Chinese Journal of Cancer

Original Article

Preliminary assessment of nasopharyngeal carcinoma incidence in the Philippines: a second look at published data from four centers

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Abstract

In endemic regions such as southern China and Southeast Asia, the annual incidence of nasopharyngeal carcinoma (NPC) ranges from 3 to 30 per 100,000. In the Philippines, the estimated incidence in 2010 was 1.2 per 100,000. However, this rate is based on data collected from registries covering only two regions in the country. Here, we report the findings from our study to better approximate the incidence of NPC in the Philippines. Between September 1, 2011 and August 31, 2012, data were collected from 49 patients from 4 different institutions—University of Santo Tomas, Makati Medical Center, Philippine Oncology Center Corporation, and Cardinal Santos Memorial Medical Center—using a NPC screening questionnaire. Crude incidence was 0.09 per 100,000. Age-standardized incidences using Segi and WHO standards were 2.08 and 1.79 per 100,000, respectively. Of the 49 patients, 31 were males and 18 were females, and 71% of patients were between 30 and 59 years old. WHO types II and III represented 22% and 78% of the subjects, respectively, and 75.5% of cases were locally advanced (stages III–IVB). Although the age-standardized incidence from the 4 institutions was numerically higher than the published age-standardized incidence (2.07 per 100,000 vs. 1.2 per 100,000), two-proportion *z*-test showed no significant difference between them ($P = 0.68$). A more concerted effort is needed for a better approximation of the country's NPC disease burden.

Key words Nasopharyngeal carcinoma, incidence, Philippines

Nasopharyngeal carcinoma (NPC) is rare (annual incidence, <1/100,000) in most parts of the world. However, it is endemic in regions such as southern China and Southeast Asia, where the annual incidence ranges from 3 to 30 per 100,000 persons[1,2]. NPC has two different age distributions depending on the risk population. Low-risk groups tend to have a bimodal distribution between the ages of 15–25 and 50–59[3]. However, incidence in high-risk groups increases in persons aged from 30 to 60 years[3]. Age distribution among sexes is similar[4], but the incidence is 2–3 times higher in males than in females[3]. Histologic distribution of NPC also differs among the risk populations. Keratinizing carcinoma (WHO type I) is more commonly seen in low-risk populations, occurring at a frequency of 25% compared to just 1% in high-risk counterparts[1]. TNM stage is the most important prognostic factor[3]. High T category portends worse local control, whereas high N category portends higher distant metastases[3]. NPC—stages I to IVB and even some metastatic cases—is primarily treated with radiation therapy.

NPC incidence in the Philippines, according to GLOBOCAN 2008[5], was 1.2 per 100,000 (age-standardized rate). Prior to this, the incidence of NPC had been slightly higher (**Table 1**). However, these rates may not accurately reflect the incidence of the disease throughout the country because these data were only based on registries of Manila (National Capital Region or NCR) and Rizal[2,6]. Furthermore, attendant to the limited scope of the population-based registry, a bell-shaped distribution of the disease across the archipelago is assumed; but should cases cluster outside of the sampled areas, they may not be captured. On a global scale, NPC is clustered in regions of varying endemicity. Even in China, individual regions have distinct incidences and their populations are at variable risk for developing the disease. Yet, incidence in the Philippines was determined based only on data from registries covering two regions. We hypothesize, based on observation of cases at our center, that a significant number of cases are not captured by the registries and that NPC incidence in the Philippines may be underreported. It is,

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doi: 10.5732/cjc.013.10010

Table 1. Age-standardized incidence of nasopharyngeal carcinoma (NPC) in the Philippines shows an unexpected decrease in 2008

Publication	Year	Age-standardized incidence (per 100,000 population)	
		Males	Females
Ngelangel *et al.*[6]	1993–1995	6.2	6.2
CI5 Vol. VIII[11]	2002		
Manila		7.2	2.5
Rizal		5.0	1.9
CI5 Vol. IX[8]	2007	5.8	2.4
GLOBOCAN 2008[5]	2008	1.2	1.2

therefore, important to better approximate the incidence of NPC in the Philippines.

In line with this, we partnered with radiation oncology centers in the Philippines through the Philippine Radiation Oncology Society to collect data and better approximate NPC incidence. Our rationale was that all NPC patients, at some point in their disease management, will pass through a radiation department, making it a logical catch basin for data gathering. This was likewise appealing because there are only 20 radiation departments in the entire archipelago. This small number makes potential data gathering a less arduous task, as less coordination is required compared with using hospital- or population-based registries.

The objectives of this study were to approximate the annual incidence of NPC using data from different radiotherapy facilities in the Philippines, and to identify the distribution of incident cases based on geography, age, histologic pattern, stage, and sex.

Patients and Methods

Institutional Review Board approval was obtained and the study started on September 1, 2011. All 20 oncology centers in the Philippines were invited to participate via invitation at various meetings and symposia of the Philippine Radiation Oncology Society.

Four centers (University of Santo Tomas, Makati Medical Center, Philippine Oncology Center Corporation, and Cardinal Santos Memorial Medical Center) consented and participated in data collection. Follow-up recruitment (second and third invitations) was undertaken among the remaining 16 oncology centers, but all declined to take part in the study.

All patients newly diagnosed with NPC between September 1, 2011 and August 31, 2012 were included in the study. A written consent was obtained from the attending radiation oncologists to allow data gathering from their patients. Data was collected using an NPC screening questionnaire. The crude incidence rate and age-standardized rate—using both the Segi and WHO population standards[7,8]—were calculated. Geographic distribution, age distribution, sex distribution, and stage distribution were also determined. The AJCC/UICC 7th edition[4] was used to determine clinical stage. In determining geographic distribution of the disease, patients were asked about their province of origin, not necessarily their place of current residence.

Two-proportion *z*-test was performed to determine significant difference between the 2010 incidence and the study incidence. A value of $P < 0.05$ was considered significant.

Results

Incidence

Between September 1, 2011 and August 31, 2012, the data of 49 NPC patients were obtained. One patient had Chinese lineage (grandfather). Crude incidence and age-standardized rates were determined only for Luzon because of the limited number of patients (two) from Visayas and Mindanao.

Crude incidence was 0.09 per 100,000 persons. Age-standardized rates, using the Segi population standard[7,8] and the WHO population standard[7], were 2.07 and 1.78 per 100,000 persons, respectively (**Table 2**). Two-proportion *z*-test showed no significant difference between the age-standardized rates of 1.2 per 100,000 persons and our rate of 2.07 per 100,000 persons ($P = 0.68$). The age-standardized incidences using Segi and WHO standards in Luzon were 2.19 and 2.05 per 100,000 persons in males and 2.10 and 1.63 per 100,000 persons for females, respectively.

Geographic distribution

Table 3 shows the distribution of subjects per region, which was further subdivided by province. Approximately one-third of the cases occurred in patients from central Luzon, and 10 occurred in patients from the National Capital Region: Caloocan ($n = 3$), Manila ($n = 2$), Marikina ($n = 1$), Parañaque ($n = 1$), Pasig ($n = 1$), and Quezon City ($n = 2$). For one of the patients from the National Capital Region, the municipality of origin was not solicited.

Age distribution

The number of cases increased with age, peaking at the 50–59 year age range (**Table 4**). More than half (71%) of the cases occurred

Table 2. Age-standardized incidence of NPC in the Philippins was computed using Segi and World Health Organization (WHO) standards

Age (years)	No. of cases	Segi standard (%)[8,9]	Age-standardized incidence (Segi)	WHO standard (%)[9]	Age-standardized incidence (WHO)
0–4	0	12	0	8.86	0
5–9	0	10	0	8.69	0
10–14	1	9	0.021,2	8.60	0.022,2
15–19	0	9	0	8.47	0
20–24	3	8	0.071,6	8.22	0.069,7
25–29	2	8	0.047,7	7.93	0.048,2
30–34	5	6	0.159,1	7.61	0.125,5
35–39	6	6	0.191,0	7.15	0.160,3
40–44	5	6	0.159,1	6.59	0.144,9
45–49	5	6	0.159,1	6.04	0.158,1
50–54	6	5	0.229,2	5.37	0.213,4
55–59	7	4	0.334,2	4.55	0.293,8
60–64	4	4	0.191,0	3.72	0.205,3
65–69	2	3	0.127,3	2.96	0.129,0
70–74	0	2	0	2.21	0
75–79	0	1	0	1.52	0
80–84	1	0.5	0.381,9	0.91	0.209,9
⩾ 85	0	0.5	0	0.63	0
Total	47	100	2.072,6	100	1.780,2

in patients between the age of 30 and 59 years.

Sex distribution

Among the 49 cases, there were 31 males and 18 females (**Table 4**), representing a male-to-female ratio of 1.7:1.

Histologic distribution

The majority of cases (38 of 49, 78%) were WHO type III. WHO type II was less frequent (11 of 49 cases, 22%). There were no cases of WHO type I.

Stage distribution

Table 5 shows the spread of cases between the stages of NPC. Of all 49 cases, 37 (75.5%) were locally advanced stage (stages III–IVB), 9 (18.4%) were early stage (stages I–II), and only 3 (6.1%) were metastatic (stage IVC).

Discussion

This small series from four centers in the Philippines has computed age-standardized incidence for NPC of 2.19 and 2.05 per 100,000 persons in males and 2.10 and 1.63 per 100,000 persons in females using the Segi and WHO standards, respectively. The computed age-standardized rates in this study are numerically higher than the GLOBOCAN rate of 1.2 per 100,000 persons[5]. Despite the difference not being statistically significant when compared to the Philippine and GLOBOCAN reports, it should be kept in mind that the source of the data in itself is limited, coming from only four institutions. In spite of this, we have documented rates numerically higher than national estimates[2,5]. Intuitively, it would be a safe assumption that the involvement of government centers with higher volumes of patients would probably drive the computed age-standardized rates higher. However, this runs counter to a hypothesis in the 2010 Philippine Cancer Facts and Estimates that the "2005 Philippine Cancer Facts and Estimates was most probably overestimated, while the 2010 estimates on cancer incidence could be closer to the real situation"[2]. Notably, however, the 2010 Philippine Cancer Facts and Estimates were determined using the latest GLOBOCAN statistical methods, which were also used in the more limited analysis we report here[2,5].

A striking observation in our series is that patients originally from northern and central Luzon provinces make up a large number of the cases of NPC. These cases would not have been captured in the GLOBOCAN report as the latter was based on the 2010 Philippine Cancer Statistics, where only residents covered by the population-based Manila and Rizal registries would have been included[2,5]. While this may represent a geographic bias in the location of the center with the most cases seen (University of Santo Tomas), the number of cases seen to the west and south of University of Santo Tomas are

Table 3. Geographic distribution shows that a large proportion of cases are from Central Luzon

Region	Province	No. of cases	Region	Province	No. of cases
National Capital Region	Total	11	Western	Aklan	1
Cordillera (CAR)	Abra	0	Visayas	Antique	0
	Apayao	0		Capiz	0
	Benguet	1		Guimaras	0
	Ifugao	0		Iloilo	0
	Kalinga	1		Negros Occidental	0
	Mountain province	0		Total	1
	Total	2	Central	Bohol	0
Ilocos Region	Ilocos Norte	1	Visayas	Cebu	0
	Ilocos Sur	0		Negros Oriental	0
	La Union	2		Siquijor	0
	Pangasinan	5		Total	0
	Total	8	Eastern	Biliran	0
Cagayan Valley	Batanes	0	Visayas	Eastern Samar	0
	Cagayan	1		Leyte	0
	Isabela	0		Northern Samar	0
	Nueva Vizcaya	1		Samar	0
	Quirino	0		Southern Leyte	0
	Total	2		Total	0
Central Luzon	Aurora	1	Zamboanga	Zamboanga del Norte	0
	Bataan	0	Peninsula	Zamboanga del Sur	0
	Bulacan	5		ZamboangaSibugay	0
	Nueva Ecija	4		Total	
	Pampanga	3	Northern	Bukidnon	0
	Tarlac	2	Mindanao	Camiguin	0
	Zambales	1		Lanao del Norte	0
	Total	16		Misamis Occidental	0
CALABARZON	Batangas	3		Misamis Oriental	0
	Cavite	1		Total	0
	Laguna	0	Davao	Compostela Valley	0
	Quezon	0		Davao del Norte	1
	Rizal	0		Davao del Sur	0
	Total	4		Davao Oriental	0
MIMAROPA	Marinduque	0		Total	1
	Occidental Mindoro	1	SOCCSKSARGEN	Cotabato	0
	Oriental Mindoro	2		Sarangani	0
	Palawan	0		South Cotabato	0
	Romblon	0		Sultan Kudarat	0
	Total	3		Total	0
Bicol	Albay	0	Caraga	Agusan del Norte	0
	Camarines Norte	0		Agusan del Sur	0
	Camarines Sur	1		Surigao del Norte	0
	Catanduanes	0		Surigao del Sur	0
	Masbate	0		Total	0
	Sorsogon	0	ARMM	Basilan	0
	Total	1		Lanao del Sur	0
				Maguindanao	0
				Sulu	0
				Tawi-Tawi	0
				Total	0

Table 4. Age and sex distribution are similar to distributions seen in intermediate and high incidence regions

Age	Males	Females	Total
Younger than 20	1	0	1
20–29	4	1	5
30–39	6	5	11
40–49	7	3	10
50–59	8	6	14
60 and above	5	3	8
Total	31	18	49

Table 5. Most cases were diagnosed in the locally advanced stage (stages III–IVB)

Stage	TNM	No. of cases
I	T1N0	1
II	T1N1	2
	T2N0	0
	T2N1	6
III	T1N2	1
	T2N2	9
	T3N0	2
	T3N1	1
	T3N2	5
IVA	T4N0	3
	T4N1	5
	T4N2	5
IVB	TanyN3	6
IVC	TanyNanyM1	3

still much lower compared with the north. Whether this observation also represents true clustering can only be answered by more robust data gathering.

It must also be kept in mind that NPC is an endemic malignancy, with different regions showing varying levels of risk. Even within China, Cantonese regions show higher endemicity than Hokkien, though incidence in the latter is higher than the general worldwide incidence[9]. In the Sarawak region, the NPC incidence of Bidayuh is higher than the Malaysian incidence in general[10]. It would also be logical to assume that incidence would vary among different regions in the Philippines where NPC is present. Indeed, we report here that Central Luzon (region 3) had more cases than other regions.

The histologic and peak age distribution reflects what is normally seen in high- and intermediate-risk regions for NPC. However, the male-to-female ratio shows lower male preponderance than what has been reported in these areas[3]. Most cases of NPC are also advanced stage (stages III–IVB).

Although an attempt was made to include all oncology centers in the Philippines, only four centers participated in the effort contributing 49 patients. While our series does not have enough cases to adequately challenge the published incidence of NPC, it does raise the question of whether the samples used in generating the Philippine and GLOBOCAN data are truly representative. It also shows that gaps in data collection and reporting may be present, as the geographic area where we documented the most cases of NPC are not covered by the present registries.

We recommend that data be continuously gathered and that more centers participate in this process. Efforts by government and private enterprise to make the data more robust would also be of help in more accurately determining the true incidence of NPC in the Philippines. If data gathering is still limited, collecting information from representative centers, whether by geographic location or by patient volume, may also aid in estimating the country's incidence. This, however, would still require the participation of other institutions.

Received: 2013-01-14; revised: 2013-05-14;
accepted: 2013-07-05.

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