

# Pediatric Hepatoblastoma: A Single-Institution Case Series

Jessica Sawaya,<sup>1</sup> Joyce McRae,<sup>1</sup> Georgi D. Mladenov,<sup>2</sup> Andrei Radulescu.<sup>3</sup>

## Abstract

**Introduction:** Hepatoblastomas comprise up to two-thirds of malignant liver masses in childhood and rank as the third most common malignant neoplasm in children under the age of three. Treatment and prognosis are highly dependent on tumor staging and characteristics. Our study's aim is to analyze the clinical findings and outcomes of hepatoblastoma at our institution. **Methods:** After Institutional Review Board (IRB) approval was granted from Loma Linda University #5240020, we conducted a retrospective review on all patients under the age of 18 with a diagnosis of hepatoblastoma between February 2000 to January 2022. Variables assessed included demographics, work up, surgical intervention, recurrence, and mortality. **Results:** Fifteen patients were diagnosed with hepatoblastoma within that timeframe. Mean age was 18.7 months. Associated comorbidities included three patients with prematurity, one patient with Beckwith-Wiedemann Syndrome, and two unique presentations each of Prune Belly Syndrome and grade IV/V vesicoureteral reflux. There were four mortalities, two due to relapse in disease, one due to pulmonary and CNS metastasis at diagnosis, and another due to sepsis and multi-organ failure. Eleven patients continued monitoring without tumor recurrence. All patients were treated based on the Children's Oncology Group (COG) guidelines. **Conclusion:** Risk stratification is an important component of hepatoblastoma management. Our cohort demonstrated novel comorbidities of Prune Belly Syndrome and vesicoureteral reflux. Eleven patients received neoadjuvant chemotherapy that allowed for subsequent surgical resection. Our mortalities were associated with tumor metastasis and recurrence consistent with elevated alpha-fetoprotein (AFP) values. Future research should involve multi-institutional studies focusing on comorbidities and genetic analysis.

## Introduction

Hepatoblastoma is the most common primary hepatic malignant tumor in children and is the third most common malignant neoplasm in those under three years of age following neuroblastoma and nephroblastoma, respectively.<sup>1,2</sup> They account for up to 60% of malignant liver masses in childhood and 1% of all pediatric cancers with the highest incidence in those below the age of four.<sup>1-3</sup> The incidence in males is approximately 1.5 times higher than in females.<sup>2,4,5</sup> Nevertheless, hepatoblastoma remains a rare malignancy with an incidence in the United States of 10.5, 5.2, and 0.1 cases per 1 million children in the age groups of younger than one year, one to four years, and five to nine years, respectively.<sup>3</sup> Certain factors, including low birth weight (<1500 grams), exposure to the neonatal intensive care unit (NICU), Beckwith-Wiedemann Syndrome, Familial adenomatous polyposis (FAP), Trisomy 18, and maternal or paternal smoking prior to conception are associated with the development of hepatoblastoma.<sup>3,5,6</sup>

In most cases, hepatoblastoma has no presenting symptoms other than a palpable mass in the right upper abdominal quadrant.<sup>2,6-8</sup> Symptoms such as nausea, vomiting, weight loss,

and weakness begin to occur at more advanced disease states as the enlarging tumor begins to compress nearby organs.<sup>4,6,7</sup> Serum AFP is elevated in 80 to 90% of patients and can be used as a marker for treatment response and relapse.<sup>3,7-9</sup> Patients whose AFP level is below 100 ng/mL are considered to have poor prognosis.<sup>3,7,8</sup>

Treatment and prognosis are highly dependent on tumor staging and characteristics, including resectability, metastasis, response to chemotherapy, and histological component. A staging system defined by the International Childhood Liver Tumors Strategy Group (SIOPEL) called Pre-treatment extent of disease (PRETEXT) evaluates the extent of disease based on these factors and is beneficial for treatment planning.<sup>1,6,9</sup> The Children's Oncology Group (COG) stratifies treatment based on very low-risk, low risk, intermediate risk, and high-risk tumors requiring either primary resection alone, primary resection with either adjuvant therapy, neoadjuvant therapy or both, or liver transplant.<sup>10</sup> Due to advances in imaging modalities, surgical management, liver transplant, and chemotherapy protocols, overall survival has increased from thirty to seventy percent over the past three decades.<sup>1,2,7,11</sup>

<sup>1</sup> Third-year Medical Student. Loma Linda University School of Medicine, Loma Linda, CA, USA.

<sup>2</sup> MD. Division of Pediatric Surgery, Department of Surgery, Loma Linda University Children's Hospital, Loma Linda, CA, USA.

<sup>3</sup> MD, PhD. Division of Pediatric Surgery, Department of Surgery, Loma Linda University Children's Hospital, Loma Linda, CA, USA.

**About the Author:** Jessica Sawaya is currently a third-year medical student of Loma Linda University School of Medicine, CA, USA. She has recently published an article regarding gun violence in pediatric patients and is interested in pursuing a career in Cardiothoracic Surgery.

## Correspondence:

Jessica Sawaya

Address: Loma Linda University School of Medicine 11175 CA 92350, USA

Email: [ARadulescu@llu.edu](mailto:ARadulescu@llu.edu)

Editor: Francisco J. Bonilla-Escobar  
Student Editors: Eleni Georgiadi, SeShreya Sirivolu,  
Copyeditor: Leah Komer  
Proofreader: Laeeqa Manji  
Layout Editor: Daniela Collazos

Submission: Jun 5, 2024  
Revisions: Jul 11, Oct 27, 2024  
Responses: Jul 17, Nov 11 2024  
Acceptance: Nov 16, 2024  
Publication: Nov 19, 2024  
Process: Peer-reviewed

Given the rarity of this condition, we conducted a retrospective study on pediatric patients at our hospital with a diagnosis of hepatoblastoma to analyze patterns in clinical findings, treatment, and overall outcomes. Due to the smaller sample of patients, it was determined that a case series was best suited for this study's design.

## Methods

All patients under the age of 18 who presented to Loma Linda University Children's Hospital between the years of 2000 and 2022 with a diagnosis of hepatoblastoma were included in this retrospective case series (IRB approval #5240020). Cases were abstracted from an internal database. Each case was evaluated via the electronic medical record including review of radiological studies, operative reports, and histopathological results. Variables assessed included patient demographics (date of birth, age, sex, race, ethnicity, weight, height, BMI), primary diagnosis, tumor stage and location (using the PRETEXT system), lab values (including AFP), comorbidities, chemotherapeutic and surgical treatment, surgical events, tumor histopathology, relapse, and mortality. This case series has been reported in line with the PROCESS Guideline.<sup>16</sup>

## Results

A total of 15 patients were included in the study ranging from three months to four years of age with a mean age of 18.7 months ([Table 1](#)). Ten patients were male. Twelve patients were born at full term, with three patients born premature and four patients spending time in the NICU, one for pneumothorax and the other for a respiratory infection. Congenital conditions were present in seven patients including Prune Belly Syndrome (2), Beckwith-Wiedemann Syndrome (1), polyuric renal failure (1), bilateral grade IV vesicoureteral reflux, left sided grade V vesicoureteral reflux (2), cryptorchidism (1), and midgut malrotation (1). With regards to mass location, seven cases were in the right lobe of the liver, six cases in the left lobe of the liver, and two cases spanned both the right and left lobes. All patients presented with elevated AFP values, ranging between 1,210 and 1,248,500 ng/mL with an average of 303,294.2 ng/mL. Diagnosis of a liver mass was made via Computed Topography (CT) scan of the abdomen and pelvis and definitive diagnosis of hepatoblastoma was confirmed with biopsy ([Figure 1](#)). At the time of diagnosis, three patients demonstrated pulmonary metastasis with one patient having additional metastasis to the brain ([Table 1](#)).

Eleven patients underwent planned neoadjuvant chemotherapy following tumor biopsy due to initial tumor characteristics not being amenable to surgical resection ([Table 2](#)). [Neoadjuvant chemotherapy here is defined as chemotherapy administered prior to surgical intervention with the goal of shrinking the tumor.] Seven patients were enrolled in the AHEP0731 protocol consisting of cisplatin (CDDP) alone (2), cisplatin, 5-fluorouracil, and vincristine (C5V) (1), cisplatin, 5-fluorouracil, vincristine, and doxorubicin (C5VD) (2), vincristine, irinotecan, and temsirolimus (1), or carboplatin with doxorubicin alternating with vincristine (1)

depending on risk stratification and Tumor Board discretion. Four patients underwent tumor resection, and two patients had liver transplants. One patient who had pulmonary metastasis at the time of initial diagnosis had a thoracotomy with resection of metastatic pulmonary nodules prior to hepatectomy. Following surgery, these patients received postoperative chemotherapy, including C5V (1), CDDP (1), and C5VD (2). Within the group of patients enrolled in the AHEP0731 protocol, two patients ultimately died, one due to progression of pulmonary and CNS metastasis who was unable to undergo surgery secondary to severe thrombocytopenia and the other due to complications from tumor recurrence following neoadjuvant chemotherapy, tumor resection, and postoperative chemotherapy.

Of the four patients who were not enrolled in the AHEP0731 protocol, two received C5V, one received cisplatin, vincristine, and amifostine, and one received only cisplatin and amifostine. Two of these patients underwent tumor resection and received postoperative chemotherapy with C5V and amifostine. The remaining two patients only underwent liver biopsy, and both received post-procedural chemotherapy, one with C5V and amifostine and the other with CDDP. The latter patient died due to multi-organ failure and sepsis secondary to pneumonia.

Four patients were treated primarily with surgical management. All four patients underwent tumor resection or hepatectomy and three patients received postoperative chemotherapy with C5V and amifostine (2) and C5VD (1). One patient who received postoperative chemotherapy died due to tumor recurrence with pulmonary metastasis.

In terms of histologic patterns determined via liver biopsy or tumor resection, six patients were found to have mixed fetal embryonic pattern, three had a pure fetal pattern, one had a pure embryonal pattern, one had a macrotrabecular pattern, one had a mixed epithelial-mesenchymal pattern, and three patients' subtype were unavailable from retrospective chart review. No mortalities or tumor recurrences occurred in patients with the pure fetal histology. Two mortalities occurred in a patient with mixed fetal embryonal pattern. Tumor recurrence and mortality occurred in one patient with macrotrabecular and one patient with mixed epithelial-mesenchymal pattern.

Patients were followed on average for nine years following diagnosis, with a range of two years from most recent diagnosis in 2022 up to 19 years. For those that underwent surgical management, there were no reported intraoperative or immediate postoperative complications. Except for the four mortalities, the remaining eleven patients had no reports of tumor recurrence.

## Discussion

Hepatoblastoma can occur in children of any age. However, it most commonly presents in children between six months and three years of age, with a mean age of diagnosis at 16 months

**Table 1.** Summary of Reported Cases.

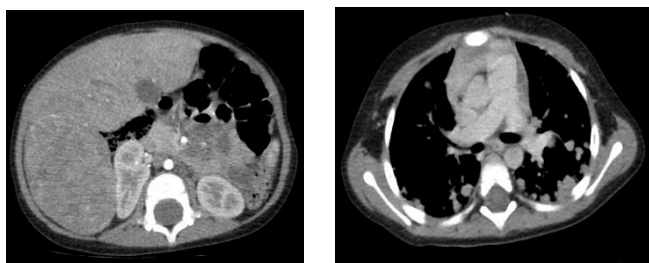
Case No.	Age	Sex	Comorbidities	Diagnosis	Metastasis at Diagnosis	Recurrence
1	3 mos	Female	None	Mixed fetal/embryonal hepatoblastoma	None	None
2	2 y	Female	None	Unspecified Hepatoblastoma	None	None
3	2 y	Female	Beckwith-Wiedemann Syndrome, Bilateral Sensorineural Hearing Loss	Macrotrabecular Hepatoblastoma	None	Yes, Pulmonary. Deceased
4	4 y	Female	Fetal Alcohol Syndrome, Developmental Delay, Bilateral Grade IV Vesicoureteral Reflux	Mixed epithelial/mesenchymal hepatoblastoma	None	Yes. Deceased
5	4 y	Female	None	Fetal hepatoblastoma	None	None
6	4 mos	Male	None	Mixed fetal/embryonal hepatoblastoma	None	None
7	8 mos	Male	None	Unspecified Hepatoblastoma	None	None
8	11 mos	Male	Premature (36 weeks) with NICU Stay, Prune Belly Syndrome, Chronic Kidney Disease	Fetal hepatoblastoma	None	None
9	11 mos	Male	None	Mixed fetal/embryonal hepatoblastoma	Pulmonary	None
10	11 mos	Male	None	Unspecified Hepatoblastoma	None	None
11	13 mos	Male	Prune Belly Syndrome, Left Grade V Vesicoureteral Reflux, Polyuric Renal Failure, Cryptorchidism, Midgut Malrotation	Embryonal hepatoblastoma	None	None
12	13 mos	Male	Premature (36 weeks) with NICU Stay	Fetal hepatoblastoma	None	None
13	15 mos	Male	NICU Stay for Pneumothorax at Birth	Mixed fetal/embryonal hepatoblastoma	Pulmonary	None
14	2 y	Male	Premature (32 weeks) with NICU Stay, Reactive Airway Disease	Mixed fetal/embryonal hepatoblastoma	None	Deceased
15	2 y	Male	None	Mixed fetal/embryonal hepatoblastoma	Pulmonary, Brain	Deceased

and rarely develops in children over five years.<sup>1,3,7</sup> If hepatoblastoma does present in those over five years of age, prognosis is typically poor in comparison to those less than one year of age.<sup>3,8,11</sup> In our cohort of 15 patients, the mean age of diagnosis was 18.7 months, with a range between three months and four years, consistent with the literature. Three of a total of four mortalities occurred in children trending toward the older extreme of our age range at two, three, and four years of age.

Many factors have been reported to be associated with hepatoblastoma including low birth weight, male gender, Neonatal Intensive Care Unit (NICU) exposure, preeclampsia, polyhydramnios and oligohydramnios, high maternal pre-pregnancy weight, treatment for infertility, and maternal or paternal smoking prior to conception.<sup>3,5,6</sup> Certain conditions also present with higher incidence in those with hepatoblastoma in comparison to the general United States population, such as Familial Adenomatous Polyposis (FAP), Beckwith-Wiedemann

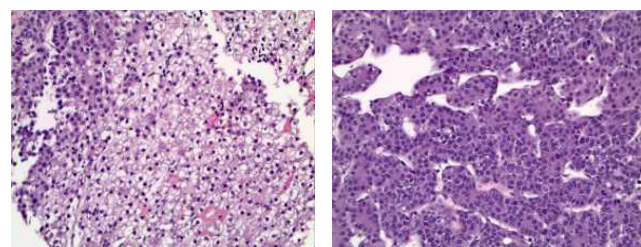
Syndrome, and Trisomy 18.<sup>3,5,6</sup> Our patients' comorbidities are consistent with previously published associations including NICU exposure due to prematurity, respiratory disease, and Beckwith-Wiedemann Syndrome.<sup>3,5,6</sup> Conditions not commonly found in the literature that were present in our patients include two cases of Prune Belly Syndrome, one of which was associated with left grade V vesicoureteral reflux, and one case of polyuric renal failure, bilateral grade IV vesicoureteral reflux, cryptorchidism, and midgut malrotation. Both Prune Belly Syndrome and vesicoureteral reflux are congenital anomalies of the kidney and urinary tract (CAKUT). Hepatoblastoma has been found in association with hypodysplastic glomerulocystic kidney, renal agenesis, and dysplastic kidney in prior case reports.<sup>12-15</sup> A common genetic alteration present within 70-80% of hepatoblastoma cases include upregulation of the Wnt/ $\beta$ -catenin pathway, which is also responsible for renal development.<sup>16, 17</sup> Therefore, hepatoblastoma may have a common underlying genetic mechanism with CAKUT.<sup>18</sup>

**Figure 1.** Case 15.



**Legend:** (A) Computed tomography (CT) of the abdomen and pelvis demonstrating a large hepatoblastoma measuring 16.2 cm x 9.9 cm x 9.7 cm in the right lobe of the liver and smaller lesion in the left liver lobe at 2.5 cm. (B) CT chest showing multiple soft tissue nodules throughout bilateral lungs, measuring up to 1.4 cm in diameter, later found to be metastasis. Given extensive pulmonary and CNS metastasis at the time of diagnosis, patient was unable to undergo surgical management and ultimately died secondary to the significant disease burden.

**Figure 2.** Case 6.



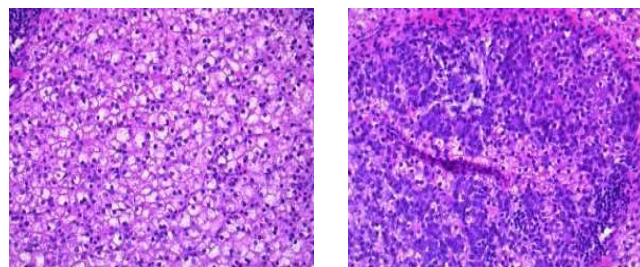
**Legend:** (A) Preoperative biopsy pathology demonstrating fetal epithelial pattern. (B) Preoperative biopsy pathology demonstrating embryonal component.

Most cases of hepatoblastoma are asymptomatic, with the main presenting factor being a palpable mass in the right upper quadrant. Five of our patients presented with a palpable abdominal mass or abdominal distension, with only four patients who presented with symptoms of abdominal pain. About one fifth of the cases presented with extrahepatic disease at the time of diagnosis.<sup>11</sup> Metastasis of hepatoblastoma primarily travels to

the lungs which may present with symptoms of difficulty breathing, cough, and hemoptysis.<sup>7</sup> Metastasis at diagnosis indicates a poor prognosis.<sup>3,19</sup> Three patients presented with pulmonary metastasis at the time of diagnosis. Two of these patients were successfully treated with either resection of the pulmonary nodules and chemotherapy or chemotherapy alone. The other died from progression of the effects of his metastatic disease.

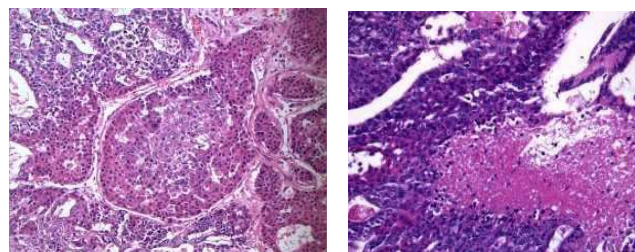
Imaging studies such as ultrasound, Magnetic Resonance Imaging (MRI), CT with intravenous contrast, angiography, or liver scintigraphy can aid in determination of tumor location, segmental extension or proximity to hepatic vessels.<sup>1,7,8</sup> The gold standard for diagnosis of hepatoblastoma is tumor biopsy.<sup>1,6,7</sup> All of our patients were preliminarily assessed with an abdominal and pelvic CT scan and definitive diagnosis was made with image-guided or open tru-cut liver biopsy.

**Figure 3.** Case 12.



**Legend:** (A) Preoperative biopsy pathology demonstrating hepatoblastoma with sheets and cords of tumor cells resembling fetal hepatocytes. (B) Preoperative biopsy pathology demonstrating adjacent area of tumor with a more primitive appearance of the tumor cells which is associated with a more favorable prognosis.

**Figure 4.** Case 3.



**Legend:** (A) Surgical pathology demonstrating macrotrabecular growth pattern with broad islands of neoplastic hepatocytes. (B) Surgical pathology demonstrating central necrosis within an area of microtrabecular growth. This is a rare subtype of hepatoblastoma with histologic findings similar to hepatocellular carcinoma. This patient ultimately died secondary to tumor recurrence with pulmonary metastasis.

A common treatment course for hepatoblastoma includes both pre- and postoperative chemotherapy and tumor resection with partial liver resection or liver transplant if the former is not feasible.<sup>7</sup> Complete resection of the tumor can be curative, however, only 50% of patients have tumors that can be resected at the time of diagnosis.<sup>1,11,19</sup> In our cohort, only four patients were treated with upfront surgical intervention. Neoadjuvant chemotherapy reduces tumor size allowing up to 87% of patients

to be eligible for complete surgical resection.<sup>1,2,11,19</sup> Resection was possible for four of our patients after neoadjuvant treatment. Postoperative chemotherapy further decreases the risk of tumor relapse and addresses any postoperative tumor residual.<sup>2</sup> From our study, eleven patients had postoperative chemotherapy after Tumor Board discussion. In the case of lung metastases,

metastasectomy. Liver transplant is preferred for cases in which the tumor cannot be completely resected due to vascular involvement, in tumors that are unresponsive to chemotherapy, or with multifocal tumors.<sup>1,9,10</sup> Two of our patients had liver transplant in combination with chemotherapy due to unresectable tumors and no tumor recurrence or mortality at 4 and 8 year follow-up, respectively.

**Table 2.** Summary of Treatment Interventions.

Case No.	Pre-operative or Initial Chemotherapy	Surgical Intervention	Postoperative or Definitive Chemotherapy	Outcome
1	None	Right hepatic lobectomy	C5V + Amifostine	Alive
2	Vincristine + Cisplatin + Amifostine	Exploratory Laparotomy with Resection	C5V + Amifostine	Alive
3	None	Hepatectomy	C5VD	Deceased
4*	C5V	Resection of hepatoblastoma	C5V	Deceased
5*	CDDP	Liver transplant	CDDP	Alive
6*	CDDP	Right extended hepatectomy	None	Alive
7	Cisplatin + Amifostine	None	C5V + Amifostine	Alive
8	None	Partial liver resection	C5V + Amifostine	Alive
9	C5V	Resection of hepatoblastoma	C5V + Amifostine	Alive
10*	Carboplatin + Doxorubicin + Vincristine	Liver Transplant	None	Alive
11	None	Resection of hepatoblastoma	None	Alive
12*	C5VD	Resection of hepatoblastoma	C5VD	Alive
13*	C5VD	Partial hepatectomy, small bowel and omentum excision, thoracotomy with resection of pulmonary nodules	C5VD	Alive
14	C5V	None	CDDP	Deceased
15*	Vincristine + Irinotecan + Temozolomide	None	None	Deceased

**Legend:** denotes AHEP0731 Protocol C5V=cisplatin, 5-fluoruracil, vincristine; CDDP=cisplatin; C5VD= cisplatin, 5-fluoruracil, vincristine, doxorubicin

neoadjuvant chemotherapy may be used to achieve remission, however, surgical resection is required if the tumors persist.<sup>7</sup> One of our patients underwent a thoracotomy for pulmonary

Histopathological subtypes serve as major prognostic considerations for pediatric liver tumors.<sup>8</sup> Many histological types exist for hepatoblastoma including epithelial, mesenchymal, mixed epithelial and mesenchymal, and undifferentiated. Epithelial types can further be divided into embryonal, fetal, pleomorphic, anaplastic, small cell, undifferentiated, and cholangioblastic macrotrabecular subtypes.<sup>6</sup> Fetal epithelial hepatoblastoma is made up of cells that resemble fetal hepatoblasts during embryonic development and generally has a more favorable prognosis.<sup>11,19</sup> Embryonal epithelial hepatoblastoma resembles the liver at 6-8 weeks of gestation and is the most common presenting pattern.<sup>18</sup> Uncommon histological patterns include cholangioblastic macrotrabecular epithelial and mixed epithelial-mesenchymal hepatoblastoma.<sup>14</sup> The former displays a macrotrabecular growth pattern akin to hepatocellular carcinoma and accounts for only about 5% of all cases.<sup>18</sup> Mixed epithelial-mesenchymal hepatoblastoma contains mesenchymal components including fibroblastic stroma, muscle, osteoid, and cartilage.<sup>11</sup> Consistent with the literature, most of our patients (40%) presented with a mixed fetal embryonic pattern ([Figure 2](#)), 20% had pure fetal histology ([Figure 3](#)), 6.7% had a pure embryonal histology, 6.7% had macrotrabecular hepatoblastoma ([Figure 4](#)), 6.7% demonstrated a mixed epithelial-mesenchymal pattern, and 20% did not have a histology pattern available upon retrospective review. There was no recurrence or mortality in all patients with hepatoblastoma of pure fetal histology. Two mortalities occurred with mixed fetal embryonic pattern with one due to progression of metastasis at the time of diagnosis and the other due to multi-organ failure and sepsis. The other two mortalities occurred in the macrotrabecular and mixed-epithelial-mesenchymal pattern due to recurrence after initial treatment. A cohort study conducted at a neighboring institution demonstrated similar findings with fetal and epithelial subtypes associated with increased overall survivability and lowest risk of relapse or death with pure fetal subtypes.<sup>21</sup>

Following treatment, patients diagnosed with hepatoblastoma are monitored for up to five years. AFP values are monitored as elevations could potentially indicate residual tumor or tumor relapse, which is a major cause of mortality among patients following treatment.<sup>2,7</sup> All patients in our cohort who achieved remission following treatment had normalization in AFP values, and the two with relapse demonstrated elevation in AFP levels (168,430 ng/mL and 1,422 ng/mL). In a recent study by Srinivasan et. al., they noted poor prognosis in patients with tumor relapse. There was a six percent survival to 36 months in those with refractory or relapsed disease. In addition, they found that a decline in AFP of more than 90% was associated with improved

three-year survival.<sup>22</sup> Therefore, monitoring of AFP values is an important diagnostic clue to disease recurrence.

While this study presents a sizable number of a rare condition, our sample size is not large enough to allow for significant statistical analysis. Given the retrospective nature of this study, some data is missing from older cases and the reasoning behind treatment decisions was not always clear. Future studies should be directed towards compiling a larger cohort of patients into a multi-institutional study with a specific focus on genetic analysis of hepatoblastoma and associated comorbidities.

## Summary – Accelerating Translation

Hepatoblastoma is a rare malignancy of the liver that presents most commonly in children under the age of three. Current treatment is highly dependent on tumor staging and characteristics and consists of chemotherapy, surgical management, or a combination of both based on individual risk category. The purpose of our study is to analyze the clinical findings, treatment, and outcomes of pediatric hepatoblastoma at a single free-standing children's hospital.

We conducted a retrospective review of all patients under the age of 18 with a diagnosis of hepatoblastoma between the years of 2000 to 2022. We assessed patient demographics, work up, surgical intervention, recurrence, and mortality.

A total of fifteen patients were found to have a diagnosis of hepatoblastoma within the designated time frame with a mean age of 18.7 months at diagnosis. Our results demonstrated presentations of known associated comorbidities including that of prematurity (3), Beckwith-Wiedemann Syndrome (1), and neonatal intensive care unit stay (4) as well as unique conditions including Prune Belly Syndrome (2) and vesicoureteral reflux (2), otherwise not documented in the literature. All patients presented with elevated alpha-fetoprotein (AFP) values at diagnosis with an average level of 303,294.2 ng/mL.

Three patients were treated with chemotherapy alone, two of which died, one secondary to pulmonary and brain metastasis at the time of diagnosis and the other due to sepsis and multi-organ failure. One patient was treated with only surgical management and three patients were treated with surgical intervention followed by postoperative chemotherapy, one of whom died due to tumor recurrence and pulmonary metastasis. Eight patients underwent neoadjuvant chemotherapy administered prior to surgical intervention with the primary goal of shrinking the tumor and six of these patients also received postoperative chemotherapy, one of which died due to tumor recurrence.

Six patients had histologic presentations of mixed fetal embryonic pattern, three had a pure fetal pattern, one had a pure embryonal pattern, one had a macrotrabecular pattern, one had a mixed epithelial-mesenchymal pattern, and three patients' subtype was unavailable from retrospective chart review. Two mortalities occurred in the mixed fetal embryonal pattern group and both patients with the macrotrabecular and mixed epithelial-mesenchymal pattern had tumor recurrence and mortality.

Categorizing a patient's tumor stage and risk is an important component of hepatoblastoma management for appropriate treatment. The unique comorbid conditions in our cohort, including Prune Belly Syndrome and vesicoureteral reflux, fall into the category of congenital anomalies of the kidney and urinary tract (CAKUT), proposing a possible common underlying genetic mechanism with hepatoblastoma. Our cohort demonstrated that neoadjuvant chemotherapy allows for excision of initially unresectable tumors with good, long-term disease-free outcomes. Our mortalities were associated with tumor metastasis, tumor recurrence, and certain histological factors which may serve as poor prognostic factors. Both of our tumor recurrences presented with elevated AFP values, therefore, long term monitoring of this marker is critical in the patient's post-treatment care plan. Future research can include larger cohort of patients in a multi-institutional study with specific focus on genetic analysis of hepatoblastoma and associated comorbidities.

## References

- Küpesiz, F. T., Akinel, A. N., Akbaş, H., Sivrice, Ç., Kintrup, G. T., Karagüzel, G., et al. Multidisciplinary Management of Pediatric Hepatoblastoma: A 20-Year Single-Center Experience. *The Turk J Gastroenterol.* 2022;33(12):1069.
- Zhang Y, Zhang W, Tang S, Chen L, Yi Y, Zhang P, et al. A single-center retrospective study of pediatric hepatoblastoma. *Oncology Lett.* 2016 Nov 1;12(5):3919-25.
- Pateva, I. B., Egler, R. A., & Stearns, D. S. Hepatoblastoma in an 11-year-old: Case report and a review of the literature. *Medicine.* 2017 Jan 1; 96(2): e5858.
- Lack, E. E., Neave, C., & Vawter, G. F. Hepatoblastoma: A clinical and pathologic study of 54 cases. *Am J Surg Pathol.* 1982 Dec 1;6(8):693-705.
- Spector, L. G., & Birch, J. The epidemiology of hepatoblastoma. *Pediatr Blood Cancer.* 2012 Nov;59(5):776-9.
- El Asmar, A., & El Rassi, Z. Hepatoblastoma in childhood, long term survival achieved: 2 case reports and literature review. *Int. J. Surg. Case Rep.* 2016 Jan 1;21:55-8.
- Hager, J., & Sergi, C. M. Hepatoblastoma. Exon Publications. 2021 Apr 6:145-64.
- Hiyama, E. Pediatric hepatoblastoma: diagnosis and treatment. *Transl. Pediatr.* 2014 Oct;3(4):293.
- Meyers, R., Hiyama, E., Czauderna, P., & Tiao, G. M. Liver tumors in pediatric patients. *Surg. Oncol. Clin. N. Am.* 2021 Apr 1;30(2):253-274.
- Kulkarni, S., Brauer, D. G., Turmelle, Y., Stoll, J., Nadler, M., Chapman, W. C., et al. Surgical therapy for pediatric hepatoblastoma in the USA over the last decade: analysis of the national cancer database. *J Gastrointest Cancer.* 2021 Jun; 52:547-556.
- Bharti S, Bharti JN, Sinha A, Yadav T. Common and rare histological variants of hepatoblastoma in children: a pathological diagnosis and review of the literature. *Gastrointest. Tumors.* 2021 Apr 8;8(2):41-6.
- Abdul-Rahman OA, Edghill EL, Kwan A, Enns GM, Hattersley AT. Hypoplastic glomerulocystic kidney disease and hepatoblastoma: a potential association not caused by mutations in hepatocyte nuclear factor 1β. *J Pediatr Hemato Oncol.* 2009 Jul 1;31(7):527-9.
- Sattler B, Gunawan B, Lorf T, Müller D, Ringe B, Füzesi L. Undifferentiated small-cell hepatoblastoma. *Der Pathologe.* 2000 Nov 1;21(6):456-9.
- Sebestyen J, Garg U, Lewing KB, Warady BA, Abdel-Rahman S, Blowey DL. Cisplatin pharmacokinetics in a child receiving peritoneal dialysis. *Pediatr Nephrol.* 2010 Jun;25:1185-9.
- Khosla A. Hepatoblastoma and congenital dysplastic kidney. *J Pediatr Surg.* 1990 Aug;25(8):924.
- Majidinia M, Aghazadeh J, Jahanban-Esfahiani R, Yousefi B. The roles of Wnt/β-catenin pathway in tissue development and regenerative medicine. *J Cell Physiol.* 2018 Aug; 223(8):5598-612

17. Becknell B, Pais P, Onimoe G, Rangarajan H, Schwaderer AL, McHugh K, Ranalli MA, Hains DS. Hepatoblastoma and prune belly syndrome: a potential association. *Pediatr Nephrol.* 2011 Aug;26:1269-73.
18. Sharma, D., Subbarao, G., & Saxena, R. Hepatoblastoma. *Seminars in diagnostic pathology.* 2017 Mar 1 (Vol. 34, No. 2, pp. 192-200). WB Saunders.
19. Perilongo, G., Malogolowkin, M., & Feusner, J. Hepatoblastoma clinical research: lessons learned and future challenges. *Pediatr Blood Cancer.* 2012 Nov; 59(5):818-21.
20. Agha RA, Sohrabi C, Mathew G, Franchi T, Kerwan A, O'Neill N for the PROCESS Group. The PROCESS 2020 Guideline: Updating Consensus Preferred Reporting Of Case Series in Surgery (PROCESS) Guidelines, *Int. J Surg.* 2020;60
21. Zhou S, Malvar J, Chi YY, Stein J, Wang L, Genyk Y, Spoto R, Mascarenhas L. Independent assessment of the children's hepatic tumors international collaboration risk stratification for hepatoblastoma and the association of tumor histological characteristics with prognosis. *JAMA Netw Open.* 2022 Feb 1;5(2):e2148013-.
22. Srinivasan S, Prasad M, Parambil BC, Shrimal A, Gollamudi VR, Subramani V, Ramadwar M, Khanna N, Baheti AD, Gala K, Patil V. Treatment outcomes and prognostic factors in children with hepatoblastoma using a risk-stratified approach. *Pediatr Blood Cancer.* 2023 Jul;70(7):e30302.

---

### Acknowledgments

None.

### Conflict of Interest Statement & Funding

The Authors have no funding, financial relationships or conflicts of interest to disclose.

### Author Contributions

Conceptualization: AR, JS. Data Curation: JS, JM, GM. Investigation: JS, JM, GM, AR. Supervision: AR. Writing - Original Draft: JS, JM. Writing Review Editing: JS, JM, AR.

### Cite as

Sawaya J, McRae J, Mladenov G, Radulescu A. Pediatric Hepatoblastoma: A Single-Institution Case Series. *Int J Med Stud.* 2025 Jan-Mar;13(1):60-66.

*This work is licensed under a [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/)*

ISSN 2076-6327

This journal is published by [Pitt Open Library Publishing](https://pittopenlibrarypublishing.com/)

