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Histopathological Profile of Solid Tumours of Childhood and Infancy in Northwest Punjab, India

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Abstract

Malignancy is a major cause of childhood death in developed world and in developing countries like India, paediatric tumours are on the rise. Appropriate management of paediatric tumours requires epidemiological data in different geographical areas. Present study was conducted to classify and find out the histopathological profile of solid tumours of childhood and infancy in 15 years from January 1999 to December 2013. In our study of 168 paediatric tumours, 108 (64.29%) were benign, and 60 (35.71%) were malignant. Maximum incidence of paediatric tumours was seen in the age group of 11-14 years (41.67%) and least in the age group of <1 year (10.71%), with male to female ratio of 1. Amongst the benign tumours, soft tissue tumours were most common (56.48%), with highest incidence of vascular tumours (57.36%). Amongst the malignant tumours, most common were Lymphomas (36.67%) and amongst lymphomas, Hodgkin's lymphomas were more common (63.64%) than non- Hodgkin's lymphoma (36.36%).

Keywords: Histopathological Profile, Solid Tumours, Childhood, Infancy, Benign, Malignant, Paediatric Tumours.

Introduction

Incidence of paediatric tumours is on the rise all over the world. Malignancy is the second most common cause of childhood death in developed world, accounting for 10%-12.3% of all childhood deaths. In developing countries like India childhood mortality is still due to malnutrition and infections, but paediatric tumours are also rising in number.[1,2]

Children below 14 years of age constitute a little over one-third of the total population (all ages) but form less than five percent of the total cancer burden in the population based cancer registries in India.[3,4] Nonetheless, cancers in childhood are important for several reasons. Geographic and ethnic differences in the occurrence of childhood cancer have been described.[5] An increased risk of childhood cancers has been described to be associated with certain genetic conditions or syndromes such as chromosomal abnormalities, DNA repair disorders, congenital anomalies, hereditary immune deficiency states, and other hereditary syndromes.[6,7]

Paediatric cancers differ markedly from adult cancers in their nature, distribution and prognosis. Childhood cancers are unique in the sense that they arise from embryonal cells and thus, respond to chemotherapy.[1] Virtually any tumour may be encountered in children, however in general, benign tumours are far more common in infancy and childhood than malignant ones; of the former, hemangiomas are the most common. Most benign tumours are of little concern, but on occasion they cause serious complications by virtue of their location or rapid increase in size. Regarding solid tumours, CNS tumours, lymphomas and sarcomas are the dominant tumours in children, while carcinomas are more common in adults.[8] Cancer statistics for adults are largely classified according to the site of the tumour. Childhood cancers, however, are more naturally classified using a system which also takes histology into account. The International Classification of Childhood Cancer (ICCC) divides these cancers into 12 diagnostic groups, with further subgroups and divisions.[9]

Appropriate management of paediatric tumours requires complete epidemiological data of paediatric tumours in different geographical areas and combined efforts of paediatrician, paediatric oncologist and pathologist. A literature search shows that there is paucity of studies on the histologic review of the childhood tumours in general and benign tumours in particular.[10,11] In an effort to better understand the epidemiology of tumours in children, a retrospective review of the tumours, diagnosed histopathologically, was carried out, since hospital registries are the only available source of information for assessing the disease pattern in community.

Materials and Method

This study was done in the Department of Pathology, Guru Gobind Singh Medical College, Faridkot, Punjab, India, during a total period of 15 years from January 1999 to December 2013.

Inclusion Criteria: The material for the study included records of all the children, aged 0- 14 years, diagnosed histopathologically with solid tumour, (both benign and malignant tumours diagnosed in children were included, while leukaemias were excluded).

Methodology: The method of study included the retrieving and analysis of clinical details and records of the patients available in the Department of Pathology, Guru Gobind Singh Medical College, Faridkot, Punjab,

India. The tissues were fixed in (10%) formalin, processed and 5µm thick sections were stained with hematoxylin-eosin stain. The slides were reviewed by 2 senior Pathologists and the findings were noted in detail as per protocol. Immunohistochemistry and special stains were applied for confirmation. Clinical details, gross specimen and histological findings were studied and correlated. The tumours were analyzed according to age, sex and histopathological diagnosis. The clinical data of these patients were collected from the request form, which included name, age, sex, site of tumour, and other relevant information, and performas were filled accordingly.

Classification: Malignant paediatric solid tumours are classified as per the 3rd ICD-O classification 1996[9] (International Classification of Childhood Cancer) edited in the year 2000 and of benign tumours according to the tissue of origin. (Table 1)

Results and Discussion

Out of the total 6650 tumours reported in this department over 15 years, 168 were diagnosed as paediatric tumours comprising 2.53% of the total. Overall incidence was equal in male and females (M:F=1).

Table 2-5 show the spectrum of tumours, male to female ratio and site wise distribution of cases.

The benign paediatric tumours were 108 in number and comprised 2.96% of 3650 benign tumours, whereas malignant tumours were 60 in number and consisted 2% of 3000 malignant tumours received over fifteen year period. Other authors have also reported the incidence to be 2%[1] - 4.4%.[2]

Maximum number of paediatric tumours were seen in the age group of 11-14 years (41.67%), with equal frequency in both males and females (M: F=1). A M:F ratio of 1.5- 1.6 has been quoted by similar studies.[2,11] As reported by other authors,[11,12] benign tumours (64.29%) were more common than malignant tumours (35.71%).

Table 5 shows comparison of spectrum of benign tumours in current study with other studies. The incidence of soft tissue tumours and breast tumours was more in this study than other studies. Incidence of bone tumours was almost one-third of that quoted by Ali EA & Talib[12] SHS in 2009 and Punia et al[11] in 2014, but a little more than that quoted by Lee et al[10] in 1966. Skin and adnexal tumours were less frequent than reported by Lee et al[10] in 1966, but more frequent than others.[11,12]

Table 6 compares spectrum of malignant tumours with other studies. The incidence of Lymphomas and Germ cell tumours was more in the present study than all other studies, whereas the incidence of malignant epithelial tumours was lower than other studies.

Lymphomas: Lymphomas constituted 36.67 % of all pediatric tumours, with Hodgkin's disease being more frequent than non- Hodgkin's Lymphoma, and with a male predominance. Similar findings have been reported previously.[13] National Registry of Childhood Tumours by Childhood Cancer Research group; 2006-2007[14] and Stiller CA[15] in 2007 quoted a higher incidence of lymphomas in the age group of 10-14 years but in the present study they occurred most frequently in the age group of 6-10 years.

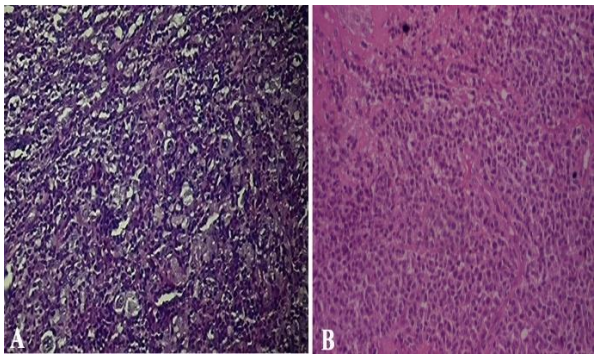

Fig. 1: A) Hodgkin's lymphoma (H & E 40X); B) Non-Hodgkin's lymphoma (H & E 40X)

Central nervous system tumours: Stiller CA[15] quoted, astrocytomas constituted over two- fifths (43%), embryonal tumours account for around a fifth (19%) of all CNS tumours in childhood and ten per cent are defined as ependymoma and choroid plexus tumours. But in the present study glioblastoma multiforme, oligodendroglioma, medulloblastoma, choroid plexus papilloma and carcinoma, all occurred with same frequency, i.e., 20%.

According to Stiller CA[15] around three-quarters (76%) of astrocytomas were diagnosed as low grade and 15% as high grade, but in this case single case of high grade astrocytoma was present, i.e., Glioblastoma multiforme (WHO grade IV). Also Stiller CA stated that, nearly three-quarters (73%) of embryonal tumours were medulloblastoma, and in this study embryonal tumors are represented by a single case of medulloblastoma.

Incidence of choroid plexus tumours has been reported to be highest in one-year-olds,[20] but in this study a single case of choroid plexus papilloma aged 5 years and a single case of choroid plexus carcinoma aged 10 years were seen.

Retinoblastoma: National Registry of Childhood Tumours by Childhood Cancer Research Group; 1996-2005,[16] quoted, around two-fifths (40%) of cases were diagnosed in the first year of life and incidence rates drop to a very low rate after five years of age. In the present study, however, 50% cases presented in the age group of 1-5 years and the rest 50% presented in the age group of 6-10 years. The male to female ratio of 1:3 was quoted by Ali EA[12] and Talib SHS. In this study all the cases were females.

Renal tumors: In this study 2 cases of nephroblastoma were present, both in the age group of 1-5 years and with a male to female ratio of 1. Similar findings were quoted by Stiller CA,[15] but Ali EA[12] and Talib SHS quoted a higher incidence in the age group of 5-9 years, with a

male to female ratio of two.

Bone tumors: Osteochondromas were the most common bone tumours in this study. However, Ewing's sarcoma was the most common bone tumor in the study by Ali EA and Talib SHS.[12] The highest incidence of bone tumours was in the age group of 11-14 years with a male to female ratio of 3.5 in the present study. Similarly, highest incidence of bone tumours was present in the age group of 10-14 years but with the male to female ratio of 1.8 in the study by Ali EA and Talib SHS.[12]

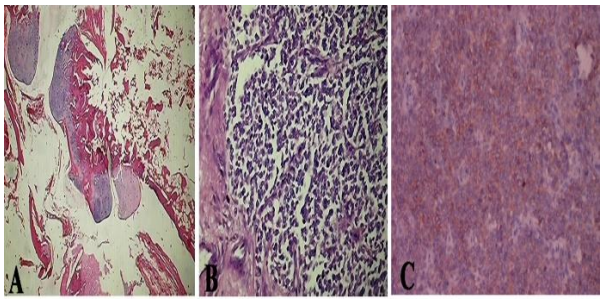

Fig. 2: Bone tumours. A) Osteochondroma (H & E, 4X);
B) Ewing's sarcoma (H & E, 40X);
C) CD 99 positivity of Ewing's Sarcoma on IHC

Out of malignant tumours, Ewing's sarcoma was more frequent than osteosarcoma. Similar finding was quoted by Ali EA and Talib SHS[12] but vice versa by Stiller CA.[15]

Stiller CA[15] quoted, over two-thirds (69%) of osteosarcomas are diagnosed in 10-14 year-olds with majority being diagnosed in the long bones of the legs (84%) and arms (12%). Similar results were seen in this study.

All cases of Ewing's sarcoma, in the present study, occurred in the long bones and more frequently in the age group of 11-14 years, with a male predominance. Similar results were quoted by Stiller CA.[15]

Soft tissue tumors: Vascular tumours were the most common soft tissue tumours in this study as reported earlier.[11,12,17] According to National Registry of Childhood Tumours by Childhood Cancer Research Group[16], around a half (51%) of all soft tissue sarcomas were rhabdomyosarcoma. In the present study also, similar findings were present. Maximum cases presented in head & neck region as reported earlier.[12] Stiller CA[15] quoted majority cases in trunk.

National Registry of Childhood Tumours by Childhood Cancer Research Group; 1996-2005,[16] also quoted, incidence of soft tissue tumours remains fairly constant throughout most of childhood, with just a small increase in the last few years. In the present study similar results were seen.

Vascular tumours were more common in the head & neck region in the present study as reported by other authors.[12,17]

According to Rosai J[8] majority of lipomas occur in the upper half of the body, particularly the trunk and neck. Similar findings were obtained in the present study.

Most cases of rhabdomyosarcoma occur in the head and neck or genitourinary tract,[16] as found in the present study.

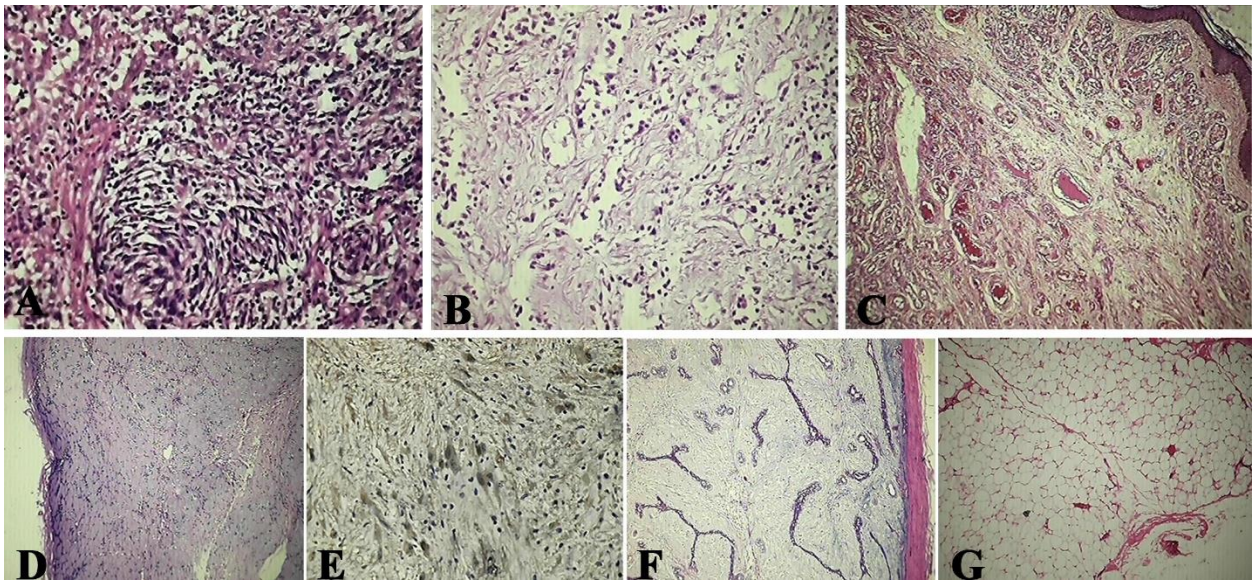

Fig. 3: Soft tissue tumours. A) Plexiform Histiocytoma (H & E, 40X); B) Rhabdomyosarcoma (H & E, 40X); C) Hemangioma (H & E, 10X); D) Schwanomma (H & E, 10X); E) S-100 positivity in Schwanomma on IHC; F) Fibroadenoma (H & E, 10X); G) Lipoma (H & E, 10X)

Germ cell and gonadal cell tumor: As reported by other authors[12,15] malignant gonadal germ cell tumours were more common than extra-gonadal teratoma. According to Stiller CA and National Registry of Childhood Tumours by Childhood Cancer Research Group; 1996-2005,[16] male gonadal germ cell tumours were most likely to be diagnosed in children less than two years old, whereas incidence of female gonadal tumours increases with age. Similar results were obtained in this study.

Yolk sac tumour is reported to be the most common testicular neoplasm,[18] but in the present study, 1 case each of yolk sac tumour, embryonal carcinoma and mixed germ cell tumour were reported.

Germ cell tumours account for 60–70% of all ovarian tumours in pediatric age group.[19,20] Similar results were obtained in the present study.

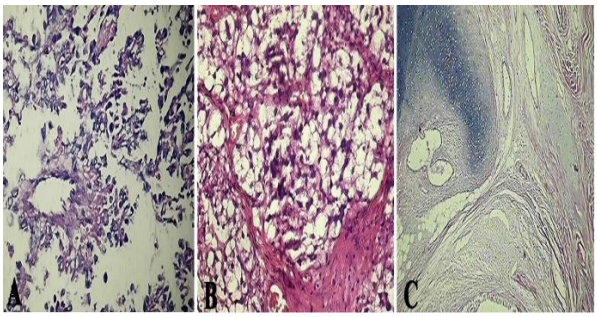

Fig. 4: Germ Cell tumours. A) Yolk sac tumour (H & E, 40X); B) Dysgerminoma (H & E, 40X); C) Mature Teratoma (H & E, 10X)

Breast tumors: Fibroadenoma is the commonest tumour of breast in late childhood and adolescence in girls.[21] Similar results were seen in the present study, with 81.25% breast tumours being diagnosed as fibroadenoma and majority presenting in the age group of 11-14 years.

Skin and adnexal tumours: Other authors have found pilomatrixoma to be the most common skin and adnexal tumour.[11,12] But in this study, pilomatrixoma and nevi occurred with same frequency. Predilection of these tumours for head and neck region and the upper extremities was noted, as reported previously.[11]

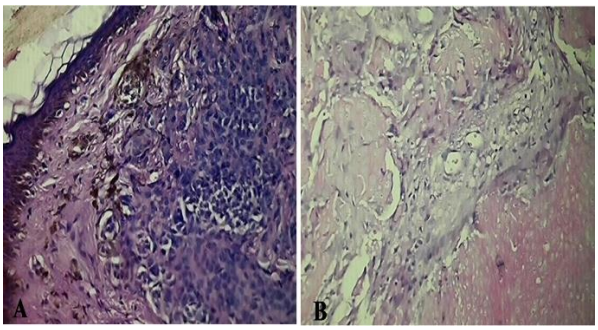

Fig. 5: Skin tumours. A) Nevus (H & E, 40X); B) Pilomatrixoma (H & E, 40X)

Conclusion

In this study of 168 pediatric tumors 108 (64.29%) cases were benign, & 60 (35.71) cases were malignant. Maximum incidence of pediatric tumors was seen in the age group of 11-14 years (41.67%), and least in the age group of <1 year (10.71%); with male to female ratio of 1. Amongst the benign tumours, soft tissue tumors were most common (56.48%), with highest incidence of vascular tumors (57.36% of soft tissue tumors). Amongst the malignant tumours, most common tumors were Lymphomas (36.67%) and amongst lymphomas, Hodgkin's lymphomas were more common (63.64%) than non- Hodgkin's lymphoma (36.36%).

Table 1: International Classification of Childhood Cancer, Third edition (ICCC-3) based on ICD-O-3[9]

I.	**Leukaemias, myeloproliferative diseases, and myelodysplastic diseases**
a) Lymphoid leukaemias b) Acute myeloid leukaemias c) Chronic myeloproliferative diseases d) Myelodysplastic syndrome and other myeloproliferative diseases e) Unspecified and other specified leukaemias	
II.	**Lymphomas and reticuloendothelial noeplasms**
a) Hodgkin lymphomas b) Non-Hodgkin lymphomas (except Burkitt lymphoma) c) Burkitt lymphoma d) Miscellaneous lymphoreticular neoplasms **e)** Unspecified lymphomas	
III.	**CNS and miscellaneous intracranial and intraspinal neoplasms**
a) Ependymomas and choroid plexus tumour b) Astrocytomas c) Intracranial and intraspinal embryonal tumours d) Other gliomas e) Other specified intracranial and intraspinal neoplasms f) Unspecified intracranial and intraspinal neoplasms	
IV.	**Neuroblastoma and other peripheral nervous cell tumours**

a) Neuroblastoma and ganglioneuroblastoma b) Other peripheral nervous cell tumours	
V.	**Retinoblastoma**
VI.	**Renal tumours**
a) Nephroblastoma and other nonepithelial renal tumours b) Renal carcinomas c) Unspecified malignant renal tumours	
VII.	**Hepatic tumours**
a) Hepatoblastoma b) Hepatic carcinomas c) Unspecified malignant hepatic tumours	
VIII.	**Malignant bone tumours**
a) Osteosarcomas b) Chondrosarcomas c) Ewing tumour and related sarcomas of bone d) Other specified malignant bone tumours e) Unspecified malignant bone tumours	
IX.	**Soft tissue and other extraosseous sarcomas**
a) Rhabdomyosarcomas b) Fibrosarcomas, peripheral nerve sheath tumours, and other fibrous neoplasms c) Kaposi sarcoma d) Other specified soft tissue sarcomas e) Unspecified soft tissue sarcomas	
X.	**Germ cell tumours, trophoblastic tumours, and neoplasms of gonads**
a) Intracranial and intraspinal germ cell tumours b) Malignant extracranial and extragonadal germ cell tumours c) Malignant gonadal germ cell tumours d) Gonadal carcinomas e) Other and unspecified malignant gonadal tumours	
XI.	**Other malignant epithelial neoplasms and malignant melanomas**
a) Adrenocortical carcinomas b) Thyroid carcinomas c) Nasopharyngeal carcinomas d) Malignant melanomas e) Skin carcinomas f) Other and unspecified carcinomas	
XII.	**Other and unspecified malignant neoplasms**
a) Other specified malignant tumours b) Other unspecified malignant tumours	
XIII.	**Not Classified by ICCC or in situ**

Table 2: Spectrum of tumours

Type of tumour	Number	%
Benign (n=108)		
Soft tissue tumours	61	56.48
Bone tumours	09	8.33
Breast tumours	16	14.82
Germ cell and gonadal tumours	05	4.63
Skin & adenexal tumours	12	11.11
Other benign tumours	05	4.63
Malignant (n= 60)		
Lymphomas	22	36.67
CNS Neoplasms	04	6.67
Retinoblastoma	04	6.67
Renal tumours	02	3.33
Bone tumours	09	15

Soft tissue tumours	07	11.67
Germ cell tumours & Gonadal tumours	10	16.67
Malignant epithelial neoplasms	01	1.66
Metastasis	01	1.66

Table 3: Age distribution and M:F ratio of various tumours

Type of tumour	Age group					M:F ratio
	<1 year	1-5 years	6-10 years	11-14 years	Total	
Lymphomas (n=22)					22	2.67
Hodgkin's	0	0	8	6	14	2.5
Non-Hodgkin's	0	1	5	2	8	3.0
CNS tumours (n=5)						1.5
Choroid plexus Papilloma	0	1	0	0	1	
Glioblastoma Multiforme	0	0	0	1	1	
Oligodendroma	0	0	0	1	1	
Medulloblastoma	0	0	1	0	1	
Choroid plexus carcinoma	0	0	1	0	1	
Retinoblastoma (n=4)	0	2	2	0	4	--
Nephroblastoma (n=2)	0	2	0	0	2	1.0
Bone tumours (n=18)						3.5
Osteochondroma	0	0	3	5	8	
Chondroblastoma	0	0	0	1	1	
Osteosarcoma	0	0	1	2	3	
Ewing's sarcoma	0	0	1	4	5	
Giant cell tumours	0	0	0	1	1	
Soft tissue tumours (n=68)	15	14	19	20	68	1.06
Germ cell and gonadal tumours (n=15)	3	3	5	4	15	0.67
Malignant germ cell tumours (n=9)						
Dysgerminoma	0	0	0	1	1	
Yolk sac tumour	0	1	0	1	2	
Immature teratoma	0	0	2	1	3	
Embryonal carcinoma	0	1	0	0	1	
Mixed germ cell tumour	0	1	1	0	2	
Brest tumours (n=16)						--
Fibroadenaoma	0	0	0	13	13	
Phylloides	0	0	1	2	3	
Skin and adenexal tumours (n=12)						1
Pilomatrixoma	0	1	2	2	5	
Nevus	0	1	3	1	5	
Fibroepithelial polyp	0	0	1	1	2	
Miscellaneous tumours (n=6)						
Pleomorphic adenoma					3	
Odontogenic tumour					1	
Adenocarcinoma intestine					1	
Metastasis intestine					1	

Table 4: Distribution of tumours according to site

Tumour	Site	%	Site	%	Site	%	Site	%
Bone tumours (n=18)	**Long bones (n=13)**		**Short bones (n=1)**		**Flat bones (n=4)**			
Osteochondroma	3	16.66	1	5.55	4	22.22		
Chondroblatoma	1	5.55	0	0.00	0	0.00		
Osteosarcoma	3	16.66	0	0.00	0	0.00		
Ewing's sarcoma	5	27.77	0	0.00	0	0.00		
Giant cell tumour	1	5.55	0	0.00	0	0.00		
Soft tissue tumours (n=68)	**Head & neck (n=32)**		**Trunk (n=22)**		**Lower limb (n=4)**		**Upper limb (n=10)**	
Vascular tumour	22	32.35	9	13.23	2	2.94	6	8.82
Fibrous tumour	2	2.94	0	0.00	1	1.47	0	0.00
Lipoma	1	1.47	7	10.29	0	0.00	1	1.47
Peripheral nerve sheath tumour	3	4.41	5	7.35	0	0.00	0	0.00
Fibrohistiocytic tumour	1	1.47	0	0.00	0	0.00	1	1.47
Rhabdomyosarcoma	3	4.41	0	0.00	0	0.00	1	1.47
Fibrosarcoma	0	0.00	0	0.00	1	1.47	1	1.47
Malignant fibrohistiocytic tumour	0	0.00	1	1.47	0	0.00	0	0.00

Table 5: Comparison of Benign tumours (%)

Tumour	Current Study (%) (n=108)	Punia et al[11] 2014 (%) (n=191)	Ali EA & Talib SHS[12] 2009(%) (n=92)	Lee et Al[10] 1966(%) (n=171)
Soft tissue tumours	56.48	50.91	39.1	48.53
Bone tumours	8.33	22.55	25	7.60
Breast tumours	14.82	8.73	4.3	5.26
Skin and adnexal tumours	11.11	8.36	2.1	26.31
Miscellaneous	9.26	9.45	29.5	12.30

Table 6: Comparison of Malignant tumours (%)

Tumour	Ali EA & Talib SHS[12] 2009(%) (n=83)	Jabeen S et al 2010[2](%) (n=1250)	Bhalodia JN & Patel MM[1] 2011 (%) (n=43)	Punia et al 2014[11] (%) (n=110)	Present Study (%) (n=60)
Leukemia, MPD, MDS	Excluded	14.3	44.18	Excluded	Excluded
Lymphomas / reticulo-endothelial neoplasms	24.09	24.2	16.27	7.27	36.67
Central nervous system tumours	16.8	3.7	6.97	23.64	6.67
Neuro- blastoma	8.4	--	6.97	0.91	--
Retino- blastoma	9.6	17.4	--	6.36	6.67
Renal tumours	10.8	6.8	9.3	--	3.33
Hepatic tumours	--	1.3	--	--	--
Malignant bone tumours	13.2	7.3	2.32	32.73	15
Soft tissue & other extra- osseous sarcomas	3.6	19.3	2.32	17.27	11.67
Germ Cell tumours	4.8			3.64	16.67
Malignant epithelial neoplasms &	2.4			7.27	1.66

malignant melanoma			11.67		
Unspecified malignant Neoplasms	6.02			--	1.66

MDS – Myelodysplastic syndrome; MPD – Myeloproliferative diseases

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