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## **A study of epidemiological study of nasopharyngeal cancer cases over a period of 5 years**

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**Abstract**

**Background:** Nasopharyngeal carcinoma is a multifactorial disease mainly affecting the Asian and North African populations including Morocco. **Aimed:** To determine the epidemiological profile of nasopharyngeal carcinoma in central India as well as its clinicopathological, therapeutic, and prognostic characteristics. **Materials and Methods:** We analyzed our hospital data between January 2018 and December 2024 with NPC and analyzed their demographic parameters and outcomes with therapy. **Results:** Nasopharyngeal carcinoma (NPC) represented 5% of all cases with a median age of 47. The most affected age group was 40–55 years (38%). Of all patients, 68% were men and 32% were women with a sex ratio of 1.9 (Male/Female). Undifferentiated nasopharyngeal carcinomas were the most common histological type affecting 92% of patients. At diagnosis, the majority of patients (96%) had an advanced stage of NPC (III, VIa, b, c) including 4% of metastatic cases (IVc). Most cases (92%) had lymph node involvement with cervical mass being the most common clinical presentation. 82% of patients received radiotherapy combined with chemotherapy. Among these patients, 44% had concurrent radiochemotherapy preceded by induction chemotherapy. The 5-year overall survival (OS) was 86% for all patients. It represented 90% for early stages, 86% for locally advanced stages, and 54% for the metastatic stage significantly. **Conclusions:** Nasopharyngeal carcinoma is a particular disease with a late declaration. It is common in Morocco as is the case in other endemic areas with a high prevalence. Patients' survival is significantly influenced by disease staging.

**Keywords** nasopharyngeal carcinoma, epidemiology, clinicopathology, therapy, survival, prognosis

**Introduction**

Head and neck carcinoma is an important public health problem mainly related to tobacco carcinogenesis. Nasopharyngeal carcinoma (NPC) is a rare head and neck cancer with an age-standardized ratio being 0.6–2.0/100,000 in males and 0.2–0.8/100,000 females worldwide.[1] However, there is significant variation in geographic distribution of the disease with the highest incidence being in Southeast Asia up to 6.4/100,000 males and 2.4/100,000 females in these regions. Chinese and Malay races appear to be at the highest risk. India, though being an integral part of Southeast Asia, has significant geographic, racial, and cultural diversity in the population which is reflected in varied incidence of cancer in various parts of the

country as well. Head and neck cancer is the leading form of cancer in males in India and ranks 5th for females.

However, NPC is unequally distributed. Highest age-adjusted rates for NPC were found in Northeast States with Kohima district in Nagaland having an incidence of 19.4/100,000 population. Our center is a regional cancer center in Southern India, catering population of Karnataka and nearby states. Although leading cause of cancer in males in our center also remains head and neck cancer, NPC remains uncommon. The disease has peculiarities in its etiopathogenesis, presentation, risk of nodal and distant metastasis, response to therapy and overall survival (OS) outcomes that stand out as compared to other head and neck cancer subsites. There are limited data on epidemiology and outcomes of NPC reported from central India. Furthermore, the studies reported have not addressed the therapeutic challenges faced in resource-constrained settings as ours. We tried to analyze our hospital data over last few years with regard to the disease epidemiology and outcomes with current therapy. This study aimed to determine the epidemiological profile and the clinicopathological, therapeutic, and prognostic characteristics of nasopharyngeal carcinoma in central India in order to better understand this complex disease.

## **Materials and Methods**

### **Study Population**

This epidemiological study was conducted on patients diagnosed with 50 nasopharyngeal carcinoma patient in Central India. We retrospectively analyzed data from January 2018 to December 2024 from our hospital. We analyzed their demographic parameters including age, gender distribution, tobacco exposure, symptoms, stage at presentation, and histology according to the WHO classification. We also recorded the therapeutic options exercised in addition to primary radiotherapy (RT) including various forms of chemotherapeutic (CT) modalities including neoadjuvant, concurrent to RT, and adjuvant setting. We analyzed responses to therapeutic modalities including CT agent used.

### **Statistical Analysis**

All statistical analysis was performed using SPSS software version 23 designed for analysis of scientific projects. Descriptive analysis of our cohort was carried out to represent the results significantly for good interpretation. Quantitative variables were presented as central tendency indicators, like the mean and the median, or/and dispersion indicators such as the standard deviation. Ordinal and nominal qualitative variables were presented as frequencies or percentages. In this case, we only calculate the mode. T-test for independent samples was used for statistical significance.

### **Variables Definition**

In this study, a wide range of variables were collected and analyzed. Prevalence, patients' age (divided into categories), sex, and origin were grouped into epidemiological data. For chemotherapy (neoadjuvant, concurrent, and palliative) and radiotherapy (curative and palliative), variables including chemotherapy regimens, and radiotherapy total dose, fractions, and duration were studied. Relapse data included variables such as relapse types (locoregional and metastatic), common sites, treatment-relapse interval, and treatment after relapse. The date of diagnosis and last news as well as the evolution data divided to under control, in treatment, death, and lost to follow-up were used in survival analysis.

### Ethical Aspects

This retrospective study was approved by the regional health directorate and the regional center of oncology of central india although it did not require ethical board approval. All patients included in this study gave their informed verbal consent prior to their inclusion as instructed by these committees. In addition, the confidentiality of information collected and the anonymity of patients were ensured.

### Observation and Results

**Table 1. Epidemiological Profile and Clinicopathological Characteristics of NPC Patients**

| Patient characteristics   |                             | Number of cases (n=50) | %  |
|---------------------------|-----------------------------|------------------------|----|
| <b>Age distribution</b>   | 10–25                       | 4                      | 8  |
|                           | 25-40                       | 6                      | 12 |
|                           | 40-55                       | 19                     | 38 |
|                           | 55-70                       | 16                     | 32 |
|                           | ≥70                         | 5                      | 10 |
| <b>Sex</b>                | Male                        | 34                     | 68 |
|                           | Female                      | 16                     | 32 |
| <b>Origin</b>             | Urban                       | 41                     | 82 |
|                           | Rular                       | 9                      | 18 |
| <b>Histological types</b> | Undifferentiated carcinomas | 46                     | 92 |
|                           | Non-keratinizing squamous   | 3                      | 6  |
|                           | Keratinizing                | 1                      | 2  |

|                            |     | squamous |    |
|----------------------------|-----|----------|----|
| <b>cTNM classification</b> | T1  | 2        | 8  |
|                            | T2  | 16       | 32 |
|                            | T3  | 17       | 34 |
|                            | T4  | 12       | 24 |
|                            | N0  | 7        | 8  |
|                            | N1  | 14       | 24 |
|                            | N2  | 24       | 48 |
|                            | N3  | 5        | 10 |
|                            | M0  | 48       | 96 |
|                            | M1  | 2        | 4  |
| <b>Cancer stage</b>        | I   | 0        | 0  |
|                            | II  | 9        | 18 |
|                            | III | 23       | 46 |
|                            | Iva | 11       | 22 |
|                            | IVb | 5        | 10 |
|                            | IVc | 2        | 4  |

### **Epidemiological Profile**

Regarding the prevalence, nasopharyngeal carcinoma represented 5% of all cases recorded between 2018 and 2024 at the regional center of oncology of Tangier. During this period, 250 cases of all cancers were recorded, including 50 cases of nasopharyngeal cancer. In our cohort, patients' age ranged from 10 to 88 years, with a peak incidence at 40–55 years old. The mean age was  $47 \pm 14.9$  years with 47.7 for men and 45.7 for women. The median age of patients was 47 years (50 for men and 49 for women). Forty-one and one tenth percent (41.1%), 25%, and 10% of NPC patients were aged between 40 and 55, 55 and 70, and 10 and 25 years, respectively. Only 10% were aged 70 years or more. In this study, the gender difference was remarkable. Of the 50 patients, 34 were men (68%) and 16 were women (32%). The majority of patients lived in urban areas (82%) compared to rural areas (18%) as shown in Table 1.

### **Clinicopathology**

Patients in our cohort had several clinical signs at the time of diagnosis; the most common were cervical mass (64%), rhinological signs (62%), otological signs (60%),

and headaches (28%), respectively. Table 1 shows the other clinicopathological characteristics of NPC patients. Undifferentiated carcinoma nasopharyngeal type (UCNT) was the most common histological type in our cohort, representing 92%. Differentiated non-keratinizing squamous and keratinizing squamous were rare, representing 28% and 2%, respectively. Regarding cTNM classification, analysis of the size and extension of the tumor (T) in patients showed that 34%, 32%, 24%, and 8% of tumors were classified T3, T2, T4, and T1, respectively. Among all patients, 96% had lymph node involvement (N1, N2, and N3). 4% of patients were metastatic (M1) at the time of diagnosis. The most common sites of metastasis were bone, liver, lymph nodes, and lung. By grouping this data into stages, 64% of patients had an advanced stage (III, IVa, IVb, IVc) of nasopharyngeal carcinoma at the time of diagnosis, while 17.8% had an early stage (II). None of these were classified as stage I. Regarding sex, 68% of female patients had locoregional advanced NPC (III, IVa, IVb) at diagnosis, whereas 80% of males had locoregional advanced stage. NPC stages compared to males and females had a p-value ( $P = .001 < .05$ ) statistically significant.

**Table 2. Initial Treatment of NPC Patients During the Follow-Up Time.**

| <b>Treatment type</b>                |                            | <b>Frequency</b> | <b>Percentage %</b> |
|--------------------------------------|----------------------------|------------------|---------------------|
| <b>Radiotherapy and chemotherapy</b> | Concurrent                 | 22               | 44                  |
|                                      | Neoadjuvant and concurrent | 26               | 52                  |
|                                      | Palliative                 | 2                | 4                   |
|                                      | Total                      | 50               | 100                 |
| <b>Chemotherapy alone</b>            | Neoadjuvant alone          | 8                | 16                  |
|                                      | Palliative                 | 2                | 4                   |
|                                      | Total                      | 10               |                     |
| <b>Radiotherapy alone</b>            | Total                      | 1                | 2                   |
| <b>No treatment</b>                  | Total                      | 2                | 2                   |

### **Initial Treatment**

In this study, the majority of patients (80%, 40 individuals) received radiotherapy combined with chemotherapy (CT), whereas 14% (individuals) received chemotherapy alone and 2% (1 individuals) received radiotherapy alone. 2% (1 individuals) of patients did not receive any treatment during the follow-up time. Regarding surgery, only 2 patients have been operated during their treatment with palliative surgery. Among the patients treated with radiotherapy combined with chemotherapy, 52% (26 patients) received induction chemotherapy before the CRT, while 44% (22 patients) had CRT directly. All metastatic patients (4%) received a palliative treatment including 2 with palliative chemotherapy and 1 with palliative chemotherapy and radiotherapy as shown in Table 2.

The most widely used drugs in neoadjuvant (induction) and palliative chemotherapy were platinum-based combinations including cisplatin–anthracycline. Single drug protocols such as gemcitabine and taxanes were also used in palliative chemotherapy. Regarding concurrent chemotherapy, cisplatin was the most used drug in our study. Radiotherapy was delivered using Volumetric Modulated Arc Therapy (VMAT), an arc-based approach of Intensity Modulated Radiotherapy (IMRT). The majority of patients in our cohort received a total dose of 70 Gy in 35 fractions of curative radiotherapy. The period of radiation varied from 2 to 88 days with a mean of 54 days during the follow-up time.

### **Relapse**

In our cohort, nasopharyngeal cancer relapse occurred in 7 cases (14%) including 3 cases (6%) with metastatic relapse, 2 cases (4%) with locoregional and metastatic relapses, and 2 cases (4%) with locoregional relapse. The bone was the most common metastatic site after relapse (64%). 15 patients of the 16 cases with relapse (93.8%) had an advanced stage of nasopharyngeal carcinoma at diagnosis. The period between the end of treatment and cancer relapse varied between 11 and 1825 days with a mean of 588.27 and a median of 310.50 days. Among these patients, 7 received after relapse treatment by the follow-up time, including 2 cases treated with palliative chemotherapy and radiotherapy, 2 cases treated with palliative chemotherapy, and one case treated with palliative radiotherapy.

### **Survival**

The mean of patients' follow-up from diagnosis was 30 months with extremes between 1 and 220 months. The mean of non-metastatic patients' follow-up was 28 months, while the mean of metastatic patients was 9.8 months. The 5-year overall survival (OS) was 86% knowing that the event (death) occurred 15 times (12 men and 3 women). The OS at 5 years was 90% for early stages (I, II), 86% for locally advanced stages (III, IVa, IVb), and 56% for the metastatic stage (IVc) with a P-value of .002 (<.05) statistically significant. Regarding sex, the 5-year OS was 82% for males and 92% for females with a p-value = .053 ( $\geq .05$ ) weakly significant. Regarding the age groups 10–25, 25–40, 40–55, 55–70 and  $\geq 70$ , the OS at 5 years was 92%, 90%, 84%, 86%, and 80%, respectively, with a p-value = .71 ( $> .05$ ) not statistically significant. The 5-year DFS was 86% knowing that the event (relapse) occurred in 16 cases.

### **Discussion**

Knowing that this is the first epidemiological and clinical study of nasopharyngeal carcinoma in central India with the absence of a cancer registry, these results give an idea of the epidemiological profile and the clinical characteristics of this type of cancer in Morocco and particularly in central India.

## Epidemiological Profile

In central India, as is the case in other endemic areas, nasopharyngeal carcinoma is one of the most common cancers with a high prevalence. In this study, NPC represented 5% of all cases reported between 2018 and 2024. This result gives an idea about the prevalence although it included all patients recorded at the regional center of oncology of Tangier during that period even if some of them were diagnosed way before. Our prevalence is higher than that found in Casablanca (1.8%) during the period from 2008 to 2012 (Cancer registry of Casablanca 2008–2012) and almost similar to that found by Arfaoui et al (4.9%) in Rabat between 1994 and 2004.[2-3]

Internationally, the prevalence of nasopharyngeal carcinoma was 3.2% (3-year period) according to the International Agency for Research on Cancer (IARC) which is lower than the prevalence of this study.[4] In our cohort, patient's ages ranged from 10 to 88 years with a median of 50 years old. Abdullah et al found a median age of 51 years in a study of 266 NPC patients, whereas Alami et al found a median age of 47 years in a study of 163 NPC patients. [5] The most common age group in this study was 40–55 years. These results converge at the national level with Arfaoui et al.'s study and internationally with the results of IARC.[6] Unlike the majority of cancers, nasopharyngeal carcinoma also affects young people. [7] 8% of patients in our cohort were between 10 and 25 years old at diagnosis, knowing that children under 15 are normally treated in pediatric centers except for some rare cases. Without this condition, the percentage of young NPC patients could be greater. These results are similar to what Daoud et al. found.[8] This might be explained by the genetic predisposition which contributes to the development of NPC at a younger age. T/F). These the sex disparity was remarkable in this study with a higher risk for males and a sex ratio of (M/F). These results are consistent with the literature data. [9] The sex difference may be due to the great exposure of men to NPC risk factors including toxic substances and occupational factors such as wood dust and chemical fumes. [10] Further studies on this level should be done.

Our results showed a predominance of urban origins (82%) over rural origins (18%) which converge with the results of Wei et al. in China. [11] This could be explained by the difficulty of access to diagnosis and treatment in rural areas and the urbanization of central Indian people.

## Clinicopathology

In the early stages of the disease, nasopharyngeal cancer may not cause any symptoms. Clinical signs of NPC appear as the tumor grows in nearby tissue. Cervical mass caused by lymphadenopathy was the most common symptom in this cohort, followed by rhinological signs, including nasal congestion and epistaxis, otological signs such as hearing loss and tinnitus, and headaches. Other symptoms such as eye signs,



neurological signs, and weight loss have been reported less frequently. These results converge with the literature data.[9]

The non-specificity of the symptoms and the complex anatomy of the nasopharynx make the diagnosis of NPC difficult which could explain why most patients are diagnosed at an advanced stage. In this study, undifferentiated carcinoma (UCNT) was the most common histological type of nasopharyngeal cancer with 96% of cases. These results are consistent with all studies like Bahannan A et al and Wided BA et al confirming that UCNT is the predominant type of NPC in endemic areas. [12-13] Thirty-five and seven tenth percent 34%, 32%, 24%, and 8% of tumors in our cohort were classified T3, T2, T4, and T1, respectively. Of the 50 patients, 86% had lymph node involvement. In a study of 83 NPC patients in Taiwan, Liu et al found that 42% of patients had T2 tumors, 28% had T4, 23% had T1, and 7% had T3. Of the 83 patients, 77% had lymph node involvement. [14] Bahannan et al and Raissouni et al found cervical nodal metastasis in 78.9% and 80% of patients, respectively. [13,15] T-stage and N-stage were shown to be significant prognostic factors in NPC. [14] In this study, 6% were metastatic at the time of diagnosis with bone, liver, lymph node, and lung being the most common sites of metastasis. These results are similar to the literature data. [16]

One of the particularities of NPC is that the majority of patients are diagnosed at an advanced stage. In this study, 82% of patients had an advanced stage (III, IVa, IVb, IVc) of nasopharyngeal carcinoma including the metastatic stage (4% IVc). Marnouche et al and Mak et al. also found a high percentage of patients with an advanced stage of NPC (85.5% and 66.1%, respectively). [17] These results confirm that NPC is a late-declaration cancer. The detection of anti-EBV antibodies and other serological markers such as Cyfra 21 can predict this type of cancer, hence their usefulness in early diagnosis. [18] More studies at this level should be done. In this study, only 68% of females had locoregional advanced NPC, compared to 80% of males who had locoregional advanced disease. This difference in NPC stages between men and women was statistically significant, which might result in a better prognosis for female patients compared to males.

### **Treatment Modalities**

Nasopharyngeal carcinoma is a radiosensitive tumor, which makes radiotherapy the first choice for treating early stages. Many studies have shown that the addition of chemotherapy to radiotherapy has several benefits, including improved clinical outcomes and survival in patients with locally advanced stages of NPC. In this study, 80% of patients received an initial treatment of radiotherapy (RT) combined with chemotherapy (CT). Among these patients, 54% received induction chemotherapy before the CRT. Wang et al. and Tan et al. performed a meta-analysis in which they confirmed that the addition of induction chemotherapy to CRT to treat advanced stages of NPC improves overall and progression-free survival. [19] In our cohort,

patients without treatment (2%) and patients treated with chemotherapy (14%) or radiotherapy alone (2%) are either lost to follow-up or have not yet started or completed their treatment by the follow-up time. According to several studies, palliative chemotherapy and radiotherapy, as well as surgery in some cases, play an important role in controlling the disease and prolonging the survival of patients with recurrence or metastasis. [20] In this study, 7 patients (14%), including 3 metastatic cases and 3 relapse cases, received palliative treatment, mainly CT and RT. Only one patient has been operated on during their treatment (palliative surgery). The most commonly used CT protocols in this study were platinum-based drugs such as cisplatin combined with anthracycline for neoadjuvant and palliative CT and cisplatin alone for concurrent CT. Zhou et al. found that docetaxel, cisplatin, and fluorouracil (TPF)-based induction CT plus CRT results in better survival outcomes with manageable toxicities compared with CRT alone or double-drug-based induction CT. [21] Zhang et al. showed that the addition of gemcitabine and cisplatin induction CT to cisplatin CRT improves patients' survival. The radiotherapy dose is usually 2 Gy per fraction, 5 days per week, with a total dose of 70 Gy in 49 to 50 days. In our series, the majority of patients received a total dose of 70 Gy in curative RT (VMAT-IMRT). The treatment period varied from 2 to 88 days, with a mean of 54.54 days by the follow-up time. Interruption during RT treatment has been reported to reduce local control and the survival of patients. [22] These delays can be due to treatment tolerance and/or logistic issues. The use of IMRT to target the tumor more precisely by increasing the radiation dose seems to be more promising than conventional RT in treating nasopharyngeal carcinoma. Several studies have shown that it contributed to an absolute improvement in locoregional control and survival, as well as a lower incidence of toxicities. [23] Recent studies and clinical trials focus nowadays on new treatment modalities such as immunotherapy, gene therapy, and targeted therapies. Regarding this latter, monoclonal anti-EGFR antibodies such as cetuximab and nimotuzumab are among the most studied targeted therapies. Adoptive transfer of autologous EBV-specific cytotoxic T cells and inhibition of checkpoints such as PD-1 and CTL-4 to activate the immune system are used as immunotherapy strategies. Significant cytotoxicity mediated by apoptosis was obtained using a technique of gene therapy that consists of introducing a viral vector (adenovirus) containing a transgene whose expression is under the transcriptional regulation of the latent origin of the replication of repeated sequences (oriP) of the Epstein-Barr virus. [24]

## **Recurrence**

Among all patients, 12.4% presented NPC recurrence, with a higher rate of metastatic relapses compared to locoregional relapses. Like other studies, the most common site of metastatic recurrence in our cohort was the bone. These results are similar to the literature data. [25] In this study, the median interval between the end of treatment and NPC relapse was 316 days. When this period is less than 90 days (1 case), the tumor is said to be resistant to treatment. Therapeutic failure and NPC recurrence may be due to the presence of hypoxic tumors, which are known to be radioresistant. [26]

## Survival Functions

With a mean follow-up of 28 months, the overall survival (OS) of all patients at 5 years was 86%. Marnouche et al. found a 5-year OS of 68%. Internationally, Mak et al. found a 5-year OS of 70.7% in Singapore, whereas Anne Lee et al. reported a 5-year OS of 75% in Hong Kong. [27] In our cohort, the DFS at 5 years was 87.6%. Marnouche et al. reported a 5-year DFS of 81.1% in Rabat, Morocco. In Malaysia, Phua et al. found a poor DFS of 48.4%. According to several studies, the OS and DFS improve when patients are treated with IMRT instead of conventional RT and with concurrent radiochemotherapy instead of RT alone. The five-year overall survival in our cohort for early stages, locally advanced stages, and metastatic stages was 90%, 86%, and 54%, respectively, which confirms that NPC stages significantly impact patients' survival. These results were consistent with those of several studies showing that the NPC stage is the most important prognostic factor for NPC. Regarding sex, the 5-year overall survival was higher in women (90%) compared to men (84%), with a weakly significant a weakly significant p-value.. These results were similar to the literature data showing a female advantage with a higher survival rate. Lu et al. and OuYang et al. suggest that the favorable prognosis of female NPC patients is not only attributable to the early diagnosis and treatment but might also be attributed to some intrinsic biologic factors of female patients, such as hormonal differences. [28] In this study, OS at 5 years was lower for patients aged 70 years or more (80%) and for the age group 40–54 years (68%), which is the most affected age category. The age groups were 10–24, 25–40, and 55–70, with a p-value not statistically significant. In an Indonesian study, Hutajulu et al. showed that age was an independent predictor of the OS. [29]

## Strength and limitation

The limited data accessibility and the study size are considered limitations of the study, although the latter represents the first study of its kind in central India. It relates to the national plan for the prevention and control of cancer.

## Conclusion

It is becoming more and more difficult to ignore the role of nasopharyngeal cancer, as is the case in other endemic areas, hence the importance of carrying out epidemiological studies and establishing cancer registries. NPC remains a complex malignancy with a late diagnosis, representing one of the most frequent cancers in central India. It is characterized by its epidemiological profile and its clinicopathological, therapeutic, and prognostic factors. This study will contribute to the understanding of this type of cancer by improving prevention and patients' follow-up. It will also allow us to study the molecular and genetic parts of nasopharyngeal carcinoma to subsequently improve therapeutic pathways and the early diagnosis of this disease.

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