Short Communication

High Incidence of Nasopharyngeal Carcinoma in Native People of Sarawak, Borneo Island

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Abstract

Nasopharyngeal cancer (NPC) is generally a rare malignancy with a few well-known exceptions, notably South-East China. In this article, we describe evidence of a high risk of NPC in the population of Sarawak State, Malaysia, and particularly in one native ethnic group. Sarawak State is one of the two provinces of Malaysia located on the island of Borneo. The native population (71.6%) includes the Iban, Malay, Bidayuh, Melanau, and diverse smaller ethnic groups. The Chinese are the largest nonindigenous group (27.5%). We identified 392 newly diagnosed cases (292 males and 100 females) of NPC in 1996–1998 in Malaysian citizens, permanent residents of Sarawak. Age-standardized rates by sex and ethnic group were compared with the highest rates in the world. The age-adjusted rate (ASR) in Sarawak residents was 13.5/100,000 [95% confidence interval (CI) 12.2–15.0] and 6.2/100,000 (95% CI 5.7–6.7) in males and females, respectively. The risk in the Bidayuh people was 2.3-fold (M) and 1.9-fold (F) higher than the Sarawak average, and about 50% higher than that in Hong Kong—the highest recorded by any population-based registry for the same period. Local dietary habits, environmental exposures, and genetic susceptibility deserve investigation in this population. (Cancer Epidemiol Biomarkers Prev 2004;13(3):482–486)

Introduction

Nasopharyngeal cancer (NPC) is generally a rare malignancy, although there are a few well-known exceptions. The highest rates are recorded among Chinese living in the South-East of China, where age-standardized rates reach 21/100,000 in males. Moderately high rates occur in the countries of South-Eastern Asia, in Northern Africa and among natives of the Arctic Region (1). Rates are otherwise below 1/100,000 (1). In this article, we describe a high risk of NPC in the native population of Sarawak State, Malaysia.

Materials and Methods

Sarawak State is one of the two provinces of Malaysia which are located in the North of the island of Borneo. The native populations include the Iban (29.9%), Malay (22.1%), Bidayuh (8.4%), Melanau (5.4%), and other smaller ethnic groups (5.8% altogether). Chinese comprise the largest non-indigenous group (27.5%). Less than 1% are of other ethnic origin (Indians, Eurasians, Javanese, and Bugis) (2). The Malay and the Chinese are concentrated in urban administrative and marketing centers while the Iban and other native people reside in the rural areas (2).

The Department of Radiotherapy and Oncology of the Sarawak General Hospital in Kuching is the only one serving the State of Sarawak. Because radiotherapy is the essential treatment for this malignancy, virtually all eligible cases, histologically confirmed, are referred to this center. If not previously performed, histopathology examination is carried out at the hospital. A computerized file of all cases treated is maintained in the Department. Records include personal identification items (citizenship, residential details, and self-reported ethnic group), tumor characteristics coded according to ICD-O 2nd revision (3) and stage at presentation as well as the date of diagnosis. We identified 392 cases (292 males and 100 females) diagnosed in 1996–1998 in Malaysian citizens, who were permanent residents of Sarawak. All were histologically verified. Sixty percent of the cases had been diagnosed in Sarawak General Hospital; the others were referred from 13 other hospitals in the State.

Sarawak State is served by a population-based cancer registry initiated in 1996 and promoted by the Ministry of Health. At the time of assembling the data for this study, the registry's database was still incomplete for the period of interest. Nevertheless, any NPC cases recorded in the registry were included in our file. Completeness was further improved by incorporating information on 42 cases, identified from death certificates in the same period and mentioning NPC, which could not be linked

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with any record in our file [Death Certificate Only (DCO) cases]. Reliable routine mortality data are not available for Malaysia (4). Denominators for the calculation of rates are the population estimates of year 2000 census (2) by sex, age, and ethnic group.

Crude and age-adjusted rates (ASRs) and rate ratios (RRs) comparing the incidence by ethnic group to the overall ASR in Sarawak, and their confidence intervals (CIs), are presented. Rates were adjusted by direct standardization to the world standard (5). The 95% confidence limits were calculated after logarithmic transformation (6).

Results

The annual number of cases was rather stable, ranging from 152 in 1996 to 145 in 1998. The proportion of DCO cases was rather constant at around 8% (M) and 14% (F). The age range was 7–86 years, mean ± SD were 47.7 ± 14.6. Eighty-eight percent of the cases were stage 3 or 4 at presentation. The histological types of the 381 cases characterized were 238 undifferentiated carcinomas (62%) of which 7 were lymphoepithelial type, and 143 squamous cell carcinomas (38%) of which 119, non-keratinizing.

Crude and age-standardized rates and RRs by sex and ethnic group are given in Table 1. Ethnicity was missing for three cases (one male and two female). The ASR in Sarawak resident citizens was 13.5/100,000 (95% CI 12.2–15.0) and 6.2/100,000 (95% CI 5.7–6.7) in males and females, respectively. The risk in the Bidayuh people was 2.3-fold (M) and 1.9-fold (F) higher than the Sarawak average, and about 50% higher than the highest recorded by any other population-based registries around the same period (Fig. 1) (Hong Kong where rates were $21.4/10^5$ in males and $8.3/10^5$ in females). Incidence rates in Malay and Chinese residents of Sarawak were very similar to those registered in Singapore for the same ethnic groups (Fig. 1) (1). The risk in the native Iban people was close to the province average, ASR (M) = $13.1/10^5$ (95% CI 9.5–18.0) and ASR (F) = $5.6/10^5$ (95% CI 4.6–7.0), while the smaller group of Melanau was at lower risk, ASR (M) = 5.2 (95% CI 4.3–6.2), ASR (F) = 1.1 (95% CI 1.0–1.2). The other remaining two indigenous groups, Iban and Melanau, showed rates within the range of the selected top 10 in the world (Fig. 1).

Incidence rates peaked in age-group 50–59 and declined thereafter consistent with the age-specific distribution of other high-risk populations (Fig. 2).

Discussion

We present new data on the incidence of NPC in the population of Sarawak State, Malaysia. Ten percent of the cases were included only on the basis of a death certificate diagnosis. All others were confirmed by histology. There are no reliable mortality statistics for this population to allow us a check of the completeness of these data, but we can exclude overreporting. The incidence rates were calculated based on the census of 2000, although this probably overestimated the population at risk in 1996–1998, given the increasing population size of Sarawak (14.6% between 1991 and 2000), for all races (2, 7). In Malaysia, registers of all households in urban and rural areas are maintained and updated by the local governmental administration. A major update and review takes place at every census survey. Ethnic group recorded at census is self-reported also for the smaller ones of native tribes. There are no reasons therefore to expect that the coverage and completeness of census denominators are of different quality for the different ethnic groups. The sense of racial identity is deep-rooted in this society so that misclassification

Table 1. Numbers of cases, crude, and age-standardized rates/100,000 (world) in Sarawak 1996–1998 by ethnic group and sex

	All cases						DCOs excluded				
	Cases	Crude	ASR	RR	95% CI of RR		Cases	Crude	ASR	RR	95% CI of RR
Males											
Sarawak	317	10.4	13.5	1		Sarawak	292	9.6	12.6	1	
Malays	36	5.1	7.8	0.6	(0.4–0.9)	Malays	31	4.4	6.7	0.5	(0.4–0.8)
Chinese	99	12.0	12.6	0.9	(0.7–1.2)	Chinese	87	10.5	11.0	0.9	(0.7–1.2)
Melanau	6	3.5	5.2	0.4	(0.3–0.5)	Melanau	5	2.9	4.2	0.3	(0.3–0.4)
Bidayuh	58	23.1	31.5	2.3	(1.7–3.1)	Bidayuh	55	21.9	29.4	2.3	(1.7–3.1)
Iban	99	10.9	13.1	1.0	(0.7–1.4)	Iban	96	10.6	12.6	1.0	(0.7–1.4)
Other native	18	9.9	13.7	1.0	(0.8–1.3)	Other native	17	9.3	13.1	1.0	(0.8–1.3)
Others	1	7.7	11.0	0.8	(0.7–1.0)	Others	1	7.7	11.0	0.9	(0.7–1.1)
Females											
Sarawak	114	3.8	6.2	1		Sarawak	100	3.4	5.8	1	
Malays	13	1.9	2.8	0.5	(0.3–0.6)	Malays	12	1.8	2.7	0.5	(0.3–0.6)
Chinese	32	4.1	4.0	0.6	(0.5–0.9)	Chinese	24	3.1	3.0	0.5	(0.4–0.7)
Melanau	1	0.6	1.1	0.2	(0.2–0.2)	Melanau	1	0.6	1.1	0.2	(0.2–0.2)
Bidayuh	22	8.8	11.8	1.9	(1.6–2.4)	Bidayuh	19	7.6	10.6	1.8	(1.4–2.3)
Iban	43	4.8	5.6	0.9	(0.7–1.1)	Iban	41	4.5	5.4	0.9	(0.7–1.2)
Other native	2	1.2	0.9	0.2	(0.1–0.2)	Other native	2	1.2	0.9	0.2	(0.1–0.2)
Others	1	8.9	16.8	2.7	(2.4–3.1)	Others	1	8.9	16.8	2.9	(2.6–3.3)

Note: Rate ratios and 95% CIs, comparing ethnic groups *versus* Sarawak.

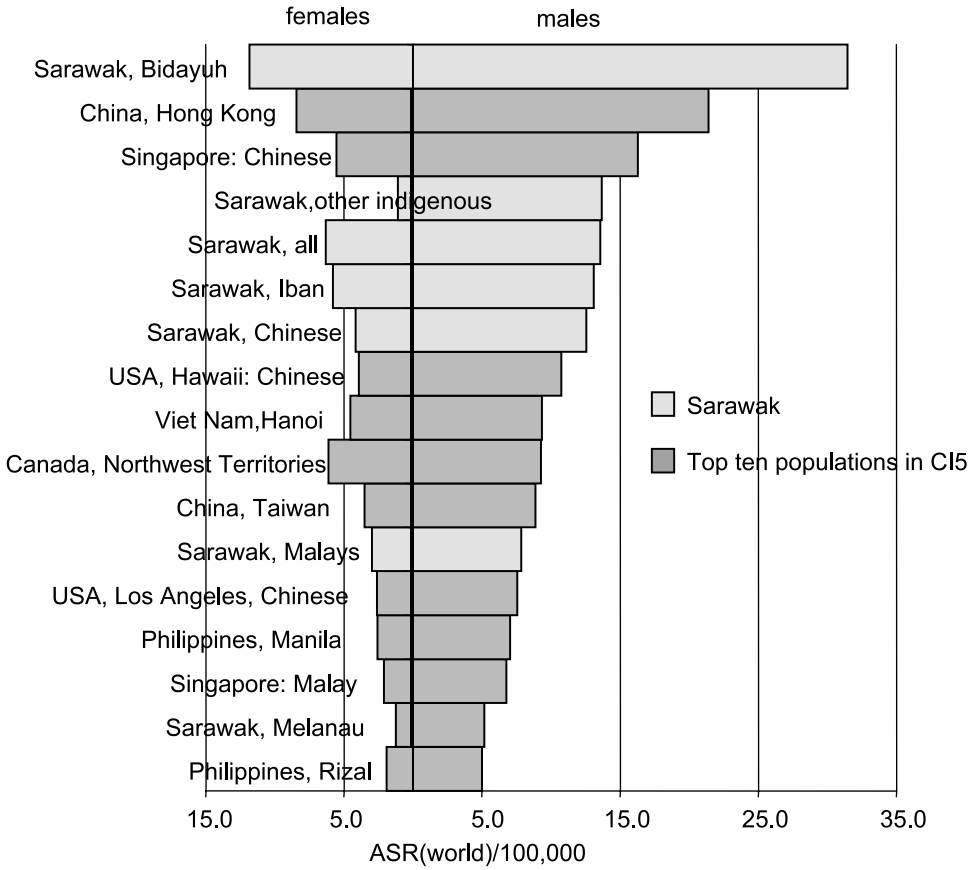

Fig. 1. Age-standardized rates (100,000) of NPC in Sarawak and in the 10 populations in Cancer Incidence in Five Continents, vol. 8 (1) with the highest rates.

between racial groups is unlikely (8). Crude rates of NPC cases from histopathology series were reported to be high, among non-Chinese Mongoloid populations of Sarawak and Sabah (the other Malaysian province located on the island of Borneo), in the 1960s (9) and confirmed in subsequent work (10) although at that time, only relative frequencies or crude rates could be estimated. The risk of NPC was also reported high in a group of native children including some from Sarawak, treated in Kuala Lumpur (11). Prasad and Rampal (12) conducted a survey of histologically confirmed cases diagnosed in 1988 in peninsular Malaysia and found the highest rates among Chinese with Malays being intermediate and Indians at low risk, confirming the early work by Armstrong (13–15) who also showed a pattern of risk in Chinese subgroups similar to that described elsewhere. We were able to assess the magnitude of the phenomenon and provide comparative age-standardized figures showing that native Sarawak people exhibit the highest rates in the world. Incidence is moderately high in several other countries in South-East Asia such as Thailand and Viet Nam where Chinese immigrants have mixed with the local population for centuries. Studies of migrants from high-risk Asian countries to the United States show that such individuals retain a relatively high risk, compared with the US population (16–18) as do North African migrants to Israel (19). The high risk in native people of Sarawak, however, is unlikely to be the result of blending with citizens of Chinese descent that in this country, as in Singapore, are a distinct ethnic group.

Established causes of NPC are the ubiquitous EBV (20), tobacco smoking (21), and consumption of Chinese-style salted fish, particularly in childhood (22–24). Salted fish has been shown to increase the risk of the disease in Malaysian Chinese (25) while no studies linking NPC to specific dietary habits of native people have been published. In the high-risk Hong Kong population, incidence rates have declined by 30% from 1980 to 1995 (1, 26), proving that environmental factors are a relevant component of the aetiology of the disease. Nevertheless, because of the peculiar geographical distribution of the disease, which does not match the prevalence of the factors described, none of these alone is likely to be sufficient to cause the disease. Interaction between environmental causes and genetic predisposition would be consistent with the wide range of risk in the world and variable association with established risk factors, as well as with the pattern of risk observed in migrant populations. Some haplotypes of the HLA system have been associated with increased risk of NPC in several high-risk populations including Malay (27–30) but susceptibility genes have not been identified as yet. A specific Km allele that was associated with NPC cases

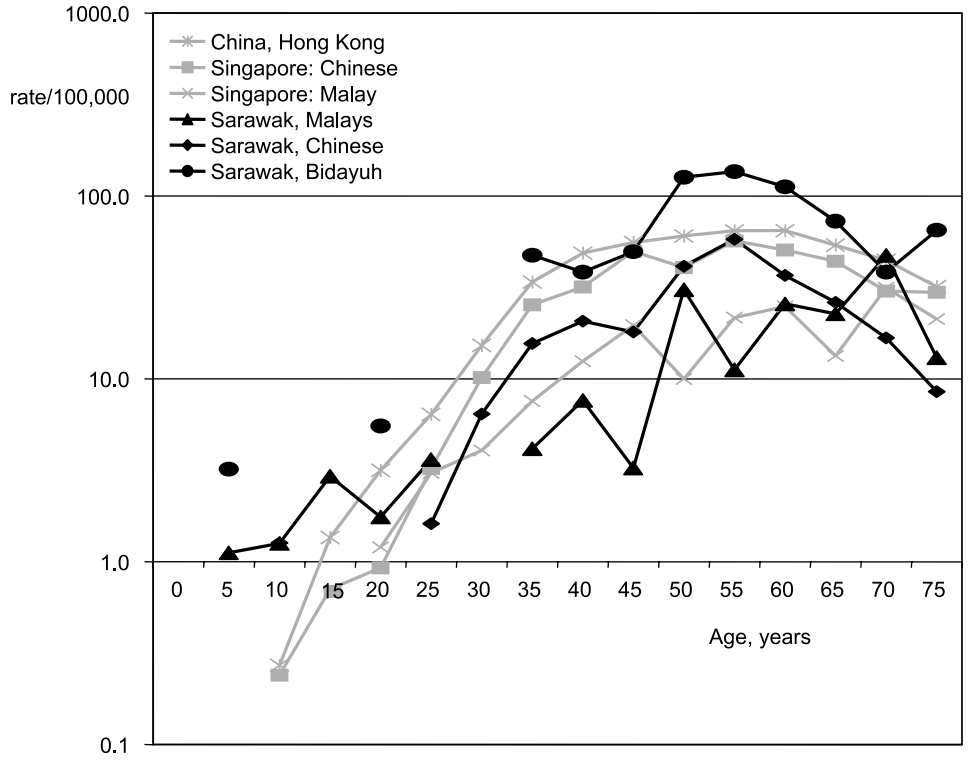

Fig. 2. Age-specific incidence rates of NPC in Sarawak, 1996–1998, Singapore, 1993–1997 (1) and Hong Kong, 1993–1997 (1), by ethnic group. Males.

from Northern Africa was not more common in NPC Malaysian Chinese or Malay patients compared to controls (31). The people of Sarawak might be an example of genetic drift suitable for studies of genetic linkage. Traditional dietary habits and immune response to EBV also deserve further investigation.

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