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Estimation of Serum Alpha 1 Antitrypsin in Oral Leukoplakia Patients

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Abstract: ***Introduction: Oral leukoplakia is the most common premalignant lesion of oral cavity. Leuko means 'white' and plakia means 'patch'. These lesions are often associated with carcinogenic exposures, such as use of tobacco, alcohol. Alpha 1 antitrypsin is a protein belonging to serpin superfamily. As a type of enzyme inhibitor it protects tissues from enzymes of inflammatory cells specifically from neutrophil elastase. Method: This clinical study included 60 patients from 2013- 2015. 30 patients each in study and control group. Result: Males were more affected from oral leukoplakia as compared to females. In study group serum a1at range was 0.70-1.60 g/l, whereas control group range was recorded 0.90-1.90 g/l. p value was highly significant. Conclusion: In the absence of alpha 1 antitrypsin neutrophil elastase is free to break down elastin, which contributes to elasticity of lungs, resulting in respiratory complication such as emphysema, COPD. The results obtained in clinical study were inconclusive of role of A1AT in oral leukoplakia pathogenesis.***

Keywords: oral leukoplakia, premalignant lesion,alpha-1- antitrypsin, anti-proteinase.

1. Introduction

Any lesion that increases the thickness of epithelium causes it to appear white by increasing the distance to vascular bed because of thickening of keratin layer.

Normally the mucosa appear coral pink due to reflection of light when translucency of the mucosa is lost due to above mentioned factors.[4]

The term leukoplakia was first used by Schwimmer in 1877 to describe white lesion of tongue, which represented syphilitic glossitis. It is most frequent premalignant lesion of oral cavity. As defined by WHO leukoplakia is 'a white patch or plaque that cannot be characterized clinically or pathologically as any other lesion.[3]

Alpha 1 antitrypsin is a pan proteinase protein mainly synthesized and secreted by hepatocytes and additional quantities by monocytes, lung alveolar cells, macrophages, enterocytes and endothelial cells with a reference range in blood of 1.5-3.5 g/l. It is a glycoprotein that functions as major inhibitor of tissue proteases including trypsin, chymotrypsin, collagenase, and renin.[14] The occurrence of A1AT in extra hepatic sites is important since it inhibits the growth of tumour cells. Thus, the increased level of protease activity in malignant cells might be due to deficiency of protease inhibitors in these cells.[2] The purpose of this study is to estimate the levels of A1AT in oral leukoplakia patients and to establish co-relation between significance of A1AT in leukoplakia patient.

2. Method

This clinical study included sixty patients, divided into study and control group with thirty patients in each group. The patients in study group were followed up for one year. Out of 30 patients 26 were male and 4 were female. In male patients, 20 had homogeneous leukoplakia (fig.1) and 6 had non homogeneous leukoplakia (fig.2). In females, homogeneous and non homogeneous was equally present in four patients. Subjects were recruited with the following eligibility criteria-

1) Patients with clinically diagnosed oral leukoplakia.
2) Patients not undergoing any form of treatment for their lesions.
3) Devoid of immunocompromised diseases.

In control group, thirty patients were included who had no premalignant lesion or condition, and had no previous history of any deleterious habit.

From these screened patients 5ml of blood was drawn using standardized procedures, allowed to coagulate at room temperature for one hour and sent to laboratory for serum alpha 1 antitrypsin values evaluation.

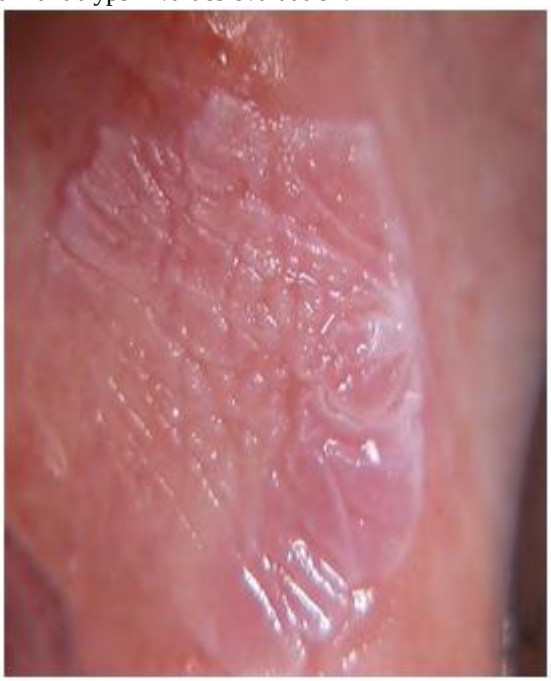
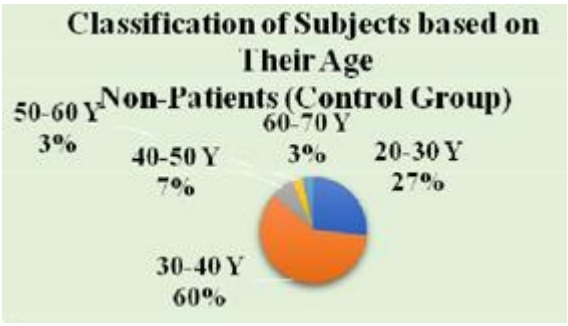
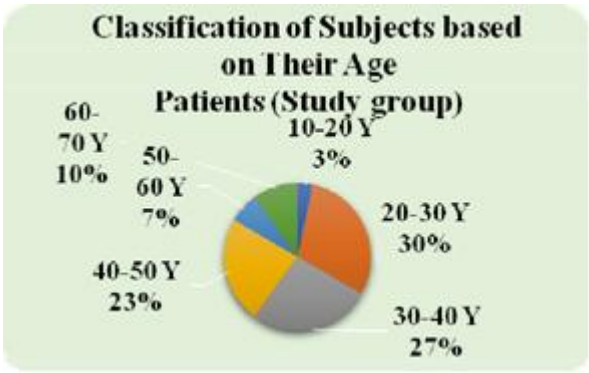


Figure 1: homogeneous leukoplakia

Figure 2: Non-homogeneous leukoplakia





Overall comparison of Alpha-1-antitrypsin levels (g/l)

Comparison of Alpha-1-antitrypsin levels between genders (g/l)

	Control	Study
Mean	1.28	1.06
SD	0.27	0.21
Minimu	0.90	0.70
Maximum	1.90	1.60
No. of Patients	30	30
T value=3.467, P Value=0.000		

3. Results

In study group out of 26 male patients had homogenous leukoplakia and majority of lesions were seen on buccal mucosa, and lesions on palate and commissure had a count of 2 each.

All 4 female subjects had homogenous type on buccal mucosa. We observed in study that type and site which was in abundance was homogenous and buccal mucosa respectively.

4. Discussion

Precancerous lesion is defined as "morphologically altered tissue in which cancer is more likely to occur than its apparently normal counterpart".[4]

	Non-Patients (Control Group)		Patients (Study group)	
	Female	Male	Female	Male
Mean	1.29	1.28	0.90	1.07
SD	0.29	0.27	0.00	0.21
Min	1.00	0.90	0.90	0.70
Max	1.90	1.80	0.90	1.60
Count	10	20	1	29
Student T Test on Mean Values	T Value=0.141, P value=0.445		T Value=-0.789, P value=0.218	
Chi Square Test on Count	Chi Square=3.333, P Value=0.068		Chi Square=26.133, P Value=0.000	

According to WHO (1978) leukoplakia is defined as "a white patch or plaque that cannot be characterized clinically or pathologically as any other disease".[11]

Oral leukoplakia is a well known premalignant lesion. It was first reported by Schwimmer in 1877 to describe white lesion of tongue. Pindborg et al describe it as "predominantly white lesion that cannot be characterized clinically or pathologically as any other definable lesion".[3,10]

According to Axell et al (1983), it is a whitish patch or plaque that cannot be characterized clinically or pathologically aas any other diseases and it is not associated with any physical or chemical causative agent except the use of tobacco.[1]

On the basis of clinical appearance leukoplakias are classified into homogenous and non homogenous (speckled or nodular) leukoplakia.

Homogenous leukoplakia constitute 84% of all leukoplakia and are characterized by thin, smooth surface fissures. On the other hand non homogenous leukoplakia develop surface irregularities and are referred to as granular or nodular and comprise 3% of all leukoplakia.[3,12]

Oral leukoplakia occurs most frequently in tobacco users, which is most often smoked or chewed. Alcohol, chronic irritation, candida albicans, human papilloma virus, genetic predisposition, vitamin A, B_{12} , and vitamin C deficiency have been put forth as other etiological factors for leukoplakia.[6,8]

Action of alpha 1 antitrypsin is directed primarily towards tissue rather than proteolytic enzymes, suggesting that it might be synthesized in other cells other than hepatic. Its occurrence in extra hepatic sites may be important since it inhibits the growth of tumour cells.[2]

The prevalence of leukoplakia in various population shows a wide range. In India, between 0.2 to 4.9% of population over 15 years of age was found to have leukoplakia (Mehta

et al 1972).

Of interest is the examination of the annual incidence of leukoplakia in those who do not use tobacco (0.6 per 1,000) versus those who use betel quid (1.3 per 100,00). In smokers this rises to an incidence of 4.2.

While an incidence of 8.9 has been reported among those who smoke and also use smokeless tobacco (Mehta, 1972).[9]

The gender distribution of leukoplakia varies widely from one survey to another. There differences are attributed to variation in tobacco habits (Roed-Petersen et al 1972).

Waldron and Shafer et al demonstrated increased frequency of leukoplakia in women. However, in our study more severely affected patients were males.[11,13]

The anatomical distribution of leukoplakia, varies with the form of tobacco used. Kaugars et al noted that with the use of snuff, the location was in the buccal vestibule under the contact of snuff product. In our study the most commonly affected site was buccal mucosa, followed by commissure and palate.[8]

Kanemitsu Shirasuna et al examined the immunoreactive levels of A1AT and trypsin inhibitory capacity in patients of oral malignant tumour. They observed that patients with squamous cell carcinoma had increased levels of alpha one antitrypsin but no significant differences among healthy control subjects.[7]

Bagdasarian A et al reported that proteolytic enzymes are associated with normal and neoplastic tissue. Therefore protease inhibitor might also be involved in control of cell functions. In their study an inhibitor was isolated and purified from ovarian carcinoma that exhibited functional and physical similarity to normal ovarian A1AT protease inhibitor.[2]

5. Conclusion

A1AT is a protease inhibitor which is synthesized in the liver and protects lung alveolar tissues from destruction by neutrophil elastase. A1AT deficiency is a common autosomal recessive condition (1:1600 to 1:1800) in which liver disease results from retention of abnormal polymerized. A1AT in the endoplasmic reticulum of hepatocytes, and emphysema results from alveolar wall damage.

The clinical consequences of A1AT deficiency in childhood are haemorrhagic disease in infancy, cholestasis in infancy, or chronic liver disease. Lung disease attributable to A1AT deficiency does not occur in childhood, but is closely linked to smoking in adults. Membranoproliferative glomerulonephritis, panniculitis, and necrotising vasculitis are associations with A1AT deficiency in adult life. A1AT is a protease inhibitor belonging to the serpin superfamily. It is generally known as serum trypsin inhibitor. Alpha 1-antitrypsin is also referred to as alpha-1 proteinase inhibitor (A1PI) because it inhibits a wide variety of proteases. It protects tissues from enzymes of inflammatory cells, especially neutrophil elastase, and has a reference range in blood of 1.5 - 3.5 gram/liter, but the concentration can rise many fold upon acute inflammation.

In its absence, neutrophil elastase is free to break down elastin, which contributes to the elasticity of the lungs, resulting in respiratory complications such as emphysema, or COPD (chronic obstructive pulmonary disease) in adults and cirrhosis in adults or children.

A total of 60 patients, 30 each in control and study group were included in our study. The age between 20-70 years were included both males and females, with 49,11 in number respectively. Blood sample of each patient was taken and evaluation of serum A1AT was done.

Observations were compiled and results were statistically analyzed. In study group the mean value of A1AT was recorded at 1.06±0.21. In control group the mean value of serum A1AT was observed 1.28±0.27. The P value in both groups was found to be highly significant (P=0.000).

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