

# Meta-analysis on risk factors of squamous cell carcinoma of the tongue in young adults

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## Abstract

Tongue squamous cell carcinoma (TSCC) generally affects the older age group exposed to tobacco for an extended period. However, recent research points out that there is an increased incidence of TSCC in the younger age group without any traditional risk factors making TSCC as a distinct biological entity in this group. This study aims to assess the prevalence and risk factors of tongue carcinoma in the younger group of patients. This article included studies that addressed the TSCC involving young patients and that which are PubMed indexed. Initially, 390 articles were considered; but after refined evaluation, 123 articles had their titles and abstracts matching to this present work. After the extraction of the case reports, review articles and the articles without the assessment of the parameter of harmful habits, we have included only 23 articles in the sample matching the title. The statistical analysis was formed by using chi-square tests using IBM SPSS ver. 20.0. The cohort of the younger population in these studies was mostly in the 35- to the 45-year age group. The majority of reports (64%) classified the patients below 40 years of age as a young group. Though male predominance is reported to be 55%, female patients are also more affected (40%) in the younger age group compared with, the more typical and usual group of head and neck carcinoma patients. TSCC in older adults predominantly reported in tobacco users (70%) whereas in young adults, TSCC was associated with a higher incidence in nonsmokers (53%); the causes of these cancers in young adults remain unclear. The identification of the potential risk factors aside from traditional factors is vital to control the incidence of TSCC in young patients.

**Keywords:** Prevalence, risk factors, tongue cancer, young patients

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**Received:** 11.04.2019, **Accepted:** 12.06.2019

## INTRODUCTION

Oral squamous cell carcinoma (OSCC) represents about 90%–95% of all intraoral malignancies.<sup>[1]</sup> Nearly 100,000 cases are reported every year in India. The

reported incidence was also high in other countries such as Sri Lanka, Bangladesh and Pakistan.<sup>[2]</sup> A recent report revealed that about 45% of all oral cavity cancers were tongue SCC (TSCC).<sup>[3]</sup> TSCC is the most frequently

Access this article online	
Quick Response Code:	Website: www.jomfp.in
	DOI: 10.4103/jomfp.JOMFP_118_19

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**How to cite this article:** Mohideen K, Krithika C, Jeddy N, Bharathi R. Meta-analysis on risk factors of squamous cell carcinoma of the tongue in young adults. *J Oral Maxillofac Pathol* 2019;XX:XX-XX.

occurring cancer in young age group patients.<sup>[4-7]</sup> This early rising onset TSCC incidence will be proportionately higher in the nearby future.<sup>[4]</sup> The better understanding of TSCC in young patients will enable us to provide better therapeutics to improve the prognosis of the patients.

**METHODOLOGY**

The present paper provides the findings of meta-analysis on the theme of “Prevalence and risk factors of TSCC in young patients”. The search was performed from October 2018 to March 2019 through the PubMed database (US National Library of Medicine) in the English Language. The descriptors “SCC,” “tongue” and “young,” taken from the Medical Subject Headings, were used. After screening and refinement of the titles and abstracts of the retrieved articles, articles were selected according to the inclusion and exclusion criteria. Studies emphasizing TSCC affecting young patients were included. Case reports, reviews and researches deviating from TSCC in young patients were excluded.

The analyzed variables were author, publication year, country of data collection, sample size, age group, sex and the presence of harmful habits. These fragments of data were noted in a specific form.

From the methodology used, 390 articles were initially retrieved. After search refinement, 267 articles were not related to study title, and abstract were excluded. In the remaining 123 articles, after extraction of the review articles and case reports, only 28 articles were carefully chosen. Among these articles, only 23 investigations demonstrated an association between tobacco and alcohol use, which were selected relevantly for this article. The statistical analysis was formed by using chi-square tests using IBM SPSS ver. 20.0.

**RESULTS**

Regarding the country of study, ten works were carried out in the USA. The remaining works were reported in various countries. As for the sample size, the number of participants ranged from 3 to 76 in young individuals.

These studies often utilized different age thresholds for defining “young.” The selected cohort of younger age group was varied: individuals considered young were those aged ≤30 years (23%) [Table 1].<sup>[7-13]</sup>

Among the reported studies, 13 reports designated patients with <40 years as the younger group (64%) [Table 2].<sup>[3,4,6,14-23]</sup>

The other reports described patients with <45 years (13%) as the young group [Table 3].<sup>[24-26]</sup>

The predominance of the male sex was found in twelve of the published studies.<sup>[3,4,9,10,12,15-17,19,20,23,24]</sup> There were two reports conducted only in the female population, and also, there were no gender details in one reported study.<sup>[6,18,26]</sup>

Concerning the relationship with harmful habits in the young group, 15 investigations demonstrated less association (<50%) between tobacco use and TSCC,<sup>[4,6-10,13,16-18,21-25]</sup> of which one report presented with nearly half of the participants with positive association,<sup>[26]</sup> seven reported studies showed more than 50% of association with tobacco use,<sup>[3,11,12,14,15,19,20]</sup> and only five reports showed more than 50% of association with alcohol use.<sup>[4,11,16,17,20]</sup>

Among the 23 studies, only ten reports compared the data with the older age group [Table 4].

Of which, eight reported studies demonstrated more than 50% of association with tobacco use in the older age group<sup>[6,7,19,20,22-24,26]</sup> and only two reports displayed lesser association (<50%) with tobacco use [Table 4].<sup>[3,25]</sup>

The comparison within the selected groups could be made, but the comparisons between the younger and older groups could not be achieved due to insufficient data.

The reported studies had taken the cohort of patients between 35- to the 45-year age group to categorize the true “young” population. Comparison of TSCC within the different age group of younger patients exhibited statistically significant differences. The present study showed male predominance in the younger age group ( $P < 0.01$ ). The data also expressed the fact that more than 50% of

**Table 1: Assessment of tongue carcinoma in younger age group ≤30 years**

Authors	Country	Total cases	Young cases, n (%)	Male/female	Tobacco/alcohol, n (%)
Venables and Craft <sup>[8]</sup>	Brazil	819	13 (2)	4/9	2/0 (15)
Byers <sup>[9]</sup>	USA	418	11 (3)	7/4	0
Newman et al. <sup>[10]</sup>	USA	13	13 (100)	7/6	5/4 (38/31)
Sankaranarayanan et al. <sup>[7]</sup>	India	307	22 (7)	10/12	5/2 (23/9)
Oliver et al. <sup>[11]</sup>	UK	3	3 (100)	1/2	2/1 (67/67)
Mallet et al. <sup>[12]</sup>	France	52	52 (100)	34/18	33/15 (63/28)
Morris et al. <sup>[13]</sup>	USA	50	10 (20)	2/8	1/2 (10/20)

**Table 2: Assessment of tongue carcinoma in younger age group ≤40 years**

Authors	Country	Total cases	Young cases, n (%)	Male/female	Tobacco/alcohol, n (%)
Jones <i>et al.</i> <sup>[14]</sup>	Canada	121	11 (9)	4/7	6/1 (55/9)
Sarkaria and Harari. <sup>[15]</sup>	USA	14	6 (43)	5/1	4/0 (67)
Atula <i>et al.</i> <sup>[16]</sup>	Finland	34	34 (100)	22/11	15/18 (44/53)
Friedlander <i>et al.</i> <sup>[17]</sup>	USA	72	36 (50)	20/16	15/22 (42/61)
Myers <i>et al.</i> <sup>[14]</sup>	USA	64	64 (100)	37/27	26/35 (41/55)
Vargas <i>et al.</i> <sup>[18]</sup>	USA	34	17 (50)	0/17	3/0 (18)
Hyam <i>et al.</i> <sup>[19]</sup>	Australia	129	15 (12)	9/6	8/6 (53/40)
Siriwardena. <sup>[6]</sup>	Srilanka	30	23 (77)	-	7/0 (30)
Liao <i>et al.</i> <sup>[20]</sup>	Taiwan	296	76 (26)	71/5	70/44 (92/58)
Harris <i>et al.</i> <sup>[21]</sup>	USA	25	25 (100)	10/15	12/0 (48)
Fang <i>et al.</i> <sup>[22]</sup>	China	176	15 (8)	6/9	5/2 (33/13)
Qahtani <i>et al.</i> <sup>[23]</sup>	KSA	61	8 (13)	6/2	1/3 (13/38)
Jeon <i>et al.</i> <sup>[3]</sup>	Korea	117	23 (20)	15/8	12/11 (52/48)

**Table 3: Assessment of tongue carcinoma in younger age group ≤45 years**

Authors	Country	Total cases	Young cases, n (%)	Male/female	Tobacco/alcohol, n (%)
Danieli S <i>et al.</i> <sup>[24]</sup>	USA	87	30 (34)	22/8	12/0 (40)
Park <i>et al.</i> <sup>[25]</sup>	Korea	85	23 (27)	11/12	5/6 (22/26)
Goepfert <i>et al.</i> <sup>[26]</sup>	USA	54	18 (33)	0/18	9/3 (50/17)

**Table 4: Assessment of tongue carcinoma in older age group**

Authors	Old cases, n (%)	Male/female	Tobacco/alcohol, n (%)
≥30 years			
Sankaranarayanan <i>et al.</i> <sup>[7]</sup>	285 (93)	-	217/51 (76/18)
≥40 years			
Hyam <i>et al.</i> <sup>[19]</sup>	114 (88)	75/39	82/69 (72/60)
Siriwardena <i>et al.</i> <sup>[6]</sup>	7 (23)	-	7/0 (100)
Liao <i>et al.</i> <sup>[20]</sup>	220 (74)	194/26	174/103 (79/47)
Fang <i>et al.</i> <sup>[22]</sup>	161 (91)	113/48	109/72 (68/45)
Qahtani <i>et al.</i> <sup>[23]</sup>	53 (87)	30/23	34/22 (64/41)
Jeon <i>et al.</i> <sup>[3]</sup>	94 (80)	51/43	41/42 (44/45)
≥45 years			
Danieli S <i>et al.</i> <sup>[24]</sup>	57 (65)	-	47/0 (82)
Park <i>et al.</i> <sup>[25]</sup>	62 (73)	40/22	27/25 (43/40)
Goepfert <i>et al.</i> <sup>[26]</sup>	36 (67)	25/11	20/6 (55/17)

the patients were nonsmokers and nondrinkers within the younger age group. Habitual tobacco use is statistically not significant within the younger group ( $P > 0.05$ ). There is statistical significance in alcohol use within the younger group ( $P < 0.01$ ) [Table 5].

Comparison of habitual usage of tobacco is statistically significant within the older age groups ( $P < 0.01$ ). These reports are also depicting that the majority of patients, i.e., nearly 70% were tobacco users and only 36% of patients were alcohol users in the older age group [Table 6].

## DISCUSSION

OSCC predominantly affects men of sixth and eighth decades of life. In India, oral cancer is the third most common cancer and accounts for 30% of all cancers.<sup>[27]</sup> The carcinomatous change typically occurs as a consequence of the incremental accumulation of mutations which on the long run lead to neoplastic

initiation and progression.<sup>[28]</sup> However, there is a significant increase in the prevalence of OSCC in young adults during the recent decades.<sup>[29]</sup> The exposure of the oral epithelium to potential carcinogens at a very young age might reduce the latency period of carcinogenesis in this group.<sup>[30]</sup>

The incidence of OSCC in the younger population has risen from 0.4% to 13%.<sup>[4,5,31-35]</sup> The data from some developed countries like the UK showed that 6% of all oral cancers occurred in young people under the age of 45 years in both men and women.<sup>[2]</sup> Hart *et al.* report stated that about 16% of OSCC occur in younger patients of <45 years of age.<sup>[36]</sup> The alarming rise in early-onset cancer occurrence is estimated to be 16% to 28% of all oral malignancies seen at various institutions in different parts of India.<sup>[37]</sup>

The site predilection of primary OSCC differs in the younger group patients. The tongue is the most frequently affected subsite in the younger group oral cancers.<sup>[4-7,38-41]</sup> Few studies

**Table 5: Comparison of tongue carcinoma within the younger age group**

Description	Groups	n (%)	$\chi^2$	Statistical significance
Age (years) Prevalence	≤30	124 (23)	368.91**	P<0.01** (significant at 1% level)
	≤40	353 (64)		
	≤45	71 (13)		
Sex	Male	303 (55)	25.66**	P<0.01** (significant at 1% level)
	Female	221 (40)		
	Unknown	24 (4)		
Tobacco	Users	258 (47)	3.74 <sup>(NS)</sup>	P>0.05 (NS)
	Nonusers	290 (53)		
Alcohol	Users	175 (32)	143.08**	P<0.01** (significant at 1% level)
	Nonusers	373 (68)		

\*\*Significant at the 0.01 probability level. NS: Non-significant at the 0.05 probability level

**Table 6: Comparison of tongue carcinoma within the older age group**

Description	Groups	n (%)	$\chi^2$	Statistical significance
Age (years) Prevalence	≥30	285 (26)	541.92**	P<0.01** (significant at 1% level)
	≥40	649 (60)		
	≥45	155 (14)		
Tobacco	Users	758 (70)	334.86**	P<0.01** (significant at 1% level)
	Nonusers	331 (30)		
Alcohol	Users	390 (36)	175.36**	P<0.01** (significant at 1% level)
	Nonusers	699 (64)		

\*\*Significant at the 0.01 probability level

analyzed the carcinoma of the younger group and stated that nearly 25% of the patients appear to have TSCC.<sup>[20,25]</sup> The percentage of young TSCC patients at Texas M. D. Anderson Cancer Centre, Houston increased from 4% to 18%, and rising incidence was noted in the US population at large.<sup>[4]</sup>

Funk *et al.* reported that of all head and neck SCC, 76% were TSCC that occurred in patients <35 years old.<sup>[42]</sup> In India, tongue carcinoma appears to develop at an earlier age with the highest incidence reported between 40 and 45 years of age.<sup>[43]</sup> Few reports conveyed that 8%–10% of TSCC belonged to the younger age group of lesser than 40 years old.<sup>[22,44]</sup> A global study concerning a total of 22 tumor registries, especially investigating the TSCC in young patients (<45 years), emphasized a yearly increase ranging from 0.4% to 3.3%.<sup>[45]</sup> The young age consideration should be given only to those below the age of 30 years to obtain meaningful comparison.<sup>[46]</sup> The age selection criteria should be defined clearly for the young group. The present study showed that the prevalence of TSCC is statistically significant in both the different sets of the younger group and older groups ( $P < 0.01$ ). Some authors have tried to assess the differences and factors involved in the etiology of TSCC, by comparing them with those in older patients.<sup>[3,6,7,19,20,22-26]</sup>

Opinion regarding gender predilection for TSCC in young remains divided. The predominance of the male sex is found in thirteen of the published studies with

$P < 0.01$ .<sup>[3,4,6,9,10,12,15-17,19,20,23,24]</sup> The present report displayed the statistical significance in gender predilection within the younger group ( $P < 0.01$ ). There was also an increased incidence of tongue cancer in female patients when compared with the typical group of oral cancer patients.<sup>[7,8,11,13,14,21,22,25]</sup> Few other studies also support that there was female gender predilection in the younger group. Patel *et al.* published the analysis of incidence and survival data from the Surveillance, Epidemiology and End Results. This data revealed that the overall incidence of TSCC was increasing in young Caucasian women.<sup>[47]</sup> Bektas-Kayhan *et al.* report revealed that nearly 80 % of patients were young (<40 years old) and the patients were equally distributed in both the genders.<sup>[48]</sup> The effects of passive smoking on health issues should also be considered for increasing cancer incidence in female patients. These variances highlight the value of documenting the history of environmental smoke exposure. This attributed difference in gender predilection could also be due to the presence of various cultural or behavioral characteristics in the diverse group of different populations.

The lateral border of the tongue is the most frequently affected site for TSCC in younger age. The reports revealed that nearly 70% of TSCC occurred in the lateral border of the tongue.<sup>[5,49,50]</sup> Falaki *et al.* found that most of the TSCCs involved the lateral border.<sup>[51]</sup>

Tobacco and alcohol consumption were the main causative factors for OSCC among older adults.<sup>[35]</sup> The present study is also depicting that the majority of patients, i.e., nearly 70% were tobacco users and 36% of patients were alcohol users. The use of tobacco or alcohol is statistically significant within the older age groups ( $P < 0.01$ ).

Only four reported studies had conveyed that the traditional risk factors could be the causative factor for TSCC in the young group too.<sup>[12,15,20,52]</sup>

Similarly reports revealed that nearly half of their younger group were smokers and only to the lesser extent reported with alcohol abuse.<sup>[14,19]</sup> The present study also evidences the lesser association of alcohol use, i.e., 32% within the younger groups, and it is statistically significant within the younger groups ( $P < 0.01$ ).

Few other reported studies had found that there is a positive association of chewing tobacco use with early-onset TSCC.<sup>[20,53]</sup> Some authors reported that in India, betel quid chewing with tobacco is a possible carcinogenic agent in the rising incidence of the young group (<35 years) oral cancer.<sup>[18,54]</sup> These studies were brought out the potential role of areca nut into attention.<sup>[55]</sup> Some specific racial



groups in India did not show cancer transformation even though they constantly chew betel nut for a longer period.

Oral submucous fibrosis (OSF) is associated with betel quid and areca nut chewing, mostly prevalent in the population of South East Asia. The previous history of the presence of the potentially malignant oral disorders could significantly increase the risk of malignancy.<sup>[56]</sup> A study in Srilanka showed a higher percentage of OSF reported with OSCC in patients of below 50 years age group (23.8% vs. 21%).<sup>[57]</sup> The recently reported study in India revealed that the incidence of TSCC concomitant with OSF was estimated to be around 25%.<sup>[58]</sup> Oliver *et al.* reported that the malignant transformation might predict nearly 5% in existing atrophic or erosive form of lichen planus lesions occurring in the high-risk sites of the floor of the mouth and lateral border of the tongue which could be easily susceptible to carcinogens.<sup>[11]</sup> Zhang *et al.* concluded that the genetic changes that occur during lichen planus malignant transformation were different from those of other potentially malignant disorders such as leukoplakia.<sup>[59]</sup> The young patients who report with persistent ulceration, OSF, leukoplakia, erythroplakia, erosive lichen planus or swellings with no apparent local cause should always be suspected of malignant transformation. Hence, biopsies should be advised in a timely fashion without ignoring their symptoms. For those cases, an appropriate referral is recommended, which will ensure prompt investigation and earlier initiation of treatment to increase the chances of successful treatment.

Some of the reports stated that marijuana use might be a potential risk factor associated with the increased incidence of tongue and tonsil SCC in young adult cases.<sup>[39,60]</sup>

However, there are other reports which claim that the etiological factors for TSCC in young are different from those responsible for OSCC in the older group.<sup>[3,7,9,14,23]</sup> Myers *et al.*'s and Newman *et al.*'s study showed that nearly half of their patients were nonsmokers and non drinkers.<sup>[4,10]</sup> Majority of the reports conveyed that TSCC in young patients was not associated with the use of tobacco or alcohol.<sup>[4,6-10,13,16-18,21-25,61]</sup> Similar findings were also reported in India that tongue cancer is on the increase in nonsmoking and nondrinking males.<sup>[62]</sup> Many of the recent reports showed that more than 80% of the patients with lingual carcinoma aged below 35 years had no evidence of any common risk factors.<sup>[7,23,38]</sup> Morris *et al.*'s study showed about 70% of patients did not report to have any habit history.<sup>[13]</sup> The exposure to common risk factors is also of short duration in younger patients.<sup>[33,63]</sup> Martin-Granizo *et al.*'s study exposed that the tongue and floor of the mouth cancers were usually not associated with carcinogenic factors, but carcinoma of other sites of the oral

cavity may have previous exposure history for carcinogens.<sup>[64]</sup> Sankaranarayanan *et al.*, specified that the factors other than tobacco and alcohol might be the causative factor for oral tongue cancers in young people.<sup>[7]</sup> The present report also supports the fact that more than 50% of the patients were nonsmokers and nondrinkers within the younger age group. Habitual tobacco use is statistically not significant within the younger group ( $P > 0.05$ ). Since there is less association with traditional risk factors, TSCC in the younger group might be considered as different entity from the older population.

There is also increasing incidence reported in female patients who did not practice any habit in the young group compared with the old age group.<sup>[6,13,18,21,22,65]</sup> The history of passive smoking was unavailable through the retrospective records which had not yet been studied.<sup>[18]</sup> The absence of conventional risk factors was significantly noted in the more proportion of younger female patients, so TSCC in this group might be associated with diverse etiology.<sup>[63]</sup>

The presence of primary cancers in other parts of the body of the patient along with added instability of immune system could also be the causative factor for carcinogenesis.<sup>[66]</sup> Morris *et al.* conveyed that previous history of the Fanconi's anemia should also be considered as a known risk factor for TSCC in young adults.<sup>[13]</sup> This statement was also supported by Kaplan *et al.*'s report.<sup>[67]</sup>

The positive family history would presumably carry a significant role among risk factors for young patients since the other conventional risk factors require relatively long periods of exposure. Genetic predisposition or familial antecedents may be etiology for young cancer cases,<sup>[5,18]</sup> but the genetic events are unclear.<sup>[11]</sup> The detailed genetic counseling is mandatory for patients of 20–30 years old presenting with associated syndromic characteristics and suggestive family history to thoroughly evaluate the general disease background.<sup>[68]</sup> Hirota *et al.*'s study showed the high rate, i.e., 84.6% of positive family history for malignancy in these younger group patients (compared to 29.6% in older group patients) at a significant level.<sup>[5]</sup> Considering the hereditary nature of carcinogenesis, it is crucial to analyze sites of occurrence of malignant neoplasms in parents and descendants.<sup>[69]</sup>

Some researchers have proposed that TSCC in younger patients may represent a significantly different entity at the genetic level.<sup>[70]</sup> The phenotypic differences may likely be brought about the difference in genotypes in the patients affected by these cancers.<sup>[21]</sup> Schantz *et al.* stated that the initiation of cancer in younger age group people might be associated with genetic susceptibility to carcinogens with an increased predisposition to mutagen-induced DNA damage

or decreased DNA repair mechanisms.<sup>[71]</sup> The alterations in the DNA repair pathway, genetic stability surveillance or cellular growth regulations may result in an increased possibility of developing oral cancers.<sup>[68]</sup>

Chronic trauma in the form of long-standing irritation from orthodontic appliances,<sup>[13]</sup> denture flanges,<sup>[48,72,73]</sup> broken dental restorations,<sup>[72]</sup> sharp teeth,<sup>[48]</sup> and the position of the mandibular second molar<sup>[74]</sup> may also play a vital role in the initiation and stimulation of neoplastic progression. Hence, it is meaningful to document the recent history of therapeutic procedures endured by the patients.

The clinical profile of TSCC may look similar for young and old group, but the risk factors for the young patients are different from that of the elderly population.<sup>[35]</sup> The factors linked with the majority of TSCC in young patients remain indistinguishable. Many recent reports stress that the generally implicated etiologic factors may not be fully applicable to this age group.<sup>[41,47,51,70,75]</sup> The tongue cancer in this group of patients might be associated with multifactorial etiology.<sup>[4,12,15,16,21,32,34,51]</sup> The exposure to external factors other than traditional factors and lifestyle should also be investigated in the young group. Hart *et al.*'s study discussed that these malignancies positively occur as the result of the interactions of constitutional and environmental factors.<sup>[36]</sup>

Some of the factors such as viruses,<sup>[72]</sup> dental status,<sup>[72,76,77]</sup> occupation and environmental exposure,<sup>[78]</sup> dietary factors,<sup>[31]</sup> iron deficiency<sup>[79]</sup> and immunodeficiency<sup>[80]</sup> have also been implicated as cofactors in the genesis of tongue cancer.

Only a few studies reported a consistent link between the risk factors studied and the development of carcinoma in young patients. Hence, it is still not possible to reveal the etiology of oral cancer in younger adults, and it remains uncertain. According to these reported studies, some time-dependent factors in association with changing behavior should also be reviewed for etiology.

The biological behavior of oral cancer in younger patients is under debate. The physiologic response to risk factors and the clinical behavior of cancers in younger patients may be different.<sup>[81,82]</sup> This substantial difference was attributed to the differing basis of carcinogenesis at the genetic level of both groups.<sup>[25]</sup> Hence, they are speculated to have an altered ability to metabolize procarcinogens and carcinogens,<sup>[83]</sup> and they have been suggested to show different clinical characteristics and disease progression from that of older patients.<sup>[84]</sup> Jeon *et al.* presented poorer

clinical outcomes for younger patients when compared with the older patients.<sup>[3]</sup> The younger adults with TSCC had a higher locoregional recurrence rate than older patients.<sup>[17]</sup> Few studies point out that the biological behavior of SCC in younger patients is likely more aggressive compared to those affecting elderly patients.<sup>[38,51]</sup> Conversely, TSCC in the younger group was not presented with poorer outcomes when compared to a matched group of control patients in other reports.<sup>[26,85]</sup> One of the main factors which is influencing the different study outcome may be the selected young age cutoff range varies from 30 to 45 years. Because of these factors, researchers have started searching for the discrete mutations linked with the disease in young patients to find the little differences at the genetic level between these groups.

## CONCLUSION

Many retrospective studies are limited in their small sample size with various inherent bias resulting in conflicting reports. Prognosis of younger and older group carcinomas is bound to differ since etiology is likely dissimilar for these cases. Therefore, complete documentation of the habits along with other risk factors exposure is mandatory. Further investigations with multicentric approaches are required to identify etiology, biological behavior and the molecular mechanisms by which young patients, despite the absence of risk factors, go on to develop tongue cancers have to be emphasized. Finding such factors could eventually throw some light about the preventive measures of implementation and management protocol, and also, it may provide some evidence on prognostic markers to reduce the patient's morbidity and mortality and to improve their quality of life.

## Acknowledgments

Our sincere thanks to Mr. Syed Imran Maktoum, Director, Kalbani Group, for supporting us in the present work.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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