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LIPID PROFILE ESTIMATION IN ORAL MALIGNANT AND PREMALIGNANT LESIONS

Pathology

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ABSTRACT

Introduction: Oral malignancy is usually preceded by lesions which are non-malignant to begin with and which are therefore been termed as premalignant. Many premalignant lesions and conditions like leukoplakia, erythroplakia, oral lichen planus, oral submucous fibrosis have malignant potentials.

Aims: To evaluate the serum lipid profile in premalignant lesions and conditions like Oral Leukoplakia, Oral Submucous fibrosis and in Oral squamous cell carcinoma and its comparison with the lipid profile among control groups.

Material and method: A total number of 225 patients were selected for the study from the OPD in Chandra Dental College and Hospital, Barabanki, U.P. the patients were selected under the criteria mentioned below. Patients with clinically evident and histopathologically confirmed with oral submucous fibrosis, oral lichen planus, oral leukoplakia, erythoplakia, and oral malignancy, for leukoplakia patients with histopathological confirmation sample collection was done, for patients with Oral Submucous Fibrosis after histopathological confirmation, sample collection was done and for Oral Malignancy sample collection was done after histopathological confirmation were included in this study.

Result: In Control Group (1 Vs 3), the mean HDL (mean± s.d.) of patients was 72.9885± 8.6803. In Malignant Group (1 Vs 3), the mean HDL (mean± s.d.) of patients was 38.2000± 3.5106. Distribution of mean HDL with Group (1 Vs 3) was statistically significant ($p<0.0001$). In Control Group (1vs3), the mean VLDL (mean± s.d.) of patients was 36.8640± 3.0412. In Malignant Group (1vs3), the mean VLDL (mean± s.d.) of patients was 26.1600± 1.5905. Distribution of mean VLDL with Group 1vs3 was statistically significant ($p<0.0001$). In Control Group1 vs3, the mean LDL (mean± s.d.) of patients was 96.4448± 12.7468. In Malignant Group1 vs3, the mean LDL (mean± s.d.) of patients was 94.8000± 5.9233. Distribution of mean LDL with Group 1 Vs3 was not statistically significant ($p=0.3125$).

Conclusion: There was statistically significant decrease in plasma total cholesterol, TG, LDL, VLDL and HDL observed in malignant patients as compared to the premalignant control group. The low lipid levels associated with Oral malignancy indicates that there is inverse relationship between oral cancer and serum lipid profile. Decrease in the lipid levels may be considered as a useful biochemical marker in the early diagnosis of oral malignancy.

KEYWORDS

Oral malignancy, serum lipid profile, Oral Leukoplakia, Oral Submucous fibrosis and in Oral squamous.

INTRODUCTION

Cancer is the second-leading cause of death worldwide after cardiovascular disease, which take >14 million lives in 2012 (Torre et al. 2015). There will be an increase in number in next few years as a result of the aging human population and the prevalence of cancer risk factors increasing worldwide. From the public health perspective this statistics is alarming, and there must be a question, "what exactly constitutes a cancer case?". The definition of cancer continued to evolve in the recent years with the advancement of the basic biologic field. Even the current established hallmarks of malignancy (Hanahan and Weinberg 2011)[1] is also revised continuously and the complexity involved in distinguishing between cancerous and noncancerous tissue is revealing day by day. Globally there may be a difference in clinical definitions of the morphological threshold between an invasive tumor and a preinvasive carcinoma in situ, and even within an individual hospital two pathologists may disagree whether a diagnosis of dysplasia versus malignancy should be applied to a particular biopsy specimen.

Oral malignancy is usually preceded by lesions which are non-malignant to begin with and which are therefore been termed as premalignant. Many premalignant lesions and conditions like leukoplakia, erythroplakia, oral lichen planus, oral submucous fibrosis have malignant potentials.

Various biochemical studies have shown that during tumour development various substances alter quantitatively in the serum and are referred to as tumor markers. So, if we find the biochemical changes occur even before frank cancer has occurred, we can predict even in the oral tissues.

Lipids are essential biomolecules for maintenance of various biological functions which includes stabilization of deoxyribonucleic acid helix, cell growth and division in normal as well as in malignant tissues. Various studies have been done by several researchers in the usefulness of variations in blood cholesterol levels in diagnosis and treatment of various diseases. A major risk factor for coronary heart diseases is increased levels of cholesterol; on the other hand, the decreased level of cholesterol has been associated with an increased risk of malignancy.

Cholesterol is an amphipathic lipid which is an essential structural component of all cell membranes and the outer layer of plasma lipoproteins. It is present either as free cholesterol or combined with a long-chain fatty acid, as cholesteryl ester in tissues and in plasma lipoprotein.[2] Fundamentally, the development of a malignancy requires the uncontrolled and excessive proliferation of cells. These rapidly forming cells need many basic components well above the normal limits which are used in physiological process. For various biological functions including the cell division and the growth of normal and malignant tissues major cell membrane component is essential, and in the formation of this cell membrane component lipids is one of the most important component.. Lipid stores are diminished due to increased use of lipids by this rapidly dividing cells.[3]

AIMS AND OBJECTIVES

To evaluate the serum lipid profile in premalignant lesions and conditions like Oral Leukoplakia, Oral Submucous fibrosis and in Oral squamous cell carcinoma and its comparison with the lipid profile among control groups.

1. To determine the serum levels of Total cholesterol (TC), Low density lipoprotein (LDL), High density lipoprotein (HDL), Very Low density lipoprotein (VLDL), Triglycerides (TG) of patients

with potentially malignant disorders like Oral Leukoplakia, Oral Submucous fibrosis and its comparison with the lipid profile among control groups.

2. To determine the serum levels of Total cholesterol, Low density lipoprotein, High density lipoprotein, Very Low density lipoprotein, Triglycerides of patients with Oral squamous cell carcinoma and other oral malignant lesions and its comparison with the lipid profile among control groups.
3. To see the changes in the levels of serum lipid profile during the pathogenesis of oral malignant and premalignant lesions or conditions.
4. To determine the altered levels of serum lipid, and if any changes found that could be used as a biochemical marker for oral premalignant diseases or oral cancer.

MATERIALS AND METHODS

A total number of 225 patients were selected for the study from the OPD in Chandra Dental College and Hospital, Barabanki, U.P. the patients were selected under the criteria mentioned below.

Inclusion criteria:

- Patients with clinically evident and histopathologically confirmed with oral submucous fibrosis, oral lichen planus, oral leukoplakia, erythoplakia, and oral malignancy.
- For leukoplakia patients with histopathological confirmation sample collection was done.
- For patients with Oral Submucous Fibrosis after histopathological confirmation, sample collection was done.
- For Oral Malignancy sample collection was done after histopathological confirmation.

Exclusion criteria:

- Patients with immunocompromised conditions
- Pregnant patients
- Patients underwent/undergoing radiotherapy and chemotherapy
- Patients with multi-organ conditions

For the purpose of the study further grouping of the patients is done.

- Group 1: 75 patients with oral malignancy
- Group 2: 75 patients with oral premalignant lesions and conditions
- Group 3: 75 patients of healthy individual

RESULT AND DISCUSSION

This study is performed for estimation of Lipid Profile in Oral Malignant and Premalignant lesions in three groups which are malignant group (Group 1) consisted of 75 patients with the age range 30 to 70 years. The second group was of 75 patients with premalignant lesions and conditions with the age range from 28 to 70 years. The third group comprised of healthy individuals (control group) with the age range from 28 to 70 years. The significance of this study is that unrestricted lipid inside the malignant cell is directed into leading as saturated fat esters considerably that actuality out from the tissue to the flowing HDL despite the free cholesterol is ascending as of production in the cancer cells which cause the reduction in intensities of HDL in tumour patients. The reduced intensity serves like an indicator with productive pointer in the primary recognitions or oral carcinoma or change of precancerous lesions or conditions to a carcinoma Sabea D. W. (2020). The change in lipid levels may have an early diagnostic or prognostic role in the oral premalignant lesions/conditions and oral cancer.

Kumar et al (2018)[4] also found in their study that oral cancer mainly occurs in the older age group as they found fourth to fifth decade of age group was most vulnerable to cancer and mean age for precancerous disease is 34.15(range 21 to 52). Similarly our study also observed the mean age for malignant patients was 55.7 and the mean age of premalignant patient was 44.6.

In our study we observed the peak age incidents of patients mean in each group to be from 44.6 to 55.7 with SD ±9.5 to 10.7 which is accordance with the observation reported by **Sharma et al (2018),** and **Vaish et al(2019)**[5]**.** This age related incidents suggests that time dependent factor results in the initiation and promotion of genetics events that results in malignant change and the diminished immune surveillance been in the older age group.

Cholesterol ester is a stored form of cholesterol found in most tissues which is transported as cargo in the hydrophobic core of lipoproteins. Recent studies by **Kaul D (2000)** [6]**and Kaur M (1998)** discovered a novel cell surface cholesterol sensor designated as receptor-CK which was not only shown to be ubiquitously present in various human organs but also regulated (by its signaling pathways) various genes involved in cholesterol homeostasis (HMG CoA reductase; HMG CoA synthase; Apo-B-specific LDL receptor); cell growth (Cyclin D; C-fos; etc); cell death (Bc1-2) through a 47kDa transcription factor (which derived from cleavage of 125kDa SREBP) having affinity for genomic sterol regulatory clement (SRE) sequence as well as through other transcription factor. Cholesterol often found distributed non randomly in domains in membrane. Study suggests that cholesterol exerts many of its action by maintaining a specialized type of membrane domain termed as lipid rafts. This lipid rafts enriched in cholesterol and sphingolipids, and have been thought to act as platform through which signal transduction events are coordinated.

Another study by **Pratap M et al (2018)**[7] also found a decrease levels of TC, TG, LDL and VLDL in the study group compare to control. They also found that mean lipids were reduced significantly with the advance staging of OSMF as advance stage of OSMF has a high chances of malignant transformation. Our study showed that there is significant decrease in TC, TG, HDL, LDL in oral cancer patients compared to premalignant diseases except VLDL which was not much significantly reduced.

Lohe et al (2010)[8] found a significant decrease in serum TC, TG, HDL, VLDL in oscc and premalignant disease compared to control but no significant decreased in LDL in OSCC and Premalignant disease compared to control which was consistent with our study. But in comparing OSCC with premalignant disease they found a significant decrease in VLDL and TG in OSCC patients which was consistent with our study except VLDL which was not significantly decrease in our study in OSCC compared to premalignant disease. They also found no significant decrease in TC and HDL in OSCC compared to premalignant disease which was inconsistent with our study.

The study done by **Goyal S et al (2013)**[9] on 90 patients for the estimation of serum lipid profile in oral precancerous lesions and conditions showed that there was not statistical significant changes in value of serum lipid profile in either the oral tobacco habit group or the oral precancer group which was consistent with our study as LDL levels has shown increased mean value of 100.03 with a SD 4.6. the findings was not consistent with the study conducted by **Khurana M et al (2000), Neki NS (2002) and Kshitiz et al (2010)**[10] who found raised total cholesterol, triglycerides, LDL, VLDL and lower HDL levels in tobacco users respectively.

In studies conducted by **Singh S et al (2013)**[11] **and Chawda J D et al (2011),** serum LDL and VLDL levels did not revels any significant difference in between cancer and control group, which is not consistent with their study as in our study as compare to the control group, there is decrease in the LDL and VLDL.

Mehta R et al (2014) found a significant decrease in serum TC, HDL and TG level in oral cancer and precancerous disorders compared to control. Similarly **Gaddikeri K et al (2016)**[12] performed a study in which they found a significant decreased in TC, TG, HDL, LDL, VLDL in oral cancer and precancerous disorders compared to control which was consistent with our study except LDL which was increased in premalignant disorders compared to control and not much significantly decreased LDL levels in oral cancer compared to control. They also found a significant decrease in TC, TG and HDL in oral cancer compared to premalignant diseases, which is in accordance with our study. They found a significant increase in VLDL level in OSCC compared to premalignant diseases which is inconsistent with our study as we did not found any significant decrease in VLDL levels in OSCC compared to premalignant diseases as similar to the study done by Mehta R et al (2014)32 as they found significantly reduced VLDL levels in OSCC compared to premalignant diseases.

They also found non-significant decrease in LDL in OSCC compared to premalignant disease. But we found a significant decrease in LDL in OSCC compared to premalignant disease.

The result of our study is inconsistent with the study done by **Goel P et al (2014)**, which showed that increased levels of serum lipid TG and VLDL, and total cholesterol and LDL in normal limits as our study showed that increased LDL level. Since **Chao et al (1975)** reported

that neoplastic cells directly utilize cholesterol for their metabolism resulting in hypolipidemia. Therefore cholesterol should be restored at the earlieast in cancer patients to avoid condition that may speed up morbidity and mortality.

A study done by **Kanthem R K et al (2015)**[13] evaluating serum lipid profile in OSMF patients found a statistical significant reduction in levels of TC and HDL as the clinical stage of OSMF advances when comparing OSMF patients with respect to clinical staging, but no differences was found in the values of TG, VLDL, LDL as the staging advances. But when comparing the histological grading of the OSMF advances, they found a statistically significant reduction in the levels of TC, TG, HDL, VLDL and LDL levels.

Acharya S et al(2016)[14] in their study on 120 patients with age range from 20 to 75 years found a statistically significant decrease in serum TC, TG, HDL, LDL levels in OSCC patients compare to healthy control. Similar result has also been found in our study. It may be due to the deregulation of lipid synthesis / accusation pathways in tumour cells could be responsible in part for the aberrant serum lipid profile seen in cancer patients. Endogenous lipogenesis as one of this pathway has historically been considered the principal source of fatty acids in cancer cells. It may contribute to cancer progression by multiple mechanisms as they provide cancer cells with membrane building blocks, signaling molecule and an energy source to support their rapid proliferation and survival.

Agrawal AG et al (2021)[15] showd that the serum TG, TC, HDL, VLDL and LDL was decreased in OSCC and premalignant diseases compared to control which was also observed in our study as we found a decreased serum TC, TG, HDL, VLDL and LDL in OSCC patient compared to control. They also found that there is a decrease in serum TC, TG, LDL and VLDL in OSCC patients compared to premalignant as we also found a decreased serum TC, TG, LDL, VLDL in OSCC patients compared to premalignant. But our study showed a decreased HDL also in OSCC compared to premalignant which was not similar with the previous study.

We observed a decreased VLDL and TG levels in cancer patients compare to the controls. The low levels of cholesterol may be due to the process of carcinogenesis as cholesterol is an essential constituent of LDL, HDL and VLDL. The LDL receptors are necessary for metabolism and circulating LDL and here by 80% of plasma LDL are clear through the receptors, thus this result in reducing the plasma cholesterol levels. The deficient LDL receptor remove plasma LDL at a lower rate and hence elevated levels of LDL are seen in plasma **[Brown MS et al (1981)[16].**

CONCLUSION

In our study Smoking and tobacco use in other forms were the most common factor in both Malignant and premalignant patients which were statistically significant.

It was found that Total cholesterol was lower in Malignant patients compared Premalignant and control which was statistically significant.

Triglyceride was significantly lower in malignant patient and HDL was also significantly lower in malignant patient compared to premalignant and control.

We found that LDL and VLDL were lower in Malignant patients compared Premalignant and control which were statistically significant.

We concluded that there was statistically significant decrease in plasma total cholesterol, TG, LDL, VLDL and HDL observed in malignant patients as compared to the premalignant control group. The low lipid levels associated with Oral malignancy indicates that there is inverse relationship between oral cancer and serum lipid profile. Decrease in the lipid levels may be considered as a useful biochemical marker in the early diagnosis of oral malignancy.

Table: Distribution of mean Total cholesterol, TG, HDL, VLDL and LDL: Group

		No.	Mean	SD	Min.	Max.	Median	p-value
Total cholesterol	Control	75	206.3840	14.3781	172.0000	261.0000	205.0000	<0.0001
	Malignant	75	159.1600	7.4526	140.0000	177.0000	159.0000	
	Premalignant	75	173.0667	7.4204	148.0000	194.0000	173.0000	
TG	Control	75	184.3227	15.2055	154.0000	228.0000	182.0000	<0.0001
	Malignant	75	130.8133	7.9486	114.0000	149.0000	132.0000	
	Premalignant	75	145.4667	10.8171	124.0000	175.0000	143.0000	
HDL	Control	75	72.9885	8.6803	47.1400	95.0000	72.0000	<0.0001
	Malignant	75	38.2000	3.5106	31.0000	49.0000	38.0000	
	Premalignant	75	44.2533	6.2668	33.0000	60.0000	42.0000	
VLDL	Control	75	36.8640	3.0412	30.8000	45.6000	36.4000	0.0006
	Malignant	75	26.1600	1.5905	22.8000	29.8000	26.4000	
	Premalignant	75	32.4453	29.0522	24.8000	280.0000	28.5000	
LDL	Control	75	96.4448	12.7468	68.0000	68.0000	95.2000	0.0008
	Malignant	75	94.8000	5.9233	76.8000	76.8000	95.4000	
	Premalignant	75	100.0347	4.6096	89.6000	89.6000	100.2000	

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