Oral submucous fibrosis and plasma lipid profile

Oral cancer (OC) is the leading cause of morbidity and mortality due to cancer in India and is most commonly preceded by clinically definable premalignant lesions and conditions. One of the most common oral precancerous conditions prevalent in India is oral submucous fibrosis (OSMF).

OSMF is a chronic disease of the oral cavity, which is characterized by an epithelial and sub epithelial inflammatory reaction, followed by fibroelastic changes in the submucosa. Around 7-12% of oral submucous fibrosis cases undergo malignant transformation.[1]

Early detection of these lesions can drastically improve the treatment outcomes and prognosis in such patients. Carcinoma development is an intricate complex mechanism and the multifactorial causation makes it more difficult to find specific prognostic and therapeutic biomarkers. Thus, the development of newer diagnostic and predictive approaches that are less invasive, economical, and amenable to repeated sampling is imperative.

Lipids are major cell membrane components essential for various biological functions including cell growth and division of normal and malignant tissues. Altered circulatory cholesterol levels have been implicated in the etiology of various cancers like breast cancer and colorectal cancer.[2] Rose *et al*., were the first to report an inverse relation between blood cholesterol levels and risk of developing cancer.[3] It has been proposed that lower levels of blood cholesterol are associated with an increased risk of cancer occurrence.[4] However, the reports on altered lipid levels in oral malignancies and potentially malignant disorders (PMDs) are few and conflicting.[5,6]

In oral malignancies, the blood cholesterol undergoes significant and early changes. Because of rapidly proliferating tumor cells, there is reduction in blood cholesterol levels due to increased demand. There are many theories put forth explaining the association of altered lipid profile and potentially malignant or malignant disorders:[7]

- Newly forming and rapidly proliferating malignant cells need many basic components such as lipids well above the normal physiological limits, leading to diminished lipid stores
- Tobacco induces generation of free radicals and reactive oxygen species responsible for high rate of oxidation/peroxidation of polyunsaturated fatty acids (PUFA), which affects cell membrane and in turn lead to increased utilization of lipids
- Low cholesterol levels may be causally associated with occurrence of these cancers.

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But, the question that still remains unanswered is "whether altered lipid profile is causative factor for oral malignancy/PMDs or is a result of the disease process?"

The dearth of studies in this area of research is a major reason for the limited information available as well as the limited utility of these findings at present. The studies that tried to look into the role of lipid profile as potential biomarker were either small cohort studies or those that did not look at premalignant conditions specifically.[8] Patel *et al*., evaluated the largest number of patients with PMDs and had 63% patients with OSMF in their study.[9] They reported significant decrease in total cholesterol and HDL cholesterol levels (P = 0.04 and 0.00, respectively), thus strengthening the fact that there is an inverse relation between plasma cholesterol levels and PMDs. They even compared tobacco users with non-tobacco users group, which many other studies did not, and showed that tobacco users have lower levels of plasma cholesterol as compared to non-tobacco users.

The inverse relation between decreased plasma lipid profile and malignancy/PMDs was highlighted in all the studies, but they were plagued by lack of statistically significant sample size. A few authors also suggested that hypolipidemia may be a late effect occurring during the process of carcinogenesis rather than being the cause.[10]

Kumar *et al*. also evaluated patients with OSMF and their correlation with plasma lipid levels.[11] The authors have shown the inverse relationship between plasma lipids and OSMF as reported in literature as well, but have limitation of small sample size. Also, it fails to clarify whether decreased lipid levels were the preceding factor for development of OSMF or the result of disease process. Nevertheless, this study strengthens the available evidence and provides an insight into this aspect and definitely warrants further research.

Presently, there is no strong evidence present to support hypolipidemia as a causative factor for developing cancer, still the fact that plasma lipid levels reduce during the process of carcinogenesis can act as a potential diagnostic biomarker. We believe that currently available information should be used not only to look for a diagnostic marker but also to prognosticate the development of PMDs into malignancy. Exploring this concept will pave the way for future research to understand the complex mechanism of lipid metabolic pathways and use this information to identify and develop it as a potential prognostic biomarker.

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