

## Research Article

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# Neuroblastoma in Iraq-KRG-Sulaimani

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### Abstract

**Background:** Neuroblastoma is the third most common cancer in pediatric age group; it is the most common malignancy in the first year of life. The majority of the patients (50-65%) have advanced disease at diagnosis. Diagnoses, staging investigations and risk categorization have a great success in neuroblastoma, trying to classify the patient into risk groups according to the age, stage and molecular study and this in turn has important value in the treatment strategies. Despite of this improvement in the early diagnosis and treatment protocol, neuroblastoma stills one of the malignant diseases that are associated with high morbidity and mortality.

**Objectives:** This six years prospective study was an initial effort to evaluate the pattern of presentation, studying the correlation between age, sex and site of primary tumor with the stage of neuroblastoma in our patients.

**Patients and Methods:** this study spans over a period of six years from February 2008 to February 2014. Sixty two patients with newly diagnosed pediatric neuroblastoma were admitted to Hiwa Hematology/Oncology hospital included in this study. Age, sex, clinical patterns, staging and important laboratory findings were assessed.

The patients staged according INSS. We divided our patients into three groups according to the risk categories.

**Results:** Data analyzed using SPSS software, version 13 and P-value obtained by Chi-square test, a median age at diagnosis was about 24 months with male predominance. Most common site of the primary tumor was the abdomen; approximately 69% of our patients with neuroblastoma studied were stage 4.

**Conclusion:** The stage in our study was age dependent but it was neither depending on the sex nor the site of the primary tumor.

**Keywords:** Neuroblastoma; Risk groups; Sex distribution; Site of primary tumor; Sulaimaniya province

## **1. Introduction**

Neuroblastoma is the most common extracranial solid tumor in infancy. It is an embryonal malignancy of the sympathetic nervous system arising from neuroblasts (pluripotent sympathetic cells). In the developing embryo, these cells invaginate, migrate along the neuraxis, and populate the sympathetic ganglia, adrenal medulla, and other sites. The pattern of distribution of these cells correlates with the sites of primary disease presentation [1].

Age, stage, and biological features encountered in tumor cells are important prognostic factors and are used for risk stratification and treatment assignment [2, 3]. The differences in outcome for patients with neuroblastoma are striking. Patients with low-risk and intermediate-risk neuroblastoma have excellent prognosis and outcome. However, those with high-risk disease continue to have very poor outcomes despite intensive therapy. Unfortunately, approximately 70-80% of patients older than 18 months present with metastatic disease, usually in the lymph nodes, liver, bone, and bone marrow. Less than half of these patients are cured, even with the use of high-dose therapy followed by autologous bone marrow or stem cell rescue [1, 4, 5].

## **2. Patients and Methods**

Sixty two patients with newly diagnosed pediatric neuroblastoma were admitted to Hiwa Hematology/Oncology hospital in the Sulaimaniya province of Iraqi Kurdistan were included in this study. They were studied prospectively from February 2008 to February 2014.

### **2.1 Inclusion criteria**

1. All children aged 15 years or younger.
2. Both male and female.
3. Histopathologically proved neuroblastoma made either by A or B.
  - A. From tumor tissue by light microscopy (with or without immunohistology) and/or increased urine catecholamines.
  - B. Bone marrow aspirate or trephine biopsy contains tumor cell and increased urine catecholamines.
4. Newly diagnosed patients who were not treated previously by chemotherapy.

### **2.2 Exclusion criteria**

1. Age more than 15 years.
2. Relapsed neuroblastoma or previously treated with chemotherapy.

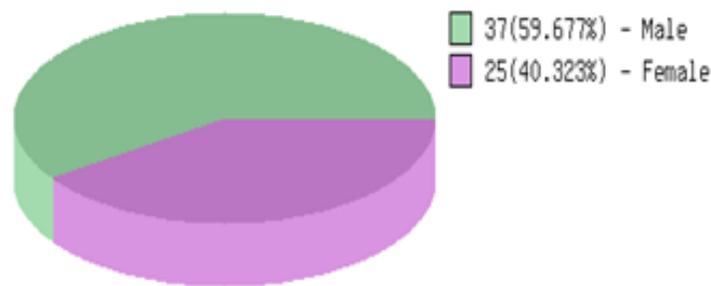
Study requirements included: All the targeted patients had their Sulaimaniya facilities of histopathological diagnosis, CBC, liver function test, renal function test, serum electrolyte, serum LDH, serum ferritin level, abdominal U/S, CXR, CT-scan and/or MRI of the primary site, chest and abdomen and bone marrow aspirate and trephine biopsy.

**2.3 Statistics**

Data analyzed using SPSS software, version 13 and P-value obtained by Chi-square test. P-value <0.05 was considered significant.

**3. Results**

Among 62 patients with neuroblastoma studied, 37 patients (59.677%) were male and 25 patients (40.323%) were female. The male: female ratio was 1.48:1. Figure 1 shows the sex distribution.

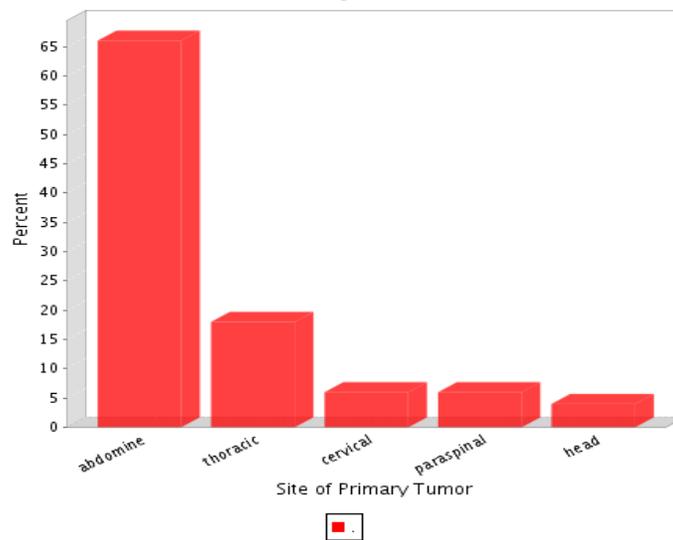


**Figure 1:** Sex Distribution of NBL.

A median age at diagnosis was about 24 months with peak age of incidence was between 1-5 years. Table 7 shows the number and percentage of the cases in relation to the age. The most common site of the primary tumor was the abdomen which was the primary site of the tumor in 41 out of 62 patients (66.12%), followed by thoracic primary which occurred in 11 patients (17.74%), Para spinal primary in 4 patients (6.45%), cervical primary occurred in 4 patients (6.45%) and head primary which was happened in 2 patients (3.22%).

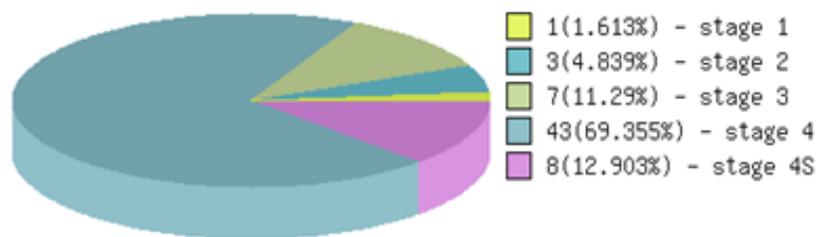
Age in years	No. of patients	Percent (%)
< 1	19	30.64
1-5	31	50
6-10	10	16.12
11-15	2	3.22

**Table 1:** Age Distribution of NBL at Diagnosis.



**Figure 2:** Site of Primary Tumor (Percentage).

Figure 2 shows the percent of the patients in relation to the site of the primary tumor. Among the 62 patient with neuroblastoma studied 43 patients (69.35%) were stage 4, 8 patients (12.9%) were stage 4S, 7 patients (11.29%) were stage 3, 3 patients (4.83%) were stage 2 and 1 patient (1.61%) was stage 1. Our study showed that there is significant correlation between age and staging with localized disease (stage 1 and 2) occurred more in younger age and advanced stage (stage 3 and 4) found in older children.



**Figure 3:** Stage Distribution of NBL.

Table 2 shows the relation between age and the stage. Chi square test showed that the difference among the stages and the age was statistically significant (P- value =0.049).

Age (years)	Stage 1 No. (%)	Stage 2 No. (%)	Stage 3 No. (%)	Stage 4 No. (%)	Stage4S* No. (%)	Total No. (%)
< 1 year	1 (5.26)	1 (5.26)	3 (15.78)	8 (42.10)	6 (31.57)	19 (100)
1-5 years	0	2 (6.45)	3 (9.67)	26 (83.87)	-	31 (100)
6-10 years	0	0	1 (10)	9 (90)	-	10 (100)
11-15 years	0	0	0	2 (100)	-	2 (100)

\*From the definition of stage 4S, it is just occur in infancy.

**Table 2:** Staging in Relation to Age (P- value=0.049).

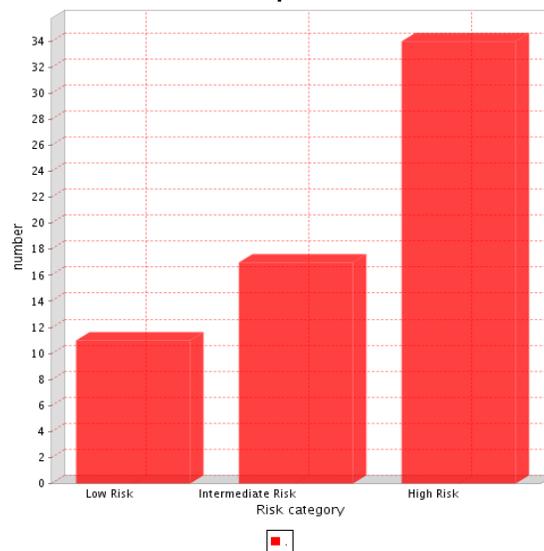
Stage	Male No./total (%)	Female No./total (%)
Stage 1	0/37	1/25 (4)
Stage 2	2/37 (5.4)	1/25 (4)
Stage 3	4/37 (10.81)	3/25 (12)
Stage 4	26/37 (70.27)	17/25 (28)
Stage 4S	5/37 (13.51)	3/25 (12)

**Table 3:** Sex in Relation to the Stage (P-value =0.809).

Stage	Abdomen No. (%)	Thoracic No. (%)	Cervical No. (%)	Para spinal No. (%)	Head No. (%)	Total No. (%)
Stage 1	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)
Stage 2	2 (66.66)	1 (33.33)	0 (0)	0 (0)	0 (0)	3 (100)
Stage 3	6 (85.71)	1 (14.28)	0 (0)	0 (0)	0 (0)	7 (100)
Stage 4	24 (55.81)	9 (20.93)	4 (9.3)	4 (9.3)	2 (4.65)	43 (100)
Stage 4S	8 (100)	0 (0)	0 (0)	0 (0)	0 (0)	8 (100)
Total	41	11	4	4	2	62 (100)

**Table 4:** Primary Site of NBL in Relation to stage (P-value=0.897).

This study found that there was no statistic significant correlation between sex and staging as there was no effect of the sex upon staging (P-value =0.809). The relation between the primary site of the tumor and staging is shown in table 10 (P-value=0.897). Among the 62 patients with NBL studied, 34 patients (54.84%) were high risk group, 17 patients (27.42%) were intermediate risk group and 11 patients (17.74%) were low risk group. Figure 4 shows the number of patients according to the risk categories of NBL.



**Figure 4:** Number of Patients According to the Risk categories of NBL.

#### 4. Discussion

Neuroblastoma is the most common extracranial solid tumor in childhood. It is an embryonal malignancy of the sympathetic nervous system arising from neuroblasts (pluripotent sympathetic cells). Age, stage, and biological features encountered in tumor cells are important prognostic factors and are used for risk stratification and treatment assignment. Low-risk and intermediate-risk neuroblastoma have excellent prognosis and outcome. However, those with high-risk disease continue to have very poor outcomes.

The total number of cases studied was sixty two, over a period of six years. We found that males were affected more than female with male: female ratio was 1.48:1; this ratio is higher than male: female ratio in most large studies which was 1.1:1 [1]. It is also higher than the male: female ratio in USA which was 1.2:1 [6]. Peak age incidence at presentation in our study was (1-5) years which was represent (50%), this was similar the result of cooperative group studies at POG and CCG institution from 1986 to 2001 which also showed peak age incidence between (1-5) years.

A median age at diagnosis was about 24 months in our study which is higher than that showed at POG and CCG institution from 1986 to 2001 which was of about 19 months [1]. This higher median age at diagnosis in our study might result from possibly delayed diagnosis of the disease in our community because of the poor family knowledge regarding the disease and absence screening program.

The most common site of the primary tumor in this study was the abdomen which represent approximately (66.1%) followed by thoracic primary (17.74%), Para spinal primary (6.45%), cervical primary occurred in (6.45%) and head primary which was happened in (3.22%). According to the international figure, abdominal primary was also the most common site at presentation and it was seen in (65%) [1, 7]. The majority of the patients had advanced disease at the time of diagnosis, approximately (69.35%) of the patients had stage 4 at presentation, (12.9) were stage 4S, (11.29%) were stage 3, (4.83%) were stage 2 and only (1.61%) was stage 1. This result means that our patient is

more likely to have advanced stage (stage 3 and 4) than those observed in the international figure (50 to 60% of all neuroblastoma cases present with metastases) [1, 8]. This higher percentage of advanced disease at diagnosis might be due to delayed medical care and absence of screening program.

We also discovered that there is a strong correlation between age and staging as the proportion of patients presenting with localized, regional, or metastatic disease is age dependent. Localized disease (stage 1 and 2) occurred more in younger age and advanced stage (stage 3 and 4) found in older children. This result is again similar to the international Figure 1.

In our study we found no correlation between sex and the stage of neuroblastoma at the time of diagnosis. Also there was no relation between the primary site of neuroblastoma and stage of the disease. Most of the patients were classified as high risk group (54.84%), followed by the intermediate risk group (27.42%) and only (17.74%) were low risk group.

## **5. Conclusion**

Neuroblastoma was higher in male than female in our community. Peak age group was 1-5 years; a median age at diagnosis was about 24 months. It is extremely rare after the age of 10 years and the majority of the patients presented with abdominal primary at the time of diagnosis.

Most of the patients had distant metastases at presentation (stage 4 disease). There was strong correlation between age and advanced stage which meant that stage is age dependent. Neither there was relation between the primary site of the tumor and the stage nor significant correlation between the sex of the patients and the stage. Despite absence of MIBG, bone scan, cellular and molecular study for proposed risk stratification system for purpose of risk categories, (54.84%) of our patients got high risk category.

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