



Sinonasal Cancer: A National Population-based Study in Iran

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Abstract

Background: Cancer is a leading cause of death in the 21st century. Sinonasal malignancies comprise less than 0.5% of all cancers. There are limited epidemiologic studies on them.

Objectives: The current study aimed to estimate the patient demographics, as well as the incidence rates of nasal cavity and paranasal sinuses (NC-PNS) cancers, using a population based registry.

Methods: The current study was a descriptive cohort using the Iranian national population based cancer registry (INPCR) data in 2016. The incidence rate of NC-PNS cancer and its distribution considering age, gender, geographical location and histopathology were determined.

Results: A total of 258 cases (62.4 % males) were included in the study. Age standardized incidence rate (ASIR) of NC-PNS cancer was 0.36 per 100,000 population. ASIR had the highest value in the 7th, 8th, and 6th decades of life, in descending order. Squamous cell carcinoma (SCC) was the most common histopathologic subtype (23.64%). The most frequent non-epithelial cancer were hematopoietic and lymphatic malignancies (12.40%). The most prevalent site of involvement was the nasal cavity (43.02%), followed by the maxillary sinus (24.81%). The geographical distribution of NC-PNS cancer did not follow any particular pattern. The highest crude incidences were detected in Chahar-Mahal-Bakhtiari, Kerman, and West Azarbaijan in decreasing order.

Conclusion: As evidenced by the obtained results, NC-PNS cancers are rare malignancies. Men in their fifties and older are at a higher risk of involvement. Epithelial cancers are more prevalent, among which SCC is the most common histopathologic subtype.

Keywords: Incidence, Iran, Nasal cancer, National program of cancer registries, Paranasal sinus cancer

1. Background

Cancer is recognized as a leading cause of death in the 21st century (1). It was the first or second cause of death before the age of 70 in 2019, with an increasing burden. (2). Moreover, the cancer incidence rate has increased over time due to aging, the growth of the population, and a higher age-specific incidence rate (3). The age-standardized incidence rate of cancer (ASIR) in Iran was 150.90 per 100,000 in 2015 (4). Cancer-related mortality is estimated to be 53,000 cases annually (5). Mortality incidence rates (MIR) of cancer were 61.85 and 39.55 per 100,000 of population in males and females, respectively (6).

Nasal Cavity and paranasal sinuses (NC-PNS) malignancies comprise about 0.2% and 0.1% of all cancers (excluding non-melanoma skin malignancies) among men and women, respectively (7). The reported ASIRs among males and females are less than 1 and 0.5 per 100,000 (8). There is complex histological diversity in the nose and paranasal sinuses (PNS) (9). Squamous cell carcinoma (SCC) is the most common histology of NC-PNS cancers (10). Exposure to radium, nickel, leather, and wood dust

are known risk factors (7). In particular, inhaled wood dust is considered the main risk factor for adenocarcinoma (7, 11).

2. Objectives

Moreover, an association of cigarette smoking and Human Papilloma Virus (HPV) with NC-PNS cancers has been detected (7, 12). The most common initial symptoms are nasal obstruction, rhinorrhea, and epistaxis (13). Neurological, ophthalmological, and dental symptoms are observed in advanced stages of NC-PNS cancers (7). Tumors diagnosed at later stages carry a worse prognosis (7,14).

Considering NC-PNS cancer rarity, the epidemiologic data about NC-PNS cancer is limited (15). In light of the aforementioned issues, the present study aimed to evaluate for the first time the epidemiology of NC-PNS cancer in Iran in 2016.

3. Methods

This research was designed as a descriptive cohort study among patients with definitive NC-PNS cancer from 2016-2017 (from March, 21st 2016 to

March 21st, 2017). The source of data was the Iranian National Population based Cancer Registry (INPCR) which was confirmed by the Iranian Ministry of Health and Medical Education (MOHME). The study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences. The national and provincial population of Iran in 1395 SH was used according to the official statistics published by the Statistical Center of Iran (SCI).

The INPCR data are gathered through a special application called Sima-ye-Saratan from all medical universities in Iran. The main sources of information are report forms of pathology laboratories. Other sources are patients' medical files in hospitals and death reports from the mortality registry. Each newly diagnosed case of cancer receives a code. In the clinical and paraclinical records, or in case of death, the same code is used to report. Using this code, the national identification (ID) number, and other demographic information, duplicated cases are accurately detected and omitted. The mortality information is matched with the cancer registry data in order to detect those patients with death certificate only (DCO) diagnoses. Rechecking of data quality is performed by the INPCR secretariates to determine data validity and completeness. The evaluation of data quality is performed by matching all patients' information, including age, gender, date and place of birth, tumor location and morphology, primary or metastatic cancer, as well as the date and place of diagnosis (16).

The final data of the year 2016 was the main resource for our statistical analysis. We used the International Classification of Disease for Oncology (ICD-O-3), the first revision of the third edition. For extracting cases with NC-PNS cancers, the codes C30.0 (the nasal cavity) and C31 (accessory sinuses) and their subdivisions were searched. Microsoft Excel and Stata 14 were used for data analysis. All patients were divided into nine ten year age groups (0-9, 10-19, 20-29...80+). Crude incidences and ASIR were determined both among all patients and also separately in cases with the nasal cavity and PNS malignancies, considering their gender, geographical pattern, morphological group, and sites of origin. The

WHO World Standard Population was used for standardization (17).

4. Results

The total number of patients with NC-PNS cancer registered in 2016 consisted of 258, 161 (62.4 %) males and 97 (37.6 %) females. The mean age was 56.39±18.64 (SD) years for all patients, including 55.96±19.48 (SD) and 57.12±17.22 (SD) years for men and women, respectively. The most common site of NC-PNS cancer was the nasal cavity. The maxillary sinus was the most frequent location of involvement among paranasal sinuses (Table 1). Comparing the frequency of patients in each decade of life, the most common ages of involvement with the nasal cavity and PNS cancers were the seventh (23.42%) and sixth (21.77%) decades of life, respectively (Table 2).

The calculated ASIR among all cases was 0.36 per 100,000 of the population. Crude incidence rates and ASIR in each decade of life were estimated. The highest values of ASIR in descending order were detected in the 7th, 8th, and 6th decades of life (Table 3). Overall crude incidence rates of NC-PNS cancer, as well as nasal cavity and PNS cancers, were determined separately in each province of Iran. The highest incidences of nasal cavity and PNS cancer were detected in Khuzestan in the south of Iran and South Khorasan in the northeast of Iran respectively. The results of crude incidence rate estimation indicated that Chahar-Mahal-Bakhtiari a western province was the most common geographical site of NC-PNS cancer involvement (Figure1).

The analysis of demographic characteristics of all patients by different histopathologic diagnoses revealed that SCC was the most common morphology (23.64%). In this group of patients, the most frequent age of involvement was the 7th decade of life (32.79%). Epithelial malignancies, including SCC, adenoid cystic carcinoma (ACC), adenocarcinoma, and other epithelial carcinomas, made up 66.4% of all known cases (141 of 213 cases). The most common non-epithelial cancers were hematopoietic and lymphatic malignancies (Table 4).

Table 1. Demographics of patients with the nasal cavity and paranasal sinuses cancer in Iran (2016)

| | Total (%) | Gender | | Age, year |
|------------------------|-------------|---------------|------------|---------------|
| | | Male | Female | Mean ±SD |
| | | Frequency (%) | | |
| Nasal cavity | 111 (43.02) | 75 (46.58) | 36 (37.11) | 56.71 ± 19.67 |
| Paranasal Sinuses | 147 (56.98) | 86 (58.50) | 61 (41.50) | 56.16 ± 17.88 |
| Maxillary sinus | 64 (24.81) | 39 (24.22) | 25 (25.77) | 53.01 ± 19.48 |
| Ethmoid sinus | 4 (1.55) | 4 (2.48) | 0 | 54.75 ± 16.87 |
| Frontal sinus | 4 (1.55) | 3 (1.86) | 1 (1.03) | 57.25 ± 12.84 |
| Sphenoid sinus | 14 (5.43) | 6 (3.73) | 8 (8.25) | 50.21 ± 14.32 |
| Overlapping lesion | 3 (1.16) | 2 (1.24) | 1 (1.03) | 69 ± 24.63 |
| Accessory sinus, NOS | 58 (22.48) | 32 (19.88) | 26 (26.80) | 60.43 ± 16.14 |
| All Sino-nasal cancers | 258 | 161 (62.40) | 97 (37.60) | 56.39 ± 18.64 |

NOS: not otherwise specified, SD: standard deviation

Table 2. Age distribution of patients with nasal cavity and paranasal sinuses cancer in Iran (2016)

| | Nasal Cavity cancer | | | Paranasal Sinuses cancer | | | All Sinonasal cancer | | |
|----------------|----------------------|---------------|--------------|--------------------------|---------------|---------------|----------------------|---------------|---------------|
| | Total | Male | Female | Total | Male | Female | Total | Male | Female |
| | Frequency (%) | | | | | | | | |
| Age means (SD) | 56.71 (19.67) | 55.85 (19.89) | 58.5 (19.37) | 56.16 (17.88) | 56.05 (19.23) | 56.31 (15.94) | 56.39 (18.64) | 55.96 (19.48) | 57.12 (17.22) |
| 0-9 | 1 (0.90) | 0 | 1 (2.78) | 4 (2.72) | 3 (3.49) | 1 (1.64) | 5 (1.94) | 3 (1.86) | 2 (2.06) |
| 10-19 | 1 (0.90) | 1 (1.33) | 0 | 0 | 0 | 0 | 1 (0.39) | 1 (0.62) | 0 |
| 20-29 | 9 (8.11) | 7 (9.33) | 2 (5.56) | 4 (2.72) | 4 (4.65) | 0 | 13 (5.04) | 11 (6.83) | 2 (2.06) |
| 30-39 | 15 (13.51) | 12 (16.00) | 3 (8.33) | 16 (10.88) | 8 (9.30) | 8 (13.11) | 31 (12.02) | 20 (12.42) | 11 (11.34) |
| 40-49 | 16 (14.41) | 12 (16.00) | 4 (11.11) | 23 (15.65) | 14 (16.28) | 9 (14.75) | 39 (15.12) | 26 (16.15) | 13 (13.40) |
| 50-59 | 16 (14.41) | 8 (10.67) | 8 (22.22) | 32 (21.77) | 17 (19.77) | 15 (24.59) | 48 (18.60) | 25 (15.53) | 23 (23.71) |
| 60-69 | 26 (23.42) | 17 (22.67) | 9 (25.00) | 30 (20.41) | 16 (18.60) | 14 (22.95) | 56 (21.17) | 33 (20.50) | 23 (23.71) |
| 70-79 | 13 (11.71) | 8 (10.67) | 5 (13.89) | 27 (18.3) | 16 (18.60) | 11 (18.03) | 40 (15.50) | 24 (14.91) | 16 (16.49) |
| 80≤ | 14 (12.61) | 10 (13.33) | 4 (11.11) | 11 (7.48) | 8 (9.30) | 3 (4.92) | 25 (9.69) | 18 (11.18) | 7 (7.22) |

SD: Standard Deviation

Table 3. Age standardized incidence rate (per 100,000) of nasal cavity and paranasal sinuses cancers in Iran (2016)

| Age groups | Cases (N) | Sino nasal Crude Incidence rate | Total Sino nasal cancer ASR | Sino nasal cancer ASR in Male | Sino nasal cancer ASR in Female | Total nasal cavity cancer ASR | nasal cavity cancer ASR in Male | nasal cavity cancer ASR in Female | Total paranasal sinuses cancer ASR | paranasal sinuses cancer ASR in Male | paranasal sinuses cancer ASR in Female |
|--------------|------------|---------------------------------|-----------------------------|-------------------------------|---------------------------------|-------------------------------|---------------------------------|-----------------------------------|------------------------------------|--------------------------------------|--|
| 0-9 | 5 | 0.0370 | 0.0065 | 0.0076 | 0.0053 | 0.0013 | 0 | 0.0027 | 0.0051 | 0.0080 | 0.0025 |
| 10-19 | 1 | 0.0089 | 0.0015 | 0.0030 | 0 | 0.0015 | 0.0030 | 0 | 0 | 0 | 0 |
| 20-29 | 13 | 0.0890 | 0.0144 | 0.0241 | 0.0045 | 0.01 | 0.0153 | 0.0044 | 0.0044 | 0.0090 | 0 |
| 30-39 | 31 | 0.1982 | 0.0292 | 0.0373 | 0.0210 | 0.0141 | 0.0223 | 0.0057 | 0.0151 | 0.0153 | 0.0149 |
| 40-49 | 39 | 0.3767 | 0.0476 | 0.0623 | 0.0323 | 0.0195 | 0.0288 | 0.0099 | 0.0281 | 0.0348 | 0.0216 |
| 50-59 | 48 | 0.6596 | 0.0654 | 0.0680 | 0.0628 | 0.0220 | 0.0218 | 0.0219 | 0.0436 | 0.0464 | 0.0408 |
| 60-69 | 56 | 1.3163 | 0.0879 | 0.1069 | 0.0701 | 0.0410 | 0.0550 | 0.0274 | 0.0471 | 0.0487 | 0.0453 |
| 70-79 | 40 | 1.9379 | 0.0722 | 0.0874 | 0.0572 | 0.0234 | 0.0291 | 0.0179 | 0.0487 | 0.0572 | 0.0401 |
| 80 + | 25 | 2.2809 | 0.0351 | 0.0482 | 0.0206 | 0.0196 | 0.0268 | 0.0118 | 0.0154 | 0.0236 | 0.0080 |
| Total | 258 | 6.9050 | 0.3598 | 0.4448 | 0.2738 | 0.1521 | 0.2022 | 0.1017 | 0.2076 | 0.2430 | 0.1732 |

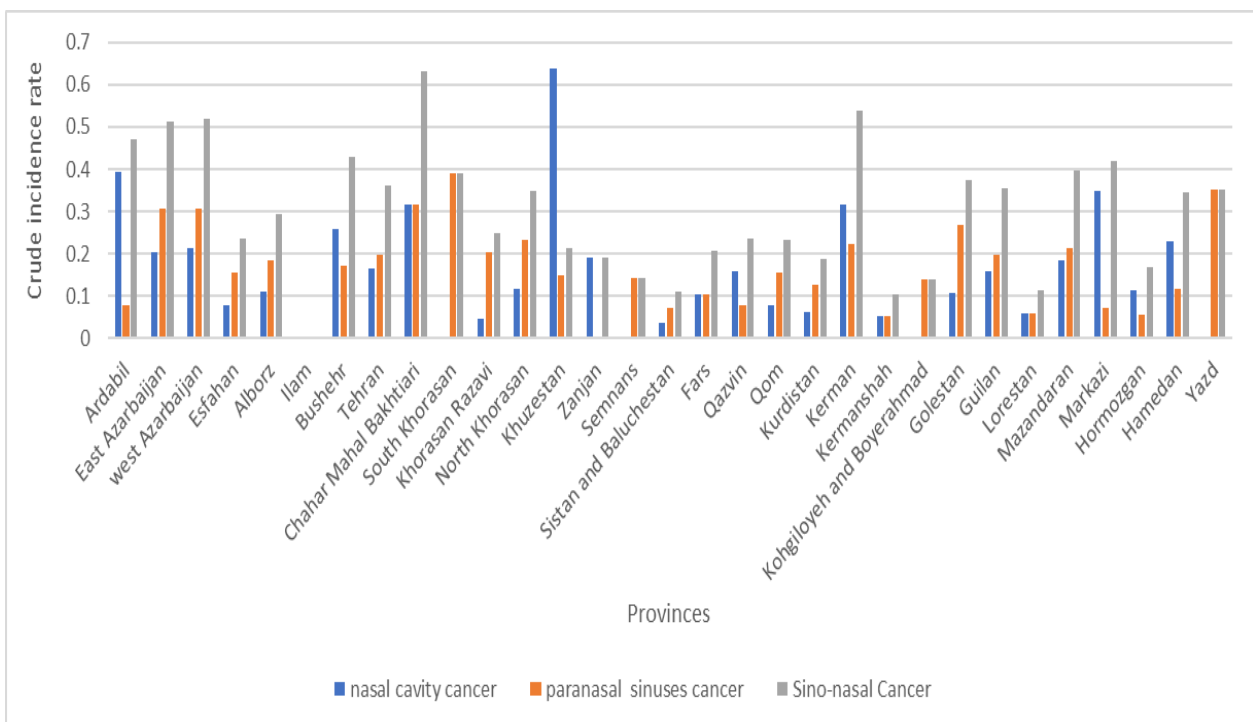


Figure 1. Nasal cavity and paranasal sinuses cancer crude incidence rates in different provinces of Iran (2016)

Histopathologic subtypes of the nasal cavity and PNS were analyzed separately, considering patients' gender. The most frequent PNS and nasal cavity

malignancies in men and women were SCC. Hematopoietic and lymphatic malignancy of the nasal cavity was as frequent as SCC in females (Figure 2).

Table 4. Demographics of patients with nasal cavity and paranasal sinuses cancer by histopathologic subtypes in Iran (2016)

| | All Sino-nasal cancers | Squamous cell carcinoma | Hematopoietic and lymphatic cancer | Adenocarcinoma | Adenoid cystic carcinoma | Sarcoma | Melanoma | Neuroblastoma and neuroectodermal cancer | Other epithelial carcinomas | unknown |
|-------------------------|------------------------|-------------------------|------------------------------------|----------------|--------------------------|-----------|-----------|--|-----------------------------|------------|
| Total N (%) | 258 | 61 (23.64) | 32 (12.40) | 21 (8.14) | 23 (8.91) | 18 (6.98) | 10 (3.88) | 12 (4.65) | 36 (13.95) | 45 (17.44) |
| Gender N (%) | | | | | | | | | | |
| Male | 161(62.40) | 42 (26.09) | 16 (9.94) | 10 (6.21) | 15 (9.32) | 9 (5.59) | 6 (3.73) | 7 (4.35) | 27 (16.77) | 29 (18.01) |
| Female | 97(37.60) | 19 (19.59) | 16 (16.49) | 11 (11.34) | 8 (8.25) | 9 (9.28) | 4 (4.12) | 5 (5.15) | 9 (9.28) | 16 (16.49) |
| Age (year) N (%) | | | | | | | | | | |
| 0-9 | 5 (1.93) | 0 | 1 (3.13) | 0 | 0 | 1 (5.56) | 0 | 1 (8.33) | 1 (2.78) | 1 (2.22) |
| 10-19 | 1 (0.39) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.22) |
| 20-29 | 13 (5.02) | 2 (3.23) | 2 (6.25) | 0 | 0 | 2 (11.11) | 0 | 4 (33.33) | 1 (2.78) | 2 (4.44) |
| 30-39 | 32 (12.36) | 5 (8.20) | 1 (3.13) | 4 (19.05) | 4 (17.39) | 5(27.78) | 1 (10.00) | 2 (16.67) | 4 (11.11) | 5 (11.11) |
| 40-49 | 39 (15.06) | 10 (16.39) | 4 (12.50) | 2 (9.52) | 9 (39.13) | 5(27.78) | 1 (10.00) | 1 (8.33) | 4 (11.11) | 3 (6.67) |
| 50-59 | 48 (18.53) | 15 (24.59) | 8 (25.00) | 8 (38.10) | 2 (8.70) | 3 (16.67) | 1 (10.00) | 1 (8.33) | 4 (11.11) | 6 (13.33) |
| 60-69 | 56 (21.62) | 20 (32.79) | 5 (15.63) | 1 (4.76) | 4 (17.39) | 1 (5.56) | 3 (30.00) | 2 (16.67) | 10 (27.78) | 10(22.22) |
| 70-79 | 40 (15.44) | 6 (9.84) | 7 (21.88) | 5 (23.81) | 4 (17.39) | 1 (5.56) | 3 (30.00) | 1 (8.33) | 6 (16.67) | 7 (15.56) |
| ≥80 | 25 (9.65) | 3 (4.92) | 4 (12.50) | 1 (4.76) | 0 | 0 | 1 (10.00) | 0 | 6 (16.67) | 10(22.22) |

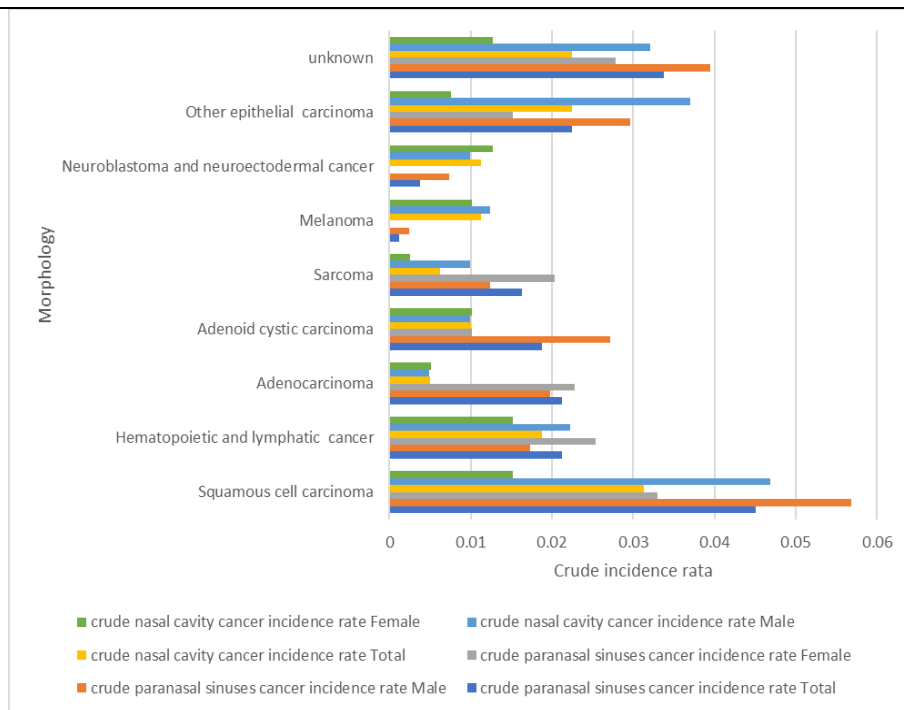


Figure 2. Crude incidence rates of nasal cavity and paranasal sinuses cancers by histopathologic subtypes and gender in Iran (2016)

5. Discussion

As evidenced by the results of this study, the most common site of NC-PNS cancer was the nasal cavity. The maxillary sinus was the most frequent location of involvement among paranasal sinuses. The most common ages of involvement with the nasal cavity and PNS cancers were the seventh and sixth decades of life, respectively. The most frequent PNS and nasal cavity malignancies in men and women were SCC.

There are few epidemiological surveys about malignancies of PNS and the nasal cavity. It may be due to the rarity of these cancers and the lack of organized cancer registry systems all over the world.

SEER (Surveillance, Epidemiology, and End Results) is a database covering the registered cases of cancer in some states of the United States, confirmed by the National Cancer Institute. Turner and Reh studied NC-PNS cancers over the years (1973-2006) and obtained valuable information about the behavior of these malignancies (18). A newer version of SEER has been used by other authors to extend the population and duration of research (1973-2011). They introduced complementary findings about histopathology and specific sites of involvement (14). To the best of our knowledge, the current study is the first population based survey on NC-PNS cancers in Iran, with the highest number of cases focusing on

geographical disturbance, site specific, and histopathologic incidence rates. Moreover, we studied NC-PNS cancer incidence rates in a period of time before the Covid-19 pandemic. Therefore, the results can be used later for comparison between NC-PNS cancer incidence rates before and after the pandemic. We found two epidemiologic studies on NC-PNS cancers in Iran. They were intra institutional studies over 8 and 10 years periods in Shiraz (center of Iran) and the northeast of Iran. They reviewed only 71 and 69 cases, respectively (19, 20). The comparison between the number of included cases in the above mentioned studies and the current population-based research (258) demonstrated that having access to a large number of cases is one of the most important advantages of utilizing a national cancer registry system. This is more valuable, especially when encountering such a rare malignancy. On the other hand, the geographical variety which is presented in this type of database causes an increase in the external validity (18). Iran has a great diversity considering various ethnicity, social behavior, food habits, traditions, and different climate; These factors can affect the prevalence of cancer in different provinces. In addition, the use of a population based resource decreases possible geographical bias. Another outstanding feature of INPCR the database used in this study is the coverage of all 31 provinces of Iran. Many countries have their own national cancer registry but without coverage of the whole population.

The demographic characteristics of our patients were similar to other studies. We found a male to female ratio of 1.66, similar to an intra-institutional study in Iran. Nevertheless, this ratio, according to another Iranian research, was 1.8, with a mean age of 51.07 years, five years less than the estimated mean age in the present study (20). The most common primary sites of tumor involvement, according to the current study, were the nasal cavity followed by the maxillary sinus, which is consistent with other studies (14, 20). Despite what was expected, we found that the frequency of cancers in the ethmoid sinus was lower than in the sphenoid sinus.

Almost according to all previous studies, even studies involving some not all of the prevalent morphologies of NC-PNS malignancy, cancers involving ethmoid sinus were more common than sphenoid and frontal sinuses (10, 21, 22). The possible explanation for this inconsistency may be due to the relatively high percentage (22.48%) of tumors involving accessory sinus, not otherwise specified (NOS). Many ethmoidal cancers were diagnosed in the advanced stages with invasion to other PNS. Consequently, they were probably categorized in the NOS group.

The most common histopathologic subtype in the present study similar to previous studies was SCC (7, 14, 15, 18, 23). Hematopoietic and lymphatic cancers

were found to be the most common non-epithelial malignancies. It was well-matched with other previous Iranian surveys (18, 20). We could not find any explanation for the geographical distribution pattern of NC-PNS cancers since there was no remarkable similarity considering ethnicity, social behavior, food habits, traditions, and climate between provinces with similar NC-PNS cancer incidence rates. The most important shortcoming of the current research was the relatively short duration of the study. However, we believe that it is a good starting point and will continue with more extensive and long-lasting surveys. We did not have access to some important information, such as stages of the disease, different types of treatments, and patient's survival rates. Planning a prospective study can resolve these limitations.

6. Conclusion

NC-PNS cancers are rare malignancies. According to this epidemiological study in Iran, from March 21st, 2016 to March 21st, 2017, patients in their fifties and older are at higher risk of involvement. Epithelial malignancies are more prevalent, and among them, SCC is the most frequent morphology. The most common non-epithelial cancers are hematopoietic and lymphatic malignancies. The most common site of origin is the nasal cavity, followed by the maxillary sinus.

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Footnotes

Conflicts of Interest: The authors have no conflicts of interest.

Author's contributions: Concept: Matin Ghazizadeh, MEA, Design: MEA, Literature search: MatG, FH, MarG, Data acquisition: FH, Data analysis: FH, Statistical analysis: FH, Manuscript preparation: MatG, MarG, MEA, Manuscript editing: MatG, FH, MEA, Manuscript review: MatG, FH, MarG, MEA.

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