**ORIGINAL ARTICLE**

# Rhabdomyosarcoma in Pediatric Population; a 5 year experience at Children's Hospital, Lahore

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## ABSTRACT

**Background:** Soft tissue sarcomas comprise 7% of all malignant tumours in children with Rhabdomyosarcoma being the commonest soft tissue sarcoma. In Children Embryonal Rhabdomyosarcoma (ERMS) and alveolar (ARMS) are the most common subtypes. Patients younger than 10 years of age have more chances of developing ERMS and >10 years are likely to have ARMS. There are two important prognostic factors in Rhabdomyosarcoma namely age at diagnosis and histological features.

**Aim:** To study the morphology and frequency of Rhabdomyosarcoma among pediatric population.

**Methods:** A retrospective cross sectional study including all cases of Rhabdomyosarcoma among the children diagnosed under 15 years of age were included. All specimens were fixed in 10% buffered formalin, routinely processed under standardized protocol conditions for paraffin embedding, sectioned and finally stained with hematoxylin and eosin. Immuno-histochemical stains including Desmin and Myogenin were applied by standard protocol.

**Results**: A total of 61 cases were diagnosed as Rhabdomyosarcoma during the study period. All cases were of ERMS type. Out of them, 38(62.2%) were males and 23 (37.7%) were females with male to female ratio of 1.7:1. Majority of the tumors were seen; 34 cases (55.7%) in age range of 1-5 years. However, there were two cases (3%) in which the age was not mentioned. Out of 61 cases, head and neck was the most common site for Rhabdomyosarcoma, 18 cases (29%) followed by genitourinary system,17 cases (28%). There were 5 cases (8.2%) in which site was not mentioned. All the diagnosed cases were confirmed by IHC.

**Conclusion:** Rhabdomyosarcoma is, the most common soft tissue sarcoma in pediatric population with predominant involvement of head & neck and genitourinary system. Majority of the patients presented before the age of 5 years. ERMS is the predominant type, with male preponderance.

**Key words:** RMS, children, sarcomas, head & neck, abdomen, genitourinary system.

## INTRODUCTION

Soft tissue sarcomas (STS) comprise about 7% of all malignancies in children and adolescents under the age of 20 years. Rhabdomyosarcoma (RMS) accounts for about 40% of all pediatric STS. The incidence of RMS is 4.5 cases/million children/adolescents per year in American population and in more than 50% of cases, RMS occurs during the first decade of life[1]. RMS, is composed of cells with histopathologic features of striated muscle in various stages of embryogenesis. RMS is derived from primitive undifferentiated mesenchymal cells[2,3] and due to the wide distribution of striated muscle across the body, these tumors may appear anywhere in the body and cause symptoms accordingly. However, due to some unknown mechanism the head and neck area is the most frequently involved site[4,5].

Based on the histological and biological features of the tumor, RMS is classified as embryonal (ERMS) and alveolar (ARMS)[6]. Pleomorphic sarcoma botryoid is an ERMS variant comprising 6% of all RMS with a distinctive gross appearance of polypoid or grape-like structures and the histologic features include aggregates of tumor cells tightly abutting an epithelial surface/cambium layer. ERMS has an earlier age of onset (the majority of cases occur before 10 years of age) and has better prognosis[7]. ARMS is the second most common subtype about 30% of all RMS. In contrast and unlike ERMS, it is more common in adolescents and young adults, with a peak incidence between 10 and 25 years of age. By definition, it has a monomorphic population of primitive cells with round nuclei and features of arrested myogenesis.

Pleomorphic rhabdomyosarcoma (PRMS) is another variant of RMS, occurring mainly in the paients ranging from sixth to seventh decades of life. Spindle cell/sclerosing RMS is a newly described entity comprising 5-10% of all rhabdomyosarcomas[8,9]. All variants of RMS are more common in males. ERMS is more common in whites, whereas, no such gender, racial and geographic predominance is seen in ARMS. ERMS frequently occur in head and neck while ARMS reportedly occurs in extremities[10, 11].

The current study was carried out to reveal the epidemiologic data including age, gender and site as well as the pathological findings both microscopic and immunohistochemical in a series of patients diagnosed over a period of 5 years in the largest pediatric hospital of Pakistan.

The objective was to study the morphology and frequency of Rhabdomyosarcoma among pediatric population.

## MATERIALS AND METHODS:

A retrospective cross sectional study was conducted in the Histopathology department, CH&ICH,Lahore. All cases of Rhabdomyosarcoma diagnosed among the children under 15 years of age, from 1st January, 2013 to 31st December, 2017 were included. All specimens were fixed in 10% buffered formalin, followed by paraffin embedding,

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sectioning and finally staining with haematoxylin and eosin using standard procedures. In addition to types and site of the tumor, patient demographics including sex and age were also be recorded.Immunohistochemical stains including Desmin and Myogenin were applied by standard protocol. All biopsies of children below 15 years of both genders were included while poorly fixed biopsy specimen were excluded.

## RESULTS

A total of 61 cases were diagnosed as RMS during the period of five years from 2013 to 2017. The predominant subtype was ERMS and two cases (3.27%) were of sarcoma botryoides sub type (Fig 3)

Out of the total 61 cases, 38(62.2%) were males and 23 (37.7%) were females with male to female ratio of 1.7:1 . A distinct male predominance was observed.

The tumors were categorized in 3 different age groups comprising of 5 years each. (Table 1) Majority of the tumors were seen in age range of 1-5 years 35 cases (59.3%) followed by 6-10 years 10 cases (16.9%) and 11-15 year 14 cases (23.7%). However, there were two cases (3%) in which the age was not mentioned. So percentage was calculated to 59 number of cases.

Regarding the site, the commonest location for RMS was head and neck, 18(29%), closely followed by genitourinary system with 17(28%) Abdominal cavity was another commonly involved site, 12(19.6%). However, thorax 4(6.5%) and extremities 5(8.2%) were comparatively less frequently involved location. There were 5 cases (8.2%) in which site were not mentioned. Breakdown of site in head & neck & genitourinary cases is shown in Table 2 & 3.

Immunohistochemical stains including desmin and myogenin were applied on 58 cases out of 61 and positive results were observed in overwhelming majority cases.

Of the total cases included in the study, 49 (87.5 %) were incisional biopsies, 7 (12.5%) were excisional biopsies and 5 blocks were received for second opinion. A panel of other immunohistochemical markers including LCA, CK, WT1, NSE were applied on 20 cases for categorizing round blue cell tumors. All showed negative results for lymphoma, carcinoma, germ cell tumors, Wilms tumor and neuroblastoma .

Table 1: Age wise Distribution of RMS in the present study

| **Age groups** | **n** |
|---|---|
| 1-5 years | 35(59.3%) |
| 6-10 years | 10(16.9%) |
| 11-15 years | 14(23.7%) |
| Total | 59(100%) |

Table 2: Break Down of ERMS in Head & Neck location

| | |
|---|---|
| Nasophyrnx | 4 |
| Cheek | 3 |
| Eye | 2 |
| Cervical lymph node | 2 |
| Neck | 2 |
| Post auricular | 2 |
| Parotid / submandibular | 1 |
| Occipital | 1 |
| Temporal muscle | 1 |

Table 3: Break down of genito urinary cases

| | |
|---|---|
| Urinary bladder | 5 |
| Pelvic mass | 5 |
| Vaginal vault | 3 |
| Ureter | 2 |
| Scrotal mass | 1 |
| Prostate | 1 |

## DISCUSSION

Rhabdomyosarcoma is the most common soft tissue sarcoma seen in infants and children[1]. RMS is further categorized into three main subtypes including embryonal, alveolar and pleomorphic RMS[6]. ERMS was the only subtype seen in infancy and children as observed in the present study. However, Zubair etal[10] and Ognianovic et al[1] diagnosed ERMS in 87.4% and 60% respectively in their studies. In the present study ,no case of ARMS was observed opposite to the finding by Newton et al who observed 31% ARMS in his study[12]. This conflict may be due to the lesser number of cases and only children less than 15 years are included in the study .

In the present study, ERMS showed male predominance with male to female ratio of 1.7:1, similar to Azam et al. Sarcoma Botryoid,a variant of ERMS accounted for 3.27% in the present study contrary to Zubair et al and Newton et al who observed Sarcoma Botryoid in 9.4% and 6% respectively [10,12]. This variant typically occurs in mucosa lined hollow organs such as nasal cavity, nasopharynx, urinary bladder and vagina.

Head and neck was the commonest location for ERMS in the present study, followed by genitourinary system which was similar to findings of Yasmin, Christ and Pappoo[13,15,16] .Among the ERMS occuring in head and neck,as shown in table 3 the nasopharynx was the commonest location followed closely by cheek whereas Zubair et al reported paranasal sinus as the predominant site of involvement in head and neck region. We found urinary bladder to be predominent site of origin in cases of genito urinary region as shown in table 3. Similar results were obsereved by Zubair et al.

We diagnosed 8.2% cases in extremities contrary to Azam et al who found extremites as a frequent site of involvement followed by head and neck.[13]. Maximum number of cases were seen in the age group of 1-5 years followed by age group of 6-10 years (Table 1). This observation is consistent with the finding of Gurney and Ognianovic.

We used Desmin and Myogenin as the main immunomarkers in the present study to confirm the diagnosis and the sensitivity shown by myogenin was 80%. Other studies have supported similar results.[17]

## CONCLUSION

ERMS is common RMS in pediatric population with predominant involvement of head & neck and genitourinary system. Children in the age range of 1-5 years were most commonly diagnosed with Rhabdomyosarcoma. Males were predominantly involved in the present study.

**Limitation of study:** There is relatively small number of cases in the present study and certain types like Alveloar,

Sclerosing/Pleomorphic were not diagnosed during this period. Population based studies are required to calculate the exact incidence of this tumour.

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