

## CLINICAL OUTCOMES OF LYCOPENE AT DIFFERENT STAGES OF ORAL CANCER TREATMENT

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### **Abstract**

**Keywords:** *Lycopene, oral.*

Oral cancer is a major problem in the Indian subcontinent where it ranks among the top three types of cancer in the country and is eighth most common cancer worldwide [1]. It is often preceded by precancerous or premalignant lesions and conditions such as leukoplakia, erythroplakia and oral submucosal fibrosis. Subjects: A total of 142 patients presented with clinical signs and symptoms of premalignant and malignant stages of Oral Cancer were enrolled in the study. Among them 39 patients were excluded for the reasons of patients expired (n=5), not reported for the next follow up (n=23), posted for radiation (n=2) and for surgery (n=9) during the study period. After exclusion of above 39 patients, 103 patients were eligible to include in the study, of them 88 were males and 15 were females. Socio demographic data of the patients: In the present study amongst 103 eligible patients 88 (85.43%) were males and 15 (14.56%) were females. Majority of the patients were uneducated that constitute of 70.87% (n=73) while educated patients percentage was 29.12% (n=30). 67.96% (n=70) of patients were identified from rural area and rest of 32.04% (n=33) were from urban area. CONCLUSION

In the present study substantial improvement and decrease in disease severity was observed with selected (lycopene) antioxidant therapy in different stages of oral cancer patients. Thus, antioxidants are overall favorable for early cases of oral premalignant lesions and conditions to cease and delay the disease progress.

### **Introduction**

Oral cancer is a major problem in the Indian subcontinent where it ranks among the top three types of cancer in the country and is eighth most common cancer worldwide [1]. It is often preceded by precancerous or premalignant lesions and conditions such as leukoplakia, erythroplakia and oral submucosal fibrosis [2]. World Health Organization (WHO) defined leukoplakia as a white patch or plaque that cannot be characterized clinically or pathologically as any other disease and is not associated with any other physical or chemical causative agent [3]. Two main clinical types of leukoplakia are recognized, being homogeneous and non homogeneous leukoplakia. WHO defined erythroplakia as a fiery red patch that cannot be characterized clinically or pathologically as any other definable disease. It is much less common than leukoplakia but it has the greatest potential for malignant transformation. Erythroplakia is often flat with a smooth or granular surface [4]. Oral sub mucosal fibrosis (OSMF) is a chronic disorder characterized by fibrosis of the mucosal lining of the upper digestive tract involving the oral cavity, oropharynx and frequently the upper third of the oesophagus [5]. The major risk factors are tobacco (both smoked and smokeless forms), betel quid chewing and alcohol. More than 4000 different chemicals are found in tobacco and tobacco smoke. More than 60 of these chemicals are known to cause cancer.

Antioxidants may be regarded as those substances which will significantly delay or inhibit the oxidation of a substance and protect the body against oxidative damage. Insufficient levels of antioxidants or inhibition of antioxidant enzymes causes oxidative stress and damage or kills the cells. The antioxidants act by breakage of chain reaction, reducing concentration of reactive oxygen species, scavenging initiating radicals, chelation of transition

metal catalyst [6]. Lycopene is a major carotenoid found in tomato which has potent anticancer activity in many types of cancer. The antioxidant properties of lycopene are thought to be primarily involved in its preventive effects in chronic diseases. It also has potent benefits in oral potentially malignant lesions. Because of its high number of conjugated dienes, lycopene is one of the most potent antioxidants, with a singlet oxygen quenching ability twice as high as that of  $\beta$ -carotene and 10 times higher than that of  $\alpha$ -tocopherol. Lycopene has been ranked as highly potent antioxidant followed by  $\alpha$ -tocopherol,  $\alpha$ -carotene,  $\beta$ -cryptoxanthin, zeaxanthin,  $\beta$ -carotene and lutein [7].

## Materials And Methods

**Study centre:** Subjects for the present study were enrolled from a private clinic, Sai Shree cancer hospital, located at Warangal, Telangana, India. This centre is providing outstanding services to the patients with all types of cancers, since 1995.

**Subjects:** A total of 142 patients presented with clinical signs and symptoms of premalignant and malignant stages of Oral Cancer were enrolled in the study. Among them 39 patients were excluded for the reasons of patients expired (n=5), not reported for the next follow up (n=23), posted for radiation (n=2) and for surgery (n=9) during the study period. After exclusion of above 39 patients, 103 patients were get eligibility to include in the study, of them 88 were males and 15 were females.

Institutional Human Ethics Committee reviewed and authorized the study protocol (MGM/VCOP/PHARM D/V/2015/15/07/3). After explanation of the study intension to patients, Patient Informed Consent (PIC) was obtained from all participated patients.

**Study design:** After the patients allowed to their regular clinical diagnosis, screening of subjects for the study was done. Then participants underwent set of pre programmed steps, first obtaining PIC to access their data and their partaking in the study, second if patients were identified with potential risk factors counselling was made to trigger off to halt the habits then, followed by an observation of a set of symptoms (like burning sensation, taste change, dryness of mouth, excessive salivation, ulcers, vesicles and difficulty in speaking, swallowing, and hearing) in an individual patient prior and after antioxidant therapy with lycopene (**Fig 1**).

## Results

**Socio demographic data of the patients:** In the present study amongst 103 eligible patients 88 (85.43%) were males and 15 (14.56%) were females. Majority of the patients were uneducated that constitute of 70.87% (n=73) while educated patients percentage was 29.12% (n=30). 67.96% (n=70) of patients were identified from rural area and rest of 32.04% (n=33) were from urban area (**Fig 2**).

The age incidence of patients was shown in **Table 1**. It is perceptible that highest incidence was found between the age groups 20 to 29 (n= 36; 34.95%) followed by 30 to 39 (n=30; 29.13%) and 40 to 49 (n=21; 20.39%).

Among the various predisposing factors, chewing of smokeless forms of tobacco was identified as common etiological factor. Consuming of gutkha was found to be high i.e., 66.02% (n=68), next gutkha along with tobacco, smoking, and alcohol was found to be low 17.47% (n=18) (**Fig 3**).

**Clinical staging and treatment out comes with antioxidants drug (Lycopene):** Study patients were distributed according to their clinical stage (**Table 2**). Patients presenting with premalignant lesions were found to be more and the percentage is 49.51% (n=51). On the whole leukoplakia cases were found to be in top (n=43; 41.74%). Next to leukoplakia, oral submucosal fibrosis (OSMF) was found to be high i.e., 24.27% (n=25) followed by buccal mucosal cancer with 16.5% (n=17).

The various symptoms prior to the anti oxidant therapy as reported by the patients are shown in **Table 3**. The number is calculated for the total of 103 patients and for possessing of more than one symptom patient was fall over in the other category. 95.14% (n=98) patients complained of burning sensation. Next to this 73.79% (n=76) patients reported with difficulty in swallowing, 65.05% (n=67) patients were observed with difficulty in mouth opening followed by 31.07% (n=32) were with vesicles and ulcers. Whereas 21.36% (n=22), 20.39% (n=21), 16.50% (n=17) and 2.91% (n=3) patients were found with taste change, excessive salivation, difficulty in speaking and with dryness of mouth respectively.

After the treatment with antioxidant drug Lycopene for a period of 3 months, symptoms of burning sensation of mouth was relieved in 70.48% (n=69) of cases. Difficulty in mouth opening was relieved in 74.62% (n=50) of cases. Symptom of difficulty in swallowing was relieved in 43.42% (n=33), where as difficulty in speaking was relieved in 58.82% (n=10). Dryness of mouth and excessive salivation are improved in 66.67% (n=2) and 23.80% (n=5) respectively. Vesicles and ulcers were cured in 68.75% (n=22) of cases.

## Discussion

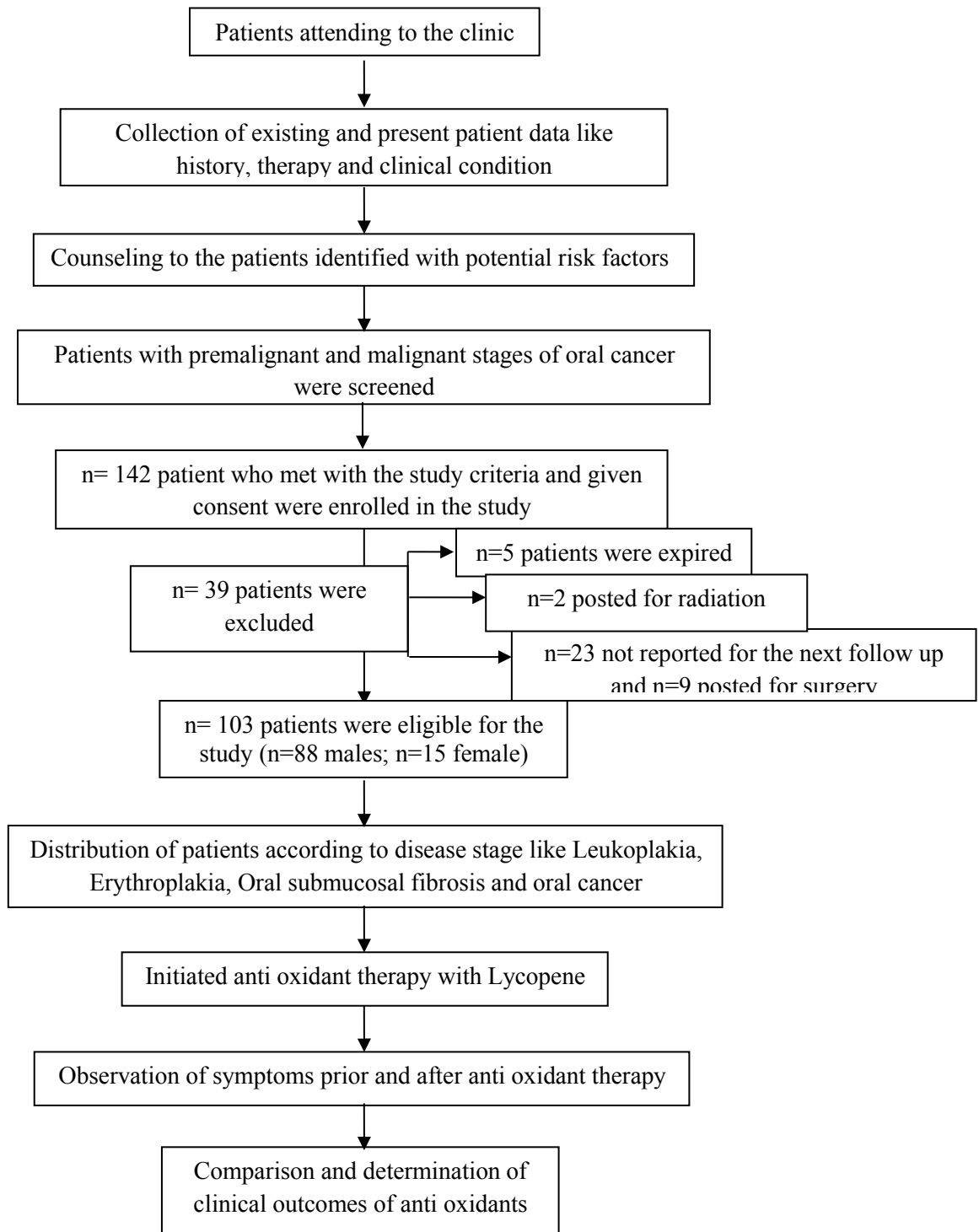
Present study results revealed highest incidence of premalignant stages in 3<sup>rd</sup> and 4<sup>th</sup> decade of life i.e., 64.07% (66 out of 103 cases) and were between ages of 20 to 40 years. This corresponds with Rohit *et.al.*, [8] who recorded 44 out of 64 cases (68.75%) to be in 3<sup>rd</sup> and 4<sup>th</sup> decades. Kamal *et.al.*, [9] has also reported highest incidence of 43.3% in the 3<sup>rd</sup> decade of life.

Although premalignant stages affect both sexes, male predominance for this condition has been noted in many studies. Present study also revealed the same (85.43%) with high male predominance and the male to female ratio was 5.9:1, the value is near to the earlier studies conducted by Hazarey *et.al.*, [10] and Burungale *et.al.*, [11] which shown male to female ratio of 4.9:1 and 7:1 respectively. Even studies from China showed higher prevalence among males. The reason for male predominance may be because of high consumption of gutkha and other related products among youngsters. Moreover males are the working gender and money earner among Indian subcontinent. Areca nut/betel quid, gutkha is chewed for variety of reasons such as stress reliever, mouth freshener, improving concentration and digestion after food. Whereas females are more conscious about their aesthetic values and it is considered socially unacceptable for a female to get gutkha from gutkha vendors. Majority of females in present study were addicted to areca nut or betel quid.

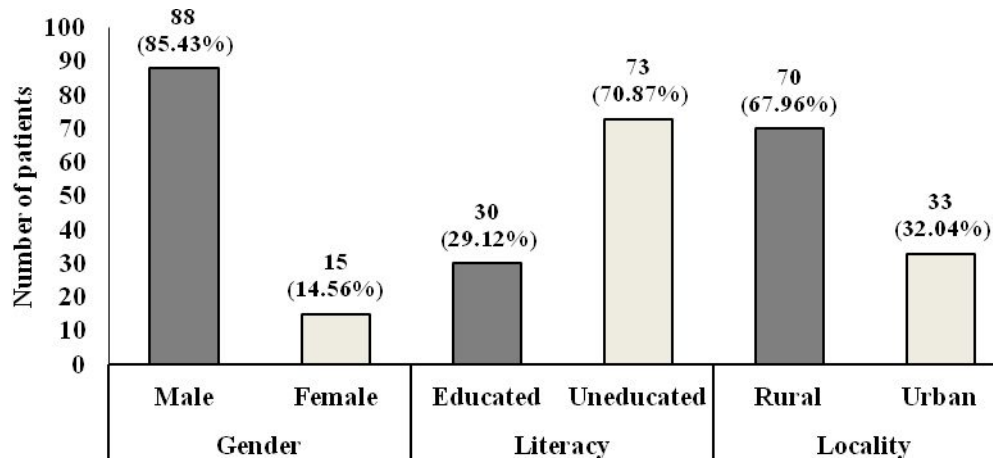
Almost all the patients have as a minimum habit of taking either forms of tobacco. Present study found that most common etiological factor is gutkha chewing seen in 66.02%. These findings are in agreement with the reports given by Vanaja *et.al.*, [12] and Supadminidevi *et.al.*, [13] Syeda *et.al.*, [14] who concluded that the occurrence of premalignant condition is faster and more severe in gutkha chewers as compared to other forms of areca nut products chewers but it is contrast to the study findings of Santhosh & Sneha [15] who reported areca nut was the common etiological factor.

Lycopene was used as the antioxidant in present study patients and the specificity of using lycopene is significant from the findings of Niranzena & Arjun [7] they concluded that lycopene is efficacious in improving the mouth opening and reducing other symptoms in patients with oral sub mucosal fibrosis with no side effects. However, in most of the studies only a few symptoms were examined with antioxidant therapy to assess the role of antioxidants. But, present study resolute a set of symptoms to assess the clinical outcomes of antioxidants therapy more effectively.

Present study resulted in improvement or decreasing severity of disease condition in patients treated with antioxidant lycopene therapy. Burning sensation was improved in 70.48% patients this finding is quite high with the findings of Borle & Borle [16] who observed 58.18% relief from these symptom in their cases. This study also bears significant resemblance to Rohit *et.al.*, [8] whose study findings showed 70% improvement of burning sensation symptom on post antioxidant therapy



*Fig 1: Flow chart explaining methodology*



*Figure 2. Socio demographic data of the patients*

*Table 1. Patients distribution based on age incidence*

S. No	Age group (years)	Total (n=103)	
		n	Percentage
1	20-29	36	34.95%
2	30-39	30	29.13%
3	40-49	21	20.39%
4	50-59	8	7.76%
5	60-69	6	5.82%
6	70-79	1	0.97%
7	80-89	1	0.97%

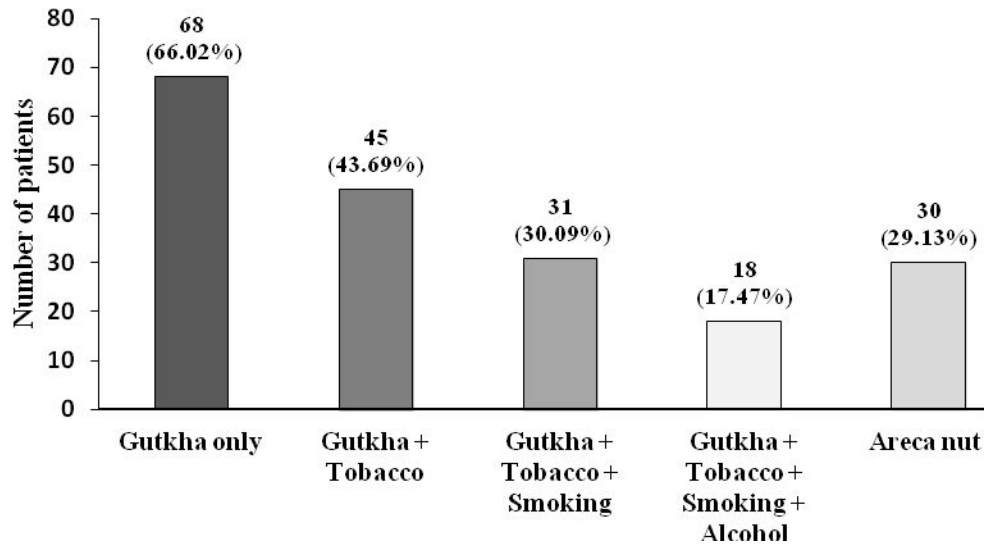


Figure 3. Type of predisposing factors

Table 2. Distribution of patients according to their clinical stage

Disease stage	Number of patients & Percentage (n=103)
<b>Premalignant lesions</b>	
Leukoplakia	43 (41.74%)
Erythroplakia	8 (7.7%)
<b>Premalignant condition</b>	
Oral submucosal fibrosis (OSMF)	25 (24.27%)
<b>Oral cancer</b>	
Tongue cancer	3 (2.9%)
Palate cancer	5 (4.8%)
Buccal mucosal cancer	17 (16.5%)
Erythroplakia with OSMF	1(0.97%)
Leukoplakia with OSMF	1(0.97%)

Table 3. Showing the effect of antioxidants on symptoms in patients with different stages of oral cancer

S. No	Symptoms	No. of cases (n)	percentage	Outcome of Antioxidant therapy			
				Improvement		No improvement	
				n	percentage	n	percentage
1	Burning sensation	98	95.14%	69	70.48%	29	29.59%
2	Difficulty in mouth opening	67	65.05%	50	74.62%	17	25.37%
3	Difficulty in swallowing	76	73.79%	33	43.42%	43	56.58%

4	Taste change	22	21.36%	15	68.18%	7	31.81%
5	Dryness of mouth	3	2.91%	2	66.67%	1	33.33%
6	Excessive salivation	21	20.39%	5	23.80%	16	76.19%
7	Difficulty in speaking	17	16.50%	10	58.82%	7	41.17%
8	Vesicles and ulcers	32	31.07%	22	68.75%	10	31.25%

### Conclusion

In the present study substantial improvement and decrease in disease severity was observed with selected (lycopene) antioxidant therapy in different stages of oral cancer patients. Thus, antioxidants are overall favorable for early cases of oral premalignant lesions and conditions to cease and delay the disease progress. Hence, it offers non invasive option that yields significant improvement. In conclusion, antioxidant therapy should be coupled with cessation of predisposing factor to improve patient disease condition.

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### Conflict of interests

All authors report no conflict of interest

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