

# Evaluation of serum lipid profile and ABO blood groups in oral cancer and tobacco associated oral lesions among Sriganganagar Population; A Case control study

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## ABSTRACT

**Introduction:** Oral cancer (OC) is among the major cause of morbidity and mortality in India and is mostly preceded by clinically definable premalignant lesion and/or conditions. Role of alterations in serum lipid profile in oral cancer and the incidence of OC in various blood groups remain controversial.

**Aims and objectives:** To evaluate and compare the variations in serum lipid profile (total cholesterol, total triglycerides, low density lipoproteins, very low density lipoproteins, high density lipoproteins) and ABO/Rh blood groups in oral cancer and tobacco associated oral lesion. **Materials and methods:** Thirty patients with OC (Group 1), 30 patients with tobacco related lesions (Group 2), 30 tobacco abusers (TAs) with no lesions (Group 3), and 30 age and gender matched healthy controls (Group 4) were included in the study. Serum lipid profile including total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), Very low density lipoprotein (VLDL), and triglycerides (Tg) were evaluated in each patient using a semiautomatic autoanalyzer STAT fax-3300 Ark Diagnostics and the blood group of the patients was determined by placing a drop of blood on the slide and treating with anti-A, anti-B and Anti-Rh sera. Difference in lipid profile and blood groups in various groups was determined.

**Results:** LDL was lower and HDL was higher in group 1 as compared to group 4. The mean TC in group 3 was more than the Group 1 and Group 2. The mean VLDL was also more in Group 3. No significant correlation was found in the prevalence of ABO/Rh blood group in study Group. **Conclusion:** There was no significant relation between lipid profile and ABO Rh blood Groups in oral cancer and tobacco associated oral lesion patients.

**Key words:** Lipid profile, ABO Rh blood groups, Oral cancer, tobacco related lesions

## I. INTRODUCTION

Oral cancer (OC) is the most life threatening disease of oral tissues, causing a major health problem in India. Oral cancer is the sixth most common cancer worldwide. Most prevalent cancer related to the consumption of tobacco, areca nut, alcohol and other carcinogenic products.<sup>1-3</sup> Several studies have shown clearly that oral cancers either develop from precancer or are associated with it.<sup>5,6,7,9-17</sup> The problem of oral precancer and cancer in India has been investigated extensively and its incidence has been shown to be really high.<sup>19-22,24</sup> Biochemical studies in evaluation of cancer have shown that various substances alter quantitatively in the serum during tumor development and are referred to as tumor markers. So, if the biochemical changes occur even before frank cancer has occurred, risk of developing cancer in individuals with oral precancerous lesions and conditions can be predicted.<sup>27-46</sup> Cholesterol is an amphipathic lipid and it is an essential structural component of all cell membranes and of the outer layer of

plasma lipoproteins. Fundamentally the development of a malignancy requires the uncontrolled and One such component which forms major cell membrane components essential for various biological functions including cell division and growth of normal and malignant tissues is lipids.<sup>48,50,51,53-63</sup> Lipid stores are diminished due to increased use of lipids by these rapidly dividing cells. More than 20 genetically determined blood group systems are known today but the ABO blood groups are sensitive than other blood grouping system in detecting antigen responsible for cancers. The expression of certain blood group carbohydrates antigens on the surface of cancer cells thus can be regarded as an end product of tumor progression that can be used as useful prognostic and diagnostic markers.<sup>65,66,68-69</sup> With this background, the present study was conducted to evaluate the definitive biochemical changes in serum lipid profile with histological grading of patients of OC and tobacco associated oral lesions along with prevalence of ABO blood groups in these patients

## II. MATERIALS & METHODS

### SOURCE OF DATA

This prospective study included a total of 120 subjects, both male and female of age 20- 85 years, who visited the department of Oral Medicine & Radiology, Surendera Dental College and Research Institute for routine dental check-up. This study was conducted from July 2018 to July 2020. The subjects were divided into following four Groups:

**Group I:** Consisted of 30 histopathologically diagnosed cases of OC. These patients were graded histologically into - well differentiated, moderately differentiated and poorly differentiated carcinomas.

**Group II:** Consisted of 30 cases of tobacco associated oral lesions (except diagnosed OC cases). These lesions were biopsied and examined for the presence or absence of dysplasia. Dysplasia was graded as – mild, moderate and severe.

**Group III:** Consisted of 30 subjects indulged in some tobacco consumption habit but without any clinically evident oral lesion. This Group was equally subdivided further depending on the tobacco use into: **Group III A:** Consisted of 15 subjects indulged in tobacco smoking habit. **Group III B:** Consisted of 15 subjects indulged in smokeless tobacco habit.

**Group IV:** consisted of 30 age and gender matched healthy controls without any history of tobacco abuse and without any evidence of oral lesions.

### METHOD OF COLLECTION OF DATA

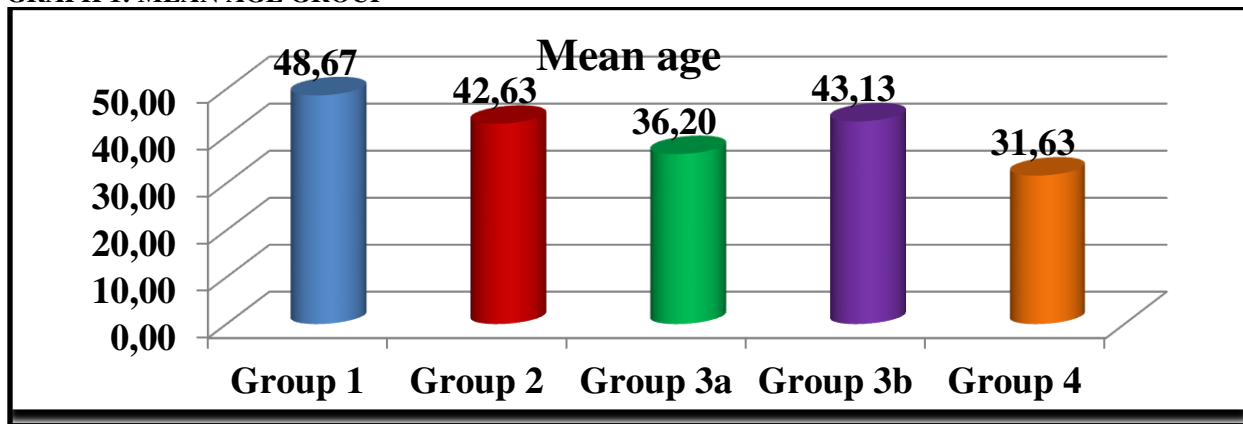
The patients reporting to the department OPD were evaluated thoroughly by making them seated comfortably on a well-equipped dental chair. After explaining the nature of the study, the written and informed consent was taken from each patient. The institutional ethical committee clearance (IEC) was obtained before the start of the study. The patients were made to rinse with diluted 0.2% Chlorhexidine gluconate mouthwash before clinical intraoral examination. Each Patient's demographic data, BMI, detailed history of tobacco habits (type, duration, frequency, site etc) general and medical history and clinical examination was carried out in a systematic manner. Then the hard and soft tissue intra-oral examination was carried out for each patient followed by localized intra-lesional examination if any, to reach the provisional diagnosis. When there was a clinical evidence of oral cancer/precancerous lesion (Group I and II), incisional/excisional biopsy was performed for histopathological grading. The patients satisfying the selection criteria of the study were subjected for BMI and haematological examination (including Lipid profile & ABO/Rh blood Group determination).

## III. RESULTS

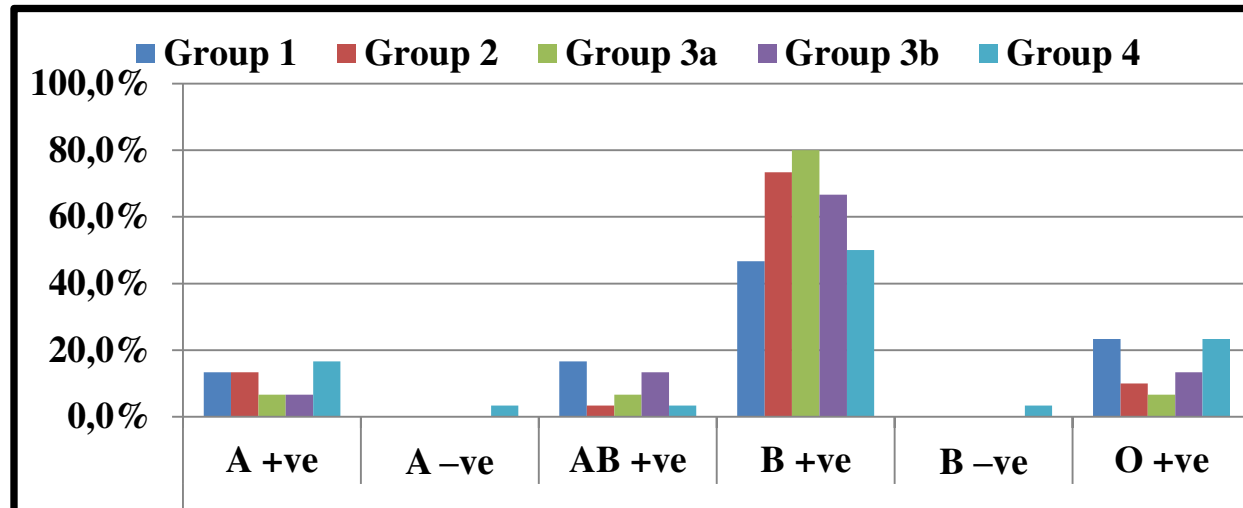
The over-all mean age of the patients was 40.65±13.71 years with significant difference between the groups with group 4 having significantly lesser age compared to group 1, group 2 and group 3. There was no difference in the distribution of blood groups between the different groups. Most common blood group among the study population was B+ve (60.8%) followed by O+ve (16.7%), A+ve (12.5%), AB+ve (8.3%), A-ve (0.8%) and B-ve (0.8%). The mean total cholesterol did not differ between group 1 (175.84±60.71), group 2 (166.40±19.51), group 3a (174.69±21.47), Group 3b (177.09) and group 4 (171.85±14.64). The mean HDL cholesterol was significantly more among Group 1 (46.63±8.95) compared to group 2, group 3a, 3b and group 4 (41.67±3.96, 41.43±3.08, 41.55±2.54) and 39.07±2.33 respectively). The mean LDL cholesterol was significantly more among Group 4 (116.91±13.06)

compared to group 1, group 2 and group 3a,3b(97.69±40.63, 98.40±23.18, 105.46±20.97 and 105.77±27.53 respectively).The mean VLDL cholesterol was significantly more among group 1, group 2 and group 3a,3b (28.18±22.68, 28.85±11.12, 27.99± 6.67 and 31.01±5.39 respectively)compared to Group 4 (17.88±2.86). The mean Triglycerides was also significantly more among group 1, group 2 and group 3a,3b (137.75±114.23, 139.38±44.97, 144.60± 33.77 and 156.35±26.93 respectively)compared to Group 4 (90.10±14.63).No significant difference in mean total cholesterol was found for the inter-group comparisons (175.84±60.71, 166.40±19.51, 174.69±21.41, 177.09±29.71 and 171.85±14.64 respectively). The mean HDL cholesterol was significantly more among Group 1 (46.63±8.95) compared to group 2, group 3a, group 3b and group 4 (41.67±3.96,41.43±3.08, 41.55±2.54 and 39.07±2.33 respectively) (**Table 1**).The mean LDL cholesterol was significantly more among Group 4 compared to group 1, group 2, group 3a and group 3b (**Table 2**). The mean VLDL cholesterol and Triglycerides level was significantly more among group 1, group 2, group 3a and group 3b compared to Group 4. (**Table 3,4**). Correlation between histopathologically diagnosed oral cancer and lipid profile was also studied (**Table 5**).

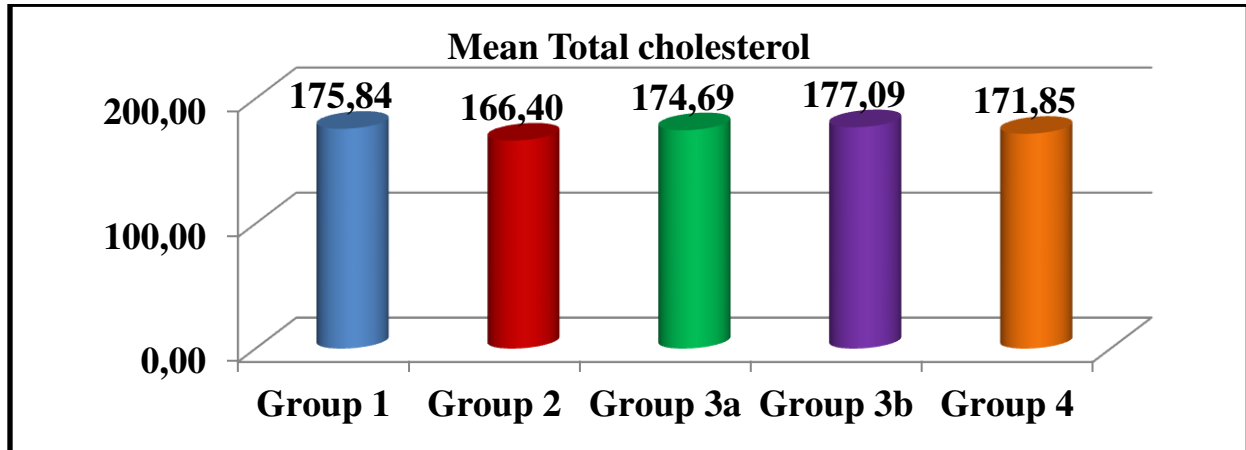
GRAPH 1: MEAN AGE GROUP



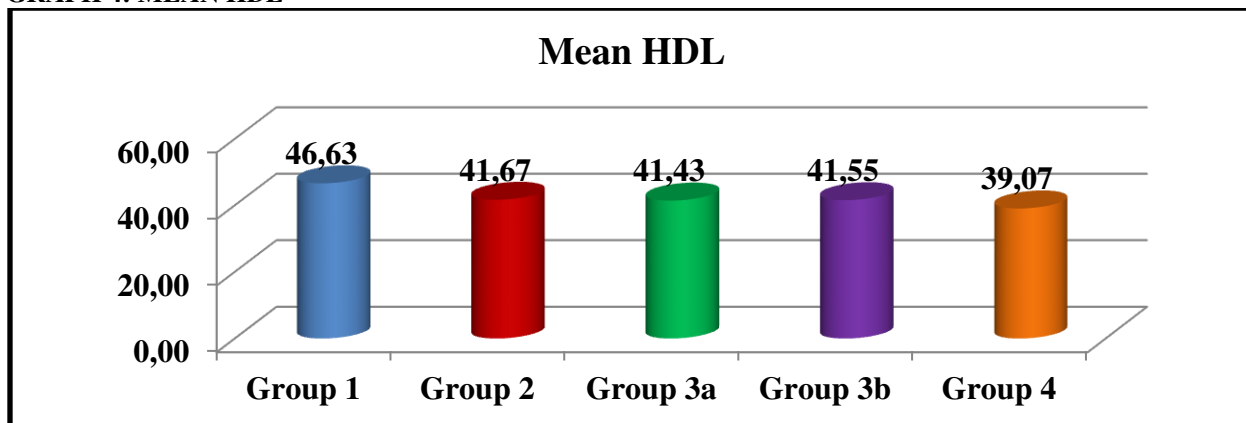
GRAPH 2: BLOOD GROUPS IN VARIOUS GROUPS



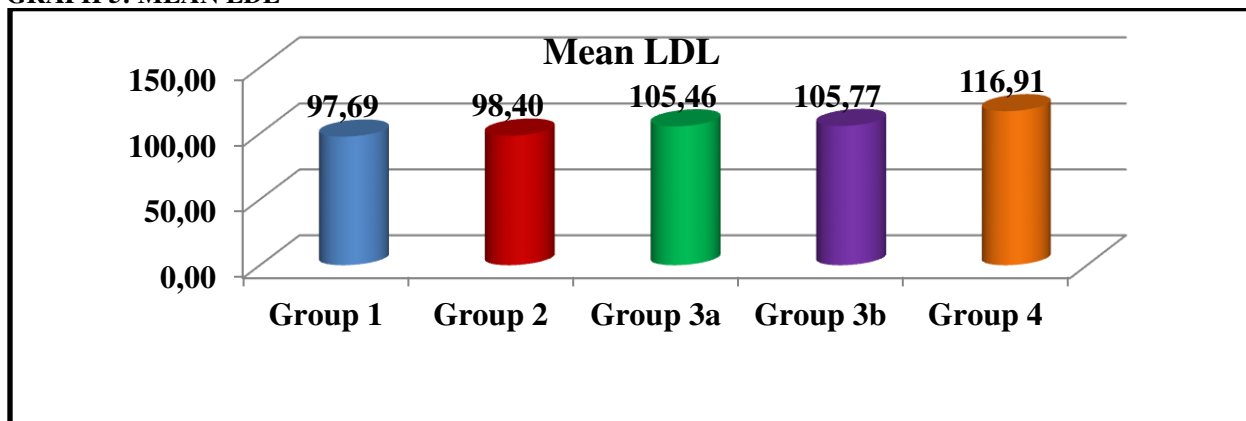
GRAPH 3: MEAN TOTAL CHOLESTROL



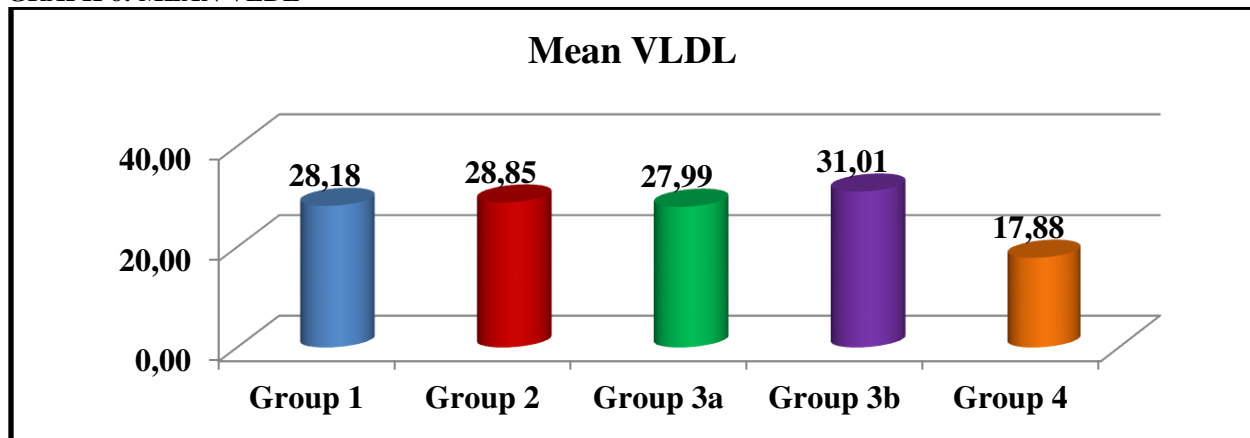
GRAPH 4: MEAN HDL



GRAPH 5: MEAN LDL



GRAPH 6: MEAN VLDL



GRAPH 7: MEAN TRIGLYCERIDE LEVEL

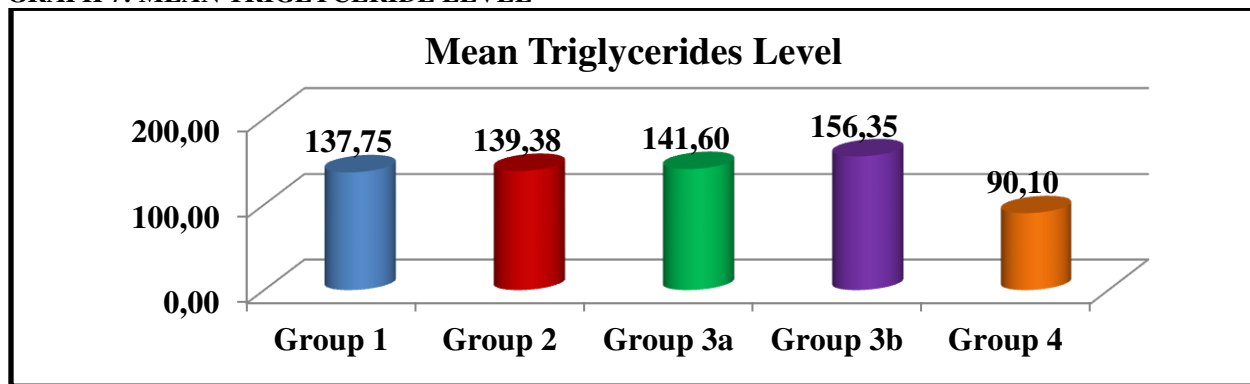


Table 1: INTERGROUP COMPARISON OF MEAN HDL

		Mean Difference	p-value
Group 1	Group 2	4.95	0.004*
Group 1	Group 3a	5.19	0.022*
Group 1	Group 3b	5.07	0.027*
Group 1	Group 4	7.56	< 0.001*
Group 2	Group 3a	0.24	1.000
Group 2	Group 3b	0.12	1.000
Group 2	Group 4	2.61	0.565
Group 3a	Group 3b	-0.12	1.000
Group 3a	Group 4	2.37	1.000
Group 3b	Group 4	2.49	1.000
<b>Post-hoc bonferroni test</b>			<b>* Significant difference</b>

Table 2: INTERGROUP COMPARISON OF MEAN LDL

		Mean Difference	p-value
Group 1	Group 2	-0.71	1.000
Group 1	Group 3a	-7.77	1.000
Group 1	Group 3b	-8.08	1.000
Group 1	Group 4	-19.21	0.042*
Group 2	Group 3a	-7.06	1.000
Group 2	Group 3b	-7.37	1.000

Group 2	Group 4	-18.50	0.046*
Group 3a	Group 3b	-0.31	1.000
Group 3a	Group 4	-11.45	0.048*
Group 3b	Group 4	-11.13	0.049*
<b>Post-hoc bonferroni test</b>			<b>* Significant difference</b>

**Table 3: INTERGROUP COMPARISON OF MEAN LDL**

		Mean Difference	p-value
Group 1	Group 2	-0.67	1.000
Group 1	Group 3a	0.19	1.000
Group 1	Group 3b	-2.83	1.000
Group 1	Group 4	10.30	0.029*
Group 2	Group 3a	0.85	1.000
Group 2	Group 3b	-2.16	1.000
Group 2	Group 4	10.97	0.016*
Group 3a	Group 3b	-3.01	1.000
Group 3a	Group 4	10.12	0.046*
Group 3b	Group 4	13.13	0.020*
<b>Post-hoc bonferroni test</b>			<b>* Significant difference</b>

**Table 4: INTERGROUP COMPARISON OF MEAN TRIGLYCERIDES**

		Mean Difference	p-value
Group 1	Group 2	-1.64	1.000
Group 1	Group 3a	-3.85	1.000
Group 1	Group 3b	-18.60	1.000
Group 1	Group 4	47.65	0.046*
Group 2	Group 3a	-2.22	1.000
Group 2	Group 3b	-16.96	1.000
Group 2	Group 4	49.28	0.034*
Group 3a	Group 3b	-14.75	1.000
Group 3a	Group 4	51.50	0.042*
Group 3b	Group 4	66.25	0.014*
<b>Post-hoc bonferroni test</b>			<b>* Significant difference</b>

**Table 5: CORRELATION BETWEEN HISTOPATHOLOGICALLY DIAGNOSED ORAL CANCER AND LIPID PROFILE**

Grading	Total cholesterol		Triglyceride		LDL		HDL		VLDL	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Well differentiated carcinoma	171.65	71.68	129.79	91.07	93.97	43.85	45.99	8.49	26.47	18.09
Moderate differentiated carcinoma	155.33	23.43	100.10	1.85	107.51	25.55	48.80	8.48	33.61	33.34
Poorly differentiated carcinoma	191.06	42.58	166.20	67.58	90.53	36.24	43.93	15.04	22.13	3.35
P-value	0.625		0.631		0.695		0.655		0.675	

#### IV. DISCUSSION

Lipids are major cell membrane components essential for various biological functions including cell growth and division of normal and malignant tissues. The changes in lipid profile have long been associated with cancerous and precancerous conditions because lipids play a key role in maintenance of cell integrity.<sup>4</sup> Oral cancer is the leading cause of morbidity and mortality in India and is most commonly preceded by clinically definable premalignant lesions and conditions. Usefulness of variations in tissue/ blood cholesterol levels. The over-all mean age of the patients was  $40.65 \pm 13.71$  years with significant difference between the groups with group 4 having significantly lesser age compared to Group 1, Group 2 and Group 3. Also in line, Kumar et al,<sup>10</sup> found that the highest incidence for both genders was seen in the age group 50-59 years and the lowest incidence for both genders was in youngest age group (<20 years). These findings are also consistent with the studies conducted by Mehta R et al,<sup>52</sup> Ashutosh K,<sup>97</sup> Singh S,<sup>47</sup> and Mallik M<sup>98</sup> where the mean age of patients suffering from OSCC is  $50.10 \pm 7.66, 51.40, 51.07, 52$  yrs respectively. These studies imply that the incidence of OSCC is higher above 40 yrs of age. More than 20 genetically determined blood group systems are known today but ABO blood groups are sensitive than other blood grouping system in detecting antigen responsible for cancers as ABO blood group genes are mapped at 9q34.2 region in which genetic alteration is common in many cancers. Thus, blood group antigen expression may be affected by genetic change of tumor, the loss or presence of blood group antigens can increase cellular motility or facilitate the interaction between tumor cells and endothelial cells of distant organs.<sup>77,78</sup> There was no difference in the distribution of blood groups between histopathologically diagnosed cases of OC, tobacco associated oral lesions, tobacco consumption habit with no lesion and no history of tobacco and no oral lesion. Most common blood group among the study population was B+ve (60.8%) followed by O+ve (16.7%), A+ve (12.5%), AB+ve (8.3%), A-ve (0.8%) and B-ve (0.8%). Rao et al<sup>70</sup> stated that the susceptibility of head and neck malignancies is highest among the individuals of B, A, O, AB blood group with Rh antigen positivity, in descending order and least susceptibility was found among O negative individuals. Koul et al<sup>75</sup> reported that blood group B (37.5% and 56.1, respectively) was the commonest followed by group A (35% and 31.3%, respectively). In some malignancies, serum cholesterol undergoes early and significant changes. Low levels of cholesterol in the proliferating tissues and in blood compartments could be due to the rapidly dividing cells in malignancies. Several prospective and retrospective studies have shown an inverse association between blood lipid profiles and different cancers.<sup>82</sup> Some scientists have observed an inverse trend between lower serum cholesterol and head and neck cancer as well as oesophageal and colon cancers.<sup>91</sup> Similar findings were reported by Patel et al.<sup>26</sup> In current study, the mean total cholesterol did not differ between oral cancers ( $175.84 \pm 60.71$ ), tobacco associated oral lesions ( $166.40 \pm 19.51$ ), tobacco consumption habit with no lesion ( $175.89 \pm 25.47$ ) and no history of tobacco and oral lesion ( $171.85 \pm 14.64$ ). Similar to our findings, Whig et al<sup>18</sup> reported that Active smoking raised the low density lipoprotein cholesterol and very low density lipoprotein cholesterol levels whereas high density lipoprotein cholesterol content was lowered, thus resulting in decreased ratios of HDL/Tc and HDL/LDL. The passive smokers also showed slightly higher levels of LDL and VLDL but lower levels of HDL, and a lower HDL/LDL ratio. Vural et al<sup>23</sup> reported that the levels of all lipid fractions were increased in both Actinic Keratosis(AK) and Basal cell carcinoma(BCC). A significant increase in phospholipids and total lipids was found in BCC. Serum cholesterol, phospholipids, triglyceride, and total lipid concentrations of AK patients were significantly higher than those of the control group. When BCC and controls were compared, a significant increase in phospholipids and total lipids was seen. Serum cholesterol in BCC patients was significantly lower and serum phospholipid levels were significantly higher with  $p < 0.05$  than those in the AK group. The mean LDL cholesterol was significantly more among Group 4 ( $116.91 \pm 13.06$ ) compared to Group 1, Group 2 and Group 3 ( $97.69 \pm 40.63, 98.40 \pm 23.18$  and  $105.62 \pm 24.05$  respectively). The mean VLDL cholesterol and Triglycerides level was significantly more among Group 1, Group 2 and Group 3 ( $28.18 \pm 22.68, 28.85 \pm 11.12$  and  $29.50 \pm 6.15$  respectively) compared to Group 4 ( $17.88 \pm 2.86$ ). Gupta SA<sup>90</sup> observed a significant decrease in plasma total cholesterol, HDLC, and triglycerides in the patients with the precancerous lesions and conditions as compared to the controls which is in accordance with this study except for triglyceride levels. The decrease in plasma cholesterol in Squamous cell carcinoma cases maybe due to enhanced lipid peroxidation due to decline in antioxidants.<sup>90</sup> No significant difference in mean total cholesterol was found for the inter-group comparisons ( $175.84 \pm 60.71, 166.40 \pm 19.51, 174.69 \pm 21.41, 177.09 \pm 29.71$  and  $171.85 \pm 14.64$  respectively). The mean HDL cholesterol was significantly more among Group 1 ( $46.63 \pm 8.95$ ) compared to group 2, group 3a, group 3b and group 4 ( $41.67 \pm 3.96, 41.43 \pm 3.08, 41.55 \pm 2.54$  and  $39.07 \pm 2.33$  respectively). The mean LDL cholesterol was significantly more among Group 4 compared to Group 1, Group 2, Group 3a and Group 3b. The mean VLDL cholesterol and Triglycerides level was significantly more among Group 1, Group 2, Group 3a and Group 3b compared to Group 4. Khurana et al<sup>24</sup> revealed almost similar results reporting that High density lipoprotein-cholesterol was lower both in smoker ( $P < 0.01$ ) as well as in tobacco chewers than the controls. Both smokers and tobacco chewers had higher

values of total cholesterol, low density lipoprotein cholesterol, very low density lipoprotein-cholesterol and, triglycerides as compared to non-smoker, non-tobacco chewer group whereas the differences in levels of lipids in smokers and tobacco chewers were not statistically significant. Radha and Raut<sup>70</sup> had the finding that TC, HDL and LDL levels were higher, while TG and VLDL levels were lower in tobacco chewers with oral lesions as compared to tobacco chewers without oral lesions. Neki et al<sup>25</sup> results revealed that mean TC, LDL, and VLDL were significantly higher in smokers with  $p < 0.05$  as compared to non-smokers. Mean serum TG levels in smokers were significantly high with as compared to non-smokers. Mean serum HDLC was significantly lower in chronic smokers as compared to non-smokers. Garg Det al<sup>49</sup> evaluated the alterations in serum lipid profile in untreated patients of oral submucous fibrosis (OSMF), oral leukoplakia, and oral lichen planus and proven cases of oral cancer with respect to healthy controls. Decrease in plasma total cholesterol, triglycerides, HDL, LDL and VLDL in the subjects with the oral precancer and oral cancer as compared to the controls was statistically significant. There was also decrease in plasma levels of TGL and VLDL in oral cancer subjects as compared to precancer subjects. Thus, it was found that there is an inverse relationship between plasma lipid levels and patients. Many of the pioneer workers have somewhat comparable results.<sup>71,74,76,79-81</sup> Vijay et al<sup>8</sup> stated that the serum level of HDL, VLDL, TGL, TC and LDL were significantly reduced in the oral leukoplakia group. TGL were highest in patients who had mild dysplasia and lowest TC, while, moderate dysplasia cases had highest TC and lowest TG, LDL, VLDL, HDL. The authors concluded that reduced levels of lipid profile in cases of leukoplakia could be due to tobacco habits that reduced the lipid fractions, Naiket al<sup>64</sup> showed that the plasma levels of HDL, VLDL, TGL and ratio of HDL and LDL was significantly reduced in patients with OSCC and OL and Ealla et al<sup>67</sup> also found significant decrease in TC, TG, LDL and VLDL, HDL in gutkha chewers and OSMF patients as compared to controls. The habit of tobacco consumption is a known etiologic factor for development of oral precancerous diseases and head/neck cancer.<sup>92,93</sup> Many of the pioneer workers have somewhat comparable results.<sup>83-89,95</sup> Cholesterol which is an amphipathic lipid is an essential structural component of all cell membranes. It is present either as free cholesterol or combined with a long-chain fatty acid, as cholesteryl-ester in tissues and in serum lipoprotein. It is synthesized from acetylCoA in many tissues and is ultimately eliminated as cholesterol or bile salts from the body. In the circulation, lipoprotein transports free cholesterol and it readily equilibrates cholesterol in other lipoproteins and in membranes.<sup>94-96</sup>

## V. CONCLUSION

There was no significant difference in mean total cholesterol among various Groups. The mean HDL was significantly more in Group 1 as compared to Group 2, 3a, 3b and 4. The mean LDL was significantly more in group 4 as compared to Group 1, 2, 3a, 3b. The mean VLDL was significantly lesser in Group 4 as compared to Group 1, 2 and 3a, 3b. The mean triglycerides was significantly lesser in Group 4 as compared to Group 1, 2, 3a, 3b. There was no significant difference in the distribution of blood groups among Group 1, 2, 3a, 3b and 4. To conclude according to our study lipid profile parameters and ABO/RH blood groups cannot act as a diagnostic/prognostic marker in OC and tobacco related lesions.

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