



Sex difference in the incidence of nasopharyngeal carcinoma in Hong Kong 1983–2008: Suggestion of a potential protective role of oestrogen

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Available online 11 August 2012

KEYWORDS

Nasopharyngeal carcinoma
Sex ratio
Sex difference
Aetiology
Oestrogen

Abstract Background: Nasopharyngeal carcinoma (NPC) shows a male predominance in incidence while the underlying reasons have rarely been explored.

Methods: We analysed incident cases of NPC recorded in Hong Kong Cancer Registry during the period 1983–2008. All cases were divided into 5-year age groups. Age group specific incidence rates of NPC by sex and male to female ratios in incidence rate by age group were calculated. A curve fitting approach was taken to quantitatively describe the age-specific incidence rates of NPC using non-linear regressions.

Results: During the period 1983–2008, a total of 27,579 new cases of NPC were identified (20,060 males and 7519 females) in Hong Kong. The overall male to female ratio of the annual age-standardised incidence rates of NPC ranged 2.2–3.1. The male to female ratio of NPC incidence increased with age until peaking at ages 55–59 years and showed a decline thereafter. An additional minor increase at ages 15–19 years was also observed. Modelling of the age-specific incidence curves suggested divergent slopes for men and women and a delay in increasing incidence with age among females, by around 5–10 years before menopause ages.

Conclusion: The age-dependent pattern of the sex difference in the incidence of NPC could not be completely explained by known risk factors for NPC. The contributions of intrinsic exposures, such as sex hormones, merit consideration and further investigations.

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1. Introduction

Nasopharyngeal carcinoma (NPC) is a malignancy with remarkable ethnic and geographical variations in incidence. NPC is rare in most parts of the world with age-adjusted incidence rates less than 1 per 100,000 persons per year irrespective of sex.¹ However, high incidence rates of NPC are noted in certain areas, especially in Southern China and Hong Kong. The age-adjusted incidence rates of NPC among males and females in Hong Kong in 2008 were 14.9 and 4.8 per 100,000, respectively.² NPC has been for decades a leading cause for cancer incidence among Hong Kong males under the age of 50 years.³

The age-specific curve of incidence rates of NPC differed greatly across different populations. In most low-risk populations, the incidence rate of NPC monotonically increases with age, which is similar to that of most types of epithelia cancers.^{4–6} However, in high-risk regions, such as Southern China and Hong Kong, it increases with age until peaking around ages 50–59 years and then declines with age.^{7,8} A minor peak among adolescents and young adults was also observed in several populations with low risk of NPC.^{1,4,9–11} The distinct features of age distributions of incidence rates of NPC suggest different aetiological profiles that are related to age.

A common feature of the incidence rates of NPC across populations is the male predominance. In most populations, the male to female ratio of incidence rate of NPC is approximately 2–3:1.^{1,6} Such a male predominance in incidence of NPC may be partly explained by differences between the sexes in the prevalence of some environmental risk factors, such as smoking and hazardous occupational exposures. It is also possible that some intrinsic exposures, such as sex hormones, could account for the observed male predominance by a protective effect of endogenous oestrogen but this postulation has been rarely examined.

In the present study, we described the sex difference in the incidence of NPC in Hong Kong during the period 1983–2008. We also examined the putative effect of oestrogen, using age as a proxy, on the incidence of NPC. It was hypothesised that a protective effect of oestrogen on the development of NPC would be reflected by a decline in the male to female sex ratio of the NPC incidence after usual menopausal ages due to decreased hormonal protection in females. This study also aimed to examine whether the male predominance in NPC incidence is related to a delayed development in females, as previously suggested in upper gastrointestinal adenocarcinomas which are also cancers with remarkable male predominance.^{12,13} Aetiological implications of the results are discussed hereby.

2. Materials and Methods

All newly diagnosed NPC cases during 1983–2008 were identified from Hong Kong Cancer Registry, a

population-based cancer registry. It is a member of the International Association of Cancer Registries (IACR) and contributes regularly to “Cancer Incidence in Five Continents” publications of the IACR. Population data during the corresponding period were obtained from the Hong Kong Census and Statistics Department.

Cases were divided into five-year groups beginning from ages 0–4 years. All cases aged 85 years or older were combined as one group. For each age group, the incidence rate of NPC was calculated separately for each sex by dividing the number of cases by the corresponding population. The male to female ratios of incidence rates of NPC were calculated by dividing the incidence rates in males by those in females, and then plotted against age group. To evaluate potential time period effects, results were stratified into three periods: 1983–1991, 1992–2000, and 2000–2008. We also performed subgroup analyses stratified by histological subtype.

A curve fitting approach was taken to quantitatively describe the age-specific incidence rates of NPC by sex using non-linear regressions.^{12–14} The equation $I_{(t)} = a \times (t - d)^b \cdot (1 - kt)$ modified from previous studies was fitted to age-specific incidence data using the SOLVER function of Microsoft Excel. In this equation, $I_{(t)}$ is the age-specific incidence rate of NPC (1/100,000 person-years) at age t (the mean age of the group), a is a scaling factor, b is a power term, d is the a delay term for the time between birth and age of increased incidence above zero and k is an empirical term to be described. A logic “if” function was used in Excel such that when $t < d$, $I_{(t)} = 0$. Thus only when $d > t$ was $I_{(t)} > 0$.

3. Results

During the period 1983–2008, a total of 27,579 new cases of NPC were identified (20,060 males and 7519 females). The crude annual incidence rates of NPC ranged 20.6–31.9 per 100,000 and 6.7–11.9 per 100,000 for males and females, respectively. The age-standardised incidence rates with the World Health Organisation (WHO) standard population (2000) as reference steadily decreased from 35.6 per 100,000 person-years in 1983 to 14.9 per 100,000 person-years in 2008 for males, and from 12.7 per 100,000 person-years in 1983 to 4.8 per 100,000 person-years in 2008 for females.

The age-group specific incidence rates of NPC and the male to female ratios in the incidence rate during 1983–2008 are shown in Table 1. The incidence rate of NPC increased with age until it peaked between the ages 50–54 years in males and 50–64 years in females, and subsequently declined at older ages. The incidence rate in females at the ages of 20–49 (adulthood before menopause age) was lower than that at the ages of 50 or above (after menopause age) and the difference was statistically significant ($P < 0.01$). The overall male to female ratio of the annual age-standardised incidence

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