Malignant Pediatric Tumors In Najaf

Safa M. Mahdi Al-Obaidi (F. R. C. S.)

Summary:

Back ground : *cancer is one of the leading causes of death in children .In young children , particularly infants , the aberrant genetic processes that fail to safeguard against the clonal proliferation of cell with unregulated growth potential occur very early in life and progress very quickly .*

Objectives :- *To study the epidemiology of malignant pediatric tumors regarding age ,sex ,,regional distribution and clinicpaothological findings in Najaf province*

Patients and method :- *35 pediatric cancer cases were collected between January 2000 and January 2002 .The cases were analyzed according to age sex , regional distribution , frequency of malignancies type of operation , and the histopathological results after operation.*

Results :- *The peak age incidence was (4-8) years, male to female ratio was (1.06: 1) .The three most common malignancies were lymphoma (40%) , Wilm's tumor (14,3%) and Neuroblastoma (14,3%) .The abdominal viscera are the commonest sites followed by head and neck . Poorly differentiated tumors are more prevalant than well differentiated ones. Incisional. biosy operations constitute about 65% of cases.*

Conclusion :- *To our knowledge this is the first study which highlight's the epidemiology pathology presentation and lines of treatment of pediatric tumors. Late presentation of cases was remarkable in this study so public education about early attendance to general practitioner and early referral to pediatric specialist or surgeon will improve the progress of pediatric cancer*

Keywords *malignant pediatric malignancy , lymphoma, Wilm's tumor.*

J Fac Med Baghdad
2006; Vol. 48, No.2
Received Oct. 2005
Accepted Jan. 2006

Introduction :

Cancer is second only to trauma as the leading cause of death in children[1]. Relatively few malignant tumors in children currently are treated solely by surgical excision most are treated by a combination of surgical resection, chemotherapy and radiotherapy. Thus the successful treatment of a child with malignant tumor requires the co-operation approach of surgeons, pediatric oncologist, and radiotherapists [2,4].

Adult cancers usually form in epithelial tissues and are believed often to be the result of along biological process related to the inter-action of exogenous exposures with genetic and other endogenous characteristics among susceptible people. However in young children, particularly infants, the aberrant genetic processes that fail to safeguard against the clonal proliferation of cell with unregulated growth potential occur very early in life and progress very quickly. Due to the unique clinical genetic, and epidemiologic characteristics of cancer in infants [3,4], it is becoming increasingly apparent that the study of infant cancer may lead to further understanding of the mechanism of carcinogenesis.

* *Department of Surgery College of Medicine University of Kufa*

Common pediatrics tumors:

A. Malignant lymphoma:

Tumors arising from lymphoid tissue account for 10-15 percent of childhood malignancies in the western world and up to 50 percent of tumors in African children.

The malignant lymphoma are divided into two groups, Hodgkin's disease & non- Hodgkin's lymphomas. Each of these groups is further subdivided on the basis of cell type, any may involve the liver, spleen, bone, bone narrow, lung or skin as well as lymphatic tissue.

1. Non-Hodgkin's lymphoma:

The (NHL) are more common in childhood than HD, and there is an even greater preponderance of males. There is one age peak at 4-5 years. And another at 10 to 11 years. These rapidly growing aggressive tumors occur in the abdomen, the anterior mediastinum and lymph node of the head and neck as well as peripheral sites. [5-6-7]

2. Hodgkin's disease:

Perhaps by coincidence, 10 years is the mean age of diagnosis of Hodgkin's disease in all patient's up to 15 years of age.

Although Strum and Rappaport were unable to document the diagnosis of Hodgkin's disease in children under 3 years of age the youngest patient among three other reviews was 2 years old [8,9].

In these three series covering a total of 223 patients there was a (90%) preponderance in boys in the under 10 age groups. By the mid teen years,

the male: female ratio is 1.4:1, or the same as in adult.

B. Neuroblastoma:

Neuroblastoma is a common pediatric malignant tumor that arises from neural crest tissue and has aboard spectrum of clinical behavior, and usually affect children in 1st 5 years of life. Approximately 50% of patients present with disseminated disease, and with the exception of infants (age 0-11 months) have a poor prognosis [10]. In cases with out detectable metastasis at diagnosis, surgical excision of the primary tumor radically, or with minimal local residual disease, may be sufficient therapy for most patients with low stage neuroblastoma, as residual disease does not usually grow or metastasis and may spontaneously regress. [11]

Several recent studies implicate angiogenesis in the regulation of neuroblastoma growth. In primary neuroblastoma tumors high vascular index correlates with MYCN amplification metastasis and poor outcome where a low tumor vascularity is associated with a better prognosis, localized stage and favorable history [12,13,14].

C. Teratoma

Teratoma, by definition, are tumor that are composed of multiple tissue containing at least 2 germ-layer derivative foreign to the part of the body in which they arise. Of all the teratoma seen in infants and children, sacrococcygeal (SCT) account to nearly 40% of all cases [15]. Even so, sacrococcygeal teratoma is rare with reported incidence of 1 in 35000 to 40000, live birth [16-17]. The majority of SCT cases are apparent at birth and are more common in female accounting for about 75% [15]. In SCT the size of the tumor does not correlate with the likelihood of recurrence or poor out come [18-19], but the age at diagnosis and treatment as well as histological evaluation and stage at the time of resection are important prognostic factor.

D . Wilms tumor:

This is common solid intra abdominal tumor (malignant) in children. It affects 450-500 children annually in the USA. Neuroblastoma is most common, but they are not all confined to the abdomen. It has a peak incidence of at 3-5 years of age. Present as abdominal or flank mass with abdominal pain, asymptomatic hematuria and occasionally fever. Other presentation malaise weight loss, anaemia, left varicocele (obstructed left renal rein), hypertension.[20]

Operation is for both treatment and staging to determine further therapy. The abdomen is explored by a large transverse incision and both kidneys are visualized .Nephrectomy is done, nodes are biopsied to determine extent of disease[21].

Further treatment with chemotherapy or radiotherapy depend on staging and histology (favorable vs non-favorable) of tumor. Non favorable histologic characteristic are: anaplasia (enlarged nucleus 3x, hyperchromatism, mitosis) sarcomatous or rhabdoid degeneration.

Disease-free survival is 95% for stage I and approximately 77% for all patients. Poor prognosis for those with lymph node, lung and liver metastasis.[22]

E. Rhabdomyosarcoma:

Most common soft tissue sarcoma in infants and children and represents about 5-15% of all solid malignant tumor. It has a peak incidence at age 2-5 years second group between 10-15 years of age. Tumors of pelvic organs and head and neck are more prevalent in infancy and early childhood, while the paratesticular rhabdomyosarcoma are largely a disease of adolacents and young adults[20-21-22].

F. Liver tumors:

Hepatoblastoma and hepatocellular carcinoma are the most common malignant tumor of liver. These represents about 2% of all malignancies in childhood and 15% of malignant abdominal masses.

Hepatoblastoma (HB) is the most common primary malignant neoplasm of the liver in childhood. Mostly seen in males less than four years of age. Diagnostic work up (ultrasound, chest Xray, CT-scan) in predicting resectability and tumor extension. Diagnostic laparotomy will decide resectability. Markers associated to this tumor are: alpha fetoprotein and gamma, glutamyl tranferase II. Only reliable chances of cure is surgical excision although half are unresectable at dx. Unresectable tumor can be managed with pre-operative chemotherpy[20-21].

Hepatic resection has provided the only cures. In patient with initially unresectable tumor or in post resection patients. Chemotherapy is employed. Among those patients in whom the entire tumor can be resected, survival is 80% at two years. Unresectable tumors have a poor prognosis ADR (adriamycin) is the principal chemotherapeutic agent.[20-21-22]

Patients and Method

A total of 35 children representing all pediatric malignant tumors seen in the Teaching hospital in Al-Najaf. between January 2000 and January 2002. The cases were analyzed according to sex, age, and regional distribution and frequency of malignancies. Age was broken down into three groups: < 4 years, 4-8 years and 9-12 years. All the patients were operated up on in Najaf teaching hospital and specimens of tissues resected sent for histopathology, by which grading and staging of the tumors was done and further treatment adopted accordingly. All the obtained results were analyzed, compared and assessed.

Results:

In this prospective study 35 patients were collected there was 18 males and 17 females patients with ratio of male: female (1.06:1). Age of patients was ranged from 3 months up to 12 years with the mean age of 7 years. There was 12 patients < 4 years age, 7 males and 5 females, 14 patients between 4-8 years age, 8 were females and 6 males and 9 patients from 9-14 years age, 5 were males and 4 females.(Table 1)

Table (1): Age and sex distribution of pediatric cancer

Age/years	F	%	M	%	Total
< 4	5	14.3	7	20.0	12
4-8	8	22.9	6	17.1	14
9-12	4	11.4	5	14.3	9
Total	17	48.6	18	51.4	35

The age and sex distribution in relation to pediatric cancer cases in our study is shown in fig. 1 & 2

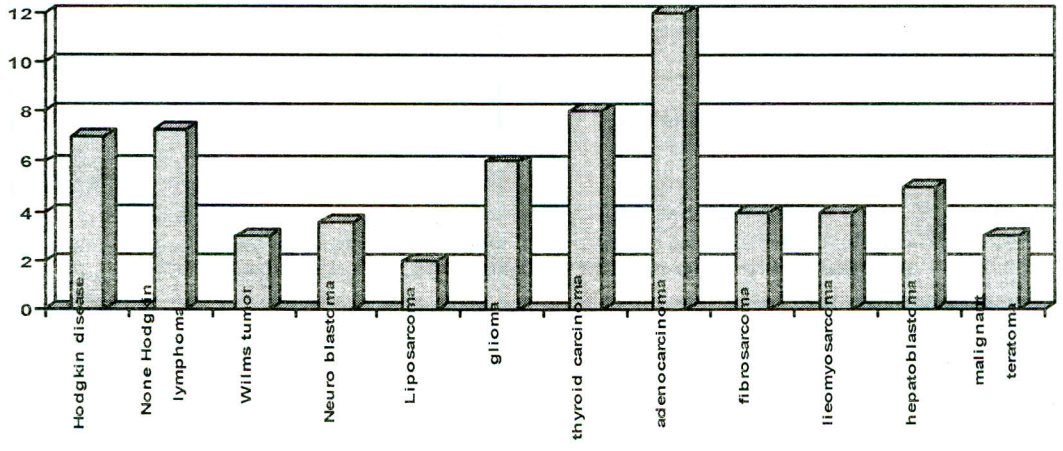

Fig. (1): Distribution of age in relation to pediatric cancer

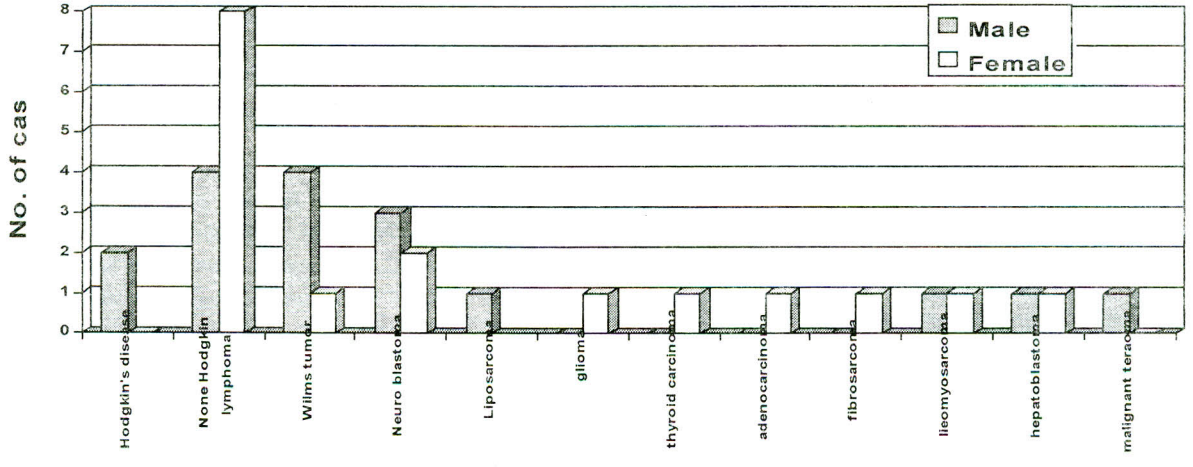

Fig. (2): Sex distribution of pediatric cancer

Most of patients were from Al-Najaf governorate. 18 of patients were from rural areas, 17 from urban areas. as shone in table (2)

Table (2): Distribution of pediatric cancer in relation to their residence

Cancer type	Rural	Urban	Total
Lymphoma (HD) and (NHL)	9	5	14
Wilms tumor	1	4	5
Neuroblastoma	3	2	5
hepatoblastoma	1	1	2
Malignant teratoma	0	1	1
Liposarcoma	1	0	1
Congenital fibrosarcoma	0	1	1
Adenocarcinoma	1	0	1
Glioma	1	0	1
Retinoblastoma	1	0	1
Lieomyosarcoma	0	2	2
Papillary thyroid carcinoma	0	1	1
Total	18	17	35

The three most common malignancies accounting for (68.6%) of the total cases are shown in fig. (3). Lymphoma (40%) (n=14), Wilms tumor (14.3%) (n=5) and neuroblasotma (14.3%) (n=5).

The patients had been complaining from different signs and symptoms which made them seeking for medical treatment as shown in table (3).

Table (3): Clinical presentation of pediatric cancer

Type of cancer	No. of cases		Clinical presentation
None Hodgkin lymphoma	12	3	Acute appendicitis
		5	Abdominal mass
		4	Others (Abd. Pain, weight loss, malabsorption)
Hodgkin's disease	2		Cervical mass
Wilms tumor	5	4	Flank mass
		1	Haematuria
Neuroblastoma	5	2	Lion mass
		1	Ascites
		2	Abdominal mass
Hepatblastoma	2		Hepatic mass
Liposarcoma	1		Anal mass (obstructing the anal canal)
fibrosarcoma	1		Huge pelvic mass (up to epigastric level)
Adenocarcinoma	1		Bleeding per rectum
Lieomyosarcoma	2	1	Haematuria
		1	Melena
Glioma	1		Headache + right side hemi paresis
Retinoblastoma	1		Proptosis of eye

Malignant teratoma	1		Coccygeal mass
Thyroid papillary carcinoma	1		Solitary thyroid nodule + single lymph node enlargement

The most common 4 sites involved in pediatric malignant tumors were intestine (37.14%) (n=13), kidney (14.3%) (n=5), liver (5.7%) (n=2), neck (8.6%) (n=3) adrenals (14.3%) (n-5) as shown in table (4).

Table (4): Distribution of pediatric cancer according to the sites involved

Site involved	No. of cases	%	Final histopathological diagnosis
Intestine	13	37.1	12 Non- Hodgkin's Lymphoma 1 adenocarcinoma
Kidney	5	14.3	Wilm's tumor
Liver	2	5.7	Hepatoblastoma
Retina	1	2.9	1 retinoblastoma
Neck	3	8.6	2 Hodgkin disease 1 papillary thyroid carcinoma
Adrenals	5	14.3	Neuroblastoma
Stomach	1	2.9	Lieomyosarcoma
Coccyx	1	2.9	Malignant teratoma
Brain	1	2.9	Glioma
Pelvis	1	2.9	fibrosarcoma
Urinary bladder	1	2.9	Lieomyosarcoma
Anal canal	1	2.9	Liposarcoma

There was much variation in the histopathological results of the cancer cases ranging from low grade (well differentiated) to high grade (poor differentiated), one as shown in table (5). The majority of these tumors were reported as intermidate or high grade histopathologicaly.

Table (5): Histopathological grading of pediatric malignancies

Cancer type	No. of cases		Histopathological notes
Non Hodgkin lymphoma	12	1	low grade (well differentiated)
		9	intermediate grade
		2	high grade (poorly diffrenetiated)
Hodgkin's disease	2	1	Mixed type
		1	Nodular sclerosis
Wilms tumor	5	3	Intermediate grade
		2	High grade
Neuroblastoma	5		High grade
Hepatoblastoma	2		High grade
Liposarcoma	1		Mixed round cell & well differentiated
Adenocarcinoma	1		Well differentiated

Fibrosarcoma	1	High grade
Lieomyosarcoma	2	Intermediate grade
Glioma	1	Low grade
Retinoblastoma	1	High grade
Malignant teratoma	1	High grade
Thyroid papillary ca.	1	Low grade

All of the collected cases had been operated upon. Different type of surgical therapy had been adopted ranging from complete resection of the tumor, Debulking (palliative) operation and some of cases only incisional biopsy was taken because of their inoperability as shown in table (6).

Table (6): Operations that had been applied for pediatric cancer

Cancer type	No. of cases		Type of operation
Intestinal lymphoma	12	7	Resection of the mass
		5	In-operable (involved large segment)
Hodgkin's disease	2		Excisional biopsy
Wilms tumor	5		Nephrectomy
Neuroblastoma	5	2	Excision of the mass
		3	Inoperable (incisional biopsy)
Hepatoblastoma	2		Inoperable (incisional biopsy)
Fibrosarcoma	1		Inoperable (incisional biopsy)
Liposarcoma	1		Debulking operation (palliative)
Adenocarcinoma	1		Abdominoperineal resection
Lieomyosarcoma	2	1	Partial gastrectomy
		1	Partial cystectomy
Glioma	1		Incisional biopsy
Papillary thyroid carcinoma	1		Total lobectomy (right lobe + isthmus)
Retinoblastoma	1		Excisional biopsy
Teratoma	1		Excisional biopsy

The above table shows that the majority of these tumors (about 65% of cases) could be resected radically or palliatively at time of presentation. In the remaining cases only incisional biopsy was done.

Discussion

The number of patients reviewed in this study was (35) over a period of 2 years and to our knowledge there was no similar published study in Najaf governate

The age distribution of cases reveals that patients between 4-8 years has consistently accounted for (40%) of the total cases over the years. This is due mainly to the number of cases of lymphoma in this age group. These are comparable to other study, James G.et al[23] which showed the age of peak cancer incidence among children occurred during the 1st year of life, other study, Young JL et al [24] showed a peak age incidence 2-5 years.

Hepatoblastoma is similar to neuroblastoma, retinoblastoma and Wilm's tumor (nephroblastoma) in that it is an embryonal malignancy with the age of peak incidence occurring during very early childhood. Lymphomas are extremely rare in infant, Ashcraft KW study[25]. This is similar to our study.

M:F ratio for whole cases was (1.06:1). The male to female ratios of incidence rates for selected cancer types are illustrated in figure (2). None of the sex differences were very pronounced.

The three most common malignancies of pediatric age group in this study were lymphoma, neuroblastoma and Wilms tumor with incidence rate of (40%, 14.3%, 14.3%) respectively in comparison with other study[24] where leukaemia accounted for 25-30% and the CNS for 20-25% of these tumor. The next most common category is the lymphoma which comprise 10-15% of childhood cancer. Neuroblastoma and Wilms tumor each account for 8% of all childhood malignancies.[25]

Other study showed that the 5 most common tumor are leukaemia made up (26.2%), lymphoma (31.3%) and CNS tumor (15%), soft tissue sarcoma (9%) and eye tumor (7%)..[24]

(51.4%) of the patients came from rural area and (48.6%) from urban area. So there is no pronounced difference of cancer distribution according to their residence. This may be due to increase in the socioeconomic state of rural areas and irradication of special type of diseases associated with malignancy such as malaria, which is associated with Burkitt lymphoma. .[24]

In our study the histopathological grading of the tumors reveals that most of them were either intermediate or high grade while only few cases were low grade malignancy. This is may be due to the unique genetic and epidemiologic characteristics of cancer in infants, so in young children particularly infants the aberrant genetic processes that fail safeguard against the clonal proliferation of cells with an unregarded growth potential occur very early in life and progress very quick according to Grans SL study .[20]

All of the patients were admitted to hospital either as an emergency or elective clinical cases and had been subjected to a variable types of operations ranging from complete surgical resection of malignancy to only debulking surgery as a palliative therapy in 65% of case in our study. The remaining cases were inoperable with disseminated malignancy, so only incisional biopsy was taken. In other studies resectability rate ranges from 70 – 80 % due to early presentation [25,26] .

In our study 33/35 (94%) of cases needed chemotherapy or radiotherapy post-operatively the only two cases exempted were adenocarcinoma of rectum and papillary thyroid carcinoma. In Gosfeld study [11] and sharma S. study [26] all cases of malignant pediactric tumors were treated by surgery followed by chemotherapy and/or radiotherapy.

Conclusion:

Late presentation of cases was remarkable in this study so public education about early attendance to general practitioner and early referral to pediatric specialist or surgeon will improve the prognosis of pediatric cancer in Najaf province as compared to similar studies else where .[20-23-25] . Improved survival with pediatric malignant tumors has been positively influenced by multidisciplinary cooperative methods using surgery chemotherapy and/or radiotherapy.

Acknowledgement

The author would like to thank the support of Dr. Asaad AL-Janabi (Ph.D Pathology) and Dr. Mohammed H. Al- Dabbagh (M.B.Ch.B.,D.S.) for their great assistance in preparing this paper .

References:

1. *Rockville, HEW, Public health service: Vital statistics of United States, 1975, vol. 2, part B.*
2. *Farber S: the control of cancer in children neophsia in childhood. Twelve annual conference on cancer 1967 university of Texas , Chicago, year book, 1969, pp 321 – 27.*
3. *Kenny LB, Reaman GH; special considerations for the infants with cancer-pizjo P, Poplack D, Editors, principle and practices of pediatric oncology, 3rd edition. Philadelphia, PA: Lippincott–Raven 1997: 343 – 356.*
4. *Gurney JG, Ross JA, Wall DA, Bleyer WA, Severson RK, Robison LL. Infant cancer in the US: histology–specific incidence and trends, 1973 to 1992. J Pediat. Hematol Oncol, 1997; 19: 428-432.*
5. *Murphy SB, Davis LW: Hodgkin's disease and the non Hodgkin's lymphomas in childhood. Semin Oncol. 1: 17, 1974.*
6. *Murphy S. Hustu H, Rivera G, et al: End results of treading children with localize non- Hodgkin lymphoma with a combined modality approach of lessened intensity J. Clin, Oncol. 1: 326, 1983.*
7. *Jenkin R, Anderson J, Chilcote R, et al: The treatment of localized non- Hodgkin lymphoma in children: A report from the children cancer study group-J Clin. Oncol. 2: 88097, 1984.*
8. *Strum SB, Rappaport H: Hodgkin's disease in the first decade of life. Pediatrics 46: 748, 1970.*
9. *Norris DG, Burgert Eo Jr, Cooper HA et al: Hodgkin's disease in childhood. Cancer 1975 36: 21-25,.*
10. *Garaventa A, Bernardi B, Piarica C, Don Francesco A. for the Italian co-operative group for neuroblastoma. Localized but unresectable neuroblastoma: treatment and out-come of 145 cases. J. Clin. Oncol. 1993; 11: 1770.*
11. *Grosfeld JL. Risk-based management current concepts of treating malignant solid tumors of childhood. J. Am. Coll. Surg. 1999, 189, 407.*
12. *Shimada H. et al. International neuroblastoma pathology classification for prognostic evaluation of patients with peripheral neuroiblastic tumors a report from the children's cancer group. Cancer 2001; 92;2451.*
13. *Nitschke, R; Cangir A, Crist W, Berry DH. Intensive chemotherapy for metastasis neuroblastoma: a sowth west oncology group study. Med. Pediatr. Oncol. 1980; 8: 281-288.*
14. *Green DM, Tarbell NJ, Shamberyer J. Solid tumors of childhood in Derita VT, Hellman S, Rosenberg SA editors. Principles and practice of oncology, 5th Ed., Philadelphia: Lippincott-Raven; 1997: P. 2099.*

15. Tapper D, Lack EE, Teratomas in infancy and childhood: a 54-year experinetal at the children hospital medical center. Ann surg., 1983; 198: 398-410.
16. Ein SH, Mancer K, Adeyemi SD, malignant sacro coccygeal teratoma endodermal Sinus, Yolk sac tumor in infants and children: a 32-year review J. Pediatr. Surg. 1985; 20: 473-7.
17. Schropp KP, Lobe TE, Rao B, et al. Sacrococcygeal teratoma: The experience of four decades, J. Pediatr. Surg. 1992; 27: 1075-9.
18. Altman RP, Randolph, Lilly TR. Sacrococcygeal, teratoma: American Academy of Pediatric surgical section survey-1973. J. Pediatr. Surg.1974; 9: 389-98.
19. Carney JA, Thompson DP, Johnson CL, et al. Teratoma in children clinical and pathological aspect J. Pediatr. Surg. 1972; 7: 271-81.
20. Gans SL, Grosfelf Jay L: Current concept of pediatric oncology, seminars in pediatric surgery, 1993; 2(1): 1-82.
21. Aschraft KW, Holder TM. Ped. Surgery, 2nd edition. Philadelphia W-B Saunders company, 1993.
22. Grosfeld JL, Common problems in pediatric surgery. 1st edition. ST Louis-Mosby year book, 1991.
23. James G, Gurney, Malcolm A, Smith, Julic A, Ross carcinoma among infant; 1997: 148-156.
24. Young JL, Miller RW: Incidence of malignant tumors in U.S children. J. Pediatr., 1975; 86: 254.
25. Ashcraft K.W . Murphy J.P, Sharp R.J and Sigalet D.L.(2001) Pediatric Surgery ,3rd .ed W.B Saunders , Philadelphia .
26. Sharma S. Mishra K. , Khanna G. , Solid tumors of childhood , the Indian J. of pediatrics , 2004, V.71, I. 6, P 501-504.