RESEARCH ARTICLE

# Epidemiology and Histopathological Spectrum of Head and Neck Cancers in Bihar, a State of Eastern India

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## Abstract

**Head and neck cancers are amongst the commonest malignancies, accounting for approximately 20% of the cancer burden in India. The major risk factors are tobacco chewing, smoking and alcohol consumption, which are all preventable. This retrospective study presents data from the histopathology register for a five year period from 2002-2006 at Patna Medical College and Hospital, a tertiary care hospital drawing patients from the entire Bihar state, the 3rd most populous state of India with the majority of the population residing in rural areas. Incidence rates based on sex, age, site of lesion, including age standardized incidence rates for males and females, with mean age of presentation, distribution of histological variants and year wise trend were calculated. Out of 455 head and neck neoplasias, 241 were benign while 214 were malignant. The most common age group for all malignant biopsies was 7th decade for males and the 5th decade for females. Malignant cases were commoner in males than females with the male:female ratio of 3.1:1, which was found to be statistically significant by the chi-square ($\chi^2$) test. The crude rate and age standardized incidence rate was 0.05 and 0.06 per 100,000 population respectively. Squamous cell carcinoma (SCC) contributed about 96% of all cases, with grade I being the most common. Larynx was the most common site for malignancy, the supraglottic region being its most commonly affected sub-site. This observed incidence patterns in the region are a reminder of widespread unawareness, low healthcare utilization with virtually non-existent cancer programs. It also underlines the need to advocate for reliable cost-effective programs to create awareness, for early detection and plan appropriate management strategies. There is a compelling demand for a cancer registry in this region as well as proper implementation of preventive measures to combat this growing threat of cancer, many of whose risk factors are preventable.**

**Keywords:** Head and neck cancers - epidemiology - squamous cell carcinoma - histopathology - Bihar - Eastern India

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## Introduction

Head and neck cancers (HNC) are amongst the commonest malignancy in India and globally, accounting for around 20% cancer burden in India. HNC comprise of soft tissue neoplasms of oral cavity including lips, nasal cavity and paranasal sinuses (PNS), pharynx, larynx and salivary glands. The consumption of tobacco in various forms such as smoking, bidi, betel quid (paan) along with alcohol are the major 'preventable' risk factors. Both tobacco and alcohol are dose-dependent (Basu et al., 2008) and synergistic risk factors. Betel quid chewing is rampant in Bihar, an important risk factor of oral cancer (Ekramuddaula et al., 2011). Tobacco consumption continues to grow at 2-3% per annum, and by 2020 it is predicted that it will account for 13% of all deaths in the country (Jandoo et al., 2008). Recent studies have shown an inverse relationship of fruits and vegetables intake with HNC (Chuang et al., 2012; Edefonti et al., 2012) while a diet rich in red meat and fats pose increased risk (Edefonti et al., 2012). Lack of nutrients like Vitamin B12 and Folate might have synergetic effect, alongwith habit of tobacco consumption on the process of carcinogenesis (Raval et al., 2002). The people belonging to lower socioeconomic group tend to have higher risk of HNC (Agarwal et al., 2011). Recently HNC have been proposed to have a viral aetiology like Human Papilloma Virus (HPV) (Elango et al., 2011; Rautava et al., 2012), Epstein-Barr Virus (EBV) as well as being associated with various chromosomal deletions and other alterations, most frequently involving the chromosomes 3p, 9p, 17p, 13q and mutations in tumor suppressor genes like p53 (Cadoni et al., 2012). Overexpression of p53 in the margins of tumor could be a gross predictor of clinical outcome (Jalali et al., 2011). Another p63 gene is reported to play a role in the normal cellular and carcinogenetic proliferation P63 4A4+Y4A3 marker can be used for a confirmatory diagnosis of the squamous cell carcinomas of HNC (Khan et al., 2012). Furthermore increasing oropharyngeal incidence has been associated with HPV (Saba et al., 2011).

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While mouth and tongue cancers are more common in the Indian sub-continent, nasopharyngeal cancer is more common in Hong Kong, with pharyngeal and/or laryngeal cancers being more common in other populations (Sankaranarayanan et al., 1998). Oropharynx is reported to be the commonest site of lesion from northeast India while in northern India larynx is reported to be the commonest malignant site with nose being the commonest site for benign lesions. This variation in incidence of cancers by sub-site of head and neck is mostly related to the relative distribution of major risk factors such as tobacco or betel quid chewing, cigarette or bidi smoking and alcohol consumption. Some degree of misclassification by sub-sites is a clear possibility in view of the close proximity of the anatomical sub-sites (Mehrotra et al., 2005).

Globally incidence of HNC is higher in males compared to females. India has the highest rate of HNC among females (Sankaranarayanan et al., 1998). Mean age of presentation lies in the 5th-6th decade for the Asian population as compared to 7th-8th decade among the North American population (Jacques et al., 2011). Incidence of oral cancer in South-East Asia and of oral cavity plus nasopharyngeal cancer in East Asia follows the global HNC pattern.

Bihar, a state of eastern India is the 3rd most populous state with more than two-thirds of population residing in rural areas. The cancer incidence & distribution in Eastern India as well as Bihar has not been reported in detailed manner, especially for HNC. Though there are few research papers from neighboring states of Bihar showing cancer incidence in their region only, no specific HNC incidence in population of Bihar is reported. Being the most rapidly developing state of India, harboring a good portion of Indian population predominantly living in rural areas with lack of effective awareness programs, there is a special requisite to address the cancer threat in this region. This study was conducted at Patna Medical College & Hospital, the tertiary care hospital located in the state capital which attracts patient from entire Bihar state, including referrals.

## Materials and Methods

This is a retrospective study based upon the records obtained from histopathology register of department of Pathology, Patna Medical College & Hospital, Patna from years 2002 to 2006. The study was approved by the local ethics committee. Total number of biopsy specimen submitted were obtained from the register then the number of head and neck biopsies were sorted out. Above retrieved data was collated on the basis of age, gender, site of biopsy and histopathological diagnosis. Data collected were classified on the basis of ICD-10 (International Classification of Diseases 10th Revision) categories C00-C14 (cancer of the lip, oral cavity and pharynx) and C32 (larynx). Incidence rate based on age, gender & site, crude rate (CR), age standardized incidence rate (ASR) for males and females, age of presentation, distribution of histological variants associated with site and sub-site of lesion as well as year wise trend were determined. Statistical analysis was done for total number of males and females observed for HNC by the chi-square ($\chi^2$) test and p value for its preponderance in males was calculated. CR and ASR were calculated based on 2001 census statistics of Bihar (http://gov.bih.nic.in/Profile/CensusStats-01.htm). The total population was 82878796 with sex ratio of 921 females per 1000 males.

## Results

During the years 2002-2006, a total of 5479 biopsies were submitted to the department of Pathology, Patna Medical College & Hospital for histopathological examination. Of these 5479 biopsies, 768 were of the head and neck region. Among these, 455 were diagnosed to be head and neck neoplasia; of which 241 were benign and 214 were malignant (Table 1).

Benign cases were more common in males (60.17%) as compared to females (39.83%) with a male:female ratio of 1.5:1. Similarly, malignant cases were much more common in males (75.7%) than females (24.3%) with a male:female ratio of 3.1:1. Thus male:female malignant ratio was almost double to that of the ratio in benign cases (Figure 1). This difference of HNC incidence between males and females, being more common in males was found to be statistically significant ($p = 0.00157$).

Year wise distribution revealed a steady increase in the total number of biopsy submitted to the department. 2006 showed around two and half times the number reported in 2001 (Figure 2). Age wise distribution showed that the period of life from 30-69 years was most commonly affected by malignant neoplasm, while it was rare below 30 years of age. The most common age group for all malignant biopsies was the 60-69 years age group or the 7th decade of life. In males the same 60-69 years age group was the commonest followed by the 50-59 years age group. While in females the 40-49 years age group is

**Table 1. Incidence of Benign and Malignant Head Neck Neoplasm in Different Gender**

| Type (↓) Sex (→) | Male | Female | Total |
|---|---|---|---|
| Benign | 145 | 96 | 214 |
| Malignant | 162 | 52 | 241 |
| Total | 307 | 148 | 455 |

**Table 2. Histopathological Variants Observed in Different Head Neck Neoplasms**

| HP diagnosis | Male | % | Female | % | Total | % |
|---|---|---|---|---|---|---|
| Benign | 145 | 47.23 | 96 | 64.86 | 241 | 52.97 |
| SCC in situ | 16 | 5.21 | 3 | 2.03 | 19 | 4.18 |
| SCC – I | 56 | 18.24 | 17 | 11.49 | 73 | 16.04 |
| SCC – II | 31 | 10.10 | 10 | 6.76 | 41 | 9.01 |
| SCC – III | 19 | 6.19 | 8 | 5.41 | 27 | 5.93 |
| SCC – IV | 13 | 4.23 | 7 | 4.73 | 20 | 4.40 |
| AdenoCa | 2 | 0.65 | 1 | 0.68 | 3 | 0.66 |
| Small Cell Ca | 10 | 3.26 | 1 | 0.68 | 11 | 2.42 |
| Spindle Cell Ca | 3 | 0.98 | 0 | 0 | 3 | 0.66 |
| Verrucous Ca | 1 | 0.33 | 1 | 0.68 | 2 | 0.44 |
| Others | 11 | 3.58 | 4 | 2.70 | 15 | 3.30 |
| Total → | 307 | 67.47 | 148 | 32.53 | 455 | 100 |

*SCC-Squamous Cell Carcinoma; Ca-Carcinoma

**Table 3. Sites of Various Head Neck Neoplasms**

| Site of lesion (↓) | Benign | Malignant | Total |
|---|---|---|---|
| Nose & PNS | 135 | 25 | 160 |
| Nasopharynx | 16 | 0 | 16 |
| Larynx | 11 | 73 | 84 |
| Oral cavity & Oropharynx | 20 | 59 | 79 |
| Ear | 11 | 6 | 17 |
| Salivary Glands | 14 | 3 | 17 |
| Neck | 9 | 7 | 16 |

*PNS-Paranasal sinuses

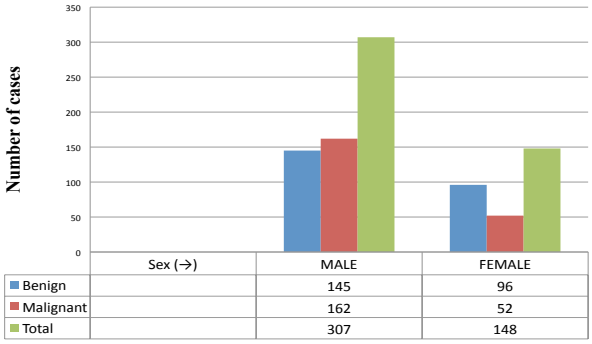


**Figure 1. Gender Distribution of Head Neck Neoplasms.**

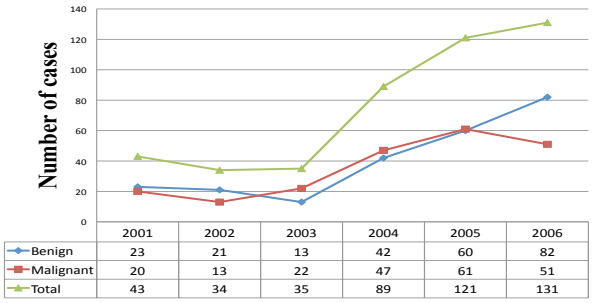


**Figure 2. Annual Distribution of Head Neck Neoplasms.**

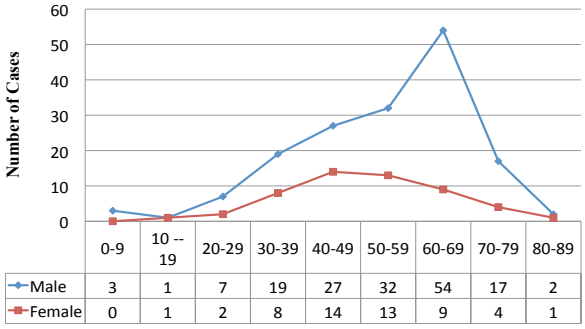


**Figure 3. Age Distribution of Head Neck Neoplasms.**

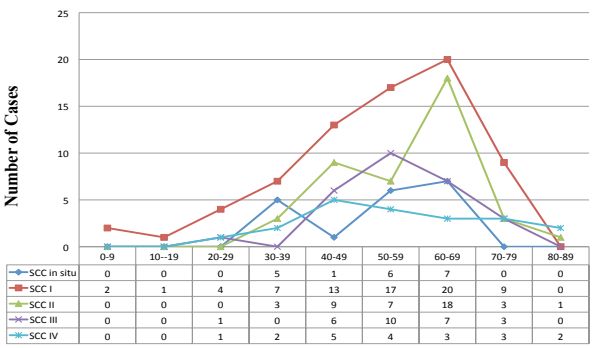


**Figure 4. Age Distribution of Squamous Cell Carcinoma of Head Neck Neoplasms.** SCC- Squamous Cell Carcinoma.

commonest which was closely followed by 50-59 years (Figure 3).

The CR was 0.05 per 100,000 population and ASR was 0.06 per 100,000 population.

Histopathological pattern showed Squamous Cell Carcinoma (SCC) and its subtypes contributing to about 96% of all cases in both males and females. The most common type among malignant biopsies was SCC grade I (16.04%), followed by SCC grade II (9.01%). This pattern was also exhibited in their separate distribution between males and females. SCC in situ was more common in males. SCC showed an unusually high incidence in males in comparison to females (Table 2).

Adenocarcinoma was rarely observed with almost equal percentage in both the genders. SCC in situ, SCC grade I, SCC grade II were more common in the 60-69 years age group, which was the also the age group with highest malignancy incidence. SCC grade III was more common in 50-59 years age group, while SCC grade IV was more common in 40-49 years age group. SCC was rare below the age of 30 years, with minimum incidence in 10-19 years age group (Figure 4).

Larynx was the most common site for malignancy and supraglottic region being its most commonly affected sub-site. Vocal cord was the most commonly involved sub-site in benign cases of larynx. Oral cavity region, including tongue & oropharynx was the second most common site with buccal mucosa being its most common sub-site, followed by the tongue. Nasopharynx had the minimum cases of malignant lesions. Nose & PNS region presented the most cases of benign lesions (mainly by polyps) followed by oral cavity region. Neck showed the minimum number of benign cases (Table 3).

## Discussion

There was progressive increase in the number of biopsies submitted to the department during the period of study. In addition to increase in number of cancer cases, this can also be attributed to several other reasons like increased awareness of people towards health, increased accessibility to health facilities and increased attraction towards these public-funded hospitals in these 6 years.

The malignant male:female ratio observed (3.1:1) was higher than that of a northeastern-india (2.9:1) (Abhinandan et al., 2006), and lower than from northern-india (3.8:1) (Mehrotra et al., 2005). This male to female ratio was reported to be lower in other studies from India (Jussawalla et al., 1980; Chaturvedi et al., 1987; Manjari et al, 1996; Thakur et al., 2001) ranging from 1.5:1 to 2.1:1. The higher male preponderance in this region may be due to almost exclusive use of alcohol and tobacco by males, specially the gutkha, pan-masala which are rarely used by females in this region. Though bidi-smoking, betel quid (paan) and areca nut chewing is practiced among rural females, but to a lesser extent compared to males. This could also be due to the prevailing local socio-cultural mindset facilitating males to better healthcare accessibility leading to higher diagnosis in them. India also reports the highest incidence of head neck cancers in females in comparison to other parts of world (Sankaranarayanan et

al., 1998). Among benign cases, male to female ratio is 1.5:1 which was near to that reported from northern India 1.43:1(Mehrotra et al., 2005).

The observed peak age incidence of 60-69 years was higher to that reported from northeastern and northern India where it was 50-59 years. This could be attributed to people coming late for diagnosis, starting tobacco use at an older age or some factors or habits locally present causing increased incubation period. Females are seen mostly in age group 40-49 years, closely followed by 50-59 years. This may be due to prevalent poorer nutritional status of woman as compared to males. Prevailing social ideas leading to preferential care of male child to female in same household may also be a reason as new research has shown high incidence of head neck cancers in people with lowest consumption of fruits and vegetables (La Vecchia et al., 1997). Also females maybe having some predisposing factors, which if present make them early targets, with shorter incubation periods. Head neck malignancies were rare below 30 years age group which suggests a strong relation between duration of tobacco consumption and subsequent cancer development.

Interestingly the CR (0.05 per 100,000) and ASR (0.06 per 100,000) were very low compared to other reports, which need to be interpreted in an appropriate manner. As many HNC cases are not reaching higher centers due to lesser access of healthcare among the rural population, as well as due to prevailing regional mindset, patients often resort to locally available and sometimes cheaper alternative medical therapies thus getting deprived of a proper cancer diagnosis at a higher center. Low socio-economic status, illiteracy, ignorance of patients often act as a barrier in getting their primary symptoms of HNC checked with proper workup; thus also preventing their diagnosis.

In this study, larynx was the commonest site involved followed by oral cavity and oropharynx similar to north India, while northeast India reports oropharynx as the commonest. This may be ascribed to more smoking habits in this population, specially bidi which is a form of crude cigarette without filter. There are reports stating development of laryngeal cancers with smoking habits (Jussawalla et al., 1984; Gangadharan et al., 1997). India has highest incidence of oral cavity and oropharynx malignancies (Sanghvi et al., 1989) among all malignancies. Nose and paranasal sinuses were commonest site of benign lesion reflected in both this as well as the study from north India. This could be attributed to rampant allergic and seasonal rhinosinusitis which itself is a predisposing factor for nasal polyps.

SCC grade I was common among 60-69 years which was also the most prevalent age group for malignancies. This inference was identical to north India where SCC grade I was common among 50-59 years which was the most prevalent age group. Similar age pattern for SCC grade II was observed. SCC grade III was reported to be common in 40-49 years both here and in north India.

Other than cigarettes, many forms of tobacco are used in this region. Probably the most common tobacco use is the smokeless-chewable khaini; which is an oral preparation of tobacco and slaked lime kept for long hours in the buccal sulcus. This habit is a potential risk factor for various precancerous conditions and oral cancer. Bidi; an inexpensive indian cigarette without filter is made with tobacco flakes wrapped in tendul leaves which is a popular local smoking habit among poor population, including females. Gutkha is a preparation of crushed areca nut, tobacco, catechu, paraffin and slaked lime with some flavorings and is very popular among young people. Betel quid (paan) is a chewable preparation of betel leaf enclosing chopped areca nut, slaked lime, powered tobacco and catechu. Hookah is another form of smoking where flavored tobacco smoke is passed through water and then inhaled. Paan and hookah are equally popular among the affluent class of society.

This being a single-centre study carries some limitations, but still provides a present outlook of HNC in this region, as there has been no previous report on HNC epidemiology in this region. This analysis can serve as a primary survey regarding HNC spectrum for directing future population based cancer studies as well as for planning prevention programs. A thorough population based study of HNC in this region is urgently warranted with establishment of a cancer registry which must be regularly updated, reported and reviewed. There is ignorance of HNC along with indiscriminate use of tobacco, alcohol and smoking across all classes and ages which require widespread dissemination of specific prevention programs, such as information-education-counseling (IEC) programs stressing upon cessation of all forms of tobacco use, its hazards, lifestyle modification and change in dietary habits. HNC if detected early have high cure rates, so there should be campaigns regarding health education to facilitate screening and early diagnosis in population. The existing health infrastructure should be further upgraded and equipped with better diagnostic tools to screen cancer patients, as most of the HNC patients are misdiagnosed, late-diagnosed or remain undiagnosed. Since cancer prevention programs are virtually non-existent, national cancer control programs should be effectively implemented and followed in this region.

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