



Head and neck cancer in a developing country: A population-based perspective across 8 years

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SUMMARY

Head and neck cancer (HNC) has been studied in different regions of the world but little is known about its incidence patterns in the Middle East and Egypt.

In this study from Egypt's only population-based registry, we analyzed data from 1999 to 2006, to estimate incidence, incidence rate ratios (IRRs) and 95% confidence intervals (CIs) categorized by age, district and subsites.

Overall urban incidence of HNC was twice or more that of rural incidence for both males (IRR = 2.59; 95% CI = 2.26, 2.97) and females (IRR = 2.00; 95% CI = 1.64, 2.43). Highest urban–rural difference for males was seen in 40–49 years (IRR = 2.79; 95% CI = 1.92, 4.05) and for females in 30–39 years (IRR = 2.94; 95% CI = 1.60, 5.40). Among subsites, highest incidence among males was for larynx (1.53/10⁵) and among females for gum and mouth (0.48/10⁵). Maximum urban–rural difference in males was for paranasal sinus (IRR = 4.66; 95% CI = 1.88, 11.54) and in females for lip (IRR = 8.91; 95% CI = 1.89, 41.98).

The study underscores the patterns of HNC incidence in Egypt while indicating the need for future analytical studies investigating specific risk factors of HNC in this population.

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Introduction

Head and neck cancer (HNC) are a group of malignancies involving oral cavity, pharynx, ear/nose, and larynx. Among the 10 most common incident cancers in men worldwide, 90% of HNC is squamous cell carcinomas (SCC).¹ Each year there are approximately 560,000 new cases of and 300,000 deaths due to HNC.² The highest incidences of HNC in the world are found in South Asia, and parts of central and southern Europe.² By far, the most common risk factors associated with HNC are tobacco and alcohol use with significant interaction observed between the two.³ Other observed risk factors are poor oral hygiene⁴ and the human papillomavirus (HPV) 16 in tongue, tonsil and oropharyngeal HNC and, in particular, non-smoking cases of HNC.⁵ In South Asian countries the risk of HNC is further aggravated by smoking of *bidis* which increases

the incidence of cancer of hypopharynx and larynx⁶, and chewing tobacco, betel quid and areca-nut.⁷

Within the Middle East, rates of smoking are high^{8,9} although alcohol consumption is limited. This is especially true for Egypt where smoking rates are increasing for both cigarettes and water-pipe.⁹ However, there have been very few studies depicting the magnitude or etiologic factors of HNC in the Middle East and Egypt. Previous hospital-based studies from Egypt showed that HNC constitutes about 17–20% of all malignancies.^{10,11} The majority of cases are diagnosed at advanced stages^{12–14}, and the suspected risk factors of subsites varied by tumor site and place of residence in small-scale hospital-based studies.^{15–17} A report of the Middle East Cancer Consortium (MECC) of the National Cancer Institute in Bethesda, USA, depicted that Egypt had one of the highest overall incidence rates of cancer of oral cavity and pharynx (5.5/10⁵) among the MECC countries, equal to the rate seen in Israeli Jews.¹⁸ As such, we conducted this study to investigate the incidence of different clinical subsites of HNC in Egypt's only population-based cancer registry in the Province of Gharbiah. We also explored the demographic and geographical patterns of HNC to

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better understand the regional differences of the disease and generate hypotheses regarding the HNC etiology.

Patients and methods

Study population

The study population consisted of men and women diagnosed with HNC from 1999 through 2006 from the Gharbiah population-based cancer registry (GPCR) comprising the following sites: lip, tongue, gum, mouth (floor, palate, other), salivary glands, tonsils, pharynx (oro-, naso- and hypopharynx), and nose and ear. For each case, the following information from routinely-collected registry data was obtained: registry number, age at diagnosis, address, address code, smoking status, occupation, basis of diagnosis, tumor grade, stage, morphology, medical record number, and place of referral. Data were stripped of all personal identifiers and their analyses were approved by the University of Michigan Institutional Review Board and the Gharbiah Cancer Center Ethics Committee.

Gharbiah population-based cancer registry

The Gharbiah population-based cancer registry, founded in 1998 as a part of the Middle East Cancer Consortium (MECC) and funded by the US National Cancer Institute (NCI), is located in Tanta, the capital of Gharbiah province.^{9,18} Through an active registration process, data on cancer cases are collected from various sources in the province. For this study, yearly HNC cases came from three locations; the Tanta Cancer Center (40–50%), Gharbiah Cancer Society (10–12%) and Tanta University Hospital (10–12%). Data obtained from these hospitals and centers were entered in a manner that ensured strict quality control checks and avoided repetition of cases using the International Agency for Research on Cancer (IARC) software CanReg4. Registrars were trained in data extraction and entry methods, and are periodically monitored by faculty of Emory School of Public Health, IARC, and the MECC.¹⁸

Gharbiah province

The Gharbiah province is an administrative region located 90 km north of Cairo in the Nile delta region and has eight districts, each with a capital city (Figure 1). Tanta city also serves as the capital of the province. Gharbiah has a population of more than 4 million people, 49% of whom are women. Approximately 30% of the

population resides in urban areas and almost 47% of the female population is below the age of 20, according to the 2006 Central Agency for Public Mobilization and Statistics (CAPMAS) national census of Egypt.¹⁹

Census data

The 1996 and 2006 CAPMAS censuses were used to obtain data on men and women residing in Gharbiah²⁰, and linear regression was used to estimate the population during each study year. The linear growth rates of eight districts were applied to the urban and rural populations within those districts to determine urban and rural populations from 1999 through 2006. The census data consisted of 16 age categories at 5 year intervals. Six age categories were created from these by collapsing the age categories below 29 years followed by 10 year intervals. These population figures formed the denominators to calculate the overall, age-specific, and urban–rural incidence rates for HNC and its subsites.

Urban–rural classification

Urban and rural designations were made according to the CAPMAS definitions.²⁰ Urban areas consisted of all the capital cities of the eight districts of the province, while the remaining areas in the province were considered rural. Each case in the registry was assigned a residence code based on their residential address that follows the CAPMAS coding which was used to classify cases as urban or rural.

Statistical analysis

Descriptive statistics and incidence rate analyses were completed using SAS (Version 9; SAS Institute, Cary, NC). Crude and age-adjusted incidence rates were calculated for Gharbiah province, each of the eight districts, and urban and rural areas for the province. Age-specific incidence rates for the entire population and for urban vs. rural areas for each of the six age categories. The six age categories were 0–29, 30–39, 40–49, 50–59, 60–69 and 70 or more. Direct age-adjusted incidence rates were calculated by using Gharbiah's 2006 population as the standard. We then calculated urban–rural incidence rate ratios (IRR) and 95% confidence intervals (CI) using Poisson regression. We also calculated incidence rates specific to HNC subsites and compared overall

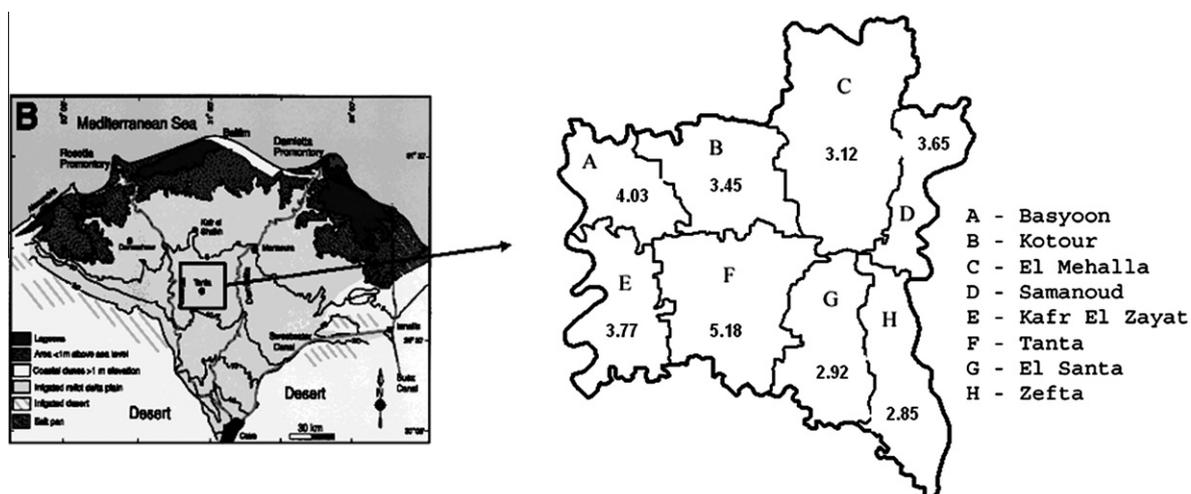


Figure 1 Distribution of head and neck cancer incidence in the districts of Gharbiah, Egypt.

rates to US SEER, as well as compared urban and rural incidence rates.

Results

A total of 1140 cases of HNC were identified in Gharbiah, Egypt from 1999 to 2006 with 64.3% of all cases being male (Table 1). More than half of the cases were in the 50–69 year age-category (50.71%). Most cases belonged to the two largest districts of Tanta (33.07%) and El Mehalla (21.4%). Almost 40% of males were current or former smokers although more than half of the cases had missing information on smoking (52.02%). Most cases were detected at localized stage (28.42%) and had been detected by histopathological confirmation of the primary (91.84%) (Table 1).

Overall incidence of HNC was approximately twice among males (4.76/10⁵) than in females (2.73/10⁵) (Table 2). Overall age-specific incidence was highest in the 70+ age group in both males (44.09/10⁵) and females (18.39/10⁵). Overall urban incidence of HNC was twice or more that of rural incidence for both males (IRR = 2.59; 95% CI = 2.26, 2.97) and females (IRR = 2.00; 95% CI = 1.64, 2.43). Highest urban–rural difference for males was seen in the 40–49 year age-category (IRR = 2.79; 95% CI = 1.92,

4.05) while for females it was in the 30–39 year age-category (IRR = 2.94; 95% CI = 1.60, 5.40) (Table 2).

Highest overall incidence of HNC was in Tanta (6.79) followed by Samanoud (5.24) for males, and Tanta (3.57/10⁵) followed by Basyoon (3.11/10⁵) in females (Table 3). Highest urban–rural differences were observed in El-Santa (IRR = 8.52; 95% CI = 5.02, 14.46) followed by Kotoor (IRR = 6.98; 95% CI = 3.88, 12.57) among males. Among females, highest urban–rural differences were present for Kotoor (IRR = 7.41; 95% CI = 3.45, 15.91) followed by Kafr El-Zayat (IRR = 5.92; 95% CI = 3.22, 10.87) (Table 3).

On analyzing incidence of HNC by subsite (Table 4) we discovered that the highest incidence among males was for larynx (1.53/10⁵), nasopharynx (0.65/10⁵), gum and mouth (except floor) (0.49/10⁵), and tongue (0.42/10⁵). Among females, the highest incidence was observed for gum and mouth (except floor) (0.48/10⁵), nasopharynx (0.40/10⁵), hypopharynx (0.40/10⁵), and salivary glands (0.34/10⁵). Highest urban incidence of HNC subsites among males was present for larynx (3.09/10⁵), nasopharynx (1.12/10⁵), tongue (0.69/10⁵), and gum and mouth (except floor) (0.67/10⁵) with a similar order seen for rural males as well (Table 4). Among urban females highest incidence of HNC subsites was observed for gum and mouth (except floor) (0.76/10⁵), nasopharynx (0.74/10⁵), salivary glands (0.54/10⁵), and hypopharynx (0.50/10⁵). Among rural

Table 1
Distribution of head and neck cancer patients in Gharbiah, Egypt 1999–2006.

Variables	Overall		Male		Female	
	N	%	N	%	N	%
Total	1140	100	733	64.30	407	35.70
<i>Age at diagnosis</i>						
Age 0–29	81	7.11	47	6.41	34	8.35
Age 30–39	93	8.16	51	6.96	42	10.32
Age 40–49	201	17.63	111	15.14	90	22.11
Age 50–59	291	25.53	192	26.19	99	24.32
Age 60–69	287	25.18	202	27.56	85	20.88
Age 70+	187	16.40	130	17.74	57	14.01
<i>Urban–rural</i>						
Urban	579	50.79	386	52.66	193	47.42
Rural	561	49.21	347	47.34	214	52.58
<i>District</i>						
Tanta	377	33.07	251	34.24	126	30.96
El Mehalla	244	21.40	145	19.78	99	24.32
Kafr El-Zayat	109	9.56	66	9.00	43	10.57
Zefta	95	8.33	61	8.32	34	8.35
Samanoud	82	7.19	59	8.05	23	5.65
El-Santa	82	7.19	56	7.64	26	6.39
Kotoor	75	6.58	48	6.55	27	6.63
Basyoun	76	6.67	47	6.41	29	7.13
<i>Smoking status</i>						
Current smokers	151	13.25	150	20.46	1	0.25
Non-smokers	273	23.95	83	11.32	190	46.68
Former smokers	123	10.79	122	16.64	1	0.25
Unknown	593	52.02	378	51.57	215	52.83
<i>Stage at diagnosis</i>						
In situ	15	1.32	12	1.64	3	0.74
Localized (stage I lymphoma)	324	28.42	216	29.47	108	26.54
Regional – direct extension	190	16.67	117	15.96	73	17.94
Regional-lymph nodes	128	11.23	83	11.32	45	11.06
Regional-direct extension and lymph nodes	89	7.81	57	7.78	32	7.86
Regional-stage II lymphoma	85	7.46	33	4.50	52	12.78
Distant-stage III and IV lymphomas	120	10.53	87	11.87	33	8.11
Unknown	189	16.58	128	17.46	61	14.99
<i>Basis of diagnosis</i>						
Death certificate	11	0.96	9	1.23	2	0.49
Clinical	2	0.18	1	0.14	1	0.25
Clinical/radiographic	9	0.79	2	0.27	7	1.72
Cytology/hematology	18	1.58	10	1.36	8	1.97
Histology of metastasis	53	4.65	34	4.64	19	4.67
Histology of primary	1047	91.84	677	92.36	370	90.91

Table 2
Comparison of urban–rural age-specific incidence^a of head and neck cancer by gender in Gharbiah, Egypt (1999–2006).

Age group	Male				Female			
	Overall	Urban	Rural	IRR ^b (95% CI)	Overall	Urban	Rural	IRR ^b (95% CI)
Age 0–29	0.49	0.89	0.34	2.65 (1.50, 4.68)	0.36	0.50	0.30	1.68 (0.85, 3.34)
Age 30–39	2.55	3.37	2.20	1.53 (0.87, 2.70)	1.99	3.56	1.21	2.94 (1.60–5.40)
Age 40–49	6.33	11.14	3.99	2.79 (1.92, 4.05)	5.89	8.10	4.63	1.75 (1.16, 2.64)
Age 50–59	16.28	22.37	12.86	1.74 (1.32, 2.29)	11.01	12.68	10.14	1.25 (0.83, 1.89)
Age 60–69	31.47	46.69	22.39	2.09 (1.59–2.75)	13.53	20.20	10.35	1.95 (1.27, 3.00)
Age 70+	44.09	69.43	30.63	2.27 (1.60, 3.23)	18.39	31.80	12.80	2.48 (1.49, 4.13)
Total	4.76	8.35	3.22	2.59 (2.26, 2.97)	2.73	4.17	2.08	2.00 (1.64, 2.43)

CI = confidence interval.

^a All incidence is per 100,000.

^b IRR = incidence rate ratio.

Table 3
Comparison of urban–rural incidence^a of head neck cancer for districts by gender in Gharbiah, Egypt (1999–2006).

Districts	Male				Female			
	Overall	Urban	Rural	IRR ^b (95% CI)	Overall	Urban	Rural	IRR ^b (95% CI)
Tanta	6.79	9.34	4.79	1.95 (1.51, 2.52)	3.57	3.87	3.32	1.17 (0.82–1.66)
El Mehalla	3.67	5.31	2.42	2.19 (1.57, 3.06)	2.57	2.76	2.42	1.14 (0.77, 1.69)
Kafr El-Zayat	4.51	11.10	2.95	3.76 (2.30, 6.14)	3.03	8.93	1.51	5.92 (3.22, 10.87)
Zefta	3.58	7.70	2.46	3.13 (1.88, 5.21)	2.12	3.70	1.68	2.20 (1.11, 4.37)
Samanoud	5.24	8.86	4.39	2.02 (1.17, 3.50)	2.06	3.75	1.66	2.26 (0.95, 5.35)
El-Santa	3.93	20.27	2.38	8.52 (5.02, 14.46)	1.90	5.97	1.52	3.92 (1.65, 9.29)
Kotoor	4.43	20.43	2.93	6.98 (3.88, 12.57)	2.46	11.78	1.59	7.41 (3.45, 15.91)
Basyoun	4.95	10.00	3.51	2.85 (1.61, 5.03)	3.11	8.57	1.52	5.62 (2.67, 11.84)

CI = confidence interval.

^a All incidence is per 100,000.

^b IRR = incidence rate ratio.

Table 4
Comparison of incidence^a of head neck cancer for subsites by urban–rural status within genders, and with SEER in Gharbiah, Egypt (1999–2006).

Head and neck cancer subsites	Male				Female				ASW ^c	
	Overall	Urban	Rural	IRR ^b (95% CI)	Overall	Urban	Rural	IRR ^b (95% CI)	Gharbiah incidence	SEER incidence
Lip	0.25	0.48	0.16	3.01 (1.60, 5.67)	0.07	0.17	0.02	8.91 (1.89, 41.98)	0.23	0.88
Tongue	0.42	0.69	0.30	2.33 (1.43, 3.80)	0.27	0.37	0.22	1.65 (0.88, 3.08)	0.49	2.80
Gum and mouth-other	0.49	0.67	0.41	1.64 (1.04, 2.60)	0.48	0.76	0.36	2.11 (1.33, 3.35)	0.67	1.64
Mouth-floor	0.03	0.02	0.03	0.78 (0.08, 7.46)	0.02	0.04	0.01	4.46 (0.40, 49.15)	0.03	0.71
Salivary glands	0.37	0.63	0.26	2.41 (1.43, 4.05)	0.34	0.54	0.24	2.23 (1.28, 3.88)	0.51	1.25
Tonsils and oropharynx	0.27	0.50	0.18	2.82 (1.54, 5.18)	0.27	0.28	0.26	1.07 (0.55, 2.08)	0.37	1.71
Larynx	1.53	3.09	0.86	3.58 (2.76, 4.65)	0.15	0.30	0.08	3.90 (1.64, 9.30)	1.32	3.61
Nasopharynx	0.65	1.12	0.45	2.52 (1.7, 3.73)	0.40	0.74	0.24	3.03 (1.81, 5.08)	0.70	–
Piriform sinus	0.16	0.17	0.15	1.16 (0.5, 2.72)	0.07	0.07	0.08	0.84 (0.22, 3.15)	0.18	–
Hypopharynx	0.34	0.48	0.28	1.71 (0.98, 2.96)	0.40	0.50	0.36	1.39 (0.82, 2.33)	0.49	–
Other	0.06	0.11	0.04	2.91 (0.78, 10.84)	0.07	0.06	0.07	0.96 (0.25, 3.69)	0.08	–
Ear/nose	0.06	0.09	0.05	1.86 (0.50, 6.94)	0.12	0.22	0.08	2.79 (1.10, 7.06)	0.10	–
Paranasal sinus	0.14	0.30	0.07	4.66 (1.88, 11.54)	0.08	0.13	0.06	2.23 (0.72, 6.91)	0.13	–

CI = confidence interval.

^a All incidence is per 100,000.

^b IRR = incidence rate ratio.

^c ASW = age-standardized to the world population.

females the highest incidence of HNC subsites was in the following order: gum and mouth (except floor) (0.36/10⁵), hypopharynx (0.36/10⁵), tonsils and oropharynx (0.26/10⁵), salivary glands (0.24/10⁵), and nasopharynx (0.24/10⁵). For males, maximum urban–rural difference was detectable for paranasal sinus (IRR = 4.66; 95% CI = 1.88, 11.54), larynx (IRR = 3.58; 95% CI = 2.76, 4.75), and lip (IRR = 3.01; 95% CI = 1.60, 5.67). Among females, maximum urban–rural differences were observed for lip (IRR = 8.91; 95% CI = 1.89, 41.98), floor of the mouth (IRR = 4.46; 95% CI = 49.15), and larynx (IRR = 3.90; 95% CI = 1.64, 9.30) (Table 4).

On comparing age-standardized HNC incidence by subsite in Gharbiah with age-standardized incidence from SEER we discovered a lower incidence in Gharbiah for all subsites compared to

SEER although incidence of laryngeal cancer was highest in both Gharbiah (1.32/10⁵) and SEER (3.61/10⁵) (Table 4).

Discussion

In this first study describing the epidemiology of HNC in Egypt using data from the only population-based cancer registry, we revealed higher incidence of HNC among males than females and higher incidence in urban than rural populations. Overall, the incidence of HNC was highest in the 70+ age group in both males and females. Highest urban–rural differences were observed in the 40–49 year age group in males and 30–39 year age group in

females. Among districts, the highest overall HNC incidence was observed in Tanta and Samanoud districts among males, and Tanta and Basyoon districts among females. Highest urban–rural differences were found for El-Santa and Kotoor districts for males, and Kotoor and Kafr El-Zayat districts for females. The subsite analysis showed that males had the highest overall incidence for larynx and nasopharynx while females had the highest overall incidence for gum and mouth (except floor) and nasopharynx. The highest urban–rural incidence was observed for the subsites of paranasal sinus and larynx among males, and lip and floor of the mouth among females.

The overall highest incidence in the 70+ age group in both males and females might be related to previous extensive nutritional deficiencies and environmental exposures to nitrates a few decades ago in Egypt.^{17,21,22} The highest urban–rural differences were observed in 40–49 year age group in males and 30–39 year age group in females could be due to the increasing and higher smoking rates in men in urban than rural areas and the possible viral etiology in younger women in urban compared to rural areas. The decline in age of incidence of HNC was also reported in the U.S.²³ and is often attributed to increasing incidence of HPV-related HNC. Unfortunately, using registry data we have inadequate information on smoking history, which could indicate the frequency of non-smoking and likely HPV-related cases of HNC. The Surveillance Epidemiology and End-Results (SEER) analysis showed that since the mid-1990s, females in the US between 10 and 40 years of age had an increase in the incidence of oral and pharyngeal cancers contrary to previous periods.²³ HPV and other sexually transmitted diseases were suspected in the decline of the age incidence in the US²³ and might be the reason for the age decline also in Egypt too. The highest rates observed in the two districts of Tanta and Samanoud among males and females in Tanta and Basyoon could be due to the higher smoking rates in urban areas (Tanta), and environmental pollution, infection and malnutrition in the two districts of Samanoud and Basyoon. The highest urban–rural differences seen for the districts of El-Santa and Kotoor for males, and the districts of Kotoor and Kafr El-Zayat for females might be related to differences in pollution risk factor information between urban and rural areas^{24–26} and higher smoking rates in urban than rural areas.^{27–29} While previous studies highlighted the possible regional difference in pollution between urban and rural areas in those districts, our previous research in the region has also shown regional differences in incidence of liver, bladder, breast, and endometrial cancers in those particular districts.^{30–33} The higher subsite incidence rate for larynx and nasopharynx and for gum and mouth (except floor) and nasopharynx for females might also be related to variable smoking rates, infection, and regional environmental pollution. The overall incidence of all subsites (except for larynx) was lower in Egypt than in SEER. This may indicate a difference in risk factors, including genetic susceptibility and diet between these two populations. However, the similarity between the Egyptian registry and SEER with respect to the incidence of laryngeal cancer underscores the importance of the association between smoking and laryngeal cancer in both countries.

Previous studies highlighted the importance of smoking in HNC in pooled international analysis of the HNC consortium³⁴ and smoking and alcohol.³⁵ Meta-analysis of 62 studies showed the association between HPV in oral cancers and HNC.³⁶ In studies from India, coal was associated with hypopharyngeal/laryngeal cancer risk³⁷, and cooking fumes exposure in childhood, tobacco and marijuana smoking, food contamination, and EBV in relation to nasopharyngeal cancer were reported from Algeria, Tunisia, and Morocco.^{38–40} Previous small-scale hospital-based studies that were limited to one or a few subsites in Egypt suspected that nitrates, malnutrition, Herpes Simplex Virus and Candida infection as possible risk factors.^{15–17}

Our study has several strengths. The population-based nature of the study on a relatively long time period is a major strength. The quality control measures of the data by IARC and NCI provides confidence about the data quality. These data clearly show a gradient of risk between different regions of Egypt. In the future, the heterogeneity of both traditional and novel risk factors in Egypt, including smoking, infection, environmental pollution, will provide a unique opportunity for understanding the etiology of the disease. It should be noted though that a usual limitation of all population-based registries is the limited number of variables available to allow for extensive investigation of the etiology of cancer. Future studies will build upon this work to investigate the epidemiologic and molecular characteristics of these cancers in this unique population.

This study is the first to quantify the magnitude of HNC from a population-based perspective from a long period of the registry. The study underscores the high-incidence age groups and the regional variations in subsites by urban–rural residence of patients. Future studies could benefit from the results of this study to tailor specific analytical studies to investigate specific viral etiology, such as HPV, environmental exposures to nitrates or other risk factors, and smoking in the etiology of this disease.

Conflicts of interest statement

None declared.

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