OUTCOMES AND CLINICAL EXPERIENCE IN PEDIATRIC HEPATOBLASTOMA: A THREE-YEAR STUDY

Dr. A. M. Shahinoor[1], Dr. Rowson Ara[2], Dr. Salma Akter Munmun[*3]

[1]*Medical Officer, Department of Paediatric Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh*
[2]*Medical Officer, Department of Obstetrics and Gynecology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh*
[3*]*Medical Officer, Department of Obstetrics and Gynecology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh*
**Corresponding Author: Dr. Salma Akter Munmun*

KEYWORDS

Pediatric Hepatoblastoma, Clinical Presentation, Treatment Modalities, Outcomes, Survival

ABSTRACT:

Background: Hepatoblastoma is the most common primary malignant liver tumor in children, accounting for 50-60% of pediatric liver cancers. This study aimed to evaluate the clinical presentation, treatment modalities, and outcomes of pediatric hepatoblastoma over a three-year period to refine therapeutic approaches and improve patient survival and quality of life. **Aim of the study:** The aim of the study was to evaluate the clinical presentation, treatment modalities, and outcomes of pediatric hepatoblastoma over a three-year. **Methods:** This retrospective study was conducted at the Department of Pediatric Surgery and Pediatric Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from June 2017 to June 2020. It included 22 pediatric hepatoblastoma patients, with data collected from medical records on demographics, clinical presentation, treatment, and outcomes. Outcome measures included overall survival, event-free survival, recurrence, and complications. Data were analyzed using SPSS version 25. **Results:** In 22 pediatric hepatoblastoma patients, median age was 1.5 years, with male predominance (54.5%). Most presented with abdominal mass (77.3%). PRETEXT I was common (63.6%); median AFP was 400,000 ng/mL. All received chemotherapy (72.7% neoadjuvant); 90.9% underwent surgery (72.7% complete resection). Three-year survival was 85.0%; recurrence was 18.0% (mostly lung metastases). Postoperative complications included respiratory issues (9.0%). **Conclusion:** This study emphasizes the importance of early diagnosis, multimodal treatment, and vigilant postoperative care in achieving favorable outcomes for pediatric hepatoblastoma, despite challenges such as recurrence and complications.

INTRODUCTION

Hepatoblastoma is the most prevalent primary malignant liver tumor in children, responsible for 79% of all liver tumors in this population and nearly two-thirds of primary malignant liver cancers in the pediatric age group.[1,2] Although rare, it remains the most common form of liver cancer in children, making up 50-60% of pediatric primary liver cancers.[3] The incidence of hepatoblastoma has been on the rise, with an annual increase of 4.3% from 1992 to 2004.[4,5,6,7] It is most frequently diagnosed in children under the age of 5, highlighting its significance in pediatric oncology. Although the exact cause of hepatoblastoma is not fully understood, higher rates have been observed in children born prematurely or with very low birth weights.[8,9,10]

The treatment of hepatoblastoma has traditionally aimed at achieving long-term survival, with complete surgical resection remaining the cornerstone of therapy.[11,12] Chemotherapy is commonly used to shrink the tumor in cases where the lesions are initially deemed unresectable or to treat any residual microscopic disease following surgery.[13] Prior to the 1970s, surgery alone was the main approach, but survival rates were as low as 20-30% due to the lack of effective postoperative chemotherapy.[14] Modern treatment strategies, especially the combination of surgery and chemotherapy, have led to significant improvements in survival outcomes.[15] However, managing hepatoblastoma continues to present challenges, necessitating accurate staging and a multidisciplinary approach to navigate the complexities of treatment and achieve the best possible survival rates.

The PRETEXT (Pretreatment Extent of Disease) staging and serum alpha-fetoprotein (AFP) levels are pivotal in determining the treatment strategy and predicting the prognosis of hepatoblastoma (HB). The Children's Hepatic Tumour International Collaborative (CHIC) has refined the PRETEXT staging system, highlighting the importance of combining chemotherapy and surgery as the primary treatment, given the tumor's responsiveness to chemotherapy.[15,16] Key factors in PRETEXT staging, such as involvement of the hepatic and portal veins, extrahepatic spread, multifocal tumors, and distant metastasis, are critical for assessing risk. Moreover, low AFP levels (<100 ng/ml or 100–1000 ng/ml) are associated with poorer outcomes, with PRETEXT class IV patients aged 3-7 years experiencing particularly unfavorable prognoses.[17,18] These staging elements guide treatment decisions, including the use of chemotherapy to shrink tumors for resection in cases of recurrence.

Treatment for hepatoblastoma (HB) typically involves a combination of chemotherapy, surgical resection, and liver transplantation.[19] Chemotherapy is often administered as neoadjuvant therapy to shrink the tumor before surgery, particularly in cases that are initially resectable. For resectable HB, complete surgical resection remains the first-line treatment at diagnosis.[20,21] However, for unresectable cases, liver transplantation is considered. While upfront surgery is ideal, only a subset of patients can undergo it directly, with many requiring neoadjuvant chemotherapy (NCT) to improve resectability. This approach has significantly enhanced survival rates, particularly for high-risk patients.[22] When combined with accurate staging and AFP monitoring, these treatment strategies offer improved outcomes, though challenges persist, especially in cases of distant metastasis or postoperative recurrence.

Pediatric hepatoblastoma (HB) outcomes are shaped by clinical presentation, PRETEXT staging, serum alpha-fetoprotein (AFP) levels, and treatment strategies. While most patients present with abdominal mass and pain, favorable outcomes are often associated with early-stage disease and appropriate treatment modalities. The standard approach involves chemotherapy and surgery, with a focus on neoadjuvant therapy and achieving complete tumor resection. Despite significant advancements in treatment, recurrence and metastasis remain challenges in patient prognosis. Although survival rates are promising, postoperative complications highlight the need for improved management strategies. This study aimed to evaluate the clinical presentation, treatment modalities, and outcomes of pediatric hepatoblastoma over a three-year period, providing essential data to refine therapeutic approaches and further enhance patient survival and quality of life.

OBJECTIVE

- The aim of the study was to evaluate the clinical presentation, treatment modalities, and outcomes of pediatric hepatoblastoma over a three-year.

METHODOLOGY & MATERIALS

This observational, retrospective study was conducted at the Department of Pediatric Surgery and Pediatric Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between June 2017 and June 2020. A total of 22 pediatric patients diagnosed with hepatoblastoma were included in the study, selected based on specific inclusion and exclusion criteria for the evaluation of clinical presentation, treatment modalities, and outcomes.

Inclusion Criteria:

- Pediatric patients (aged ≤5 years) diagnosed with hepatoblastoma.
- Availability of complete clinical, diagnostic, and follow-up data.

Exclusion Criteria:

- Patients with incomplete medical records or insufficient follow-up data.
- Patients diagnosed with other types of liver tumors or malignancies.

Written informed consent was obtained from the parents or guardians of all participants, ensuring their awareness of the study's purpose and procedures while maintaining confidentiality and anonymity. Data were collected by reviewing medical records, including demographic characteristics (age and gender), clinical presentation (abdominal mass, pain, weight loss, jaundice), diagnostic details (PRETEXT staging, serum AFP levels), treatment modalities (chemotherapy—neoadjuvant/adjuvant, cisplatin-based; surgery—complete resection or transplantation; adjuvant therapy), and follow-up data (survival, recurrence, postoperative complications). Outcome measures included overall survival (OS), event-free survival (EFS), recurrence rates (local or distant), and postoperative complications (respiratory issues, intra-abdominal collections, wound infections, bile leaks). Descriptive statistics were used to summarize demographic, clinical, and treatment data, with continuous variables reported as medians and ranges, and categorical variables as frequencies and percentages. Data analysis was performed using SPSS version 25.

RESULTS

Table 1: Demographic and Clinical Characteristics of the Study Population (n=22)

Variable		Number of patients	Percentage
Age (In years)	<1 year	7	31.8
	1-3 years	9	40.9
	>3 years	6	27.3
	Median (Range)	1.5 years (1 month – 5 years)	
Gender	Male	12	54.5
	Female	10	45.5
Clinical Presentation	Abdominal mass	17	77.3
	Abdominal pain	11	50.0
	Weight loss	5	22.7
	Jaundice	2	9.1

This table summarizes the demographic and clinical features of the 22 pediatric patients diagnosed with hepatoblastoma. The median age at diagnosis was 1.5 years (range: 1 month – 5 years), with 7 patients (31.8%) diagnosed before 1 year of age, 9 patients (40.9%) between 1-3 years, and 6 patients (27.3%) older than 3 years. A slight male predominance was observed, with 12 males (54.5%) and 10 females (45.5%). The most common clinical presentation was an abdominal mass, occurring in 17 patients (77.3%), followed by abdominal pain in 11 patients (50.0%), weight loss in 5 patients (22.7%), and jaundice in 2 patients (9.1%).

Table 2: Distribution of PRETEXT Stages and Serum AFP Levels in the Study Population (n=22)

Variable		Number of Patients	Percentage (%)
PRETEXT Stage	I	14	63.6
	II	4	18.2
	III	3	13.6

	IV	1	4.5
Tumor Marker	**Median (Range)**	Serum AFP (ng/mL)	400,000 (2,000 – 5,000,000)

This table outlines the distribution of PRETEXT stages and serum AFP levels in the study cohort. The majority of patients were diagnosed with PRETEXT stage I (14 patients, 63.6%), followed by stage II (4 patients, 18.2%), stage III (3 patients, 13.6%), and stage IV (1 patient, 4.5%). The median serum AFP level at diagnosis was 400,000 ng/mL, with a range from 2,000 to 5,000,000 ng/mL.

Table 3: Treatment Modalities and Surgical Outcomes in Pediatric Hepatoblastoma Patients (n=22)

Treatment Variable	Number of Patients	Percentage (%)
Chemotherapy	22	100.0
- Neoadjuvant	16	72.7
- Cisplatin-based	12	54.5
Surgery	20	90.9
- Complete Resection	16	72.7

This table outlines the treatment modalities and surgical outcomes for the pediatric hepatoblastoma patients in the study. All 22 patients (100.0%) received chemotherapy, with 16 patients (72.7%) undergoing neoadjuvant chemotherapy and 12 patients (54.5%) receiving cisplatin-based chemotherapy. Regarding surgery, 20 patients (90.9%) underwent surgery, with 16 patients (72.7%) achieving complete resection.

Table 4: Treatment Outcomes in Pediatric Hepatoblastoma Patients (n=22)

Outcome	Number of Patients (n)	Percentage (%)
3-year Overall Survival (OS)	19	85.0
Deaths	3	15.0
Recurrence (Total)	4	18.0
- Local recurrence	1	4.5
- Distant metastasis (lung)	3	13.5

This table presents the three-year overall survival (OS) and recurrence rates in pediatric hepatoblastoma patients. The OS rate was 85.0% (n=19), with 15.0% (n=3) of patients succumbing to the disease. Recurrence occurred in 18.0% (n=4) of cases, with 4.5% (n=1) experiencing local recurrence and 13.5% (n=3) developing distant metastases to the lungs.

Table 5: Postoperative Complications in Pediatric Hepatoblastoma Patients

Complication	Number of Patients (n)	Percentage (%)
Respiratory complications	2	9.0
Intra-abdominal collection	2	9.0
Wound infection	1	4.5
Septic shock	1	4.5
Bile leak	1	4.5

Table 5 presents the frequencies and percentages of postoperative complications observed in pediatric hepatoblastoma patients. Respiratory complications and intra-abdominal collections were the most common, affecting 2 patients (9.0%) each. Wound infection, septic shock, and bile leak were each

observed in 1 patient (4.5%). These findings emphasize the importance of postoperative monitoring and timely intervention to manage potential complications effectively.

DISCUSSION

This study highlights the clinical presentation and outcomes of pediatric hepatoblastoma over a three-year period at a tertiary care hospital in Bangladesh. Hepatoblastoma, the most common malignant liver tumor in children, requires a multidisciplinary approach for optimal management. The findings emphasize the predominance of abdominal mass as the initial presentation and the critical role of chemotherapy and surgical resection in achieving favorable outcomes. The high overall survival rate emphasizes the effectiveness of current treatment protocols, while the observed recurrence and postoperative complications highlight the need for vigilant follow-up and timely intervention.

The baseline characteristics in this study, including age, gender distribution, and clinical presentation, were consistent with findings from Sriniworn et al.[23] This comparability suggests that variations in outcomes were likely influenced by factors beyond demographic differences. A slight male predominance (54.5%) was observed, aligning with previous reports. Abdominal mass was the most common clinical presentation (77.3%), followed by abdominal pain (50.0%), weight loss (22.7%), and jaundice (9.1%), reflecting typical hepatoblastoma symptoms. The median age at diagnosis was 1.5 years (range: 1 month – 5 years), similar to the distribution reported by Zhang et al.[24] These findings highlight the characteristic presentation patterns of pediatric hepatoblastoma, emphasizing the importance of early recognition and diagnosis in clinical practice.

The distribution of PRETEXT stages and serum AFP levels in this study were similar to those reported by Shukla et al. The majority of patients presented with PRETEXT stage I tumors (63.6%), which aligns with Shukla et al.'s[25] findings where stage I was the most commonly observed, reinforcing the tendency for hepatoblastoma to be diagnosed at an earlier stage. The distribution of other stages (II, III, and IV) followed a typical pattern, with fewer patients in the higher stages. The median serum AFP level of 400,000 ng/ml (range: 2,000 to 5,000,000 ng/ml) was also consistent with Shukla et al.'s report,[25] underlining AFP as a key biomarker for hepatoblastoma diagnosis and monitoring. These findings emphasize the reliability of serum AFP levels in reflecting tumor burden and the stage of disease, further supporting its role in guiding clinical management and prognosis in pediatric hepatoblastoma cases.

In this study, chemotherapy was administered to all patients, with a predominant use of neoadjuvant chemotherapy (72.7%), aligning with the findings of Ang et al.[26], who similarly utilized neoadjuvant chemotherapy to shrink the tumor prior to surgical resection. The use of cisplatin-based regimens (54.5%) in this cohort mirrors their approach, where cisplatin remains the cornerstone of chemotherapy for hepatoblastoma due to its established efficacy. As for surgical treatment, 90.9% of patients underwent surgery, with a significant proportion (72.7%) achieving complete resection. This is consistent with their results, where complete resection was a common and crucial step in achieving favorable long-term outcomes. In both studies, complete surgical resection was associated with improved prognosis, further emphasizing the importance of early diagnosis and effective neoadjuvant chemotherapy in the management of hepatoblastoma. These similarities underline the consensus on treatment strategies, with both chemotherapy and surgery being key components of the therapeutic approach in hepatoblastoma management.

Our study's 3-year overall survival (OS) rate of 85% is comparable to the 5-year OS of 85.7% reported by McAteer et al.[27], indicating that survival outcomes remain favorable over different follow-up periods. Similar to their findings, surgical resection played a crucial role in achieving better survival rates, emphasizing the importance of complete tumor removal in hepatoblastoma management. Additionally, our recurrence rate of 18%, with 13.5% distant metastases (lung) and 4.5% local recurrence, aligns with the findings of Shukla et al.[25], who reported a recurrence rate of 16.7%, primarily due to distant metastases. This similarity suggests that despite advancements in surgical and chemotherapeutic approaches, recurrence remains a significant challenge, particularly distant

metastases, which continue to be the most common form of disease relapse. The consistency between our findings and those of previous studies highlights the ongoing need for long-term surveillance, aggressive multimodal treatment, and early intervention strategies to improve disease-free survival and reduce recurrence rates in pediatric hepatoblastoma patients.

In our study, respiratory complications were the most frequently observed postoperative issue (9.0%), similar to the findings reported by Ang et al.[26] This study also noted intra-abdominal collections (9.0%) as a notable complication, highlighting the risk of postoperative infections and fluid accumulation. Wound infections (4.5%) and bile leaks (4.5%) were also observed, reinforcing the importance of meticulous surgical technique and postoperative wound care to minimize these risks. Additionally, septic shock (4.5%) was documented, emphasizing the potential for severe post-surgical infections, especially in settings with limited intensive care resources. While these complication rates are comparable, differences in perioperative care, infection control measures, and surgical expertise may influence outcomes. Addressing these challenges through improved perioperative monitoring, antibiotic stewardship, and critical care support could further reduce postoperative morbidity in pediatric hepatoblastoma patients.

Limitations of the study

This study had some limitations:

- The study was conducted in a selected tertiary-level hospital.
- The sample was not randomly selected.
- The study's limited geographic scope may introduce sample bias, potentially affecting the broader applicability of the findings.

CONCLUSION

This three-year study of pediatric hepatoblastoma patients highlights the importance of early diagnosis and multimodal treatment in improving outcomes. The majority of patients presented with an abdominal mass and were diagnosed at early PRETEXT stages, with significantly elevated serum AFP levels. All patients received chemotherapy, and most underwent successful surgical resection, achieving a high overall survival rate. However, recurrence, particularly distant metastases, and postoperative complications such as respiratory issues and intra-abdominal collections, remain significant challenges. These findings emphasize the need for timely intervention, comprehensive treatment strategies, and vigilant postoperative care to enhance outcomes in pediatric hepatoblastoma.

REFERENCES

1. Tsay PK, Lai JY, Yang CP, Hung IJ, Hsueh C, Tsai MH, Jaing TH. Treatment outcomes for hepatoblastoma: experience of 35 cases at a single institution. Journal of the Formosan Medical Association. 2011 May 1;110(5):322-5.
2. Schnater JM, Aronson DC, Plaschkes J, Perilongo G, Brown J, Otte JB, Brugieres L, Czauderna P, MacKinlay G, Vos A. Surgical view of the treatment of patients with hepatoblastoma: Results from the first prospective trial of the International Society of Pediatric Oncology Liver Tumor Study Group (SIOPEL-1). Cancer. 2002 Feb 15;94(4):1111-20.
3. von Schweinitz D. Hepatoblastoma: recent developments in research and treatment. InSeminars in pediatric surgery 2012 Feb 1 (Vol. 21, No. 1, pp. 21-30). WB Saunders.
4. Litten JB, Tomlinson GE. Liver tumors in children. The oncologist. 2008 Jul 1;13(7):812-20.
5. Hadzic N, Finegold MJ. Liver neoplasia in children. Clinics in liver disease. 2011 May 1;15(2):443-62.
6. Darbari A, Sabin KM, Shapiro CN, Schwarz KB. Epidemiology of primary hepatic malignancies in US children. Hepatology. 2003 Sep;38(3):560-6.

7. Linabery AM, Ross JA. Trends in childhood cancer incidence in the US (1992–2004). Cancer: Interdisciplinary International Journal of the American Cancer Society. 2008 Jan 15;112(2):416-32.
8. Maruyama K, Ikeda H, Koizumi T, Tsuchida Y, Tanimura M, Nishida H, Takahashi N, Fujimura M, Tokunaga Y. Case-control study of perinatal factors and hepatoblastoma in children with an extremely low birthweight. Pediatrics International. 2000 Oct 29;42(5):492-8.
9. Ikeda H, Hachitanda Y, Tanimura M, Maruyama K, Koizumi T, Tsuchida Y. Development of unfavorable hepatoblastoma in children of very low birth weight: results of a surgical and pathologic review. Cancer: Interdisciplinary International Journal of the American Cancer Society. 1998 May 1;82(9):1789-96.
10. Oue T, Kubota A, Okuyama H, Kawahara H, Nara K, Kawa K, Kitajima H. Hepatoblastoma in children of extremely low birth weight: a report from a single perinatal center. Journal of pediatric surgery. 2003 Jan 1;38(1):134-7.
11. JM S. Surgical view of the treatment plans of patients with hepatoblastoma: results from the first prospective trial of the International Society of Pediatric Oncology Liver Tumor Study Group. Cancer. 2002;94:111-20.
12. Perilongo G, Shafford E, Plaschkes J. SIOPEL trials using preoperative chemotherapy in hepatoblastoma. The Lancet Oncology. 2000 Oct 1;1(2):94-100.
13. Shukla PJ, Barreto SG, Qureshi SS, Hawaldar R, Shrikhande SV, Ramadwar MR, Banavali S. Hepatoblastoma: a single institutional experience of 18 cases. Pediatric surgery international. 2008 Jul;24:799-802.
14. Evans AE, Land VJ, Newton WA, Randolph JG, Sather HN, Tefft M. Combination chemotherapy (vincristine, adriamycin, cyclophosphamide, and 5-fluorouracil) in the treatment of children with malignant hepatoma. Cancer. 1982 Sep 1;50(5):821-6.
15. Czauderna P, Lopez-Terrada D, Hiyama E, Häberle B, Malogolowkin MH, Meyers RL. Hepatoblastoma state of the art: pathology, genetics, risk stratification, and chemotherapy. Current opinion in pediatrics. 2014 Feb 1;26(1):19-28.
16. Meyers RL, Tiao GM, Dunn SP, Langham MR. Liver transplantation in the management of unrespectable hepatoblastoma in children. Front Biosci (Elite Ed). 2012;4:1293–302.
17. Czauderna P, Haeberle B, Hiyama E, Rangaswami A, Krailo M, Maibach R, Rinaldi E, Feng Y, Aronson D, Malogolowkin M, Yoshimura K. The Children's Hepatic tumors International Collaboration (CHIC): novel global rare tumor database yields new prognostic factors in hepatoblastoma and becomes a research model. European Journal of cancer. 2016 Jan 1;52:92-101.
18. Meyers RL, Maibach R, Hiyama E, Häberle B, Krailo M, Rangaswami A, Aronson DC, Malogolowkin MH, Perilongo G, von Schweinitz D, Ansari M. Risk-stratified staging in paediatric hepatoblastoma: a unified analysis from the Children's Hepatic tumors International Collaboration. The Lancet Oncology. 2017 Jan 1;18(1):122-31.
19. Kremer N, Walther AE, Tiao GM. Management of hepatoblastoma: an update. Current opinion in pediatrics. 2014 Jun 1;26(3):362-9.
20. Hong JC, Kim J, Browning M, Wagner A, Lerret S, Segura AD, Zimmerman MA. Modified associating liver partition and portal vein ligation for staged hepatectomy for hepatoblastoma in a small infant: how far can we push the envelope?. Annals of surgery. 2017 Aug 1;266(2):e16-7.
21. Pham TA, Gallo AM, Concepcion W, Esquivel CO, Bonham CA. Effect of liver transplant on long-term disease-free survival in children with hepatoblastoma and hepatocellular cancer. JAMA surgery. 2015 Dec 1;150(12):1150-8.

22. Trobaugh-Lotrario AD, Katzenstein HM. Chemotherapeutic approaches for newly diagnosed hepatoblastoma: past, present, and future strategies. Pediatric blood & cancer. 2012 Nov;59(5):809-12.
23. Sriniworn A, Anuntkasol M, Laorwong S, Poocharoen W, Niramis R. Clinical outcomes of hepatoblastoma: an experience of 37 cases. The Thai Journal of Surgery. 2015 Dec 30;36(4).
24. Zhang Y, Huang D, Zhang W, Tang S, Chen L, Yi Y, Zhang P, Liu A, Zhi T. Study on the experience on clinical characteristics and the outcome of pediatric hepatoblastoma. Biomedical Research. 2017 Jan 1;28(16):7315-21.
25. Shukla PJ, Barreto SG, Qureshi SS, Hawaldar R, Shrikhande SV, Ramadwar MR, Banavali S. Hepatoblastoma: a single institutional experience of 18 cases. Pediatric surgery international. 2008 Jul;24:799-802.
26. Ang JP, Heath JA, Donath S, Khurana S, Auldist A. Treatment outcomes for hepatoblastoma: an institution's experience over two decades. Pediatric surgery international. 2007 Feb;23:103-9.
27. McAteer JP, Goldin AB, Healey PJ, Gow KW. Surgical treatment of primary liver tumors in children: outcomes analysis of resection and transplantation in the SEER database. Pediatric Transplantation. 2013 Dec;17(8):744-50.