

## RESEARCH ARTICLE

# Time Trend Analysis of Oral Cancer in Iran from 2005 to 2010

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### Abstract

**Background:** There is a considerable lack of understanding of oral cancer incidence, especially its time trend in Iran. In this study, the authors aimed to analyze time trend of oral cancer incidence with a focus on differences by gender in a period of six years - from 2005 to 2010. **Materials and Methods:** Both population-based cancer registry and national cancer registry (NCR) data based on pathologic reports from 2005 to 2010 were obtained from the Ministry of Health and Medical Education (MOHME). Population data were also received from Statistical Centre of Iran. Age-standardized incidence rates (ASRs) based on the World Standard Population were then calculated. Finally, Negative Binomial regression was run for time trend analysis. **Results:** The maximum ASR for males was calculated as 2.5 per 100,000 person-years in 2008 and the minimum was observed as 1.9 per 100,000 person-years in 2005 and 2006. Meanwhile, the maximum ASR for females was estimated as 1.8 per 100,000 person-years in 2009 and the minimum was calculated as 1.6 per 100,000 person-years in 2005 and 2006. Additionally, in females, incidence risk ratio (IRR) did not show a clear decreasing or increasing trend during the six years. Nevertheless, in males an increasing trend was observed. The maximum IRR adjusted for age group and province, for females was reported in 2009 (IRR=1.05 95% CI: 0.90-1.23), and for males was estimated in 2010 (IRR=1.2 95% CI: 1.04 - 1.38). **Conclusions:** Our findings highlight disparities between oral cancer incidence trends in males and females over the six years from 2005 to 2010.

**Keywords:** Oral cancer - Iran - trend - epidemiology - incidence

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### Introduction

Oral cancer is the most prevalent cancer among the head and neck cancers (HNCs) (Dobrossy, 2005). Generally, cancers of the oral cavity and oropharynx, grouped together, supposed to be the sixth most common cancer in the globe (Ferlay et al., 2010) and considered as a global health problem (Warnakulasuriya, 2009b). They accounted for an estimated 400,000 incident cases and 223,000 deaths during 2008 (Chaturvedi et al., 2013). The highest incidence rate of oral cavity cancer is reported in Asia (Warnakulasuriya, 2009b; Rao et al., 2013) and certain parts of Africa (Warnakulasuriya, 2009b). In south-central Asia, oral cavity cancer is the third most common type of cancer. In India, the age standardized incidence rate of oral cancer is the highest in the world (Warnakulasuriya, 2009b) is reported as 12.6 per 100,000 populations (Petersen, 2009). Additionally, recent studies also have reported Sri Lanka and Pakistan as hot spots of oral cavity cancer (Warnakulasuriya, 2009b; Rao et al., 2013). Among Asian countries, there is a growing trend in India, Pakistan and Taiwan, and conversely a decreasing one for Sri Lanka and the Philippines (Rao et al., 2013).

Globally, oral cancer incidence among males is higher

than females (Rao et al., 2013), which traditionally would be due to higher smoking (Amtha et al., 2014) and alcohol consumption in males (Petersen, 2009). Tobacco use is the strongest risk factor, especially for oral cavity cancer (Simard et al., 2014). Two of the most frequent risk factors are tobacco (Warnakulasuriya et al., 2005; Khalili, 2008; Rao et al., 2013; Simard et al., 2014) and alcohol use (Tramacere et al., 2010; Warnakulasuriya, 2009a). According to a systematic review, tobacco use is a more important risk factor than alcohol consumption in oral cavity cancers (Radoi and Luce, 2013).

In Iran, ASR of HNCs has increased from 4.8 in 2003 to 7.4 per 100,000 in 2009 (Mirzaei et al., 2015). According to GLOBOCAN 2012 age-standardized incidence rate of lip and oral cavity cancer for males and females worldwide were estimated as 5.5 and 2.5 per 100,000 populations, respectively. Meanwhile, in Iranian males and females were calculated as 2.2 and 1.8 per 100,000 person-years in the same order (Ferlay et al., 2012). Moreover, a systematic review in Iran from 1990 to 2014, revealed male/female ratio as 1.91 for oral cancer (Maleki et al., 2015). In essence, lip and oral cavity cancer ranks as 13th for males and 16th for females among all cancers in Iranian population (Ferlay et al., 2012).

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There are few studies concerning time trend of oral cancer incidence in Iran (Mousavi et al., 2009; Razavi et al., 2012). In this study, the authors aimed a) to calculate age-standardized rates (ASRs) by year, gender and province, and b) to analyze time trend of oral cancer incidence with a focus on differences by gender in a period of six years-from 2005 to 2010-in Iran.

**Materials and Methods**

In our study, oral cancer includes totally ICD-10: C00-14: cancers of the lip, tongue and mouth (oral cavity) [ICD-10: C00-06], salivary glands [C07-08], oropharynx [ICD-10: C09-C10], and other pharyngeal sites [C11-14].

We have used both population-based cancer registry and national cancer registry (NCR) based on pathologic reports from 2005 to 2010. The data assembled by Ministry of Health and Medical Education (MOHME). After that, Duplicates were excluded. Population data was

also obtained from Statistical Centre of Iran. We used 2003 and 2006 census data and for estimating of the population in the other years used 1.29% average annual population growth rate in Iran (Iran, 2015).

All analyses were conducted separately among men and women and were run with Stata version 14. First, according to population and oral cancer data, crude rates were estimated by year, sex and province. Afterward, ASRs were calculated by year, sex and province based on the World (WHO 2000-2025) Standard Population. Although due to over dispersion using Poisson regression was rejected for time trend analysis, Negative Binomial regression was run instead.

**Results**

During this 6-year period, 9113 new cases were recorded. Number of new cases were counted up 5298 (58.13%) for males and 3815 (41.86%) for females;

**Table 1. Age-standardized Incidence Rate (per 100,000 person-years) of Oral Cancer by Gender, Year and Province**

Province	2005		2006		2007		2008		2009		2010		Geographical location
	F	M	F	M	F	M	F	M	F	M	F	M	
Markazi	0.8	1.4	0.9	1.1	0.8	1.6	1	1.8	1.5	1.7	1	2	Center
Gilan	1.7	2.8	1.2	2.1	1.1	2.6	0.9	1.7	1.7	2.1	2.3	2.4	North
Mazandaran	1.3	2.7	1.9	1.7	1.9	2.5	1.6	2.2	1.4	1.8	1.5	1.8	North
East Azarbaijan	1.1	1.7	0.5	0.6	2.4	3.9	2	3.5	2	3.4	1.6	2.3	Western North
West Azarbaijan	1.4	1.2	1.3	0.8	2	2	0.4	1.3	1.4	2.8	1.4	2.4	Western North
Kermanshah	1	2	1.7	1.8	2.1	2.7	1.7	2.3	1.1	2	0.7	2	West
Khouzestan	1.7	1.3	1.7	2.3	1.9	2.2	2.2	3.3	2.7	2.5	2.1	2.1	Western South
Fars	2	2.4	1.4	1.7	1.4	2.4	1.7	1.4	1.9	1.8	1.8	2.3	South
Kerman	1.5	1.2	1	1.9	2.1	0.7	1.4	2.1	2.1	3.6	1.9	1.7	South
North Khorasan	0.6	1.7	1.1	2.8	0.8	2.4	1.8	2.8	1	1.7	1.4	2.7	Eastern North
South Khorasan	1.1	0.3	1.5	1.5	1.1	1.3	1	1.6	1	1.1	1	1.8	East
Razavi Khorasan	1.3	1.8	1.7	2.8	1	2.6	2	1.3	1.4	1.9	2	2.8	East
Isfahan	2.2	1.7	1.3	1.9	2	2.5	1.2	1.6	1.8	2.2	1.6	1.7	Center
Sistan and baluchestan	1.5	1.4	1.8	2	1.9	2.5	2.3	2.6	2	2.2	3.5	2.1	Eastern South
Kordestan	1.1	2	1.4	1.5	0.7	1.9	2.1	2	1.2	2.9	0.8	3.8	West
Hamedan	0.6	1.5	1.6	1.5	1	2.2	1.5	1.9	1.2	2.1	0.9	2.4	West
Chaharmahal and bakhtiary	1	1.3	1.6	1	1	2	2	1.5	1.4	2.8	0.7	2.3	Center
Lorestan	1.2	1.4	0.7	1.9	1.1	1.7	0.5	2.2	0.8	2.4	0.7	1.6	West
Ilam	1.6	0.8	1.4	0.9	2.1	2.5	0.4	0.8	0.4	1.5	0.9	1.5	West
Kohgilue and buyer ahmad	0.5	3.5	0.5	1.3	2.3	2.6	1.1	1.7	0.8	2	0.3	3	Center
Boushehr	0.9	3.1	1.7	1.4	1.1	1.6	0.5	1.1	1.3	1.9	0.2	2.5	South
Zanjan	1.6	1.7	1.1	2.3	0.7	1.5	0.8	2.7	0.8	1	0.7	1.5	Center
Semnan	1	0.3	1.6	1.9	2.8	3.5	2.2	2.4	2.8	0.9	0.8	2.4	Center
Yazd	2.8	1.8	2.7	2.2	2.4	1.9	1.5	2	2.8	1.1	2.6	3.7	Center
Hormozgan	1.4	2.7	1.8	2.3	2	1.4	1.1	1.4	1.6	1.8	2.6	2.6	South
Tehran	1.9	2.5	2.1	2.3	1.7	2.7	2.3	3.2	1.9	2.8	2.2	3.1	Center
Ardebil	1.3	0.9	1.4	1.3	1	2.1	1.3	1.8	0.5	3.1	1.1	1.4	Western North
Qom	1.4	1.7	1.8	3.7	1.1	2.3	1.4	2.3	1.4	0.9	1	1.6	Center
Qazvin	2.3	2.6	2.8	1.3	1.5	2.8	2.6	1.5	1.5	2	2	2.4	Center
Golestan	0.5	1.2	0.5	1.8	1.9	1.3	1.4	2	2.3	1.9	1.7	2.4	North

\* Female = F, Male = M

therefore a 1.38 gender ratio was calculated.

The maximum ASR for males was calculated as 2.5 per 100,000 person-years in 2008 and the minimum was observed as 1.9 per 100,000 person-years in 2005 and 2006. Meanwhile, the maximum ASR for females was estimated as 1.8 per 100,000 person-years in 2009 and the minimum was calculated as 1.6 per 100,000 person-years in 2005 and 2006. In addition, ASRs in both genders showed a growing trend (Figure 1).

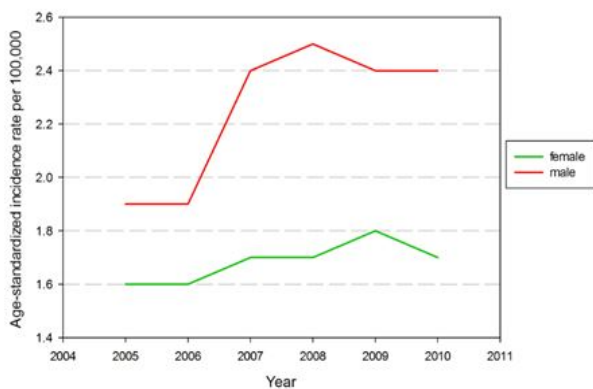
In both genders the maximum and minimum ASR were observed over 64 years and under 40 year age groups,

respectively. In males, ASR indicated a growing trend in over 64 years and 40 - 64 year age groups. However, ASR for patients under 40 years was stable during the 6-year period. Albeit in females, the same as males ASR for persons under 40 was in a stable condition, ASR in patients over 64 years and 40 - 64 years not revealed a specific increasing trend over the 6-year period (Figure 2).

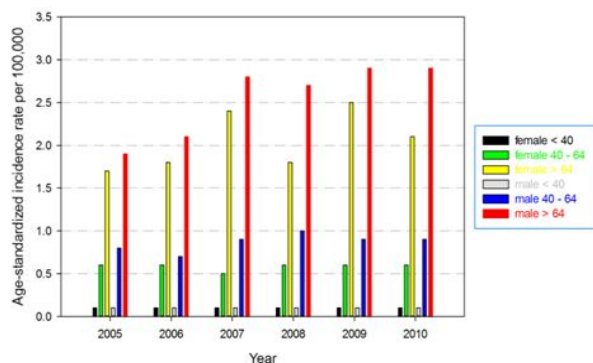
Table 1 indicated that the maximum and minimum ASRs for females were observed as 3.5 in Sistan and Baluchestan province and 0.2 per 100,000 person-years in Boushehr province both in 2010, respectively. However,

**Table 2. Time Trend Analysis of Oral Cancer Incidence by Gender**

Variable	Female		Male	
	IRR (95% CI)	P-value	IRR (95% CI)	P-value
<b>Year</b>				
2005	Reference	---	Reference	---
2006	0.79 (0.67 – 0.93)	< 0.001	0.83 (0.72 – 0.97)	0.02
2007	1.03 (0.88 – 1.21)	0.63	1.19 (1.03 – 1.37)	0.01
2008	0.96 (0.82 – 1.12)	0.65	1.18 (1.03 – 1.36)	0.01
2009	1.05 (0.90 – 1.23)	0.49	1.19 (1.03 – 1.37)	0.01
2010	0.99 (0.85 – 1.16)	0.95	1.20 (1.04 – 1.38)	0.01
<b>Age group (year)</b>				
< 40	Reference	---	Reference	---
40 - 64	8.30 (7.41 – 9.30)	< 0.001	9.56 (8.64 – 10.58)	< 0.001
> 64	27.73 (24.70 – 31.14)	< 0.001	27.31 (24.61 – 30.32)	< 0.001
<b>Province</b>				
Markazi	Reference	---	Reference	---
Gilan	1.49 (1.01 – 2.18)	0.04	1.43 (1.04 – 1.98)	0.02
Mazandaran	1.59 (1.09 – 2.32)	0.01	1.32 (0.96 – 1.82)	0.08
East Azarbaijan	1.63 (1.12 – 2.36)	< 0.001	1.66 (1.22 – 2.27)	< 0.001
West Azarbaijan	1.30 (0.88 – 1.92)	0.17	1.08 (0.78 – 1.50)	0.62
Kermanshah	1.39 (0.92 – 2.09)	0.11	1.29 (0.92 – 1.81)	0.13
Khuzestan	2.05 (1.42 – 2.95)	< 0.001	1.48 (1.08 – 2.02)	0.01
Fars	1.74 (1.21 – 2.51)	< 0.001	1.30 (0.95 – 1.77)	0.09
Kerman	1.73 (1.17 – 2.53)	< 0.001	1.14 (0.82 – 1.60)	0.4
North Khorasan	1.12 (0.67 – 1.88)	0.65	1.44 (0.97 – 2.14)	0.06
South Khorasan	1.10 (0.65 – 1.85)	0.71	0.77 (0.48 – 1.23)	0.28
Razavi Khorasan	1.72 (1.31 – 2.48)	< 0.001	1.84 (1.23 – 2.68)	< 0.001
Isfahan	1.70 (1.18 – 2.45)	< 0.001	1.24 (0.91 – 1.69)	0.16
Sistan and baluchestan	2.12 (1.43 – 3.13)	< 0.001	1.24 (0.88 – 1.75)	0.2
Kordestan	1.20 (0.77 – 1.86)	0.4	1.45 (1.03 – 2.06)	0.03
Hamedan	1.12 (0.73 – 1.71)	0.59	1.21 (0.85 – 1.71)	0.27
Chaharmahal and bakhtiary	1.27 (0.77 – 2.08)	0.33	1.06 (0.70 – 1.60)	0.77
Lorestan	0.77 (0.48 – 1.23)	0.28	1.16 (0.81 – 1.65)	0.39
Ilam	0.71 (0.35 – 1.44)	0.34	0.77 (0.45 – 1.30)	0.33
Kohgilue and buyer ahmad	0.87 (0.46 – 1.64)	0.68	1.41 (0.92 – 2.16)	0.1
Boushehr	0.90 (0.52 – 1.57)	0.73	1.26 (0.84 – 1.88)	0.25
Zanjan	0.79 (0.46 – 1.34)	0.39	1.10 (0.74 – 1.64)	0.61
Semnan	1.85 (1.15 – 2.96)	0.01	1.16 (0.75 – 1.80)	0.48
Yazd	2.46 (1.63 – 3.70)	< 0.001	1.35 (0.93 – 1.97)	0.11
Hormozgan	1.74 (1.14 – 2.66)	0.01	1.20 (0.83 – 1.73)	0.32
Tehran	2.17 (1.53 – 3.07)	< 0.001	1.82 (1.36 – 2.43)	< 0.001
Ardebil	1.05 (0.66 – 1.67)	0.82	1.10 (0.75 – 1.60)	0.6
Qom	1.30 (0.81 – 2.08)	0.26	1.32 (0.90 – 1.93)	0.15
Qazvin	2.13 (1.40 – 3.22)	< 0.001	1.32 (0.91 – 1.92)	0.13
Golestan	1.47 (0.96 – 2.23)	0.07	1.11 (0.77 – 1.59)	0.56



**Figure 1. Trend of Oral Cancer Age-standardized Incidence Rate (per 100,000 person-years) by Gender During 2005 to 2010**



**Figure 2. Age-standardized Incidence Rate (per 100,000 person-years) of Oral Cancer by Gender and age Group During 2005 to 2010**

for males the maximum was calculated in 2007 as 3.9 per 100,000 person-years in East Azarbaijan and the minimum were estimated in 2005 as 0.3 per 100,000 person-years in South Khorasan and Semnan provinces.

Using Negative Binomial regression, time trend of oral cancer incidence was investigated separately for males and females. The analyses were adjusted for age group and province. We also set year 2005 as the reference group. In females, incidence risk ratio (IRR) not showed a specific decreasing or increasing trend. Nevertheless, in males an approximately increasing trend was observed (Table 2). The maximum IRR adjusted for age group and province, for females was reported in 2009 (IRR=1.05 95% CI: 0.90-1.23), and for males was estimated in 2010 (IRR=1.2 95% CI: 1.04-1.38). Furthermore, the interaction between year and province was checked, however, it was not statistically significant.

## Discussion

In this study, the authors aimed to analyze time trend of oral cancer incidence in Iran for a six-year period from 2005 to 2010. According to Negative Binomial regression, the results indicated that even though oral cancer incidence showed an increasing trend for males, there were not any clear trends for females.

Oral cancer consisted of approximately a variety of definitions; different sites of oral cavity and pharynx make this variation. In some studies all sites of oral cavity and pharynx, altogether, cited as oral cancer (Warnakulasuriya,

2009b). In this study oral cancer definition includes totally ICD-10: C00-14: cancers of the lip, tongue and mouth (oral cavity) [ICD-10: C00-06], salivary glands [C07-08], oropharynx [ICD-10: C09-C10], and other pharyngeal sites [C11-14]. Since oral health considered as a noteworthy part of general health, WHO Global Oral Health Programme was run as one of the technical programmes within the Department of Prevention of Noncommunicable Diseases (PND). The objectives of the programme are developing global policies in oral health promotion and oral disease prevention. It was believed that oral diseases and conditions, including oral cancer, have a considerable effect on oral health (Petersen, 2005). Some sun-national studies in Iran, worked on trends of cancers generally, and their results have showed an increasing trend in incidence of different cancers (Keyghobadi et al., 2014; Zahedi et al., 2014). In general, there are numerous studies concerning trend analysis of oral cancer in different parts of the globe (Kingsley et al., 2008; Bezerra de Souza et al., 2012; Antunes et al., 2013; Ariyawardana and Johnson, 2013; Hernandez-Guerrero et al., 2013; Guo et al., 2013; Auluck et al., 2014; Braakhuis et al., 2014). Simard et al. (2014) studied international trend of HNC incidence rate and found incidence rate of oral cavity cancer might be effect of tobacco use. In fact, countries with high prevalence in tobacco use suffer high incidence, by contrast, countries with high prevalence at the time showed a cut in incidence rate (Simard et al., 2014). Moosazadeh et al. (2013) conducted a meta-analysis study on smoking prevalence in Iran. As results, prevalence of smoking in Iranian males and females from 2001 to 2012 was estimated as 21.7% and 3.6%, respectively. However, they had not observed a completely marked trend for smoking prevalence (Moosazadeh et al., 2013). Therefore, in our study high incidence of oral cancer in males might be due to the high prevalence of smoking in this group. Although we have reported a statistically significant increase in oral cancer incidence rate for males, Moosazadeh et al, had not reported a clear trend in smoking prevalence. Monteiro et al. (2013) studied trend of oral, lip and oro-pharyngeal cancers in Portugal. Their study indicated a rising trend for oral and oro-pharyngeal cancers for both genders in Portugal form 1998 to 2007. They believed this might be due to high tobacco and alcohol consumption in the last decades (Monteiro et al., 2013). Razavi et al. (2012) conducted a retrospective analytic study to investigate trend of oral cancer incidence rate in Isfahan, Iran, from 1991 to 2010. Indeed, they analyzed separately different sites of mouth. They have found oral carcinomas had a growing trend, though, not statistically significant (Razavi et al., 2012). Chaturvedi et al. (2013) studied the global trends in incidence rate of oral cavity and oropharyngeal cancers. As results, they have observed a significantly increasing trend in oropharyngeal cancer (OPC) especially in developed countries from 1983 to 2002. Furthermore, in females there was an attendant trend in incidence of oral cavity cancer (OCC) (Chaturvedi et al., 2013). McGorray et al. (2012) worked on trends in incidence oral and pharyngeal carcinoma in Florida form 1981 to 2008. According to their results, oral cancer showed a decreasing trend for both genders. Even though,

pharyngeal cancer indicated a growing trend in males, suggested a decreasing trend in females (McGorray et al., 2012). Van Monsjou et al. (2013) studied incidence of head and neck squamous cell carcinoma (HNSCC) in young patients-younger than 45 years old. They believed risk of HNSCC in the young, might be per se under the influence of genetic susceptibility factors, or a blend of extrinsic risk factors-human papilloma virus (HPV) (van Monsjou et al., 2013).

The first shortcoming of this study could be coverage rate of the cancer registry. There might be some cases of oral cancer that have not been registered by MOHME. Secular trend in cancer studies is another important issue. Hence, perhaps a six-year period is roughly short to analyzing the incidence trend. In addition, comparison of researches especially in risk factor studies might be challenged due in part to variation in oral cancer definitions (Radoi and Luce, 2013).

In conclusion, our findings highlight disparities between oral cancer incidence trend in males and females for six years. This research could pave the way for the study of the etiology and consequently we believe further research in the future is needed to establish the etiology of oral cancer in Iran, especially in hot spots.

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