Open Access

Original Article

Outcome of Hepatoblastoma in A Low-and Middle-Income Country; Single Centre Experience from Pakistan

Rabiha Manzoor, Tariq Ghafoor*, Awais Arshad, Beenish Hira, Ayesha Latif, Fouzia Khan

Department of Pediatric Oncology, Combined Military Hospital, Rawalpindi/National University of Medical Sciences (NUMS) Pakistan, *Department of Pediatric Oncology, Armed Forces Bone Marrow Transplant Centre, Rawalpindi/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To determine the survival outcome of patients with hepatoblastoma (HB) treated at a tertiary care hospital of Pakistan.

Study Design: A prospective cohort study.

Place and Duration of Study: Pediatric oncology unit, Combined Military Hospital, Rawalpindi Pakistan from Jan 2013 to Dec 2023.

Methodology: All cases of hepatoblastoma (HB) diagnosed in individuals aged up to 12 years were enrolled. The study primarily focused on documenting survival outcomes, encompassing both "overall survival (OS)" and "disease-free survival (DFS).

Results: In a total of 29 patients with HB, 18(62.1%) were boys. The median age at the time of diagnosis was 1.3 years (0.8 to 2.8 years). At presentation, abdominal distension was present in all 29(100%) cases whereas palpable abdominal mass, and jaundice was present in 25(86.2%), and 9(31.0%) patients, respectively. Mortality was reported in 14(48.3%) patients. The median DFS, and OS were 18.64 months (5.27 to 47.04 months), and 0.13 months (0 to 44.00 months), respectively. Surgery emerged as a significant predictor of mortality, with a striking 15.89 times higher odds of mortality if surgery was not performed (95% CI: 1.71-147.39, p=0.015). Overall, 8-year survival was 50.0%. Eight year cumulative DFS was 59.3% for standard risk, 44.4% for high risk, and 26.7% for very high risk patients. OS was 60.0% for standard risk, 44.4% for high risk, and 40.0% for very high risk patients.

Conclusion: Hepatoblastoma is a rare pediatric cancer. A very high relapse/refractory rate needs further investigation to determine the cause of failure of the treatment.

Keywords: Abdominal distension, Hepatoblastoma, Jaundice, Mortality, surgery.

How to Cite This Article: *Manzoor R, Ghafoor T, Arshad A, Hira B, Latif A, Khan F. Outcome of Hepatoblastoma in A Low-and Middle-Income Country; Single Centre Experience from Pakistan. Pak Armed Forces Med J 2025; 75(3): 495-500. DOI: https://doi.org/10.51253/pafmj.v75i3.11816*

INTRODUCTION

Primary liver cancer is regarded as a relatively rare pediatric disease on a global scale, accounting for approximately 2% of all pediatric cancer cases.[1] The predominant subtype of primary liver cancer is hepatoblastoma (HB), constituting roughly 67–90% of instances, with a notably higher occurrence among children under 5 years old.[2,3] The prevalence of HB exhibits variations worldwide, with a greater incidence observed in infants. In the US, Europe, and South Africa, the estimated incidence rates are 0.8–1.5, 1.2, and 0.61 per million children, respectively.[4-6]

Historically, relying solely on surgical intervention yielded unfavorable outcomes, with a mere 20% to 30% chance of survival.[7-8] The landscape changed significantly with the invention of neoadjuvant and adjuvant chemotherapy, leading to a substantial improvement in survival rates, ranging from 70% to 80%.[8] Consequently, chemotherapy plays a crucial role in the comprehensive treatment of HB, serving not only to assist surgical excision but also to thwart local recurrence and manage metastatic disease. In the United States, a study reported 81.5%, 71.6%, and 69% for 1, 5, and 10-year survival rates, respectively.[9] Abdelahamid et al from Egypt documented 3-year event-free and overall survivals for HB as 46%, and 67%, respectively.[10]

Despite the abundance of global epidemiological and clinical studies, there is a noticeable dearth of research on the outcomes of HB, particularly in the context of Pakistan. This study was specifically designed to shed light on the epidemiological characteristics of HB in Pakistan and to analyze the factors that influence the survival of children diagnosed with this condition. The overarching goal is to provide valuable evidence that can contribute to the enhancement of prognosis for children grappling with

Correspondence: Dr Rabiha Manzoor, Department of Pediatric Oncology, Combined Military Hospital, Rawalpindi Pakistan

Received: 14 Mar 2024; revision received: 04 May 2024; accepted: 07 May 2024

hepatoblastoma. The primary objective of this study is to ascertain the survival outcomes of patients with HB who received treatment at a tertiary care hospital in Pakistan. By focusing on this specific population within the Pakistani healthcare setting, the research aims to fill a critical gap in knowledge, ultimately fostering a better understanding of the disease's dynamics and treatment outcomes in this region.

METHODOLOGY

This prospective cohort study was carried out in the "Pediatric oncology unit at the Combined Military Hospital (CMH) Rawalpindi, Pakistan from January 2013 to December 2023.

Inclusion Criteria: All newly diagnosed cases of HB aged up to 12 years and undergoing treatment during the study period were included.

Exclusion Criteria: Parents or guardians who did not want their children to be part of this study were excluded. Patients unwilling to undergo advised treatment were also not included in this research.

All patients during the duration of study were included due to unpredictable nature of hepatoblastoma, Hepatoblastoma is a rare pediatric liver cancer, and its occurrence can vary greatly across different geographic regions and populations. Approval from "Institutional Review Board" was acquired (543). Informed and written consents from the parents or guardians of the study cases were obtained. Detailed medical history as well as clinical information were documented at the time of enrollment. Socio-demographic and clinical information of all patients were noted. Relevant laboratory investigations were performed. The HB was diagnosed on the basis of clinical features, typical imaging findings, raised alpha fetoproteins (AFP) levels and biopsy findings. Decision of biopsy was not uniform and was based on physician preference. The "contrast enhanced computed tomography (CT)" chest ,abdomen and pelvis were done for proper pretext staging of HB. Based on pretext and additional anatomical information or additional pretext criteria (like regional lymphadenopathy "N",portal vein involvement "P",distant metastasis "M" Multifocality "F",Hepatic vein involvement "H", Caudate lobe involvement), patients were further classified as standard risk (pretext 1 2 3,AFP>100ug/dl), high risk (pretext 4 ,AFP >100ug/dl and additional pretext criteria) or very high risk (metastasis or AFP<100ug/dl).

Before February 2020, patients were treated on SIOPEL 6 guidelines where patients were given 6 cycles of Cisplatin only. Response assessment was done with contrast enhanced CT after 4 cycles of Cisplatin and AFP was repeated prior to each cycle. Patients with significant reduction in the size of mass, operatable disease and falling levels of AFP were considered to have adequate response. Stagnant or raised AFP levels or progressively increasing size of the mass were classified as inadequate response. The CCLG 2020 guidelines were used after February 2020. Standard risk patients were given 6 cycle of Cisplatin while high risk and very high risk patients were treated on more intensive chemotherapy Carboplatin and Doxorubicin. Response assessment criteria was same as in SIOPEL 6.1 Those with adequate response had surgery by a multidisciplinary team which was followed by post operative chemotherapy. Patients with inadequate response were shifted to more intensive chemotherapy before surgery. A special database was designed to record all study data. Patients underwent hospitalization for the initiation of chemotherapy. Following the initial phase, subsequent chemotherapy sessions were administered either as inpatient treatments or in a daycare setting, allowing for outpatient care. Outdoor cases were admitted immediately in case of fever or any other related clinical issues. Patients not admitted in the hospital were reviewed in outdoor clinics during chemotherapy visits as per protocol. During the neutropenic period, no prophylactic antimicrobial or colony-stimulating factors were administered. However, all instances of febrile neutropenia were managed with inpatient care involving the administration of broad-spectrum intravenous antibiotics. The criteria for defining fever included a single oral temperature exceeding 38°C or two readings surpassing 37.5°C taken at least 2 hours apart. Neutropenia was characterized by "absolute neutrophil count (ANC)" falling below 1000 cells per microliter.[10] Febrile patients with an ANC below 1000 were subjected to a treatment regimen involving a combination of Piperacillin-Tazobactam and Amikacin. If fever persisted after 48 hours, Piperacillin-Tazobactam was replaced with Meropenem. Empirical addition of Amphotericin B occurred if the fever persisted beyond 96 hours. Regular blood and blood products transfusions were administered, with a hemoglobin transfusion threshold set at 8.0 g/dL. Platelet transfusion thresholds were established at 10x10^9/L for

asymptomatic patients and 20x10^9/L for febrile patients.[11] The period from the date of morphological complete response until the occurrence of disease progression, relapse, or death, with censoring at the last contact date (January 31, 2024), was defined as "disease-free survival (DFS)". On the other hand, the interval from the day of diagnosis to the last follow-up day or death was defined as "overall survival (OS)".

"IBM-Statistical Package for Social Sciences", version 26.0 was used for data analysis. Quantitative data were described as Mean±SD or median and inter-quartile range (IQR). Frequency and percentages were shown to represent qualitative data. Chi-square test was performed to analyzed categorical data whereas independent sample t-test or Mann-Whitney U test were applied to compare quantitative data. In univariate analysis, factors with *p*-value below 0.20 were further analyzed employing Cox proportional hazard model. Kaplan-Meier survival curves were employed to estimate DFS and OS. *p*-values less than 0.05 was considered significant.

RESULTS

During the study period, a total of 33 new HB cases were registered. Four (12.1%) patients abandoned the treatment, so these 4 cases were excluded from the final analysis. In the remaining 29 patients, 18(62.1%) were boys and 11(37.9%) girls, representing boys to girls ratio of 1.6:1. The median age at the time of diagnosis was 1.3 years (0.8 to 2.8 years), ranging between 3 months to 7 years. The mean duration of symptoms was 1.83±0.85 months, ranging between 1 to 3 months. Right lobe was involved in 17(58.6%) patients, 7(24.1%) left lobe, while both lobs were involved in 5(17.2%). At presentation, abdominal distension was present in all 29(100%) cases whereas palpable abdominal mass, and jaundice were present in 25(86.2%), and 9(31.0%) patients, respectively. Hyperbilirubinemia, and tansaminitis were noted in 9(31.0%), and 7(24.1%) patients respectively. Tumor staging was 1, 3, and 4 in 1(3.4%), 24(82.8%), and 4(13.8%) cases. Fifteen (51.7%) patients belonged to standard risk group, 9(31.0%) high risk, and 5(17.2%) very high risk group. Histopathology examination was performed in 24 patients and it was found that epithelial type, and mixed epithelial and mesenchymal patterns were found among 15, and 9 patients respectively. Pulmonary metastatic disease was present in 4(13.7%) patients. Pre-treatment tumor extension PRETEXT staging 1, 2, 3, and 4 were noted in 4(13.8%), 14(48.3%), 7(24.1%), and 4(13.8%) patients, respectively. Additional pretext evaluation showed multi-focal disease, nodal involvement, portal vein involvement, and nodal as well as portal vein involvement in 2(6.7%), 4(13.8%), 1(3.4%), and 2(6.7%) cases respectively. Twenty four (82.8%) patients were given Cisplatin protocol while PLADO protocol was used in remaining 5(17.2%) cases. Response to chemotherapy was adequate in 18(62.1%) patients. The most common chemotherapy complication was febrile neutropenia, and cardiomyopathy, noted in 12(41.4%), and 1(3.4%) caserespectively, whereas 16(55.2%) patients did not experience any chemotherapy related complications. Seventeen (58.6%) patients underwent surgery. One (5.8%) patient had upfront surgery while remaining 16 (94.2%) had Neoadjuvant Chemotherapy followed by surgery. Liver transplantation was done in one (5.8%) patient. Post-surgery infection was reported in 2(11.8%) patients. One Mortality was reported in 14(48.3%) patients (7 due to treatment related mortality, 7 relapsed or refractory disease). There are 15 patients, who are still alive and on follow ups. Overall, the median DFS, and OS were 18.64 months (5.27 to 47.04 months), and 0.13 months (0 to 44.00 months), respectively. Age above or equal to 1 year (85.7% vs. 46.7%, p=0.027), lower hemoglobin below 8 g/dl (28.6% vs. 0%, p=0.006), surgery done (21.4% vs. 93.3%, p<0.001), and relapsed disease (50.0% vs. 6.7%, p=0.009) were significantly associated with mortality. Table-I is showing association of characteristics of HB patients with mortality. Table-II is showing comparison of abnormally distributed quantitative data with respect to mortality.

The Cox-Proportional Hazard Model (table-III) was employed to investigate predictors of mortality in patients with HB. For age, children aged ≥12 months exhibited a 1.10 times higher odds of mortality compared to those <12 months (95% CI: 0.12-10.24, p=0.927). Hemoglobin levels <8 g/dl were associated with a 1.68 times higher odds of mortality (95% CI: 0.28-10.27, p=0.574) compared to levels ≥8 g/dl. Notably, the presence of hyperbilirubinemia showed a trend, with an odds ratio of 5.14 (95% CI: 0.98-26.94, p=0.053). Treatment with Cisplatin did not significantly influence mortality compared to PLADO (Odds Ratio =1.74, 95% CI: 0.45-6.72, p=0.420). Surgery emerged as a significant factor, with a striking 15.89 times higher odds of mortality if surgery was not performed (95% CI: 1.71-147.39, p=0.015). The relapse status did not exhibit a statistically significant impact

on mortality (Odds Ratio =1.44, 95% CI: 0.40-5.18, *p*=0.578).

Table-I: Association of Characteristics of Hepatobalstoma Patients with Mortality (n=29)

Characteristics		Mortality		*p*-value
		Yes (n=14)	No (n=15)	
Gender	Boys	9(64.3%)	9 960.0%)	0.812
	Girls	5(35.7%)	6(40.0%)	
Age (years)	<1	2(14.3%)	8(53.3%)	0.027
	≥1	12(85.7%)	7(46.7%)	
Duration of symptoms (months)	<1	7(50.0%)	6(40.0%)	0.762
	1-2	3(21.4%)	5(33.3%)	
	>2	4(28.6%)	4(26.7%)	
Hemoglobin (g/dl)		8.74±1.13	10.26±1.55	0.006
Hemoglobin (g/dl)	<8	4(28.6%)	0	0.026
	≥8	10(71.4%)	15(100%)	
Hyperbilirubinemia		6(42.9%)	3(20.0%)	0.184
Transaminitis		3(21.4%)	4(26.7%)	0.742
Lob involved	Right	9(64.3%)	8(53.3%)	0.470
	Left	2(14.3%)	5(33.3%)	
	Both	3(21.4%)	2(13.3%)	
Pulmonary metastatsis		2(14.3%)	1(6.7%)	0.501
PRE-treatment tumor extension staging	1	2(14.3%)	2(13.3%)	0.707
	2	6(42.9%)	8(53.3%)	
	3	3(21.4%)	4(26.7%)	
	4	3(21.4%)	1(6.7%)	
Tumor staging	1	0	1(6.7%)	0.617
	3	12(85.7%)	12(80.0%)	
	4	2(14.3%)	2(13.3%)	
Risk groups	Standard	6(42.9%)	9(60.0%)	0.645
	High risk	5(35.7%)	4(26.7%)	
	Very high risk	3(21.4%)	2(13.3%)	
Treatment protocol	Cisplatin	10(71.4%)	14(93.3%)	0.119
	PLADO	4(28.6%)	1(6.7%)	
Surgery done		3(21.4%)	14(93.3%)	<0.001
Disease status	Relapsed disease	7(50.0%)	1(6.7%)	0.009
	No relapse	7(50.0%)	14(93.3%)	

Overall, 8 year survival for HB patients was 50.0%. Eight-year cumulative DFS was 59.3% for standard risk, 44.4% for high risk, and 26.7% for very high risk patients. OS was 60.0% for standard risk, 44.4% for high risk, and 40.0% for very high-risk patients. Details about the cumulative DFS and OS during the study period are shown in Figure-1.

DISCUSSION

The current study represents the most extensive cohort of pediatric HB cases, encompassing individuals from all regions of the country. Overall, 8-year survival for HB patients was 50.0%. Eight-year cumulative DFS was 59.3% for standard risk, 44.4% for high risk, and 26.7% for very high-risk patients. OS was 60.0% for standard risk, 44.4% for high risk, and 40.0% for very high-risk patients. Data from developed world shows 5-year survival rate of 66%, higher for patients undergoing liver transplant or resection with rates of 93%, 82%, and 82% for 1, 5, and 10-year survival, respectively.[4,12] A multi-center study on 153 HB children in China reported a 6-year survival rate of 83.3%±3.1%.[13] Our findings stand aligned with the contemporary world in terms of DFS and OS.4,13,12 Another study such as a 5-year survival rate of 86.3±5.0% in Shanghai and 54.6% in Beijing, China.[14] Another study reported that advanced stages of HB were associated with low survival rates, ranging from 75.0% in stage II to 20.2% in stage IV.[15]

Table-II: Comparison of Abnormally Distributed Quantitative data with respect to mortality (n=29)

Parameters	X		*p*-value
	Yes (n=14)	No (n=15)	
Leukocytes count (109/L)	13.75(5.85)	13.30(9.80)	0.694
Platelets (109/L)	575.50 (468.00)	566.00(535.00)	0.663
AFP (ug/L)	97100.00(398413.00)	51000(334113.00)	0.861

Values shown in Median (Interquartile range); Mann-Whiteny U test applied

Table-III: Cox-Proportional Hazard Model for Predictors of Mortality(n=29)

Predictors		Odds ratio	95% Confidence Interval (lower-upper)	*p*-value
Age (months)	<12	Reference		0.927
	≥12	1.10	0.12-10.24	
Hemoglobin (g/dl)	<8	1.68	0.28-10.27	0.574
	≥8	Reference		
Hyperbilirubinemia	Yes	5.14	0.98-26.94	0.053
	No	Reference		
Treatment protocol	Cisplatin	1.74	0.45-6.72	0.420
	PLADO	Reference		
Surgery	Not done	15.89	1.71-147.39	0.015
	Done	Reference		
Disease status	Relapse	1.44	0.40-5.18	0.578
	No relapse	Reference		

In this study, surgery emerged as a significant factor, with a striking 15.89 times higher odds of mortality if surgery was not performed (95% CI: 1.71-147.39, *p*=0.015). A study by Yu *et al*., from China reported inability to undergo surgery, and male gender to be significantly linked with mortality.[16] Research in the previous years have emphasized the

significance of surgical interventions in improving prognosis of patients with HB.[17,18] Despite more than 60% of tumors initially appearing unresectable, about 40% become amenable to resection after chemotherapy.[19,20] Liver transplantation emerges as the optimal solution for the remaining 20% of tumors, providing a potential cure opportunity for children with advanced HB.[21] Further exploration of the relationship between gender and the prognosis of childhood HB is deemed necessary. This entails a more in-depth analysis to understand how gender may influence the outcomes of children with HB. It is also crucial to consider and examine the potential differences in prognosis among various countries and regions. The impact of geographical and cultural factors on the prognosis of childhood HB warrants closer investigation to discern potential variations in outcomes based on geographic or regional disparities. Such comprehensive analyses will contribute to a more nuanced understanding of the factors affecting the prognosis of childhood HB and provide valuable insights for tailored and effective treatment strategies. The present study reports the most extensive and detailed data about the profile and outcomes of children having HB in Pakistan.

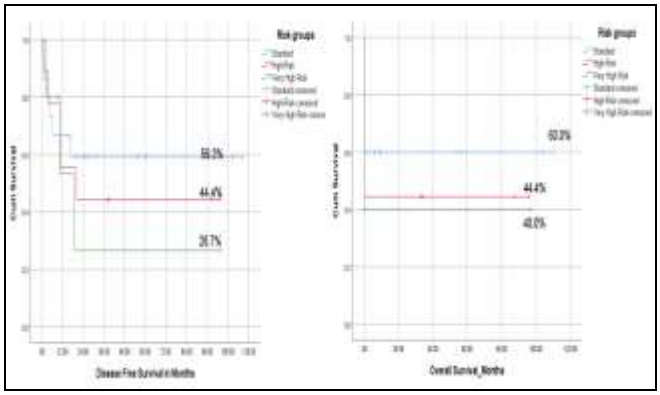

Figure-1: Disease free Survival and Overall Survival of Patients with Respect to Hepatoblastoma Risk Stratification

LIMITATIONS OF STUDY

Single center study design and a relatively small sample size were some of the limitations of this study. We are also unable to calculate the financial impact of HB on the affected families during the study period.

CONCLUSION

Hepatoblastoma is a rare pediatric cancer. A very high relapse/refractory rate needs further investigation to determine the cause of failure of the treatment. Further studies should explore large scale data involving long follow up duration needs to be planned to further record the outcomes.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

RM & TG: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

AA & BH: Data acquisition, data analysis, approval of the final version to be published.

AL & FK: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Di Giuseppe G, Youlden DR, Aitken JF, Pole JD. Pediatric hepatic cancer incidence and survival: 30-year trends in Ontario, Canada; the United States; and Australia. Cancer 2021; 127(5): 769-776. https://doi.org/10.1002/cncr.33319
2. Jeong SU, Kang HJ. Recent updates on the classification of hepatoblastoma according to the International Pediatric Liver Tumors Consensus. J Liver Cancer 2022; 22(1): 23-29. https://doi.org/10.17998/jlc.2022.02.24
3. Luo H, Huang T, Lu Q, Zhang L, Xi Y, Yang Y, et al. Molecular prevalence of HBB-associated hemoglobinopathy among reproductive-age adults and the prenatal diagnosis in Jiangxi Province, southern central China. Front Genet 2022; 13: 992073. https://doi.org/10.3389/fgene.2022.992073
4. Stiller CA, Pritchard J, Steliarova-Foucher E. Liver cancer in European children: incidence and survival, 1978-1997. Report from the Automated Childhood Cancer Information System project. Eur J Cancer 2006; 42(13): 2115-2123.
5. Moore SW, Millar AJ, Hadley GP, Ionescu G, Kruger M, Poole J, et al. Hepatocellular carcinoma and liver tumors in South African children: a case for increased prevalence. Cancer 2004; 101(3): 642-649. https://doi.org/10.1002/cncr.20398
6. Espinoza AF, Scheurer ME, Chambers TM, Vasudevan SA, Lupo PJ. A population-based assessment of metastatic hepatoblastoma in Texas reveals ethnic disparities. Front Public Health 2023; 11: 1049727. https://doi.org/10.3389/fpubh.2023.1049727
7. Exelby PR, Filler RM, Grosfeld JL. Liver tumors in children in the particular reference to hepatoblastoma and hepatocellular carcinoma: American Academy of Pediatrics Surgical Section Survey--1974. J Pediatr Surg 1975; 10(3): 329-337. https://doi.org/10.1016/0022-3468(75)90095-0
8. Brown J, Perilongo G, Shafford E, Keeling J, Pritchard J, Brock P, et al. Pretreatment prognostic factors for children with hepatoblastoma-- results from the International Society of Paediatric Oncology (SIOP) study SIOPEL 1. Eur J Cancer 2000; 36(11): 1418-1425. https://doi.org/10.1016/s0959-8049(00)00074-5

9. Vinayak R, Cruz RJ Jr, Ranganathan S, Mohanka R, Mazariegos G, Soltys K, et al. Pediatric liver transplantation for hepatocellular cancer and rare liver malignancies: US multicenter and single-center experience (1981-2015). Liver Transpl 2017; 23(12): 1577-1588. https://doi.org/10.1002/lt.24847
10. Abdelahamid S, Khedr RA, El Wakeel M, Younes A, Ahmed G, Elkinaai N, et al. Hepatoblastoma in Developing Countries; Eight Years of Single Centre Experience. J Cancer Ther 2018; 9: 793-806. https://doi.org/10.4236/jct.2018.910065
11. Benjamin RJ, Anderson KC. What is the proper threshold for platelet transfusion in patients with chemotherapy-induced thrombocytopenia? Crit Rev OncolHematol 2002; 42(2): 163-171. https://doi.org/10.1016/s1040-8428(01)00182-2
12. 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 Surg. 2015; 150(12): 1150-1158. https://doi.org/10.1001/jamasurg.2015.1847
13. Yuan XJ, Wang HM, Jiang H, Tang M, Li Z, Zou X, et al. Multidisciplinary effort in treating children with hepatoblastoma in China. Cancer Lett. 2016; 375(1): 39-46. https://doi.org/10.1016/j.canlet.2016.02.051
14. Wang TY, Han YL, Gao YJ, Xu M, Gu S, Yin MZ, et al. Retrospective Analysis of Childhood Hepatoblastoma in a Single Centre in China. Clin Oncol (R Coll Radiol) 2019; 31(7) :471-478. https://doi.org/10.1016/j.clon.2019.03.044
15. Zhang Y, Zhang W, Tang S, Chen L, Yi Y, Zhang P, et al. A single-center retrospective study of pediatric hepatoblastoma. Oncol Lett 2016; 12(5): 3919-3925. https://doi.org/10.3892/ol.2016.5195
16. Yu W, Liu X, Li J, Xi Z, Jin J, Huang H, et al. A single-center retrospective analysis of childhood hepatoblastoma in China. Gland Surg 2020; 9(5): 1502-1512. https://doi.org/10.21037/gs-20-710
17. Vasudevan SA, Meyers RL, Finegold MJ, Dolores L, Ranganathan S, Dunn SP, et al. Outcomes of children with well-differentiated fetal hepatoblastoma treated with surgery only: Report from Children's Oncology Group Trial, AHEP0731. J Pediatr Surg 2022; 57(10): 251-256. https://doi.org/10.1016/j.jpedsurg.2022.05.022
18. Murawski M, Weeda VB, Czauderna P. Surgical management in hepatoblastoma: points to take. PediatrSurg Int 2023; 39(1): 81. https://doi.org/10.1007/s00383-022-05356-z
19. Hishiki T. Current therapeutic strategies for childhood hepatic tumors: surgical and interventional treatments for hepatoblastoma. Int J Clin Oncol 2013; 18(6): 962-968. https://doi.org/10.1007/s10147-013-0625-7
20. Rammohan A, Rela M, Kumar GV, Scott JX, Shanmugam N, Reddy MS, et al. Outcomes for high-risk hepatoblastoma in a resource-challenged setting. BJS Open 2020; 4(4): 630-636. https://doi.org/10.1002/bjs5.50297
21. Leiskau C, Junge N, Mutschler FE. Long-Term Outcome Following Liver Transplantation for Primary Hepatic Tumors-A Single Centre Observational Study over 40 Years. Children (Basel) 2023; 10(2): 202. https://doi.org/10.3390/children10020202