1, 2). Many factors are known to be associated with the development of cancer including genetic factors, lifestyle, diet, reduced physical activity, infections and exposure to chemicals and radiation (3-5). The success of immunotherapy drugs in cancer has reinitiated the interest in understanding the relation between cancer and other diseases that weaken the immune system, like diabetes and HIV (6-8). Diabetes is one of the major health concerns especially in countries like India (9). Although diabetes is considered as a metabolic disorder, scientists are increasingly seeing it as an autoimmune disease, where the immune system attacks the insulin-producing beta cells in the pancreas and destroys them (10).

The relationship between cancer and diabetes was a topic of intense debate in scientific community for a long time and a good number of studies have been carried out to find out whether there is any association between these two major diseases (11-13). Based on a study conducted among Japanese men and women, Inoue et al concluded that diabetes was associated with a significantly higher risk of cancer than those without diabetes (14). There have been many studies on the biological links between cancer and diabetes which revealed intracellular pathways commonly shared by these diseases. Diabetes may influence the neoplastic process by mechanisms like hyperinsulinemia, hyperglycemia or chronic inflammation (15-18). Insulin acts through its effects on IGF- 1 which can initiate many signaling pathways which in turn stimulate proliferation, invasion and metastasis (19). It can also cause a reduction in the synthesis of sex hormone binding globulin, increasing the bioavailability of hormones (20). The elevated sex hormones are associated with a higher risk of breast, endometrial and other cancers. Untreated hyperglycemia may facilitate neoplastic proliferation because there is a high requirement for glucose by cancer cells Based on this understanding, many anti-diabetic drugs like metformin, phenformin and thiazolidine-diones have been tested and showed anticancer properties, suggesting a relationship between cancer and diabetes (21-22). In addition to insulin lowering action, Metformin inhibits cell proliferation, and cause partial cell cycle arrest in cancer cells. The therapeutic effect of Metformin was tested for different types of cancers and positive results were obtained for prostate and hepatocellular carcinoma (23-24). Most of the reported studies on the relation between cancer and diabetes are done among western population, and very little study is reported from data collected among Indian patients. Since many known causative factors for cancer like eating habits, lifestyle, physical activity, environmental factors, etc. are different for Indian population, a good understanding of the relationship between diabetes and cancer may be useful in devising better therapeutic approaches to treat cancer. In an effort to understand whether there is any pronounced link between these diseases, we evaluated the diabetic conditions of about 138 cancer patients who were on chemotherapy. In addition to diabetic condition, we also analyzed other related parameters like age, obesity and alcoholic use to see whether these parameters also have any link to cancer and diabetes (25).

MATERIALS AND METHODS

A prospective observational study was conducted at a tertiary hospital. 157 cancer patients undergoing treatment for different types of cancer was included in the study. Demographic data, blood sugar levels, HbA1C levels, drug treatment history, alcohol consumption, and obesity data were collected during the 4 months study period. Complete diabetes data was available for only 138 patients. To study the association between diabetes and cancer, the data of these patients only were considered.

Fasting blood sugar (FBS), post prandial blood sugar (PPBS) and whole glycated hemoglobin (HbA1c) levels of patients undergoing treatment for cancer were collected. These parameters were estimated in a biochemistry lab using a Biochemical Analyzer. Internationally accepted norms were used for the classification of diabetes (Normal, Prediabetes, Diabetes) based on FBS, PPBS, and HbA1c levels and is represented in Table 1 (26).

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Table 1: Classification of diabetes based on FBS, PPBS and HbA1C levels

FBS/PPBS/HbA1C	Sugar Level	Classification
Fasting Blood Sugar after 8 to 12 hour fasting	< 100 mg/dL 100 to 125 mg/dL > 126 mg/dL	Normal Prediabetes Diabetes
Post-prandial blood sugar (2 hours after taking food)	< 140 mg/dL 140 to 199 mg/dL >200 mg/dL	Normal Prediabetes Diabetes
HbA1C	< 6% 6-6.5% >6.5%	Normal Prediabetes Diabetes

RESULTS

Patient and treatment History

Out of the 157 patients in the study, the mean age was 52 years (18-80 years). 81 were males and 76 were females. For the convenience of data analysis, they were classified into different age groups with 10 years difference between the ages. Maximum number of patients were in the age group 50 – 59 years (31%). Among the patients, 33% were alcoholics and 3% were obese (Table 2). Majority of patients were in stage III or IV of cancer. Average treatment time on chemotherapy was about 3 months, with minimum 4 days and maximum 8 months duration.

Table 2: Baseline Characters: n=157

Demographic Data	No.of patients	Percentage
Age in years		
<30	10	6%
30 - 39	12	8%
40 - 49	30	19%
50 - 59	48	31%
60 - 69	36	23%
≥70	13	8%
Gender		
Male	81	52%
Female	76	48%
Obese	3	2%
Alcoholic	33	21%
Immunocompromised	1	1%

Number of diabetic/pre-diabetic patients

The number of diabetic and pre-diabetic cases determined by three diagnostic methods are given in Table 3. By FBS method, 35 patients were pre-diabetic and 20 were diabetic. The number of pre-diabetic and diabetic patients by HbA1C method was 30 and 16 respectively. While the pre-diabetic cases determined by

the three methods were similar, FBS and HbA1C methods showed higher number of diabetics as compared to that detected by PPBS.

Table 3: Prevalence of Diabetes and Pre - diabetes as determined by three methods

Diabetic/Pre-diabetic	FBS	PPBS	Hb1Ac
% Diabetic	14.2	3.6	11.6
% Pre-diabetic	24	24.6	21.9

Sex Distribution of patients with Diabetes

The number of patients with diabetes was classified based on gender and the data is given in Table 4. Analysis shows that majority of the patients were pre-diabetic with almost equal frequency among males and females

Table 4: Sex Distribution: Patients with pre-diabetic and diabetic conditions

Patient Sex distribution	FBS	HbA1c
Diabetic		
Male	12	9
Female	8	7
Pre-diabetic		
Male	19	15
Female	16	15

Distribution of cancer types among the patients included in the study

Among the 157 patients included in this study, 46 different types of cancers were observed. Table 5 shows the different types of cancers observed in the study grouped into 13 classes of cancers. Maximum number of patients were with Lung cancer followed by esophageal cancer and breast cancer. Lung cancer, multiple myeloma and cervical cancer patients were mostly pre-diabetic (Table 6)

Table 5: Major Cancer types of patients in the study

Cancer Types	Number of Patients
Head and Neck Carcinomas	30
Esophageal Carcinomas	11
Gastro-Intestinal Carcinomas	20
Lung Carcinoma	13
Breast Carcinoma	11
Haemato-lymphoid Carcinomas	18
Myelomas	9
Genito-urinary Carcinomas	12

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Gynaecological Cancers	9
Testicular Cancers	2
Skin Cancers	2
Sarcomas	4
Neurologic Tumors	2

Table 6: Diabetic and Pre-diabetic conditions of cancer patients from FBS and HbA1c measurement

Type of Cancer	Total	FBS		HbA1c	
		Pre-Diabetes	Diabetes	Pre-Diabetes	Diabetes
Ca Lung	16	8	1	5	1
Ca Esophagus	11	1	2	1	0
Ca Breast	11	0	1	2	2
Multiple Myeloma	9	3	2	2	2
Ca Cervix	8	2	2	5	0

Diabetic condition of patients on Cisplatin treatment

Cisplatin was the major drug used for the chemotherapy of the cancer patients and all of them patients were also given Dexamethasone. On analyzing the data, it was found that 15.9 % were diabetic by FBS method and 11.3% by HbA1C method.

Diabetic condition of obese and alcoholic patients:

Analyzing the diabetes patients who were alcoholic showed some important observations. Out of the 46 alcoholic patients, 9 were women. As shown in Table 7, about 40% of the patients were diabetic/ pre-diabetic on analyzing by FBS and HbA1c levels. However, obesity was seen in only 3 patients.

Table 7: Percent of alcoholic patients who are diabetic or diabetic + pre-diabetic

Diabetic condition	Percent of diabetic/pre-diabetic		
	FBS	PPBS	HbA1c
Diabetic	19.1	4.3	21.3
Pre-diabetic	21.2	27.6	23.4
Diabetic + Pre-diabetic	40.3	31.9	44.7

DISCUSSION

In India, as the incidence of both diabetes and cancer are increasing, we aimed to study if there is any association between the two in Indian population. The number of cancer patients included in the present study was limited to 157 and there were 46 different types of cancers (grouped into 9 major cancer types, Table 6), making it difficult to find out whether there is a statistically significant correlation between cancer and diabetes in general, and specific type of cancers and diabetes in particular.

The data used in this study was generated by estimating the levels of the commonly used diabetes parameters FBS, PPBS and HbA1C levels of cancer patients. Among these three diagnosis methods, FBS and HbA1c detection methods showed higher incidence of diabetic cases as compared to PPBS methods (Table 2). Maximum percentage of diabetic cases was observed when detected by HbA1C method. The correlation coefficient calculated for FBS vs PPBS and FBS Vs HbA1C was significantly lower than 1 indicating poor correlation between these diagnostic methods, particularly between FBS and PPBS. This may be due to (a) the effect of the cancer drug on FBS and PPBS, (b) high variability in the glucose measurement and (c) not adhering to the recommended timings/conditions for Blood glucose measurement. Since HbA1C is a measure of the long term diabetic condition, this may be a better indicator of the diabetic condition of the patients.

Maximum number of diabetes patients was seen in the 50-59 age group (24 %). It is in line with the reported correlation of cancer and diabetes with the age of the patients (27). The diabetic cases among cancer patients was relatively higher (14.2 % by FBS and 11.6 % by HbA1C) as against the average value reported for general population (8.5-8.7 %). It was also surprising to note that >20% were pre-diabetic by all the three detection methods. The pre-diabetic cases among Indian population from different states is reported to be in the range of 8-15 % (28). The diabetic conditions of patients with different types of cancer indicated marginally higher incidence of diabetes patients with multiple Myeloma, lung, breast and cervical cancer. Since the sample size was small, it has to be considered as indicative numbers. Effect of chemotherapy on diabetic condition of patients was also analyzed. In most of the cases, cancer treatment was for less than 5 months duration. Cisplatin was the most common drug used in the chemotherapy. To see whether this treatment has any effect on diabetic condition, the FBS, PPBS and HbA1C values of the patients taking this treatment was analyzed separately. The number of pre-diabetic and diabetic cases was marginally higher in these patients. Based on the limited data available, and the fact that the drug treatment duration was not very long, it is difficult to conclude whether Cisplatin treatment had any effect on the diabetic condition of the patients. It could also be due to the fact that most patients on cisplatin also receive concurrent dexamethasone to prevent vomiting (29).

The diabetic condition of the cancer patients who were alcoholic showed that the prevalence of diabetes was high in them. Diabetic condition was significantly higher for these group – 19.1 % as compared to the average value of 14.2% for all the patients in the study.

The limitation of our study was that the sample size was small and hence we could not analyze the correlation between diabetes and individual cancer types. We took patients on all phases of cancer treatment; a study only on newly diagnosed treatment naïve cancer patients would give us better information.

CONCLUSIONS

Analysis of diabetes data collected from cancer patients indicated marginally higher incidence of diabetes and pre-diabetes among the cancer patients as compared to the reported values for global general population. The number of patients who were pre-diabetic was also significantly high. In the study on the effect of cancer chemotherapy treatment on diabetes, we found that the patients undergoing Cisplatin chemotherapy treatment had higher occurrence of diabetes/pre-diabetes along with alcohol intake.

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