Original Research Article

A Comparative Study of Serum Fucose, Hs C Reactive Protein Levels & Lipid Profile in Oral Cancer, Leukoplakia and Oral Submucous Fibrosis

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Abstract

Introduction: Cancer is the second leading cause of death worldwide. Eleven million new cases of cancer are diagnosed every year. India has the highest incidence of oral squamous cell carcinoma in the world. Serum as a diagnostic tool, has gained lot of attention in last three decades. **Methodology:** This study was conducted in Department of Biochemistry, Index Medical College and Research Centre, Indore, Madhya Pradesh. **Results:** The result of this study revealed that statistically significant difference between the parameters between the groups. **Conclusion:** It can be concluded that, the change in biochemical markers such as lipid levels may have a diagnostic or prognostic role in the early diagnosis or prognosis for oral premalignant and malignant lesions.

Keywords: Leukoplakia, Oral Submucous Fibrosis, Serum Fucose.

Introduction

Oral cancer is one of the leading causes of mortality and morbidity. The early detection of cancer appears to take a lead when assessing the treatment and patient prognosis. For easy early detection biochemical markers pertaining to that respective cancer are a way ahead than other specialized techniques or tools[1]. The use of specialized biomarkers is one of the leading areas for research and innovation and help in not only early diagnosis but over the period their measurement promises treatment assessment as well.

Various human secretions and body fluids show biochemical markers in their composition, as and when secreted by the cancer cells[2]. The glycoproteins synthesized by the cancer cells are released into the body fluids. Glycoproteins contain galactose, mannose, glucosamine, galactosamine, sialic acid or fucose as the carbohydrate residue[3]. The presence of tumor cells increases the process of fucosylation (addition of L-fucose at the terminal end of the oligosaccharide chain) which stimulates cellular proliferation, adhesion, metastasis and even prevents the detection of tumor cells by escaping the cell recognition.

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The increased fucosylation causes an increase of biomarkers in body fluids and works as an easy tool for detection of tumor cells within an individual[4]. Hence, monitoring serum/tissue fucose levels could be a promising approach for the early detection, diagnosis, and prognosis of various cancer types[3].

Oral cancers are preceded by various stages of pre-cancerous lesions or conditions such as leukoplakia, oral submucous fibrosis etc. These pre-cancerous conditions are a leading diagnosis factor for forthcoming well-defined cancers and their early detection helps in improving patient condition and defining treatment towards better prognosis[5]. The cycle of conversion of pre-malignant condition to a malignant transformation is accompanied by altered glycosylation within the cells and tissues of the body[4-6]. Altered glycosylation of glycoconjugates cause changes in biological events due to acquired defects in this enzymatic process. Early detection of malignant transformation improves the clinical outcome of patients. The search for a biomarker that could predict the changes in the premalignant lesions would immensely help in the recognition of high-risk lesions. Therefore, if patients with clinically suspicious lesions can be analyzed with biomarkers along with routine histopathological tests for the prediction of its malignant potential, the chances of minimizing them morbidity and mortality was high.

Hs CRP, a typical systemic inflammation marker, were first discovered in the plasma of patients during the acute phase of pneumococcal pneumonia. HsCRP is produced in hepatocytes in response to inflammatory cytokines such as interleukin (IL)-1, tumor necrosis factor (TNF)-α, and IL-6[5]. Thus, its level in tissue fluids

marks the underlying conditions of inflammation and cellular proliferation.

One of the important components responsible for the maintenance of cell integrity is lipids, which are also required for various biological functions like cell division and growth of normal and malignant tissues. Free radicals and reactive oxygen species are formed due to tobacco carcinogens which cause oxidation/ peroxidation of polyunsaturated fatty acids. This peroxidation further releases peroxide radicals which alter the essential constituents of the cell membrane leading to their involvement in carcinogenesis/ tumorigenesis[8]. The lipid peroxidation causes an increased utilization of lipids such as total cholesterol, lipoproteins and triglycerides. The increased requirement of accomplished either from circulation, by synthesis through the metabolism or from degradation of major lipoprotein Fractions like very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), or high-density lipoprotein are an indicator towards cancer marker.

Thus, the assessment of these (vide supra) biomarkers takes the lead in diagnosis and treatment prognosis of either a precancerous lesion or well-developed cancers.

Methodology

Study Area

This study was conducted in Department of Biochemistry, Index Medical College, Malwanchal University, Indore (M.P.).

Study Population

The study included 200 participants within age group of 15-60 years, divided into 4 groups.

Group I, II and III included 50 patients each with clinical and histo-pathological proven oral leukoplakia, oral submucous fibrosis and oral cancer respectively attending the OPD, Index Medical College, Indore. Group IV included 50 age and sex matched healthy subjects, from patients' attendants to serve as controls.

Group I: 50 Oral leukoplakia patients

Group II: 50 Oral submucous fibrosis patients Group III: 50 Oral cancer patients

Group IV: 50 Healthy controls

Data Collection

Blood (5.0ml) was collected by venipuncture which is the preferred method of blood sampling that causes less pain than heel prick. Winged steel needle 23 gouge was used for the purpose in all subjects as well as patients. The sample was processed in research laboratory after collection of blood sample; and centrifuged for 10 min at3000 rpm at room temperature. The supernatant was transferred in the fresh tube with proper labeling for the analysis of serum fucose and serum CRP.

All the parameters were assessed by standard estimation tests for subjects in all groups. The serum fucose level was estimated by Winzler method.

The Serum Hs C Reactive Protein (HsCRP) was estimated by Immunoturbidimetry. The serum lipid levels were determined by CHOD/PAP method (Cholesterol oxidase/peroxidise amino phenazone test)

TGL was determined by GPO/PAP method.

LDL cholesterol was assessed according to the formula by Friedwald et al, LDL= TC–(HDL+TG/5)

VLDL was calculated by the formula - To estimate VLDL-C, divide the triglyceride value by 5 if the value is in mg/dL

Data Analysis

Data analysis was done by using ANOVA for variance and the significance of mean difference between the groups was done by Tukey's post hoc test.

Results

The study results are categorized as demographic distribution, biomarker analysis comparison and correlation.

The frequency distribution between genders is shown in table I, the result was non-significant for gender distribution between the groups. The mean age and standard deviation were also non-significant between the groups, as shown in table I.

The result shows a statistically significant difference between the parameters between the groups. The post hoc Tukey's HSD determined the comparison of means between the pairs. For serum fucose the results were significant for majority of the pairs, except for comparison between group 2: group 3 and group 2: group4 (with $p>0.05$). For Hs CRP the values were significant between the groups with $p<0.05$. The analysis for CHL was however variable where post hoc Tukey's HSD was non-significant when compared with control group but was significant between the groups with pre-malignant and malignant conditions.

The results show statistically significant p value between the groups. The comparison of all parameters/ biomarkers was significantly variable when compared with group 4 subjects.

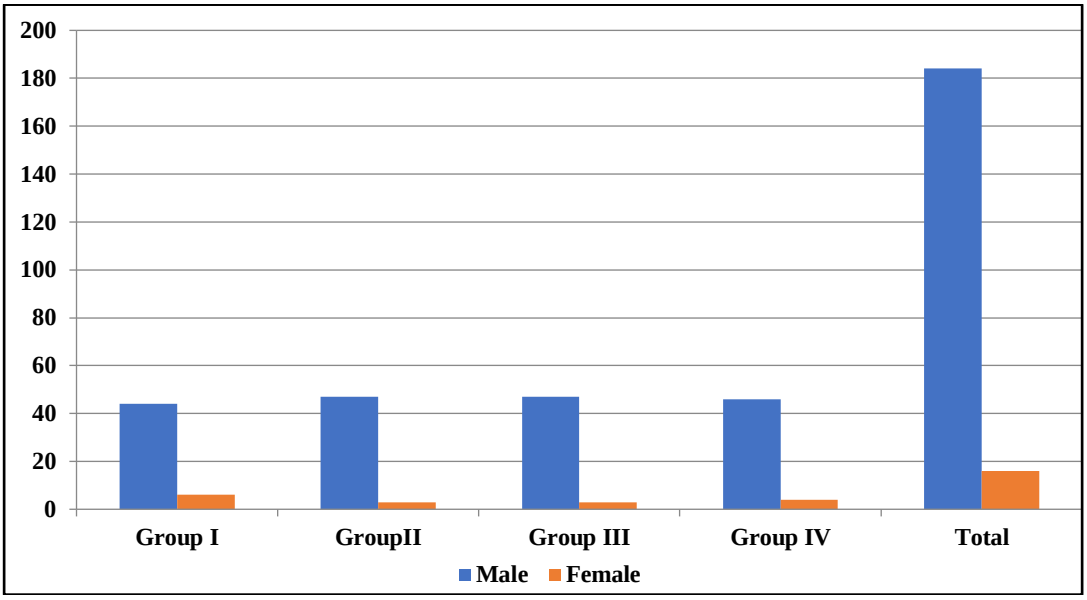

Fig I: Frequency distribution and mean age of groups; NS=non-significant

Table 1: Mean and standard deviation (SD) for Serum fucose, Hs CRP and total cholesterol

Groups	S. fucose (mean±SD)	f-ratio/Pvalue	Hs CRP(mean±SD)	f-ratio/P value	CHL (mean±SD)	f-ratio/P value
I	7.22±1.28	34.69/ < .00001. The result is significant at p < .05.	3.168±0.86	56.42/ < .00001. The result is significant at p < .05.	174.72±25.27	20.78/ < .00001. The result is significant at p < .05.
II	37.83±23.42		3.92±1.0		180.4±34.42	
III	35.28±21.01		3.67±0.95		187.3±39.02	
IV	46.63±26.16		5.56±1.01		142.44±21.17	

Table 2: Mean and standard deviation (SD) of lipid markers in study groups

Groups	TGL (mean±SD)	f-ratio/P value	HDL (mean±SD)	f-ratio/P value	LDL (mean±SD)	f-ratio/P value	VLDL (mean±SD)	f-ratio/P value
I	168.12±71.64	10.53/<.00001 The result is significant at p < .05	40.12±3.9	2.68/ <.00001 The result is significant at p < .05	103.04±29.23	3.73/.012218 The result is significant at p < .05	34.36±13.77	6.03/.000284 The result is significant at p < .05
II	177.76±68.89		40.84±3.073		107.28±33.09		34.76±13.45	
III	176.18±55.55		39.36±3.91		117.14±28.84		32.10±17.93	
IV	121.96±15.53		38.94±3.56		100.24±12.41		24.36±3.91	

Discussion

Oral cancer is the most common type of cancer in the head and neck region with an annual incidence Visible changes are detectable in the oral mucosa in the form of white or red patches before the occurrence of oral squamous cell carcinomas (OSCCs), therefore the current study design to evaluate the biomarkers for their determination and correlation in understanding the disease. Apart from this it sets a cut off value for each marker in the case which gives a clear picture to the clinician to aid the better treatment protocol and assessing the condition so prevention and early detection of such potentially malignant disorders (PMDs) have the potential of not only decreasing the incidence but also improving the survival of those who develop oral cancer.

Increased level of different glycoproteins has been associated with different types of malignancies, like higher serum fucose level found in cancer of the cervix, breast, oral cavity, and lymphoma. Glycoconjugate molecules expressed in the plasma membrane of mammalian cells have also been reported to be associated with cell-to-cell adhesion, tumor progression, and metastasis[8]. Measurement of protein-bound carbohydrates of glycoproteins has been used as an index to glycoprotein levels now more recent trend need to be used to measure the amount of given monosaccharide as a measure of glycoproteins.

Lipids in malignant tumors are not only necessary for providing the membrane constituents of proliferating cells but are also needed for energetic, biophysical and signalling pathways that drive tumorigenesis. Dysregulated lipid metabolism is a hallmark of cancer[2]. Cancer specific modifications of the lipid metabolism can affect the production of specific signalling lipids, such as factors derived from poly-unsaturated fatty acids and alter the availability of specific Fatty Acids (FA) pools required for protein modification[3,4].

This study is aimed at evaluation of serum fucose, Hs CRP and lipid profile in oral submucosa fibrosis, leukoplakia, and Oral Cancer and the results obtained showed the very high significance for serum fucose levels in oral submucosa fibrosis, leukoplakia, OC group as compared with healthy individuals. Analysis of the markers can be an additional tool for diagnosis, prognosis, and treatment monitoring of cancer patients. Therefore, the evaluation of serum l-fucose would be of good help in assessing early malignant change in increasing the accuracy of clinical diagnosis and also in assessing the spread and invasiveness of OC, OSMF, and leukoplakia also found that there was an increase in serum lipid profile and serum CRP in cancer group when compared to premalignant and malignant group. The elevated level of CRP is most likely a response secondary to tumor necrosis, local tissue damage, and associated inflammation in patients with malignancies. The increasing tumor cells release cytokines into the blood. These cytokines act on the hepatocytes of liver to synthesis and release acute phase proteins i.e, CRP. Thus, CRP concentration is increased in blood serum in malignant group when compared to premalignant group and in control group. But the CRP is not a specific inflammatory factor. There are many stimuli, including certain chronic infections or inflammatory conditions, smoking, obesity and trauma, which may also account for mild increase in CRP. In our study other conditions which causes increase in serum CRP and included only subjects with premalignant and malignant conditions were excluded. Lipids in malignant tumors are not only necessary for providing the membrane constituents of proliferating cells but are also needed for energetic, biophysical and signalling pathways that drive tumorigenesis. Thus, concentrations of the lipids were decreased in cancer conditions where there was excessive utilization of lipids for cell membrane synthesis and to drive for tumorigenesis. So this study provides strong base regarding the raise of CRP protein in cancer patients and decrease of serum lipid profile in cancer patients which was proved also in some other studies. By evaluating the serum CRP level even though it is not possible to diagnose the type of lesion or underlying systemic condition as it is a nonspecific marker, but it was helpful to predict the prognosis of the disease.

Conclusion

This study concludes that the change in lipid levels may have a diagnostic or prognostic role in the early diagnosis or prognosis for oral premalignant and malignant lesions. The lower plasma lipid status may be a useful indicator for initial changes occurring in neoplastic cells. So, our study opens new prospects for serum lipid profile to be a diagnostic marker for identifying the precancerous and cancerous conditions.

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