

# Clinico-Histocytopathological Profile of Paediatric Head and Neck Malignant Neoplasms: A Mini-Review

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## ABSTRACT

Head and neck malignant neoplasms are reported to be the tenth most common cancer globally. They are associated with potential morbidity and mortality because of their tendency to interfere with vital functions of life such as breathing, swallowing, speech, hearing, vision, taste and smelling. Contrary to what was seen in the past where infectious diseases were the leading causes of paediatric morbidity and mortality, non-infectious diseases for example head and neck cancers are now spearheading the morbidity and mortality observed in paediatric population in Africa. This review aims at discussing the clinico-histocytopathological profile of various paediatric head and neck malignant neoplasms in different countries across the World.

## BACKGROUND

Head and neck malignant neoplasms are cancerous neoplasms occurring in the nasal cavities, paranasal sinuses, nasopharynx, oral cavity, oropharynx, hypopharynx, larynx, ear, eye, scalp, orofacial bones, thyroid and salivary glands and they are reported to be the tenth most common cancer globally with associated potential morbidity and mortality (1-3). Malignant neoplasms involving the head and neck are associated with high morbidity and mortality because of their tendency to interfere

with vital functions of life such as breathing, swallowing, speech, hearing, vision, taste and smelling (4,5).

Only 2% of all malignant tumours occur in infancy and childhood. It has been reported that, ethnic and geographic variations in the distribution of different types of childhood malignancies may be attributed to the interplay of varied causative factors such as exposure to ultraviolet light, chemical carcinogens, oncogenic viruses, genetic factors and cultural practices among various populations (6-8).

Head and neck malignant neoplasms constitute up to 5-50% of all malignancies seen globally and on average, about 85% of malignancies seen in children occur in developing countries where majority of such countries are in Africa and this estimate is expected to increase above 90% over the next two decades (4,6).

Paediatric cancers have been found to be second only to accidental trauma as a cause of death in children aged 5 to 14 years in developed countries. Contrary to what was observed in the past decades of life where cancers were reported to be rare in paediatric population in developing countries, the trend has now change with studies showing an increasing incidence of head and neck cancers in

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these countries. Globally there is an estimated number of 650000 new cases worldwide (1,4,6).

Even though paediatric cancers were once very rare but recent reports suggest that they are becoming a major source of mortality. Children constitute a significant proportion of the population in many developing countries for example about one-third of the general population in developing countries comprises of paediatric population and therefore proper documentation of paediatric malignancies including head and neck cancers is of paramount importance in planning medical services, resource allocation and policy formulation in such countries (1,4,10,11).

In developing countries, gender disparity in the diagnosis of paediatric malignant neoplasms may be exaggerated because of poor resource settings compounded by economic and cultural factors where males are given more medical attention than females (9,10).

There has been diversity on the clinico-histocytopathological profile of various head and neck malignant neoplasms in paediatric patients as it has been reported by different sources and the aim of this mini-review is to highlight on such profile in different countries across the World which is vital in planning medical services, resource allocation and policy formulation in such countries.

### **Clinico-histocytopathological Profile of Paediatric Head and Neck Malignant Neoplasms**

#### **(I) Gender disparity in relation to paediatric head and neck malignant neoplasms**

Studies have consistently shown head and neck cancers to be more common among males than females and ranging from a male to female ratio of 1.3:1 to 3.4:1 (1,7,9,11,13,15,16-22) and also in other countries such as Nigeria and Ghana, male to female ratio was reported to be 1.3:1 (17,20,21,23,24). Males were markedly more affected than females in Iran where the male to female ratio was reported to be 3.4:1 (7).

From various studies which were conducted on paediatric head and neck malignant neoplasms, lymphoma was found to be predominantly a male disease with male to female ratio ranging from 1.61:1 to 8:1 and males were more affected than females in one of the study which was conducted in Nigeria where male to female ratio was 8:1 but smaller incidence of males being more affected than females in another study which was conducted in the same country was also reported (1, 7, 13, 19, 20, 25, 26). Sarcoma was reported to be more of a male disease than being a female disease with male to female ratio ranging from 1.5:1 to 1.7:1 and more incidence of males being more affected by sarcomas than females was reported in Nigeria with male to female ratio being 1.7:1 and this was contrary to what has been observed from a study which was conducted in Iran where sarcomas were found to be exclusively a female disease (100%)

Several studies have also shown carcinomas to be predominantly a male disease with male to female ratio ranging from 2:1 to 7.5:1 (1,7,28) though other studies reported no sex predilection with carcinomas (13,19,26).

When thyroid malignancies are to be considered, a study from Nigeria revealed follicular thyroid carcinoma to be a disease of female predominance similar to papillary thyroid carcinoma with each accounting a female to male ratio of 3:1 (1).

Neural malignancies for example neuroblastomas were reported in two studies to have no sex predilection and in one study it was reported to have male predominance with male to female ratio being 2:1 (1,2,25).

Studies from India and Ghana have shown retinoblastoma to be consistently more common in males than females (male to female ratio being 1.6:1) even though one study from Mongolia has shown different results where no sex predilection was found in patients who were diagnosed to have retinoblastoma (29-31).

## **(ii) Anatomical sites for paediatric head and neck malignant neoplasms**

There is a great diversity on the anatomical sites for paediatric head and neck malignant neoplasms and this fact can be exemplified through the reviewed literatures as follows:

Four studies which did not give specific anatomical components of the neck such as hypopharynx, larynx or oropharynx reported the neck to be the most common site for paediatric head and neck malignant neoplasms where a study from the United States of America reported the neck (thyroid gland) to be affected in 22.1% of the cases and two studies which were conducted in Iran also concluded the neck to be the commonest site for the cancers and this was reported to account for 36%-41% of the cases and such predominance was also observed in a study which was carried out in Nigeria (4,7,13,32).

Oral cavity was observed in two studies to be the commonest site for head and neck cancers where one study from Nigeria reported it to be affected in 36.8% of the cases and the other documented study is from Tanzania where the oral cavity was reported to be affected also in 37.3% of the cases though this study had included both paediatric and adult patients and therefore no specificity to paediatric patients alone was laid in this study(4,33). These findings appear to be different from what was found in another study from Nigeria where the eye/orbit (39.96%) was found to be the commonest anatomical site for paediatric head and neck malignancies and other common sites from the study were the nasopharynx (6.27%), paranasal sinuses (2.64%), nasal cavity (2.35%) and thyroid gland (2.06%) (1).

The nose/paranasal sinuses were found to be the commonly affected anatomical site in a study which was done in Nigeria where it was affected in 30% of the cases and this finding appears to be similar to what was observed in another study which was conducted in the same country where the respiratory tract was found to be the commonest site even

though the respiratory tract was a composite of several sites such as nasal cavity, nasopharynx, oropharynx, hypopharynx and larynx and they were affected in 43.2% of the cases (2,22).

A study which was conducted in Tanzania though not specific for paediatric patients only reported the sinonasal region to be the commonest anatomical site for head and neck cancers accounting for 24.7% of the cases and this was followed by the larynx where it was afflicted in 20.4% of the cases and from this study patients below the age of 20 years with head and neck cancers constituted 5.3% of all the cases and from this study the larynx was predominantly not affected in paediatric patients as it was reported to be more commonly affected in patients after the age of 40 years (12).

Regarding malignant tumours of the salivary glands, the parotid gland was reported to be more affected than the submandibular gland in a study which was conducted in the United States of America and it was affected in 88.7% of the cases unlike the submandibular gland which was afflicted in 8.9% of the cases. This finding appears to be similar to what was observed in the study which was conducted in Tanzania where the parotid gland was the only salivary gland that was affected by malignant tumours even though this study included both paediatric population and adults (12,14). Several other studies have also shown the salivary glands (major and minor) to be common sites for head and neck cancers (2,13,14).

Other less common specific anatomical sites reported from various studies include; tongue, skin, (face and scalp) oesophagus, ear, lips, nasopharynx, oropharynx and hypopharynx, maxilla, mandible (13,32,33)

Regarding maxillofacial bones, the mandible were reported to be the commonest bone to be affected by malignant neoplasms as it has been reported in several studies from Nigeria and Tanzania where one study from Nigeria shows predominance of the mandible over the maxilla with a ratio of mandible to

maxilla affliction being 1.22:1 and another study from Tanzania found all the malignant neoplasms of bones belonging to the head and neck region to be located in the mandible and were exclusively osteosarcoma. Similarly, a study from Iran also reported the mandible to be the only site that was affected by malignant neoplasms in the head and neck region when maxillofacial bones were taken into consideration. These findings appears to be different what was reported from a study which was conducted in Nigeria where the maxilla was found to be predominated by malignant neoplasms belong to the head and neck region with the maxilla to mandible affliction ratio being 2.1:1 (2,7,13,34).

### **(iii) Clinical features for paediatric head and neck malignant neoplasms**

Regarding lateralization of retinoblastoma, unilaterality has been observed in majority of the cases ranging from 67.6% to 82.6% and leukocoria was reported to be the predominant sign ranging from 78% to 87% of the clinical manifestations of retinoblastoma. The second most common clinical feature of retinoblastoma reported from several studies was proptosis where a study from India reported proptosis to be the second most common clinical feature and this accounted for 17% of cases and a study from Ghana also reported the same clinical feature to be the second most common and it accounted for 34.8% of the cases (29-31,35).

Similarly, a study from Taiwan revealed proptosis to be the third most common clinical manifestation of retinoblastoma and this was an affliction of 17% and in this study the second most common manifestation was strabismus accounting for 38% of the cases. These findings appears to differ from what was reported by Essuman et al and Chawla et al where strabismus accounted for 21.7% and 5.5% of the clinical manifestations of the neoplasm respectively (29-31,35).

Studies from different parts of the world have shown neck mass (cervical lymphadenopathy) to be the most common clinical presentation of

nasopharyngeal carcinoma (ranging from 32.3% to 96.7%) and this was followed by epistaxis in majority of the cases (35.7% to 66.7%). The other commonly reported clinical feature was hearing loss where a study from Kenya reported it to occur in 37.6% of the cases and another study from Nigeria revealed an affliction of 66.7% (36-38).

A study from Nigeria established other presenting complaints to be nasal blockage (63.3%), otalgia (46.7%), diplopia (40%), cranial nerve palsy (20%) and seizures which was reported in 10% of the cases. Contrary to this observation, a study from Kenya reported other clinical manifestations such as; trismus (20.8%), ear blockage (20%), dysphagia (14.4%), tinnitus (13.6%), facial numbness (11.2%), proptosis (10.4%), nasal growth (10.4%), otalgia/ear ache (8.8%), diplopia and poor vision each accounting for 6.4% of the cases, dysphonia (5.6%) and nasal discharge (0.4%) (37-39).

In a study which was conducted by Choudhry et al in India, Burkitt's lymphoma (BL) had the following clinical features in its manifestations; facial bones involvement (34.6%), peripheral lymph nodes (13.4%) and apart from head and neck involvement by BL, other affected sites included the abdomen (40.4%), concurrent facial bones and abdominal involvement were reported in 3.8% of cases from the study. Regarding facial bones, maxilla was more affected by BL than the mandible with an affliction ratio of 1.2:1 respectively. Proptosis was reported in 2.4% of cases whereas soft palate involvement in 4.8% of the cases was observed from the same study (40).

A study by Mwanda in Kenya found "a swelling" to be the main complaint by patients with Burkitt's lymphoma. Jaw swelling (51.6%) was the most commonly reported clinical feature whereas other clinical manifestations reported from the study were abdominal swelling (25%), combined jaw and abdominal swelling (13.8%) and other complaints from the study accounted for 9.6% of the cases (41).

Sinonasal cancers have variable clinical manifestations and some studies have shown nasal

obstruction to be the commonest clinical feature where one study from Finland reported nasal obstruction in 35% of the cases and in Nigeria there is a study which reported it in 100% of patients. On top of that, a study which was conducted by Poursadegh et al in Iran revealed facial swelling (66.6%) to be the commonest clinical presentation among patients with sinonasal cancers and these findings appears to differ from what was reported in the aforementioned studies (42-44).

Similarly, several other studies have shown nasal obstruction to be among the clinical presentations even though not leading as the prominent manifestations and this can be seen in a study which was conducted in Iran where it accounted for 27.5% of the cases and in Ghana it accounted for 12% of the cases. This appears to be different from what has been observed in several other studies such as in Michigan where the commonest manifestation was nasal pain (34%) and a study from Ghana by Opoku-Buabeng reported epistaxis (23%) to be the commonest clinical manifestations among patients with sinonasal cancers. Other clinical manifestations reported from several other studies include; hyposmia, anosmia trismus, palatal swelling, sinus tenderness, facial paraesthesia, nasal mass, palatal ulcer, dental luxation, dental pain, diplopia, chronic otitis media, pharyngeal mass, loosening of teeth, tinnitus, ear fullness and hyponasal speech (42-46).

#### **(iv) Histocytopathological types of paediatric head and neck malignant neoplasms**

Generally, between 70% to 90% of head and neck malignant neoplasms are epithelial in origin and squamous cell carcinoma constitutes 66.7% of carcinomas and 47.8% of head and neck cancers (2). About 30% of all lymphomas are reported to occur in the head and neck region and they comprise the second most primary malignancy in the head and neck region whereas about 15% to 20% all sarcomas are diagnosed in the same region (2). Literatures reports osteogenic sarcoma, rhabdomyosarcoma, malignant fibrous histiocytoma and angiosarcoma as the most common histological variants of

sarcoma in the head and neck region (2,9) Salivary gland cancers is reported to constitute about 1% of all head and neck malignant neoplasms (47).

Studies from different parts of the world have shown lymphoma to be the commonest histological type and ranges from 20% to 59.79% (2,9,15,17-21). Of the histological variants of lymphoma reported from various studies, Hodgkin lymphoma was reported to be predominant over Non-Hodgkin's lymphoma (17,19,24,25,33,48).

However, findings from other studies reported Non-Hodgkin's lymphoma to be predominant over Hodgkin's lymphoma (7,18). It's only the study which was conducted in Nigeria which reported an equal prevalence of Hodgkin's and Non-Hodgkin's lymphomas where each accounted for 44.4% of the cases (26). In several other studies, Burkitt's lymphoma was shown to be more prevalent over other types of lymphoma ranging from 36% to 79.6% of the cases (9,11,34). This appear to be different from several other studies which reported carcinoma to be the predominant histological type of paediatric head and neck cancer ranging from 45.3% to 97.4% (4,7,12,13,17).

Of the histological types of carcinoma reported, squamous cell carcinoma was found to be the predominant variant accounting for 44% to 74.3% of cases even though it was reported by Albright to occur in less than 2% of paediatric patients (7,12,14). From a study which was conducted in North Eastern Nigeria, the most common histological type which was identified was reported to be retinoblastoma accounting for 32.3% of the cases (26). Similarly, retinoblastoma was reported in several other studies ranging from 3.03% to 32.3% (1,9,15-17,20,24,26,32,52).

Contrary to other studies which reported lymphoma and carcinoma as the predominant histological variants, a study which was conducted in sub-Saharan Africa revealed neural malignancies (35.3%) to be the commonest histological type (1). Neural malignancies were also reported in paediatric patients in several other studies accounting for

0.61% to 5.7% of the histological types of head and neck malignant neoplasms in such population (9,12,15,25) and no neural malignancy was reported in a study from Tanzania by Gilyoma et al though the study was not limited to paediatric patients only (4).

Another study which was conducted among Nigerian children showed the predominant histological type to be rhabdomyosarcoma accounting for 31% of the cases (17). Other histological variants of sarcoma reported from different parts of the world include osteogenic sarcoma, malignant fibrous histiocyoma, angiosarcoma, fibrosarcoma, fibromyosarcoma, Ewing's sarcoma, osteosarcoma, chondrosarcoma, dermatofibrosarcoma, Kaposi's sarcoma(2,4,7,9,18,53).

Of the thyroid cancers reported from various studies, papillary thyroid carcinoma was the predominant type in one of the study which was conducted in the United States of America (14). In another study which was conducted in India no consistent results was found because the predominant histological type of thyroid cancer was reported to be medullary thyroid carcinoma (15).

From the available literatures, the least commonly reported head and neck malignant neoplasms among paediatric patients was found to be Langerhans cell histiocytosis or eosinophilic granuloma and hereby two studies reported it to be one of the histological types of head and neck cancers where it accounted for 0.61% and 8.6% in two different studies from India and Iran respectively. Similarly, there are other reported histological types of head and neck cancers and these include mucoepidermoid carcinoma (6.2%-9.1%), adenocarcinoma (3.5%-36.7%), adenoid cystic carcinoma (3.3%-7.4%) and olfactory neuroblastoma (0.61%)(7,12,16,18,19).

#### **(v) Anatomical sites in relation to various histocytopathological types of paediatric head and neck malignant neoplasms**

Several studies from different parts of the world have shown the nasopharynx to be more commonly affected by carcinomas where one study from

Nigeria reported the nasopharynx to be affected by carcinomas in 40% of the cases whereas another study from the same country accounted the nasopharynx to be affected by head and neck malignant neoplasms in 94.6% of the case. Similarly, a study from Tanzania which involved both paediatric population and adults reported the nasopharynx to be predominated by carcinomas in 12.4% of the cases. These findings however appears to be different from what was observed in one study from Nigeria where the nasopharynx was affected mainly by lymphomas (12,18,26).

From the available literatures, larynx was rarely affected by malignant neoplasms in paediatric patients and only one study from Nigeria reported the larynx to be affected by squamous cell carcinomas and it was found in a single child who was found to have cancer of the larynx (26).

Paranasal sinuses were found to be more affected by carcinomas where a study from Nigeria reported the paranasal sinuses to be affected by carcinomas in 91.4% of the cases and such finding appears to be similar to what was observed in Tanzania where the sinonasal region (nasal cavity and paranasal sinuses) was affected in 23.9% of the cases though this study had involve both paediatric and adult patients. Contrary to what was reported in these studies, sarcomas were reported to be predominant in the paranasal sinuses from a study which was conducted in Nigeria where 50% of the cancers in the paranasal sinuses were constituted by rhabdomyosarcoma (12,18,26).

Regarding malignant neoplasms of the major salivary glands, there are scanty literatures that has documented paediatric salivary gland malignant neoplasms and only one study from Nigeria reported salivary gland neoplasms to be constituted mainly by carcinomas as per their histocytopathological profile and this accounted for 27% of the cases (26).

The eye has variability in terms of the predominant histological type and this can be evidenced from a study which was conducted in Nigeria where carcinomas were found to be predominant (59.4%)

followed by retinoblastomas (34.4%) and the least reported histological variant from the study was lymphomas (6.2%) (26). This appears to be different from what was reported in one study from the United States of America where majority of neoplasms of the eye/orbit were found to be retinoblastoma (14).

Regarding neuroendocrine malignancies, majority were observed in the nasal cavity and this can be evidenced from several studies in different parts of the world such as the findings from a study which was conducted in Nigeria where all neuroendocrine malignancies occurred in the nose. This appear to be similar to what was reported from a study which was conducted in the same country where neurogenic tumours occurred mainly in the nasal cavity and this accounted for 10% of all the cases. Moreover, olfactory neuroblastoma as one of the neurogenic tumours was reported to occur exclusively in the sinonasal region (nasal cavity and paranasal sinuses) (2,12,26)..

The oral cavity has been observed to be predominated by carcinomas and this can be exemplified from several studies for example a study from Nigeria reported the oral cavity to be predominated by carcinomas in 91.7% of the cases even though other histological variants such as sarcoma (8.3%) were also encountered in the same anatomical site from that study. This however appear to be similar to what was observed in the same country from a study which reported the oral cavity to be affected commonly by carcinomas (2,26).

When an ear is to be considered as one of the anatomical sites for paediatric head and neck malignant neoplasms, there is a study which was conducted in Nigeria and this reported the middle ear to be more commonly affected by lymphomas whereas the external ear was afflicted by primitive neuroectodermal tumour (PNET) and temporal bone by Langerhans histiocytosis (18).

Regarding maxillofacial bones, there is a variability in terms of the predominant histological variants

where in one study which was conducted in Nigeria, the mandible was found to be more commonly affected by lymphomas (37.1%) and this appears to be different from what was observed in a study from the same country where the mandible was found to be predominated by sarcomas and this accounted for 30% of the cases. Moreover, the former study found sarcomas (30.2%) and carcinomas (13.9%) to be other histological variants and the latter study found carcinomas (2.7%) to be next to sarcomas in terms of predominance (2,13).

By considering the maxilla as one of the maxillofacial bones, one study from Nigeria reported sarcomas (37.7%) to be the most common histological variant in this site and this was followed by lymphomas (31.4%) and carcinomas (20.3%). This appears to be different from what was observed in a study which was conducted from the same country where carcinoma (11.7%) was found to be predominant in the maxilla and this was followed by sarcoma (10%) and lymphoma (4.8%) (2,13).

## CONCLUSIONS AND RECOMMENDATIONS

There is still a great variability in the clinico-histocytopathological profile of head and neck malignant neoplasms among paediatric patients across various geographical areas of the World. This call upon every institution dealing with paediatric cancers to have special paediatric head and neck cancer registry which will be of help in planning medical services, resource allocation and policy formulation in such countries and ultimately fighting against paediatric morbidity and mortality.

## CONFLICT OF INTEREST

No any conflict of interest

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