

# Histopathological patterns of nasopharyngeal carcinoma in Sudan

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## ABSTRACT

**الأهداف:** من أجل دراسة الأنماط النسيجية للسرطان الغدي الأنفي البلعومي (NPC) بين المرضى السودانيين الذين تمت معالجتهم في معهد الطب النووي، بقسم الأورام والأحياء الجزيئية (INMO) وذلك لمقارنتها مع السلاسل العالمية التي تم نشرها.

**الطريقة:** تمت دراسة ومراجعة سجلات المرضى المصابين بالسرطان الغدي الأنفي البلعومي (NPC) والذين تلقوا العلاج بمعهد الطب النووي بقسم الأورام والأحياء الجزيئية بوادي ميداني - السودان، خلال الفترة ما بين عام 2000م وحتى 2005م. أجريت القياسات الطبية والتي اشتملت على مراجعة الأنماط النسيجية للسرطان الغدي الأنفي البلعومي (NPC) وفقاً لمنظمة الصحة العالمية (WHO)، والتصنيف والعمر ونوع الجنس والموضع والأخلاق الطبية ومرحلة المرض. شملت الدراسة جميع الأنماط الأخرى للسرطان الأنفي البلعومي (NPC) مع الأنسجة الموجبة، بينما تم استبعاد الأنماط الأخرى التي لديها الأنسجة (الورم اللمفاوي، والورم اللحمي). تم استعمال برامج التحليل الإحصائي الرقمي (SPSS) لإدخال البيانات والتحليل.

**النتائج:** بلغ العدد الإجمالي للمرضى المصابين بالسرطان الغدي الأنفي البلعومي 103 (NPC) مريضاً، تتراوح أعمارهم ما بين 11-82 عاماً، وبلغ العمر الوسطي 41 عاماً وبلغ متوسط العمر 45.5 عاماً. نسبة الذكور إلى الإناث 2:1. بلغ نمط الأنسجة - 3 لمنظمة الصحة العالمية WHO-73.8% من الحالات. بلغ نمط الأنسجة 2- لمنظمة الصحة العالمية WHO-26.2%. لم يكن هنالك حالات للنمط الأول حسب تصنيف منظمة الصحة العالمية (WHO) في دراسة السكان هذه. كان انتفاخ العنق أكثر أعراض الحالات حضوراً (77.8%).

**خاتمة:** كان هناك تشابه في نمط تصنيف الورم الغدي الأنفي البلعومي (NPC) لتلك التي تمت رؤيتها في المناطق المستوطنة مثل جنوب الصين. الأنسجة المسيطرة كانت من النمط الثالث حسب تصنيف منظمة الصحة العالمية. هنالك حاجة إلى البحث عن عوامل الخطر للسرطان الغدي الأنفي البلعومي (NPC) في السودان.

**Objective:** To study the histological patterns of nasopharyngeal carcinoma (NPC) in Sudanese patients and to compare them with the internationally published series.

**Materials:** A retrospective review for records of NPC patients treated in the Institute of Nuclear Medicine, Molecular Biology and Oncology (INMO), Wadmedani, Sudan, during the period 2000-2005 was conducted. Parameters included in the review were histological types of NPC according to the World Health Organization (WHO) classification, age, gender, locality, ethnicity, and stage. All cases of NPC with positive histology were included while other types of histology (lymphoma, sarcoma) were excluded. The SPSS software was used for data entry and analysis.

**Results:** Total number of patients with NPC was 103. Age range from 11-82 years, median was 41 years, and mean was 45.5 years of age. Male:female ratio was 2:1. The WHO histology type-3 was 73.8% of cases, WHO type-2 was 26.2%, and there was no case of WHO type-1 found in this study population. Neck swelling is the most common presenting symptom (77.8%).

**Conclusions:** Pattern of NPC classification resembles those seen in endemic areas like South China. Dominant histology was WHO type-3. Identifying risk factors for NPC in Sudan is required.

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Head and neck cancers are common in Sudan, nasopharynx cancer (NPC) is the most common. Histology is a prognostic feature in management of NPC and its distribution varies between endemic and non-endemic regions around the World.<sup>1</sup> Nasopharyngeal carcinoma is epidemiologically and histologically different from other head and neck cancers. It is an Epstein-Barr virus (EBV), associated carcinoma of epidermoid origin and endemic in South China, North Africa, and the Mediterranean basin. It commonly has poorly differentiated or undifferentiated pathology with a high incidence of cervical lymph node metastasis and great radiosensitivity and chemosensitivity.<sup>1</sup> It has been demonstrated that EBV is harbored in almost every NPC tumor, regardless of the degree of differentiation and geographic distribution.<sup>2-5</sup> The highest incidence of NPC is found in South China, Hong Kong, Singapore, and the United States citizens of Chinese origin.<sup>6</sup> The incidence rates in the Caucasian race are low. In China, the incidence rate is low in North China (3 cases per 10<sup>5</sup> people) but high in the South (25-50 cases per 10<sup>5</sup> people), Canton province is the most affected area.<sup>7</sup> Other sites with high incidence are North Africa and the Mediterranean basin. In the Middle East, it is common in Saudi Arabia, where it ranks first among all head and neck cancers and 17th among all cancers.<sup>8</sup> The WHO classifies NPC into 3 types according to histology. Keratinizing squamous cell carcinoma is WHO type 1. Non-keratinizing carcinoma is WHO type 2. Undifferentiated carcinomas and lymphoepithelioma are WHO type 3. Epstein-Barr virus association is reported to be strongly associated with types 2 and 3.<sup>3,4</sup> Risk factors in endemic areas include EBV, salty diet, volatile nitrosamines, and human leukocyte antigen haplotype.<sup>9</sup> However, in non-endemic regions, the disease is associated with alcohol and tobacco use.<sup>9</sup> Literature on NPC incidence and histological patterns in Sudan is scarce. Incidence is difficult to estimate in Sudan due to lack of population-based cancer registry. This hospital-based study reflects the prevalence of NPC in this region of Sudan and provides classification according to WHO-typing.

**Methods.** This is a retrospective review study. Records of NPC patients treated in the Institute of Nuclear Medicine, Molecular Biology and Oncology (INMO) during the period from January 2000 to December 2005 were reviewed for histology classification according to WHO-classification. The local ethical committee approval was obtained prior commencement of this study. Other parameters like gender, age, race, locality, clinical presentation, and stage were also studied. All positive cases with histology reports of biopsies obtained from nasopharynx or metastatic cervical lymph node were included. Tumors evident in nasopharynx were

identified either clinically or radiologically. Exclusion criteria include all cases diagnosed clinically and patients with primary nasopharyngeal lymphoma and sarcoma. Tumors arising from neighboring sites like the nose or sinuses and extending to the nasopharynx were also excluded.

Results were tabulated and presented in simple percentage form. Correlation significance was tested using the SPSS and *p* value. *P* value is considered statistically significant if the value of null hypothesis is < 0.05.

**Results.** Total number of patients treated during the period of the study was 116. Five records were excluded due to absence of histopathological evidence of NPC and 8 cases of primary non-Hodgkin lymphoma were excluded. The male to female ratio was 2:1. The median age was 41 years, and mean age was 45.5 years. Patients' characteristics are shown in Table 1. The peak age group was between 40-60 years old (45%). Difference in age specific groups affected, and gender of the patients is not statistically significant (*p*=0.86). Most cases were Gezira State inhabitants (61.2%), other neighboring States included Sinnar (15.5%), Gadarif (8.7%), and the rest from the other neighboring States. The most

**Table 1** - Patients' characteristics.

Characteristic	Number of patients (%)
Total patients	103
<i>Age group</i>	
10-20	16 (15.5)
21-30	11 (10.7)
31-40	14 (13.6)
41-60	46 (44.7)
61-70	14 (13.6)
> 70	2 (1.9)
<i>Gender</i>	
Male	67 (65)
Female	36 (35)
<i>Histology</i>	
WHO-1	
WHO-2	27 (26.2)
WHO-3	76 (73.8)
<i>Cervical lymphadenopathy</i>	
Positive	80 (77.7)
Negative	23 (22.3)
<i>Ethnic group</i>	
Northern Arab	63 (61.2)
others	40 (38.9)
<i>Stage</i>	
Stage IVA	21 (20.38)
Stage IVB	64 (62.13)
Stage IVC	3 (2.91)
Stage I, II, III	15 (14.56)

WHO - World Health Organization

common race group affected was Northern Sudanese Arab (61.2%).

**Histology.** The dominant histology was WHO type 3 with contribution in 73.8% of cases and WHO type 2 was 26.2%. No single case had the WHO type one histology subtype. No significant correlation was found between gender and the disease histology ( $p=0.87$ ). All patients less than 20 years old had WHO-3 histology (15.5%).

**Neck swelling.** Presentation with neck swelling was observed in 77.8% of cases. All cases of positive cervical lymphadenopathy were diagnosed clinically. Presence of neck swelling was not statistically significantly between the 2 main types of histology ( $p=0.96$ ).

**Stage.** Locally advanced and metastatic disease was observed in 85.4% of patients. Locally advanced disease includes all cases with any cranial nerve palsy, cervical lymphadenopathy or T4 lesions. Common sites for distant metastases were bone, lung, and liver.

**Discussion.** Nasopharyngeal carcinoma is common in this region of Sudan and tends to affect a young age group, presents late, and the dominant histology is undifferentiated type. Gezira State, where INMO is located, is sited south of Khartoum and exactly at the center of Sudan, and this may explain the domination of cases from Gezira State. In Sudan, besides INMO there is another center in the Capital of Sudan (Khartoum). They are the only 2 centers dedicated to care for cancer patients in Sudan. Nasopharyngeal carcinoma is the second most common male solid tumor from records of patients treated in INMO. The median age of cases in this series of studied patients was similar to that reported from South China and Saudi Arabia, but it is 5-10 years less than reported median age in the West.<sup>8-10</sup> Peak age group is similar to those reports from Hong Kong with more than 60% of patients diagnosed before the age of 50 years.<sup>11</sup> The male to female ratio was slightly less than that reported from the Middle East, the South Asian region and western series with a male to female ratio of 2.7, 3 and 2.5.<sup>12</sup> The types of histology in this series were WHO-2 and WHO-3 which is similar to reports from other endemic areas. Chinese born in Hong Kong and Taiwan, most often present with undifferentiated carcinoma while non-Chinese Americans most often present with keratinizing squamous cell carcinoma.<sup>13</sup> High risk populations have a larger proportion of poorly differentiated carcinomas (WHO type 3).<sup>10</sup> However, WHO types 2 and 3 were not common in non-endemic areas. It has been reported in the United States, that most NPC in North America were WHO-1 keratinizing squamous cell carcinoma (75%).<sup>14</sup> No single case in this series presented with WHO type 1, keratinizing squamous cell carcinoma. The majority of

pediatric population affected by NPC will have WHO-3 histology.<sup>14</sup> In this series of patients, all cases less than 20 years of age were WHO type 3, undifferentiated carcinoma or lymphoepithelioma. In Tunisia, Uganda, Sudan, and Nigeria, 10-20% of cases of NPC occur in children, similar to this series (20%), while in China it is less than 1%.<sup>15</sup> Children with NPC differ from their adult counterpart in having a closer association with EBV, and nearly always the histology is of undifferentiated or lymphoepithelioma type (WHO-3).<sup>16</sup>

Beside geographic and cultural risk factors, race is a potential risk for NPC. In American-born Chinese the incidence is lower than in Chinese inhabitants of South China but, their incidence is still higher when compared with non-Chinese Americans.<sup>17</sup> In this study, the race is not significant for NPC ( $p=0.58$ ). The high incidence of NPC in the North Arab race may be attributable to the domination of this race in the region compared to other races. Neck node metastasis is the most frequent presentation for NPC in this series similar to reports from Hong Kong and China, where the percentage of neck lymph node involvement was more than 50%.<sup>18</sup> Lack of a population-based cancer registry in Sudan will make the hospital-based registries the only available and valuable way at the present time to assess the prevalence and clinical behavior of cancer in Sudan. The only limitation of this study is the small number of patients.

In conclusion, NPC is common in the Sudanese population and tends to affect a younger age group with male predominance. Most cases present with nodal involvement or locally advanced disease. Patients had similar features of histology seen in endemic regions with predominance of WHO-3 histology type. A population-based cancer registry is needed. Studies to look for potential risk factors of NPC in Sudan are needed. Further studies to determine the association between the dominant poorly differentiated NPC-type and EBV infection are also required. The outcome of treatment in retrospective or prospective studies is worth evaluating. The provision of specialist services and awareness of the medical staff and the public should play an important role in early diagnosis and better chances for cure.

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