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Assessment of Pre-Operative Random Blood Glucose in Oral Precancer and Oral Squamous Cell Carcinoma- An Original Research

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Abstract

Background: Oral cancer is one of the most common cancers occurring in South- East Asian region. There is growing evidence that hyperglycemia plays a contributing role in oral cancer progression. The current study aims to estimate pre-operative random blood glucose level in oral pre-cancer and oral cancer subjects.

Materials & Method: A total of 150 subjects (50 participants in each group). 2.5 ml of blood samples from each subject were drawn in sodium fluoride vials. Plasma was obtained by centrifuging the blood at 2000 rpm for 10 min. Random blood glucose levels were assessed using GOD-POD method.

Results: The mean values of Random blood glucose were higher in oral cancer and oral pre-cancer cases when compared to glucose. Comparison was done by One-way ANOVA the value was statistically in significant.

Conclusion: Random Blood glucose alone does not play a role. However, concomitant analysis with oral glucose tolerance with glycosylated hemoglobin might pave way to delineate the role of hyperglycemia in oral cancer and pre-cancer.

Introduction

Hyperglycemia, or high blood glucose, is a condition in which an excessive amount of glucose circulates in the blood, which develops when the body has too little insulin, or when the body cannot use insulin properly.[1] Nowadays, researchers mainly focus on the impacts of hyperglycemia on eyes, kidneys, nerves, and heart; little attention has been paid to the roles of hyperglycemia in cancer.[1] Given the prevalence of hyperglycemia-related conditions existing in cancer patients, the relationship between hyperglycemia and cancer should arouse enough attention.

Oral Cancer is the most common cancer in India in males and second most common cancer in females.[2] Despite serious efforts, oral cancer survival rates remain low.[2] Patients with various types of cancer have been examined in many clinical studies for proof of abnormalities in carbohydrate metabolism. The clinical evidence indicated a positive association between neoplasia and concomitant abnormalities in glucose metabolism.[3]

Bowen et al suggested that a single Random blood Glucose ≥ 100 mg/dl is more strongly associated with undiagnosed diabetes than traditional risk factors.[4] It has been suggested that abnormal Random Blood Glucose values are a risk factor for diabetes and should be considered in screening guidelines.[4]

The current study aims to compare preoperative random blood glucose level in oral cancer, oral pre-cancer and

control subjects.

Material and Methods

This is a prospective cohort study. Institutional Ethical Clearence and informed consent from subjects were duly obtained. A total of 150 subjects participated in the study. The subjects were divided into three groups.

Group A: 50 subjects with clinical and histopathologically confirmed cases of Oral Cancer

Group B: 50 subjects with clinical and histopathologically confirmed cases of Oral Pre-cancer (Includes Oral Leukoplakia, Erythroplakia, Oral Submucous Fibrosis)

Group C: 50 subjects of normal healthy control

2.5 ml of blood samples from each subject were collected in (sodium fluoride) vials. Plasma was obtained by centrifuging the blood at 2000 rpm for 10 min. We used R-BC Laboratory Centrifuge for centrifugation and Systronics 169 spectrophotometers for colorimetric estimation. Enzymatic Determination of Blood Glucose was done by GOD-POD method.

Principal: Glucose oxidase (GOD) catalyzes the oxidation of glucose to gluconate. Hydrogen peroxide (H2O2), thus formed, in the presence of peroxidase (POD) igets detected by a chromogenic oxygen acceptor, phenol, 4-Aminophenazone (4-AP):

β-D-Glucose+O_2 + H_2O $\xrightarrow{GOD}$ Gluconate+H_2O_2

H_2O_2 + Phenol + (4-AP) $\xrightarrow{POD}$ Red Quinone dye + H 2O.

The intensity of the color formed is proportional to the glucose concentration in the serum.

Assay Procedure: The following parameters were used: Wavelength.....505nm (500-510), Cuvette.....1cm.light path

Temperature.....37°C

We adjusted the instrument to zero with distilled water. Then, Pipetted into clean dry test tubes labeled as Blank (B), Standard (S), and Sample.

Addition Sequence	Blank	Standard	Sample
Glucose mono reagent	1.0ml	1.0ml	1.0ml
Glucose standard	-	0.01ml	-
Sample	-	-	0.01ml

Table 1: Comparison between Three groups by One-Way Anova Test

It was well mixed and incubated at 37°C for 5 min or at 15- 25°C. (25°C) for 10 min. We then measured the absorbance of the standard and test sample against blank after incubation the color is stable between 15-30min. and recorded at spectrophotometer at 535nm. The calculation was done using following formula:

Glucose (mg/dl) = Sample / Standard x100

Results

The mean Random blood sugar (RBS) in the oral cancer group were101.44± 18.282mg/dl; in oral pre-cancer group were 100.48±34.187mg/dl and in normal control group were 91.6909 ±17.365 mg/dl. (Figure 1) The three group were statistically analyzed by One-way ANOVA test where p value is considered as <0.05 (Table-1) The comparison between the three groups were found to be statistically non-significant. (p=0.079)

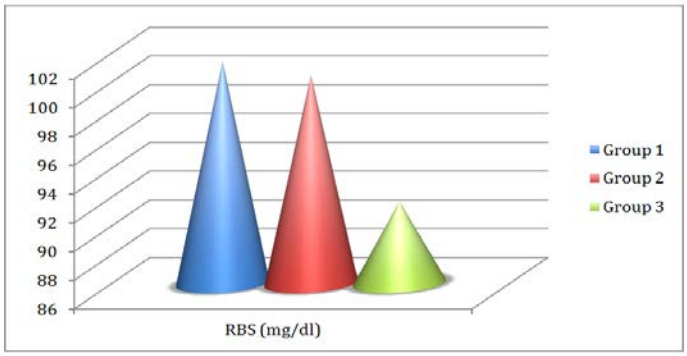

Fig.1: Mean Random Blood Sugar level in three groups

Discussion

Epidemiologic evidence in the past suggested that people with diabetes are at significantly higher risk for many types of cancer.[5] It has been recognized that diabetes plays a crucial role in the development of solid organ malignancies including liver, [6, 7] pancreatic, [6, 8] colorectal,[6, 9] breast,[10, 11] endometrial [16–18],[12-14] and bladder cancers [19, 20].[15,16] A recent meta-analysis demonstrated a considerable increase in cancer mortality related to endometrial, breast, and colorectal cancers in patients with preexisting diabetes compared with individuals with normal glycemic status.[17]

The elevated glucose concentration facilitates the synthesis of tumor cell DNA, as malignant cell metabolism relies on the pentose phosphate pathway. [18] Due to oxidative balance failure, advanced glycation end products (AGEs) accumulate, which generates the release of free radicals, cytokines and growth factors.[19] These harmful products cause extracellular matrix damage and increase the permeability of the basal membrane, thereby promoting the spread of cancers. It has already been shown that matrix metalloproteinase levels increase in DM, which facilitates the local distribution of tumor cells and the formation of metastases.[3, 20] AGEs enhance the expression of their receptor, RAGE, which is one of the main regulatory factors underlying tumor cell invasion (25). [21]

Hyperglycemia also increases the agglutination of blood cells, which causes micro-embolization, blood vessel obstruction and hypoxia.[22] As non-oxidative anabolic pathways play a leading role in tumor cell metabolism, these cells are able to multiply even in hypoxic conditions [23] In cases of diabetes, elevated glucose levels potentiate ribose generation and DNA replication by tumor cells.[24] Hyperglycemia also promotes the spread of carcinomas and tissue damage due to the Glut-1 glucose transporter. Indeed, the rate of Glut-1 expression significantly correlates with the increased mortality and lower life expectancy of oral cancer patients.[25]

Dikshit et al revealed that diabetic women are at increased risk of developing leukoplakia and erythroplakia.[26] Ujpal et al found that that amongst people with diabetes, the prevalence of precancerous lesions was higher than in the control group.[27] According to Albrecht et al, prevalence of oral leukoplakia was higher among diabetic patients compared with control group.[28] Dietrich et al studied that with a positive history of diabetes had more than 2-fold increase in risk of oral leukoplakia.[29]

The mean value of Random blood sugar was higher in two case groups (oral cancer and oral pre-cancer) when compared with controls, the value were statistically in significant. To ascertain the exact role of hyperglycemia in oral cancer and oral pre-cancer, a collaborative study of impaired glucose tolerance, random blood sugar level along with glycosylated hemoglobin with larger sample size may prove to be beneficial.

RBS	Between Groups	3060.717	0	1530.359	2.579	.079
	Within Groups	89598.348	150	593.367		
	Total	92659.065	150			

Conclusion

To conclude, mean Random blood sugar level was higher in oral cancer and oral pre-cancer groups when compared with normal healthy controls although the result was statistically not significant. However, there are few confounding bias linked with Random blood sugar level

and oral pre-cancers association. Primarily only random blood sugar level alone cannot be defined to play a role. The use of anti-diabetic drugs in subjects may alter the value of random blood sugar levels. Further studies with larger sample size and concomitant analysis of impaired oral glucose tolerance test (OGTT) and glycosylated hemoglobin ($HB_1A_{c)}$ along with due consideration of other confounding factors will prove to be beneficial in oral cancer and oral pre-cancer therapeutic outcomes.

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