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Impaired Glucose Tolerance and its Association to Oral Cancer

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Abstract

Background: Diabetes mellitus is a serious and leading health problem worldwide and is associated with severe acute and chronic complications that negatively influence both the quality of life and survival of affected persons. Growing epidemiologic evidence suggests that people with diabetes are at significantly greater risk for cancer in general and recent studies also demonstrated that glucose intolerance was associated with a higher risk of oral cancer death, beginning in the prediabetic range of glucose intolerance.

Aim: We undertook this study with the aim of finding out an association between impaired glucose tolerance and oral cancer along with finding out prevalence of other risk factors for oral cancer.

Subjects and Methods: 45 cases and 45 controls were selected for the study. Oral glucose tolerance was performed on subjects who satisfied inclusion criteria and were willing to sign informed consent form.

Results and Conclusion: Fifty three percent of the cases had abnormal glucose tolerance as compared to Thirty one percent of the controls. It was statistically significant with a p value of 0.032. To conclude, hyperglycemia (which includes IFG, IGT and diabetes) increase the risk of oral cancer two folds, however Impaired Glucose tolerance alone as defined by ADA does not appear to play a role.

Keywords: Diabetes Mellitus; Oral cancer; Impaired glucose tolerance

Introduction

Non-Insulin Dependent Diabetes mellitus (NIDDM) is rapidly becoming a common chronic disease among the urban population. At the same time, the morbidity and mortality associated with oral cancer is increasing despite exhaustive research. Is Diabetes Mellitus/ Impaired Glucose Tolerance (IGT), a known risk factor for oral cancer? There are studies on the inflammatory lesions of the periodontal tissues and the oral mucosa in patients with DM [1,2]; these oral alterations are more serious in untreated or inadequately treated diabetic patients[2] but there are hardly any studies on Diabetes Mellitus and its association with oral cancer. Studies state that altered metabolism as in DM leads to break down in oxidation equilibrium leading to elevated glucose concentration, excessive formation of free radicals, leading to reduced activities of the antioxidant scavengers bringing out serious damages in the biological structures even at a molecular level [3,4]. Diabetes mellitus is associated with increased risk, as well as worse outcome, of various malignancies including endometrial, colon and pancreatic cancers [5]. The present study proposes a novel hypothesis for an etiological association between prediabetes/ IGT, diabetes as a risk for cancers of the oral cavity. A large population of India is habituated to vices like tobacco and alcohol; hence we would also like to throw light on the relation between alcohol and tobacco in the causation of oral cancer. There are similar studies reported in the west but very few among Asians [6], since there is considerable heterogeneity in the genetic background and lifestyle between Asian and Western populations, it is of value to review the influence of pre-diabetes on the risk of oral cancer.

Materials and methods

Study population

Our study subjects involved patients with oral cancer, who visited for treatment to any of these three tertiary care hospitals of Manipal Hospital between Octobers to December 2013. Ethics committee approval was obtained from Institutional Ethics Committee and informed consents were taken from study participants. Expected Sample size was calculated using following figures: Expected proportion of Impaired glucose tolerance in control group=15%, Anticipated odds ratio=3, Calculated proportion of impaired glucose tolerance among cancer patients=35% and accordingly the power of the study was calculated as 80%. The number of subjects recruited for the study was 45 subjects and 45 controls, the controls were people from general population who were not known to be suffering from any illness. Each participant completed a self-administered questionnaire covering medical history, family history of cancer, antidiabetic treatment, smoking habits, alcohol intake, and leisure-time physical activity. Smoking and alcohol intake were classified as either current use or not. At the baseline examination, we performed a 75 g oral glucose tolerance test between 8:00AM and 10:30AM after at least 8 hour overnight fast. Plasma glucose levels were measured by means of the glucose oxidase method. Glucose tolerance was classified according to ADA diagnostic criteria 2002 [7].

Statistical analysis

The collected data was fed in computer in MS excel and the analysis was performed using the statistical package SPSS version 11.5. The quantitative variables were analyzed using student 't' test and ANOVA.

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The qualitative variables were analyzed using chi square test. A 'p' value less than 0.05 was taken as statistically significant. The statistical significance of differences in the mean values and frequencies of risk factors was estimated by means of analysis of covariance and logistic regression analysis, respectively.

Results

Our study subjects and controls were age and gender matched. More than a third of the cases (36%) were in the 5th decade of their life; about 24% of them were in their sixties. Twenty percent of the cases were between 40 and 50 years. Only 4% of the cases were in their seventies. 46% of our study subjects were diabetic, 54% of the cases were hyperglycemic as compared to thirty one percent of the controls. Seventy one percent of them were males. Majority of the cases (75.6%) did not have any family history of oral cancer. More than half of the cases 58% consumed tobacco in the study population and among controls, 64% did not consume tobacco. Among those with habits in the study group, 65.3% of them were smokers, 34% of them were paan chewers and 23% of them were paan chewers as well as smokers. Among the study population, half of the cases (53.33%) had a history of alcohol consumption, whereas 51% of controls did not consume alcohol (Tables 1 and 2).

Discussion

Abnormal glucose was found in nearly half of the cases with oral cancer in comparison with control, while nearly quarter of the controls had abnormal glucose tolerance. This can be due to associated insulin resistance in type II DM. Chronically increased levels of insulin resulting in hyperinsulinaemia, have been associated with colon cancer and cancer of breast, pancreas and endometrium. These tumourogenic effects of insulin could be directly mediated by insulin receptors in the preneoplastic target cells or might be due to related changes in endogenous hormone metabolism [8]. Recent studies say that insulin promotes the synthesis and biological activity of insulin like growth factors 1(IGF1) which act as a growth factor that promote cell proliferation and inhibits apoptosis. There is evidence that the effect of IGF-1 might be related to p53 mutations, which are quite common in head and neck malignancies [9,10]. Several prospective population-based studies have assessed the association between diabetes and cancer death, but laboratory parameters used were fasting plasma glucose levels [11,12] or post prandal glucose levels [13,14].

More than half of our study subjects were regular abusers of tobacco either in smoking form or smokeless form. Nearly half of them had a history of alcohol usage, this is consistent with the study done in Kerala [15].

Majority of the cases were males and there is a statistically significant association in men for the development of oral cancer. It is possible that males and females reported history of diabetes differently and due to social reasons females report to doctors quite late. Men are likely to represent patients with poorer metabolic control, leading to higher levels of insulin, and probably more oxidative damage to DNA. It has been proposed that poor diabetic control is associated with an increased cancer risk due to enhanced oxidative damage to DNA [16,17]. The present study clearly demonstrated that higher fasting plasma glucose and 2 hour post prandial glucose levels were significantly associated with increased risks of oral cancer. These associations remained robust even after adjustment for other confounding factors, like consumption of tobacco and alcohol. Interestingly we found that the risk of cancer death was increased significantly not only in diabetic subjects but also in subjects with impaired glucose tolerance as compared with subjects with normal glucose tolerance. These findings highlight the clinical value of early management of hyperglycemia, even in the prediabetic range, to prevent cancer death.

	Cases	Controls
Normoglycemic	21 (46%)	31 (68.8%)
Hyperglycemia(IFG+IGT+DM)	24 (54%)	14 (31.2%)
Impaired Fasting Glucose (IFG)	7 (29%)	10 (70%)
Impaired Glucose Tolerance(IGT)	6 (25%)	4 (30%)
Diabetes Mellitus(DM)	11 (46%)	0
Mean Fasting Blood Sugar(mg/dl)	96 ± 12	87 ± 14
Mean 2 hour OGTT(mg/dl)	108 ± 22	111 ± 25

Table1: Glycemic parameters of cases and controls.

	Cases	Controls
Normal OGTT	21	31
Impaired OGTT	6	4
Impaired fasting Glucose	7	10
Diabetes Mellitus	11	0

Table 2: Glucose tolerance among cases and controls.

Conclusions

The following conclusions were drawn, hyperglycemia (which includes IFG, IGT and diabetes) increase the risk of oral cancer two folds, and however Impaired Glucose tolerance alone as defined by ADA does not appear to play a role. Several potential confounders of the association between DM and cancer incidence were accounted for in the analysis, although the possibility of residual confounding factors cannot be denied. However, numerous potential confounders were controlled in the present study. We did not obtain information about the use of some antidiabetic drugs that could improve insulin resistance and reduce the risk of cancer. In summary, the current study suggests that a pre-existing DM is positively associated with the incidence of oral cancer, but the role of IGT I in the causation of oral cancer has to be reviewed with a large sample size study. Given the increasing epidemic of DM in recent years, it is time to be on the move and start preventive programs aimed at those with DM, so as to prevent cancer.

Strength

The strength of the present study is its prospective design, which prevents recall bias.

Limitations

Small sample size remains the weakness of this study. In our study serum insulin level estimation was not done, which is the most appropriate test to determine the insulin resistance, this was due to financial constraints.

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