

BENHAZI UNIVERSITY – FACULTY OF MEDICINE
DEPARTMENT OF PEDIATRIC



Current Status of Childhood Malignancies in Hematology

Oncology Department at Children Hospital- Benghazi

دراسة الوضع الحالي لأورام الاطفال بقسم امراض الدم بمستشفى الأطفال- بنغازي

Prepared by: - Dr. Hameda. A .Altoboli.MBBCh.

Supervised by: - prof. Amina Beayou / MSc, MD.

This presentation is submitted in partial fulfillment of the
requirement for the degree of Master in pediatrics

Benghazi -2013

Acknowledgement

In the name of God Most Merciful Most
compassionate

I sincerely wish to show my gratitude and
appreciation to supervisor prof. AMINA BEAYOU
for her great support guidance and patients over
the period of this research.

Thanks also to my father, my husband and sisters for
their moral support and encouragement during the
course of this study.

I would also like to express my thanks to all staff in
Hematology Oncology Unit

Dedication

To my, brother, Husband, Sisters, and kids

CONTENTS

1. Summary -----	1
2. Introduction -----	3
3. Literature Review-----	5
3-1. <u>Leukemia</u> -----	9
3-2. <u>Brain tumors</u> -----	11
3-3. <u>Lymphomas</u> -----	12
3-4. <u>Renal tumors</u> -----	13
3-5. <u>neuroblastoma</u> -----	14
3-6. <u>Bone tumors</u> -----	15
3-7. <u>Retinoblastoma.</u> -----	16
3-8. <u>Hepatic tumors</u> -----	16
3-9. <u>soft tissues sarcomas</u> -----	16
3-10. <u>Germ cell tumors</u> -----	18
3-11. <u>Nasopharyngeal carcinoma</u> -----	18
4. Aim of the study -----	19
5. Patients and Methods -----	20
6. Results -----	21
7. Discussion -----	38
8. Conclusion -----	43
9. Recommendation -----	44
10. References -----	45
11. Arabic Summary-----	51

T A B L E S L I S T

Table-1: Distribution of malignancies by residence of patients -----	
-----24	
Table -2: Distribution of malignancies according to patients gender-----	
-----27	
Table -3 : Distribution of patients according to type of malignancy and age---	
-----30	
Table -4 : Distribution of patients according to types of leukemia-----	
-----31	
Table-5:Distribution of leukemia patients according to stage of treatment----	
-----32	
Table -6 : Distribution of the lymphoma patients according to it`s types-----	
-----33	
Table -7 : Distribution of CNS tumors according to histopathology-----	
-----34	
Table -8 : Distribution of the patients by sites of malignancy-----	
-----36	
Table -9:Distribution of the patients by stages of malignancy-----	
-----37	

FIGURES LIST

Graph 1: Distribution of the patients(n=315) according to treatment status---	
-----	-21
Graph -2: Distribution of children according types of malignancies-----	
-----	-23
Graph- 3: Distribution of patients according to gender-----	
-----	-25
Graph- 4: Distribution of patients according to age-----	
-----	-28

A B B R E V I A T I O N

ICCC.....	International classification of childhood cancer .
ACCIS.....	Automated childhood cancer information system.
AIRTUM.....	The italian association of cancer registries.
EUROCARE.....	European cancer registry.
AIEOP.....	Associazione Italiana Ematologia Oncologia Pediatrica.
APC.....	Annual percentage change.
ALL.....	Acute lymphocytic leukemia.
ML.....	Myeloid leukemia.
CML.....	Chronic myeloid leukemia.
AML.....	Acute myeloid leukemia.
HL.....	Hodgkin lymphoma.
NHL.....	Non Hodgkin lymphoma.
SNS.....	Sympathetic nervous system.
RMS.....	Rhabdomyosarcoma.
SEER.....	Surveillance ,Epidemiology ,and End results program
CNS.....	Central nervous system.
PNET.....	Primitive neuroectodermal tumor.

1. S U M M A R Y

Objective: - The objective of this study is to have over view about the clinical and demographic profile of 315 child with malignant tumors at children hospital Benghazi which serves all the Eastern part of Libya as well as part of the south. All children with cancer, aged 0 – 15 years diagnosed by means of histological or cytological examination registered to this institute and still coming up to last time of data collection (august -2013) either to the department for treatments or clinic for follow up were included in this study.

.

Patients and Methods: - The study has two sections, one involve 161 child who are still active in chemotherapy in the Hematology Oncology Department. The second section presents children who had finished their chemotherapy and coming for follow up in the Hematology Oncology Clinic.

Exclusion criteria: Deaths as well as those patients who finished their chemotherapy and did not come for follow up for more than one year.

This study was a descriptive case study. The data was gathered retrospectively and classified according to all types of cancers, from the patients' charts using a designed Performa. The following data was collected; patients' Demographics: gender, date of birth, and admission, residence and investigations (complete blood count, bone marrow, result of histopathology) sites as well as the stages of the disease which were performed at time of their diagnosis also included.

Result: A total of (315) patients with malignancy, from them 161 child (52 %) are still taking chemotherapy. Forty five percent from total malignancy were leukemia, followed by lymphoma (16%).

One hundred fifty one (48%) were from Benghazi and (65%) from them had leukemia. Sixty six percent of solid tumor were from outside Benghazi .In general Male to Female ratio 1.3:1, while in lymphoma males outnumbered females giving M:F ratio 4.4:1. In contrast to retinoblastoma and germ cell tumors where M: F ratio 1:1.5 and 1:2 respectively.

Eighty two percent of them less than 10 years of age, 134 (42%) between 1-4 years, only 2 patients were 15 years old.The highest age group was in bone and germ cell tumors with median of 11.5 years.

Eighty three percent of leukemias were acute lymphoblastic leukemia.Only one case of chronic myeloid leukemia (0.7%).Near half of the patient (48%) were in the last stage of treatment (maintenance).Fifty seven percent of lymphoma was Hodgkin lymphoma. Thirty six percent of brain tumor was medulloblastoma followed by astrocytoma(20%).

Most of the tumor arise from abdomen 72 (42%) among them 47/72 were wilm`s tumors, seventy eight percent (78%) of neuroblastoma cases arise in the abdomen, 35/69 of head and neck tumors were lymphomas with (20/35) were Hodgkin lymphoma. Majority of lymphoma and wilm`s tumors (2/3) patients presented at stage III while near two third of neuroblastoma patients (60 %) came at stage IV.

Conclusion: Near half of the malignancy was leukemia , more than half of patients were from outside Benghazi, most of solid tumor were from sub urban and rural areas. Most of solid tumors patients presented at late stages.

Recommendation: Education of the population about the malignancy for early detection by those responsible for the education of health professionals, patients and family educator, caregivers,and the public cancer education. Establishment of national registry of childhood malignancy should be developed for conducting farther studies in the whole country.

2.INTRODUCTION

Cancer is relatively rare in childhood, with around 1 in 500 child developing some form of cancer by 14 years of age. This equates to just under 140 cases per million child. Each year around 1500 child are diagnosed with cancer in the UK, accounting for just 0.5% of the total cancers diagnosed in all ages. The International Classification of Childhood Cancer (ICCC) divides these cancers into 12 diagnostic groups, with further subgroups and divisions.¹

The incidence of cancer is higher in boys than girls (ratio of around 1.2: 1.0), and in both sexes the highest overall rates occur in the under five, though CNS tumors' had the greatest variation in incidence.²

They differ markedly from adult cancers in their nature, distribution and prognosis. The patterns of childhood cancers in America and Europe are almost the same, with leukemia and central nervous system tumors accounting for over one-half of the new cases. In contrast, lymphoma is the most common prevailing cancer of this age group in Africa.³

Very little is known about the causes of most childhood cancers. Several rare genetic syndromes, such as Down syndrome, Fanconi anemia and Li-Fraumeni syndrome, are associated with an increased risk of certain cancers in childhood. Some cancers occur when genes are altered during the early stages of a child's development. There is also evidence that some childhood leukemias may develop after an abnormal response to infection early in life.⁴

Near the last four decades there have been major advances in the development of successful treatment strategies for childhood cancers. For every ten children

diagnosed with cancer, almost eight now survive for five years or more, compared with fewer than three in ten in the late 1960s. Retinoblastoma has the highest

survival rate of any childhood cancer, with 99% of children being cured, and Hodgkin's disease is 95%.⁵

There are estimated to be around 26,000 childhood cancer survivors alive in Great Britain. Most long-term survivors are cured of their cancer, though intensive treatments mean that some experience higher death rates, or have increased risks of a range of physical, psychological and social health problems, compared to the general population.⁶

Although cancer is rare in childhood, it is the most common cause of death from disease in children aged 1-14 years and accounts for just under a fifth of all deaths in this age group. Each year almost 300 child die from cancer in the UK. Brain and CNS tumors are the most common cause of cancer death, accounting for around a third of all cancer deaths in childhood. Leukemias account for a slightly lower proportion of cancer deaths and tumors of the sympathetic nervous system account for around a tenth.⁷

This study was conducted in Hematology Oncology Department and Clinic at Children Hospital in Benghazi City, the second city in Libya located in the north east. This Hospital is a referral center; it serves all the eastern part of Libya as well as part of the south. The department capacity is 30 bed, with around 800 child registered in the department and clinic (with different hematology and oncology problem). Patients enrolled in this study (315) either still taking chemotherapy in the department (161) or finished their treatment (154) and came for follow up.

So we conduct this study to have over view bout clinical and demographic profile of 315 child aged from 0 – 15 years diagnosed by means of histological or cytological examination registered to this Institute.

3.LITERATURE REVIEW

Worldwide the annual number of new cases of childhood cancer increase, with more is increasing by 1.1% every year in Europe, but the rate of change as well as the direction is different for individual cancer types. The incidence of CNS tumors is increasing by 1.7%, lymphomas by 0.9%, and leukemias by 0.6%. On the other hand the incidence of bone tumors, liver tumors, and retinoblastoma is unchanged. Part of these increases can be explained by changes in diagnostic methods and registration practices, but other environmental and lifestyle factors may have a role.^{8,9}

A retrospective study of childhood malignancy at Olabisi Onabanjo University Teaching Hospital, Sagamu, Nigeria, during an 11-year period, from January 1996 to December 2006, showed that, out of 77 children were diagnosed with malignant tumors (an average of seven diagnoses per year); 46 were boys (60%), giving a male-to-female ratio of 1.5 : 1. The age distribution of patients was 1-18 years. There were 42 diagnoses (55%) in the 1-5-year age group and 68 malignancies (88%) were diagnosed at ages of 12 years or younger. Lymphomas were the most prevalent malignancy identified, accounting for 31 diagnoses (40%). Burkett's lymphoma constituted the majority of malignancies (28 cases; 36%), followed by retinoblastoma (16 cases; 21%) and nephroblastoma (11 cases; 14%). Other malignancies included germ cell tumors (6), neuroblastomas (4), osteosarcomas (3), rhabdomyosarcomas (3) and non-Hodgkin's lymphomas (3). One case each of medullary thyroid carcinoma, adenocarcinoma of the rectum, invasive mucinous carcinoma of the colon was also identified.

They concluded that Burkett's lymphoma is the most common childhood malignant tumor. With the rising incidence of childhood malignancy in resource-poor countries.¹⁰

In another study done at institute for Medical Biostatistics, Epidemiology and Informatics, University of Mainz, Germany 2000. They reports childhood cancer incidence and survival rates as well as time trends and geographical variation. They use Automated Childhood Cancer Information System (ACCIS) and EUROCORE, according to these data, which refer to the International Classification of Childhood Cancer, they found that leukemias at 34%, brain tumors at 23%, and lymphomas at 12%, represent the largest diagnostic groups among the under 15 year olds .The most frequent single diagnoses are: acute lymphoblastic leukemia, astrocytoma, neuroblastoma, non-Hodgkin lymphoma, and nephroblastoma. There is considerable variation between countries. Incidence rates range from 130 (British Isles) to 160 cases (Scandinavian countries) per million children. Incidence rates have shown an increase over time since the mid of the last century. In Europe, the yearly increase averages 1.1% and ranges from 0.6% for the leukemias to 1.8% for soft-tissue sarcomas. The probability of survival has risen considerably over the past decades, with the EUROCORE data showing an improvement of the relative risk of death by 8% when comparing the 2000-2002 time spans to the 1995-1999 periods. Regarding the years 1995-2002, the data show an overall 5-year survival probability of 81% for Europe and similar values for the USA.¹¹

A 3rd study done on the cancer incidence and survival in Italian pediatric and adolescent patients in the period 2003-2008. The study based on data collected by the network of Italian cancer registries (AIRTUM). Data covering 47% of the Italian population below age 20 years. In this period, 31 cancer registries reported 4,473 incident malignant neoplasm, 2,855 in children and 1,618 in adolescents. Cancer incidence rates were 164 cases per million in children aged 14 years or below and 269 cases per million in patients aged 15-19 years. Limited geographical variations emerged. In children (0-14 years) a significant increase in malignant cancer incidence was observed until 1997 (APC: +3.2%), followed by a plateau (APC: -1.1% not

statistically significant). Until the late nineties, a statistically significant increase was also observed in the incidence of all leukemia's in males (APC: +5.7%), lymphoid leukemia's (APC: +5.6%), representing 80% of all leukemias, Hodgkin and non-Hodgkin lymphomas (APC: +6.3%). A significant decrease emerged for lymphoid leukemia starting in 1995 (APC: -1.9%), while no substantial change in cancer incidence rates was observed in the last decade of observation for all malignant tumors and lymphomas. In addition, no variation emerged for malignant (according to the most recent classification) central nervous system (CNS) tumors, while an annual increase of 1.8% (significant) was observed in the period 1988-2008, when non-malignant tumors were included. Increases in cancer incidence were observed throughout the study period for neuroblastoma (APC: +1.9%) and epithelial tumors or melanoma (APC: +4.1%). In the period 1998-2008, in addition to lymphoid leukemia's, a significant decrease was observed for all malignant neoplasm, lymphomas in girls, CNS tumors (males and females), and renal tumors in girls, while no increases were observed in this age group. Cancer mortality in children showed a persistent decrease for all neoplasm and even for more frequent cancer sites or types, and mortality rates for cancer were three-fold higher in the early Seventies than in 2008. In addition, five-year survival after cancer diagnosis increased in the last three decades and was still increasing in the period 2003- 2008, reaching 82% in children and 86% in adolescents. In the period 2008-2010, 4,488 children (0-14 years) were treated in one of the AIEOP clinical centers and we estimate, based on the above-presented incidence rates, that they represented 92% of all cancer cases in Italy. The expected number of cancer cases in children aged between 0 and 14 years of age is approximately 7,000 in the period 2016- 2020, while the corresponding figure for adolescents between 15 and 19 years of age is 4,000, with no relevant variation in comparison with the previous five-year period.¹²

A 4th study done in Gezira State, Central Sudan 2003-2008. It is a retrospective study to determine the patterns of childhood cancers in Gezira State, Central Sudan

using hospital records. All children with cancer, aged 1 – 15 years diagnosed by means of histological or cytological examination admitted to the Institute of Nuclear Medicine, Molecular Biology and Oncology from May 2003 – December 2008 were included in the study.

The results showed a pattern of childhood lymphoma as the most common cancer (42.8%) followed by acute lymphoblastic leukemia (19.8%) and kidney tumor (12.8%). The prevalence of cancer was found to be higher among boys (64.7%) than girls (35.3%) with a rate of 1.8:1. Most of the children admitted with cancer were from rural areas (66.1%) compared to (33.9%) from urban areas. With Conclusion: Lymphoma, acute lymphoblastic leukemia and bone tumor commonly occurred in children above 5 years in contradistinction to kidney tumor and retinoblastoma which was prevalent in children less than 5 years of age.¹³

Study done in Trinidad and Tobago from the period 2001-2006, with age from 0-14 years .The data were extracted from the National Cancer Registry of Trinidad and Tobago and the Eric Williams Medical Sciences Complex: The crude incidence rate of childhood cancer was 1.9 per 100 000 patient years. One hundred and forty-five cases were reviewed for the six-year period with an incidence rate of 7.5 per 100 000. The highest incidence was in children < 5 years: 14 per 100 000 per year for males and 11.4 per 100 000 per year for females.

Leukemia and central nervous system tumors formed the majority of the cancers (58.6%), however nephroblastoma was more common than neuroblastoma especially in females < 5 years: 2.7 per 100 000patients / yr. compared with 1.2 per 100 000 patients / year for neuroblastoma. The incidence of all childhood cancers did not vary across counties; however, there was a higher incidence of leukemia in three counties.

Conclusion: childhood cancer is lower than in developed countries. There are some unique findings in the incidence of nephroblastoma in girls less than five years of age and the relatively higher incidence of leukemia in three counties¹⁴

A study done in Aga Khan university- Karachi in 2006. This study is based on the data of Karachi South published in the Cancer Incidence in the Five Continents. They found that the pattern of childhood malignancies in Karachi is predictable, with the lymphoid and hematopoietic malignancies forming the most common diagnostic group, tumors of the eye and brain forming the second diagnostic group and tumors of the bones forming the third most common malignancy in both genders. Subsequently mesothelial and soft tissue tumors, oral cavity and pharynx, urinary tract, digestive organs and thyroid and endocrine malignancies formed the descending list of malignancies in males .Oral cavity and pharynx are atypical inclusions as childhood malignancies and reflect the high prevalence of associated risk factors. In females, malignancies of the genital system, mesothelial and soft tissue tumors, skin, thyroid and endocrine malignancies and malignancies of the respiratory tract formed the hierarchical descending list of tumors.¹⁵

3-1: Leukemias: Leukemias are the most commonly diagnosed cancer in children, accounting for around a third (31%) of all cases. Incidence peaks in boys and girls at the ages of two to three years respectively, and subsequently decreases with age thereafter. Acute lymphoblastic leukemia (ALL) is the most common type of childhood leukemia by far myeloid leukemia was predominantly observed in the older childhood age groups.¹⁶

A study done in Oncology Department of Allama Iqbal Medical College-Lahore, from July 2006 to June2008 . A retrospective analysis of 1000 cancer patients were seen of whom 115 (11%) were children (under 15 years age). The commonest childhood malignancy was leukemia accounting for (54%) or 62 cases. Second commonest was non-Hodgkin lymphoma (16%), 82% were acute lymphoblastic leukemia, 16% were acute myeloid leukemia, with a single rare case of chronic myeloid leukemia. Fifty one cases of acute lymphoblastic leukemia were seen

ranging in age from 2.5 to 15 years (mean age 8.1 years). A significant peak occurred at 2.5-5 years. ALL showed predominance for boys with a male to female ratio of 1.6:1. Majority (66%) of patients belonged to middle socioeconomic group followed by low socioeconomic status (28%), 6% patients were from the high socioeconomic status. Eight patients gave history of prolonged exposure to pesticides. No clustering of leukemic cases was seen within the family. The duration of symptoms ranged from 10 days to 6 years with a mean duration of 165 days (or 5.5 months). Fifty six percent patients belonged to the performance status I and II (as defined by the WHO criteria) on presentation, 44% to performance status III and IV. The commonest complaint was fever (79%), followed by bone pains (67%) and weight loss/malaise (40%). Almost half of the patients (47%) had bleeding diathesis on presentation, 58% had hepatomegaly and 60% splenomegaly. Lymphadenopathy was present in 66% of cases, majority (87%) their patients had received no prior chemotherapy or radiation, 11% received chemotherapy in another institution and one patient had chemotherapy, radiotherapy and bone marrow transplantation earlier. Ten patients (16%) had acute myeloid leukemia. The male to female ratio was 2:1 and (78%) belonged to middle class and (22%) to low socioeconomic status, their age ranged from 3-15 years with a mean of 10.6 years and a median of 10 years. The small number of patients did not allow determination of peak age distribution. The duration of symptoms prior to presentation ranged from 20 days to 10 months with an average of 5 months. No patient had an obvious history of exposure to chemicals or radiation and had been healthy prior to the present illness. On presentation, (51%) of patients had a performance status of I or II and (49%) of III and IV. The main complaints were fever (67%) followed by weakness, malaise, weight loss, bleeding and pallor, all of which were equally frequent (33% in each category) and 67% had bleeding problems on admission. A smaller number of patients had hepatomegaly (22%) and splenomegaly (33%) as compared to patients of ALL. Lymphadenopathy was seen in (32%) of cases; 78% of patients had no previous therapy whereas 22% had received chemotherapy earlier.¹⁷

3-2: Brain Tumors: Intracranial and spinal cord tumors are the second most frequent type of childhood cancer after leukemia, accounting for around 20% of cases in many regions of the world, yet there have been few studies of their incidence by histological type and sub site.¹⁸

A study done in Department of Pediatrics, University of Oxford, UK 2000.

Age-specific and age-adjusted incidence rates were calculated from data in the study, (International Incidence of Childhood Cancer, coordinated by the International Agency for Research on Cancer). They found : the highest age-adjusted incidence, 31.4 per million, was observed in the Nordic countries, and rates between 24 and 27 per million were found in most other predominantly white Caucasian populations. In the US, black children had a significantly lower incidence (21.7) than whites (26.4). Lower rates were seen in South America, Africa and Asia, the lowest being those for Chinese populations, and for blacks in Africa, both below 15 per million. Among white populations, astrocytomas were the commonest histological type, often with an incidence of at least 10 per million, followed by medulloblastomas, 5-6 per million, and ependymomas, 2-4 per million. In other regions with lower incidence rates, these three types accounted for similar proportions of the total. Black children in the US had a higher incidence of craniopharyngiomas than whites and there was an unusually high incidence of pineal tumors in Japan, 0.9 per million compared with 0.3-0.4 in many other countries.

They concluded that, the low recorded total incidence in developing countries may be partly due to under ascertainment. Differences in total incidence or in relative frequencies of particular histological types between Western countries and Japan and between ethnic groups in the US suggest a substantial contribution of genetic predisposition in their etiology.¹⁹

3-3: Lymphomas: Lymphomas are rare before the age of two; incidence increases with age thereafter such that lymphomas account for nearly a fifth (19%) of all childhood cancers. There are lymphoma accounts for around two-fifths (41%) of all lymphomas diagnosed in children. Incidence increases steadily after the age of two until the last few years of childhood, where there is a much sharper increase such that two thirds of all childhood Hodgkin lymphomas are diagnosed in 10–14 year-olds. NHL (excluding Burkett lymphoma) accounts for 44% of lymphomas in children. Incidence of NHL increases sharply in the first few years of childhood and subsequently increases more gradually with age. a six times higher risk in males for Hodgkin's disease and thrice the risk for non-Hodgkin's Lymphoma was observed, with a high peak in the 5-9 year age group.^{20,21}

A study done in Aga Khan University - Karachi in 2006.

The result showed during 1999-2006, as low upward variation in the annual incidence of NHL was observed. The increase in the incidence affected all age groups in both genders. During this period, the mean age of childhood lymphoma was 7.9 years (95% CI 6.3; 9.4) in males and 8.4 years (95% CI 6.1; 10.6) in females. The youngest male patient was 2 years and the youngest female patient was 3 years; the oldest male and female children were 14 and 13 years respectively. The component of childhood NHL was 10.4% and 9.3% in males and females respectively. The adult to childhood ratio (A: C) was 8.6 in males and 10.7 in females.

Children and adolescents were at the highest risk of developing NHL, 0-4 years OR 4.5 (95% CI 0.3; 6.7) in males, 5.4 (95% CI 0.3; 9.8) in females; 5-9 years, OR 8.9 (95% CI 0.2; 12.2) in males, 10.1 (95% CI 0.2; 16.4) in females and 10-14 years, OR 5.0 (95% CI 0.3; 6.7) in males, 5.8 (95% CI 0.3; 8.2) in females.¹⁵

3-4: Renal tumors: Around 6% of childhood cancers are renal tumors and nephroblastoma (Wilms tumor) accounts for 90% of these. It is slightly different to the other principal embryonal tumors in that incidence rates have a slightly later peak in one- to three years old .The majority (90%) of nephroblastomas occur in one kidney only.²²

In University of Oxford, Department of Pediatrics, UK 2000. The International Agency for Research on Cancer has coordinated a worldwide study of childhood cancer incidence, with data from over 50 countries. They represent the results on renal tumors. Wilms' tumor was the most common malignant kidney tumor in all regions. It is sometimes considered to be an 'index cancer of childhood' but it is clear from the present study that there is at least a threefold difference in incidence between the age-standardized annual rates of over 10 per million in the Black populations in the United States and Nigeria and those of around three per million in several East Asian populations. In White Caucasian populations, Wilms' tumor had an annual incidence of 6-9 per million, accounting for 5-7% of all childhood cancer. It was almost everywhere equally common in boys and girls, but the sex ratio in East Asia was M/F = 1.4:1. Age distributions were similar among White Caucasian and Black populations, with the peak incidence in the second year of life. In East Asia, however, 25-40% of the total incidence occurred in infants aged less than 1 year, compared with around 15% in many Western series. Other studies have shown that, in the United States, Wilms' tumor has a lower incidence among Asian children than among Whites or Blacks and tends to occur at a younger age. The variation in patterns of incidence of Wilms' tumor along ethnic rather than geographical lines suggests that genetic predisposition is important in its etiology. Renal carcinoma in childhood is rare throughout the world, with little sign of international variation. It accounted for a higher proportion of childhood renal tumors in East Asia but this was attributable to the lower incidence of Wilms' tumor in that region.²³

3-5: Neuroblastoma: Tumors of the sympathetic nervous system (SNS) account for 6% of childhood cancers overall, and nearly all of this group are neuroblastomas (including ganglioneuroblastomas). Neuroblastoma is one of the principal embryonal tumors and is the most frequently occurring solid tumor in infants under the age of one, accounting for around a fifth (19%) of all cancers diagnosed in this age group. The incidence of neuroblastoma is rare after the age of five .Almost one half (46%) of neuroblastomas develop in the adrenal gland; other abdominal primary sites account for just over one quarter (26%) of cases, and thoracic sites account for 13%.²⁴

In department of Pediatrics, University of Oxford, UK 2000: The International Agency for Research on Cancer has coordinated a worldwide study of childhood cancer incidence, with data from over 50 countries. They present the results for neuroblastoma. In predominantly white Caucasian populations the age-standardized rate was 7-12 per million, and 6-10% of all childhood cancers were neuroblastomas. Rates were highest in the first year of life (25-50 per million, 30% of total neuroblastoma incidence), and decreased with age to 15-20 per million (50% of the total) at age 1-4, 2-4 per million (15%) at 5-9 and 1-1.5 per million (5%) at 10-14. In the United States, black children had an incidence of 8.5 per million compared with 11.5 among Whites; Blacks tended to be older than Whites at diagnosis. The highest rate in Africa was in Bulawayo, Zimbabwe (8.0 per million) and the lowest in West Nile, Uganda, with no cases registered. Incidence in Israel was similar to that in many white populations, with Jews having a particularly high rate. In other parts of West Asia neuroblastoma had a low relative frequency, suggesting that incidence is low. Rates were also low throughout much of southern and eastern Asia, including India and China. Incidence in Japan was somewhat higher, though less than in Western countries, with the deficit most pronounced in the first year of life; these data relate to the period before mass screening of infants for neuroblastoma in the regions concerned. Incidence was generally higher in regions and among ethnic

groups enjoying a higher standard of living, though previous studies within single countries had suggested that neuroblastoma is more common among less affluent groups. Blacks in Africa and the United States may have a weaker genetic predisposition to neuroblastoma, but some of the deficit in many developing countries is likely to be due to under-diagnosis.²⁵

3-6:Bone tumors: Around 4% of childhood cancers are malignant tumors of the bone. Incidence rates are very similar in both sexes and increase steadily with age overall, malignant bone tumors account for around a tenth (9%) of all cancers diagnosed in 10-14 year-olds. The most common types of malignant bone tumors are osteosarcoma (accounting for 55% of cases) and Ewing tumor and related bone sarcomas (39% of cases). Osteosarcoma is extremely rare under the age of three; incidence increases with age thereafter such that over two-thirds (70%) of osteosarcomas are diagnosed in 10-14 year-olds). The vast majority of osteosarcomas are diagnosed in the long bones of the legs (84%) and arms (12%). Ewing tumor and related bone sarcomas are mainly peripheral primitive neuroectodermal tumors(PNETs) of the bone. Tumors' can arise at a variety of sites, the most common being the long bones of the legs (38%) and the pelvis (23%). Incidence peaks in the last few years of childhood, with a male excess in 10-14 year-olds.^{26,27,28.}

3-7:Retinoblastoma:Retinoblastoma is another principal embryonal tumor and accounts for 3% of all cancers diagnosed in children around two-fifths (42%) of cases are diagnosed in the first year of life and incidence rates drop to a very low rate after five years of age, Around two-thirds (63%) of retinoblastoma as are diagnosed in one eyeonly.²⁹

3-8:Hepatic tumors: Tumors of the liver are rare in childhood, with around one child in every million being diagnosed with the condition every year .This group is broadly divided in to hepatoblastoma and hepatic carcinomas, which account for around four-fifths (81%). and one-fifth (18%) of cases, respectively .Hepatoblastomas are the rarest of the four principal embryonal tumors , and are most likely to be diagnosed in children under two.³⁰

3-9: Soft tissue sarcomas : The wide-ranging group of soft tissue sarcomas accounts for 7% of all childhood cancers overall. Incidence is similar in both sexes in early and late childhood, but is markedly higher in boys between the ages of three and eight. Just over half (53%) of all soft tissue sarcomas are rhabdomyosarcoma, which can occur in almost all parts of the body. The incidence of rhabdomyosarcoma is highest in three-year-olds .Ewing and Askin tumors of soft tissue and PNET soft tissue collectively account for 15% of all soft tissue sarcomas. These tumors mainly occur in the trunk (62%), with the remainder being evenly divided between the head and neck and the limbs. Incidence remains fairly constant throughout most of childhood, with just a small increase in the last few years.³¹

Study done in Division of Pediatric Surgery and Division of Surgical Oncology University of Miami Miller School of Medicine, Miami, Florida2003.

The SEER registry was examined for patients with RMS < 20 y old, to examine incidence and outcomes for rhabdomyosarcoma (RMS).They found that;1544 patients were identified for an incidence of 0.4414/100,000 per year. Males outnumbered females 3:2. Tumors were classified as embryonal (67%), alveolar (32%), and pleomorphic (1%). Alveolar and pleomorphic RMS were more common in adolescents, whereas embryonal type was more common in younger children (P = 0.0001).Pleomorphic (47%) and alveolar (39%) RMS commonly presented with

distant disease, in contrast to embryonal (25%). Most patients had surgical resection (81%) and radiotherapy (63%). Overall, 5- and 10-y survival was 60% and 57%, respectively. Univariate analysis identified higher survival for age < 10 y, local stage, favorable site, embryonal type, <5 cm tumor size, and surgical resection. Multivariate analysis identified non-embryonal type (HR 1.451), non-favorable site (HR 1.570), no surgery (HR 1.726), age ≥ 10 y (HR 1.734), 1973–1978 diagnosis year (HR 1.730), and distant disease (HR 3.456) as independent predictors of mortality.

They conclude: Embryonal histology, the most common type of pediatric RMS, presents in young children and has better prognosis than alveolar or pleomorphic types. Patients with embryonal tumors, favorable tumor location, age < 10 y, localized disease, and surgical resection have improved survival.³²

3-10: Germ cell tumors: Gonadal and germ cell tumors account for 3% of all childhood cancers. The pattern by age and sex varies greatly by tumor type. Malignant gonadal germ cell tumors account for 42% of this group; male tumors are most likely to be diagnosed in children less than two years old, with incidence rising again in teenagers, whereas the incidence of female tumors increases with age (Tumors originating within the brain and spine account for more than a third (34%) of all gonadal and germ cell tumors and are more common in older children.³³

3-11:-Nasopharyngeal carcinoma :A retrospective study of sixty-five previously untreated patients younger than 16 years of age diagnosed and treated at the Ibn Rochd Centre in Casablanca between 2001 and 2007. Forty-four percent of them were stage T3 to T4 and 66% stage N2 or N3. All patients were irradiated. Prior adjuvant chemotherapy was administered in 33 patients. Thirteen patients were lost to follow-up five-year overall survival was 42% and disease-free survival 38%. Ten relapses occurred at local and/or regional sites. Six patients have distant metastases. All 24 patients with relapse or persistent disease died despite salvage therapy. Stage,

histology and dose of radiation, were statistically significant prognostic variables. Patients treated with chemotherapy followed by irradiation had a better outcome than those treated with radiation alone. And they conclude: Nasopharyngeal carcinoma in children is a rare chemo sensitive tumor. However, conclusive treatment guidelines cannot drawn from this series and prospective co-operative studies are needed for the development of more effective and less toxic therapeutic strategies.³⁴

4. OBJECTIVE OF THE STUDY

The objective of this study is to have over view about the clinical and demographic profile of 315 child with malignant tumors at children hospital Benghazi which serves all the Eastern part of Libya as well as part of the south. All child with cancer, aged 0 – 15 years diagnosed by means of histological or cytological examination registered to this Institute and still coming up to last time of data collection (august -2013) either to the department for treatments or clinic for follow up were included in this study.

5. PATIENTS AND METHODS

A total of 315 patients with malignancy are registered and followed up at Children Hospital in Benghazi. The study has two sections, one involve 161 child who are still active in chemotherapy in the Hematology Oncology Department. The second section presents children who finish their chemotherapy and coming for follow up in the Hematology Oncology Clinic.

Exclusion criteria: Those Patients who finished their chemotherapy and did not come for follow up in last 1 year as well as deaths.

It is a descriptive case series study .The data was gathered retrospectively and classified according to types and sites of cancer, from the patients' charts using a designed Performa. The following data was collected; patients' Demographics: gender, date of birth, and admission , residence and investigations (complete blood count, bone marrow, result of histopathology) and also stage of the disease which were performed at time of their diagnosis were included.

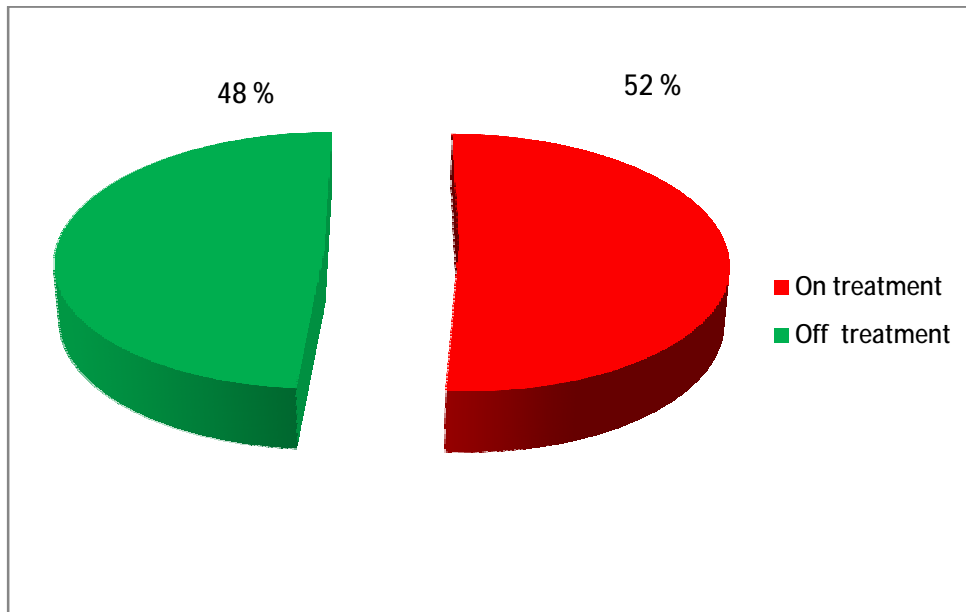
Data analysis: Data was analyzed manually and interpreted in term of percentage, mean and median.

The study period was 8 months, 4 months for data collection and literature review, 4 months for analyzing the data and thesis writing .

6. RESULTS

A total of (315) patients diagnosed with malignancy in Hematology Oncology Department, from them 161 child (52 %) are still taking chemotherapy in the department and the rest of them finished their chemotherapy and came for follow up at the clinic.

Graph (1) below illustrates patients according to treatment status.

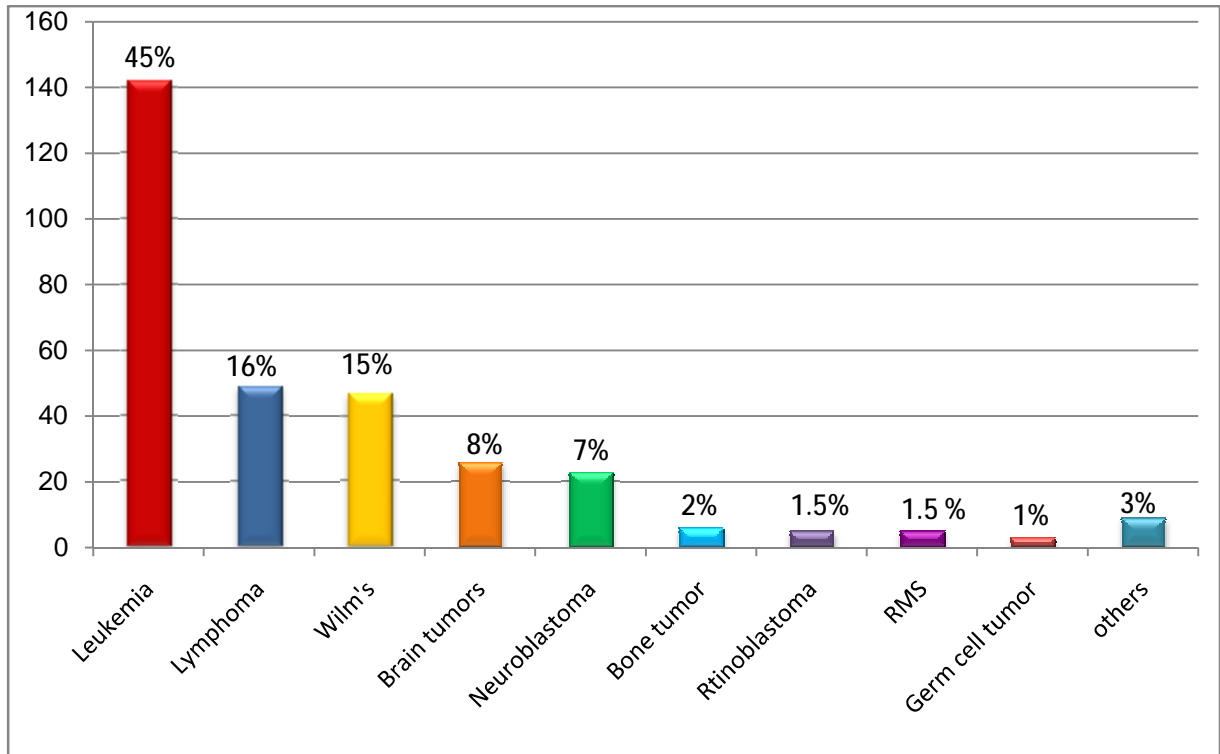


Graph-1: Distribution of children according to treatment status

6-1. Analysis of patients by types of malignancies and their Residence

- Leukemia contribute to 45% of the malignancy, followed by lymphoma and wilm`s tumor, with equal numbers of rhabdomyosarcoma and retinoblastoma cases.
- Urban residence nearly equal to suburban and rural residence with (151) 48% were from Benghazi city.
- In Benghazi the leukemic cases outnumbered the lymphoma and solid tumors cases, with 65% of leukemia were from Benghazi.
- In contrast 66% of solid tumors were from outside Benghazi.

Graph (2) and table (1) below illustrates the distribution of patients according to types of malignancies and residence.



Graph-2: Distribution of children according to types of malignancies

NB: RMS (Rhabdomyosarcoma), others include(hepatoblastoma, adrenal carcinoma, nasopharyngeal carcinoma ,pleuroblastoma).

Table -1: Distribution of malignancies by residence of the patients.

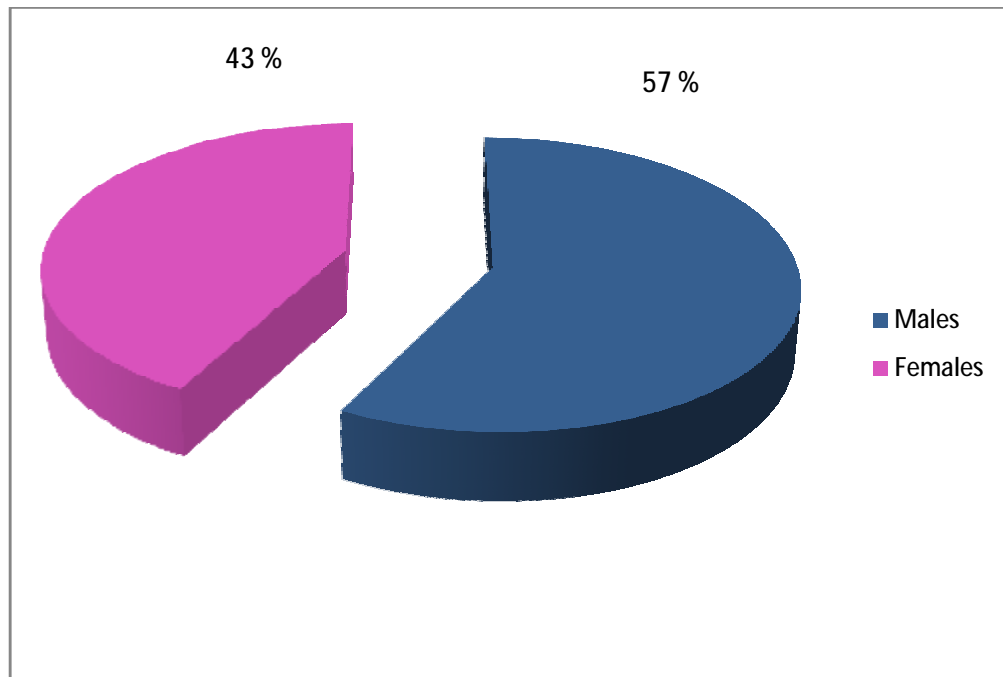
Residence	Type of malignancy				Total	
	Leukemia		Solid tumor			
	No.	%	No.	%	No.	%
Benghazi	93	65	58	34	151	48
East	45	32	88	51	133	42
West	4	3	6	3	10	3
South	0	0	21	12	21	7
Total	142	100	173	100	315	100

6 -2.Demographic Characteristics (n=315)

6-2-1. **Gender:** Males outnumbered females with:

- One hundred eighty two child (57 %) were males.
- Male to Female ratio (1.3:1).

Graph (3) below illustrates the gender of patients included in the study



Graph-3: Distribution of patients according to gender

6-2-2: Analysis of various malignancies according to gender:

- In lymphoma male outnumbered four times the female with M: F ratio 4.4:1.
- The opposite were found in retinoblastoma and germ cell tumors with M:F ratio 1:1.5 and 1:2 respectively

Table (2) below illustrates various malignancies according to gender of patients included in the study

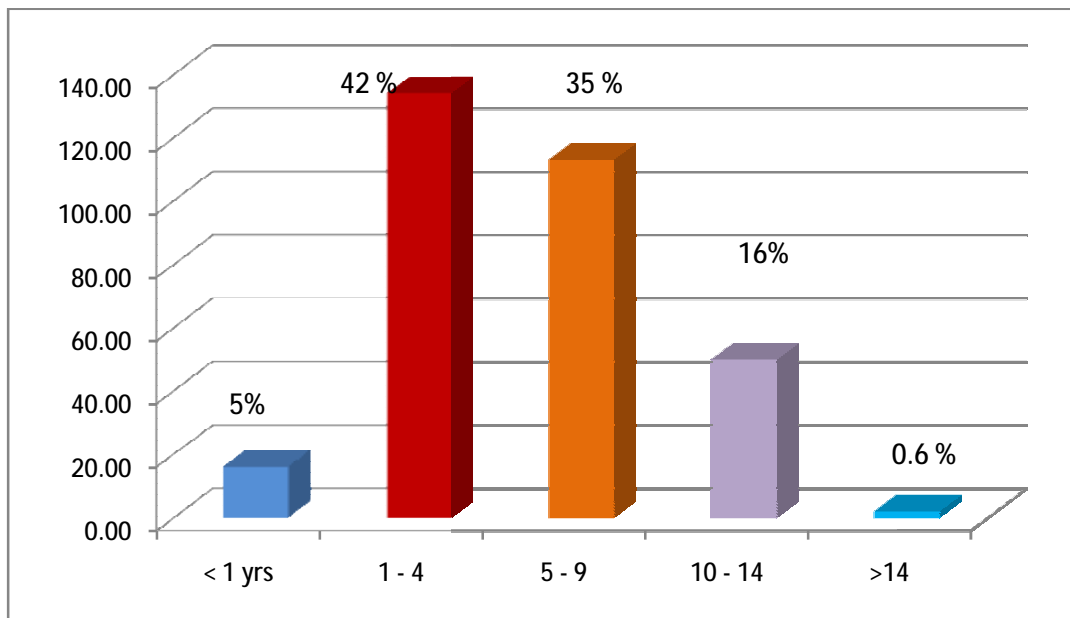
Table -2: Distribution of malignancies according to patients gender

Type of malignancy	Gender		Total		M:F ratio
	Male	Female	No.	%	
Leukemia	78	64	142	45	1.2:1
Lymphoma	38	11	49	16	4.4:1
Wilm`stumor	24	23	47	15	1:1
Brain tumors	13	13	26	8	1:1
Neuroblastoma	13	10	23	7	1.3:1
Bone tumor	4	2	6	2	2:1
Rhabdomyosarcoma	3	2	5	1.5	1.5:1
Retinoblastoma	2	3	5	1.5	1:1.5
Germ cell tumor	1	2	3	1	1:2
Others	5	4	9	3	1:1
Total	182	133	315	100	100

6-2-3. Age:

- Their age ranged from 0-15 years.
- Majority of the patients (82 %) of all childhood cancer diagnosed before 10 years of age with high peak (42%) from 1-4 years.
- Only 2 patients were 15 years old.

Graph (4) below illustrates the age of patients included in the study



Graph-4: Distribution of patients according to age

6-2-4: Type of malignancy and age:

- The highest age for malignancy were in bone and germ cell tumors with median of 11.5 years for each one of them.
- While neuroblastoma and wilm`s tumors develop in younger Age group.

Table (3) below show analysis of age of the patients by (mean, median, and peak age incidence) for each malignancy.

Table-3: Distribution of patients according to type of malignancy and age

Type of malignancy	Range of age	Median	Mean-+SD	Peak age
<i>Leukemia</i>	<i>0.3-14 yrs</i>	<i>4</i>	<i>3.4±1.8</i>	<i>2-4yrs</i>
<i>NHL</i>	<i>1-14 yrs</i>	<i>6</i>	<i>6.6±3.2</i>	<i>5-9 yrs</i>
<i>HL</i>	<i>4-14 yrs</i>	<i>8</i>	<i>7.8±2.5</i>	<i>5-9 yrs</i>
<i>Brain tumor</i>	<i>0.2-12 yrs</i>	<i>4</i>	<i>5.2±3.7</i>	<i>1-4 yrs</i>
<i>Neuroblastoma</i>	<i>0. 8-11 yrs</i>	<i>3</i>	<i>3.2±2.6</i>	<i>1-4 yrs</i>
<i>Wilm`s</i>	<i>0.6-11 yrs</i>	<i>3</i>	<i>3.5±2.1</i>	<i>1-4yrs</i>
<i>Bone tumors</i>	<i>6-15 yrs</i>	<i>11.5</i>	<i>10.6±3.6</i>	<i>10-14 yrs</i>
<i>Rhabdomyosarcoma</i>	<i>1-9 yrs</i>	<i>4</i>	<i>3.4±1.8</i>	<i>5-9 yrs</i>
<i>Retinoblastoma</i>	<i>1.4-13 yrs</i>	<i>5</i>	<i>5.4±4.5</i>	<i>5-9 yrs</i>
<i>Grem cell</i>	<i>10-15 yrs</i>	<i>11</i>	<i>13±2</i>	<i>11-14</i>
<i>others</i>	<i>0.5-13 yrs</i>	<i>3</i>	<i>5.6±4.6</i>	<i>1-4 yrs</i>

6-3. Analysis of Leukemia, lymphoma and CNS tumors

6-3-1. Analysis of Leukemias

- Eighty three percent of leukemias were acute lymphoblastic leukemia.
- Only one case of chronic myeloid leukemia (0.7%).
- Nearly half of the patient (48%) were in the last stage of treatment (maintenance).

Tables (4, 5) demonstrate types of leukemia and stage of treatments

Table-4: Distribution of patients according to types of leukemia

Type of leukemia	Gender		Total No.	%
	M	F		
<i>ALL</i>	65	54	119	83
<i>AML</i>	11	10	21	14.7
<i>CML</i>	1	0	1	0.7
<i>Biphasic</i>	1	0	1	0.7
<i>Total</i>	78	64	142	100

Table-5: Distribution of leukemic patients according to stage of treatments

6-3-2. Analysis of Lymphoma

- More than half of patients (57%) of lymphoma were Hodgkin.

Table (6) show types of lymphomas

Table-6: Distribution of lymphoma patients according to its types

<i>Type of lymphoma</i>	<i>Gender</i>		<i>Total No.</i>	<i>%</i>
	<i>M</i>	<i>F</i>		
<i>Hodgkin</i>	20	8	28	57
<i>Non Hodgkin</i>	20	1	21	43
<i>Total</i>	40	9	49	100

6-3-3. Brain tumors:

- Medulloblastoma contributing 36% of brain tumour followed by astrocytoma 20%.

Table(7) show the histopathological types of brain tumors

Table-7: Distribution of CNS tumors according to histopathology

<i>Type of histopathology</i>	<i>No.</i>	<i>%</i>
<i>Medulloblastoma</i>	9	36
<i>Astrocytoma</i>	6	20
<i>Ependymoma</i>	3	12
<i>Ganglioneuroma</i>	3	12
<i>Unclassified</i>	5	19
<i>Total</i>	26	100

6-4: Analysis of malignancy according to its sites, stages and relapse:

6-4-1. sites and stages

- *Most of the tumor arise from abdomen(72) 42 %, among them 47/72 were wilm`s tumors.*
- *Seventy eight percent Of neuroblastoma cases arise in the abdomen.*
- *Thirty five /sixty nine (35/69) of head and neck tumors were lymphomas with 20/35 were Hodgkin.*
- *Majority of lymphoma and wilm`s tumors (2/3) patients presented at stage III and IV.*
- *Nearly two third of neuroblastoma patients (60%) came at stage IV.*
- *Stages of other tumors not included in the study because they are not registered in the files of the patients.*

Tables (8, 9) demonstrates sits and stages of the tumors

Table-8: Distribution of malignancy by it is site .

Type	Head & neck	Chest	Abdomen	Pelvis	Trunk & limbs	Total No.
<i>HD</i>	20	15	2	1	0	38
<i>NHL</i>	15	5	1	0	0	21
<i>Wilm`stumor</i>	0	0	47	0	0	47
<i>Brain tumors</i>	26	0	0	0	0	26
<i>Neuroblastoma</i>	1	2	18	2	0	23
<i>Bone tumours</i>	0	0	0	1	5	6
<i>Retinoblastoma</i>	5	0	0	0	0	5
<i>Rhabdomyosarcoma.</i>	1	0	0	0	4	5
<i>Germ cell tumors</i>	0	0	0	3	0	3
Ø <i>Others</i>	1	2	4	0	2	9
<i>Total NO.</i>	69	24	72	7	11	183

Ø Others : include nasopharyngeal carcinoma, hepatoblastom, pleuropulmonary carcinoma.

Table- 9: Distribution of patients by stage of malignancy.

Type of malignancy	stage				Total
	I %	II %	III %	IV %	
Lymphoma	3 6%	15 1%	19 38%	12 24%	49 100%
Wilm's tumor	7 5%	13 27%	16 34%	11 23%	47 100%
Neuroblastoma	1 5%	3 5%	4 20%	12 60%	20 100%

NB: in 3 patients stages of neuroblastoma were not written in the file

7. D I S C U S S I O N

Childhood cancer varies in different regions of the world, where acute leukemia account around a third of all. It is common in populations of high socio-economic status and in all industrialized countries.^{7,35} Much of variation is recorded in the incidence of brain tumors, they are the second most common childhood cancer after leukemia, they account for (20-25%)^{18,36} In developing countries, brain and spinal tumors are usually outnumbered not only by leukemias but also by lymphomas.³⁷ while lymphomas are common in developing countries with Burkett's lymphoma being the commonest subtype It is the highest in tropical Africa.^{3,38}

The incidence of Wilm's tumor and Ewing's sarcoma varies largely on ethnic lines, indicating a strong role for genetic predisposition. The highest incidence occurs among black populations and West India, they account (5-7%) and (4%) respectively. Non-heritable retinoblastoma represent (2.5-4%) of all childhood cancers.^{39,40}

In united states approximately(32%) of childhood cancers were leukemia followed by CNS tumors (17%), lymphoma (11%) with: NHL(6%)HD(5%) .Neuroblastoma(7%) Wilms tumour(6%), Rhabdomyosarcoma (3%) Retinoblastoma (3%), Osteosarcoma (3%),Ewing's (1.5%), numerous rare tumors types account for the reminder.^{7,41}

These trends are similar to us in leukemia regarding its order and place as it's the most common malignancy represent (45%) from all cases which is slightly higher than Europe and America but lower than Lahore were leukemia represent

fifty four percent(54%)^{17,42} and (65%)of our cases were from Benghazi city in contrast to solid tumors were(66%) from outside Benghazi .

But lymphoma constituting (16%) from all our cases which is higher than Europe and north America^{8,43}, but near to developing country and Africa .As Libya is part of Africa for this reason lymphoma coming second in order after leukemia .

In solid tumors which need special surgery as CNS , bone tumor and retinoblastoma , as well as travelling of patients abroad and exclusion of deaths making pitfall in comparing like with like(pattern of malignancies)which was not feasible in our study. and we acknowledge this fact.

Over all cancer in childhood is more common among males than females and M:F ratio in the most of resource rich countries is around (1.2:1).² In study done in Nigeria the males are more affected giving males: females ratio 1.5:1.¹⁰ Another study done in India in 2006 using different population based registries they found the M :F ratio in Mumbai and delhi (1.34:1) and (1.92:1) respectively.⁹ In agreement with these in our study out of 315 patients (182)(57%) were male, giving M:F ratio (1.3:1). With some variation from one type of malignancy to another.

In lymphoma a striking male to female predominance is found by (4.4:1) which is comparable with other study where males six times more affected in Hodgkin lymphoma and three times in non-Hodgkin lymphoma than females.²⁰⁻²¹ while in wilm`s and brain tumor male and females almost equally affected as other researcher finding.⁴⁴

Females predominance was observed in germ cell tumor and retinoblastoma with M:F ratio(1:2),(1:1.5) respectively .The same was revealed by others in germ cell tumors where in teenager the female more affected than males while more males in younger age group³³, but in retinoblastoma there is no six variation.²⁹

According to monogram done in united states over 20 years includes 29,659 cancer cases in person younger than 20 years⁴⁵, as well as a study done in Trinidad and Tobago¹⁴they found that the average age specific incidence is higher for children younger than 5years old. And also in Nigeria 55% of patient were between (1-4).¹⁰

In our study we classify the patients age to 5 age groups according to the International Classification for Childhood Cancer(ICCC){<1,1-4,5-9,10-14,>14}⁴⁶. In agreement with them (47%) of our patients were less than 5 years with 82% younger than 9 years .

In leukemia a marked peak in early childhood has appeared in Kuwait , Britain and elsewhere with high incidence of acute lymphoblastic leukemia at age(2-3) years.⁴⁷

However in lymphoma the incidence rises steeply with age, and its rare in less than 5years. Non Hodgkin lymphoma has peak incidence between seven and ten and its increase in early adolescence.^{1,20,21}

In agreement with previous studies the peak age incidence of leukemia patients ranged from (2-4)years with mean (3.4±1.8). In lymphoma the median age was 6 years with peak age 5-9 years, and only 6 of them less than (5)years.

We get (77%) of brain tumor cases diagnosed before(10)years of age with peak incidence(1-4) years which the average age for occurrence reported by others, where (95 %) have presented by (10)years with peak in the first (5)years of Life.⁴⁸

In wilm`s tumor the peak incidence at third year of life ,over (75%) of children affected are under (4)years, and at least (90%) under (7) years at diagnosis.⁴⁹

The median age of onset Neuroblastoma is (20) years making it the most frequent malignant tumor in early childhood.⁵⁰In retinoblastoma (75%) of patients are diagnosed before age of three.²⁹Most of wilm`s tumor in this study(47%) occur before age of 5years with peak age incidence (1-4) years. In neuroblastoma the peak age among our cases was (3) year which is slightly older than reported in the previous literature .

The highest peak age incidence of Rhabdomyosarcoma was(5-9) year which is older in comparing with other study where they have two peaks: from (2-6) years and(15-19)years.³²

While in bone tumor the overall peak age is (10-14)years, with (12) years in females and (16) years in males correlating with average age for pubertal development ^{26,27,28}. Germ cell tumor increase in teenager ³³,the same was revealed in our patients with peak age incidence (10-14)years for both of them .

Eighty percent of all childhood leukemia were ALL, AML making(15-20%), CML(2-5%) and(0.5)% for acute mixed lineage.⁵¹Which is similar to our results where ALL and AML comprises(83%) and (14.7%) respectively with one single case of chronic myeloid and biphasic leukemia each.

Eighty five (85 /142)(60%) of leukemic cases diagnosed in the last 2 years and still taking chemotherapy. and as leukemia account for slightly lower proportion of cancer deaths these giving rise to this high percentage of leukemia in our patients in contrast to others.

In contrast to others¹⁷Hodgkin lymphoma was more common(57%) than non Hodgkin in our patients,and in both of them the most sit of lymph node involvement was cervical with (20/28) patients and (15/21)pateints respectively while the mediastinal lymph node involvement was more in Hodgkin lymphoma

with (15/28) patients in contrast to NHL were only(5/21)of cases has mediastinal lymph node involvement .

Histologically medulloblastoma was the most frequently observed (36%) brain tumors followed by astrocytoma, while as reported by many authors astrocytomas were the commonest.¹⁹

The most frequent anatomical sites of neuroblastoma was abdomen (60%) pelvis (6%) , neck (2%), chest (15%) (52). which is comparable to our finding were 78% of the cases their tumor arise in the abdomen.

In 2005 the international union against cancer reported that worldwide more than more than 160.000 children are diagnosed with cancer per year, and about 90000 die from cancer because of late presentation due parental ignorance and poverty, and poor health facilities ,it has also been estimated

that more than 85% of childhood cancer occurred in resource poor country,⁵³In agreement with them the majority of our patients with solid tumors presented at advanced stages which influence the prognosis and increase the risk of relapse ,more than half of lymphoma(62%) and wilm`s tumor(57%) presented at stages III and IV, while in others just one third of their patients presented at this stages.^{17,49}

Also we have (20 %) of neuroblastoma patients presented at stage III and(60%) with stage IV , which nearly similar to others were satge III and IV present in twenty percent(20%) and (45%)of their patients respectively.⁵⁰

Primary hepatic neoplasm are a rare embryonal tumor and account only (1-2%) from all childhood cancer with two third Hepatoblastoma and one third Hepatocellular carcinoma(HCC) (85%) diagnosed before 5th years of age.⁵⁴

We have two male patients one hepatoblastoma, other hepatocellular carcinoma. both of them from Ejdabia. their age (1.5) and (8) years respectively.

Hepatoblastoma diagnosed 7-2012 HCC diagnosed in 10-2012. tumor resection was done for both of them as well as chemotherapy.

Nasopharyngeal carcinoma more common in second decade of life with male predominance, has high degree of association with Epstein –Barr virus³⁴.

One Case of Nasopharyngeal carcinoma. male from Derna diagnosed 2003 at age of (9) years, treated with radiotherapy and chemotherapy .

8. C O N C L U S I O N

- Near half of the malignancy was leukemia among them 83% was acute lymphocytic leukemia. followed by lymphoma (with Hodgkin more than non-Hodgkin) and wilm`s tumor.
- More than half of patients were from outside Benghazi
- Most of the leukemia patients were from Benghazi, while the solid tumor were from sub urban and rural areas.
- Male outnumbered the females.
- Forty two percent (42%) of patients were between 1-4 year.
- 42% of malignancy are at abdomen followed by head and neck.
- Most of solid tumors patients presented at late stages.

9.RECOMMONDATION

- Updating electronic data base in Hematology Oncology department and clinic is highly recommended.
- Education of the population about the malignancy for early detection ,by those responsible for the education of health professionals, patients and family educator, caregivers, and the public cancer education .
- Establishment of Hematology Oncology Centres in the east to give good health serves in that areas.
- Establishment of a more advanced laboratory investigations for proper diagnosis .
- Establishment and maintaining a National registry of child hood malignancies.
- Conducting further studies in the whole country is paramount, that should include deaths to give clear picture about the epidemiology of childhood cancer in our society.

ملخص الدراسة باللغة العربية

الهدف: الحصول علي نظرة عامة عن الوضع الديموغرافي والصحي لثلاثمئة وخمسة عشر (315) طفل مصاب بالسرطان في مستشفى تعليمي في شمال شرق ليبيا, بنغازي هي ثاني أكبر مدينة في ليبيا، و تتضمن كل الجزء الشرقي من ليبيا وكذلك جزء من الجنوب. كل الأطفال المصابين بالسرطان الذين تتراوح أعمارهم بين 0- 15 عاما الذين شخضوا عن طريق الفحص النسيجي أو الخلوي المسجلين بهذا المستشفى وما زالوا يتابعون إما القسم للعلاج أو عيادة للمتابعة شملتهم هذه الدراسة.

الطرق والمرضى: - هذه الدراسة لديها قسمين، واحد يشمل 161 طفل الذين لا يزالون نشطين في العلاج الكيميائي في قسم علم الأورام أمراض الدم. ويعرض القسم الثاني الأطفال الذين أنهوا العلاج الكيميائي يتابعون في عيادة أمراض الدم والأورام.

معايير الاستبعاد: الوفيات وكذلك المرضى الذين أنهوا العلاج الكيميائي ولم يأتوا للمتابعة منذ عام.

وكانت هذه الدراسة دراسة وصفية سلسلة من الحالات. وقد جمعت البيانات بأثر رجعي وفقا لتصنيف جميع أنواع السرطانات، من الملفات الخاصة بالمرضى باستخدام تصميم خاص. وقد تم جمع البيانات التالية؛ التركيبية السكانية المرضى: الجنس، وتاريخ الميلاد، والدخول، والإقامة والتحليل (تحليل الدم الكامل، ونخاع العظام، ونتيجة التشريح المرضي) وكذلك مرحلة المرض التي أجريت في وقت تشخيصهم . وأدرجت أيضا مواقع للأورام والانتكاس.

النتائج: ما مجموعه (315) مريض الذين يعانون من الأورام الخبيثة، منها 161 طفل (52%) لا يزالوا يتلقون العلاج الكيماوي . 45% من اجمالي الأورام كان سرطان الدم يليه سرطان الغدد الليمفاوية 16%.

مائة وواحد وخمسين طفل (48%) مريض كانوا من بنغازي و65% منهم كانوا يعانون من سرطان الدم اللوكيميا. 66% من الأورام الصلبه كانت من خارج بنغازي .في العموم نسبة الذكور للإناث (1.3:1)، بينما (44:1) نسبة الذكور للإناث في سرطان الغدد اللمفاوية وعلى النقيض في سرطان الشبكية وسرطان الخلية حيث كانت نسبة الإناث اكثر، (1.5:1) (1:2) على التوالي.

82% من المرضى أعمارهم أقل من 10 سنوات، (134) 42% بين (1-4) سنوات، ومريضين فقط عمراهما 15 سنة الفئة العمرية أعلى كانت في أورام العظام وأورام الخلية.

83% من سرطان الدم (اللوكيميا) كان سرطان الدما للمفاوي لحاد. و فقط حاله واحدة من سرطان الدم النخاعي المزمن (0.7%). حوالي 48% أي ما يعادل نصف الحالات في المراحل النهائية للعلاج. 57% من الحالات تعاني منسرطان الغدد اللمفاوية و36% من سرطان الدماغ النخاعي وسرطان الدماغ النجمي 20%

اغلب الأورام تنشأ من البطن 72 (42%) عدد 47 من سرطان الكلى (الولمز)، و78% من حالات النيوروبلاستوما منشأها البطن، و عدد 35 من اجمالي 69 من أورام الرأس والرقبه كانت لسرطان الغدد

اللمفاوية و عدد 20 نوع هودجكينن اجمالي 35. كما أن اغلبية (2/3) من سرطان الغدد اللمفاوية وسرطان الكلى (ولمز) تشخص في المرحلة الثالثة وتقريبا ثلثي اورام النيوروبلاستوما 60%تشخص في المرحلة الرابعة.

التوصيات: تعليم السكان حول الورم الخبيث للكشف المبكر، وينبغي إنشاء السجل الوطني لأورام الأطفال لإجراء دراسات أبعء في البلد كله كما انا الدراسات المستقبلية يجب ان تشمل الوفيات لتعطي صورة واضحة عن الاورام السرطانية في مجتمعن.

REFERENCES

1. Gray M, Kupfer MD .Childhood Cancer Epidemiology. E medicine: 12,2009 [www.Emedicine.com].
2. Michelle Condren, Lisa Lubsch, et al .Long term Follow-up of Survivors of Childhood Cancer .Indian Journal of Pediatrics. January, 2005; 72: 151-53.
3. Parkin DM ,Sitas F, Chirenje M, et al .Cancer in indigenous African-burden, Distribution and trends .Lancet Oncol.2008; 30: 683-692.
4. Tinat G ,Bougeard S,Baert- Desurmont ,et al. Version of the Chompret criteria for Li Fraumeni syndrome. Journal of Clinical Oncology.2009; 27:108–9.
5. Alfred Grovas M.D. Amy Fremgen Ph.D. Amanda Rauck M.D, et al. The national cancer data base report on patterns of childhood cancers in the United States. American Cancer Journal .2003; 50:123-26.
6. Stiller C. Childhood Cancer In Britain: Incidence survival mortality. Oxford J. 2007; 5:120-34.
7. Xie Y, Davies SM, Xiang Y, et al. Trends in leukemia incidence and survival Cancer in the United States (1973-1998).cancer. May2003; 97(9):2229-35.
8. Kanavos P. The rising burden of cancer in the developing world. Ann Oncol. 2006;17:815-23.
9. Epidemiology of childhood cancer in India. Indian journal of cancer.2009; 46: 264-73.
- 10.Agboola AO, Adekanmbi FA, Musa AA, et al. Pattern of Childhood Malignant Tumors, In A teaching Hospital In south-western Nigeria. Med.J. Aus.2009; 190:12-14.
- 11.Peter .kaatsch. Epidemiology of childhood cancer.Institute for Medical Biostatistics, Epidemiology and Informatics, University of Mainz, Germany Sep 2006; 83(9):584-7. [WWW.Medline.Com].

12. AIRTUM Working Group; CCM; AIEOP Working Group. Italian cancer figures, report 2012: Cancer in children and adolescents. *Epidemiol Prev.* 2013 Jan-Feb; 37: 225.
13. Huda M, Mohamed S. Mahfouz, et al. Patterns Of Childhood Cancer In Children Admitted To The Institute Of Nuclear Medicine, Molecular Biology And Oncology (INMO) Gezira state .*JPMA* Aug:2011; 20:45.
14. Bodkyn I, Lalchandani S. Incidence of childhood cancer in Trinidad and Tobago. *West Indian Med J* Oct. 2010 ;59:5.
15. Yasmin Bhurgri. Childhood Lymphoma And Leukemia. *J Pak Med Assoc.* ,April 2006;56:4.
16. Court-Brown, W.M., Doll, R. Leukemia In Childhood And Young Adult Life. *Br. Med. J.* 2003;30:201-205.
17. Maliha Zahid, Asif Khalid, Zaheer-ud-Din Ahmed et al. Acute Leukemias of Childhood: A Retrospective Analysis of 62 Cases. *JPMA* 2010;65:147-49.
18. Valsecchi MG, Tognoni G, Bonilla M, et al. Clinical epidemiology of childhood cancer in Central America and Caribbean countries. *Annals of Oncology* 2004;15:680-85
19. Stiller CA, Nectoux J. International incidence of childhood brain and spinal tumors. *Int J Epidemiol.* 2000 Jun; 23 :458-64.
20. Naresh KN, Jonson J, Srinivas V ,et al. Epstein –Barr virus association in classical Hodgkin disease provide survival advantage to patients and correlates with higher expression of proliferation marker in Reed –Sternberg cells. *Ann Oncol* 2000; 11:91-96

21. Bhurgri Y, Pervez S, Bhurgri A et al. Increasing incidence of non-Hodgkin's lymphoma in Karachi. 1995-2002 Asian Pac J Cancer Prev. 2005 ; 6:364-9.
22. Uba AF, Chirdan LB. Childhood Wilm's tumour: Prognostic Factors in North Central Nigeria. West Afr J Med.2007; 26:222-25.
23. Stiller CA, Parkin DM .International Variations In The Incidence Of Childhood Renal Tumors. Br J Cancer. 2000 Dec; 62:1026-30.
24. CastelV, Canete A,Navarro.S, etal. Outcomeof high-risk neuroblastoma using a dose intensity approach: improvement in initial but not in long-term results. Medical and Pediatric Oncology, 2001; 37:537-42.
25. Stiller CA, Parkin DM. International variations in the incidence of neuroblastoma. Int J Cancer. 2000 Oct 21 UK; 52: 538-43.
26. Eyre R, Feltbower E ,Mubwandarikwa, et al. Incidence and survival of childhood bone cancer in northern England and the West Midlands, 1981–2002 Br J Cancer. 2009 January ;13:188–93.
27. George T. Calvert R. Lor Randall, et al. At-Risk Populations for Osteosarcoma: The Syndromes and Beyond. Br med J,2012 ; 9: 389-92.
- 28 . Ottaviani and N. Jaffe. The Etiology Of Osteosarcoma. Cancer Treatment and Research2009; 152: 15-32.
29. Shields and J. A. Shields. Retinoblastoma management: advances in enucleation, intravenous chemo reduction, and intra-arterial chemotherapy. Current Opinion in Ophthalmology, 2010; 21: 203-12.
30. Ortega JA, Douglass EC, Feusner JH ,et al. Randomized comparison of cisplatin/vincristine/fluorouracil and cisplatin/ continuous infusion doxorubicin for treatment of pediatric hepatoblastoma: a report from the Children's Cancer Group and the Pediatric Oncology Group. J Clin Oncol 2000;18:2665-75.

31. Chirdan LB, Bode-Thomas F, Chirdan. childhood cancer: Challenge and strategies for management in developing countries. *Afr J Paediatr surg.*2009; 6:126.
- 32 . Eduardo A. Perez, M.D., Noor Kassira, et al. Rhabdomyosarcoma in Children: A SEER Population Based Study. *Journal of Surgical Research* October 2011;170:243-51.
- 33.Gobel U, Calaminus G, EngertJ, et al. Teratomas in infancy and childhood. *Med Pediatr Oncol* 2006; 31: 8-15.
- 34 . Sahraoui, A. Acharki, A. Benider, etal. Nasopharyngeal carcinoma in children under 15 years of age: A retrospective review of 65 patients .*Oxford journal* 2010 ; 10:1499-1502.
35. Linet MS et al. Interpreting Epidemiologic Research: Lessons from Studies of Childhood Cancer. *Pediatrics*, 2003;112:218-32.
- 36.Bunin GR. Nongenetic causes of childhood cancers: Evidence From International Variation, Time Trends, And Risk Factor Studies. *Toxicol Appl Pharmacol.* 2004; 199: 91-103.
37. Scott CH. Childhood cancer epidemiology in low-income countries. *Cancer*, 2007; 112: 461-72.
38. Ibrahim H, Rafindadi AH, Yinti MG. Burkitt's lymphoma in Children in Sokoto. *Nigerian Journal of Medicine* 2000;7:115-119.
39. McKinney PA et al. Patterns Of Childhood Cancer By Ethnic Group In Bradford, UK 1974-1997. *Eur J Cancer*2003; 39:92-7.
40. A roar RS ,Eden TOB, Kapoor G , Epidemiology Of Childhood Cancer In India, *Indian journal of cancer* \October -December 2009; 46:12-19.

41. Ries LAG et al, Cancer Incidence and Survival Among Children and Adolescents: United States SEER Program 1975-1995. National Cancer Institute; American Jor. 2000 ;67: 405-7.
42. Buka I. et al.Trends in Childhood Cancer Incidence: Review of Environmental Linkages. Pediatric Clinics of North America. 2007; 54: 177-203.
- 43.Gurney JG, Bondy ML epidemiology of childhood cancer .IN pizzo PA, Poplack DG, Editors .principles and practice of pediatric oncology 5th edition. Philadelphia Lippincott Williams and Wilkins.2006; 85: 2-14.
44. Kramarova E, Stiller CA: The international classification of childhood cancer .Int.J 2003.Cancer;68:759-65.
- 45.Lynn A. GLOECKLER Ries. Constance L, SEER pediatric monograph ,National cancer institute. pub med 2010.
46. Pritchard J, Imeson J, Barnesm J .et al.(1995)Results Of The United Kingdom Children `S Cancer Study Group(UKCCSG) First Wilm`S Tumor Study (UKW1) J Clin.Oncol. 1999;13:124-33.
47. Monge P. et al. Childhood leukaemia in Costa Rica, 1981–96. Paediatr. Perinat. Epidemiol. 2002; 16 :210–18.
- 48.plowman and A.D.J. Pearson. Tumor Of Central Nervous System. In Pediatric Oncology ,3rd ed, Edited by C.R. Pink,erton and P.N. Plowman published in 2004 by Chapman &Hall, London. 2004; 56:321-351.
- 49.Sunghoon Kim, MD. Pediatric Solid Malignancies: Neuroblastoma andWilms' Tumor . Surgical Clinics of North America - April 2006;86:178-83.
50. Brodeur GM Neuroblastoma: biological insights into a clinical enigma. Nat Rev Cancer.2003;3: 203-16.

51. Belson M et al. A review of Risk factors for acute leukemia in children. *Health Prospect.* 2007;15:138-45
52. Valteau-Couanet, D, Michon J, Perel, Y. Preliminary results of stage 4 neuroblastoma (NB) NB 97 protocol, *Medical and Pediatric Oncology.*2000; 35:759-62.
53. Chirdan LB , et le. Childhood Cancers: Challenges And Strategies For Management In Developing Countries ,*Afr J Paediatr Surg.* 2009; 6:26.
54. Tanimura M, Matsui I, Abe J, et al. Increased Risk Of Hepatoblastoma Among Immature Children With A Lower Birth Weight. *Cancer Res* 1998; 58 :3032-3035