

Age distribution of nasopharyngeal cancer in Saudi Arabia

Abdulwahab A. Andejani, MD, CHB, Vijayananda Kundapur, MD, DMRT, Kamal Malaker, MD, PhD.

ABSTRACT

Objective: The age standardized rate of head and neck cancer in the Kingdom of Saudi Arabia (KSA) is 5.7% with nasopharyngeal cancer (NPC) accounting for >40% of all head and neck cancers. This study intends to compare age specific incidence of NPC in KSA and other countries.

Methods. Data from the National Cancer Registry for KSA during the period 1994 through to 1996 was compared with data from the World Health Organization International Agency for Research on Cancer (ARC) in Singapore, China, Kuwait and Canada.

Results. There were 373 diagnosed Saudi patients with NPC with high incidence among the young population, with 42/373 (22 males/20 females) patients in the first 20

years of life, showing a sharp increase both in boys and girls until the ages of 12-14 years. From that point the incidence curve for both males and females separates. In females the incidence flattens without an identifiable zenith from the age of 12-14 years and above, compared with their male counterpart where they have another peak in the fifth decade.

Conclusion. Our study indicates a definite early onset of this malignancy in KSA and a similar pattern to that of China and Singapore. Definite increased incidence, at a young age among both sexes, suggests a possible underlying genetic susceptibility in Saudis.

Saudi Med J 2004; Vol. 25 (11): 1579-1582

The age standardized rate (ASR) of head and neck cancer in Kingdom of Saudi Arabia (KSA) is 5.7%. Nasopharyngeal Cancer (NPC) accounts for more than 40% of all head and neck cancers in KSA.¹ The epidemiology of NPC suggests that factors like diet, viral agents and genetic susceptibility have a major role to play.^{2,3} Certain endemic areas such as Southern China, Hong Kong, Singapore, and North Africa are well known to have a high incidence of NPC^{4,5} (Figures 1 & 2). These regions also show a higher incidence among younger age group from 15-30-years, and a second peak around the fifth decade of life. These areas are characterized by consumption of salt cured fish hence association with nitrosamines.⁶ However the strongest environmental association with

Epstein-Barr virus is also well documented in these region.⁷ In addition to this, migrant studies on the Chinese population also highlighted the environmental cause though they could not rule out the genetic etiology.^{8,9} (Figure 2, China, Shanghai) Recently genetic determinants of NPC has been suggested and they are associated with increased incidence among individuals with specific major histocompatibility profiles such as presence of H2 locus.¹⁰ Similarly the presence of so called Singapore antigen BW46 and also the presence of B17 antigen increase the risk.¹¹ In the case of association with B17 antigen, this will be characterized by earlier onset of disease at a younger age.¹¹ In a recent Chinese study¹² a set of 42 genes were identified to be expressed in both

From the Princess Norah Oncology Centre, King Abdulaziz Medical City, National Guard Health Affairs, Jeddah, Kingdom of Saudi Arabia.

Received 12th May 2004. Accepted for publication in final form 21st June 2004.

Address correspondence and reprint request to: Dr. Vijayananda Kundapur, Radiation Oncologist, Princess Norah Oncology Centre, King Abdulaziz Medical City, National Guard Health Affairs, Jeddah 21423, Kingdom of Saudi Arabia. Tel. +966 (2) 6240000 Ext. 4082/4084. Fax. +966 (2) 6247424. E-mail: kotegar@yahoo.com

malignant as well as normal nasopharyngeal epithelium (NPE). Thirteen of these were over expressed in malignant NPE and 9 others genes were suppressed in them. This suggests the possibility of genetic screening for the high risk population as in Southern China.^{12,13}

The objective of this work is to compare and find out if there are any similarities between the age specific incidence of NPC in KSA with the population of the countries already known to have a high risk of developing NPC and also compare to that of the Western population. At the same time an attempt has been made to find out if the pattern observed in KSA is similar to that observed in other Middle Eastern countries wherever data is available.

Methods. The epidemiological data pertaining to NPC in KSA for the period between 1994 and 1996 has been obtained from the National Cancer Registry (NCR). This data was compared with World Health Organization International Agency for Research on Cancer (IARC) data in Singapore, China and Kuwait.

Results. The Crude Incidence (CI) of NPC as reported for KSA stratified according to the age of onset (**Figure 3**), shows that the incidence among younger population is high almost making a peak and then plateaus (ranging from 15-30-years with a median of 24.6-years). The peak for the adult patients is occurring at a median age of 52-years (ranging from 45-59-years). There were 3 patients below the age of 4-years with one male patient and 2 patients among female sex. Age distribution for Saudi males with NPC shows a bimodal incidence with an early peak similar to that of the whole population. The higher incidence was noticed among teenagers (range from 10-19-years with a median of 14.5). However the second peak is little extended with a median age of 49.5 years (range from 30-69-years). (**Figure 3**) Age distribution for Saudi females with NPC does not show any peak. But shows a definite higher incidence among teenagers reaching to 15.8% of the total incidence of NPC among females. This merges with the incidences of NPC at other age groups forming almost a flat curve with out a definite peak (**Figure 3**). The age distribution for the NPC patients between 1979 through to 1982, from Kuwait, does show an early incidence for male sex among teenagers though the number of incidences are fewer. The peak for the incidence among adult males is not well formed however it appears during the 6th decade of life (**Figure 4**). The NPC incidence for the females in Kuwait is not the same as that observed in the KSA. There is no incidence among younger age group among females unlike the male sex and far fewer

number of cases (**Figure 4**). Age distribution of patients with NPC for the same period for Canada showed definitely 2 different age of onset for male and female sexes. Incidence of NPC below the age of 30-years was mostly among males only. The incidence pattern for females follows the same curve as that of male, though it starts diverging and comes down after 4th decade. The incidence of NPC in both sexes among adults maintains almost same ratio (**Figure 5**).

Discussion. Earlier investigators based on single institution hospital based registry have reported higher incidence of NPC¹⁴ and also higher incidence among teenagers^{15,16} and onset of disease among children.¹⁷ A large single institution review of 5000 cancer patients profile in 1994 gave the impression that the risk of developing NPC is not high compared to high risk countries.¹⁸ Our study based on age standardized national data, shows that the CI for NPC in KSA shows similar pattern of distribution as that of China and Singapore, with high incidence among young population. There were 42/373 patients in the first 20-years of life and 7/42 patients were below the age of 9-years with 3/7 below first 5-years of life. This indicates that there is definite early onset of this malignancy in KSA. This raises the possibility of underlying genetic susceptibility of the population of KSA as noted by the similarity in presentation of NPC among the population in the countries such as China and Singapore where genetic etiology has been documented. Though Kuwait shares the similar geophysical characteristics as that of KSA, the incidence pattern of NPC in Kuwait is not similar to that of the KSA. This could be possibly as of different etiological mechanisms at work. However there is definite increased incidence among teenage males. Again underlines the possible genetic etiology. However there is striking dissimilarity between the female incidences and male incidences in Kuwait with far fewer incidences among female sex and absence of NPC among young adult females or in children unlike that observed in KSA. In contrast to the pattern of incidence in KSA as well as those of high incidence countries like China and Singapore, the incidence of NPC in the West shows no increased frequency among teenagers. In general the incidence among the male and female sex is such that the ratio is maintained without any exaggerated incidence among one sex as seen in KSA as well as in China and Singapore. It is interesting to note the difference in age and sex related incidence of NPC between Saudi, Western and Chinese population. Incidence increases sharply and identically both in boys and girls till the age of 12-14-years. From that point incidence curve for both males and females separate, female being

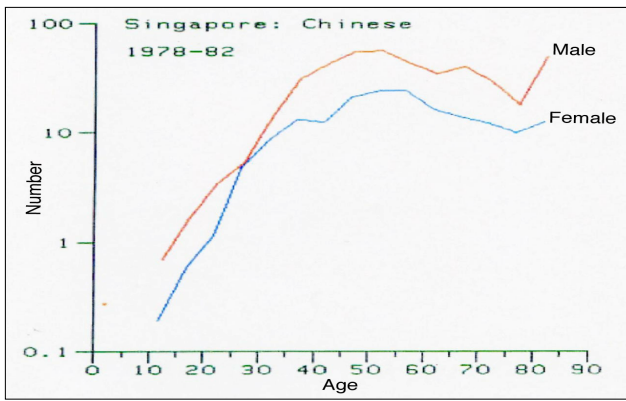


Figure 1 - Incidence of nasopharyngeal carcinoma among Singapore Chinese 1978 through to 1982.

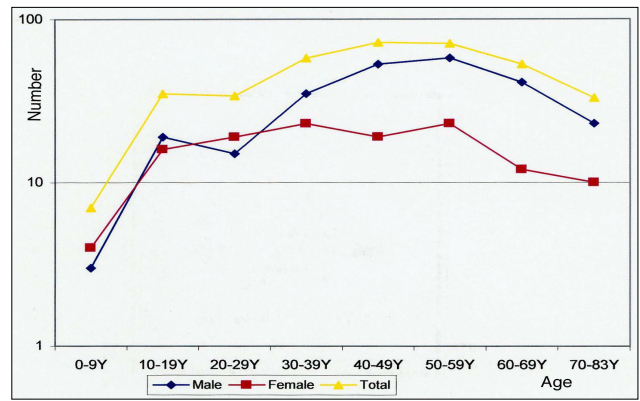


Figure 3 - Incidence of nasopharyngeal carcinoma among Saudis 1994 through to 1996.

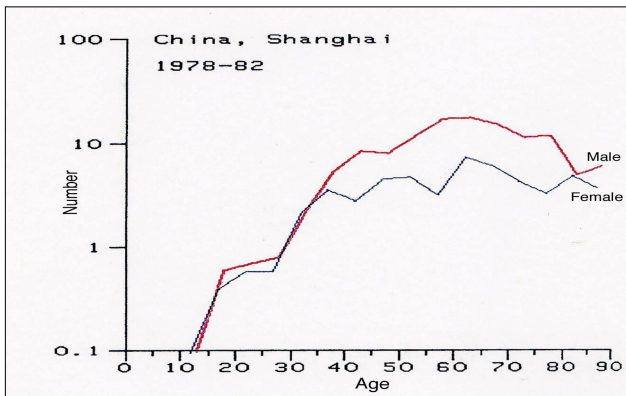


Figure 2 - Incidence of nasopharyngeal carcinoma among Chinese, Shanghai 1979 through to 1982.

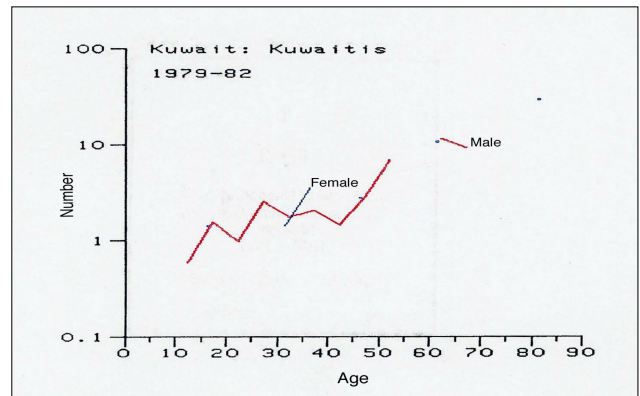


Figure 4 - Incidence of nasopharyngeal carcinoma among Kuwaitis 1978 through to 1982.

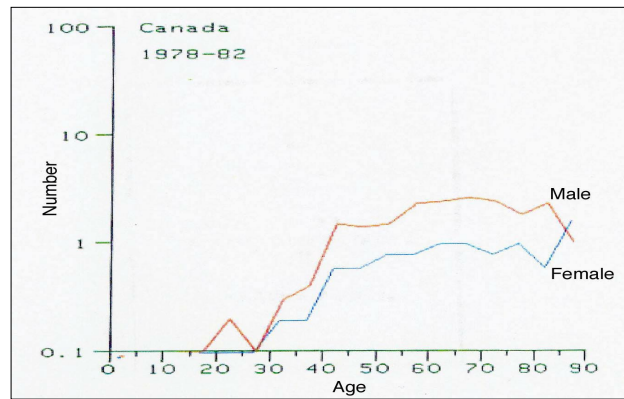


Figure 5 - Incidence of nasopharyngeal carcinoma among Canadians 1978 through to 1982.

much less. The cupolic shape remains similar in both sexes, the zenith in female being shorter in height. However it appears that in Saudi females the incidence flattens without an identifiable zenith from the age of 12-14-years and above, compared with their male counterpart. This pattern is unlike Western and Chinese female. Apart from known factors which are responsible for lower incidence of NPC in female in general, there appears to be an extra protection for Saudi female against contracting NPC. The authors postulate that starting to wear the face covering from the age of 12-14-years by Saudi females perhaps accounts for that extra protection against contracting NPC for the rest of their life. At the same time we have to keep in mind that in KSA, the majority of patients present in an advanced stage.¹⁴ Nearly 70% of these patients have undifferentiated histopathology.¹⁴ It has been well documented that Epstein Barr (EB) virus related NPC is associated with undifferentiated histology.¹⁵

In the present work we have observed that the incidence among teenage individuals in countries like China and Singapore with a known high incidence of NPC is higher compared to rest of the world. The genetic role in the etiogenesis if NPC have been noticed among these countries.^{12,13} In our present work the incidence in KSA is similar to that of countries with high incidence NPC. The higher incidence of NPC among teenage individuals in both sexes in KSA could be possibly having an underlying genetic etiology. This could be true as well for the observed higher incidence among the young Kuwaiti male population. The overall lesser incidence of NPC among the Saudi female sex in KSA and the lower incidence among Kuwaiti females could be as of the cultural and religious practice of wearing a face cover which might play a role in interfering with EB virus infection. This could suggest the possible interruption in the continuous stimulus in the cascade leading to the formation of NPC, played by EB Virus.

References

1. National Cancer Registry report 1994-1996. Riyadh (KSA): Ministry of Health; 1999. p. 49-72.
2. Henderson BE, Louie E, Jing JSH, Bwell P, Gardener M. Risk factor associated with Nasopharyngeal Carcinoma. *N Engl J Med* 1976; 295: 1101-1106.
3. Janse van Rensburg E, Van Heerden WF, Robson BA, Swart TJ, Engelbrecht S. Epstein-Barr virus strain characterization in South African patients with nasopharyngeal carcinomas. *Anticancer Res* 2000; 20: 1953-1957.
4. Whelan SL, Parkin DM, Masuyer E, editors. Pattern of cancer in five continents. Vol. V. No. 102. World Health Organization International Agency for Research On Cancer. Lyon (FR): IARC Scientific Publications; 1990. p. 116-117.
5. Higginson J, Muir CS, Munoz N, editors. Human cancer: epidemiology and environmental causes. Cambridge Monograph on Cancer Research. Nasopharynx. Cambridge (UK): Cambridge University Press; 1992. p. 256-260.
6. Yu MC, Ho JHC, Lai SH, Henderson BE. Cantonese-style salted fish as a cause of Nasopharyngeal carcinoma: report of a case control study in Hong Kong. *Cancer* 1986; 46: 956-961.
7. Fahraeus R, Fu HL, Emberg I et al. Expression of Epstein-Barr Virus enrolled proteins in nasopharyngeal carcinoma. *Int J Cancer* 1988; 42: 329-338.
8. Blitzer PH. Epidemiology of head and neck cancer. *Seminars In Oncol* 1988; 15: 2-9.
9. Fraumeni JK, Mason TJ. Cancer mortality among Chinese Americans (1950-1969). *JNCI* 1974; 52: 659-665.
10. Chan SH, Day DE, Kunaratnan N, Chia KS, Simon MJ. HLA and nasopharyngeal cancer in Chinese a further study. *Int J Cancer* 1983; 32: 171-176.
11. Simons MJ, Wee GB, Goh EH et al. Immunogenetic aspects of nasopharyngeal carcinoma IV: Increased risk in Chinese of nasopharyngeal carcinoma associated with a Chinese related HLA profile (A(2), Singapore 2. *J Natl Cancer Int* 1976; 57: 977-980.
12. Fung LF, Lo AK, Yuen PW, Liu Y, Wang XH, Tsao SW. Differential gene expression in nasopharyngeal carcinoma cells. *Life Sci* 2000; 67: 923-936.
13. Xie L, Xu L, He Z, Zhou W, Wanna L et al. Identification of differentially expressed genes in nasopharyngeal carcinoma by means of Atlas human cancer cDNA expression array. *J Cancer Res Clin Oncol* 2000; 126: 400-406.
14. Amer MH. Pattern of cancer in Saudi Arabia: A personal experience based on the management of 1000 patients Part 1. *Ann Saudi Med* 1982; 2: 203-215.
15. Clubb B et al. Nasopharyngeal carcinoma in Saudi Arabia Selected clinical and epidemiological aspects. *Ann Saudi Med* 1990; 10: 171-175.
16. Al-Ghamdi S, Maltani T, Kameswaran M, Khurana P. Head and neck cancer in referral centre in Asir region. *Ann Saudi Med* 1994; 14: 383-385.
17. Mahboubi E. Epidemiology of cancer in Saudi Arabia, 1975-1985. *Ann Saudi Med* 1987; 7: 265-276.
18. Koriech OM, Al-Kuhaymi R. Profile of cancer in Riyadh Armed Forces Hospital. *Ann Saudi Med* 1994; 14: 187-193.
19. Malaker K, Kundapur V, Andejani AW. Gender variation and nasopharyngeal carcinoma in Saudi females. Proceedings from the ISPO: Molecular Basis of Predictive Oncology and Intervention Strategies Symposium; 2004, Feb 7-10; Nice, France; 2004.
20. Hadir M, Wafa AL, Elwia T, Viajayananda K. Factors affecting outcome of treatment of advanced nasopharyngeal carcinoma. *Med J Cairo Univ* 2000; 68: 261-271.
21. Marshall P. The promise and practice of head and neck cancer therapies. Proceedings of the 37th Annual Meeting of American Society of Clinical Oncology; 2001, May 1-15; San Francisco, United States of America; 2001.
22. Feng P, Chan SH, Soo MY, Liu D, Guan M et al. Antibody response to Epstein-Barr Virus Rta protein in patients with nasopharyngeal carcinoma. A new serologic parameter for diagnosis. *Cancer* 2001; 92: 1872-1880.