SUMMARY
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Present study explores the role of Factor XIIIa (FXIIIa), Matrix metalloproteinase-9 (MMP-9) and Vascular endothelial growth factor (VEGF) in the pathogenesis of oral submucous fibrosis. Study comprises 60 clinically and histopathologically diagnosed cases of oral submucous fibrosis which formed the study group and 20 healthy individuals without any habit which formed the control group. Tissues obtained from OSMF patients were graded as Early, Moderately advanced and advanced on heamatoxyline and eosin stained sections. Expression of FXIIIa, MMP-9 and VEGF was studied immunohistochemically in tissues obtained from OSMF and compared with that of control group. Expression of markers was further correlated with the histopathological grades of OSMF. Statistical analysis was done using non-parametric tests. Interrelationship between markers was studied using Pearson’s correlation analysis. The results obtained were recorded, analyzed and corroborated leading to the following conclusions:

1. Out of 60 OSMF patients, 44 were males and 16 were females. Males were commonly affected in 2nd and 3rd decade while females were commonly affected in 3rd decade. Gutkha was the most common form of areca nut used by these patients (Males-52.57%, Females- 50%).

2. As found through standard electronic databases, present study is the first to report expression of FXIIIa in OSMF. FXIIIa expression was found in interstitial cells of connective tissue of all cases of OSMF and the expression was significantly higher in OSMF than that of normal group (p value 0.000). FXIIIacells were seen more in number juxtaepithelially, near blood vessels and in close association with collagen fibers. This may suggest their association with inflammation and fibrosis.
3. Morphologically these cells were found to be dendritic. This along with their location between inflammatory cells and near blood vessels may suggest that FXIIIa expressing cells may be macrophages.

4. FXIIIa expression was found to decrease with the increasing grades of OSMF as fibrosis increases. The difference in expression among grades of OSMF was highly significant (p value 0.000). In early grade, they were most numerous and dendritic in shape while in advanced grade they were least and appeared to be quiescent. This may suggest that FXIIIa may have significant role to play in initiation of fibrosis.

5. MMP-9 was found to be significantly raised in OSMF as compared to control group (p value (epithelium) 0.009, p value (connective tissue) 0.000). In this pioneer study MMP-9 expression was studied in different grades of OSMF. Its expression in epithelium and connective tissue increased with the increasing grades. This increase in MMP-9 expression may suggest pro-fibrotic role of MMP-9 in OSMF which needs to be explored in details.

6. Increased VEGF expression was found in epithelium as well as in connective tissue of OSMF as compared to normal oral mucosal tissues and the difference was statistically significant (p value (epithelium) 0.000, p value (connective tissue) 0.000). With the increasing grades of OSMF expression of VEGF increased. High expression of VEGF in early grade of OSMF can be related to inflammation. Its increase in moderate grade may suggest hypoxia evoked expression of VEGF.

7. Persistence of VEGF expression in advanced grade may suggest the role of VEGF in supporting the viability of the fibrotic tissue.
8. Positive correlation between FXIIIa and VEGF connective tissue (0.554) was found which may suggest that the functions of FXIIIa and VEGF could be related in fibrosis.