# CHARACTERISTICS AND TREATMENT OF HEPATOBLASTOMA IN CHILDREN AT PEDIATRIC HOSPITAL 2

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### ABSTRACT

**Objectives:** To determine the epidemiological, clinical, paraclinical characteristics and evaluate the result in treatment of hepatoblastoma (HB) at Department of Hematology-Oncology, Children's Hospital 2 from January 2011 to end of May 2019.

Method: Cases series study in combination of retrospective and prospective.

**Results:** From January 2011 to end of May 2019, there were 67 patients diagnosed with HB. The mean age at diagnosis was 22.7 ± 22.9 months with the most prevalent age group ranging from 6 months to 3 years old. The male to female ratio was 1.8/1. The most common clinical symptoms were abdominal distention and hepatomegaly, approximately 7.5% HB cases were detected accidentally by ultrasound. Nearly 60% and 80% patients presented with anemia and thrombocytosis at admission, respectively. Almost tumors were unifocal locating in the right lobe of the liver and 58.2% cases belonged to standard risk group. Assessing treatment protocol in 54 HB patients demonstrated that number of patients undergoing hepatectomy after preoperative chemotherapy accounted for 82%. The most frequent acute side effects after chemotherapy were myelotoxicity and infection. The proportion of fatal and relapsed cases was 31.5% and 12.9% respectively. Overall and event-free survival rate of the study after 3 years was 65.7% and 68.1% individually.

**Conclusion:** Hepatoblastoma is a rare malignant childhood disease, significantly response to chemotherapy followed by surgery. However mortality rate is rather high compared to worldwide reasearchs. Thus development of liver transplant is necessary to improve survival rate.

Keywords: Hepatoblastoma, chemothearapy, surgery, liver transplant.

#### **I. INTRODUCTION**

Hepatoblastoma (HB), generally observed in infants and children under 3 years old, comprises nearly 60% of all primary malignant tumors of the liver during childhood [4, 7, 8]. Most cases of HB are sporadic, but sometimes it is found to associated with some inherited syndromes such as familial adenomatous polyposis and Beckwidth-Wiedemann syndrome [7]. Incidence of HB has appeared to increase over the last 30 years [5]. The most common clinical manifestation is abdominal mass accompanying with elevated serum AFP [7]. Recent innovations in treatment have significantly increased the survival rate of patients with HB during the past few decades, including chemotherapy with platinum-based anticancer drugs combined with surgery and liver transplant [6].

In developing country like Viet Nam researches relating hepatoblastoma are limited. Particularly in Ha Noi, capital city of Viet Nam, there was a

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study of Le Thi Thuy Dung evaluating treatment response of HB in 2014. In Ho Chi Minh city, Au Duong My Phung investigated clinical features and results in cure of HB at Oncology hospital in 2008. In surgical field, Truong Dinh Khai'sstudy in 2015 assessed outcomes of hepatectomy in HB patients administered with priorchemotherapy. In general, all researches mentioned above showed optimistic result of the HB regimens applying to Vietnamese pediatric patients [1, 2, 3].

Children's hospital 2 is one of the top two pediatric hospitals in the Southern region. The department of Hematology and Oncology was established in 2011 with the aim to elaborate pediatric oncology field and relieve the burden for Oncology hospital. Since the faculty was built, there has been no report about hepatoblastoma especially treatment result and survival rate although different regimens have been carried out to save many tiny lives. Therefore, determining the characteristics and evaluating the treatment results of hepatoblastoma are necessary to not only have an overview about this disease but also premise for following studies afterward.

#### Objectives

Identify epidemiological, clinical, paraclinical features of pediatric patients diagnosed hepatoblastoma.

Evaluate treatment outcomes of hepatoblastoma: the response rate after chemotherapy, disease-free status proportion, acute side effects of anticancer drugs, three-year survival rate based on Kaplan – Meier estimator.

# **II. PATIENTS – STUDY METHODS**

#### 2.1. Study methods

Cases series study in combination of retrospective and prospective

From January to end of November 2018: retrospective figures from medical records.

From December 2018 to end of May 2019: prospective data from new patients diagnosed with hepatoblastoma.

#### 2.2. Patients

All pediatric patients under 15 years old diagnosed hepatoblastoma at Children's hospital 2 from January 2011 to end of May 2019.

#### General criterias for patient eligibility

Children under 15 years old admitted to Pediatric hospital 2 from January 2011 to end of May 2019

Diagnosis standards:

- Clinical findings: some common symptoms such as abdominal distention, hepatomegaly and upper abdominal mass.

- Serum AFP level increased comparing with normal reference values by age.

- Compatible imaging particularly abdominal CT matching hepatoblastoma, thoracic CT assessed metastasis. All images relating to disease were taken and interpreted by radiologists at Children's hospital 2.

- Histopathological result: gold standard for diagnosis. The specimen after biopsy was sent to histopathological department of University of Medicine and Pharmacy - Ho Chi Minh city for analyzation.

- If no biopsy was performed, clinical symptoms combining with suitable image and elevated AFP level were also helpful for definite diagnosis.

Pediatric patients were treated with the regimen using in Hematology – Oncology faculty depending on the risk group: SIOPEL 3 protocol for standard and high risk group and SIOPEL 4 guideline for very high risk group.

### **Excluding criterias**

Abnormal function of heart, liver and kidney at time of diagnosis.

Medical history of chemotherapy or hepatoblastoma treatment.

Medical record contains < 80% information needed or missing.

Children lost to follow-up.

\* All figures are analyzed by software Excel 2016 and SPSS 25.

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# **III. RESULTS**

Features Number of patients % Median age: 15 months Mean age:  $22,7 \pm 22,9$  months Age group 9 13.4 Under 6months 6 months - 3 years48 71.6 Above 3 years 10 14.9 Male 43 64.2 Sex Female 24 35.8 44 Hepatomegaly 65.7 **Abdominal distention** 31 46.3 Palpable abdominal mass 18 26.9 41 Anemia 61.2 53 79.1 **Thrombocytosis** 39 **Right liver tumor** 58.2 **Unifocal tumor** 53 79.1 3 4.5 HbsAg (+) 7 Lung metastases 10.4 18 38.3 Mixed fetal and embryonal type

*Table 1: Clinical and paraclinical characteristics of HB patients (N=67)* 

The mean age of pediatric patients at admission was  $22.7 \pm 22.9$  months, and the most common age group ranging from 6 months to 3 years accounted for 71.6%. Male to female ratio was 1.8/1. The differences among age groups and between two genders were statistically significant with p value < 0.05

The most frequent symptoms of HB were hepatomegaly, abdominal distention and palpable mass.

Table2:Treatment	results	of HB	(N=54)
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Features	%
Primary hepatectomy	7.4
Partial response to chemo.	70
Hepatectomy after chemo.	82
Myelotoxicity	96.3
Infection	45.6
Surgical complications	15.6

The proportion of children with anemia and thrombocytosis was 61.2% and 79.1%, respectively. All cases showed elevated serum AFP at diagnosis. Almost tumors were unifocal in the right liver. Only three cases with 4.5% presented HbsAg (+) on lab value. Lung metastases constituted 10.4% of all HB patients. The most prevalent histological sub-type was mixed fetal and embryonal with percentage of 38.3%.

Aliveness	Disease-free	66.7
With	1.9	
Death	Unresectable	22.2
After	7.4	
	Treatment complications	1.9
Relapse	Still alive	5.6
Death		7.4

Primary hepatectomy rate of this study was

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7.4%. Partial response to chemotherapy accounted for highest percentage of 70%. Preoperative chemotherapy facilitated 82% tumors becoming resectable. The common side effects of anticancer drugs were myelotoxicity and infection. About 15.6% cases had surgical complication. Diseasefree status comprised 66.7% of all patients. The most common cause of deaths was unresectable or remnant tumors with 22.2%.



Figure 1: Overall survival rate of study and by the risk group

Three-year overall survival (OS) rate of this research was  $65.7 \pm 6,9\%$ . By risk group, standard risk had the highest OS rate among groups with 87.5% (p=0.001 – statistical significance).

## **IV. DISCUSSION**

The average age at admission in our study was 22.7 months, lower than Le Thi Thuy Dung but higher than SIOPEL 3 as 24.4 and 19.1 months respectively [2, 11]. Hepatoblastoma in our country is still detected later than other developed countries. The most prevalent age group - from 6 months to 3 years old and male to female ratio 1.8/1 are

suitable for literature and researches domestically and internationally [2, 3, 7, 11].

The prominent clinical manifestations such as hepatomegaly, abdominal distention and palpable tumor were similar to Le Thi Thuy Dung [2]. Company to Zhang Y and medical literature, palpable tumor had rather high rate with 70-80% [7, 9]. Most patients with anemia and high platelets at diagnosis were also appropriate for Le Thi Thuy Dung, Truong DinhKhai and worldwide literature [2, 3, 11].

Partial response to chemotherapy accounted for 70% was the most frequent response, this result was nearly equivalent to Le Thi Thuy Dung 92.3% and SIOPEL 3 93%. After preoperative chemotherapy, resectable tumors were responsible for 82%, similar to the result of Le Thi Thuy Dung 83% and SIOPEL 93% [2, 10, 11]. Thus chemotherapy plays an important role in rising the rate of removal of tumors. The disease-free status comprised 66.7%, slightly lower than Le Thi Thuy Dung 76.1% and SIOPEL 88.2%. Comparing to mortality rate, our study was much higher 31.5% while Le Thi Thuy Dung and SIOPEL 3 recorded the number of deaths accounting for 17.4% and 5.6% individually [2, 11]. The reason for this event was due to high number of unresectable and remnant tumors while liver transplant hasn't been developed yet. The threeyear OS rate was  $65.7 \pm 6.9\%$ , matched to Truong DinhKhai 66% but lower than Le Thi Thuy Dung 88.3% and world studies [2, 3, 11]. There was a clear difference in 3-year OS rate according to the risk group with standard risk had the highest rate up to 87.5%, similar to Le Thi Thuy Dung's statistics 92.2% and SIOPEL 3 95% [2, 11]. Generally, the survival rate in our study was still low compared to foreign countries due to high rate of ineradicable tumors in the condition of developing country - high techniques such as liver transplant is still unpopular.

## **V. CONCLUSION**

Almost all hepatoblastoma patients belonged to group under 3 years old, with the common symptoms: hepatomegaly and abdominal distention

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mde was prodomonat more frequent in male with common clinical findings as enlarged liver and abdominal distention.

The disease-free rate after chemotherapy and

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surgery was 66.7%. However, a high mortality rate of 31.5% reduces survival time leading to low 3-year OS rate of 65.7%. Evolving liver transplantation field promises to improve survival prognosis.