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High Level of Estrogen in Male Oral Cancer Patients and Consumption of Smokeless Tobacco

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Abstract: *Oral cancer is the most common form of cancer and cancer-related deaths among Indian males. 70–75% of these cases are due to chewing tobacco. Estrogen and testosterone both are an important hormone for male and female. Estrogen has an important role in the development of breast cancer, ovarian cancer etc. There are very few studies available which describe the increased oral cancer incidence and level of estrogen in male oral cancer patients and use of smokeless tobacco consumption among the same type of cancer patients. Therefore, the present study has been aimed to find out the prevalence of oral cancer due to consumption of smokeless tobacco, sub-site distribution and level of estrogen in the oral cancer patients in Bihar.* In the present study 126 patients suffering from oral cancer were selected randomly. The background data obtained were categorized into sex-wise as well as age-wise oral cancer incidence, carcinoma site, frequency of oral cancer and the type of tobacco addiction among the surveyed oral cancer patients. Estrogen level in male oral cancer patients was assessed by ELISA-kit method. Addiction of khaini among all of the smoke and smokeless tobacco consuming persons in Bihar was found higher. Prevalence of oral cancer was four times higher in male patients than the female and the level of estrogen hormone in male oral cancer patients were found elevated. In conclusion, high oral cancer incidence has been observed among people of Bihar. Most popular form of smokeless tobacco is khaini mainly used by illiterate people. Elevated level of estrogen hormone in male oral cancer patients may be associated with the increased incidence of oral cancer among people of Bihar. It may further provide some evidence to understand the whole mechanism of oral cancer.

Keywords: Oral cancer, Estrogen, Smokeless tobacco, ELISA

Introduction

Oral cancer is the most common form of cancer and cancer-related deaths among Indian males. India accounts for 86% of the world's oral cancer cases, according to the study conducted in February 2011 by the National Institute of Public Health. Ninety percent of these cases are due to chewing tobacco, unlike in the west countries where smoking is the main reason. Furthermore, globally oral cancer accounts for 267,000 new cases and 128,000 deaths of which two- third cases are contributed by the developing countries (Parkin *et al*., 2002). Nearly, 8 million deaths annually are expected by 2030 due to tobacco consumption around the world (WHO, 2014). More than 50% oral cancer occur due to consumption of smokeless tobacco in India (Boffetta *et al*., 2008) and it has been shown to associate with cancers of the lip, oral cavity, pharynx, digestive, respiratory and intrathoracic organs (Pednekar *et al.,* 2011). Estrogen and testosterone both is an important hormone for male and female. Estrogen has an important role in the development of breast cancer, ovarian cancer etc. It binds with estrogen receptor α (ER α) and β (ER β) and forms a complex. This hormone-receptor complex then binds

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to the DNA which led to DNA damage or cell division of the cells.

Use of smokeless tobacco in some part of the India is acceptable mainly in Eastern, Northern and North- eastern parts of the country. Only 20% of the tobacco consumed by weight is consumed as cigarettes, 40% consumed as bidi and the rest in smokeless form (WHO 1997). In India, at least 800,000 deaths every year are related to tobacco use, out of which 700,000 are related to smoking (Reddy and Gupta, 2004). The prevalence of use of tobacco was reported to be much higher in the North-eastern states compared to other parts of India (IIPS and ORC 2000). Bihar is situated in the eastern region of India between 83^0 -30' to 88^0 -00' longitude. Geographical area of Bihar is of 38,202 sq mi (98,940 km^2) and it is a 3rd largest state by population. Due to cheap labour cost mainly, Bihar is the 6^{th} largest tobacco producing state in India. 90% population of Bihar depends upon agriculture. The land is fertile and produces several types of agricultural products including tobacco. Tobacco plays a significant role in the development of state's economy. The tobacco use is very prominent in Bihar. According to Global Adult Tobacco Survey (2009-10), 26% Indians aged 15 and above use smokeless tobacco products. In India, khaini, gutka, betel quid with tobacco, powdered tobacco snuff and other smokeless tobacco were used by 11.6%, 8.2%, 6.2%, 4.7% and 4.4% respectively (IIPS, 2009). There are Very few studies available which correlate the high incidence of oral cancer with high level of estrogen in male oral cancer patients and use of smokeless tobacco consumption among the same type of cancer patients. Therefore, the present study has been designed to find out the prevalence of oral cancer due to consumption of smokeless tobacco, sub site distribution and level of estrogen in the oral cancer patients in Bihar.

Materials and Methods

This is a Hospital record data based study of the Oral cancer patients, visiting Mahavir Cancer Sansthan Hospital from different districts of Bihar. In this study 126 patients suffering from oral cancer were selected randomly. The data obtained were categorized into sex-wise as well as age-wise oral cancer incidence, carcinoma site, frequency of oral cancer and the type of tobacco addiction among the surveyed oral cancer patients.

Tobacco use was broadly classified into four categories; smokeless, smoker, mixed (smokeless tobacco users as well as smokers) and non users. Smokeless tobacco uses include Gutka (an industrially manufactured tobacco product, containing areca nut, tobacco and other ingredients), Khaini (tobacco-lime mixtures), Pan and Betel quid (containing fresh betel leaf, lime, catechu, areca nut and tobacco.) which are very common in Bihar and other parts of the India. Estimation of estrogen in serum was done in 18 male oral cancer patients by the ELISA kit method.

Results and Discussion

Over the past several centuries, tobacco has been used in India. People use tobacco in two forms mainly i.e. smokeless or smoking tobacco. Smoked tobacco includes cigarette, bidi, cigars etc. and smokeless tobacco contains khaini, gutaka, pan with tobacco, pan masala etc. People with lower economic status usually use these form of smokeless tobacco. It has been observed that most susceptible period of tobacco use is early childhood in India (WHO 2012). According to WHO, nearly 250 million adults consume smokeless tobacco in 11 countries of South-East Asia region which contributes 90% of total global smokeless tobacco users (WHO 2014). Use of smokeless tobacco has been associated with the increased risk of oral cancer. Khaini is the most common form of smokeless tobacco used among less educated or illiterate people in India. At the beginning of the study, we found that oral cancer is the most common in the man of middle aged group between 50–60 years. Almost similar finding has been seen in

India as well as in different parts of the world (Murthy *et al.,* 2011; Petit, 2003). Smokeless form of tobacco use was predominant, and majority of the oral precancers were detected in employees using the smokeless form in a recent study (Uplap, *et al*., 2011)

In the present study, out of 126 oral cancer patients, 101 male and 25 female oral cancer patients were found. Figure 1 shows that prevalence of oral cancer in male patients. It was found nearly four times higher than in female patients. Figure 2 shows the co-relation between incidence of oral cancer and age-group of patients. Among the age groups, the highest oral cancer incidence was found among the group of 50–60 years of oral cancer patients.

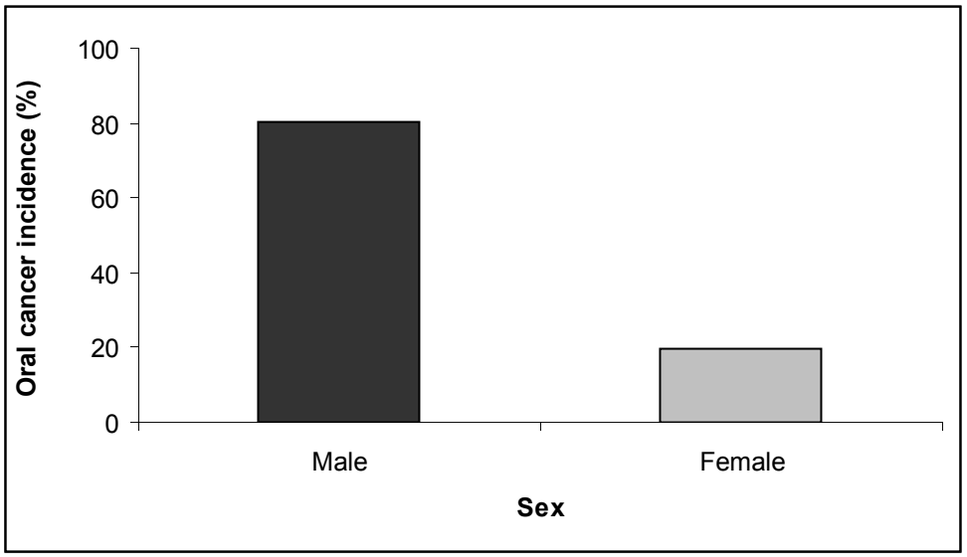

Fig. 1 Sex-wise incidence of oral cancer in Bihar.

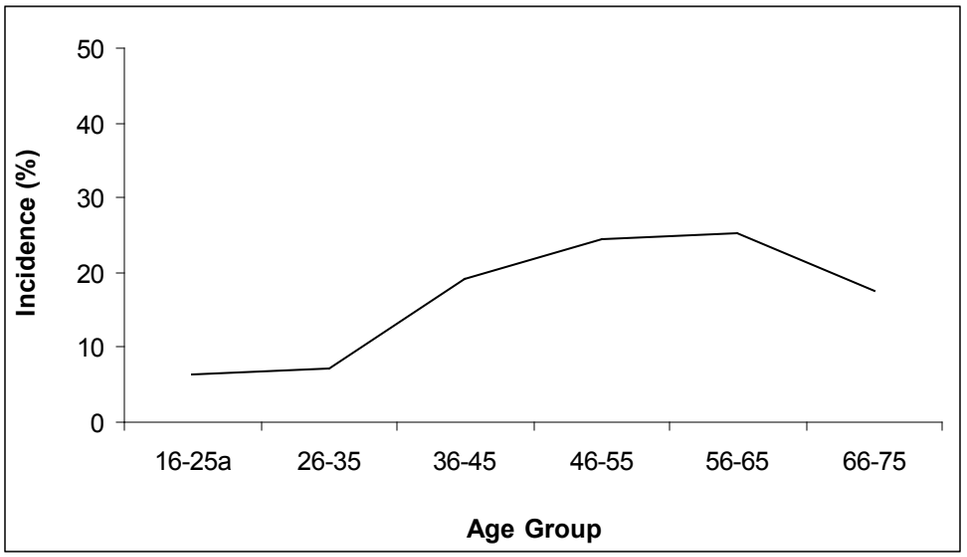

Fig. 2 Age wise incidence of oral cancer in Bihar.

Table 1 shows the site of carcinoma and frequency of oral cancer incidence in people of Bihar, India. Lower gingivo labial mucosa and tongue were the most prevalent site of oral cancer patients having the highest percentage of incidence 25.21 and 23.53 respectively.

In Figure 3, pie-chart indicates prevalence of khaini addiction (50%) among the all smoke and smokeless tobacoo consuming persons in Bihar, India. This result is consistent with some other literatures available in India. Furthermore, in addition to smoke and smokeless tobacco addiction, Pan and Gutka also contributed a significant role in the development of oral cancer.

Figure 4 shows the elevated level of estrogen hormone in male and female oral cancer patients. Estimation of estrogen hormone was done in 18 male oral cancer patients. Maximum level was found as 81.5 pg/ml. Out of 18 male oral cancer patients, 14 patients have the estrogen concentration greater than

Table 1 Carcinoma site and frequency of incidence in Bihar, India.

Site	Incidence (%)
Lower gingiva-labial mucosa (Lower alveolus)	25.21
Tongue	23.53
Buccal mucosa	15.12
Oesophagus	9.24
Tonsil	8.41
Lower lip	4.21
Upper labial mucosa (Upper alveolus)	3.36
Larynx	2.52
Pharynx	0.84
Others	4.20

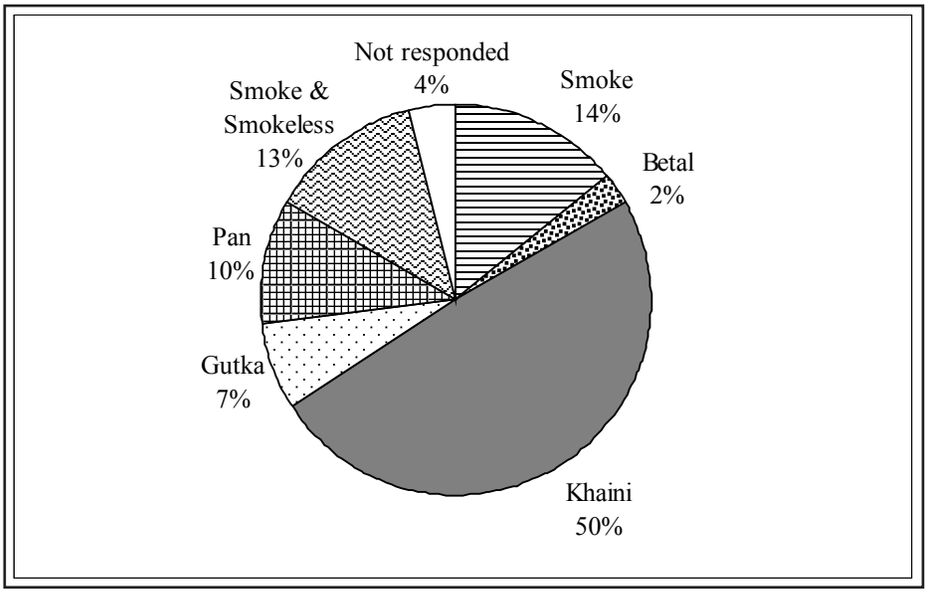

Fig. 3 Tobacco addiction among the surveyed oral cancer patients in Bihar, India.

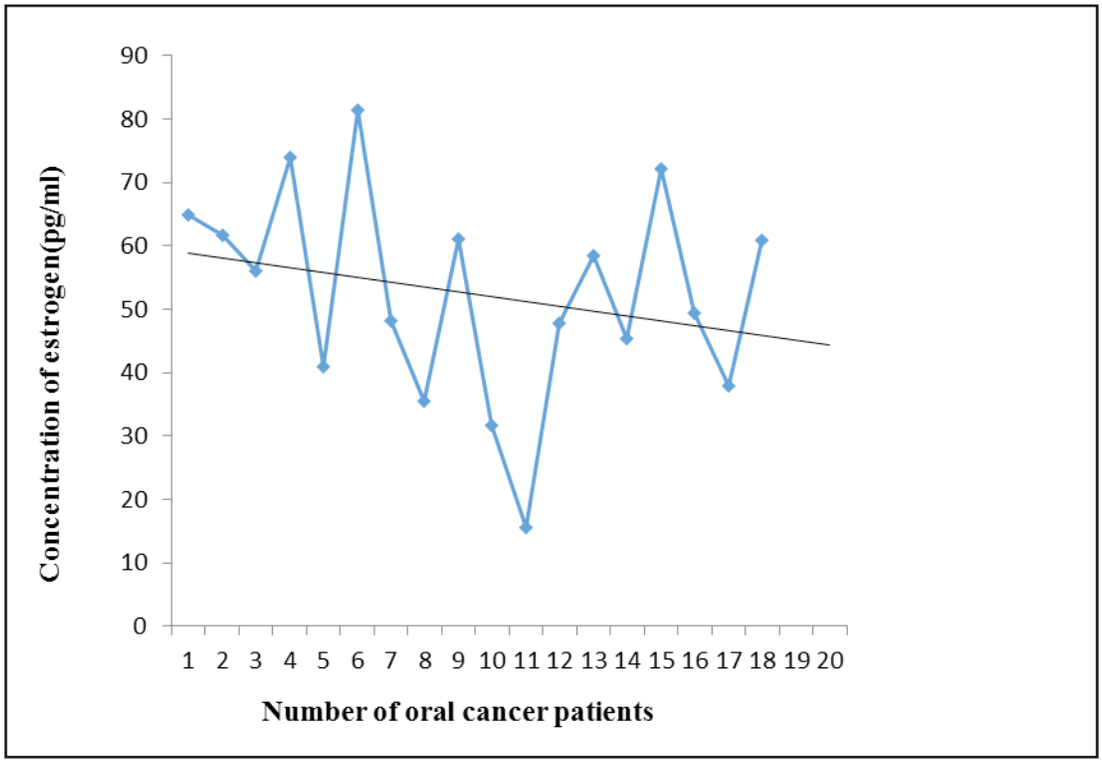

Fig. 4 Estrogen level in male oral cancer patients.

40pg/ml and minimum concentration was detected as 15.5 pg/ml in the male oral cancer patients. Estrogen has been a suspected carcinogen for the development of cancer. Some studies confirmed the positive association of elevated estrogen level with breast, ovary and endometrium cancer.

Our hospital based data provide the evidence that khaini is most prevalent risk factor among the smokeless tobacco using oral cancer patients and it is also associated with the increased risk of oral cancer with the two sites Lower gingivo-labial mucosa and tongue mainly. Government of India has banned the use of tobacco in tooth powder and toothpaste in 1992 and the Supreme Court of India upheld the decision of Government in 1997. These products however, continue to be available openly in the market (Sinha *et al*., 2003). People are using these products therefore, it is the need of time to make people aware of the adverse effects of tobacco. Further, a very significant result has been found in the present study. Elevated estrogen levels in male oral cancer patients have been observed. The exact mechanism behind this is still unclear but it may be due to conversion of testosterone to the estrogen by the enzyme aromatase. It has been shown that level of testosterone hormone in male circulation is greater than the circulation of postmenopausal women. Furthermore, testosterone level in male is similar to the K_m of aromatase, hence conversion of testosterone to estrogen has been occurred in extragonadal sites resulting the elevated level of estrogen in male (Simpson *et al*., 1999).

In conclusion, prevalence of oral cancer is very high in males in Bihar. Most popular form of smokeless tobacco is khaini which is used by illiterate people mainly. High oral cancer incidence has been observed among these people in Bihar. Elevated level of estrogen hormone in male oral cancer patients may be associated with the increased incidence of oral

cancer among people of Bihar. It may further provide some evidence to understand the whole mechanism of oral cancer.

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