

RESEARCH ARTICLE

Epidemiology of Oral Cancer in Iran: a Systematic Review

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Abstract

Background: Oral cancer stands among the 10 top causes of cancer death in the world. Considering the role of epidemiologic information on planning and effective interventions, the present study aimed to investigate the epidemiology of oral cancer in Iran. **Materials and Methods:** The required information for this systematic review study was obtained from PubMed, Google Scholar, CINAHL, SID, Medlib, Magiran and Iranmedex databases, using key words “cancer”, “oral cancer”, “squamous cell carcinoma”, “oral cavity carcinoma” and their Persian equivalents in combination with keywords of epidemiology, prevalence, etiology, frequency, and Iran from 1990 to 2014. From 1,065 related studies found, finally 25 were included to the study. **Results:** The mean age of 8,248 patients in 25 studies was 54.0 ± 15.1 years. The male/female ratio for oral cancer was 1.91. Tongue with average percentage of 29.9 was the most involved site. Regarding microscopic grade, 65.7% of cases were grade 1. SCCs, accounting for an average of 70.0%, was the most common among all types of oral cancer. In the majority of studies, smoking including cigarette, hookah, and tobacco consumption was found to be a risk factor. **Conclusions:** The epidemiological pattern of oral cancer in Iran is somewhat similar to that of other countries. Yet the information on hand in this field is limited and considering the role of epidemiological data we suggest conducting more accurate studies to catch data that is required for effective programs and interventions.

Keywords: Epidemiology - cancer - oral cancer - systematic review - Iran

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Introduction

Cancer has a reputation as a lethal disease, because about 50 percent of people receiving treatment for invasive cancers (excluding carcinoma in situ) pass away from cancer and unfortunately survival is worse in the developing countries (Greenberg and Glick, 2003; Bhurgri, 2005; Ghojazadeh et al., 2013b; Amirnia et al., 2014; Kumar et al., 2014). There were 14.1 million new cancer cases, 8.2 million cancer deaths and 32.6 million people living with cancer in 2012 worldwide (Cancer and Organization, 2014) Also in Iran annually more than 30000 death cases are reported as a result of cancer (Mousavi et al., 2009).

One of the most important types of cancers is oral cancer, in a way that is the sixth prevalent cancer, and is known as a severe increasing health and social problem in the world (Rodriguez et al., 2004). Annual incidence of 275 thousands of oral cancer has been reported and about two third of it is in developing countries and prevalence of this cancer shows high difference in terms of geographical

regions all around the world and is different in various parts of the world up to twenty times (Warnakulasuriya, 2009). In world map of prevalence of this cancer Iran stands alongside with countries such as India, Pakistan, Bangladesh, in southern region of Asia with prevalence of 20 to 36.3 in each 100 thousand people (Petersen, 2003). Oral and oropharyngeal cancer include cancer of the tongue, lip, floor of the mouth, gingiva, palate and buccal mucosa, alveolar mucosa, and oropharynx, as well as the pharyngeal tonsils and salivary glands. Males are twice as likely as females to be diagnosed with oral and oropharyngeal cancer (Chester et al.; Braakhuis et al., 2009). Squamous cell carcinoma composes more than 90% of oral cancers. The remaining oral cancers are melanomas, salivary gland malignancies, lymphomas, and sarcomas (Woolgar, 2006).

The most important well-known risk factors for oral and oropharyngeal cancer are long-term excessive alcohol consumption and tobacco use (Merletti et al., 1989; Ghojazadeh et al., 2012; Ghojazadeh et al., 2014). According to the effect of different factors on incidence

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of this cancer, and effect of sexual, age, occupational, and geographical differences on its prevalence, and other factors, epidemiological and descriptive studies in this field could be effective in planning, interventions, and decision makings (Chiba, 2001; Llewellyn et al., 2004; Rodriguez et al., 2004). Unfortunately despite the importance of these types of studies and available conflicts in prevalence, etiology, and other factors, comprehensive and proper studies have not been conducted in Iran (Delavarian et al., 2009).

Therefore current study has been designed and conducted aiming to investigate epidemiological features (ratio in men and women, their types, severity, causes, and other items) of oral cancer in studies published in Iran. It is hoped that its information would be used and effective in planning and intervention through clarifying available data in this field.

Materials and Methods

This systematic review was designed and conducted in 2013. Required information was collected at the first stage through searching Farsi keywords of “cancer”, “oral cancer”, “squamous cell carcinoma” and their combination with keywords of “epidemiology”, “prevalence”, “etiology”, “frequency”, and “Iran” and at the next stage in four databases of SID, Medlib, Magiran, and Iranmedex keywords of “squamous cell carcinoma”, “oral”, “oral cancer”, “Maxillofacial Malignancies”, “cavity” and combination with keywords of “etiology”, “Iran”, and “epidemiology” in data bases of Google scholar, CINAHL, and Pubmed. Time period of selecting articles was during 1990 to 2013. To better recognition and coverage of published articles, after searching databases, manual searching was conducted.

Inclusion criteria were: publication of article during 1991 to 2013, descriptive and epidemiological studies, and articles published in English and Persian. Exclusion criteria were: cellular, laboratory and case-report studies.

After eliminating articles with weak relevance with objectives of the study and selecting main articles, in order to ensure recognition and investigation of available articles, references of references for selected articles were also searched. Among 1065 found related articles finally after elimination of those with weak relationship to objectives of the study, 25 fully related articles were included to the study and were completely studied and investigated.

Two reviewers evaluated the articles according to the checklist of Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) and their disagreements were delivered to a third party.

After precise extraction of required data, extracted results was first summarized in an Extraction Table composed of parts for authors, year, city, period of study, population of studies, mean age of samples, male/female ratio, most involved site, commonest type of oral cancer, grade of malignancy, and factors effective on oral cancer were analyzed. Statistical analysis was performed using SPSS 16.0 .

To draw diagrams MS Excel 2013 software was used.

Reference management software of Endnote X5 was used to organize study titles and abstracts and also to identify repeated cases (Azami-Aghdash et al., 2013; Ghojzadeh et al., 2013a; Moradi Khangahi et al., 2013).

Results

Detailed characteristics of studied articles are represented in appendix 1. In 25 studied articles total 8248 patients had been investigated (Fahmy et al., 1983; Razmpa, 1997; Ansari, 2002; Yazdizadeh et al., 2003; Eshghyar et al., 2005; HoseinpourJajarm and Ghodsi, 2005; Sargeran et al., 2006; Andisheh-Tadbir et al., 2008; Razavi and Sajadi, 2008; Chamani et al., 2009; Delavarian et al., 2009; Mostaan et al., 2009; Taghavi et al., 2010; Falaki et al., 2011; Sadri et al., 2011; Aghbali et al., 2011; Aghbali et al., 2012; Aminzadeh et al., 2013; Farhad Mollashahi et al., 2013). Mean age of patients was 54.02±15.14.

Male/female ratio was varying from 0.9 to 5 and mean of this ratio was 1.91 (Figure 1).

As it is seen in Figure 1 male/female ratio has a high variation in different years (It should be mentioned that in calculating the years of this diagram the median of time period has been considered).

The most involved sites for oral cancer is been shown in Figure 2; tongue with 30 percent is the most involved part in oral cancer.

Among 25 articles, 5 articles (Razmpa, 1997; Eshghyar et al., 2005; Andisheh-Tadbir et al., 2008; Delavarian et al., 2009; Aghbali et al., 2012) had graded severity of oral cancer had been graded Figure 3; As it is seen the most

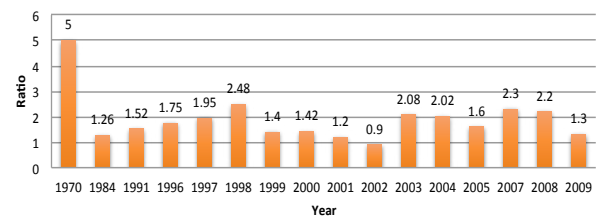


Figure 1. Male/Female Oral Cancer Ratio

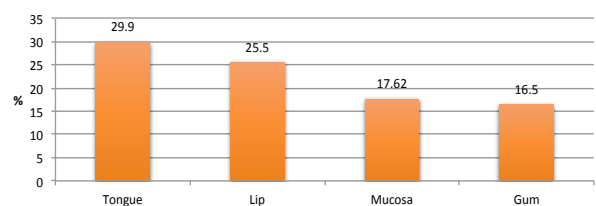


Figure 2. Frequency Distribution of Oral Cancer Severity Based on Grade

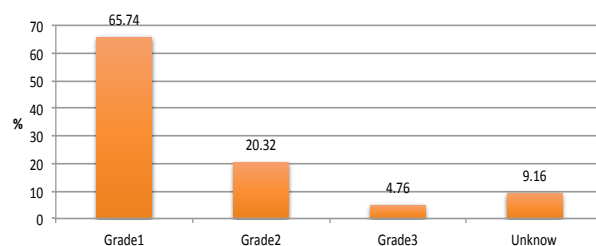


Figure 3. The Most Involved Organs in Oral Cancer Based on Repetition in Studies

Table 1. Characteristics of the Investigated Articles in the Study

R o w	Reference	City	Time pe- riod	No. of samples	Mean age of samples	Men. women prevalence ratio	The most involved sites	Common- est type (%)	Grade of malignancy (%)	Mentioned effective factors
1.	Aghbali et al 2010	Tabriz	1999- 2008	256	60.27±16.87	2.46	Tongue(30.8) lip(28.5) salivary glands(12.5)	(79) SCC	Grade 1(95.8) Grade 2 (3.6) Grade 3 (0.6)	Increase of age
2.	Eshghyar et al 2005	Tehran	1966- 2002	271	56.26	1.26	Mandibular Ridge(29) tongue(21)	-	Grade 1(59.4) Grade 2 (32.5) Grade 3 (8.1)	Smoking
3.	Aghbali et al 2012	Gilan	1999- 2008	2364	63.41±15.41	1.7	Tongue(35.2) mucosa(22.4) lip(20) gum(16)	SCC (48.7)		
4.	Delavaran et al 2009	Mash- had	2000- 2005	44	66.17±52.53	0.9	Tongue(24) mucosa(17) gum(17)	(73) SCC	Grade 1(72) Grade 2 (25) Grade 3 (3)	Cigarette an hookah
5.	Amin Zadeh et al 2012	Isfahan	2005- 2010	236	54	2.2	Larynx(20) tongue(17) mucosa(12.7) lip(20)9.3)	(65) SCC		
6.	Ansari 2002	Hama- dan	1985- 1997	386	43.5	1.52		BCC(41.4), SCC (38)		
7.	Yazdizadeh et al 2008	Gilan	1996- 2004	306	57.7±15.65	3.55	Tongue(17.3) lip(11.4) tonsils(9.48)	SCC (67)		
8.	Sadri et al 2011	Tehran	2007- 2009	170	-	-	Tongue(34.1) mucosa(29) lip(12.8)			Location of residence (north of country) and blood group A
9.	Chanlain et al	Ker- man	1993- 2002	263	59.7	2.48	Lip(49.32) tongue (22.42)	OSCC (84.7)		
10.	Ansari et al	Hama- dan	1985- 2001	249	64	2.51	Lip (39) Oral tongue(28.1) Floor of mouth(11.6)			
11.	Mosta' aan et al 2009	Iran	1995- 2005	454	61.22	1.3	Tongue (25)	-	-	-
12.	Andishe Tadbir et al 2009	Iran	2003- 2005	181	53.7±18.6	1.9	Tongue in old patients (17.5) In young patients (29.3)	SCC (68.1)	-	Cigarette
13.	Falaki et al	Mash- had	1996- 2009	158	30.19±4.24	3.1	Tongue (66)			
14.	Razmpa et al 2010	Tehran	2003- 2008	87	-	1.6	Middle (57.5) posterior (20.7) anterior(6.9)		Grade 1(46) Grade 2 (21.8) Grade 3 (4.6) Unknown (27.6)	Cigarette, denture, leukoplakia
15.	Chamani et al 2009	Ker- man	1991- 2002	334	54.55	1.75	Lip(33.8) tongue (15.3)	SCC (71.3)	-	-
16.	AndisheTadbir et al 2008	Shiraz	1992- 2007	200	56.9±15.5	1.4	Tongue (53) buccal mucosa (9.5) maxillary gingiva (9)		Grade 1(55.5) Grade 2 (18.7) Grade 3 (7.5) Unknown (18.2)	
17.	Hossein Poor Jajarm and Al- e-Davoud	Mash- had	2002- 2003	54	-	1.07	Lip (27.7) lower lip (25.9) buccal mucosa (20.3)	-	-	Cigarette or snus
18.	Mashhadi et al 2011	Za- hedan	2005- 2010	175	48.5	2.3	-			Smoking
19.	Sargeran et al 2006	Tehran	1991- 2003	1042	58.8±16	1.4	Tongue (32)			
20.	Taghavi et al 2010	Tehran	1999- 2009	67	38	-				
21.	Razavi et al 2011	Isfahan	1991- 2010	231		1.2	Gum (46) tongue (18)	SCC(60)		
22.	AndisheTadbir et al 2009	Shiraz	2002- 2007	181	53.7±18.6	1.7	Tongue (34.4)	SCC (50.8)	-	Cigarette
23.	Razmpa et al	Tehran	2003- 2008	87	-	-				-
24.	Fahmi et al 1973	Shiraz	1962- 1978	381	-	5	Lower lip Tongue	SCC (97)	-	Smoking and addiction to drugs
25.	Mollashahi et al 2012	Za- hedan	2007- 2011	98	58.46±12.89	-	-			Smoking and smoke-less tobacco

common form of oral cancer in studies was grade 1 and 9.16 percent of severities were also unknown.

Investigating results of articles showed that SCC (Squamous Cell Carcinoma) with mean of 70.05 percent is the most common type of oral cancer among all.

In the most of studies smoking including cigarette, hookah, and tobacco had been represented as risk factors for oral cancer. In one of the studies also residence location (north of country) and blood group A have been identified as risk factors for oral cancer incidence (Sadri et al., 2011).

Discussion

Cancers are one of the most important mortality reasons in human societies. In America, based on estimations one out of three or four people would suffer cancer (Jovanovic et al., 1993). In field of dentistry also oral cavity cancer could be one of reasons of referring patients to clinics and dental care centers (Kumar et al., 2014). Therefore awareness of epidemiology and other related factors could be effective in prevention, therapy, and planning for management of oral cancer.

Results of investigating articles showed that the ratio of oral cancer in men is higher than that of women. Based on results of conducted studies in other points of the world the lowest male/female ratio has been reported in Congo with 0.4 and the highest in Spain with 8.4 (Izarzugaza et al., 2001; Kayembe and Kalengayi, 2002). In this study male/female ratio of oral cancer was about 1.9 and this rate is in accordance with results of studies reported in Nigeria (Arotiba et al., 2006), Netherlands (Jovanovic et al., 1993) and Iraq (Al-Rawi and Talabani, 2008) (1.65, 1.8 and 2, respectively). According to the included studies, one of the possible reasons for higher oral cancer incidence in men could be due to higher consumption of tobacco and alcoholic products by men and in this case planning an effective interventions seems necessary to reduce consumption rate of these materials by men. The other reason for this issue could be higher exposure of men to other factors such as exposure to light which leads to lip cancer. In Shiraz in recent 40 years, male/female ratio of people suffering oral cancer has been reduced from 5 to about 1.4 (Sargeran et al., 2006). Reduction in male/female ratio of oral cancer has been clear during recent decades all around the world. First, tendency of women towards consuming alcohol and cigarette was known as the cause of this change, but it has been revealed that most of the men and women suffering oral cancer in ages below 40 are not smokers and alcohol consumers. A satisfactory reason has not been presented yet for this epidemiological change in oral cancer (Chamani et al., 2009; Aminzadeh et al., 2013).

Results of this study showed that the tongue is the most common involved site in oral cancer. In study of Delavarian et al. (Delavarian et al., 2009), Javadi et al. (Javadi, 2007), and Sargeran et al. (Sargeran et al., 2006) in Iran tongue has been also reported as the most involved site of oral cancer. It is in accordance with study by Chidzonga in Zimbabwe (Chidzonga, 2006), study by Izarzugaza et al in Basque (Izarzugaza et al., 2001), study by Gervasio et al in Brazil (Gervasio et al., 2001), and

study by Laronde et al in Canada (Laronde et al., 2008). However in some studies other sites rather than tongue have been reported as the most involved sites in oral cancer (Fahmy et al., 1983; Javaher, 2007; Shenoj et al., 2012). Therefore according to distribution of oral cancer in various sites it doesn't seem logical to focus on preventive and therapeutic plans only on one site and all sites with potential of oral cancer should be considered, but due to limitation of resources especially in health care system, in terms of need for prioritizing therapy and prevention of this cancer, it is suggested to focus on tongue to be preferred due to its high rate of involvement.

In this study in terms of microscopic grade of disease about 65 percent of cases were grade 1 which is in accordance with results of study by Delavarian in Mashhad (Delavarian et al., 2009), Aghbali in Tabriz (Aghbali et al., 2012), and study of Chidzonga in Zimbabwe (Chidzonga and Mahomva, 2006). In this study about 20% of cases were grade 2 which is different with results of study by Sasaki reporting this rate as about 65% (Sasaki et al., 2005). Sasaki et al. had only investigated people under 40 in their study and maybe the difference is due to this fact. In study of Aghbali et al., it had been revealed that there is a negative significant relationship between tumor grade and age of affected people in a way that older people had lower grade (Aghbali et al., 2012). In this condition higher grade of tumor in study of Sasaki investigating the young people is justifiable.

Investigating the results of studies showed SCC as the most common type of oral cancer with mean of 70.05 percent. This rate has been reported as 40 – 60 percent in African countries and its possible cause could be HIV related malignancies prevalence in these countries (Kayembe and Kalengayi, 2002). This percentage has been reported as higher than 90% in studies in North of Carolina and England (Llewellyn et al., 2004; Elter et al., 2005). In a study by Sugeran et al. in Australia this rate has been reported as about 98% (Sugeran and Savage, 2002). Therefore planning for effective therapy and prevention of this type of oral cancer should be in priority of health care system especially in the field of dentistry.

In most of the investigated studies on oral cancer smoking including cigarette, tobacco, and hookah has been mentioned as the most important risk factors in oral cancer. Results of most of the conducted studies in most parts of the world also confirm this point (Chandu and Smith, 2002; HoseinpourJajarm and Ghodsi, 2005; Dias and Almeida, 2007). In study of Sadri et al inhabitants of northern regions of Iran has been reported to be predisposed to oral cancer (Sadri et al., 2011). In a study by Givian et al. it seems that dietary habits of this region's inhabitants such as drinking hot tea and eating salted foods and those foods exposed to sun light are of the most importance as risk factors (Givian, 2005). This finding is in accordance with other studies recommending meat/by-products, dairy, fermented/ salted food, starch and beverage consumption as a risk factor for oral cancer (Helen et al., 2012; Amtha et al., 2014). Therefore it is necessary to increase awareness and correct dietary culture of people in this region to reduce this type of cancer.

One of the limitations of this study was impossibility

of conducting meta-analysis and estimating oral cancer prevalence rate in Iran due to problems and failure to correctly report the results or methodological problems of studies. Therefore it is recommended to researchers of this field to help this issue by overcoming these disadvantages in their future research and estimating oral cancer prevalence rate in Iran.

In conclusion, This study has drawn data from published articles which differ in study designs, to describe the scenario of epidemiology of oral cancer in Iran. Epidemiological pattern of oral cancer in Iran is somehow similar to that of other countries. This study can provide useful guidelines in order to minimize population's exposure to risk factors. Unfortunately amount of available information in this field is limited. Therefore there is a need for conducting studies with correct methodological pattern in this field is felt. For we need accurate information for making decision and planning in this field..

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