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# Pattern of Neuroblastoma Among Children in Basra Pediatric Oncology Center

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## Abstract

**Background** Neuroblastoma is a neoplasm of the sympathetic nervous system, is the second most common extracranial malignant tumor of childhood, it accounting for8% to 10% of all childhood cancers and for approximately15% of cancer deaths in children.

**Objective** To designated demographic and clinical geographies of neuroblastoma in Basra pediatric oncology center.

**Patients and Methods**A retrospective study was carried out from October 2016 till end of April 2017to assessed characteristics features of patients with neuroblastoma who have been registered and admitted to the Basrah Hospital of Pediatric Oncology center during the period from the I st of January 2004 till the end of December 2016.

**Results** The total cases of neuroblastoma admitted to the Center during that period were 179. Their age ranges from one month up to 14 years, 104 male and 75 female. A special data sheet was designed for the purpose of the study; the information was taken from patient's files; name, age (date of birth), date of admission, gender and residence. The study showed that the percentage of patients with neuroblastoma treated in Basrah Pediatric Oncology Center have increased gradually from 5% at 2004 to 13.4% at 2015.

The highest frequency of neuroblastoma was found in the age group (1-5 years) that included 117 patients 65.4%. Higher numbers of patients with neuroblastoma were from the center and northern areas of Basrah (22.3%, 12.3%) respectively and to a lesser extent in western (9%) and, southern (9%), and eastern (2.2%). Other governorates like ThiQar and Maysan account for high rates (28.5% and 21.8% respectively) of admissions in Basrah Paediatric Oncology Center.

This study revealed that most patients with neuroblastoma commonly presented with abdominal mass,gastrointestinal track symptoms and other symptom like pallor and fever, and most patients presented in stage IV (51.39%) or stage III (39.66%) of the disease. Distant metastasis occurs in 93(51.9%), the most common site of metastasis was bone marrow 72 (40.2).

The overall mortality was 92(51.4%), The outcome of patients with neuroblastoma also varied with age, the age group < one year have low percentage of death (7.8%) than the age group 1-5 year(38.0%), the mortality rate was high in last 5 years 2012-2016 (22.3%) while the years from 2008-2011, 2004-2007 percentage of mortality low (16.8%, 12.3%) respectively, the non-compliance was decrease in the last 5 year 2012-2016( 6.7%), high percentage of non-compliance in the period from 2008-2011 (7.8%).

**Conclusion** None compliance or discontinuation of treatment is an important dilemma for a disease, so increase awareness about early sign and symptoms of the disease and improving the diagnostic facilities, with psychological support in order to resolve this problem.

# Introduction

Neuroblastoma, a neoplasm of the sympathetic nervous system, is the second most common extracranial malignant tumor of childhood and the most common solid tumor of infancy [1]. The outcome of children with neuroblastoma is variable when the disease is categorized by age, stage, and clinical characteristics [2,3].

Efforts to improve the outcome of patients with neuroblastoma have focused on identification of risk groups based on clinical and biologic variables as well as intensification of therapy for high-risk cases [4]. Genetic characteristics of neuroblastoma can be divided into those with near-diploid nuclear DNA characterized by the presence of genetic aberration such as MYCN amplification,17q gain, and chromosome losses, and near-triploid tumors characterized by whole chromosome gains and losses without structural genetic aberrations, meta-analysis of prognostic markers show that MYCN amplification and DNA ploidy are of prognostic significance and currently are used along clinical factors to determine treatment include amplification of MYCN proto- oncogene (poor prognosis), and hyperdipliody of tumor cell DNA content (better prognosis). Neuroblastoma is a developmental cancer of the sympathetic nervous system that is thought to arise during neural crest cell differentiation [5]. The overall incidence is 1 case per 100,000 children, affecting approximately 700 children per year in U.S.A, [6] accounting for 8% to 10% of all childhood cancers and for approximately 15% of cancer deaths in children [1].

The median age at diagnosis is about 16 months, 95% of cases are diagnosed by 7 years of age and is rarely found in children older than 10 years [7]. The overall survival is 65%, although the majority of patients present with metastatic high-risk disease where survival rate is below 50% despite aggressive surgery and dose - intensive chemotherapy [8,9]. The incidence of neuroblastoma is slightly higher among male, than female [10]. Causal factors have not been identified and studies that suggest association between premature delivery (<33 weeks), very low birth weight (<1500g), phenobarbital) remain inconclusive [11,12], familial forms of neuroblastoma are rare, accounting for about 1% of all cases. There are few reported pedigrees of familial neuroblastoma [13]. In those families, the median age at diagnosis is 9 months, as opposed to 2 to 3 years in sporadic cases [13].

PHOX2B and anaplastic lymphoma kinase (ALK) genes have been identified as predisposition genes in hereditary cases despite incomplete penetrance [14]. One particularly informative case presented a high-level gene amplification that was strictly limited to ALK, indicating that this gene may contribute on its own to neuroblastoma development. Genetic testing for ALK and PHOX2B is therefore considered for children with a positive family history of neuroblastoma. Surveillance with screening ultrasound and urinary catecholamine metabolites is recommended for children with these heritable mutations [15,16]. Clinical appearance of neuroblastoma is dependent upon site of the tumor origin, disease extent and the presence of paraneoplastic syndrome [1]. Neuroblastoma can arise anywhere along the sympathetic nervous system. The majority of tumors (65%) arise in the abdomen, with over half of these arising in the adrenal gland. Other sites of origin include the neck, chest, and pelvis [1,17]. There is a concordance with age and site of disease with infants more likely to present with thoracic and cervical primary sites, 1% of patients have no visible primary tumor [1].

Tumors at sympathetic chain and spinal column have the potential to expand into the intraforaminal spaces and can impede on the spinal cord causing compression and neurological defects. Children with cortical bone metastases can exist with generalized bone pain and limping [18]. Tumours in the chest apex may exist with Horner's syndrome (ptosis, miosis, anhidrosis) [19].

Neuroblastoma can present as a paraneoplastic syndrome of autoimmune origin manifesting as ataxia or opsomyoclonus (dancing eyes and dancing feet). In such case, the primary tumour is in the chest or abdomen, and the brain is negative for tumour [20]. The most common sites of metastasis are the long bones and skull, bone marrow, liver, lymph nodes, and skin (subcutaneous tissue) [1,20]. The current criteria for diagnosis and staging of neuroblastoma are based upon the International Neuroblastoma Staging System (INSS) criteria. Stage 1localized tumour, complete resection with or without microscopic margins, ipsilateral nodes negative. Stage 2A localized tumour, incomplete gross resection, ipsilateral nodes negative. Stage2 Blocalized tumour, with or without gross resection, ipsilateral nodes positive, contralateral nodes negative. Stage3 unrespectable tumour that infiltrate the midline. With or without ipsilateral lymph nodes, or localized tumour with contralateral positive nodes, or midline tumour with bilateral extension. Stage4any tumour with distant metastas, Stage 4S localized primary tumour in infant <12 months, with metastases limited to skin, liver, bone marrow [1,17,20]. A new International Neuroblastoma Risk Group (INRG) staging system (INRGSS) .Stage L1 localized tumour, does not involve any vital or contiguous structure, without any IDRF. Stage L2 loco regional tumour with1 or more IDFR. Stage M distant metastases. Stage MS metastatic disease in children <18 months ofthe concept of age -dependent normal ranges of morphologic features, such as Schwannian stromal development, grade of neuroblastic differentiation, and mitosis-karyorrexis index, they used these factors to assign patients to one of three distinct risk groups (Low, intermediate and high) [1,24-26].

Treatment is imperative that a multidisciplinary approach to diagnosis and therapy be accept for all patient, tumour tissue obtained through surgical tumour biopsy is almost uniformly required to assess tumour genetic and histological feature, the requirement for surgical resection, chemotherapy or radiotherapy is depended on patient risk, exposure to chemotherapy is limited to patient who have local or advanced disease while radiotherapy limited to patient who have advanced disease and unfavourable biological characteristics. Low Risk Neuroblastoma this group includes the following patients: All patients with INSS stage 1 disease. Patients with INSS stage 2 diseases, excluding those patients older than one year at diagnosis with tumour MYCN amplification and unfavourable shimada pathology. Infants with stage 4S disease that have tumours with hyper diploidy, favourable, shimada and amplified MYCN [1]. The patients who have stage 1 are treated with surgery only. Chemotherapy has been an effective salvage therapy for patients with stage 1 disease who relapse after surgery only [27,28]. Chemotherapy can be omitted for the majority if patients who have biologically favourable but incompletely resected localized tumours (INSS stage 2A and stage 2B), with a survival rate greater than 95% [27,29]. For patients who have INSS stage 1, 2A or 2B disease. Chemotherapy should be reserved for those have localized neuroblastoma and experience life or organ-threatening symptoms. Stage 4S neuroblastoma without MYCN amplification undergoes spontaneous regression in majority of case [30]. Chemotherapy or low dose radiotherapy is reserved for patients with massive liver involvement and respiratory compromise. Young infant (<6 month of age) and children diagnosed with neuroblastoma in prenatal period typically present with small, localized adrenal tumours that have excellent survival outcomes with expectant observation [31]. Strong evidence suggests that majority of tumours in this age group will spontaneously regress without the need for surgical or medical intervention [32].

Treatment of Intermediate Risk Neuroblastoma this group include: Patients with INSS stage 3 with non- amplified MYCN and favourable shimada pathology. Infants with INSS stage 4 with non- amplified MYCN. Infants with INSS stage 4s with non- amplified MYCN and unfavourable shimada pathology [1]. Treatment contain surgical resection and moderate dose, multi-agent chemotherapy including cisplatin, doxorubicin, etoposide, and cyclophosphamide, the survival rate after surgical resection and chemotherapy is more than 90%-95% for children whose tumours show favourable characteristics [33,34].

Treatment of High-Risk Neuroblastoma this group include: Patients older than one year, with stage 4, and amplified MYCN. Patients with INSS stage 3, and amplified MYCN. Patients older than one year, with INSS stage 3, and unfavourable shimada pathology. Patients with INSS stage 2, amplified MYCN, and unfavourable shimada pathology. Patients with INSS stage 4s, and amplified MYCN standard therapy for patient with high risk neuroblastoma involved induction, local control, consolidation and treatment of minimal disease with biological agents [1]. Children with high risk neuroblastoma have long term survival rate between 25% and 35% with current treatment that consists of intensive chemotherapy, Autologous Stem Cell Transplantation (ASCT), surgery, irradiation and 13-cis-retinoic acid (isotretinoin, Accutane).Current induction chemotherapy in high risk neuroblastoma protocol includes combinations of cyclophosphamide, doxorubicin, vincristine, cisplatin and etoposide an alternative induction strategy is to add noncross-resistant cytotoxic agent into this multiagent chemotherapy, included topotecan, has activity in recurrent neuroblastoma [1,35]. Delay surgical resection after at least three cycles of induction chemotherapy offers the most optimal treatment success. While some case series suggest that aggressive removal of all primary tumour improves patient survival and or decrease local recurrence rate [36-38].

The addition of intensified myeloablative chemotherapy followed by autologous stem cell rescue has significantly improved outcomes in children with high risk disease [5,39].

# Patients and Methods

A retrospective study was carried out in the period between the 1st of October 2016 till the end of March 2017.On children less than 15 years of age who were diagnosis with neuroblastoma, patients were admitted and register in Pediatric Oncology Center at Basra Children Oncology Hospital during the period from the 1st of January 2004 till the end of December 2016.

Total cases of neuroblastoma admitted to the Center during that period were 179 cases, and their age ranged from less than one year to 14 years, the diagnosis of neuroblastoma was built on history, clinical examination, imaging studies, and histopathological examination of a biopsy specimen according to International neuroblastoma staging system (INSS) [1,17,20]. A special data sheet was designed for the purpose of the study .The following information was taken from patients files: name, age (date of birth), date of admission, gender. Residences of patients with neuroblastoma were taken and to simplify the major areas of Basra, a classification was designed by Habib OS *et al.* in 2007 [40].

Basrah governorate was separated into 5 district areas: Basrah centres, northern area (that include Qurna, Modina, Hartha), and western area (Al Zubiar district), eastern area (Shatt Al Arab and Alshlamja) and southern area (Abu Alkhaseeb and Fao). Other governorates like Thi Qar, Maysan, also were included in the sheet which also included the clinical features at presentation including symptoms and signs: fever, pallor, anorexia, weight loss and dyspnea, abdominal mass, abdominal distension, proptosis, diarrhea, subcutaneous ecchymosis, periorbital ecchymosis and others.Histopathology was reviewed; (undifferentiated neuroblastoma, ganglioneuroblastom), standard therapy for patient with high-risk neuroblastoma involved induction, local control, consolidation and treatment of minimal disease with biological agents [1]. Current induction chemotherapy in high-risk neuroblastoma protocol includes combinations of cyclophosphamide, doxorubicin, vincristine, cisplatin and etoposide, staging of tumor (I, II, III, IV, and IVs), according to International neuroblastoma staging system (INSS) [1,17,20], distant metastasis and site of metastasis (bone marrow, bone, liver, skin, and lung) were included in the sheet.

The outcome of the patient (completed treatment, on treatment, non-compliance, died) also included, non-compliance defined as the patients who dose note take a prescribed medication or follow a prescribed course of treatment [41].

179 children with neuroblastoma was study, with special data sheet was use the number of patients with neuroblastoma arrange in according to year of diagnosis, age, gender, residence, and also according to clinical feature at presentation, stage of tumour, site of primary tumour, with sites of metastasis, and type of treatment (surgery, chemotherapy or both), the outcome of patients also study according to age and also according to years of diagnosis.

Statistical analysis was done using the Statistical Packages for Social Sciences (SPSS) software version (23), data were expressed and mean age ± standard deviation was performed. Comparisons of proportions were performed by cross tab using Chi-Square test when each cell has an expected frequency of five or more. P value 0.05 was considered to be statistically significant.

# Results

Table 1 reveals that the high percentage of patients at 2009 (14.52%), then follow by 2015 (13.40%), 2013 (12.84%), and low percentage was at 2008 (3.35%).

| Years | Total number of cases | Percentage |
|---|---|---|
| 2004 | 9 | 5.03% |
| 2005 | 8 | 4.47% |
| 2006 | 9 | 5.03% |
| 2007 | 11 | 6.14% |
| 2008 | 6 | 3.35% |
| 2009 | 26 | 14.52% |
| 2010 | 9 | 5.02% |
| 2011 | 17 | 9.49% |
| 2012 | 9 | 5.02% |
| 2013 | 23 | 12.84% |
| 2014 | 19 | 10.61% |
| 2015 | 24 | 13.40% |
| 2016 | 9 | 5.02% |
| Total | 179 | 100% |

**Table 1: Distribution of patients with neuroblastoma according to years of admission.**

Table 2 shows that males are more than females (104, 75 respectively), with M/F ratio (1.4:1), most of cases had occurred in age group 1-5 years and followed by age group <1 year. And the mean age was 2.8 years.

| Age | Male | female | Total | P-Value | Male /Female ratio | Mean age(year)±SD |
|---|---|---|---|---|---|---|
| <1 year | 27 (73%) | 10 (27%) | 37 (100%) | <0.063* | 1.4:1 | 2.8 ± 2.4 |
| 1-5 years | 66 (56.4%) | 51 (43.6%) | 117 (100%) | | | |
| >5->10 years | 11 (44%) | 14 (56%) | 25 (100%) | | | |
| Total | 104 (58.1%) | 75 (41.9%) | 179 (100%) | | | |
| *P-value assessed by chi-square | | | | | | |

**Table 2: Distribution of patients with neuroblastoma in relation to the sex and age.**

Table 3 shows that most of patients were from Basrah (84 patient represent 46.8% of total admission).Other governorates like Thi Qar and Maysan represent (28.5%, 21.8% respectively of admitted cases). The p-value <0.000.

| Residence | Patients with neuroblastoma | Total No (%) | p-value |
|---|---|---|---|
| Basra | 84 | -46.80% | |
| Thi Qar | 51 | -28.50% | |
| Maysan | 39 | -21.80% | |
| Other | 5 | -2.80% | |
| Total | 179 | -100% | <0.0008* |
| *P-value assessed by chi-square | | | |

**Table 3: Distribution of patients with neuroblastoma according to their residence.**

Table 4 shows that most patients were from the center and northern areas of Basra (22.3%, 12.3% respectively), then western (5%), southern (5%) and lastly eastern areas (2.2%). p- value is <0.00001.

| Residence | Patient with neuroblastoma | p- value |
|---|---|---|
| Basra center | 40 (22.3%) | <0.00001* |
| Northern areas | 22(12.3%) | |
| Southern areas | 9(5%) | |
| Eastern areas | 4(2.2%) | |
| Western areas | 9(5%) | |
| Total | 84(46.9%) | |

**Table 4: Distribution of patients with neuroblastoma in Basra.**

Table 5 shows that most patients with neuroblastoma presented with abdominal mass (59.8%), abdominal distension (41.9%), pallor (48.6%) and fever (45.3%).

| Clinical features | No. of percentage |
|---|---|
| Fever | 81(45.3%) |
| Pallor | 87(48.6%) |
| F.T.T | 25(14%) |
| Irritability | 18(10.1%) |
| Bone pain | 23(12.8%) |
| Diarrhea | 10(5.6%) |
| Weakness | 11(6.1%) |
| Proptosis | 15(8.4%) |
| HSM | 16(8.9%) |
| Subcutaneous ecchymosis | 8(4.5%) |
| Anorexia | 14(7.8%) |
| Scalp lesion | 16(8.9%) |
| Dyspnea | 19(10.6%) |
| Weight loss | 26(14.5%) |

| | |
|---|---|
| Periorbital ecchymosis | 5(2.8%) |
| Horner syndrome | 2(1.1%) |
| Abdominal distention | 75(41.9%) |
| Abdominal mass | 107(59.8%) |
| LAP | 16(8.9%) |
| FIT | 3(1.1%) |

**Table 5: Clinical feature of patients with neuroblastoma.**

Table 6 reveals that high percentage of patients presented with stage VI (52.4%) and stage III(39.7%) of disease, and low percentage of patients presented with stage I (1.1%) and stage II (4.5%).

| **Stage of disease** | **No. of patients with neuroblastoma** |
|---|---|
| Stage I | 2(1.1%) |
| Stage II | 8(4.5%) |
| Stage III | 71(39.7%) |
| Stage VI | 92(52.4%) |
| Stage Vis | 6(3.4%) |
| Total | 179(100%) |

**Table 6: Distribution of patients according to stage of neuroblastoma at presentation.**

Table 7 reveal the high percentage of patients presented with adrenal site as the primary site of tumor (68.7%), followed by retroperitoneal (20.7%) and the least site of presentation was thoracic, cervical, pelvic (8.9%, 1.1%, 0.6%).

| **Site of neuroblastoma** | **No. percentage** |
|---|---|
| Adrenal | 123 (68.7%) |
| Retroperitoneal | 37 (20.7%) |
| Cervical | 2 (1.1%) |
| Thoracic | 16 (8.9%) |
| Pelvic | 1 (0.6%) |
| Total | 179 (100%) |

**Table 7: Site of neuroblastoma.**

Table 8 shows that (52%) patients with neuroblastoma had metastatic disease at presentation; high percentage of them had bone marrow metastasis (40.2%).then bone metastasis (6.1%), liver metastasis (3.9%), and low percentage lung metastasis (1.7%).

| **Site of metastasis** | **No. percentage** |
|---|---|
| Bone | 11 (6.1%) |
| Bone marrow | 72 (40.2%) |
| liver | 7 (3.9%) |
| lung | 3 (1.7%) |
| Total | 93 (52%) |

**Table 8: Site of metastasis in patients with neuroblastoma.**

Table 9 shows that the most common type of sympathetic nervous system tumors was undifferentiated neuroblastoma (93.8%).

| Patients with neuroblastoma | Histopathology | | Total |
|---|---|---|---|
| | ganglioneuroblastoma | Undifferentiated neuroblastoma | 179(100%) |
| | 11(6.1%) | 168(93.8%) | |

**Table 9: Distribution of patients with neuroblastoma according to histopathology.**

Table 10 shows that most patients were managed with surgery and chemotherapy (46.9%), or chemotherapy alone (44.1%).Management with surgery alone less common (6%), and patient refuse treatment about (8.4%).

| Treatment modalities | No. of percentage |
|---|---|
| Surgery | 1 (6%) |
| Chemotherapy | 79 (44.1%) |
| Surgery + Chemotherapy | 84 (46.9%) |
| Refuse treatment | 15 (8.4%) |
| Total | 179 (100%) |

**Table 10: Treatment modalities in patients with neuroblastoma**.

Table 11 illustrates high percentage of death (51.4%), follow with high percentage of non-compliance (20.7%), patient who end their therapy represent (20.1%) of all patients. P value is highly significant <0.0009.

| Outcome | No. of Percentage | P value |
|---|---|---|
| Completed treatment | 36(20.1%) | <0.0009* |
| Non compliance | 37(20.7%) | |
| On Treatment | 14 (7.8%) | |
| Died | 92(51.4%) | |
| Total | 179(100%) | |
| *P-Value assessed by chi-square | | |

**Table 11: Outcomes of patients with neuroblastoma.**

Table 12 show the age group (1-<5 years) have high percentage of death (73.9%), and group <one year (15.2%), with low percentage at age group 5->10years (10.9%). The p -value was <0.01.

| Age | Fate | | | | | p-value |
|---|---|---|---|---|---|---|
| | On treatment | finish | Non compliance | died | Total | |
| <1 year | 2 (14.3%) | 10 (27%) | 11 (30.6%) | 14(15.2%) | 37(20.7%) | |
| 1-<5 years | 6 (42.9%) | 21(56.8%) | 22 (61.1%) | 68(73.9%) | 117(65.4%) | |
| 5->10 years | 6 (42.9%) | 6 (16.2%) | 3(8.3%) | 10(10.9%) | 25(14%) | |
| Total | 14(100%) | 37(100%) | 36(100%) | 92(100%) | 179(100%) | <0.01* |
| *p-Value assessed by chi-square | | | | | | |

**Table 12: Outcome the patients with neuroblastoma according to age of presentation.**

Table 13 shows high percentage of death (15.2%) at 2015, then 2009 (12%) follow 2014 (10.9%), high

percentage of non complains (36.1%) at 2009 follow by 2013 (13.9%), 2011 (11.1%), the high percentage of patients finish treatment at 2013 (27%) , follow2014(18.9%), then 2011(16.2%). The percentage of patients still on treatment at 2016 (57.1%), 2015 (28.6%), 2013 (7.1%) and 2012 (7.1%) respectively.

| **Year of diagnosis** | **Outcome** | | | | **Total** |
|---|---|---|---|---|---|
| | **Still on treatment** | **Finish treatment** | **Non complains** | **Died** | |
| 2004 | 0 | 2 | 1 | 6 | 9 |
| %within year | 0.00% | 22.20% | 11.10% | 66.70 % | 100% |
| %within outcome | 0.00% | 5.40% | 2.80% | 6.50 % | 5.00 % |
| 2005 | 0 | 4 | 0 | 4 | 8 |
| %within year | 0.00% | 50% | 0.00% | 50% | 100% |
| %within outcome | 0.00% | 10.80% | 0.00% | 4.30 % | 4.50 % |
| 2006 | 0 | 0 | 1 | 8 | 9 |
| %within year | 0.00% | 0.00% | 11.10% | 88.90 % | 100% |
| %within outcome | 0.00% | 0.00% | 2.80% | 8.90 % | 5.00 % |
| 2007 | 0 | 1 | 4 | 6 | 11 |
| %within year | 0.00% | 9.10% | 36.40% | 54.50 % | 100% |
| %within outcome | 0.00% | 2.70% | 11.10% | 6.50 % | 6.10 % |
| 2008 | 0 | 0 | 2 | 4 | 6 |
| %within year | 0.00% | 0.00% | 33.30% | 66.70 % | 100% |
| %within outcome | 0.00% | 0.00% | 5.60% | 4.30 % | 3.40 % |
| 2009 | 0 | 2 | 13 | 11 | 26 |
| %within year | 0.00% | 7.70% | 50% | 42.30 % | 100% |
| %within outcome | 0.00% | 5.40% | 36.10% | 12% | 14.50 % |
| 2010 | 0 | 2 | 1 | 6 | 9 |
| %within year | 0.00% | 22.20% | 11.10% | 66.70 % | 100% |
| %within outcome | 0.00% | 5.40% | 2.80% | 5.50 % | 5% |
| 2011 | 0 | 6 | 4 | 7 | 17 |
| %within year | 0.00% | 35.30% | 23.50% | 41.20 % | 100% |
| %within outcome | 0.00% | 16.20% | 11.10% | 11.10 % | 9.50 % |

| | | | | | |
|---|---|---|---|---|---|
| 2012 | 1 | 0 | 0 | 8 | 9 |
| %within year | 11.10% | 0.00% | 0.00% | 88.90 % | 100% |
| %within outcome | 7.10% | 0.00% | 0.00% | 8.70 % | 5% |
| 2013 | 1 | 10 | 5 | 7 | 23 |
| %within year | 4.30% | 43.50% | 21.70% | 30.40 % | 100% |
| %within outcome | 7.10% | 27% | 13.90% | 7.60 % | 12.80 % |
| 2014 | 0 | 7 | 2 | 10 | 19 |
| %within year | 0.00% | 36.80% | 10.50% | 52.60 % | 100% |
| %within outcome | 0.00% | 18.90% | 5.60% | 10.90 % | 10.60 % |
| 2015 | 4 | 3 | 3 | 14 | 24 |
| %within year | 16.70% | 12.50% | 12.50% | 58.30 % | 100% |
| %within outcome | 28.60% | 8.10% | 8.30% | 15.20 % | 13.90 % |
| 2016 | 8 | 0 | 0 | 1 | 9 |
| %within year | 88.90% | 0.00% | 0.00% | 11.10 % | 100% |
| %within outcome | 57.10% | 0.00% | 0.00% | 1.10 % | 5% |
| Total | 14 | 37 | 36 | 92 | 179 |
| | 7.80% | 20.70% | 20.10% | 51.40 % | 100% |
| | 100% | 100% | 100% | 100% | 100% |

**Table 13: Outcome the patients with neuroblastoma according to years of presentation.**

# Discussion

Neuroblastoma is the third most common malignancy in the pediatric age group following leukemia and brain tumors [42]. This study provided important data concerning the age, stage, treatment modalities and clinical characteristics of Iraqi children in Basrah with neuroblastoma and their expected outcome. The study showed that 179 (10.91%) patients with neuroblastoma from 1640 patients with malignancy was diagnosis during 13 years, the numbers of patients with neuroblastoma were treated in Basrah pediatric oncology center increase gradually from (5%) at 2004 to (13.43%) at 2015, this may be due improved registration of cases and due to increase number of registered malignancies, also might be due to increase awareness of people about the presence of specialized center. According to neuroblastoma were significantly more common in male than female. With male: female ratio was 1.4:1 these result are comparable to study was done in Iraq - Basrah by Dawood *et al.* [41] and the result of study was done in Saudi Arabia, in Riyadh done by Al Naqib *et al.* [43] A similar result was reported by Bordbar MR *et al*. in Shiraz, south Iran [42] who observed the male is predominate sex in patients with neuroblastoma.

Regarding to the age, neuroblastoma was mostly recognized among children with age group 1-5 year, this is in

agreement with result of a study in Iraq-Basrah done by Dawood *et al.* [41], and other study in Turkey done by Aydin GB *et al.* [45] who observed that the neuroblastoma higher among this age group. Also similar to result of study done in Southern of Iran, done by Bordbar MR *et al.*, the higher detection rate in 18-60 months of age [42]. This age group is already considered as the high risk group according to International Neuroblastoma Risk Group (INRG), disagreement to the result of studies done in France by Desands E *et al.* [45] who demonstrated that the predominant in age group below one year. This is because neuroblastoma is a disease of infancy and early childhood [46]. The mean age for patients with neuroblastoma was 32 months were similar to the results of Indian study done by Kusumakumary P *et al.* mean age was 30 months, and similar to the study was done in Turkey by Aydn GB *et al.* the mean age 33 months. While other studies done in Southern Africa by Hesseling PB *et al.* the mean age was 18 months [44,47,48].

Neuroblastoma shown significance prominent distribution rate within patients were came from center of Basrah than northern areas of Basrah, this is in agreement to the result was done in Iraq-Basra, the most patients were from Basrah (center, and northern area) and this due to increase register cases [41].

In this study the major presenting complaints of patients with neuroblastoma were abdominal mass followed by GIT symptom and other like pallor, fever and weight loss, same presentations were registered in many studies but differed in their frequencies. In India [46], Saudi Arabia [43] and in Egypt [49] most patients with neuroblastoma present in advanced stage at time of diagnosis (stage III and IV), metastatic sites, included bone marrow/ bone, lymph nodes, liver, lung. Result was similar in study was done in Turkish by Aydn GB *et al*. and other done in Malaysia stage by Ng SM, Abdullah WA *et al.* but disagreement to study was done in Iran the common metastasis site is bone followed by bone marrow [42,43,50]. Delayed presentation may be due to ignorance, poverty, wrong diagnosis, and due to that some people still trust and use traditional treatment and herbal medicine by local healers.

The primary site of neuroblastoma was adrenal follow by retroperitoneal then thoracic, cervical and pelvic, similar result was observed in study was done in Saudi Arabia and other study in Iran also the primary site was adrenal and retroperitoneal [42,43].

The study revealed that undiffertaitied neuroblastoma was the most common histological finding representing about (93.8%), followed by subtype ganglio neuroblastoma (6.1%), similar result were found in Moscow study, (51) and other study in Saudi Arabia was the common histological finding neuroblastoma (70%), followed by ganglio neuroblastoma (25%), ganglio neuroma (5%) [43].

About treatment modalities, most patients with neuroblastoma were managed with chemotherapy and surgery follows with chemotherapy alone. Similar to result of study was done in Turkish by Aydn GB *et al.* demonstrated that combined modality treatment with aggressive surgery and intensive chemotherapy is needed to cure majority of neuroblastoma patients [42,43]. Also with development of methods in pediatric surgery, anesthesia, and intensive care, the role of surgery in treatment of neuroblastoma has increase [43].

Non- compliance of patients with neuroblastoma form high percentage in our study, the common reasons for non-compliance may be related to poverty, living away from the treating center, or failure to tolerate side effects of chemotherapeutic drugs, also most families that seek management for their children with cancer believe that they will die, this suspicious certainty sometimes leads to non- compliance with treatment, similar result was also observed in study was done in Nigeria [46].

High mortality was observed among patients in this study, patients, higher death occur specially among patients presented with late stage of the disease and most of death occur due to the advanced metastatic disease and

infection. High mortality was also observed in Nigeria study done by Darcy A. Kerr *et al*. and mostly occurred in patients with late stage of disease [46]. The outcome of patients with neuroblastoma varies with age because of its clinical characteristics. The age group < one year was significantly outcome better, low percentage of death than age group 1-5 year, because age younger than 1 year is a strongly favorable factor by itself, this similar to result was done in South Egypt by El-Sayed MI *et al.* and also similar to study was done in China, at Shanghai Children Hospital by Shao JB *et al.* demonstrate that patients with aged between 12 and 18 months of age have signification improved outcome compared with older children [52,53].

Regarding the outcome of children with neuroblastoma according to year of admission high mortality rate was observed in the last 5 years, this poor result relate to the problems with fundamental issues such as ignorance, inadequate drug supply and increase number of cases with increase registering of cases and lack of collaboration so increase awareness about early sign and symptoms of the disease and improving the diagnostic facilities, with psychological support in order to resolve this problem.

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