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Original Research Article

CRP AND LIPID PROFILE IN ORAL CANCER, LEUKOPLAKIA AND ORAL SUB MUCOUS FIBROSIS

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Abstract

Background: Acute-phase proteins such as C-reactive protein (CRP), fibrinogen, a protein undergo changes in their values in the presence of inflammation. Elevated levels of CRP, which serve as a prognostic indicator, have been observed in malignancies. Lipids are major components of cell membranes essential for numerous biological functions, including cell growth and normal and malignant tissue division. The potential influence of lipids in malignancy pathogenesis may involve their impact on malignant cell metabolism, proliferation, incorporation into neoplastic cell membranes, and functioning as intercellular messengers or mediators of inflammatory reactions. **Materials and Methods:** This study was conducted in Department of biochemistry in Radha Devi Jageshwari Memorial Medical College & Hospital, Turki, Muzaffarpur, Bihar. The duration of this study was from February 2023 to January 2024.This study included 4 groups. Each group included 50 participants. Group I consisted Oral leukoplakia patients, while Group II, III, IV were included Oral submucous fibrosis, Oral cancer patients & healthy controls respectively. **Result:** The result of this study revealed that significant disparities were observed in Hs CRP values among the groups with a p-value < 0.05. However, the analysis of CHL showed variability; while it was non-significant when compared with the control group, it exhibited significance between groups with pre-malignant and malignant conditions. **Conclusion:** This study concludes that these biomarkers serve as essential tool for detecting the disease at early stage and also during treatment prognosis.

INTRODUCTION

Potentially malignant disorders (PMDs) are widespread in India, particularly among South Indians, where the high consumption of areca nut and tobacco is cause for concern. In recent times, there has been a noticeable increase in cases of oral submucous fibrosis (OSMF) and oral cancer among females. Previously, PMDs were predominantly prevalent among males, attributable to the widespread use of tobacco and related products. However, in recent years, the consumption of these substances among females has risen, driven by various factors.[1,2]

OSMF causes mucosal stiffness and difficulty in mouth opening due to collagen band formation in areas such as the buccal mucosa, labial mucosa, and soft palate. If not addressed in a timely manner, OSMF is linked to malignant transformation. Identifying and preventing these PMDs promptly may lower the incidence rates and, consequently, improve the survival outcomes of patients who develop oral squamous cell carcinoma (OSCC).[3]

Oral cancer represents a significant portion of head and neck cancers, with a global incidence of 300,000 cases. It stands as a leading cause of mortality, exhibiting a less than 50% survival rate within five years. Acute-phase proteins such as C-reactive protein (CRP), fibrinogen, A protein undergo changes in their values in the presence of inflammation. Elevated levels of CRP, which serve as a prognostic indicator, have been observed in malignancies. Hepatocytes stimulated by various inflammatory cytokines like interleukin (IL)-1, IL-6, and tumor necrosis factor-α are responsible for the increased production of CRP. Past studies have demonstrated alterations in CRP levels among patients with potentially malignant disorders (PMDs). Considering this, we sought to evaluate CRP levels in patients diagnosed with oral

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submucous fibrosis (OSMF) and oral squamous cell carcinoma (OSCC).[4,5]

Among all oral malignancies, oral squamous cell carcinoma (OSCC) accounts for approximately 90%.[6] However, the use of tobacco and arecanut can also lead to potentially malignant disorders.[7] Oral cavity cancer currently ranks as the leading cause of cancer-related deaths among Indian men, often preceded by oral potentially malignant disorders such as oral leukoplakia (OL) and/or oral submucous fibrosis (OSMF).[8] The majority of patients with potentially premalignant disorders fall within the 21-30 years age group, with a male to female ratio of 6.8:1 in India.[6] Early detection is crucial for oral cancer control, and one of the main reasons behind the high mortality rate of oral cancer is the delay in diagnosing potentially malignant disorders, which serve as precursors to oral cancer.

Oxidative stress is considered a significant factor in the pathogenesis of various diseases, with antioxidant levels playing a significant role in both the pathogenesis and treatment of malignancies [8-9]. Various biochemical markers are available for precancerous and cancerous patients, with one such marker being the serum lipid profile. Lipids are major components of cell membranes essential for numerous biological functions, including cell growth and normal and malignant tissue division. The potential influence of lipids in malignancy pathogenesis may involve their impact on malignant cell metabolism, proliferation, incorporation into neoplastic cell membranes, and functioning as intercellular messengers or mediators of inflammatory reactions.[10] Associations between serum lipids, lipoproteins, and different cancers have been reported.[10] Although significant changes in blood cholesterol levels have been observed, whether hypolipidemia acts as a predisposing factor or a result of cancer remains unanswered.

In the present study, we evaluated various biochemical lipid parameters such as total cholesterol (TC), triglyceride (TGL), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) levels in OSMF, OL, and OSCC. Additionally, we correlated the lipid profile parameters studied in OL, OSMF, OSCC, and control groups.

MATERIALS AND METHODS

Study Area: This study was conducted in Department of biochemistry in Radha Devi Jageshwari Memorial Medical College & Hospital, Turki, Muzaffarpur, Bihar.

Study Duration: The duration of this study was from February 2023 to January 2024.

Study Population: This study included 4 groups. Each group included 50 participants. Group I consisted Oral leukoplakia patients, while Group II, III, IV were included Oral submucous fibrosis, Oral cancer patients & healthy controls respectively.

The detailed medical history and clinical examinations of all patients were documented using a specially designed form and conducted by a designated assessor. Patients were then classified into different groups based on their symptoms and signs, which were further confirmed through incisional biopsy taken from the relevant lesion site. The biopsy procedure, performed by an expert under local anesthesia, aimed to confirm the category of the lesion, with subjects being reassigned to appropriate groups as needed.

Venipuncture, the preferred method for blood sampling due to its lower pain intensity compared to heel prick, was used to collect 5.0ml of blood from all subjects and patients. A 23-gauge winged steel needle was employed for this purpose. Following blood collection, samples were processed in the research laboratory, centrifuged at 3000 rpm for 10 minutes at room temperature, and the supernatant was transferred to fresh tubes labeled accordingly for serum fucose and serum CRP analysis. All parameters were evaluated using standard estimation tests across all subject groups. Serum fucose levels were determined using the Winzler method, while Serum HsC Reactive Protein (HsCRP) was measured via Immunoturbidimetry. Serum lipid levels were determined using the CHOD/PAP method (Cholesterol oxidase/peroxidase aminophenazone test), and TGL was assessed using the GPO/PAP method.

LDL cholesterol was calculated using the Friedewald formula: LDL = TC – (HDL + TG/5)

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

RESULTS

The study findings are divided into four categories, each consisting of 50 participants. Group I comprised patients with oral leukoplakia, while Groups II, III, and IV included individuals with oral submucous fibrosis, oral cancer patients, and healthy controls, respectively. The results reveal a notable difference in parameters across the groups. Post hoc Tukey's HSD analysis was employed to compare the means between pairs. Significant disparities were observed in Hs CRP values among the groups with a p-value < 0.05. However, the analysis of CHL showed variability; while it was non-significant when compared with the control group, it exhibited significance between groups with pre-malignant and malignant conditions. Overall, there was a statistically significant difference (p-value < 0.05) observed between the groups for all parameters/biomarkers, particularly in comparison with subjects in Group 4.

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Table 1: Group distribution

Group I :	50	50 Oral leukoplakia patients
Group II:	50	Oral submucous fibrosis
Group III:	50	Oral cancer patients
Group IV:	50	Healthy controls

Table 2: Gender distribution

Groups	Frequency	
	Male	Female
I	44	6
II	47	3
III	47	3
IV	46	4
Total	184	16

Table 3: Mean and SD of Hs CRP in study groups

Groups	Hs CRP(mean±SD)	f-ratio/P value
I	3.168±0.86	56.42/ < .00001. The result is significant at p < .05.
II	3.92±1.0	
III	3.67±0.95	
IV	5.56±1.01	

Table 4: Mean and 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 stands out as the most prevalent form of cancer within the head and neck area, presenting with an annual incidence rate. Observable alterations in the oral mucosa, such as white or red patches, precede the onset of oral squamous cell carcinomas (OSCCs). Consequently, the present study is designed to assess biomarkers for their identification and correlation in comprehending the disease. Additionally, it establishes cutoff values for each marker, facilitating clinicians in devising more effective treatment protocols and evaluating the condition. This approach aids in the prevention and early detection of potentially malignant disorders (PMDs), which not only has the potential to reduce incidence rates but also to enhance the survival rates of individuals who develop oral cancer.[11]

Increased levels of various glycoproteins have been linked to different types of malignancies. Glycoconjugate molecules present in the plasma membrane of mammalian cells are also associated with cell-to-cell adhesion, tumor progression, and metastasis. The measurement of protein-bound carbohydrates of glycoproteins has traditionally been utilized as an indicator of glycoprotein levels, but a more recent trend suggests the need to measure the amount of specific monosaccharides as a measure of glycoproteins.[12]

Lipids play a crucial role in malignant tumors, providing membrane constituents for proliferating cells and contributing to energetic, biophysical, and signaling pathways involved in tumorigenesis. Dysregulated lipid metabolism is a hallmark of cancer. Cancer-specific modifications in lipid metabolism can affect the production of specific signaling lipids, such as those derived from polyunsaturated fatty acids, and alter the availability of specific fatty acid pools required for protein modification.[13,14]

This study aims to evaluate high-sensitivity C-reactive protein (Hs CRP) and lipid profiles in oral submucosa fibrosis, leukoplakia, and oral cancer. The results showed significantly high serum fucose levels in oral submucosa fibrosis, leukoplakia, and oral cancer groups compared to healthy individuals. Analyzing these markers can serve as an additional tool for diagnosing, prognosing, and monitoring cancer patients.

The elevated levels of CRP are likely a response secondary to tumor necrosis, local tissue damage, and associated inflammation in patients with malignancies. Tumor cells release cytokines into the bloodstream, stimulating hepatocytes in the liver to synthesize and release acute-phase proteins such as CRP. However, CRP is not a specific inflammatory factor; various stimuli, including chronic infections, inflammatory conditions, smoking, obesity, and trauma, may also contribute to mild increases in CRP.

In this study, conditions causing an increase in serum CRP, other than premalignant and malignant conditions, were excluded. Lipids in malignant tumors are essential not only for providing membrane constituents but also for driving tumorigenesis through energetic and signaling

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pathways. Therefore, concentrations of lipids decrease in cancer conditions due to excessive utilization for cell membrane synthesis and tumorigenesis.

This study establishes a strong foundation regarding the elevation of CRP protein in cancer patients and the decrease in serum lipid profiles, consistent with findings in other studies. While evaluating serum CRP levels may not diagnose the type of lesion or underlying systemic condition due to its nonspecific nature, it can help predict disease prognosis. Changes in lipid levels may play a diagnostic or prognostic role in the early detection or prognosis of oral premalignant and malignant lesions. Lower plasma lipid status may serve as a useful indicator for initial changes in neoplastic cells, offering new prospects for serum lipid profiles as diagnostic markers for identifying precancerous and cancerous conditions.

CONCLUSION

The results of present study provide the conclusion that the derangement of biochemical composition occurs during the process of carcinogenesis. These components can be easily recognised and accurately assessed and can serve as potential biomarkers for detecting a disease as early as during its premalignant stage. The serum Hs CRP levels and lipids are deranged significantly in pre-malignant as well as malignant condition. Thus, these biomarkers serve as essential tool for detecting the disease at early stage and also during treatment prognosis.

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