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Original Article

**Descriptive Study of Nasopharyngeal Carcinoma and Treatment Outcomes: An Eight Years Experience in Hadhramout National Cancer Centre, Yemen**

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**Abstract**

**Objective:** To describe the histological patterns, and to evaluate the long-term outcomes of non surgical treatment of nasopharyngeal carcinoma (NPC) in patients registered at Hadhramout National Cancer Centre (HNCC) in Mukalla City, in Hadhramout Province, Yemen.

**Methods:** Non-randomized descriptive cancer registry-based study of patients with different WHO types of nasopharyngeal cancer and different non surgical treatment modality. Data was obtained from the medical records of patients seen and followed-up at HNCC. Data was collected using Can–Reg 10 computerized program and statistical analysis done using SPSS version–17 software program.

**Results:** The study included 109 patients with NPC, males were 71(65.14%) and females were 38(34.86%), with a male to female ratio of 2:1. The mean age was 43 (range10–89 years). The majority of the patients were from Hadhramout 85(77.98%), while 24(22.2%) patients were from outside Hadhramout. The most common type of NPC seen according WHO classification was type III 82(75.24%) patients, followed by type II 15(13.76%) patients, and lastly type I 12(11%). The type III tumors of nasopharynx was the predominant type seen in younger patients. Cervical nodal metastasis was found in 86(78.9%) patients, N0 neck was observed in 23(21.1%) patients. The highest annual incidence was observed in 2011 and 2012; fourteen females and 31 males. Patients who underwent curative radiotherapy were 14(12.85%), chemotherapy were 33(30.28%), and concurrent chemoradiotherapy were 62 (56.88%) as initial cancer treatment. Deaths during follow–up period due to local recurrences of NPCs after radiotherapy, chemotherapy and chemoradiotherapy were 1(0.92%), 5(4.59%), 11(10%) respectively. The period of follow–up was 72 months. Two patients were lost from follow–up.

**Conclusion:** Our results reveal that WHO–NPC type III is the most common type seen in patients, and the predominant type in young males who presented from Hadhramout regions. Treatment outcome was best in irradiated group followed by chemoradiotherapy and lastly chemotherapy.

**Keywords:** nasopharyngeal carcinoma, incidence, histopathological pattern, treatment outcomes, Hadhramout

**Introduction**

Hadhramout Province includes four costal governorates of South Yemen: Hadhramout, Almahra, Shabwa and Socotra Island, with a population of 1,684,373. Hadhramout is the largest of the four covering an area of 161,749 Km² (29% of the total area of Yemen). A costal part of Hadhramout lies on the Arabian Sea beach in South Arabia (South of Arabian Peninsula) while the other part lies on the desert empty quarter. Hadhramout National Cancer Centre (HNCC) was founded in the capital Mukalla in 2006 as a referral centre for cancer patients. It receives patients from the above mentioned areas and from other regions neigbouring Yemeni cities.

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There has been no independent study of NPC in Yemen as to our knowledge up to the time of the current study. Different studies have reported NPCs in Yemeni patients with head and neck cancers in general, while the independent survey of NPC and its prevalence in this risky geographic area are unpublished yet.1,2,3,4

NPC is one of the top head and neck cancers in Yemen especially in Hadhramout. It causes high morbidity and mortality among young and older patients. In this region people eat dry salted fish which is known globally as one of the major risk factors associated with the epidemiology of NPC. In 2013 Badheeb et al. studied 202 patients with head and neck cancers in Hadhramout and reported that about 50% of the patients had NPCs.1 In general, an early clinical diagnosis and treatment outcomes of curative therapy of NPC have unsatisfactory background and results are controversial because of the location of the tumor and the difficulties of approach. Histological verification, cancer stages and nodal metastasis are significant prognostic factors for successful treatment of patients with NPCs.5 Traditionally carcinoma of nasopharynx differs from other head and neck cancers in endemic geographic areas, risk factors and histopathological tumor classification. High incidence are reported in China, Singapore, Indonesia, Korea, Hong Kong, and Taiwan6. The prevalence in United States and Europe is low. In our study majority of patients presented to the oncologist late with advanced tumor stages. Late presentation is one of the causes of failure of single treatment modality in cancer therapy and hence the use of more aggressive dual or triple therapy modality as initial treatment for these cases (radiotherapy, chemotherapy, surgery and combination). Unfortunately in most cases these regimens are indicated as palliative treatment. To date the incidence of NPC in Yemen is still unclear. The geographic location of Yemen is also a major risk factor similar to the other Asian, African and mediterranean countries7.

Patients and Methods

This is a cancer registry–based descriptive study. Patients personal data was obtained from medical records of patients presenting to the HNCC at Ibn Sina Teaching Hospital (ISTH) in Mukalla city, in Hadhramout, between January 2006 to December 2013. The diagnosis was established according to the clinical picture. All patients underwent head and neck palpation, inspection using posterior rhinoscopy, endoscopic nasopharyngoscopy. Histopathological study (neoplastic tissue was taken endoscopically from primary tumor or suspected cervical lymphatic nodes) and radiographic study (CT scan, ultrasound of head and neck and chest X–ray) were carried out. The topography of the nasopharyngeal cancers were classified and coded according to the International Classification of Diseases (ICD) for oncology, 3rd edition (ICD–0–10) into: (C11.0 superior wall, C11.1 posterior wall, C11.2 lateral wall, C11.3 anterior wall (choana), C11.9 tumor occupied whole nasopharynx. NPCs histologically were divided into three types according to WHO classification8: WHO–NPC type I squamous cell “keratinizing” carcinoma, WHO–NPC type II moderately differentiated nonkeratinizing carcinoma, WHO–NPC type III undifferentiated carcinoma and TNM classification was used ““T1,T2 are an early stages, T3,T4 are advanced stages”. Tumor extension and nodal metastasis: N0 neck, N+ neck “local, locoregional, distant metastasis” were assessed.

Anticancer treatment modality used included chemotherapy, radiotherapy or both. The selection of modality was based on many factors; stage of the tumor, histopathological verification, patient’s general health condition, age, comorbidity, and patient preference. Chemotherapy and radiotherapy and their combination were performed for all patients as initial treatment modality “single treatment was indicated for early stages I, II and combination for locally advanced III, IV”. Surgery was not included in the study as primary treatment. All patients were followed—up in the HNCC. Irradiated patients were reffered for curative radiotherapy to other oncology centres following diagnosis due to lack of radiotherapy facility in our hospital.

Treatment protocol

Chemotherapy:

Includes single, doubled or multi–drugs regimen for a cycle:
- Docetaxel 75mg/m2, days 1 and 8
- Cisplatine 70mg/m2 on day1
- 5 Fluoruracil 750mg/m2 on 1–5 day

Conformal Radiotherapy

The total dose given was 60 to 70 Gy in the nasopharynx and entire neck with daily divided fractions 2 Gy in 35 to 40 fractions using linear accelerat.

Exclusion criteria included: patients with head and neck cancers in other sites, surgically treated patients with head and neck malignancy, other types of nasopharyngeal tumors than WHO–NPC types I, II, III, cases diagnosed clinically only without histological or radiological evaluation and case duplication.

Data was collected using Can Reg 4 computerized program10 and was analysed by SPSS version 17 software statistical program.
The aim of the study was to describe the histological pattern of WHO–NPC types I–III and to assess the non surgical treatment outcomes of NPCs.

**Results**

Non randomized descriptive analytical study including 109 patients. The results of this study and characteristics of patients are summarized in Table 1. During the period from January 2006 to December 2013, we studied 109 patients who had different histological WHO–NPC types of nasopharynx and underwent different treatment modalities; chemotherapy and radiotherapy or both. The majority of patients came from different areas of Hadhramout 85 (77.98%), and the remaining came from outside Hadhramout 24 (22%). Seventy one (65.14%) of the patients were males and 38 (34.86%) of the patients were females, NPC affects twice males than females. Age of patients ranged between 10–89 years. More than 62(56.88%) of the patients were aged between 33–61 years. The highest incidence was in the 2011 and 2012. The highest median age was 53 years. The current study results revealed that the annual incidence and median age of patients with NPCs are variable and irregularly distributed (Figure 1, 2). In this study curative radiotherapy was performed in 14 (12.84%) patients, chemotherapy in 33 (30.28%) patients and concurrent chemo–radiotherapy in 62 (56.88%) patients.

Eighty–three (76.15%) patients had tumor in the nasopharynx and nasal cavity. The most common identified nasopharyngeal cancer stage in this study was stage IV, 25 (22.94%) patients. Locoregional and distant extension was observed in 68 (62.38%) patients.

Based on WHO–NPC classification the histological patterns were; type I keratinizing “squamous cell carcinoma” 12(11%), type II nonkeratinizing carcinoma 15(13.76%), type III undifferentiated carcinoma 82 (75.24%). Type III was the predominant type.

In the study the log–rank test (Mantel–Haenszel test) revealed that stage I was statistically significant, it showed large differences between observed and expected deaths \( P < 0.05 \) (Figure 3).

Kaplan–Meier curve shows that the best survival experience was in radiotherapy group after approximately five years of follow–up. Overall differences in survival experience between the groups are statistically insignificant (Figure 3).

Cox PH model (Cox Proportional Hazards Modeling with Covariates) shows that the age of the patient appears to increase with the annual incidence by approximately 3.6% each year. This result is statistically significant \( p < 0.05 \) (Figure 4). Comparing survival experience

<table>
<thead>
<tr>
<th>Gender</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>71</td>
<td>65.14</td>
</tr>
<tr>
<td>Female</td>
<td>38</td>
<td>34.86</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age in years</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>10–20</td>
<td>18</td>
<td>16.51</td>
</tr>
<tr>
<td>21–30</td>
<td>11</td>
<td>10.1</td>
</tr>
<tr>
<td>31–40</td>
<td>22</td>
<td>20.18</td>
</tr>
<tr>
<td>41–50</td>
<td>19</td>
<td>17.43</td>
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<tr>
<td>51–60</td>
<td>23</td>
<td>21.1</td>
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<tr>
<td>61–70</td>
<td>8</td>
<td>7.34</td>
</tr>
<tr>
<td>&gt; 70</td>
<td>8</td>
<td>7.34</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Geographic source (ethnicity) of NPC</th>
<th>F/33</th>
<th>M/52</th>
<th>77.98</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hadhramout “Hadhrami group”</td>
<td>F/10</td>
<td>M/14</td>
<td>22.02</td>
</tr>
</tbody>
</table>

**Table 1. Characteristics of Patients**

<table>
<thead>
<tr>
<th>Topographic distribution of NPC</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>C11.0 Superior wall of nasopharynx</td>
<td>7</td>
<td>6.42</td>
</tr>
<tr>
<td>C11.1 Posterior wall of nasopharynx</td>
<td>7</td>
<td>6.42</td>
</tr>
<tr>
<td>C11.2 Lateral wall of nasopharynx</td>
<td>8</td>
<td>7.34</td>
</tr>
<tr>
<td>C11.3 Anterior wall of nasopharynx (choana)</td>
<td>4</td>
<td>3.67</td>
</tr>
<tr>
<td>C11.9 Tumor occupying whole nasopharynx (unspecified)</td>
<td>83</td>
<td>76.15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grade of NPC</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>9</td>
<td>8.26</td>
</tr>
<tr>
<td>II</td>
<td>6</td>
<td>5.5</td>
</tr>
<tr>
<td>III</td>
<td>9</td>
<td>8.26</td>
</tr>
<tr>
<td>IV</td>
<td>25</td>
<td>22.94</td>
</tr>
<tr>
<td>Unspecified</td>
<td>60</td>
<td>8.26</td>
</tr>
</tbody>
</table>

**Histological patterns (WHO–NPC type)**

| I– Keratinizing carcinoma | 12  | 11 |
| II– Non–keratinizing carcinoma | 15  | 13.76|
| III– Undifferentiated carcinoma | 82  | 75.24|

**Extent (metastasis) of NPC**

| Local | 56  | 51.38|
| Regional | 12  | 11   |
| Distant | 14  | 12.85|
| Unknown | 27  | 24.77|

**Neck status**

| N0 neck | 23  | 21.1|
| N+ "nodal metastasis” | 86  | 78.9|

**Anti–cancer treatment modality**

| Radiotherapy | 14  | 12.84|
| Chemotherapy | 33  | 30.28|
| Concurrent chemo–radiotherapy | 62  | 56.88|

**Follow–up status (follow–up period 72 months)**

| Alive | 90  | 82.57|
| Dead | 17  | 15.6|
| Lost of follow–up | 2   | 1.83|
between various groups of patients, regardless of the
regime allocated for their treatment we observed that
patients allocated to radiotherapy only did the best (one
death observed in this group while 2.11 were expected
based on follow-up time observed in this group), followed
by the group concurrent chemo—radiotherapy (11 deaths
observed while 10.96 expected based on follow-up time
observed in this group), and the worst was the patients
in the chemotherapy group (5 deaths observed and 3.93
expected based on follow-up time observed in this group).

We observed that females allocated to radiotherapy did
the best (0 deaths), females on both treatment regimens
(3 deaths). While males on radiotherapy and males on
chemotherapy each (3 deaths).

In general the overall survival curves showed
statistically insignificant finding. Median survival times in
radiotherapy group was > 0.94 years, chemotherapy group
was > 6.95 years, in concurrent chemo—radiotherapy
group was > 10.1 years and 5 years respectively. The
Kaplan Meirre test revealed that none of these results
imply that median survival time in any of the treatment
group is inferior or superior to the other. In our study two
(1.83%) patients were lost from follow—up.

Discussion

NPC is the first cancer in males and the third in
females in southeast Asia. It is endemic in southeren
China\textsuperscript{11} and rare in North America and Europe\textsuperscript{12}. Cancers
of nasopharynx have a strong association with EB virus
and salt preserved fish consumption\textsuperscript{13}. Salt preserved
fish is the second risk factor with moderate to strong
association with NPCs epidemiology after EBV infection\textsuperscript{14}. NPC is one of the most common cancers of head
and neck in Southeast Asia and is prevalent among the
Chinese, especially in the Cantonese region of southern
China and occurrence in african countries is not rare\textsuperscript{15,16,17}.\textsuperscript{15,16,17}.
Recently radiotherapy is the treatment modality of choice for early stage NPCs while concurrent or neoadjuvant chemoradiotherapy is used for the treatment of locally advanced stages of NPCs. Surgery plays a minimal role in the initial management of NPC, however, it is an important treatment option for patients who experience recurrence after definitive radiotherapy or chemoradiation therapy.

The current study revealed that males are more affected than females; this is similar to studies from other Arab countries. In Saudi Arabia, Andejani et al. in their study found high incidence of patients with NPC among young population, with 42 out of 373 (22 males/20 females) patients being in their first 20 years of life, pharyngeal cancer was significantly more frequent among younger males. Nasopharynx comprised 89.5% of pharyngeal cancers. Generally, pharyngeal cancers (22.9%) were more common among males. In literature, NPCs are mostly seen in the lateral wall of nasopharynx in Rosenmuller fossa. In our study this site was affected in eight patients.

Many authors reported that concurrent chemoradiotherapy is superior to radiotherapy alone for patients with advanced NPC in endemic areas, our results are similar to these studies. These studies are consistent with our study where more than 50% of patients underwent chemoradiotherapy.

NPC is a major concern in eastern part of Nepal. In this region pharynx 25 (27.78%) was the commonest site involved by cancer. In the pharynx, malignancies at the nasopharyngeal region contributed to the bulk of the tumor constituting 12 (48.00%). Similar results were reported in the study of head and neck cancers in Hadhramout by authors in 2013.

In Nigeria, histologically, undifferentiated nasopharyngeal carcinoma was the commonest type (70%) followed by well differentiated keratinizing “squamous cell carcinoma” (20%) and differentiated nonkeratinizing squamous cell carcinoma (10%). Undifferentiated carcinoma was the commonest type of nasopharyngeal carcinoma reported from this study especially among males in the 4th and 5th decades of life. This result is in agreement with our results where the type III is the commonest type seen in younger patients.

Abuidris et al. studied 103 patients from Sudan with NPCs. Their age range was 11–82 years, according to the WHO histology; type–III was 73.8% of cases, type–II was 26.2%, and there was no type–I seen. In their study population the dominant histology was type III. Mostafa et al. studied 36 patients with NPCs and found: type–III was 25 (69%) of cases, type–II was 8 (22%), and three (9%) cases type I.

The results of our study revealed that the highest incidence was in younger patients with type III WHO NPC.

A study in Basrah province, Iraq found that nasopharyngeal carcinoma constituted 90 cases (8.9%) of a total number of 1011 patients with squamous cell carcinoma (SCC) of the head and neck malignancy. Histologically in our study the majority of NPCs are undifferentiated carcinomas.

**Conclusion**

Our results revealed that WHO–NPC type III is the most common type seen in patients, and predominant type in young males who presented from Hadhramout regions. Treatment outcome was best in irradiated group followed by chemoradiotherapy and lastly chemotherapy. Local recurrences were found in 18 patients and there were 17 deaths. Five year survival was best following radiotherapy. Further studies are needed to determine the risk factors for NPCs in our country.

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