

ORIGINAL ARTICLE

Serum lipid profile in oral submucous fibrosis: A clinico pathological study

Ranjith Kumar Kanthem, Venkateswar Rao Guttikonda

Department of Oral Pathology and Microbiology, Mamata Dental College and Hospital, Khammam, Andhra Pradesh, India

Address for correspondence:

Dr. Ranjith Kumar Kanthem,
Department of Oral Pathology and Microbiology,
Mamata Dental College, Giriprasad Nagar,
Khammam - 507 002, Andhra Pradesh, India.
E-mail: laxmichandra19@gmail.com,

Received: 11-02-2014

Accepted: 26-06-2015

ABSTRACT

Background: Lipids play a key role in the maintenance of cell integrity. These are major cell membrane components essential for various biological functions, including cell growth and division of normal and malignant tissues. Abnormal changes have long been associated with alterations in lipid profile. **Aim:** The aim of this study was to evaluate the alterations in lipid profile in oral submucous fibrosis (OSMF) patients and to compare the levels with respect to the clinical staging and histological grading. **Materials and Methods:** Fifty patients of OSMF, diagnosed clinically and histopathologically, were included as the study subjects. A group of 50 age and sex matched normal subjects without any oral pernicious habits were taken as controls. The serum lipid profile consisting of total cholesterol (TC), triglycerides (TGs), high density lipoprotein (HDL), very low density lipoprotein (VLDL) and low density lipoprotein (LDL) were analyzed using Erba Chem-5 Plus Analyzer. **Results:** Serum TC, HDL and LDL levels were significantly decreased in OSMF patients as compared to controls. As the clinical stage progresses, the TC and HDL levels were gradually reduced. All the lipid profile parameters such as TC, TG, HDL, VLDL and LDL progressively reduced as the histological grade advanced. **Conclusion:** The results of the present study showed that there is an inverse relationship between lipid profile and the presence of OSMF. The decreased serum lipid profile may be considered as a useful indicator for initial changes occurring in the cells of potentially malignant disorders like OSMF.

Key words: Cholesterol, oral submucous fibrosis, lipid profile

INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic, premalignant condition of the oral mucosa, which was first described by Schwartz in 1952.^[1] Pindborg (1966) defined OSMF as, “an insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxta-epithelial inflammatory reaction followed by a fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat.”^[2]

It is predominantly seen in Southeast Asia and Indian subcontinent with few cases reported from South Africa,

Greece and United Kingdom . The prevalence rate of OSMF in India is about 0.2–0.5%.^[3]

The importance of this disease lies in its inability to open the mouth and the highest malignant transformation rate. The malignant transformation rate of OSMF is 7–13%.^[4,5]

Although, the etiological factor in the causation of OSMF is believed to be multifactorial, Areca nut plays an important role in the disease manifestation.^[6,7] The chronic irritation caused by consumption of areca nut in the form of pan masala, gutkha causes injury thereby leading to chronic inflammation,

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DOI:

10.4103/0973-029X.164522

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How to cite this article: Kanthem RK, Guttikonda VR. Serum lipid profile in oral submucous fibrosis: A clinico pathological study. J Oral Maxillofac Pathol 2015;19:139-44.

cytokine production and development of oxidative stress. Oxidative stress and subsequent reactive oxygen species (ROS) generation can induce cell proliferation, cell senescence or apoptosis, depending upon the level of ROS production.^[8]

Accumulation of genetic alterations is the basis for the progression of a normal cell to a cancerous cell.^[9] Fundamentally, the development of a malignancy requires uncontrolled and excessive proliferation of cells. The newly forming cells would need many basic components well above the normal limits, used in physiological processes. One such component is lipid. They are major cell membrane components essential for various biological functions including cell growth and division of normal and malignant tissues. As the neoplastic disease is related to new growth, there is a greater utilization of lipids, including total cholesterol (TC), lipoproteins and triglycerides (TGs) for new membrane biogenesis. Cells fulfill these requirements either from circulation or from degradation of major lipoprotein fractions such as very low-density lipoprotein (VLDL), low-density lipoprotein (LDL) or high-density lipoprotein (HDL).^[10]

The usefulness of variations in plasma or serum lipid levels in the diagnosis and treatment of various diseases such as breast cancer, colorectal cancer, heart diseases has been studied by several workers. However, there have been only few studies that correlate the association of plasma or serum lipids with head and neck lesions.^[11]

A careful search of the literature did not reveal any research based on comparison of lipid profile with the clinical staging and histopathological grading of OSMF.

MATERIALS AND METHODS

A study was conducted on 50 clinically diagnosed and histopathologically proven patients of OSMF attending the Outpatient Department, after obtaining the Institutional Ethical Committee clearance. Case proforma including patient's consent was made to record signs, symptoms, detailed history, including habits and extended lipid profile estimation. The OSMF cases were staged clinically according to Lai *et al.*^[12] and were graded histopathologically according to Utsunomiya H, *et al.*^[13] The control group consisted of 50 normal subjects without any pernicious oral habits within similar age groups.

Fasting blood samples were collected in plain vials. Serum was collected after centrifugation and stored in the refrigerator until analyzed. Serum levels of TC, TG, HDL, VLDL and LDL were calculated by using the urban kits in ERBA Chem – 5 Plus Analyzer (TRANSASIA Bio Medicals Pvt Ltd.).

RESULTS

A total of 50 OSMF cases were included in the study. Of 50 OSMF patients, according to clinical staging,

Group A were 16 cases (32%), Group B - 15 cases (30%), Group C - 13 cases (26%) and Group D - 6 cases (12%), respectively [Figure 1]. The cases were graded histopathologically as early stage - 15 cases (30%), intermediate stage - 19 cases (38%) and - advanced stage - 16 cases (32%) [Figure 2].

Serum lipid profiles in oral submucous fibrosis patients and controls

It was observed that the mean TC levels [Table 1], HDL levels [Table 2] and LDL levels [Table 3], of OSMF patients were significantly reduced as compared with controls with a statistically significant *P* value of 0.00001 using Student's *t*-test.

It was noted that there was no change in the mean value of TGs [Table 4] and VLDL [Table 5] among OSMF patients as compared with controls with an insignificant *P* value of 1 using Student's *t*-test.

Comparison of serum lipid profile levels in oral submucous fibrosis patients of various clinical stages

The mean TC [Figure 3] and HDL [Figure 4] levels showed a progressive decrease, as the clinical stage of OSMF advances with a statistically significant *P* value of 0.0163, 0.0221 by using one-way ANOVA test.

The mean TG [Figure 5], VLDL [Figure 6] and LDL [Figure 7] levels did not exhibit any significant variation in different groups of OSMF by using one-way ANOVA test.

Comparison of serum lipid profile levels in different histological grades of oral submucous fibrosis

The mean TC [Figure 8], TG [Figure 9], HDL [Figure 10], VLDL [Figure 11] and LDL [Figure 12] levels showed a progressive decrease as the histological grade of OSMF

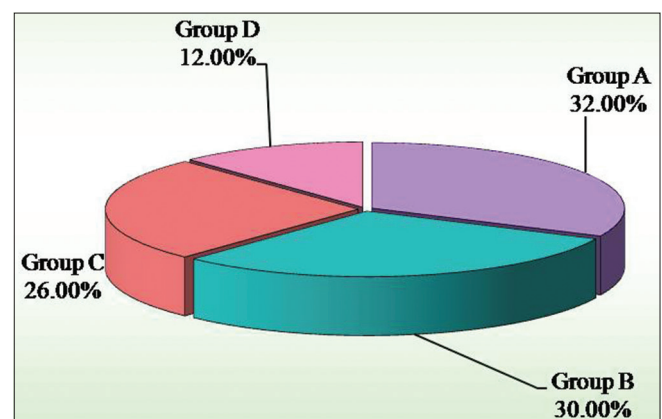


Figure 1: Distribution of oral submucous fibrosis samples by clinical staging

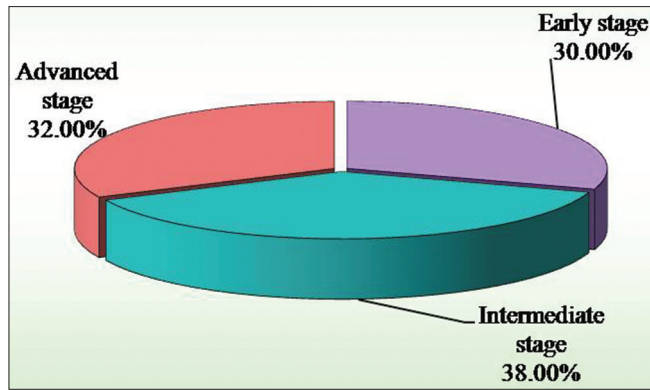


Figure 2: Distribution of oral submucous fibrosis samples by histological grading

advanced with a statistically significant P value of 0.00001, 0.00001, 0.00001, 0.00001 and 0.00001, respectively by using one-way ANOVA test.

DISCUSSION

OSMF has been identified as a precancerous condition with the highest rate of malignant transformation amongst potentially malignant disorders.^[4] Chewing betel quid has been recognized as one of the main risk factors for causation of OSMF. Carcinogens in these substances generate ROS and lipid peroxides thereby leading to tissue injury as a result of elevated lipid peroxidation, further damaging the cellular structural block, namely lipids.^[14] Hence, the present study was aimed to evaluate the lipid profile in OSMF patients.

As compared to controls, OSMF patients showed a significant reduction in the levels of TC, HDL and LDL whereas no statistically significant difference was found in the values of TG and VLDL between OSMF and control group. In the present study, serum lipid profile in OSMF patients was compared with respect to clinical staging and the results of our study showed a statistically significant reduction in levels of TC and HDL as the clinical stage of the OSMF advances. On contrary, no difference was found in the values of TG, VLDL and LDL as the staging advances. Finally, in the present study, the serum lipid profile in OSMF patients was also compared with histological grading. After statistical evaluation, it was found that a significant reduction in the levels of TC, TG, HDL, VLDL and LDL was found as the histological grade of the OSMF advances.

Cholesterol is an essential constituent of lipoprotein fractions such as LDL and HDL. Around 75% of the cholesterol is transported in the form of LDL. Human body cells restore cholesterol from LDL fraction of lipoproteins. LDL receptors are necessary for metabolizing and circulating LDL levels. High activity of the LDL receptors attributes for lowering the serum cholesterol levels.^[14] In the present study, a significant decrease was observed in serum cholesterol and LDL levels

Table 1: Comparison of OSMF group and control group with respect to TC

Groups	Mean	SD	t	P
OSMF group	147.92	10.10	-12.1748	0.00001*
Control group	180.90	16.27		

* $P < 0.05$. SD: Standard deviation, OSMF: Oral submucous fibrosis, TC: Total cholesterol

Table 2: Comparison of OSMF group and control group with respect to HDL

Groups	Mean	SD	t	P
OSMF group	31.88	5.67	-11.0602	0.00001*
Control group	44.42	5.66		

* $P < 0.05$. SD: Standard deviation, OSMF: Oral submucous fibrosis, HDL: High-density lipoprotein

Table 3: Comparison of OSMF group and control group with respect to LDL

Groups	Mean	SD	t	P
OSMF group	88.16	6.31	-8.6639	0.00001*
Control group	108.40	15.27		

* $P < 0.05$. SD: Standard deviation, OSMF: Oral submucous fibrosis, LDL: Low-density lipoprotein

Table 4: Comparison of OSMF group and control group with respect to TG

Groups	Mean	SD	t	P
OSMF group	139.40	5.38	0.0000	1.0000
Control group	139.40	5.45		

SD: Standard deviation, OSMF: Oral submucous fibrosis, TG: Triglyceride

Table 5: Comparison of OSMF group and control group with respect to VLDL

Groups	Mean	SD	t	P
OSMF group	27.88	1.08	0.0000	1.0000
Control group	27.88	1.09		

SD: Standard deviation, OSMF: Oral submucous fibrosis, VLDL: Very low-density lipoprotein

in OSMF patients, which might be a consequence of a disease that is mediated by utilization of cholesterol for membrane biogenesis.

Our study results coincided with the studies done by Kumar *et al.*,^[15] in which they showed a significant decrease in TC, HDL and LDL in patients with OSMF as compared to the controls. Their study also showed no significant changes in the levels of TGs and VLDL.

A study was done by Chalko *et al.*,^[14] observed a significant decrease in serum cholesterol and LDL in OSMF patients, coinciding with the results of our study. However, in contrast, they also observed a significantly increased TG levels in OSMF, which was not observed in our study.

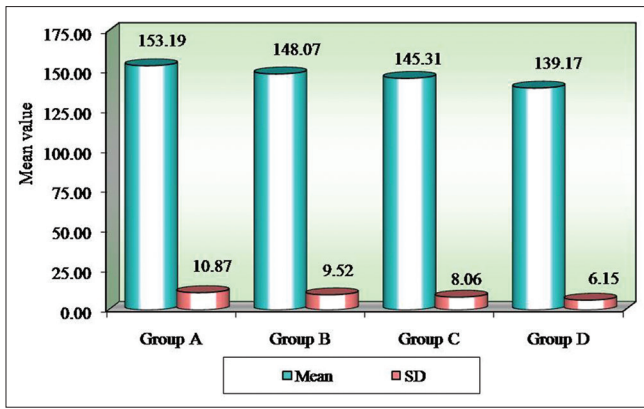


Figure 3: Comparison of clinical staging with respect to total cholesterol levels

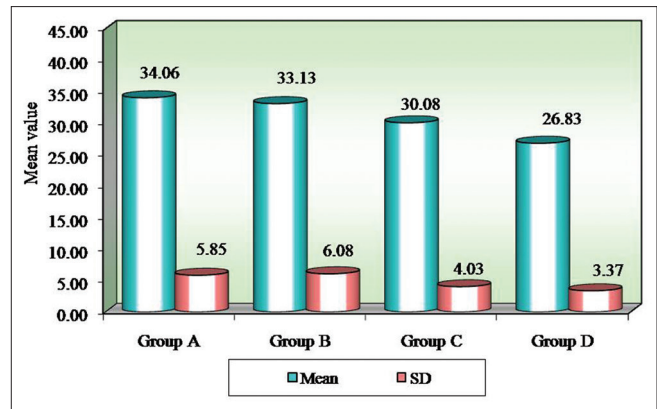


Figure 4: Comparison of clinical staging with respect to high-density lipoprotein levels

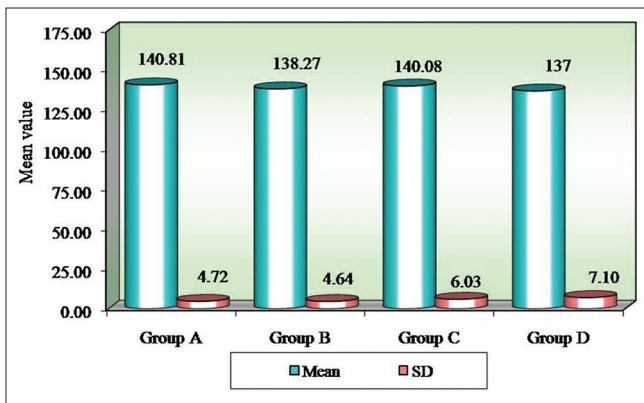


Figure 5: Comparison of clinical staging with respect to triglyceride levels

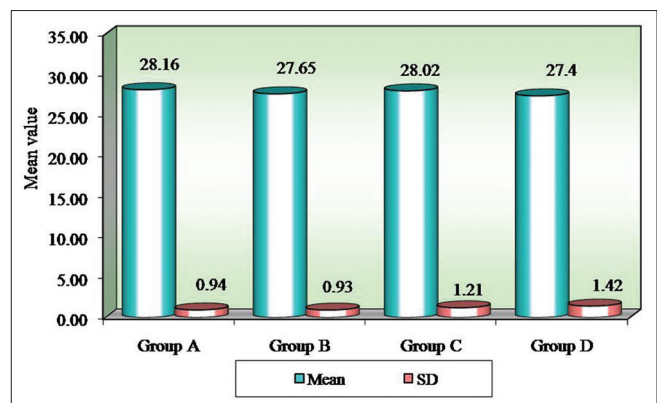


Figure 6: Comparison of clinical staging with respect to very low-density lipoprotein levels

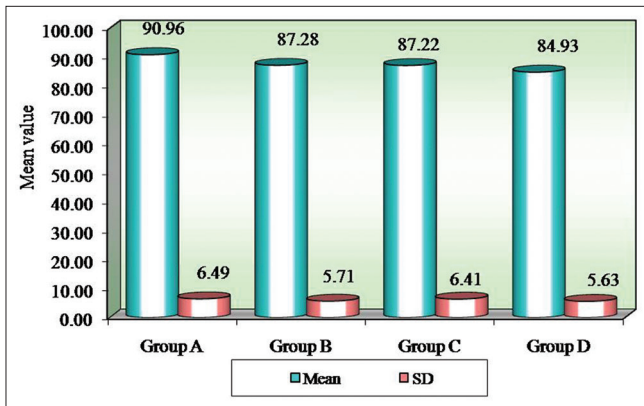


Figure 7: Comparison of clinical staging with respect to low-density lipoprotein levels

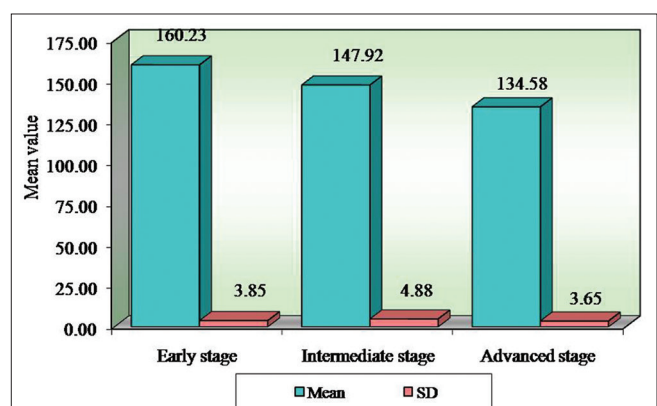


Figure 8: Comparison of histological grading with respect to total cholesterol levels

Study by Mehrotra *et al.*,^[16] found a significant decrease in plasma TC, HDL with no significant change in the levels of LDL and TGs in OSMF patients as compared to controls whereas, LDL levels was found to be decreased in the present study.

A study by Sharma *et al.*,^[17] observed a significant decrease in serum cholesterol, LDL in OSMF patients, which was similar

to the present study. In contrast to this study, they also observed increased levels of HDL, which was decreased in our study.

Gupta and Gupta,^[18] observed a significant decrease in plasma TC and HDL in patients with the precancerous lesions and conditions as compared to the controls similar to our study. In contrast to the present study, they also found a significant decrease in TGs.

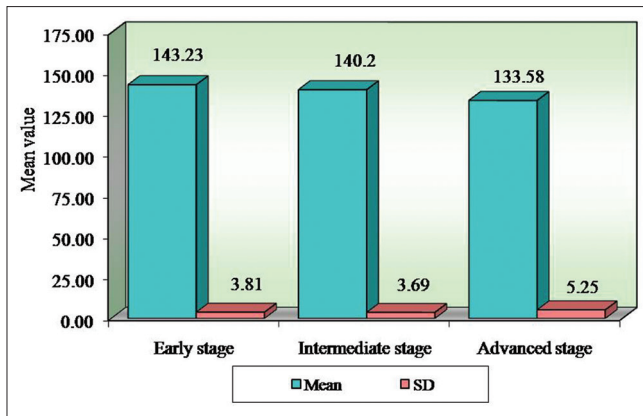


Figure 9: Comparison of histological grading with respect to triglyceride levels

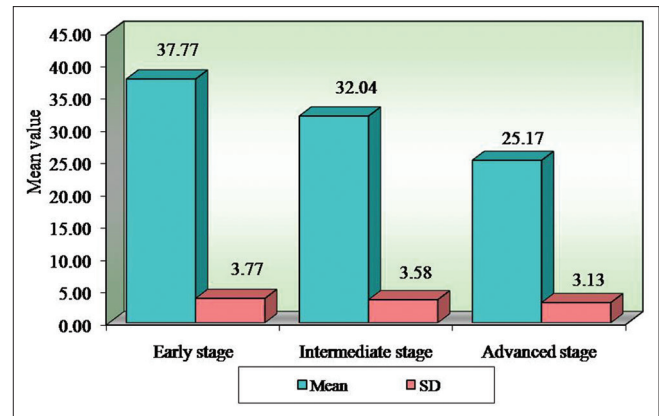


Figure 10: Comparison of histological grading with respect to high-density lipoprotein levels

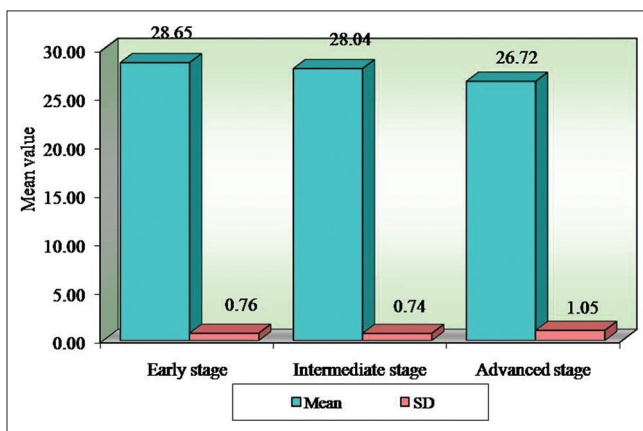


Figure 11: Comparison of histological grading with respect to very low-density lipoprotein levels

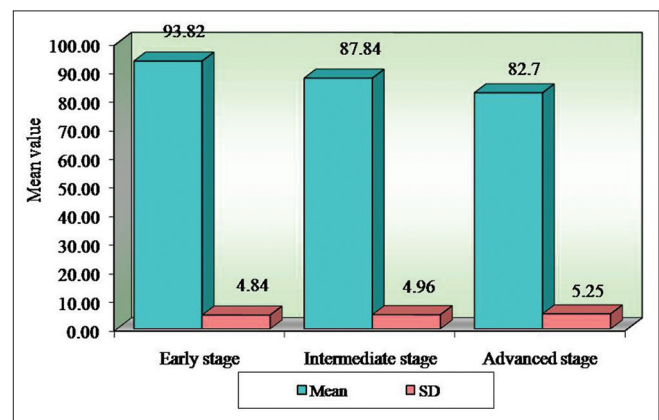


Figure 12: Comparison of histological grading with respect to low-density lipoprotein levels

In contrast to our study Goyal *et al.*^[10] found no statistically significant changes in the lipid profile parameters, namely TC, TGs, HDL, VLDL and LDL in cases of oral precancerous lesions and conditions as compared to controls.

An extensive search of English literature revealed that the present study was the first study done to evaluate the lipid profile in OSMF patients with respect to both clinical staging and histological grading. Our study results exhibited a significant decrease in all the lipid parameters, namely TC, TG, HDL, VLDL and LDL in OSMF patients with respect to histological grading as compared to clinical staging.

The results of all parameters with respect to lipid profile tested in our study are not in agreement with few above-mentioned studies done on OSMF patients. This may be due to differences between the studies when various parameters are considered individually. This variability in the values of lipid profiles in OSMF may be due to multiple reasons such as age, nutritional status, body mass index, alcohol consumption and exercise habits. The variability may also arise from methodological differences.

CONCLUSION

- The TC, HDL and LDL levels in OSMF patients were reduced as compared with controls, suggesting that a lower serum lipid profile is a useful indicator for initial changes occurring in the cells of potentially malignant disorders like OSMF
- The TC and HDL levels were decreased as the clinical stage of OSMF advances indicating their role as a reliable biochemical indicator
- All the lipid profile parameters such as TC, TG, HDL, VLDL and LDL were gradually reduced as the histological grade advanced signifying their role as the best prognostic biochemical indicator.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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