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CERTIFICATE

This is to certify that this dissertation entitled "***A CLINICAL AND HISTOMORPHOLOGICAL ANALYSIS OF PAEDIATRIC MALIGNANT NEOPLASMS"*** is the bonafide record work done by **DR. R.REVATHI** submitted as partial fulfillment for the requirements of **M.D Degree Examinations**, **Pathology** to be held in March 2007.

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MASTER CHART

INTRODUCTION

Paediatric cancers differ markedly from adult malignancies in their distribution by histology, tumour site and in prognosis. Acute lymphoblastic leukemia, brain cancers, Lymphomas and sarcomas of soft tissue and bone predominant in children and adolescence.[3,8,72,73] Unlike incidence pattern in adults where cancer rates tend to rapidly increase with increasing age, relatively wide age variability exists during development, with two peaks in early childhood and in adolescence.[16,17,19.]

During the first year of life embryonal tumour such as neuroblastoma, nephroblastoma, retinoblastoma, medulloblastoma, rhabdomyosarcoma, are most common.[3,8,18,19,46,47] These embryonal tumours combine with acute

leukemia, NHL and gliomas which together peaks in incidence from 2 to 5yrs of age, for the highest cancer incidence during childhood and adolescence other than in infancy. It appears that adolescence is a transitional period between the common early childhood malignancies and characteristic carcinomas of adulthood. The mortality rate of cancer in children is approximately 3 to 5 deaths / 1 lakh population / year.

A number of genetic conditions associated with elevated risk of childhood cancers such as DOWNS SYNDROME, NF I and II, BECKWITH WEIDEMANN SYNDROME, TUBEROUS SCLEROSIS and LI FRAUMENI SYNDROME. The risk factors for the major paediatric cancer includes ionizing radiation, non-ionizing power frequency electromagnetic field, pesticides, parental occupational chemical exposures, dietary factors and environmental cigarette smoke. The role of viruses such as polioma viruses, EBV & HTLV in etiologic importance is unclear.

In this study the paediatric cancers are broadly classified under 3 major groups i.e., soft tissue and bone sarcomas, Haematalogical and lymphoreticular malignancies and CNS neoplasms. Most authors and research workers agreed to follow this system in evaluating the incidence, prevalence, risk factors and management of pediatric cancers. In general, there is diversity in the occurrence of paediatric neoplasm all over the world. In this study, the actual incidence and presentation of paediatric neoplasm in semi urban area is evaluated with painful attention to clinical features, role of environmental factors,

consanguinity and initial cytomorphological evaluation with fine needle aspiration in proportion of cases. As Paediatric neoplasm are often anaplastic cancers, they pose a challenge to surgical pathologist.

Paediatric oncology face unique challenges because treatment with radiation, surgery and chemotherapy may adversely affects growth and development and may cause serious long term medical and psychosocial effect.[54,59,65]

Molecular cytogenetics, Immunohistochemistry and histochemical stains play a major role in determining the exact underlying pathology of various paediatric cancers.

This study is undertaken in view of evaluating the actual incidence of paediatrics neoplasms in semi urban area like Thanjavur with particular attention to the age, sex, site and histopathology of cancers. In addition, the recent literatures, journals and research publications regarding paediatric cancers are also immensely reviewed.

AIM OF STUDY

1. To evaluate the incidence and prevalence as well as trend of paediatric neoplasms in semi urban area.
2. To evaluate the clinical features, symptoms and signs associated with childhood malignancies.
3. To study paediatric tumours under three broad categories i.e haematological malignancies, soft tissue sarcomas and CNS tumours.
4. To evaluate the initial role of histochemical stains in diagnosis of haematological neoplasms.
5. To study the value of immunohistochemistry in final diagnosis of paediatric tumours.

MATERIALS AND METHODS

Children and adolescence presented with malignant neoplasms referred from Raja Mirasudhar Govt. Hospitals (RMH), Thanjavur which is affiliated to Thanjavur Medical College (TMC) during 2003 – 2005 where included in this study. A thorough clinical evaluation routine haematological investigations, ultra sonogram and CT scan (in proportion of cases) were done in each case.

A detailed history with particular attention to consanguinity, socio economic status, nutrition, radiation, exposure to pesticides, parental occupation and also similar neoplasms in other family members were also recorded.

A- HAEMATALOGICAL & LYMPHO RETICULATOR SYSTEM

The routine haematological evaluation when reveals malignancies such as acute leukemia, the slides were stained routinely with Leishman and Giemsa stains (Appendix I & II) and further subjected to histochemical evaluation with special stain such as periodic-acid-schiff and sudan black B (appendix III)

Lymph node specimen with initially suspected lymphoma are with initial cytomorphological diagnosis lymphoma were fixed in toto in buffered neutral formation and processed routinely. 3-5 micrometer sections were cut and stained with haematoxylin and eosin (appendix IV) Reticulin and CD makers (in proportion of cases) were also applied in doubtful cases for final conformation (appendix V, VI).

B - SOFT TISSUE AND BRAIN CANCERS

Like lymph node, the soft tissue cancer and brain neoplasms are also examined carefully from the reception itself and larger specimens were sliced at 1cm interval without distorting the gross pathology and fixed in neutral buffered formalin and processed routinely. 3 to 5 sections were cut and stain with routine H and E. Immunohistochemistry with GFAP marker were also performed in doubtful CNS Neoplasms.

REVIEW OF LITERATURE

The biologic nature of tumors of childhood is clinically, histopathologically, and biologically distinct from that of adult-onset malignancies. Childhood cancers tend to have short latency periods, are often rapidly growing and aggressively invasive, are rarely associated with exposure to carcinogens implicated in adult-onset cancers, and are generally more responsive to standard modalities of treatment, in particular chemotherapy.

Malignant tumors between the ages of 1 and 15 years are distinctly uncommon, but cancer remains the leading cause of death from disease in this age group. Unlike adults, in whom most cancers are of Epithelial origin (e.g., carcinomas of the lung, breast, and gastrointestinal tract) most malignant tumors in children arise from hematopoietic, nervous, and soft tissues. Another feature that distinguishes childhood tumors from those of adults is the fact that many of the former are part of developmental complexes. Examples include are part of developmental complexes. Examples include Wilms tumor associated with aniridia, genitourinary malformations, and mental retardation (WAGR complex) hemi hypertrophy of the body[26,58,69] hepatoblastoma, and adrenal carcinoma and tuberous sclerosis in blastoma, and adrenal carcinoma, and tuberous sclerosis in association with renal tumors and rhabdomyomas of the obviously developmental tumours that have evolved in utero. In addition, abnormally developed organs, persistent organ primordial, and displaced organ rests are all vulnerable to neoplastic transformation.

HAEMATOLOGICAL AND LYMPHORETICULAR MALIGNANCY

LEUKEMIA

Leukemia is the most common form of cancer in children approximately 2500 new cases of childhood leukemia are diagnosed each year in the United States. ALL and AML are diagnosed in 75 % and 20 % of the cases, respectively, and chronic myeloid leukemia in fewer than 5 %. The well – established peak incidence of childhood leukemia at age 4 years is due to ALL.[43, 53]

The FAB system divides ALL in to three morphologic subtypes [L_1, L_2, and L_3] L_1 lymphoblasts, the most common FAB type in children, have scantly cytoplasm and inconspicuous nucleoli. Blasts in the L_2 category account for 10% of cases, they are larger and more Pleomorphic in size, with abundant cytoplasm and prominent nucleoli, and they may be difficult to distinguish by morphology alone from FAB subtype M0 AML. L_3 is the rarest subtype (1% to 2%) of ALL, and these blasts have very basophilic vacuolated cytoplasm. These L_3 blasts have the same immunophenotype as well as karyotype and molecular genetic abnormalities as the tumor cells in small no cleaved or Burkitt lymphomas [L_3]

The FAB classification recognizes eight subtypes of AML (M0 to M10)

-Acute myeloid leukemia minimally differentiated

- Acute myeloid leukemia without maturation

- Acute myeloid leukemia with maturation.
- Acute myelomonocytic leukemia.
- Acute monoblastic and monocytic leukemia.
- Acute Erythroid leukemia.
- Acute megakaryoblastic leukemia.
- Acute Basophilic leukemia.
-Acute pan myelosis with myelofibrosis.
- Myeloid sarcoma.

CYTOCHEMISTRY:

Myeloperoxidase (MPO):

Myeloperoxidase activity is specific for myeloid differentiation. Myeloperoxidase activity is stable for approximately four weeks in unstain smears kept at cool room temperature. Myeloperoxidase in myeloblast is granular and often concentrated in the golgi zone. Monoblast may be negative or positive with scattered fine granules. Lymphoblasts and megakryoblasts are MPO negative.

Sudan Black B (SBB):

SBB reactivity is similar to MPO in Myeloblast and monoblast and is stable for months in unstained slides.Its specificity for the myeloid lineage is less than MPO positive cells stain more intensely than MPO. Lymphoblast are usually negative. Black granules in Neutrophils and myeloblasts.

LYMPHOMA

The lymphomas are the third most common childhood malignancy and account for approximately 10% of cancers in children. Approximately two-thirds of the lymphomas diagnosed in children are Non-Hodgkin's lymphoma (NHL) [30,31,33,41,51,56] and the remainders are Hodgkin;s disease.[4,11,16,22,61] The spectrum of NHL seen in paediatric patients differs significantly from that seen in adults.

HODGKIN'S LYMPHOMA

Hodgkin's disease is a lymphoreticular malignancy characterize by a progressive painless enlargement of lymphnodes and define by specific histopathological features include a partial or total replacement of nodal architecture by an inflammatory cellular background containing Reed- Sternberg (RS) cells and their variants.

Childhood Hodgkin's disease is a lymphoma displays characteristic epidemiological, clinical and pathological features according to various geographic areas, particularly according to the socio economic level of a country. High male to female ratio, younger age at presentation, high proportion of advanced stages and presence of constitutional symptoms, predominance of mixed cellularity type of HD disease.

WHO histological classification of Hodgkin's Lymphoma

Nodular Lymphocyte predominant Hodgkin's Lymphoma	NLPHL
Classical Hodgkin's Lymphoma	CHL
Nodular Sclerosis Classical Hodgkin's Lymphoma	NSHL
Mixed cellularity Classical Hodgkin's Lymphoma	MCHL

Lymphocyte- Rich Classical Hodgkin's Lymphoma	LRCHL
Lymphocyte-Depleted Classical Hodgkin's Lymphoma	LDHL

NON-HODGKIN'S LYMPHOMA

Non-Hodgkin's lymphoma (NHL) results from malignant cloned proliferation of lymphocytes of T-B- or intermediate cell origin.

Clinical manifestations:

Lymphoblastic NHL often present as an intrathoracic tumour, usually a mediastinal mass and is associated with dyspnoea, chest pain, dysphagia, pleural effusion and superior vena cava syndrome. Cervical and axillary lymph adenopathy is present in up to 80 % of the patient at diagnosis. Primary involvement of bone, bone marrow, testis or skin is not uncommon. [29, 37, 74, 75]

The central nervous system (CNS) may also be involved.

SNCCC present as an abdominal tumour in 80 % of united state cases in patient with abdominal pain or distention, bowel obstruction, change in bowel habits, intestinal bleeding or rarely intestinal perforation. Other sites include CNS, bone marrow and peripheral lymph nodes.

LCL occurs in many sites including abdomen and Mediastinum. Extra medullary sites include skin, bone, soft tissue. CNS involvement is rare in contrast to SNCCL and lymphoblastic NHL.

Morphology:

Morphology of large cell lymphoma:

Diffuse lymphoma composed of large transformed B cells. Four morphological variants are recognized in WHO classification: - centroblastic, immunoblastic, T cell rich/ histocytic rich and anaplastic lymphoma.

Histopathological Features:

DCBCL usually have a predominance of large transformed lympoid cells with vesicular chromatin.

Those of centroblastic type where the neoplastic cells resembles larger transformed follicular center cells have nuclei usually larger than histocytic nucleai with round to oval but sometimes more irregular nucleai contours, dispersed chromatin, one to more moderatelly prominent nucleoli, cytoplasm is generally scanty and amphophilic to basophilic.

Immunoblastic type:

Majority of the cell 90 % are immunoblasts with single centrally located nucleus an appreciable amount of basophilic cytoplasm less than 5% of the population is represented by centroblast.

T- Cell / histiocyte rich:-

In this variant the majority of the cells are non-neoblastic T cells with or without histiocytes and fewer than 10% large neoblastic B cells are present.

Anaplastic large B cell lymphoma:

Characterized by large round, oval or polygonal cells with bizarre pleomorphic nuclei which may resemble Reed – Sternberg cells.[31, 33, 34]

Anaplastic large T cell lymphoma:

Characterize by Broad morphologic spectrum however all cases contain a variable proportion of cells with eccentric, horse shoe or kidney shaped nuclei. Often with an eosinophilic region near the nucleus. Some of the cell may appear to contain cytoplasmic inclusions, they are the invaginations of the nuclear membrane. Cells with there features have been referred to as dough nut cells. ALCL have more adbundant cytoplasm. Cytoplasm may appear clear, basophilic or eosinophilic. Multiple nuclei with wreath like pattern may present. Severe cytomorphological variants have been recognized. These include 1.common 2.Lympho histrocytic 3. Small cell variants.

Morphological features of Burkitt's lymphoma:

Medium sized cells show diffuse monotonous pattern of infiltration. The cells exhibit squared borders of retracted cytoplasm and may appear cohesive. The nuclei round with clumped chromatin and contain lipid vacuoles.

A “starry sky” pattern is usually present imparted by numerous benign macrophages that have ingested apoptotic tumour cells.

Other variants are BL with plasmacytoid differentiation, A typical Burkitt or Burkitt’s like.

Lymphoblastic lymphoma:

Lymphnode show complete effacement with involvement of the capsule. A starry sky effect may present.

Partial involvement present in a para cortical location with sparing of germinal centre may occur. In some cases, the predominant population of blast has convoluted nuclei. Mitotic figure may be numerous. A small number of patients with TLBL, eosinophilia and myeloid hyperplasia has been observed.

Immunophenotyping:

Lymphoblastic lymphoma:

Tdt posstive. Variable expression of CDla, CD2, CD3, CD4, CD5, CD7, and CD8. Among these CD7 and cytoplasmic CD3 are most often positive.

Burkitt Lymphoma:

Tumour cells express membrane IgM with light chain restriction. B cell associated antigen CD19, CD20, CD22, CD10, BCL-6 cell negative for CD5, CD23, Tdt, BCL2 is not expressed.

Large cell Lymphoma:

Diffuse large B cell lymphoma express various Pan- B markers such as CD19, 20, 22 and CD79 and for cytoplasmic immunoglobulin can be demonstrated in 50 – 75 % of cases.

Anaplastic large B cell expresses CD30:

Some cases expresses CD5 (10 %) or CD10 (25 -50%) CD5 and DLBCL are negative for cyclin D1 expression.

Anaplastic large T cell lymphoma:

Positive for CD30 on the cell membrane and in the golgi region strongest reaction in large cells, smaller cells a only weakly positive or negative for CD30.

ALK staining may be cytoplasmic and nuclear or it may be restricted either to nucleus or to the cytoplasm.[50, 51, 56]

SOFT TISSUE AND BONE TUMOURS

Neuroblastoma and Ganglioneuroblastoma

About 85% of all neuroblastomas and ganglioneuromblastomas occur in the first 4 years of life, with a median age of about 21 months there are no sex-related differences in incidence rates.[12, 21, 35, 68] While almost 70% of cases arise in the adrenal gland or intra-abdominal sympathetic chain, at least 20% arise in the thorax (including the thymus).

The tumors may appear as a discrete spheroidal mass or a large bulky tumor with a multinodular surface. There may be invasion of adjacent organs or tissues.

On cross-section:

Neuroblastomas are often coarsely nodular with areas of hemorrhage and necrosis. The gross appearance can simulate a hematoma with cystic degeneration. Calcification within the tumor may appear as chalky white or yellowish punctate areas. Specimen radiography may demonstrate this to much better advantage. Cystic neuroblastomas have been reported which simulate a hematoma or adrenal cyst. Ganglio-neuroblastomas show an increased level of differentiation and this may be reflected on gross examination as a neoplasm with a more homogeneous appearance on cross-section.

Microscopically:

Neuroblastoma is the prototypic example of the "small blue cell" tumor of childhood, and usually has an ill-defined lobular or nesting pattern with thin fibrovascular septa. Markedly nested ("organoid") cases are said to carry an improved prognosis. There is often a variable amount of pale, fibrillary material between cells, representing neuritic cell processes. This neurofibrillary matrix, which has been likened to neuropil of the central nervous system, may form the center of

rosettes or broad mats with irregular contour, rarely the rosettes have a rhythmic or palisading configuration. In undifferentiated neuroblastoma the neurofibrillary matrix may be absent altogether, making diagnosis more difficult. Nuclear chromatin usually is finely dispersed in small clumps, imparting a speckled or "salt and pepper" appearance, nucleoli generally are inconspicuous although they may become prominent with ganglion cell differentiation. Anaplastic neuroblastoma has also been described but its significance remains uncertain. Other unusual histopathologic features have been reported such as a sclerosing pattern, spindle-shaped neuroblasts, stromal hyalinization, and dense lymphoplasmacytic infiltration, some of which may be related to the phenomenon of regression.

Renal tumors in children

Primary renal neoplasms are uncommon in children fewer than 500 new cases occur in the U.S.A. annually.[26, 58, 69] However, they constitute the fifth most common group of pediatric cancers and are the second most frequent abdominal malignancy of children.

The most common tumor in this group is Wilms tumor (nephroblastoma). Important because of their poor response to therapy and consequent morbidity and mortality are clear cell sarcoma and rhabdoid tumor. In children younger than three months, mesoblastic nephroma is the most common renal neoplasm and usually has a favorable prognosis. A final rare tumor, the ossifying renal tumor of infancy. Tumors such as renal cell carcinoma, lymphoma, sarcomas, neuroendocrine tumors and angiomyolipoma, which usually are found in adult kidneys, occur rarely in children but do not in most instances differ pathologically in this age group from their adult counterparts, although there is a rare oncocytoid form of renal cell carcinoma apparently only seen after treatment for neuroblastoma. Much of what we know today about the pathology of renal neopasia in childhood is the result of the work of the National Wilms' Tumor Study (NWTS) and its Pathology Center under the direction of Dr.Bruce Beckwith.

Wilms' tumor

Wilms' tumors comprise more than 80% of renal tumors of childhood.[26,58,59] Most often, they are found in children 2-4 years old (median ages for males and females, respectively, are 37 and 43 months) they are relatively uncommon in the first 6 months of life and in children older than 6 years. Wilms' tumors are rare in the neonatal period. There is a slight

preponderance of females. The tumors are bilateral in 4.4% of cases and patients with bilateral tumors average more than a year younger than patients with unilateral tumors. Associations with congenital anomalies including cryptorchidism, hypospadias, other genital anomalies, hemihypertrophy, and aniridia are well recognized. As many as 5% of patients with Beckwith-Weidemann syndrome develop Wilms tumors. Patients with the Drash syndrome also have an increased risk of developing Wilms tumors. A variety of other malformations are less frequently associated with Wilms tumors. Uncommonly, Wilms tumors have a familial association.

Macroscopic Appearances

Wilms tumors are usually large masses more than 5 cm in diameter and a third or more are larger than 10cm. Often they weigh more than 500g. The cut surfaces are typically solid, soft and grayish or pinkish resembling brain tissue. Foci of hemorrhage and necrosis are often present and cysts are common. Rarely, the tumors are extensively cystic. The tumors usually are enclosed by a prominent pseudo-capsule composed of compressed renal and perirenal tissues this, gives an appearance of circumscription and even true encapsulation. Polypoid growth in the renal pelvic cavity, mimicking sarcoma botryoides.

Histologic Appearances

Wilms tumors are typically composed of variable mixtures of blastema, epithelium and stroma, although in some tumors only two components, occasionally only one is present. Blastema consists of sheets of randomly arranged, densely packed small cells with darkly staining nuclei, frequent mitotic figures, and inconspicuous cytoplasm, resembling to some extent, other "small blue cell tumors" of childhood. Blastema is commonly arranged in three patterns – serpentine, nodular, and diffuse. Serpentine and nodular are most common and diagnostically helpful. They consist of anastomosing serpiginous or spheroidal aggregates of blastema, sharply circumscribed from the surrounding stromal elements.

MALIGNANT TUMORS OF BONE

Annual incidence of malignant tumors in United States is approximately 7 cases per million in which children younger than 15 years of age, with slightly lower incidence in black children. Osteosarcoma hosorcem is the primary malignant tumor of bone in children younger than 10 years of age followed by Ewings sarcome of bone.[1, 3,8,46]

Ostesarcoma can be defined simply as a malignant tumor in which osteoid or bony matrix is produced by the tumor cells. Osteosarcomas can be subdivided broadly into two groups, the majority occur within the bone but a small minority

occur on the surface. These two broad categories can be further subdivided depending on the clinical, roentgenographic and histologic features.

Classification of osteosarcoma

Osteosarcomas within bone

Conventional osteosarcoma

- Osteoblastic
- Chondroblastic
- Fibroblastic

Small cell osteosarcoma

Telangiectatic osteosarcoma

Low-grade central osteosarcoma

Osteosarcoma in Paget's desease

Post-irradiation osteosarcoma

Osteosarcoma in other benign precursors

Surface osteosarcomas

Parosteal osteosarcoma

Periosteal osteosarcoma

High-grade surface osteosarcoma

The clinical symptoms are quite non-specific. Patients complain of pain or swelling or both of variable duration, ranging from days to months. Pathologic fracture may be the initial symptom. The roentgenographic features of osteosarcoma are quite variable. The tumor usually gives rise to a large area of destruction of bone with extension into soft tissue. The amount of mineral present in the lesion varies and correlates somewhat with the type of osteosarcoma. As the tumor destroys the cortex, it lifts up the periosteum. This results in reactive new bone formation at the junction between the elevated periosteum and the underlying cortex. This is referred to as Codman's triangle. Rarely, an osteosarcoma is small and extremely well circumscribed, suggesting a benign lesion.

The gross appearance of osteosarcoma also is quite variable. Most have the fish-flesh appearance associated with sarcomas.[16, 17] Some are heavily mineralized and hence extremely hard. Some have large areas of obvious blue cartilage.

Microscopically, most osteosarcomas are highly malignant tumors their spindle cells have nuclei with marked pleomorphism. Conventional osteosarcoma can be further subdivided into osteoblastic, chondroblastic and fibroblastic varieties, depending on the predominant matrix.

Approxiamtely half of all osteosarcomas can be called “osteoblastic”. Characteristically, the matrix is produced as a fine network between individual tumor cells. The matrix may be in the form of unmineralized osteoid or may show mineralized trabeculae. About 25% of osteosarcomas show predominantly cartilaginous differentiation. The cartilage is in the form of lobules and the cells within lacunae show marked anaplasia. Osteoid matrix may be seen between the spindle cells or in the center of chondroid lobules. In a small biopsy specimen, osteoid may not be seen between spindle cells.

Approximately 25% of osteosarcomas have a pre-dominantly spindle cell pattern and minimal amounts of matrix production. These are called “fibroblastic osteosarcomas”.

EWINGS SARCOMA AND PNET

Ewings sarcoma and PNET are rare sarcomas of bone & soft tissues described in 1921 by Dr.James Ewing.[5, 67] Both Ewings sarcoma & PNET share in over 90% of the cases balanced translocation T (11, 22) and they are almost now universally referred as ends of a common histologic spectrum known as "Ewings family of tumor (EFTS).

In bone, Ewing's sarcoma is a rare primary neoplasm of bone comprising approximately 6% of all malignant bone tumors in the Mayo Clinic files.[5, 67] The tumor is slightly more prevalent in males than in females. The majority of patients (more than half of the Mayo Clinic patients) are in the second decade of life. It is unusual to see Ewing's tumor in patients younger than 5 years (only 2% of Mayo Clinic patients). Similarly, just over 3% of the patients were close to age 50 years. Any portion of the skeleton may be involved, but more than half of the tumors involve the long bones, usually the diaphysis.

Typical Ewing's sarcoma is composed of small round uniform cells. The nuclei are round and the nucleoli are inconspicuous. The nuclei have a rather smoky appearance. Mitotic activity usually is not prominent in typical Ewing's

sarcoma. Special stains and electron microscopy usually demonstrate cytoplasmic glycogen in up to 70% of Ewing's Sarcomas.

Askin et al described a small cell tumor of the thoracopulmonay region in childhood.[65, 67] They distinguished these lesions from Ewing's sarcoma because of unusual histologic features and suggested that they are neurally derived. In their series, the prognosis was worse than for Ewing's sarcoma. Contesso et al, compared Askin's tumor with classic Ewing's sarcoma.[65, 67] situated in other locations. They found no significant difference in the immunohistochemical profile of Askin's tumor and classic Ewing's sarcoma. The characteristic chromosomal translocation (11, 22) present in Ewing's sarcoma has been described in Askin's tumor, peripheral neuroectodermal tumor and esthesioneuroblastoma but not in primitive neuroectodermal tumor of the brain. The concept that Ewing's sarcoma may be a form of a neuroectodermal tumor has been supported by several electron microscopic tissue culture and immuno histochemical studies

Rhabdomyosarcoma

Soft tissue sarcoma occur with an annual incidence of 8.4 cases/million children younger than 15 years of age incidence in black children in 50% of that white children. Rhabdomyosarcoma accounts for more than half of the soft tissue sarcomas. The prognosis mostly slightly correlates with extent of disease at diagnosis, primary tumor site and type of treatment.

Rhabdomyosarcoma are malignant neoplasms which show morphologic, immunohistochemical, ultrastructural or molecular genetic evidence of primary skeletal muscle differentiation usually in the absence of any other pattern of differentiation.

It accounts for around 60% of childhood cases,[45,46,47] in its classical form consists of small round or spindle shaped undifferentiated (basophilic) cells, admixed with variable numbers of round strap or tadpole-shaped eosinophilic rhabdomyoblasts in a myxoid stroma. Cytoplasmic cross-striations are present in no more than 20-30% of cases but even in tumors with almost no discernible rhabdomyoblasts, desmin or muscle actin immunostains are positive in more than 95% of cases and this is therefore the most reliable means of making the diagnosis in the routine setting. Additionally, well

characterized antibodies to the protein products of specific myogenic nuclear transcription factors, MyoD1 and myogenin (myf4) are proving to be extremely useful. Occasional cases (more often of embryonal type than alveolar) show a remarkable degree of cytoplasmic differentiation becoming much more obviously rhabdomyoblastic after chemotherapy.

OTHER SOFT TISSUE SARCOMAS

The nonrhabdomyosarcomas soft tissue sarcoma (NRSTS) constitutes a heterogeneous group of tumors that account for 3 % of all childhood malignancies.[16, 17, 70, 71] Because they are relatively rare in children. Much of the information about their natural history and treatment has been derived from the studies of adult patients.

In children the median age of diagnosis is 12 years of age and male predominate (male:female ratio 2.3 : 1). Most common histologic types are synovialsarcoma (42%), fibrosarcoma (13%), Malignant fibrous histiocytoma(12%) and neurogenic tumors(10%). These tumors commonly arise in the trunk or lower extremities. Tumor size, stage, invasiveness and histologic grade correlate with survival.

RETINOBLASTOMA

Retinoblastoma is the most common intraocular tumor in childhood and the most common tumor of the retina but it is a rare malignant tumor with a prevalence of about 1/23000 live births in England 1/16000 in Holland and 1/20000 in Japan.[3,25,79] Retinoblastoma has changed from an almost uniformly fatal disease to one in which 95% of patients are cured. The genetic cause of retinoblastoma was found to be the loss of both alleles of a normal tumor suppressor gene (the Rb gene) on the long arm of chromosome 13. This gene, classified as a recessive oncogene or tumor-suppressor gene has been closed. Researchers then discovered that mutations of the Rb gene play a role in the development of a wide variety of cancers in addition to retinoblastoma.

HEPATOBLASTOMA

Hepatoblastoma accounts for only 0.2-5.8% of malignancies in childhood but for 25-45% of all primary hepatic tumors and for about 50% of those that are malignant. The vast majority 83-92% occur in patients under 5 years of age, and 66% are seen in the first 2 years of life.[8,19,32] Rarely, the tumor may be present at birth. Males are twice as commonly affected as females but the frequency becomes nearly equal in older children. A third of patients with hepatoblastoma have

some form of congenital anomaly syndrome or other childhood tumor. These include hemihypertrophy, cleft palate, talipes, cardiac and renal malformations, diaphragmatic hernia, Beckwith Wiedemann and Down's syndromes, and nephroblastoma. Cytogenetic abnormalities are common especially trisomies of chromosomes 2 and 20. Hepatoblastoma is now recognized as part of the familial adenomatous polyposis syndrome. Anecdotal case reports have attempted to link hepatoblastoma to maternal oral contraceptive use but this has been refuted by a large case-control study which also excluded alcohol smoking and HBV infection but pointed to the possible role of parental occupational exposure to metals, solvents and pigments.

Microscopically

Most hepatoblastomas fall into the mixed epithelial and mesenchymal categories if sufficient tissue is available for examination. Less common are an anaplastic small cell and a macrotrabecular variant. Other rare types are teratoid, mucoid and rhabdoid. The most recent classification recognizes six subtypes of hepatoblastoma epithelial (fetal, embryonal and fetal, macrotrabecular, small cell) and mixed epithelial-mesenchymal (with or without teratoid features). Teratoid hepatoblastomas may contain squamous epithelium, neural and melanocytic cells and endocrine components which are not found in developing or normal adult livers. The majority of hepatoblastomas consist of liver epithelial cells in various

stages of development and a mesenchymal component that is usually spindle-celled or osteoid. The epithelial component may be of several types, the presence of two or more being required for the diagnosis. Embryonal-type cells are smaller, enlongated or fusiform and darkly staining. They have hyperchromatic nuclei and little cytoplasm. They may aggregate into rosette-like clusters or appear as cords or ribbons but seldom as tubules. Fetal-type cells are polygonal and relatively large, almost the size of normal liver cells. They have round to oval nuclei and single nucleoli the cytoplasm may be granular or clear, depending on the amount of glycogen and fat. These cells are generally organized into irregular plates with bile canaliculi and sinusoids. Extramedullary hematopoiesis is commonly seen. These two cell types are invariably present and occur in varying proportions, often intimately mingled. Anaplastic small cells grow in sheets and are indistinguishable from neuroblastoma and other primitive tumors of childhood. Some tumors have a mucoid stroma. The macrotrabecular component resembles adult liver cell carcinoma. Intestinal-type glandular elements may also be seen. The mesenchymal component characteristically consists of osteoid and undifferentiated spindle-celled mesenchyme. Other elements-namely cartilage, striated muscle and neural tissue – are rarely seen. All the components of hepatoblastoma probably derive from a stem cell precursor.

IMMUNOHISTOCHEMICAL STUDIES

They have demonstrated AFP, hCG, CEA, epithelial membrane antigen (EMA), hepatic cytokeratins (8 and 18) and biliary cytokeratins (7 and 19), α_1-antitrypsin, ferritin, S-100 protein chromogranin A and neuron-specific enolase in a varying proportion of cases.[32, 46] AFP is readily demonstrable in fetal and embryonal types of cell, hCG in giant cells and vimentin in anaplastic cells; cells embedded in osteoid express cytokeratins. Ultrastructural studies have shown simple cytoplasmic organelles, few mitochondria, bile canaliculi with microvilli, dilated endoplasmic reticulum and fibrillar or amorphous inclusions.

Surgical resection is the best treatment, preceded by accurate staging and chemo/radiotherapy. Results have improved in recent years 90% of hepatoblastomas can be made respectable and the cumulative probability of survival in patients treated with intent to cure is about 2 in 3. Poor prognostic indicators are age under 1 year large tumor size, involvement of vital structures and predominance of small anaplastic cells or macrotrabeculae. Small cell lesions are

associated with a uniformly fatal outcome and the macrotrabecular type is resistant to chemotherapy. The outcome is best in those cases in which the pre-treatment serum AFP level falls by at least two logs.

ADENOCARCINOMA OF THE COLON AND RECTUM

Colorectal carcinoma rarely presents in the pediatric population. There is a male predominance, as compared with a female predominance in adults. Even in patients with predisposing condition, such as familial adenomatous polyposis and Peutz-Jeghers syndrome, cancer usually does not present until adulthood, although screening should begin during childhood or adolescence. Presenting symptoms include bloody stools or malena, abdominal pain, weight loss, and changes in bowel pattern. Signs are often vague, often resulting in a delay in diagnosis and advanced disease. The histologic subtype differs from that seen in adults, with the majority of pediatric tumors being mucinous. Treatment consists of surgical resection when possible with chemotherapy for unresectable tumors. Irradiation is useful in the treatment of rectal carcinomas.

PAEDIATRIC BRAIN TUMOURS

Epidemiology:

Primary CNS tumours are a hetrogenous group of disease. The central Nervous system tumours comprises 19 % of these astrocytoma is more common followed by medulloblastoma and ependymoma.

Paediatric brain tumours are mainly infratentorial, which is different from what is seen in adults. 59 % of the brain tumours in children are infratentorial while 41 % are supratentorial. This applies to all ages below 15 years. However the ratio is differs in the first year of life.

Higher incidence of CNS tumours in infants and young children up to 7 yrs of age compared with the older children and adolescence.

Pathogenesis:

World Health Organization (WHO) classification of tumours of CNS and meninges include five categories such as juvenile pilocytic astrocytoma, medulloblastoma / primitive neuroectodermal tumour (PNET), diffuse astrocytoma, ependymoma and craniopharyngioma constitute 80% of all paediatric brain tumours.

There are age related differences in primary location of the tumour. Within the I year of life supratentorial tumour predominate and include most commonly choroid plexus complex tumours and teratomas. From 1-10 yrs of age, infratentorial tumours predominate owing to the high incidence of juvenile pilocytric astrocytoma and medulloblastoma.

After 10 yrs of age, once again, supratentorial tumours predominate, with the diffuse astrocytomas. Most common tumours of the optic pathway and hypothalamous, the brain sterm and pineal-midbrain region occur with a greater incidence in children and adolescence than in adults.

There is little understanding of the etiology of the brain tumours. A male predominance is noted in the incidence of medullablastoma and ependymoma familial and hereditary syndromes associated with increased incidence of brain tumours account for approximately 5 % of the cases.

Cranial exposures to ionizing radiation is also associated with an increase incidence of brain tumours. Sporadic reports of brain tumours within females without evidence of a heritable syndrome. The molecular events associated with the tumorigenesis of paediatric brain tumours are not known.

Classification:

Brain tumours are classified according to histology but tumour location and extent of spread are important factors that affect the treatment and prognosis.

Immunohistochemical analysis cytogenetic and molecular genetic findings and measures of mitotic activity are increasingly used in the tumors diagnosis and classification.

The Classification of childhood brain tumours is based not only in histology but also on location. Tumours are classifiably categorized as infratentorial, sellar (or) suprasellar on cortical based.[42,46]

Clinical Manifestations

Clinical presentation of patients with brain tumours depends on the tumour location, tumour type and the age of the child. Signs and symptoms are related to the tumor causing obstruction of cerebrospinal fluid (CSF) drainage paths leading to increased intracranial pressure (ICP) and /(or) causing local brain dysfunction.

Subtle changes in the personality Mentation and /or speech may proceed the classic sign and symptoms of the brain tumours.

In young children the diagnosis of a brain tumour may be delayed because their symptoms are similar to those of more common illness such as gastro intestinal disorders.

Classic triad of Head ache, nausea and/or vomiting and papilloedema is associated with mid line (or) infratentorial tumours.

Supratentorial tumours are more commonly associated with local disorders such as motor weakness sensory changes, speech disorders, seizures and reflex abnormalities.

MEDULLOBLASTOMA

This is a primitive tumour and is a type of the primitive neuro-ectodermal tumour group. Medulloblastomas are usually solid arise from the cerebellar vermis and extend to fill the cavity of the 4th ventricle. It is the most common solid tumour of the childhood. 20 to 30% of posterior fossa tumour in childhood are Medulloblastomas and the age incidence is 5 to 8 yrs of age. It is reported that they are more common is males.[2,8,10,19,20,66]

Desmoblastic variant of Medulloblastoma Grade 4

Medulloblastoma may contain excessive fibrous connective tissue lacking reticulun (or) reticulin free zones compared with reticulin rich nature of regions of high cellularity.

Such tumours are designated desmoplastic medulloblastoma. These neoplasms are more laterally located in the cerebellum then other medulloblastomas often in young adult. The assumption is that the desmoplastic reaction is the result

of a Fibrous connective tissue proliferation by the leptomeningeal cells in the arachnoid space as a result of local invasion by the medulloblastoma cells.

ASTROCYTOMA

Astrocytomas are the most common paediatric brain tumours and comprise a heterogenous group of tumours with numerous subtypes.[42,46] Because some designations or subtypes emphasize grading (low, anaplastic, GBM) accounting for approximately 40% of the cases. These tumours occurs through out the CNS. Malignant astrocytomas are much less common on children and adolescents than in adult accounting for 7-10% of all childhood tumours among these groups.

Anaplastic Astroaytoma WHO grade III is more common than glioblastoma multiforme (WHO Grade IV).

Anaplastic Astrocytoma

The designation anaplastic emphasizes the grade of malignancy. Mitoses are considered a feature of anaplastic astrocytoma. Because the percentage of mitosis in low grade diffuse astrocytoma is so low. Quantitative features that are

shared by high grade gliomas are an increased cellular density, increased nuclear pleomorphism and increased nuclear hyperchromatism.

Histologically

Lack of low of coagulation necrosis and of microvasuclar proliferation in an astrocytic glioma distinguishes anaplastic astrocytoma from glioblastoma. But individual cells with pyknotic nuclei may be interspersed through out the anaplastic astrocytoma. So histopathology of anaplastic astrosytoma demonstrate increased cellularity, cellular and nuclear atypia, presence of mitoses compared with low grade diffuse astrocytoma.

Glioblastoma Multiforme:

It is considered a glioma that may be uniformly undifferentiated, but it contains focal astrocytoma . Mostly low grade glioma may progress to glioblastoma overt time. Many of these progressions are associated with overtime, specific genetic alteration including a loss of genetic material in chromosome 10.

Denovo Glioblastoma appears to exist as well. Although most glioblastomas are supratentorial they also occur in the brainstem and common in cerebellum.

EPENDYMAL TUMOURS

Derived from the ependymal lining of the ventricular system. Ependymoma (who grade II) is the most common of these neoplasm, occurring predominantly in childhood tumours.

Approximately 70% ependymomas in childhood occur in posterior fossa. The mean age of the patient is 6 yr, with approximately 30% of cases occurring in children younger than 3 yrs of age.

Variants

1. Ependymoma - low grade
2. Clear cell ependymoma
3. Tanycytic ependymoma
4. Sub ependymoma
5. Myxopapillary ependymoma
6. Anaplastic ependymoma (or) Malignant ependymoma

Anaplastic expendymoma – Grade 3

These are uncommon-Although these tumours are often found in the cerebrum (or) cerebellum of children and young adult.

Key Diagnostic criteria for anaplasia include

1. Increased cellularity
2. Nuclear anaplasia
3. Brisk Mitotic activity

Vascular proliferation, whether intramural (or) glomeruloid and necrosis including pseudo pallisading necrosis may be seen.

PRIMITIVE NEUROECTODERMAL TUMOURS (PNET)

PNET are the most common group of malignant CNS tumours of childhood, accounting for 20-25% of paediatric CNS tumours.

PNET has structure and staining properties of the cerebellar medulloblastomas, composed of undifferentiated (or) poorly differentiated neuroepithelial cells, identified PNET with supratentorial compartment. PNET has occurred in patients with renal tumours and renal tube defects.

PNET also occur in peripheral location. Most of the tumour associated with t(11,22) q(24, q12) chromosomal translocation and they stain with MIC – 2. The sites include those that arise from the neural crest derivatives, gonads, chest wall bone rare peripheral PNET above in the craniospinal vault.

Markers of Neuronal differentiation such as synaptophysin and protein gene product aid in the identification of PNET.

OBSERVATION AND RESULTS

This study covered a total of 132 paediatric cancers in which, 63 were hematological malignancies, 49 were soft tissue cancers and 21 were CNS Neoplasms.

In 63 Hematological cancers observed, 42 were males (66.67%) with age ranging from 2 - 15 yrs (mean age 8.2 yrs) and 21 were females (33.33%) with age ranging from 2 - 14 yrs (mean age 8.6 yrs)

Table No .1: shows total number of hematological malignancies observed during the period Jan - 2003 to December - 2005. The average incidence is 44.49%

Table No - 1

S.NO	PERIOD	TOTAL HEMATOLOGICAL CANCERS	PAEDIATRIC CANCERS	PERCENTAGE
1	Jan 2003 – June 2003	96	15	15.63%
2	July 2003 – Dec 2003	120	13	10.83%
3	Jan 2004 – June 2004	124	20	16.13%
4	July 2004 – Dec 2004	152	21	13.82%
5	Jan 2005 – June 2005	167	33	19.76%

6	July 2005 – Dec 2005	234	30	12.82%

When the children are divided in to six groups (i.e ≤ 2yrs, 2 - 4 yrs, 5 -6 yrs, 7 - 8 yrs, 9 - 10 yrs and >10 yrs) there was increased incidence of haemotological malignancies in the age group of more than 10 yrs, followed by 3 -4 yrs and 5 -6 yrs. Incidence of hematological/lymphoreticular malignancy is low at less than 2 yrs, as given in the following Table no– 2.

Table no– 2

S.NO	AGE	MALE	FEMALE	TOTAL NO.OF CASES	PERCENTAGE
1	≤ 2	4	-	4	6.6%
2	3 – 4	9	2	11	17.46%
3	5 – 6	7	4	11	17.46%

4	7 – 8	2	5	7	11.11%
5	9 – 10	5	4	9	14.29%
6	> 10	15	6	21	33.33%

Table - 2 also shows, incidence is high in male children (42 cases, - %) when compared with females (21 cases, 33.33 %).

Most of the children with hematological/ lymphoreticular malignancies were from surrounding villages, with low socio economic status, presented with following clinical symptoms as given in the Table No 3

Table No.3

S.NO	CLINICAL FEATURES	NO.OF CASES	PERCENTAGE
1	Fever	48	76.19 %
2	Anemia	52	82.54 %
3	Upper Respiratory Tract Infection	32	50.79 %

4	Jointpain(lower extremity)	15	23.79 %
5	Bony tenderness	2	3.17 %
6	Gum Hypertrophy (Fig.1)	41	1.59 %
7	Chloromas	-	-
8	Generalized lymphadenopathy	58	92.06 %
9	Spleenomegaly	55	87.30 %
10	Hepatomegaly	38	60.32 %
11	Bleeding manifestation	25	39.68 %

Most of the children presented with a triad of fever, anaemia and spleenomegaly as common presenting symptoms, and generalized lymphadenopathy is the commonest presenting symptom in children with lymphoreticular malignancies exhibiting firm, discrete, nontender enlargement of the lymphnodes.

When paediatric hematological/lymphoreticular malignancies were divided, hematological cancers were observed in 45 cases (71.43%) and lymphoid neoplasms in 18 cases (28.57%)

In 45 hematological cancers, 32 cases were acute lymphoblastic leukemia (Fig.2&Fig.3) [(ALL),(71.11%)] and [11cases,(24.44%)] were diagnosed as lymphoproliferative/lymphoma spill (Fig.6) Lesions as given in the following Table No.4. Only 2 cases of Acute Myeloid leukemia (AML, 4.44%)(Fig.4&Fig.5) was observed in this study.

Table No.4

SL.NO	HEMATOLOGICAL MALIGNANCY	NO.OF CASES	PERCENTAGE
1	ALL	32	71.11 %
2	AML	2	4.44 %
3	JCMML	-	-
4	CML	-	-
5	LYMPHOPROLIFERATIVE/LYMPHOMA	11	24.44 %

	SPILL		

Similarly, the Lymphoreticular malignancies were also divided, as shown in Table No. 5

Table No-5

SL.NO	LYMPHORETICULAR MALIGNANCY	NO.OF CASES	PERCENTAGE
1	HL	3	16.67 %
2	NHL		
	LARGECELL LYMPHOMA	10	55.56 %
	BURKITTS LYMPHOMA	2	11.11 %
	LYMPHOBLASTIC LYMPHOMA	1	5.56 %
	OTHERS	2	11.11 %

In 18 cases, 15 cases were NHL, in which large cell anaplastic Lymphoblastic type was commonly observed. Only 3 cases of Hodgkin disease (Fig.7) was observed in this study. Cases were diagnosed initially as lymphoma, further confirmation with CD Marker- CD 30 for RS cell was also done.

SOFT TISSUE NEOPLASMS (INCLUDING - ABDOMINAL AND BONE MALIGNANCIES)

In this prospective study, 48 soft tissue neoplasms were observed, in which 25 were male children (52. 08%) with age ranging from 1 month to 15 yrs (Mean age- 7.04 yrs) 23 were female (47. 92%) with age ranging from 1 month to 15 yrs (Mean age - 7.08 yrs).

The Following Table No. 6 shows the total no. of soft tissue malignancies observed during the Period from JAN - 2003 To DEC - 2005. The average Incidence is 36. 36%.

Table No-6

SL.NO	PERIOD	TOTAL NO.OF SOFT TISSUE MALIGNANCY	PAEDIATRIC CASES	PERCENTAGE
1	Jan 2003 to Dec 2003	132	12	9.1 %
2	Jan 2004 to Dec 2004	198	14	7.1 %

3	Jan 2005 to Dec 2005	282	22	7.8%

Similarly as in hematological / lymphoreticular malignancies, when the children are divided into 6 groups as given in the following Table - 6, there was increased Incidence of paediatric soft tissue malignancies in the age group of 3-4 yrs, followed by more than 10 yrs and less than 2 yrs.

The Table No-7 also shows that the incidence of soft tissue malignancies is common in males [25 cases (52.08%)] when compared with females [23 cases (47.92 %)].

Table No-7

SL.NO	AGE	MALE	FEMALE	TOTAL NO.OF CASES	PERCENTAGE
1	≤ 2	4	4	8	16.67 %
2	3 to 4	11	5	16	33.33 %
3	5 – 6	-	4	4	8.33 %
4	7 – 8	-	2	2	4.17 %
5	9 – 10	4	-	4	8.33 %
6	> 10	6	8	14	29.17 %

When the soft tissue neoplasms are categorised as given in the following

Table No -7, Neuroblastoma (Fig.8&Fig.9) with Incidence of 16. 67% (8 cases) predominates over other malignancies, followed by ovarian tumors (Fig.10&Fig.11) and extraskeletal Ewing sarcoma (Fig.12) (5 cases, 10.42%). In this study 4 cases of Hepatoblastoma, 4 cases of colorectal Adenocarcinoma and 4 cases of Retinoblostoma were also observed. Osteosarcoma, (Fig.13&Fig.14) Rhabdomyosarcoma, (Fig.15&Fig.16) Nasopharyngeal and Laryngeal neoplasms were observed only in 3 cases respectively.

Like wise, WILMS tumor, (Fig.17) once thought to be a common paediatric neoplasm was observed in only one case.

Table No.8 also show, one interesting case of Melanoma - which was observed at 3 yrs Male child in the intra - oral region, Testicular tumor (Fig.18&Fig.19) at 3 yrs and Adrenocortical neoplasm at the age of 4 yrs.

Table No – 8

SL.NO	SOFT TISSUE NEOPLASM	NO.OF CASE	PERCENTAGE	AGE
1	MALIGNANT MELANOMA	1	2.08 %	3 yrs
2	COLORECTAL MALIGNANT NEOPLASM	4	8.33 %	10 – 13 yrs
3	NASOPHARYNGEAL &LARYNGEAL NEOPLASM	3	6.25 %	13 – 15 yrs
4	OVARIAN TUMOUR	5	10.42 %	2 – 15 yrs
5	TESTICULAR TUMOUR	1	2.08 %	3 yrs
6	ADRENALCORTICAL NEOPLASM	1	2.08 %	4 yrs
7	RETINOBLASTOMA	4	8.33 %	3 – 5 yrs
8	NEUROBLASTOMA	8	16.67 %	1 – 9 yrs

9	HEPATOBLASTOMA	4	8.33 %	1 month to 4 yrs
10	EXTRASKELETAL EWING SARCOMA	5	10.42 %	3 – 10 yrs
11	RHABDOMYO SARCOMA	3	6.25 %	1 – 15 yrs
12	LOW GRADE MPNST	2	4.17 %	12 – 15 yrs
13	BONE TUMOUR – OSTEO SARCOMA	3	6.25 %	15 yrs
14	WILMS TUMOUR	1	2.08 %	4 yrs
15	SALIVERY GLAND TUMOUR	1	2.08 %	15 yrs
16	OTHERS	2	4.17 %	-

CNS NEOPLASMS

In 21 CNS tumors observed in this study, 12 cancers were seen in Male children (57.14%) with age ranging from 1-15 yrs (Mean age 8.33 yrs) and 9 were females (42.86%) with age ranging from 1-15 yrs (Mean age 8.77 yrs).

The average incidence of Paediatric CNS - neoplasm is 15.90% as given in the following Table No-9, during the period from JAN - 2003 to DEC - 2005.

Table No-9

SL. NO	PERIOD	TOTAL NO.OF CNS NEOPLASMS	PAEDIATRIC CANCERS	PERCENTAGE
1	JAN 2003 – DEC 2003	18	5	27.78 %
2	JAN 2004 – DEC 2004	21	5	23.80 %
3	JAN 2005 – DEC 2005	32	11	34.37 %

When the children with CNS Neoplasms were also divided into 6 groups, as done in the Hematological and soft tissue neoplasms, there was increased incidence of cancers during 9-10 yrs and more than 10 yrs (7 cases 33.33%) followed by 2-3 yrs and less than 2 yrs (3 cases, 14.29%)

Incidence is common in Males (12 cases 57.14%) as in soft tissue and hematological neoplasms when compared with females (9 cases 42.86 %).

Table No-10

SL.NO	AGE	MALE	FEMALE	TOTAL NO.OF CASES	PERCENTAGE
1	≤ 2	1	2	3	14.29 %
2	3 – 4	3	-	3	14.29 %
3	5 – 6	1	-	1	4.76 %
4	7 – 8	-	-	-	-
5	9 – 10	3	4	7	33.33 %
6	≥ 10	4	3	7	33.33 %

The following Table No. 11 shows Paediatric CNS - Neoplasm distribution.

Table – 11

SL.NO	CNS TUMOURS	NO.OF CASES	PERCENTAGE	AGE
1	MEDULLOBLASTOMA/PNET	8	38.09 %	4 – 11 yrs
2	EPENDYMOMA	3	14.29 %	2 – 5 yrs
3	ASTROCYTOMA	7	33.33 %	2 – 14

				yrs
4	CHORDOMA	1	4.76 %	3 yrs
5	PINEOBLASTOMA/PINEOCYTOMA	2	9.52 %	9 -15 yrs

Medulloblastoma / PNET (Fig.20&Fig.21) predominates with [8 cases (38. 09%)], in the age group of 4-11 yrs followed by Astrocytomas, (Fig.22, Fig.23 &Fig.24) [7 cases (33. 33%)] and ependymomas [3 cases (14.29%)].

2 cases of Pineoblastoma / Pineocytoma (Fig.25&Fig.26) and one case of chordoma at the age of 9-15 yrs and 3 yrs were also observed.

SPECIAL STUDIES:

In 2 cases of Acute Myeloid leukemia & 11 cases of lymphoproliferative lesions, histochemistry and Sudan black B (Fig.27 to Fig.31) was done and the results were given in the following.

Table - 12

SL.NO	**PERIPHERAL.SMEAR NUMBER**	**SUDAN BLACK B**	**PAS**	**RESULTS**
1	PS 1501/05	POSITIVE	NEGATIVE	AML

2	PS 1404/05	NEGATIVE	POSITIVE	ALL
3	PS 1395/05	NEGATIVE	POSITIVE	ALL
4.	PS 2096/05	NEGATIVE	POSITIVE	ALL
5	PS 1494/05	POSITIVE	NEGATIVE	AML

IMMUNO HISTOCHEMISTRY:

Immunohistochemical stains GFAP and CD Markers – for Astrocytomas and Hodgkin Lymphomas was also undertaken and the results were given in the following Table No-13 (Fig.32 to Fig.42).

Table No - 13.

SL.NO	IHC	MARKER	RESULT	IMPRESSION
1	HODGKIN LYMPHOMA	CD-30	NEGATIVE	NON-HODGKIN LYMPHOMA
2.	NON-HODGKIN LYMPHOMA			
	1.LARGE CELL LYMPHOMA	PAN-B MARKER CD20	POSITIVE	DIFFUSE LARGE B CELL LYMPHOMA
	2. LARGE CELL LYMPHOMA	PAN-T MARKER	POSITIVE	DIFFUSE LARGE T CELL LYMPHOMA

	3. LARGE CELL LYMPHOMA	CD3 PAN-T MARKER	POSITIVE	DIFFUSE LARGE T CELL LYMPHOMA
	4. LARGE CELL LYMPHOMA	CD3 PAN-B MARKER CD20	POSITIVE	DIFFUSE LARGE B CELL LYMPHOMA
3	CENTRAL NERVOUR SYSTEM NEOPLASM ASTROCYTOMA-GRADE III	 GFAP VIMENTIN EMA SMA DESMIN	 POSITIVE(+++) POSITIVE(+++) POSITIVE(+++) SCATTERED CELLS POSITIVE(+++) IN VESSELS AND VERY FEW TUMOUR CELLS NEGATIVE	 ATYPICAL TERATOID RHABDOID TUMOUR GRADE II
	ASTROCYTOMA-GRADE II -III	GFAP	POSITIVE(++) IN TUMOUR CELLS POSITIVE(++)	 GRADE II
	GLIOBLASTOMA MULITIFORME GRADE -IV	GFAP		

DISCUSSION

Although cancer among children is relatively uncommon, it remains a significant cause of mortality in this population and is second only to accidents as a cause of death in the age group of 5 - 14 years.

The Incidence of Paediatric cancer is increasing, in comparison with studies conducted by various research workers and literature. In our study, the incidence of Paediatric hematological malignancies is 44.49%, which is in correlation with studies conducted by Elizabeth J. Rosen MD. Resident Physician.[37,43,53,75] The average incidence of hematological Paediatric Malignancy is 1 in 630, and the relative rate of hematological cancer below 5 yrs is 40%.

In Western Population, the increased incidence of hematological malignancies is observed below the age of 5 years.[7,13,29]

In our study, the Peak incidence of hematological Malignancies is seen after 10 yrs, followed by 3-4 yrs, which is in contrast with the studies conducted by western research workers.

Probably related to low socio economic status, Poor education and lack of knowledge regarding the initial alarming symptoms of hematological Malignancies.

The most common hematological neoplasm in children is leukemia and it also stands as most common malignancy.

In our study, acute lymphoblastic leukemia is the commonest hematological neoplasm followed by lymphoma / lymphoproliferative disorders, which is well in correlation with literature.

In doubtful cases, use of histochemistry with Sudan – black B and PAS allows an initial, standard cost effective method, helpful in arriving at diagnosis.

One case of Hodgkin lymphoma, with total effacement of architecture and Polymorphous population of lymphocytes with few RS like cells, when subjected to IHC with CD Marker CD 30, a classical RS cell marker revealed total negative staining for RS cells, and positive for - B cell markers of NHL.

Lymphomas comprise approximately 24.44% of all paediatric malignancies, making them the third most common cancer.[50,51,56,57] Approximately 60% of paediatric lymphomas are non-Hodgkin's lymphoma (NHL). Boys are affected more often than girls with a 3:1 ratio and the peak incidence of NHL is between the ages of 7 and 11 years.

Histologic varieties of NHL are divided into low-, intermediate-, or high-grade categories bases upon their clinical behavior and over 90% of children have high-grade disease at presentation.[39,40,41] High-grade lesions include,

Large cell lymphomas constitute about 27% of paediatric NHL.

Lymphoblastic lymphoma occurs in 29% of paediatric cases.

The small cell noncleaved lymphomas are found in 34% of paediatric NHL and Burkitt's lymphoma (BL) is the most common of this subtype.

The evaluation of the child suspected to have a lymphoma begins, of course, with a complete history and physical. Definitive diagnosis requires tissue for pathologic evaluation, which may be obtained by a tonsillectomy or open biopsy of an involved lymph node. Because most paediatric patients with NHL present with disseminated disease, a complete staging work-up must be undertaken. This would include laboratory studies (to include LDH, LFT's and HIV), LP with CSF analysis, bilateral iliac crest bone marrow biopsy, CT of the chest, abdomen and pelvis, and bone scan. The reasoning for such an extensive work up is that accurate clinical staging is of utmost importance in assigning patients to an appropriate treatment protocol.

Hodgkin' disease (HD) is less common in the paediatric population than NHL. This occurring in children under the age of 10 years. Boys are affected more frequently than girls (3:1) although this ratio narrows after puberty (1.4: 1).

There are four histologic subtypes of HD- nodular sclerosing, mixed cellularity, lymphocyte predominance and lymphocyte depletion. Overall, nodular sclerosing and mixed cellularity are the most common subtypes of HD, but in the paediatric population the lymphocyte predominance and nodular sclerosing are seen most frequently.[4,11,14,22,61]

HD will present with asymmetric lymph node enlargement in about 90% of cases. The lymphadenopathy is described as firm, rubbery and non-tender and in the neck most often involves the supraclavicular fossa. The most common extralymphatic site of HD is the spleen, followed by the liver. Nearly one-third of patients will have associated constitutional symptoms at presentation including fever, night sweats, anorexia, weakness or loss of 10% or more of body weight.

Neuroblastoma being the most common abdominal-soft tissue neoplasm, observed in our study, as studies conducted by various research workers.

Neuroblastoma is the most common extra cranial solid tumor of childhood and accounts for 8-10% of childhood cancers. The annual incidence of these tumors is around 9 cases / 1,000,000 in children under 15 years of age. It is the most

common malignancy in children under 1 year of age and 90-95% of patients ill present before the age of 10 years. Neuroblastoma is slightly more common in boys than girls.

The cell of origin for neuroblastoma is the neural crest cell that eventually gives rise to the sympathetic nervous system. These tumors may develop from the paraspinal sympathetic ganglia, the adrenal chromaffin cells within the adrenal medulla or other various intra-abdominal paraganglia. Histologically, neuroblastoma is one of several "small blue round cell" tumors that occur in children and must be differentiated from other similar tumors such as Ewing's sarcoma, NHL, Primitive neuroectodermal tumors and undifferentiated soft-tissue sarcomas. This differentiation is aided by the use of immunohistochemical staining in which neuroblastoma will be positive for neurofilament proteins, synaptophysin and neuron-specific enclose.

The majority of primary neuroblastomas present as an intra-abdominal mass involving the adrenal gland or retroperitoneal paraganglia.[12,21,35,68]

The criteria necessary to make a diagnosis of neuroblastoma as established by the International Neuroblastoma Staging System includes either a definitive histologic diagnosis on light microscopy +/- immunohistochemistry, electron microscopy or the presence of elevated urine catecholamines, or a bone marrow biopsy demonstrating unequivocal tumor cells and the presence of elevated urine catecholamines. The metastatic work up for neuroblastoma is to that for other paediatric malignancies and includes chest x-ray, bilateral iliac crest bone marrow biopsy, bone scan, CT or MRI of the neck and abdomen.

A variety of staging systems for neuroblastoma exist that take into account tumor burden, surgical resectability and metatatic disease, The TNM criteria define Stage I disease as primary tumor <5cm with no regional or distant disease. Stage II includes tumors >5cm but <10cm with no regional or distant disease. Stage III includes tumors up to 10cm plus regional disease or tumors over 10cm +/- regional disease but without distant disease. Stage IV is defined as cases with a single primary tumor +/- regional disease and presence of distant disease. And finally, Stage V includes multicentric primary tumor +/- regional or distant disease.

Ewing sarcoma & ovarian neoplasms constitute second most common -soft tissue neoplasms.

Ewing sarcoma (ES) and primitive neuroectodermal tumour (PNET) are rare sarcomas of bone and soft tissue, described in 1921 by Dr. James Ewing and in 1918 by Dr. Arthur Purdy Stout, respectively.[5,67] Although ES and PNET were originally regarded as totally separate entries, this distinction began to blur with the description by Angervali and Enzinger in 1975 of an "extra skeletal neoplasm resembling Ewing's sarcoma" and the 1984 report of jaffe et al of "the neuroectoderminal tumour of bone".[5,67,46,47] It has subsequently been established that both ES and PNET share in over 90% of cases a balanced translocation (11; 22) (q24; q12), and they are now almost universally regarded as ends of a common histologic spectrum, known as the "Ewing family of tumours" (EFTs).

Both ES and PNET are "small round blue cell tumours" which lack obvious differentiation by light microscopy and which are composed of nearly indifferent, primitive-appearing cells at the ultra structural level. Thus, the diagnosis of EFT has traditionally been one of exclusion, although this situation has improved considerably over the last 10 years with the introduction of much better immunohisochemical markers of EFT, such as CD99 and FLII protein.

The histologic features of typical ES include a sheet-like to vaguely lobular growth pattern, well-developed capillary vasculature, and uniform cell population of round cells approximately two times the size of an endothelial cell, with a small

amount of lightly eosinophilic cytoplasm, regular nuclear contours, finely dispersed chromatin, and in apparent or small nucleoli. Geographic necrosis and individual degenerating cells (so-called “dark cells”) were also frequently present.
In this study, Hepatoblastoma, Retinoblastoma and colorectal - adenocarcinomas each constitute – 8.33% of cases.

Hepatoblastoma usually forms a single mass, is often very large when first detected and may weigh over 1000g. The tumor has a variegated appearance according to the proportion of its histologic components (i.e. brown to green, fibrous or calcified) and often shows areas of necrosis, cystic change and hemorrhage. Vascularity is usually prominent, a thin capsule may be present and the rest of the liver is normal.

The most recent classification recognizes six subtypes of hepatoblastoma: epithelial (fetal, embryonal and fetal, macrotrabecular, small cell) and mixed epithelial-mesenchymal (with or without teratoid features). Teratoid hepatoblastomas may contain squamous epithelium, neural and melanocytic cells and endocrine components which are not found in developing or normal adult livers. The majority of hepatoblastomas consist of liver epithelial cells in various stages of development and a mesenchymal component that is usually spindle celled or osteoid. The epithelial component may be of several types, the presence of two or more being required for the diagnosis. Embryonal type cells are smaller, elongated

or fusiform, and darkly staining. They have hyperchromatic nuclei and little cytoplasm. They may aggregate into rosette-like clusters or appear as cords or ribbons but seldom as tubules. Fetal-type cells are polygonal and relatively large, almost the size of normal liver cells. They have round to oval nuclei and single nucleoli, the cytoplasm may be granular or clear, depending on the amount of glycogen and fat. These cells are generally organized into irregular plates with bile canaliculi and sinusoids. Extramedullary hemopoiesis is commonly seen.

Hepatic tumors account for approximately 1% of child malignancies, with hepatoblastoma (HB) and hepatocellular carcinoma (HCC) constituting the majority.[32,54] Because of their rarity, generalizations regarding the epidemiology are difficult. Worldwide, HB occurs almost twice as often as HCC in children.

Male predominance has been pointed out in the report of Chen et al. and our study disclosed a similar result.[32,54]

Routine newborn screening by paediatrician with physical exam is the only way to find the abdominal mass but it is always too late for high stages. In the paediatric literature, several cases have been diagnosed post-natally, within

6 weeks after delivery, suggesting that HB may arise during fetal life. But only a case report could be found about antenatal diagnosis of congenital HB in uterus as initial presentation of enlarged fetal abdominal circumference at 36 weeks of gestation. Now, the prenatal sonogram is prevalent and may help to an early diagnosis of liver tumors.

Retinoblastoma is the most common intraocular tumor in childhood[3,25,8] and the most common tumor of the retina, but it is a rare malignant tumor with a prevalence of about 1 / 23,000 live births.

Common presenting features included a fungating mass prolapsed through a corneal perforation, proptosis caused by posterior orbital involvement, bulphthalmos from secondary glaucoma, neurologic manifestations related to intracranial involvement, and enlarged preauricular or submandibular lymph nodes from metastasis.

The abnormal appearance of one or both pupils. The pupil usually appears white (leukocoria). Strabismus can be present in 35% of the patients. Computed tomography aids in determining the size and location of the retinoblastoma, and

can be used to detect macroscopic extra ocular extension; microscopic spread within the optic nerve beyond the lamina cribrosa is not readily detectable with CT.

In the pathologic examination, the gross features of intraocular retinoblastoma are dependent on the growth pattern of the tumor. Five growth patterns are recognized: endophytic, exophytic, mixed endophytic-exophytic, diffuse infiltrating and complete spontaneous regression. Histopathologically, retinoblastomas are essentially malignant neuroblastic tumors that may arise in any of the nucleated retinal layers. The predominant cell is small with large basophilic nuclei of variable size and shape, and scanty cytoplasm. Mitotic figures are typically numerous. Especially in large tumors, sleeves of viable cells are present along dilated blood vessels. If the tumor cells are displaced more than 90-110.m from the vessel, they often undergo ischemic necrosis. The formation of Flexner-Winter Steiner rosettes is highly characteristic of retinoblastomas and they are found within areas of undifferentiated malignant cells exhibiting mitotic activity.

The typical Flexner-Winter Steiner rosettes are lined by tall cuboidal cells with basally located nuclei that circumscribe an apical lumen. Homer wright rosettes are less common in retinoblastoma than Flexner-Winter Steiner

rosettes. Because they are found in a variety of neuroblastic tumors, they are less specific for retinoblastoma. In these rosettes, cells are not arranged about a lumen but instead send out cytoplasmic processes that form a tangle within the center of the rosette.

Rhabdomyosarcoma are malignant neoplasms which show morphologic, immunohistochemical, ultra structural or molecular genetic evidence of primary skeletal muscle differentiation, usually in the absence of any other pattern of differentiation.

Rhabdomysarcoma falls into three main groups - embryonal, alveolar and pleomorphic - and, in general terms, the forst two groups occur mainly in children, while pure pleomorphic lesions occur almost exclusively in adult. Rhabdomyosarcoma in children occurs principally before the age of 10 years, with a peak before the age of 4 years, and shows a moderate male predominance. The most common sites are the head and neck region[45,46,47] (including orbit and meninges), followed by the genitourinary tract, followed by the limbs, and then the trunk.

As a general rule, embryonal lesions affect somewhat younger patients than the alveolar type, the latter being more frequent in adolescents; limb tumors are much more commonly alveolar than embryonal. Two other infrequent, but distinctive, clinical traits in alveolar rhabdomyosarcoma are the tendency to develop breast metastases in female patients and to present very rarely in a manner closely resembling leukemia due to extensive bone marrow involvement, without a clearly evident primary lesion. This latter pattern of disease may well represent malignant transformation of bone marrow mesenchymal stem cells ("rhabdomyoblastemia").

Embryonal rhabdomyosarcoma, which accounts for around 60% of childhood cases, in its classical form consists of small, round or spindle-shaped, undifferentiated (basophilic) cells, admixed with variable numbers of round, strap-or tadpole-shaped eosinophilic rhabdomyoblasts, in a myxoid stroma. Cytoplasmic cross-striations are present in no more than 20-30% of cases but, even in tumors with almost no discernible rhabdomyoblasts, desmin or muscle actin immunostains are positive in more than 95% of cases and this is therefore the most reliable means of making the diagnosis in the routine setting.

There have been considerable recent advance in molecular genetic means of confirming and refining the diagnosis of rhabdomyosarcoma and, particularly in paediatric oncology centers, this is becoming the standard of care.

Overall, the diagnosis of small round cell tumors in young patients has been transformed during the past twenty years. Immunohistochemistry and, more recently, molecular genetics have largely superceded hematoxylin and eosin morphology in this context since in general; they are more consistently discriminatory as is essential in the setting of significantly different treatment protocols.

Soft tissue sarcoma occur with an annual incidence of 8.4 cases/million white children younger than 15yrs of age incidence in black children is 50% of that white children.[54,59,65]

Malignancies of the kidney (renal cancers) represented 6.3% of cancer diagnosis among children younger than 15 years of age (incidence 7.9 per million) and 4.4% of cancer diagnosis for children and adolescents younger than 20 years of age (incidence of 6.2 per million).

Wilms' tumor was by far the most common form of renal cancer in children. Wilms' tumor occurred most commonly among children younger than 5 years of age, with very low incidence for 10-14 and 15-19 year olds. The highest incidence for Wilms' tumor was in the first 2 years of life, followed by steadily decreasing rates with increasing age.[26,58,69]

In our study, Osteosarcoma constitutes about 6.25% of cases. Osteosarcoma can be defined simply as a malignant tumor in which osteoid or bony matrix is produced by the tumor cells. Osteosarcomas can be subdivided broadly into two groups; the majority occurs within the bone but a small minority occurs on the surface. These two broad categories can be further subdivided depending on the clinical, roentgenographic, and histologic features.

Conventional osteosarcoma is a high-grade malignant tumor that occurs predominantly in the metaphysis of the long bones of children. Most osteosarcomas occur in adolescents and young adults. It is unusual to see an osteosarcoma in a patient younger than 5 years or older than 50 years unless there is a predisposing condition. There is a definite male predominence. The majority of conventional osteosarcomas have their epicenter in the metaphysis of a long bone. Approximately 10% occur in the shaft of the bone.

A small percentage of osteosarcoma occurs in the flat bones, such as pelvic bones and scapula. These may be related to previous irradiation or a pre-existing condition such as Paget's disease. Involvement of the bones of the hands and feet is even more uncommon.

The clinical symptoms are quite non-specific. Patients complain of pain or swelling or both of variable duration, ranging from days to months. Pathologic fracture may be the initial symptom.

The roentgenographic features of osteosarcoma are quite variable. The tumor usually gives rise to a large area of destruction of bone with extension into soft tissue. The amount of mineral present in the lesion varies and correlates somewhat with the type of osteosarcoma. As the tumor destroys the cortex, it lifts up the periosteum. This results in reactive new bone formation at the junction between the elevated periosteum and the underlying cortex. This is referred to as Codman's triangle. Rarely, an osteosarcoma is small and extremely well circumscribed, suggesting a benign lesion.

The gross appearance of osteosarcoma also is quite variable. Most have the fish-flesh appearance associated with sarcomas. Some are heavily mineralized and hence extremely hard. Some have large areas of obvious blue cartilage.

Microscopically, most osteosarcomas are highly malignant tumors; their spindle cells have nuclei with marked pleomorphism. Conventional osteosarcoma can be further subdivided into osteoblastic, chondroblastic, and fibroblastic varieties, depending on the predominant matrix.

Approximately half of all osteosarcomas can be called "osteoblastic". Characteristically, the matrix is produced as a fine network between individual tumor cells. The matrix may be in the form of unmineralized osteoid or may show mineralized trabeculae.

In our study malignant mixed germ cell tumours and gonadoblastoma constitute about 10.42 % of cases.

Malignant mixed germ cell tumours occur in children and young woman. Mixed germ cell tumours tend to be large, average size 15 cm in diameter. Their gross appearance depends on which elements are present. Elements of yolk sac tumour vary in colour, contain cystic and firm cartilaginous or bony foci.[6,24] Areas of choriocarcinoma are hemorrhagic and necrotic. Mixed germ cell tumours are ordinarily unilateral but, when dysgerminoma is present they can be bilateral.

There are two malignant elements in 80 % of mixed germ cell tumours and four or more in the reminder. The elements can be mixed together or they can grow in separate but contiguous foci. Dysgerminoma is the most frequent

element, followed by yolk sac tumour and immature teratoma. Embryonal carcinoma, choriocarcinoma and polyembryoma are rarely found.

Gonadoblastoma is a rare tumour that arises almost exclusively in abnormal gonads and contains an admixture of germ cells and sex cord cells.

The average age at diagnosis is 18 years, and 80% of gonadoblastomas are detected before the age of 20 years. Most gonadoblastomas are found when a patient is evaluated for primary or secondary amenorrhea or for an abnormally formed genital tract.

Gonadoblastoma arises in abnormal gonads, including streak gonads, indeterminate gonads, and dysgenetic testes. It is typically small, ranging from microscopic to 2-3 cm in diameter. More than 40% of cases are bilateral. The cut surface is tan or white and often contains calcified areas.

Microscopically, nests of germ cells and sex cord cells are surrounded by fibrous stroma. The germ cells resemble dysgerminoma cells. They are large and polygonal with abundant clear cytoplasm, vesicular nuclei and prominent nucleoli. Sex cord cells surround the germ cells. These resemble granulose cells, or more commonly, Sertoli cells. They surround one or more germ cells or small spaces containing eosinophilic hyaline material. The stroma surrounding a gonadoblastoma frequently is luteinized in postpubertal patients and it may contain microcalcifications. Immunostains for inhibin, vimentin, and cytokeratin are positive in the sex cord elements. The hyaline material reacts with antilaminin antibodies.

In our study, Paediatric CNS Neoplasm constitutes about 15.90% with Peak age at presentation during 9-10years and more than 10yrs. These figures are in contrast with hematological and soft tissue neoplasm in which most of the cases are seen in < 5yrs of age. The Incidence is also slightly higher in Males, with M:F of 1.3 : 1. In our study, medulloblastoma is the commonest childhood neoplasm which is in correlation with the data provided by the National Cancer Institute as well as the study conducted by the various research workers and authors.[2,10,20,66]

Two major risk group categories defined by clinical criteria are now being used:

AVERAGE RISK: Children older than 3 years with posterior fossa tumors; tumor is totally or near-totally (<1.5 cc's of residual disease) resected; no dissemination.

POOR RISK: Children 3 years old or younger or those with metastatic disease and/or subtotal resection (>1.5 cc's of residual disease) and/or nonposterior fossa location.

Astrocytomas constitute about 33.33% of cases in which 3 cases goes difficulty on diagnosis at light macroscopy level. With Immunohistochemical marker, GFAP 2 cases of grade-II anaplastic astrocytoma yielded positive result where as one case of anaplastic astrocytoma showed positivity for EMA and vimentin in association to GFAP and final impression of Atypical teratoid / rhabdiod tumor was made.

Pineoblastoma / pineocytomas constitute about 9.52 % of cases.Second most common tumour in the pineal region. Pineoparenchymal tumours arises from pinocytes. Pineoblastoma occurring predominately is childhood. Pineoblastoma is the most malignant variant and is considered a subgroup of PNETS of childhood.

Consist of sheets of crowded highly anaplastic neoplastic cells that appear undifferentiated they manifest local nuclear molding with a high mitotic rate resembling that a melulloblastoma (or) PNET and retinoblastoma.[42,46]

Flexer wintersteiner rosettes can be identified. In some tumours intermixed area containing features from pineocytoma, pineal parenchymal tumours of intermediate malignancy and pineoblastoma can be identifited pineoblastoma cannots increased malignancy and is high grade.

It shows mixed photoreceptor and neuro endocrine features immunoperoxidase for synaptophysin identifies their neuronal phenotype. Other markers such as chromogranin, tau, neurofilament, neuron specific enolase are sometime used. But less reliable than synaptophysin. Retinal S antigen reactivity reflects their photosensory differentiation.

CONCLUSION

In general, because of early detection and progress with therapeutic methods, mortality due to malignant diseases as a whole during childhood has been decreasing. Although mortality from all cancers in children fell in recent years, the incidence of childhood brain tumors is increasing.

In the present prospective study of 132 cases of Paediatric cancers evaluated with clinical light microscopy Histochemical and IHC, following conclusions are made and presented.

1. The average incidence of Paediatric malignant neoplasm is 2 %.
2. The incidence of Paediatric neoplasms are in increasing trend with new modalities of investigating procedures.
3. No classical epidermiological or socioeconomic cause is identified as an etiological feature in Paediatric cancers.
4. Paediatric cancers are common in Male children with Male to Female ratio of 1.5:1
5. The peak age of paediatric neoplasm is less than 5yrs of age.
6. Hematological malignancy acute lymphoblastic leukemia is the commonest neoplasm in childhood.
7. Histochemical stains shall have their value in differentiating acute leukemias.
8. In all cases of lymphoma, final confirmation with CD marker for treatment and prognosis is the gold standard strategy / method.

9. Neuroblastoma is the most common neoplasm following leukemia.
10. Rare tumors like colorectal adenocarcinoma Melanoma and nasopharyngeal carcinoma are also occur even in Paediatric age groups.
11. Primary CNS neoplasms are relatively rare in children, in contrast with Western population where brain tumors are common near to leukemia.
12. In case of doubtful histogenesis, Immunohistochemistry is very useful for final diagnosis.

APPENDIX-VI

IMMUNO- HISTOCHEMISTRY

Method Used:

1. 5µ thick sections were cut from the blocks received (diagnosed as lymphomas) on slides coated with Chrome alum gelatin.
2. Slides were dewaxed and dehydrated in graded alcohol.
3. Slides were immersed in 0.3 % H_2O_2 for 20 minutes to block endogenous peroxidase activity.
4. Washed in phosphate buffered saline (PBS).
5. Incubated in Primary Antibody & Pan B (CD20, clove L26 DAKO), PAN T (CD3, polyclonal, DAKO), (CD30, clove L26 DAKO) & GFAP for 20 minutes.
6. Washed in PBS.
7. Biotinylated link was applied for 20 minutes.

8. Washed in PBS.
9. Incubated in streptavin-biotin complex.
10. Washed in PBS.
11. DAB was used as chromagen.
12. Washed and canbe stained with haematoxylin.
13. Mounted with coverslip

Control run – was tonsil.

BIBLIOGRAPHY

1. Ana Ruiz – Casado, M.D., Cecilia Guzman, M.D., Jose Jimeno, M.D., David Harmon, M.D., 2003 American cancer society. Phase II study of Ecteinascidin 743 in heavily pretreated patients with recurrent osteosarcoma. Page No: 832.
2. Alastair J.W. Millar, Alan Davidson, Heinz Rode, Alp Numanoglu, Patricia S. Karinepelc, M.D., Sylvie Vincent, M.Sc., Marie Ruchoux, M.D., Robert kiss Ph.D., Roland Pochet, Ph.D., Eric Sariban, M.D., Christine Decaestecker, Ph.D., Calbindin – D28k, & marker of recurrence for medulloblastomas - 2002 American Cancer Society.

3. Ann C. Mertens, ph.D, Yutaka Yasui, ph.D, Yanliu, M.S., Marilyn Stovall, ph.D., Ray Hutchinson, M.D., Vill Ginsberg, M.D., Charles Sklar, M.D., Leslie L. Robison, ph.D., Pulmonary Couplicatious in survivers of childhood and adolescent cancer. A report from the childhood cancer surviver shedy Cancer December 1 2002/volume 95/Number 11 P.No: 2431.
4. Ann c. Merters, ph.D., Pauline A Mitby, M.P.H, Gretchen Radloff B.S., Irene M.Jones, ph,D., John Perentesis, M.D., William R.Kiffmeyar, ph.D., Joseph P. Neglia M.D., M.P.H., Anna Meadows, M.D., John D. Potter, M.D., ph,D., Debra Friedman, M.D., Debra Friedman, M.D., Yutaka Yarui ph.D., Leslie L.Robison,ph.D., Stella M. Davies, M.B.B.S., ph.D., XRCCI and glutathione – S. transferare gene Polymorphisms and susceptibility to radiotheraphy – Related Malignancies In survivers of Hodgking's diseases. 2004 American cancer society.Page No: 1463
5. AndrewL.Folpe,M.D., John R.Goldblum,M.D., Brain P.Rubin, M.D., ph.D., Bahig M. shehata,M.D., Wendy Liu, M.D., Angelo P.Deitos, M.D., and Sharon W.Weiss, M.D., Morphologic and immuno phenotypic diversity in Ewing family tumours. A study of 66 genetically confirmed cases. American J Surgical pathology, volume 29, Number 8, August 2005 Page No: 1025.

6. Arny Heerema – Mckenney, M.D., Micael R. Harrison, M.D., Barbara Bratton R.N, Jody Farrell, RN, and Charles Zaloudek, M.D., Congenital Teratoma A clinopathologic study of 22 fatal & neonatal tumors.Am J Surg Pathol.
7. Asim F. belgaumi M.D, Mohammed AL – Bakrah M.D., Mohammed AL – Mahr, M.D., Abdullah AL –Jefri, M.D., Abdulrahman Al-Musa, M.D., Mahaser saleh, M.D, Mohammed F.salim,M.D., mohammed Osman, M.D., Dayla Osman, M.D., Hassan El – Soth, M.D., Dexamethasone – associated Toxicity during induction chemotherapy for childhood acute lymphoblastic Leukemia in augmented by concurrent use of Daunomycin.2003 American cancer society Page No: 2898.
8. Alay, Hayward, Levin, Sondheimer, Current Paediatric diagnosis and treatment, Sixteenth edition.
9. Buchino JJ. Jones VF – fine Needle aspiration in the evaluation of children with lymphadenopathy – Arch Pediatric Adolescence Medicine – 1994 Dec-148(12); 1327-30.
10. Biwas G, Laskars S, Baravali SD, Gujral S, Kurkure PA, Muckaden M, Parikh PM, Nair CN. Desmoplastic small round cell Tumour: Extra abdominal and abdominal presentatious and the results of treatment.Indian Journal of Cancer/April – June 2005/Volume 42/Issue 2 (page No: 78).

11. A.R.Khan, Shuab Omer, Sumia Rashid, Syed Besina – Fine needle aspiration; diagnosis of nodal Hodgkin's lymphoma (part – II)- JK Pracatitioner – 2002; 9(4); 264-267.
12. Brain H. Kushner, M.D., AmyBudnick M.ed., MPH., Kimkramer MD., Shakeel Modak MD., Nai – Kong V.cheeng, M.D, Ph.D. Otoxicity from high dose use of platinum compounds in patients with Neuroblastoma. 2006 American cancer society Page No: 417.
13. Brian P. Quaranta M.D., Edward C.Halperin, M.D., Joanne Kurtzbeg M.D., Robert Clough, B.A., Paul L Martin, M.D., ph.D., The incidence of testicular recurrence in boys with acute leukemia treated with total body and testicular irradiation and stem cell transplantation. 2004 American cancer society Page No: 845.
14. B.Pellegrino, M.J Terrier-Lacombe, O.Oberlin, T. Lebanc, Y. Bertrand – Lymphocyte – Predominant Hodgkin's Lymphoma in children; Therapeutic abstention after initial lymph node resection- A study of the French society.
15. Benesch M, Kerbl R, Wirnsberger A, Stunzner D, Mangge II, Schenkeli R, Deutsch J – Peripheral Lymphadenopathy in childhood- recommendations for diagnostic evaluation – Klin Pediatric – Year 2000-Sep-Oct; 277-282.

16. Caroline Laverdiere, M.D., E.Anders, M.D., Kolb,M.D., Jeffrey G. Supko, ph.D., Richard Gorlick, M.D., Paul A. Meyers, M.D., Robert G. Maki,M.D., Leonard Wexler , M.D., George D. Dentri, M.D., John H. Healey, M.D,Andrew G. Huvos, M.D., Allen M.Goorlin, M.D., Rochelle Bagetell,
17. Celine Icher – de Bouyn, M.D., Serome Loclere M.D., Dominique couanet Raimondo, M.D., Hubert Ducou le Pointe, M.D., Dominique Valteau – Couanet M.D., Oliver Martmann M.D., Incidence, Risk factors, and outcome.Pediatric department, Institute Gustare – Roussy, Villquit, France September 13,2002.
18. Christopher D.M fletcher, Diagnostic histopathology of tumors, Second edition, 2 Volumes.
19. Cotran, kumar, Robbins, Pathologic basis of disease, Sixth edition.
20. Dane R. Lal, Wendy T. Su, Suzanne L. Wolden, Kenneth C. Loh, Shakeel Modak, Michael P. La Quaglia. Results of multimodal treatment for desmoplastic small round cell tumor. Journal of Pediatric Surgery (2005) 40, 251 – 255.
21. David F.Saad, Kenneth W.Gow, Zvonimir Milas, mark L.Wulkan, Laparoscopic adrenalectomy for neuroblastoma in children: A report 6 cases.Jaumal of Paediatric surgery (2005) 40, 1948 – 1950.

22. Daniel M.Green, Andrew Hyland, Maurice P. Barcos, Julie A. Reynolds, R.Jeffrey Lee, Brenda C. Hall and Michael A. Zevon-Second Malignant Neoplasms after treatment for Hodgkin's disease in childhood or adolescence – Journal of Clinical Oncology – Vol-18, No 7 (April), 2000, Page – 1492-1499.
23. Edythe A. Albano – Lymphadenopathy (Enlarged Lymphnodes or Swollen Glands) Children's Hospital & Regional Medical Center, Seattle, Washinton.
24. Francisco F. Nogales, M.D., Catalina Buritica, M.D., Siigrid Regauer, M.D., Talina Gonzalez, M.D., Am J Surg Pathology. Mucinous carcinoid as an unusual manifestation of endodermal differentiation in Ovarian Sac tumours. Volume 29, Number 9, September 2005. Page – 1247.
25. Guillermo Chantada, M.D., Adriana fandino, M.D., Maria T.G. Davila,M.D., ph.D., Julio Manzitti, M.D., Elsa Raslawski, M.D., Sandra Casak, M.D., Enrique Schvartzman, M.D., Results of a prospective study for the treatment of retinoblastoma 2003 American cancer Society. Page No: 834.
26. Hartley, John D. Daubenton, Farieda desai. Bilateral Wilm's tumours: A single center Experience with 19 cases. Department of Pediatric surgery, red cross Children's Hospitals, Capetarn, South Africa. Journal of Paediatric Surgery (2005) 40, 1289 – 1294.

27. Hoffbrand, Lewis, Iuddenhan, Post graduate haematology, Fourth edition.

28. Iochims Lymph Node Pathology – Harry Iochims.

29. Jaume Mora, M.D., David A.Filippa, M.D., Jing Qin ph,D., Norma wother,M.D., The 30 years experience at memorial sloan- Kethering cancer center 2003 American cancer Society Lymphoblastic lymphoma of childhood and the LSA2 – L2 protocol. Page No: 1283.

30. John T. Sandlund, Ching-Hon Pui, W. Mark Roberts, Victor M. Santana – Clinicopathologic features and treatment outcome of children with large cell lymphoma and the t(2;5) (p23:q35) – Blood, Vol-84, No-8 (October 15), 1994; page-2467-2471.

31. John T. Sandlund, James R. Downing and William M. Crist – Non Hodgkin's Lymphoma in Childhood – The New England Journal of Medicine – May 9 – 1996- Vol – 334 – No-19, Page – 1238-1248.

32. Jorg fuchs, M.D., Jana Rydzynski, Dietrich Von Schweinitz, M.D., Udo Bode, M.D., Hartmut Hecker, Ph.D., Peter Weinel, M.D., Dieter Harms, M.D., Rudolf Erttmann, M.D., Karl oldhafer, M.D., Alermann, Milderberger, M.D., Pretreatment Prognostic factors an treatment results in children with hepatoblastoma.A report from the German Cooperative Pediatric liver tumour study HB 94. The study committee of the cooperative

pediatric liver tumour study Hb 94 for the German Society for Pediatric Oncology and Hematology – 2002 American Cancer Society. Page-172.

33. Karados TF, Maygarden SJ, Blumberh AK, Wakely PE Jr, Frable WJ – Fine needle aspiration biopsy in the management of children and young adults with peripheral lymphadenopathy – Cancer. 1989 Feb 15;63(4): 703-7.
34. Kathrin Seidman, Marker Tieman Short pulse B-Non Hodgkin lymphoma – type chemotherapy is efficacious treatment for pediatric anaplastic large cell lymphoma a report of Berlin Frankfurt – Munslee group Trail NHC BF 90. Blood June 2001, Vol 97.
35. Keiichiro Ianaka, Masaki kanai, Jyoji Yesizawa, Yoji Yamazaki. A case of Neonatal Neuroblastoma mimicking Attman type III sacrococcygeal teratoma. Journal of Pediatric Surgery (2005) 40, 578 – 580.
36. Kenneth Gow – Lymph node Disorders – Emedicine Specialilties- June 23, 2004.

37. Laura luvone, M.D., Paolo Mariotti, M.D., Cesare-Colosino, M.D., Francesco Guzzetta, M.D., Antonia Ruggiero, M.D., Riceardo Riccardi, M.D., Long term Cognitive outcome, Brain computed Tomography Scan, and Magnetic resonance Imaging in children cured for Acute lymphoblastic leukemia. - 2002 American Cancer Society.
38. Lake AM, Oski FA – Peripheral Lymphadenopathy in childhood. Ten year experience with excisional biopsy – American Journal of diseases of children – Apr-132(4), 356-9.
39. Layfield LJ, Reichman A – Fine needle aspiration cytology: Utilization in pediatric pathology – Diseases Markers – 1990 Nov-Dec;8(6):301-15.
40. Liu ES, Bernstein JM, Sculerati N. Wu IIC – Fine needle aspiration biopsy of pediatric head and neck masses – Internal Journal Pediatric Otorhinolaryngology – 2001 Aug 20: 60(2): 135-140.
41. Lydia Pleotis Howell, Liisa A. Russell, P. Holbrook Howard, and Raymond L. Teplitz – Fine needle Aspiration Biopsy of Lymphadenopathy – Texas Pediatric Surgical Associates – (832); 325-7234.
42. Malcolm A. Smith, Borisfredlin, Lynn A, Gloeckler Rie, Richard Simon. Trends in reported evidence of primary malignant brain tumours in children in the United States. Journal of the national cancer institute, Volume 90, No.17, September 12, 1998.

43. Matteo Zignol M.D., Marta Peracchi M.D., Gloria Tridello Ph.D., Marta Pillon M.D., Federica fregonese M.D., Ruggiero D'Elia M.D., Leigi Zanesco M.D., simone cesaro, M.D., Assesment of Humoral immunity to Poliomyelitis, Tetanus, Heatitis B, Measles, Rabella, and Mumps in children after Chemotherapy 2004, American cancer society Page No: 635.

44. Marta Pillon, M.D., Maria Teresa D, Tullio M.D., Maria cartina putti, M.D., Alberto Garaventa M.D., Simone Cesaro M.D., Maria Caterina Putti,M.D., Claudio Favre M.D., Alma Lippi M.D., Gianmarco Surico M.D., Andera Di Cataldo M.D., Emanuele D' Amone, M.D., Luigi Zanesco, M.D., Angelo

Rosoten, M.D., Long - Term result of the first halian Association of pediatric hematology and oncology protocol for the treatment of pediatric B-cell, Non-Hodgkins Lymphoma (AIEOP LNH 92) 2006 American cancer society Page No: 385.

45. Michela Casanova, M.D., Andrea Ferrari, M.D., Filippo Spreafico, M.D.,Monica Ferenziari, M.D., Maura Massimino, M.D., Roberto Luksch, M.D., Graziella cefalo, M.D., Daniela Polastri, M.D., Ilaria Marcon, M.D., France fossati Bellari, M.D., Vinorelbine in Previously treated advanced childhood Sarcomas evidence of activity in Rhabdomyosarcoma.Page – 3263.

46. Mills, Carter,Greenson, Oberman, Reuter, stoler, Strin Berg's diagnostic surgical pathology, Fourth edition 3 Volumes.
47. Michael Macari, John Hines, Emil Balthazar, Alec Megibow-Mesentric Adenitis: CT Diagnosis of Primary Versus Secondary causes, Incidence and Clinical Significance in Pediatric and Adult patients – AJR-178, April-2002.
48. Miller – Childhood Cancer: Lymphoma – Kid Health for Parents, May 2002.
49. Mobley DL, Wakey PE JR, Frable MA – Needle aspiration biopsy: application to pediatric head and neck masses – Laryngoscope 1991 – May; 101(5); 469-72.
50. Moore SW – A clinical approach to cervical adenopathy – The Medicine Journal – May – 2001 – Vol-43-No-4.
51. Nada A.AIAwan, Amer S. AIHashimi, Maad M. Salman and Esam A.AlAttar – Fine needle aspiration cytology versus histopathology in diagnosing lymph node lesions – Eastern Mediterranean Health Journal – Volume 2, Issue 2, 1996 Page – 320-325.
52. Nancy Leu Harris, A revised European – American classification of lymphoid neoplasm. A proposal from the international lymphoma study group. Blood vol.8 and Sept.1994.
53. Nathan and Oski, Haematology of infancy and childhood, Sixth edition, Volume 1&2.
54. Nelson Textbook of Pediatrics, Seventeenth Edition Richard E Behrman, Robert M Kilegman, Hal B Jenson.

55. Niels E. Skakkeback, Ewa – Rajpert – De Meyto and Jourma Toppari. Testicular Cancer. Pathogenesis, Diagnosis, and Endocrine aspects. November 25, 2003. Page – 1.

56. Non-Hodgkin's Lymphoma (NHL) in children – Cancer Bacup- Principles and Practice of Paediatric Oncology (Fourth edition).

57. Olive4 S.Soldes, John G.Younger and Ronald B. Hirschl Ann Arbor, Michigan – Predictors of Malignancy in Childhood peripheral lymphadenopathy – Journaal of Pediatric Surgery – Vol-34, No-10 (October), 1999: pp-1447-1452.

58. Peter f. Ehrlich, Michael L. Ritchey, Jomas & Hauilton, Gerald M. Haase, san ou, Norman Breslow, Paul Grundy, Daniel Green, Patricia Norkool, Jennifer Becker, Robert C. Shanberger. Quality assessment for Wilm's Tumor: a report from the National Wilm's Tumor study-5. Journal of Pediatric Surgery (2005) 40, 208 – 213.

59. Pediatric Pathology, Second edition, J Thomas Stocker Louis P Dehner.

60. Pediatric Non-Hodgkin's Lymphomas in children – Diagnosis and Current Management – Indian Pediatrics – Vol 38- June 17, 2001, page – 583-588.

61. Pituch – Noworolska A, Drabik G, Kaacinaska E, Klekawka T – Lymphocyte populations in lymph nodes in different histological types of Hodgkin's disease in children – Acta Hematol – 2004; 112(3); 129-135.

62. Reddy M Pradeep, Moorchung N, Chaudhary A – Clinico-Pathological profile of pediatric lymphadenopathy – Indian Journal of Pediatrics – Year 2002 – Vol-69, Issue – 12, Page-1047-51.

63. Robert B. Lorsbach, Dominic shay-seymore, Jennifer Moore, Peter M.Banks – Cllinicopathologic analysis of follicular lymphoma occurring in children – Blood -15 March 2002-Volume 99 – number 6 – Page 1959-1964.

64. Robert Ferrer – Lymphadenopathy: Differential Diagnosis and Evaluation – American Family Physician-Oct – 15-1998.

65. Rosai & Ackerman Surgical pathology, Ninth edition, Volume 1&2.

66. Seyedf A.Amlashi, M.D., Laurent Riffand, M.D., M.Sc., Qilles Brassier, M.D., ph.D., Xavier Morandi, M.D, M.Sc., A Population – based study and review of the literature Nevoid basal cell carcinoma sybdrome. Relation with desmoplastic Medulloblastoma in infancy. 2003 American cancer society.Page No: 618

67. Smadar Avigad, ph.D., Lan J. Cohen, M.B, ch.B, Julia Zilberstein, M.Sc., Ella Liberzon, M.Sc., Yacov Goshen, M.D., Shifra Ash, M.d, Isaac Meller M.D., Yehuda Kottender, M.D., Josephine Issakov, M.D., Rina Zai Zov, M.D., Isaac

Yariv, M.D., The predictive potential of molecular detection in the non metastatic Ewing family of tumours. 2004 American cancer society. Pager No: 1053.

68. Scott M. Bradfield,M.D., James G. Douglas M.D., Douglas. S. Hawkins, M.D., Jean E. sanders, M.D., Julie R.Park, M.D., Fractionated low – dose Radiotheraphy after myeloblastine stem cell transplantation for local control in patients with high risk neuroblastoma. 2004 American cancer society.Page No: 1268.
69. Shown D. Safford, Alex J. freemerman, scott Langdon, rex Bentley, Dominique Goyeau, Paul E. Graundy, Michael A. Skinner. Decreased E. Cadherin Expression Corrlates with higher stage of Wilm's tumor. Journal of Pediatric Surgery (2005) 40, 341 – 348.Volume 29, Number 1, January 2005, Page- 29.
70. Silverberg, Delellis, frable, Principle and Practice of surgical pathology and cytopathology, Third edition, 3 Volumes.
71. Sutow, fernbach, Vietti, Clinical Pediatric Oncologh Third edition.
72. STANS Field 1985 Lymph node biopsy interpreted.
73. V Rathaus, M. Shapiro, M. Grunebaum and R.Zissin – Enlarged mesenteric lymph nodes in asymptomatic children: the value of the finding in various imaging modalities – The British Journal of Radiology 78(2005), 30-33.

74. Wancring Wen, M.D., Xiao cru shu, MD, Ph.D., John D.Potler, M.D, Ph.D., Richard K. Severson, Ph.D., Jonathan D.Buckley, M.D, Ph.D., Gregory of Reaman, M.D., Leslie L.Robinson, Ph.D., Parental medication use and risk of childhood Acute lymphoblastic leukemia. - 2002 American Cancer Society.

75. W.H.O Classification of tumors – Pathology and Genetics – tumor of Hematopoietic and Lymphoid tissue 2001.

CHART

SL.NO	HPE/PS	AGE (Years)	SEX	CLINICAL PRESENTATION	DIAGNOSIS	SPECIAL STAINS	IMMUNO HISTOCHEMISTRY
1	351/03	5	M	Axillary Node	NHL – Large cell Lymphoma	Not done	Not done
2	666/03	12	M	Intra abdominal mass	NHL-Large cell Lymphoma	Not done	CD_{20} - Positive
3	794/03	15	M	Lymph Node Biopsy	NHL- Lymphoblastic Lymphoma	Not done	Not done
4	1232/03	9	F	Sub mental node biopsy	NHL- Large cell Lymphoma	Reticulin -Positive	Not done
5	1840/03	12	M	Lymph Node Biopsy	Hodgkin lymphoma - Mixed cellularity	Not done	Not done
6	2067/03	3	M	Lymph Node Biopsy	NHL- Large cell Lymphoma	Reticulin -Positive	CD_3 - Positive
7	266/04	5	M	Lymph Node Biopsy	NHL- Large cell Lymphoma	Not done	Not done
8	939/04	8	F	Ileocaecal intussusception Lymph Node	NHL-Burkitt's Lymphoma	Not done	Not done
9	1030/04	15	F	Lymph Node Biopsy	NHL- Burkitt's Lymphoma	Not done	Not done
10	2296/04	15	M	Lymph Node Biopsy	Hodgkin's lymphoma	Not done	Not done
11	2663/04	10	M	Inguinal Lymph Node	NHL- Large cell Lymphoma	Reticulin -Positive	CD_{20} - Positive
12	2684/04	2	M	Lymph Node Biopsy	NHL- large cell Lymphoma	Not done	Not done
13	79/05	6	M	Cervical Lymph Node	NHL- large cell Lymphoma	Not done	Not done
14	80/05	3	F	Lymph Node from Ileum	NHL- Diffuse large cell lymphoma	Not done	CD_3 - Positive
15	466/05	6	M	Right- cervical Node	NHL Large cell Lymphoma	Reticulin -Positive	Not done
16	780/05	5	F	Cervical Lymphoma	NHL Large cell Lymphoma	Not done	Not done
17	1348/05	11	F	Cervical lymph Node	Lympho proliferative disorder	Not done	Not done
18	519/05	15	M	Cervical Lymph Node	Hodgkin's Lymphoma	Not done	CD_{30} - Negative
19	PS40/05	10	F	Anaemia,Hepatomegaly	Lympho proliferative disorder	Not done	Not done
20	PS235/05	3	M	Hepatomegaly, fever, Anaemia	ALL	Not done	Not done

SL.NO	HPE/PS	AGE (Years)	SEX	CLINICAL PRESENTATION	DIAGNOSIS	SPECIAL STAINS	IMMUNO HISTOCHEMISTRY
21	PS987/05	4	M	Anaemia, Generalized Lymphadenopathy	Lympho proliferative disorder	Not done	Not done
22	PS1230/05	3	M	Hepatomegaly, fever, Anaemia	ALL-L2	Not done	Not done
23	PS1341/05	7	F	Hepatosplenomegaly, Fever, Anaemia	ALL	Not done	Not done
24	PS2096/05	14	M	Hepatosplenomegaly, Fever, Anaemia	ALL-L2	PAS - Positive	Not done
25	PS2122/05	14	F	Anaemia, Generalized Lymphadenopathy	Lympho proliferative disorder	Not done	Not done
26	PS2158/05	14	M	Fever, Bleeding Manifestation, Joint Pain	Lymphoma spill	Not done	Not done
27	PS2519/05	3	M	Hepatosplenomegaly, Fever, Anaemia	ALL-L1	Not done	Not done
28	PS1501/05	9	F	Gum Hypertrophy. Bony tenderness, fever	AML-M4	Sudan BlackB Positive	Not done
29	PS1494/05	2	M	Splenomegaly. Bony tenderness, fever	AML	Sudan BlackB Positive	Not done
30	PS1404/05	13	F	Anaemia,Hepatomegaly	ALL	PAS - Positive	Not done
31	PS1395/05	8	M	Hepatosplenomegaly, Fever, Anaemia	ALL	PAS - Positive	Not done
32	PS906/05	5	M	Generalized lymphadenopathy, Bony tenderness.	Lympho proliferative disorder	Not done	Not done
33	PS1386/05	14	M	Fever, upper respiratory track infection	Lymphoma Spill	Not done	Not done
34	PS359/05	13	F	Fever, bleeding manifestation, anaemia	Lymphoma Spill	Not done	Not done
35	PS207/04	4	F	Joint pain, upper respiratory infection, fever	ALL	Not done	Not done
36	PS368/04	3	F	Anaemia, fever, hepatosplenomegaly	ALL-L1-2	Not done	Not done
37	PS392/04	10	M	Anaemia, fever, hepatosplenomegaly	ALL-L1	Not done	Not done
38	PS447/04	11	M	Anaemia, fever, hepatosplenomegaly	ALL-L2	Not done	Not done
39	PS568/04	15	M	Bleeding manifestation, anaemia	Lymphoma spill	Not done	Not done
40	PS645/04	9	M	Hepatosplenomegaly, fever	ALL-L2	Not done	Not done

SL.NO	HPE/PS	AGE (Years)	SEX	CLINICAL PRESENTATION	DIAGNOSIS	SPECIAL STAINS	IMMUNO HISTOCHEMISTRY
41	PS666/04	8	F	Generalized Lymphadenopathy,fever	Lymphoproliferative disorder	Not done	Not done
42	PS840/04	2	M	Bleeding manifestation, anaemia	Lymphoma spill	Not done	Not done
43	PS868/04	5	M	Hepatosplenomegaly, fever	ALL-L1	Not done	Not done
44	PS996/04	10	M	Fever , anaemia, splenomegaly	ALL	Not done	Not done
45	PS1059/04	4	M	Splenomegaly, fever, anaemia	ALL	Not done	Not done
46	PS1220/04	5/12	M	Anaemia,Hepatomegaly	ALL-L1	Not done	Not done
47	PS1247/04	14	M	Anaemia, fever, hepatosplenomegaly	ALL-L2	Not done	Not done
48	PS1354/04	5	F	Hepatomegaly , fever, Anaemia	ALL-L2	Not done	Not done
49	PS1358/04	4	M	Fever, upper respiratory track infection	Lymphoma spill	Not done	Not done
50	PS1359/04	4	M	Joint pain, upper respiratory infection, fever	ALL	Not done	Not done
51	PS1389/04	5	F	Anaemia, fever, hepatosplenomegaly	ALL	Not done	Not done
52	PS1539/04	15	M	Generalized Lymphadenopathy,fever	Lympho proliferative disorder	Not done	Not done
53	PS1563/04	9	M	Hepatomegaly, fever, Anaemia	ALL-L1	Not done	Not done
54	PS1742/04	13	M	Anaemia, fever, hepatosplenomegaly	ALL	Not done	Not done
55	PS1767/04	11	F	Splenomegaly, fever, anaemia	ALL	Not done	Not done
56	PS52/03	9	M	Splenomegaly, fever, anaemia	ALL	Not done	Not done
57	PS155/03	5	F	Anaemia, fever, hepatosplenomegaly	ALL	Not done	Not done
58	PS182/03	7	F	Splenomegaly, fever, anaemia	ALL	Not done	Not done
59	PS207/03	7	F	Joint pain, upper respiratory infection, fever	ALL	Not done	Not done
60	PS366/03	5	M	Anaemia, fever, hepatosplenomegaly	ALL	Not done	Not done

SL.NO	HPE/PS	AGE (Years)	SEX	CLINICAL PRESENTATION	DIAGNOSIS	SPECIAL STAINS	IMMUNO HISTOCHEMISTRY
61	PS460/03	13	M	Splenomegaly, Bony tenderness, fever	ALL-L2	Not done	Not done
62	PS981/03	11	M	Splenomegaly, fever, anaemia	ALL	Not done	Not done
63	PS572/03	7	M	Splenomegaly, fever, anaemia	ALL-L2	Not done	Not done
64	175/03	3	M	Growth oral cavity	Malignant melanoma	Not done	Not done
65	177/03	11	F	Colonic growth	Well differentiated Adeno carcinoma	Not done	Not done
66	511/03	15	F	Ovarian mass	Dysgerminoma	Not done	Not done
67	786/03	13	M	Naso pharyngeal growth	Well differentiated Squamous cell carcimona	Not done	Not done
68	866/03	2	M	Thoracic mass	Neuroblastoma	Not done	Not done
69	1251/03	8	F	Adrenal mass	Ganglioneuroblastoma/ Composit neuroblastoma	Not done	Not done
70	1657/03	12	F	Sarcoma from Anus	MFH with Storiform - Pleomorphic type	Not done	Not done
71	1771/03	3	F	Ovarian cyst	Gonodoblastoma	Not done	Not done
72	1870/03	4	F	Rt Adrenal mass	Adrenal cortical carcinoma	Not done	Not done
73	97/04	2	F	Swelling in Rt Gluteal region	Small round cell type	Not done	Not done
74	118/04	3	M	Rt Adrenal mass	Neuroblastoma	Not done	Not done
75	237/04	13	F	Anal growth	Mucinous adeno Carcinoma	Not done	Not done
76	853/04	4	F	Lt orbit prolapsed eye	Retinoblastoma	Not done	Not done
77	892/04	12	M	Recurrent growth Previous report schwannoma	Low grade MPNST	Not done	Not done
78	1058/04	10	M	Chest wall tumor	Extra skeletal Ewings sarcoma	Not done	Not done
79	1306/04	3	M	Testicular tumor	Mixed germ cell tumor (Embryonal carcinoma,yolk sac)	Not done	Not done
80	1715/04	1	F	Lt calf	Spindle cell variant of Rhabdomyosarcoma	Not done	Not done

SL.NO	HPE/PS	AGE (Years)	SEX	CLINICAL PRESENTATION	DIAGNOSIS	SPECIAL STAINS	IMMUNO HISTOCHEMISTRY
81	2039/04	10	M	Recto sigmoid annular growth	Well differentiated adenocarcinoma	Not done	Not done
82	17/05	3	F	Presacral teratoma	Mixed germ cell tumor (Yolk sac, teratoma)	Not done	Not done
83	21/05	15	M	Distal femur	Osteosarcoma	Not done	Not done
84	206/05	5	F	Lt growth nasal cavity	Embryonal Rhabmyosarcoma	Not done	Not done
85	222/05	5	F	Left Eye	Retinoblastoma	Not done	Not done
86	253/05	15	F	Left tibia anterolateral aspect	Osteosarcoma	Not done	Not done
87	779/05	11	F	Ovarian tumor Mass abdomen	Mixed germ cell tumor	Not done	Not done
88	860/05	15	M	Rt knee swelling	Osteosarcoma	Not done	Not done
89	864/05	3	M	Liver biopsy	Hepatoblastoma	Not done	Not done
90	865/05	10	M	Biopsy growth	Extra skeletal Ewing's Sarcoma	Not done	Not done
91	869/05	4	M	Kidney	Wilm's tumor	Not done	Not done
92	950/05	6	F	Biopsy	Extra skeletal Ewing's Sarcoma	Not done	Not done
93	1122/05	1	F	Mass Right Lumbar region Right adrenal Tumor	Ganglioneuroblastoma	Not done	Not done
94	1123/05	3	M	Biopsy	Ewing's Sarcoma	Not done	Not done
95	1562/05	9	M	Adrenal tumor	Neuroblastoma	Not done	Not done
96	1888/05	15	M	Sarcoma	Mesenchymal Malignant NerveSheath tumor	Not done	Not done
97	1943/05	4	M	Adrenal tumor	Neuroblastoma	Not done	Not done
98	2040/05	3	M	Right eye	Retinoblastoma	Not done	Not done
99	2235/05	15	M	Mass nasophrenia	Nasopharyngeal carcinoma - lympho epithelioma type	Not done	Not done
100	2420/05	4	M	Right eye	Retinoblastoma	Not done	Not done

SL.NO	HPE/PS	AGE (Years)	SEX	CLINICAL PRESENTATION	DIAGNOSIS	SPECIAL STAINS	IMMUNO HISTOCHEMISTRY
101	2236/05	15	M	Laryngeal Papilloma	High grade SIL with focal area of invasion	Not done	Not done
102	123/05	3	F	Ovarian tumor	Gonodoblastoma	Not done	Not done
103	27/05	6	F	Biopsy	Ewing's Sarcoma	Not done	Not done
104	126/05	4	F	Ovarian tumor	Monodermal teratoma	Not done	Not done
105	286/05	2	M	Left testicular tumor	Embryonal Rhabdomyosarcoma	Not done	Not done
106	471/05	30 days	M	Liver biopsy	Hepatoblastoma	Not done	Not done
107	472/05	4 months	M	Abdominal mass	Neuroblastoma – Undifferentiated type	Not done	Not done
108	581/05	30 days	F	Liver	Hepatoblastoma	Not done	Not done
109	957/06	4	F	Liver	Hepatoblastoma	Not done	Not done
110	1059/05	7	F	Adrenal	Neuroblastoma -Undifferentiated type	Not done	Not done
111	1224/06	15	M	Superficial parotidectomy	Low grade Muco epidermoid carcinoma.	Not done	Not done
112	270/03	4	M	Posterior fossa tumor	Medulloblastoma with area of necrosis	Not done	Not done
113	1064/03	5	M	Frontal lobe abscess	Medullo epithelioma/ Ependymoma	Not done	Not done
114	1131/03	14	M	Suboccipital	Anaplastic Astrocytoma	Not done	Not done
115	1605/03	2	F	Left Parietal Craniotomy	Ependymoma with extensive calcification	Not done	Not done
116	1698/03	2	F	SOL	Ependymoma	Not done	Not done
117	248/04	4	M	Left Temporo Parietal lesion	PNET	Not done	Not done
118	788/04	3	M	Neuroepithelial tumor	Dedifferentiated Chordoma	Not done	Not done
119	1513/04	2	M	Frontal SOL	Grade III Astrocytoma	Not done	GFAP Positive
120	1686/04	10	F	Posterior fossa tumor	Medulloblastoma	Not done	Not done

SL.NO	HPE/PS	AGE (Years)	SEX	CLINICAL PRESENTATION	DIAGNOSIS	SPECIAL STAINS	IMMUNO HISTOCHEMISTRY
121	2610/04	9	M	Posterior fossa tumor	Medulloblastoma	Not done	Not done
122	29/05	11	F	Supra sellar SOL	Astrocytoma – Grade III	Not done	Not done
123	36/05	15	F	Right frontal glioma	Astrocytoma – Grade III	Not done	Not done
124	406/05	11	F	Posterior fossa occupying lesion	Medulloblastoma	Not done	Not done
125	897/05	9	F	Posterior fossa occupying lesion	Medulloblastoma	Not done	Not done
126	1551/05	11	M	Right temporoparietal subcortical SOL	Atypical Teratoid / Rhabdoid tumour	Not done	GFAP, EMA, VIMENTIN, SMA, DESMIN - Positive
127	1657/05	10	F	Post fossa SOL	Medulloblastoma -Desmoplastic variant	Not done	Not done
128	2507/05	10	F	Lt frontal cystic lesion	Astrocytoma – Grade III	Not done	GFAP - Positive
129	56/05	15	M	Lt Pineal SOL	Pinecytoma/ Pineal parenchymal tumor	Not done	Not done
130	610/06	9	M	Posterior fossa tumor	Medulloblastoma/PNET	Not done	Not done
131	1164/06	15	M	Pineal SOL	Pineocytoma	Not done	Not done
132	1121/05	9	M	Frontoparietal region	Astrocytoma – Grade III	Not done	Not done