Chapter 21
Epidemiological Aspects in Nasopharyngeal Cancer

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Introduction

Nasopharyngeal cancer (NPC) is a rare cancer in the majority of countries, however NPC is endemic in certain regions of southern China, Southeast Asia and Africa. This paper provides descriptive epidemiology of the epithelial malignant nasopharyngeal tumours, showing incidence and survival variation by sex, age, geographic region/population and time trend. The source of data are the major website as given by the International Agency for Research on Cancer (IARC) Global Cancer Observatory [1], and the RARECAREnet European project [2], for Europe.

The differences in incidence and survival will be interpreted according to the literature.

Incidence

In 2018, 129,000 new cases of NPC were diagnosed worldwide with 85% of cases in the Asiatic population. Figure 21.1 shows the estimated number of new cases and the age-standardized incidence rates for the 10 countries in which NPC is diagnosed most common. Actually, in males the annual crude rate of incidence (per 100,000) dramatically varied between 8 in South-Eastern Asia and <1 in the European regions (Table 21.1).

In Europe (EU28) from European population-based cancer registries, 2600 new diagnoses per year (incidence) were made (1999–2007) and 18,200 people were living, in 2008, with a diagnosis of NPC (prevalence) [2]. Tables 21.2 and 21.3 show

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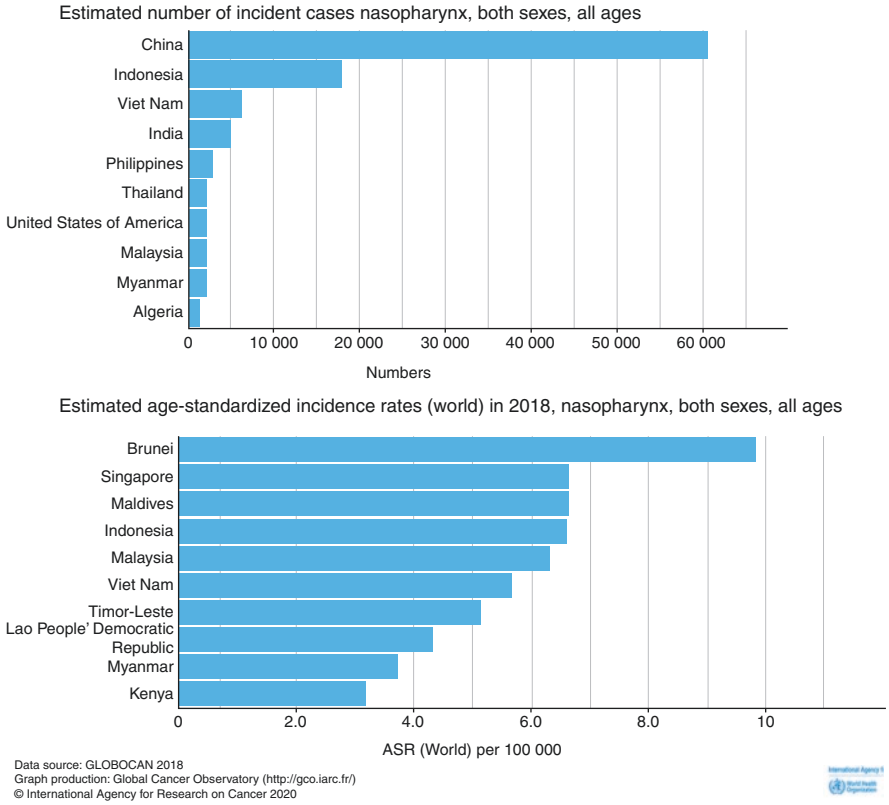

Fig. 21.1 Nasopharyngeal cancer in the ten countries with the highest incidence in 2018. From Global Cancer Observatory [1]

Table 21.1 Estimated number of new cases in 2018, nasopharyngeal cancer, males, all ages

Population	Number	Uncertainty interval	Crude rate[a]	ASR (World)[a]
Eastern Asia	46,783	[44,415.0–49,277.3]	5.5	3.9
South-eastern Asia	25,895	[22,705.8–29,532.2]	7.9	7.8
South-Central Asia	5394	[4542.2–6405.5]	0.53	0.59
Northern Africa	2331	[1726.7–3146.8]	2	2.2
Eastern Africa	2112	[1204.9–3702.1]	0.98	1.7
North America	1709	[1577.8–1851.2]	0.95	0.66
Western Asia	1642	[1321.3–2040.6]	1.2	1.3
Central and Eastern Europe	1345	[1177.2–1536.7]	0.98	0.69
South America	1273	[882.5–1836.2]	0.6	0.55
Western Africa	1170	[637.6–2146.9]	0.61	0.86
Southern Europe	1148	[920.6–1431.5]	1.5	0.97
Western Europe	903	[763.5–1067.9]	0.94	0.59
Middle Africa	515	[223.3–1187.8]	0.61	1
Caribbean	319	[204.7–497.2]	1.5	1.2

Table 21.1 (continued)

Population	Number	Uncertainty interval	Crude rate[a]	ASR (World)[a]
Northern Europe	287	[240.8–342.1]	0.56	0.37
Central America	266	[191.4–369.6]	0.3	0.32
Australia and New Zealand	145	[119.1–176.5]	0.99	0.72
Southern Africa	136	[79.3–233.3]	0.42	0.49
Melanesia	19	[5.7–63.3]	0.36	0.48
Micronesia	18	[12.2–26.6]	6.7	6.3
Polynesia	6	[3.3–10.9]	1.7	1.7

[a]Crude and age-standardized rates per 100,000
From the Global Cancer Observatory [1]

Table 21.2 Nasopharyngeal cancer in Europe, number of observed cases (obs.) and age-adjusted incidence rate (adj. rate) with (95% CI) by sex and age

	Obs.	Adj. rate
All	7439	0.429 (0.419–0.439)
Sex		
Males	5313	0.648 (0.631–0.666)
Females	2126	0.229 (0.219–0.240)
Age		
0–14 years	70	0.027 (0.021–0.034)
15–24 years	260	0.129 (0.114–0.146)
25–64 years	4862	0.571 (0.555–0.587)
65+ years	2247	0.897 (0.861–0.935)

Table 21.3 Nasopharyngeal cancer in Europe, number of observed cases (obs.) and age-adjusted incidence rate (adj. rate) with (95% CI) by time period and region

	Obs.	Adj. rate
European region		
Northern Europe	219	0.242 (0.211–0.277)
Ireland and UK	1823	0.331 (0.316–0.347)
Central Europe	1797	0.360 (0.343–0.377)
Southern Europe	2055	0.702 (0.672–0.734)
Eastern Europe	1545	0.513 (0.487–0.539)
Time period		
1995–1998	2510	0.413 (0.396–0.429)
1999–2002	2591	0.411 (0.395–0.427)
2003–2007	3227	0.400 (0.386–0.414)

From http://rarecarenet.istitutotumori.mi.it/rarecarenet/

incidence (numbers and rates) by sex, age, time period and European region. Incidence is higher in men than women with a ratio 3:1 (Table 21.2). The disease is more frequent in the elderly (65 and more years of age): the incidence rate (per 100,000/year) increases with age at diagnosis from <0.1 to 0.9 (Table 21.2).

In Europe there is an incidence gradient across countries, with the highest rates in the Southern which are 2/3 times higher than in the Northern countries. The occurrence of NPC remains constant during the period 1995–2007.

Survival

Based on about 7300 cases, survival of European patients with NPC were 76%, 57%, and 49% at 1, 3 and 5 years after diagnosis, respectively (Table 21.4). Prognosis (5-year survival) was better in younger patients, aged 15–24 years, at 73%, and dramatically reduced in the elderly, 65 years and more, at 31%. Females had a significantly better prognosis, 5-year survival, 54% versus 47% (Table 21.4).

Five-year survival was between 51% and 55% in all the European regions, except the Eastern of European countries with 36% (Table 21.5).

During the study period (1995–2007), 5-year survival slightly, but not significantly, improved.

Survival in population based studies was analyzed in terms of relative survival, which is an analogous of cause specific survival usually considered in clinical studies. Relative survival is the ratio between the observed survival of the cohort of patients belonging to a specific population (for example Belgium or Estonia) and the survival of the general population of the same country and with the same age distribution.

Table 21.4 Nasopharyngeal cancer in Europe, number of (No.) and 1, 3 and 5-year Relative Survival (RS%) with (95% CI) by sex and age

	No.	1-year RS	3-year RS	5-year RS
All	7276	76 (75–77)	57 (56–59)	49 (48–50)
Sex				
Males	5205	76 (74–77)	56 (54–57)	47 (45–49)
Females	2071	78 (76–80)	61 (59–63)	54 (51–56)
Age				
0–14 years	69	88 (81–96)	83 (75–93)	84 (75–93)
15–24 years	259	95 (92–98)	78 (73–84)	73 (67–79)
25–64 years	4791	82 (81–83)	63 (61–64)	55 (53–56)
65+ years	2157	61 (59–63)	41 (39–43)	31 (29–34)

Table 21.5 Nasopharyngeal cancer in Europe, number of (No.) and 1, 3 and 5-year Relative Survival (RS%) with (95% CI) by time period and European region

Time period	No.	1-year RS	3-year RS	5-year RS
1995–1998	1893	76 (74–78)	56 (54–59)	48 (46–51)
1999–2002	1915	73 (71–75)	54 (52–56)	47 (44–49)
2003–2007	1886	77 (75–79)	59 (56–61)	50 (48–52)
European region				
Northern Europe	218	79 (73–84)	62 (55–70)	55 (47–63)
Ireland and UK	1793	74 (72–76)	58 (56–61)	51 (48–54)
Central Europe	1764	80 (78–82)	63 (61–66)	55 (52–58)
Southern Europe	2030	80 (78–82)	60 (57–62)	51 (48–53)
Eastern Europe	1471	69 (66–71)	45 (42–48)	36 (33–39)

From http://rarecarenet.istitutotumori.mi.it/rarecarenet/

Discussion

Incidence of cancers, given by population-based cancer registries, provides the annual number of new cases of a specific cancer in a defined population/region. NPC is a rare cancer, in Europe not more than 3% of all H&N cancers [2]. Incidence together with prevalence are important for public health planning, to organize centralization of the cure and planning of clinical trials. In Europe, the number of annual cases across country ranged between 2 or less (Malta and Iceland) and 454 (Germany) [2]. The geographical variation of the incidence rates gives insight into possible factors or causes of the disease, again relevant to public health to reduce the new number of cases. The incidence variability around the world of NPC is very high and this variation has been explained by diet. According to the World Cancer Research Fund (WCRF) updated review [3], the largest review on diet, nutrition and physical activity, the major risk factors explaining the difference in incidence in populations are the consuming Cantonese style salted fish, meat and preserved non-starchy vegetable; other established causes include smoking, occupational exposure and infectious agents. There is a strong evidence of risk for NPC consuming Cantonese style salted fish and some evidence consuming red meat and processed meat; while the consumption of a greater intake of non-starchy vegetables decreases the risk of NPC. Cantonese-style salted fish contains nitrosamines and nitrosamine precursors which have been shown to induce the development of cancer. Smoking is attributable to 23% of NPC cases [3] and dust and formaldehyde are the major occupational factors associated to NPC [4]. Epstein-Barr virus (EBV) infection is an important player in this disease, but it needs other factors in addition, as only a fraction of the infected population develops NPC [3].

A recent paper, conducted in the Taiwanese population (≈160,000 participants and 115 NPC cases), showed the effect of air pollution as a risk of developing NPC [5]. The study reported a clear dose response relationship: NPC increased with the increase in nitrogen dioxide (NO_2) from 1.4 to 2.3 compared to lowest concentration levels. The same was with the fine particulate ($PM_{2.5}$) with a double risk.

There is a global reducing incidence of NPC as reported by the review by Tang et al. for the period 1970–2007 [6]. The occurrence of NPC significantly decreased in southern and eastern Asia, north America and Nordic countries with average annual percent changes (AAPCs) of −1% to −5%. Decreasing trends in NPC incidence are due to tobacco control, changes in diets and economic development. The ecological study by Lau et al. [7] investigated in some European and Asiatic countries and in the US the relationship between the NPC incidence with the consumption of salted fish, vegetables and tobacco cigarettes, from the Food and Agriculture Organization (FAO) and Census Statistics. They found markedly decreasing trends of NPC in Hong Kong which was correlated with corresponding secular changes in salted fish consumption per capita, tobacco and vegetable consumption per capita. In many countries the tobacco smoking, which is more connected to the keratinizing squamous cell carcinoma and prevalent in the non epidemic area, is reducing [6].

In Europe, NPC 5-year survival was poorer in males, in the elderly and in the Eastern countries. No progress has been observed in the first years of this century. Interestingly, from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database (1973–2013) [8], Asians showed a disease specific survival advantage over Caucasians, African Americans and Hispanics, when adjusted for sex, age at diagnosis, grade, TNM staging and treatment strategy. Asians showed a less aggressive disease characterized by non keratinizing lesions, smaller size at diagnosis, well differentiated grading and an earlier TNM stage. However, taking into account these prognostic factors in a multivariate analysis, the advantage persisted suggesting that genetic predispositions, viral agents, occupational exposures, and dietary exposures to chemical carcinogens can be responsible of the aggressiveness of the diseases. However, the African Americans had a higher rate of metastasis at the time of diagnosis and the highest proportion of no treatment with the common therapy of NPC (surgery or radiation). These results may be connected to the fact that certain minorities in the US have less access to or make use of medical care in terms of clinic visits, preventative care and diagnostic testing.

NPC is a rare cancer, therefore the correct and fast diagnosis and treatment can be obtained in high volume hospitals with a good expertise. Diagnosis and treatment in reference centres are expected to be more accurate because they benefit from large numbers of cases, which are often discussed in a multidisciplinary setting involving expert professionals. Within the RARECAREnet project [9] centralization of rare cancer patients was studied in 7 European countries, and for the head and neck group of rare cancers 75% of patients were centralised in two top hospitals in Slovenia (2 million population, 266 treatments per hospital per year), and 12 top hospitals in the Netherlands (17 million population, 201 treatments per hospital per year). The level of centralisation was lower in the other countries such as Finland, Ireland, Bulgaria, Navarra and Belgium. However, the period of study was 1999–2007 and the situation will for sure improve in some countries over time. The European Joint Action on Rare Cancers [10] and the institution of the European Reference Network for rare diseases [11] will continue to play a role in this.

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