Oral cancer incidence trends in Delhi (1990–2014): An alarming scenario

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Abstract
Background: Oral cancer ranks in the top three of all cancers in India, which accounts for over 30% of all cancers reported in the country, and oral cancer control is quickly becoming a global health priority. We have conducted an age period analysis of oral cancer incidence trends using the Population-Based Cancer Registry (PBCR) data in Delhi over a 24-year period (1990–2014) to address the trends of one of the leading cancer sites in Delhi.

Materials and Methods: The data of oral cancer proportion and incidence for the year 1990–2014 were taken from Delhi PBCR which records cancer cases from more than 180 government and 250 private facilities. The data were segregated by sex, age, and anatomical site and were analyzed to calculate age-specific incidence rates and expressed in cases per 100,000 persons/year. Results: The highest incidence for both genders was seen in the age group 50–59 years and the lowest incidence was in the youngest age group (<20 years) for all the years from 1990 to 2014. The relative proportion of oral cancer among all types of cancer in Delhi has shown alarming rise from the year 2003 onward.

Conclusion: Increasing relative proportion of oral cancer can be implicated in increased consumption of gutkha chewers in the last decade of the 20th Century. As access to health-care services and cancer-related awareness is highly variable in India, more in-depth analysis of the incidence of oral cancer in rural regions will be required.

Key words: Delhi, incidence, oral cancer

Introduction
Oral cancer (including cancers of the mouth, lip, and tongue) is a major public health problem in certain regions of Europe, Latin America, and Asia, including India where it ranks as one of the leading cancer sites among men and women in many regions. Major risk factors for oral cancer are the use of tobacco, betel quid, and alcohol. Although existing tobacco and alcohol control policies, mouth cancer incidence has been increasing in most population-based cancer registries (PBCRs) in India. In a country such as India, where access to health-care services and cancer-related awareness is highly variable, changes in incidence rates should be interpreted carefully. A more in-depth analysis of important underlying factors related to age, gender, and period for these trends can yield information for planning rationale cancer control programs. We conducted an age period analysis of oral cancer incidence trends using the PBCR data in Delhi over a 24-year time period (1990–2014) to address the trends of one of the leading cancer sites in Delhi and to better understand the differences by gender and age.

Materials and Methods
A number of cases of cancer of oral cavity were obtained for the period 1990–2014 from Delhi PBCR. Delhi PBCR was established by the Indian Council of Medical Research (ICMR) in January 1986, at the All India Institute of Medical Sciences, with the objective of generating reliable data on the magnitude, trends, and patterns of cancers in Delhi. Delhi PBCR records cancer cases from more than 180 government and 250 private facilities. The records are compiled by the National Cancer Registry Program (NCRP) of ICMR, and data are available in public domain.

The data were segregated by sex, age, and anatomical site based on the World Health Organization International Classification of Diseases for Oncology, 3rd edition (ICDO-3). We extracted information on all incident cases of cancer of the lip (C00), tongue (C01–C02), and mouth (C03–C06); gingiva (C03), floor of the mouth (C04), palate (C05), cheek mucosa, vestibule, retromolar area, and other unspecified parts of the mouth (C06). Participants were categorized into 5–10-year age groups (<20, 20–29, 30–39, 40–49, and 50–59 years). Cases above 59 years of age were excluded from the study due to less complete and accurate diagnostic data in older persons (60 + years).

The relative proportion of oral cancer among all types of cancer [Table 1] in Delhi has shown alarming rise from the year 2003 onward. We have observed a steady situation in oral cancer proportion from the year 1990 to 2003. However, during the last decade, the oral cancer incidence proportion has shown almost 150% increase, thus, making oral cancer the most common type of cancer in Delhi.

Results
The relative proportion of oral cancer among all types of cancer [Table 1] in Delhi has shown alarming rise from the year 2003 onward. We have observed a steady situation in oral cancer proportion from the year 1990 to 2003. However, during the last decade, the oral cancer incidence proportion has shown almost 150% increase, thus, making oral cancer the most common type of cancer in Delhi.

Oral cancer (International Classification of Diseases for Oncology-C00-C06)
Age-specific incidence rates of oral cancer for different age groups and for both gender populations are presented for the Delhi region in Graphs 1 and 2. In males, the highest incidence of oral cancer was seen in 50–59-year age group for the year 2012–2014. The lowest incidence was seen below 20-year age group for the year 2006–2008. In females, the highest incidence of oral cancer was seen in 50–59-year age group for the year 2012–2014. The lowest incidence was seen below 20-year age group for the year 1990–1996.

Lip cancer: (International Classification of Diseases for Oncology-C00)
In males, the highest incidence was seen in 50–59-year age group for the year 2006–2008. The lowest incidence was seen below 20-year age group for the year 1997–1998 and...
2001–2008. It was also seen in the age group of 20–29 years for the year 1999–2003. In females, the highest incidence was seen in 50–59-year age group for the year 2012–2014. The lowest incidence was seen below 20-year age group for the year 1990–2000, 2004–2008, and 2012–2014. For the age group of 20–29 years, it was seen in the year 1990–2003 and 2009–2011. For the age group of 30–39 years, it was seen in the year 1990–1996, 1999–2000, and 2006–2008 [Table 2].

**Tongue cancer: (International Classification of Diseases for Oncology-C01-C02)**

In males, the highest incidence was seen in 50–59-year age group for the year 2006–2008. The lowest incidence was seen below 20-year age group for the year 2001–2011. In females, the highest incidence was seen in 50–59-year age group for the year 2012–2014. The lowest incidence was seen below 20-year age group for the year 1990–1996, 1999–2000, and 2004–2005 [Table 2].

**Mouth Cancer: (International Classification of Diseases for Oncology-C03-C06)**

In males, the highest incidence was seen in 50–59-year age group for the year 2012–2014. The lowest incidence was seen below 20-year age group for the year 1990–1996. In females, the highest incidence was seen in 50–59-year age group for the year 2012–2014. The lowest incidence was seen below 20-year age group for the year 1990–1998, 2006–2008, and 2012–2014. For the age group of 20–29 years, it was seen in the year 1990–1996 [Table 2].

**Discussion**

A significant increasing trend in oral cancer relative proportion rate in Delhi among all cancer sites from 2004 to 2014 has been observed which is also coordinating with the steady increase in the incidence of oral cancer (lip, tongue, and mouth) among males and females from 2004 to 2014 in all the age groups. Analysis of Delhi PBCR reports has revealed a direct relation of increasing incidence of oral cancer with age, the highest incidence for both genders was seen in the age group 50–59 years, and the lowest incidence for both genders was in youngest age group (<20 years) for all the years from 1990 to 2014.

Similar trends among men and women have been reported by other PBCRs in India. NCRP data from Mumbai show a steep increase of mouth cancer incidence in men from 1999 to 2009 (3.3% each year) and a slight increase among women from 2002 to 2009. South Asian countries such as India, Sri Lanka, Pakistan, Bangladesh, and Taiwan report the highest incidence rates of oral cancer in the World due to betel quid and tobacco chewing habits, coupled with low

**Table 1: Relative proportion of cancer among all sites**

| Site specific (years) | 1990–1996 | 1997–1998 | 1999–2000 | 2001–2003 | 2004–2005 | 2006–2008 | 2009–2011 | 2012–2014 |
|-----------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Lip                   | 0.38      | 0.36      | 0.2       | 0.31      | 0.46      | 0.69      | 0.69      | 0.7       |
| Tongue                | 6.03      | 5.58      | 6.44      | 6.92      | 7.08      | 8.63      | 8.27      | 8.5       |
| Mouth                 | 4.92      | 5.29      | 4.62      | 4.65      | 6.2       | 6.36      | 7.64      | 9.15      |
| Oral cancer incidence | 11.33     | 11.23     | 11.26     | 11.88     | 13.74     | 15.68     | 16.6      | 18.35     |

*National Cancer Registry Programme: Indian Council of Medical Research, Bangalore*

**Table 2: Cancer incidence of lip, tongue, and mouth in males and females for the years (1990–2014) from Delhi registry in India**

| Year wise registry Gender | Below 20 | 20–29 | 30–39 | 40–49 | 50–59 |
|---------------------------|----------|-------|-------|-------|-------|
| **L** | **T** | **M** | **L** | **T** | **M** | **L** | **T** | **M** | **L** | **T** | **M** | **L** | **T** | **M** | **L** | **T** | **M** | **L** | **T** | **M** |
| 1990–1996 Male | 1 | 0.2 | 0 | 0.1 | 0.6 | 0.3 | 0.2 | 4 | 2 | 13.8 | 7.7 | 1.7 | 39.2 | 19.5 |
| Female | 0 | 0 | 0 | 0 | 0.4 | 0 | 0 | 1.4 | 0.8 | 0.4 | 5.2 | 3.7 | 0.1 | 12.9 | 9.2 |
| 1997–1998 Male | 0 | 0.3 | 0.1 | 0.3 | 0.8 | 0.4 | 2.5 | 2.5 | 0.3 | 15.4 | 10.2 | 2 | 29.3 | 19 |
| Female | 0 | 0 | 0 | 0 | 0.2 | 0.2 | 0.3 | 0.3 | 0.4 | 1.8 | 0.2 | 3.9 | 5.2 | 0.7 | 10.7 | 8.6 |
| 1999–2000 Male | 0 | 0.1 | 0.2 | 0 | 0.8 | 0.7 | 0.3 | 3.3 | 3.2 | 0.3 | 13.5 | 9.1 | 1 | 42.7 | 21.9 |
| Female | 0 | 0 | 0 | 0.1 | 0.3 | 0.5 | 0 | 0.9 | 2 | 0.2 | 4.9 | 4.7 | 0.7 | 11.9 | 13.8 |
| 2001–2003 Male | 0 | 0.1 | 0.2 | 0 | 0.7 | 0.6 | 0.3 | 3.3 | 3.1 | 0.9 | 16.1 | 10.7 | 0.5 | 41.7 | 21.9 |
| Female | 0.1 | 0.1 | 0.2 | 0 | 0.4 | 0.3 | 0.1 | 1.3 | 1.7 | 0.5 | 7.2 | 4.1 | 1 | 10.1 | 8.6 |
| 2004–2005 Male | 0 | 0.1 | 0.2 | 0.1 | 0.9 | 0.9 | 0.2 | 5.5 | 4.7 | 0.9 | 17 | 14 | 1.5 | 38.8 | 31.5 |
| Female | 0 | 0 | 0 | 0.1 | 0.2 | 0.2 | 0.5 | 0.1 | 0.8 | 0.9 | 0.9 | 4.7 | 0.7 | 15 | 12.2 |
| 2006–2008 Male | 0 | 0.1 | 0.1 | 0.2 | 1.3 | 1.2 | 0.4 | 6 | 6.1 | 1.7 | 17.4 | 16.8 | 4.6 | 54.6 | 37 |
| Female | 0 | 0.2 | 0 | 0.1 | 0.2 | 0.4 | 0 | 1 | 1 | 0.6 | 6.2 | 4 | 1.2 | 12.1 | 10.8 |
| 2009–2011 Male | 0.2 | 0.1 | 0.1 | 0.3 | 1.4 | 1.8 | 0.7 | 6.5 | 8.3 | 1.3 | 19.2 | 17.8 | 2.6 | 43.9 | 46.6 |
| Female | 0.1 | 0.2 | 0.1 | 0 | 0.5 | 0.7 | 0.4 | 1.4 | 1.5 | 0.6 | 5.4 | 6.3 | 0.3 | 16.2 | 11.6 |
| 2012–2014 Male | 0.2 | 0.2 | 0.1 | 0.2 | 1.6 | 2.4 | 0.3 | 11.5 | 14.2 | 1.7 | 25.7 | 30.5 | 3.6 | 44.3 | 55.1 |
| Female | 0.2 | 0 | 0.1 | 0.1 | 1.1 | 1.9 | 0.2 | 2.3 | 2.6 | 0.9 | 7.4 | 7.1 | 1.5 | 19.1 | 19.9 |

*National Cancer Registry Programme: Indian Council of Medical Research, Bangalore*
awareness, and health-care access. While Sri Lanka in recent years has shown a decreasing trend of oral cancers of about 1.9% per year ($P < 0.05$), in both men and women,[8] Taiwan[9] and Pakistan[10] have consistently showed increasing trends in both men and women. Among European countries with high incidence of oral cancer, rates in France and Slovakia have been decreasing among men and increasing among women.[11,12] Oral cancer trends have been decreasing in both men and women in all other developed countries except United Kingdom, Denmark, and the Netherlands, which show increases in recent years.[11,13,14] The decline in oral cancer incidence trends in these high-income regions is consistent with increased awareness and decline in tobacco use.[15]

Out of all cancers, tobacco-related cancer accounts for the major share. According to the World Health Organization (WHO), nearly 6 million deaths occur every year due to tobacco use, which may escalate to 8 million deaths a year by 2030.[15] India has one of the highest tobacco users in the world both in number and relative share. Tobacco is used in India in many forms such as smoking of cigarettes and beedis, chewing pan, chewing gutkha, or pan masala. India is one of the fewer countries in the world where prevalence of smoking and smokeless tobacco use is high and is characterized by dual use of tobacco (use of both smoking and smokeless tobacco products).

According to the recent National family health survey-4 study for the year 2015–2016, there were 38.9% of men who use any tobacco in urban while 48% in rural areas of India. On the other hand, 4.4% of women in urban and 8.1% in rural use any kind of tobacco. Prevalence of tobacco use in the ages of 13–15 among boys was 19% and girls 8.3% according to global youth tobacco survey of 2009.[16] Stringent tobacco control policies and programs have been in place in India since 2004, including advertisements to be restricted only to point-of-sale, prohibition of the sale of tobacco products to children <18 years of age and near educational institutions, health warnings, and declaration of product contents on packs.[3]

The emergence of newer, chewable flavored forms of tobacco along with several other ingredients, called gutkha has changed the trends in the tobacco market.[17] Gutkha contains areca nut, slaked lime, catechu, condiments, and powered tobacco. Gutkha has been commercially available since 1975.[18] Gutkha is exported to 22 countries worldwide, this shows its spreading usage. Numerous brands of pan masalas and gutkhas are being advertised and sold in Indian markets without impunity in the name of flavor, fragrance, and freshness. Due to its flavored taste, easy availability, and cheapness, it is popular among poor children. Gutkha is sold as loose or in small pouches. The market of Gutkha in India is about the worth of INR150bn-INR200bn.[19] Five million children in India are estimated to be addicted to gutkha, who are under the age of 15 years.[19] Gutkha is found to have 3095 chemical ingredients, of which 28 are proven carcinogens. We suspiciously assume the Gutkha as the main culprit, in causing the steep increase of oral cancer incidence proportion as Gutkha gained its popularity in Delhi region in the last decade of the 20th Century.

Based on several reports indicating health hazards caused, efforts are undertaken to ban the production, consumption, sale, storage, and transportation of gutkha and pan masala by many states in India. Tamil Nadu banned gutkha in 2001 followed by Andhra Pradesh, Goa, Maharashtra, and Rajasthan in August 2002. Until May 2013, 26 states had banned gutkha. Gutkha is banned under the provision to ban any food product containing harmful adulterants in the centrally enacted Food Safety and Regulation (Prohibition) Act 2011.

Recognizing the significance of tobacco cessation, 13 tobacco cessation clinics were started in 2002 by the Ministry Of Health and Family Welfare, Government of India, with the support of the WHO India Country Office, and were increased to 19 to provide tobacco cessation interventions. To strengthen implementation of the tobacco control provisions the Government of the India piloted National Tobacco Control Program in 2007–2008. The program is under implementation in 21 out of 35 States/Union territories in the country. National Guidelines for Treatment of Tobacco Dependence have also been developed and disseminated by the Government in 2011, to facilitate training of health professionals in tobacco cessation.[15] With these recent developments in tobacco control, the incidence of mouth cancers was expected to decrease. However, to date, the enforcement of these policies has been weak or insufficient[6] which is reflected in the increasing trend observed in our study.

**Conclusion**

The increasing trends of oral cancer that we observed in Delhi, and in both men and women have underscore the public health importance of targeted programs to decrease the prevalence of risk factors in young men and women, as Delhi continues to observe increase in the rate of oral cancer.

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**Conflicts of interest**

There are no conflicts of interest.

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Results and Discussion

In all the four cases, CML was suspected on the basis of complete history, general physical examination, and laboratory investigations. Using multiplex RT-PCR, an unexpected band at 230 bp [Figure 1] was obtained from all the patients.

Sequencing of the amplified product was performed as per the instructions of The BigDye® Terminator v3.1 Cycle Sequencing Kit (ABI, Japan) reagents (Applied Biosystems). The samples were placed in autosampler tray, and the purified reaction product was electrophoresed at 50°C in ABI 310 genetic analyzer. At the end of the run, the sequence was analyzed with sequence analysis software which confirmed b2a3 fusion transcript. On the basis of these findings, CML with b2a3 fusion transcript was suspected, and DNA sample from these four patients was tested in our laboratory for BCR-ABL translocation and BCR/ABL a3 type transcripts may have a better prognosis with BCR/ABL a3 type transcripts lack part of the ABL SH3 domain, which is present in the BCR-ABL-positive patients.

Multiplex RT-PCR which is used in our laboratory for the detection of characteristic PS findings. Using multiplex RT-PCR, an atypical fusion transcript was suspected, and DNA sample from these four patients was tested in our laboratory for BCR-ABL translocation. This method allowed us a reliable detection of typical BCR-ABL breakpoints in CML patients. This is also supported by literature that there is a frequency of b2a3 variant transcript was 0.9% among all of CML type transcripts lack part of the ABL SH3 domain, which is present in the BCR-ABL-positive patients.

In a total of 1350 BCR-ABL-positive CML patients, 4 (0.01%) samples showed this rare b2a3 fusion transcript encoding a 203-kDa protein. The other rare fusion transcript e19a2 encoding a 230-kDa protein has also been reported in 0.30% of cases of CML patients. In our study, two rare fusion transcripts e2a2 (125 bp) and e19a2 (808 bp), and e1a2 (310 bp) was negative, but it showed a positive band at 203 bp. It is likely that the large size of e19a2 (808 bp) makes it difficult to amplify using multiplex RT-PCR which is used in our laboratory for the detection of characteristic PS findings. Using multiplex RT-PCR, an atypical fusion transcript was suspected, and DNA sample from these four patients was tested in our laboratory for BCR-ABL translocation. This method allowed us a reliable detection of typical BCR-ABL breakpoints in CML patients. This is also supported by literature that there is a frequency of b2a3 variant transcript was 0.9% among all of CML type transcripts lack part of the ABL SH3 domain, which is present in the BCR-ABL-positive patients.

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One of the modifications of RT-PCR is nested multiplex RT-PCR. It is possible that the nested multiplex RT-PCR may fail to detect certain rare BCR-ABL fusion transcript type, as many commercially available and laboratory-developed primer sets do not cover such rare fusion transcript type.