

### Study of Biochemical Parameters in Oral Submucous Fibrosis

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#### Abstract

Oral Submucous Fibrosis (OSMF) is a chronic insidious disease with precancerous potential. Since the last decade, there has been constant rise in OSMF in India. This rise in OSMF in India has been attributed to the increased consumption of areca nut. The present study is aimed to estimate serum biochemical parameters i.e. urea, uric acid and creatinine in Early Oral Submucous Fibrosis (EOSMF). The study subjects were divided into 2 groups i.e. Group-I (Early Oral Submucous Fibrosis), Group-II (controls). Group-I includes n=30 patients of clinically diagnosed and histopathologically proven of Early Oral Submucous Fibrosis (EOSMF). They were in the age group of 25-65 years. Group-II (controls) were age and sex-matched, apparently healthy volunteers (n=30) were included in this study. Serum biochemical parameters i.e. urea, uric acid and creatinine were analyzed in all study subjects by Automated Biochemistry Analyzer - ERBA XL 180. Serum urea in Group-I shown mild difference

(Mean) when compared with Group-II. There was a decreased (Mean) of serum uric acid observed in Group-I when compared with Group-II. Whereas increased serum creatinine values (Mean) seen in Group-I when compared with Group-II. It is suggested that analysis of biochemical parameters can be helpful in mass screening of the early oral submucous fibrosis.

**Keywords:** Oral submucous fibrosis, Areca nut, Biochemical Parameters, Urea, Uric acid, Creatinine

#### Introduction

Oral Submucous Fibrosis (OSMF) is a high risk precancerous condition, chronic debilitating disease of the oral cavity characterized by inflammation and progressive fibrosis of the submucous tissues (Lamina Propria and deeper connective tissue).

Oral Submucous Fibrosis (OSMF) is a disease associated with the chewing of areca nut, an ingredient of betel quid and is prevalent in South East Asian populations. Pindborg in 1966 defined OSMF as "An insidious chronic

disease affecting any part of the oral cavity and sometimes pharynx, although occasionally preceded by and/or associated with vesicle formation, it is always associated with Juxtaepithelial inflammatory reaction followed by fibro elastic changes in the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa causing trismus and difficulty in eating". The association of betel quid chewing, oral submucous fibrosis and oral squamous cell carcinoma is quite profound in Indian subcontinent [1].

The term areca nut is used to denote the unhusked whole fruit of the areca nut tree and term betel nut is used exclusively to refer to the inner kernel or seed which is obtained after removing husk. The betel nut has psychotropic and anti helminthic property due to presence of areca alkaloids. Four alkaloids have been conclusively identified in biochemical studies-arecoline, arecaidine, guvacine & guvacoline, of which arecoline is the main agent. These alkaloids have powerful parasympathetic properties which produce euphoria and counteract fatigue [2].

Areca nut chewing is known to cause local trauma and injury to the oral mucosa due to its abrasive nature. This could be more severe in users of pan masala and gutkha due to their fine particulate nature, with the high probability of particle adhesion to the traumatized mucosa, leading to morphological changes and membrane damage. This continuous local irritation by pan masala, gutkha (or) areca nut can lead to injury related chronic inflammation, oxidative stress and subsequent Reactive Oxygen Species (ROS) generation can induce cell proliferation, cell senescence (or) apoptosis, depending upon the level of ROS production. During chronic exposure, these events can lead to preneoplastic lesions in the oral cavity and subsequently to malignancy [3].

The narrowing of the vessels is seen initially in superficial mucosa and in later stages, it spreads to deeper connective tissue. Presence of dilated vessels in advanced stages of OSMF is reported, altogether making the vascularity in OSMF a matter of conjuncture[4].

Urea is an organic compound and plays a vital role in the metabolism of nitrogen-containing compounds. It is a waste product from dietary protein and is also filtered into urine by the kidneys [5, 6]. Urea nitrogen is a normal waste nitrogen product found in blood that comes from the breakdown of protein from foods [7].

Uric acid is the final product of purine metabolism in humans and its circulating concentrations are regulated by the balance in its production and excretion [8]. Uric acid is a known antioxidant and thus may prevent cancer by mopping up free radicals that may cause cellular and genetic injury. It is also aid to help in stabilization of ascorbate in biological fluids and because its serum concentrations is higher than that of ascorbate, it is thought to potentially have a higher antioxidant property than ascorbate [9, 10].

Creatinine phosphokinase is an enzyme which is released due to muscle damage in different systemic diseases. Hence this is used as biomarker to find out the extent of muscle damage or the progress of a disease [11]. Oral Submucous Fibrosis is due to excessive chewing over many years can be explained against the fact over use of the buccal musculature. The muscle response to injury or over use for a long period of time, the levels of creatine phosphokinase are altered in different muscles in different parts of the body [12]. The primary factor for muscle damage is due to proteolysis. IL 6, IL1, ANS TNF ALPHA are found increased in submucous fibrosis patients which are factors which help in proteolysis [13].

The present study was taken up to estimate biochemical parameters i.e. Urea, Uric acid and Creatinine levels in serum of Early Oral Submucous Fibrosis (EOSMF) and compared those levels with controls.

**Materials & Methods**

This study was carried out in the Department of Biochemistry (2018-19) at College of Dental Sciences and Hospital, Bhavnagar, Gujarat, India. The study protocol was approved by the institutional ethics committee. And a written consent form taken from all study subjects.

**Inclusion Criteria**

1. The all study subjects were males. All study subjects divided into 2 groups i.e. Group-I (Early Oral Submucous Fibrosis), Group-II (controls).
2. Group-I includes n=30 patients of clinically diagnosed and histopathologically proven of Early Oral Submucous Fibrosis (EOSMF). They were in the age group of 25-65 years.
3. Habit of chewing areca nut or one of its commercial preparations, with the presence of burning sensation, dry mouth and blanching of oral mucosa were included in Group-I.
4. Group-II (controls) were age and sex-matched, apparently healthy volunteers (n=30) were included in this study.

**Exclusion Criteria**

1. Patients with systemic disease or any major illness
  2. Chronic alcoholics
  3. Renal failure
- 5ml of random venous blood sample was collected from the all the subjects in a sterile disposable syringe which was transferred into centrifuge tubes and was allowed to clot for 30 minutes. Serum was separated with centrifugation at 3000 rpm for 10 minutes.

The serum levels of Urea, Uric acid and Creatinine were estimated by Automated Biochemistry Analyzer - ERBA XL 180.

**Results**

The results of this study showed that mild difference in serum levels of urea in Group-I when compared with Group-II. Serum uric acid levels are decreased in Group-I when compared with Group-II. And Serum creatinine levels are increased in Group-I when compared with Group-II.

**Table-I: Age distribution in Group-I (Early OSMF) and Group-II (Controls)**

Age in years	Group-I (n=30)	Group-II (n=30)
25-35	14 (40.66%)	14 (40.66%)
36-45	09 (30%)	09 (30%)
46-55	05 (16.66%)	05 (16.66%)
56-65	02 (06.66%)	02 (06.66%)

**Table-II: Comparison of Urea, Uric acid and Creatinine in Group-I (Early OSMF) with Group-II (Controls)**

Parameters	Group-I (Early OSMF)	Group-II (Controls)
Urea (mg/dl)	25.93±7.42	26.8±7.47
Uric Acid (mg/dl)	3.05±0.17	3.9±0.29
Creatinine (mg/dl)	2.8±0.75	0.85±0.17

The descriptive results were expressed as Mean and Standard Deviation.

**Discussion**

Oral cancer quite common in India. Several thousands of persons are affected by oral submucous fibrosis, Oral cancer developing from a precancerous lesion is quite

common phenomenon these days. The harmful habits such as use of tobacco intake in both smoking and smokeless forms, pan masala and Gutkha chewing and products which contain areca nut are the main causative agent for premalignant disorders [14].

The present study selected 30 study subjects (Early Oral Submucous Fibrosis) and 30 healthy subjects (controls) in the comparable group. The study population comprised fully of males. The present study to assess the impact of areca nut chewing on biochemical parameters i.e. urea, uric acid and creatinine in early oral submucous fibrosis when compared to controls.

The present study shows a mild difference in levels of urea, clear variation in the serum uric acid, creatinine values between normal subjects and early oral submucous fibrosis. This shows that changes in biochemical values do occur in the premalignant state of the body. A literature stating such variations in urea, uric acid and creatinine levels in early oral submucous fibrosis in Deepak Narang *et al* [15].

It is also possible that the effect of serum uric acid on etiology of cancer may vary from type of cancer to another; low serum uric acid may be associated with increased risk of oral and lung cancer for instance. The muscle response to injury or over use over long period of time, the levels of creatine phosphokinase are altered in different muscles in different parts of the body.

### **Conclusion**

Early detection and identification of oral pre-malignancy or malignancy help in management of the disease and improve survival rates. Estimation of serum biochemical parameters like urea, uric acid and creatinine as a part of biochemical assessment, which may be of proactive intervention for high-risk groups.

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### **References**

1. Pindborg JJ, Sirsat SM: Oral submucous fibrosis. *Oral Surgery Oral Medicine & Oral Pathology*, 1966; 22: 764-79
2. Hoffmann D, Brunnemann KD, Prokopczyk B, Mirjana V, Djordjevic: Tobacco specific N-nitrosamines and areca derived N-nitrosamines: chemistry biochemistry, carcinogenicity and relevance to humans. *J Toxicol Env Health* 1994;41:1-52.
3. Nair U, Bartsch H, Nair J. Alert for an epidemic of oral cancer due to use of the betel quid substitutes gutkha and pan masala: a review of agents and causative mechanisms. *Mutagenesis* 2004; 19:251-62.
4. Rajendran R, Paul S, Mathews PP, Raghul J, Mohanty M. Characterization and quantification of mucosal vasculature in oral submucous fibrosis. *Indian J Dent Res.* 2005;16:83-89.
5. Akbar D, Mohammad M, Shadi T, et al. Anemia and thrombocytopenia in acute and chronic renal failure. *Int J Hematol Oncol Stem Cell Res.* 2013;7:34-39.
6. Ossman DH, Marouf BH, Ameen KH. Effect of extracorporeal unfractionated heparin on hematological and electrolyte markers in hemodialyzed patients. *JPPA.* 2014;4:431-439.
7. Rusul Arif AA, Haider S. A study of some biochemical changes in patients with chronic renal failure undergoing hemodialysis. *Int J Curr Microbiol App Sci.* 2014;3: 581-586.
8. Voruganti VS, Nath SD, Cole SA, et al. Genetics of variations in serum uric acid and cardiovascular risk

- factors in Mexican Americans. *J Clin Endocrinol Metab.* 2009;94: 632-638.
9. Ames BN, Cathcart R, Schwiers E, Hochstein P. Uric acid provides an antioxidant defense in humans against oxidant-and radical-caused aging and cancer: Ahypothesis. *Proc.Natl.Acad.Sci.USA.* 1981;78:6858-6862
  10. Kolonel LN, Yoshizawa C, Nomura AM, et al. Relationship of uric acid to cancer occurrence in a prospective male cohort. *Cancer Epidemiol Biomarkers Prev.* 1994;3:225-228.
  11. Paola Brancaccio, Giuseppe Lippi, Biochemical markers of muscular damage. *Clin Chem Lab Med* 2010; 48(6)
  12. Dean Dessem and Richard M, Lovering. Repeated Muscle Injury as a Presumptive Trigger for Chronic Masticatory Muscle Pain, *Pain Research and Treatment*, 2011.
  13. VV Kamath, K Satelur and Y Komali. Biochemical markers in oral submucous fibrosis. A review and update. *Dent Res J (Isfahan).* 2013 Sep-Oct; 10(5): 576-584.
  14. Joseph BB, George S. Level of Serum Creatine Phosphokinase in Oral Submucous Fibrosis - A Biochemical Study. *Int J Cur Res Rev.* 2015; 7(13):74-78.
  15. Deepak Narang, Vanita Rathod, Fatima Khan, Jaideep Sur. Estimation of urea, uric acid and creatinine in pathogenesis of OSMF: a randomized blind trial - *Int J Bioassays.* 2015; 4(11): 4582-4585.