TUMI HEALTH SCIENCES RESEARCH
e-ISSN 3084-7915

TUMI Health Sciences Research
Calderón-Villavicencio, L. TUMI Health Sci. Res. 2026;1(3):1–7
https://doi.org/10.64716/aqkevp15

ORIGINAL RESEARCH **OPEN ACCESS**

Postchemotherapy alpha-fetoprotein and baseline PRETEXT groups in young children with hepatoblastoma in Lima, Peru

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ABSTRACT

Background: Biochemical markers and anatomical staging describe different aspects of hepatoblastoma and require interpretation according to treatment timing. **Objective:** To assess the association between postchemotherapy serum alpha-fetoprotein (AFP) categories and baseline pretreatment extent of tumor (PRETEXT) groups in young children with hepatoblastoma at a referral hospital in Lima, Peru. **Methods:** A retrospective analytical record review included 30 eligible patients from 37 identified during 2018–2024. Age, sex, baseline and postchemotherapy AFP, baseline PRETEXT group, and pulmonary metastasis were extracted from clinical records. Frequencies and percentages described the sample. Associations were assessed using the Fisher–Freeman–Halton exact test; Pearson chi-square and Cramér's V were also calculated. **Results:** Eighteen patients (60.0%) were male. All patients had baseline AFP >1,000 ng/mL. After neoadjuvant chemotherapy, AFP was <100 ng/mL in 17 patients (56.7%), 100–1,000 ng/mL in three (10.0%), and >1,000 ng/mL in ten (33.3%). PRETEXT groups I, II, III, and IV accounted for 10.0%, 20.0%, 30.0%, and 40.0%, respectively. Pulmonary metastasis was documented in 14 patients (46.7%). The association between postchemotherapy AFP and baseline PRETEXT was not statistically significant (exact $p = 0.287$; Pearson $\chi^2 = 8.131$, six degrees of freedom, $p = 0.229$; Cramér's $V = 0.368$). **Conclusions:** Lower AFP categories were frequent after chemotherapy, including among children with extensive baseline hepatic involvement. These findings describe the joint distribution of biochemical and anatomical findings without establishing an association or prognostic performance.

Keywords: Hepatoblastoma; Alpha-Fetoproteins; Neoplasm Staging; Child, Preschool; Infant; Peru.

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Journal homepage: https://tumijournal.com/index.php/health-sciences-research/en
https://doi.org/10.64716/aqkevp15
Editor-in-Chief: Yovana Melisza Gutierrez-Polanco

Received: September 06, 2026
Revised: October 15, 2026
Accepted: October 25, 2026
Available online: November 1, 2026

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Introduction

Hepatoblastoma is the most common primary malignant liver tumor in young children, although it remains rare at the population level. Its presentation and management differ from those of adult liver cancer, requiring coordinated pediatric oncology, radiology, pathology, and surgical assessment. Contemporary treatment combines systemic therapy with complete tumor removal, with liver transplantation considered in selected patients whose tumors cannot be adequately resected [1,2]. Clinical series remain valuable for describing the patients treated in referral settings, where the distribution of disease extent may differ from that in population-based or trial cohorts.

Serum alpha-fetoprotein (AFP) is used during diagnosis and follow-up, but its interpretation depends on age, treatment timing, and the clinical question. A concentration obtained at diagnosis has a different meaning from one obtained after chemotherapy or during surveillance for relapse. Reports examining AFP monitoring emphasize that biochemical findings must be interpreted in their clinical context [3]. In a recent cohort, AFP measured after the fourth chemotherapy cycle contributed prognostic information when evaluated alongside post-treatment imaging and event-free survival [4]. Such evidence supports studying AFP alongside anatomical assessments while distinguishing a cross-tabulated association from a validated prediction of outcome.

The pretreatment extent of tumor (PRETEXT) system describes tumor distribution within four hepatic sections and records additional features through annotation factors. Its anatomical groups depend on the number and contiguity of tumor-free sections, rather than simply the number of affected sections [5]. Imaging recommendations distinguish the baseline PRETEXT assessment from the post-treatment extent of tumor (POSTTEXT) assessment used after chemotherapy [6]. This distinction is essential when comparing an initial anatomical classification with a biomarker measured later in treatment.

The relationship between AFP and disease extent is also influenced by tumor biology and clinical selection. A retrospective series of 316 children identified baseline AFP, PRETEXT IV, vascular invasion, and distant metastasis among factors associated with prognosis [7]. Molecular studies have further demonstrated intratumoral heterogeneity and differing chemotherapy responses in patient-derived models [8]. These findings provide a rationale for examining biochemical and anatomical features together, but they do not imply that a single AFP category can substitute for imaging or histopathology.

The objective of this study was to assess the association between postchemotherapy AFP categories and baseline PRETEXT groups in young children with hepatoblastoma treated at a pediatric referral hospital in Lima during 2018–2024. Secondary objectives were to describe age and sex, AFP categories before and after neoadjuvant chemotherapy, baseline hepatic involvement, and pulmonary metastasis. Characterizing these findings in a Peruvian referral setting provides local clinical evidence and a basis for more detailed studies of treatment response and risk stratification.

Materials and methods

Study design and setting

A retrospective observational analytical study was conducted through review of medical records at a public tertiary pediatric referral hospital in Lima, Peru. Records corresponded to patients managed during 2018–2024. The analysis related an AFP measurement obtained after neoadjuvant chemotherapy to the PRETEXT group established at diagnosis. Treatment decisions were made as part of routine clinical care. Reporting followed the applicable Strengthening the Reporting of Observational Studies in Epidemiology recommendations [9].

Participants and sampling

The accessible population comprised 37 pediatric patients with hepatoblastoma. Non-probability convenience sampling yielded 30 eligible records for analysis. Eligibility required a histopathologically confirmed diagnosis in one of the study age groups (<1 year or 1–5 years) and clinical documentation of baseline AFP, AFP after neoadjuvant chemotherapy, and baseline abdominal computed tomography permitting PRETEXT classification. Records were excluded for incomplete required clinical information, suspected secondary hepatic neoplasms, or other benign or malignant liver conditions. The final sample was determined by eligibility and availability of the required records.

Variables and clinical definitions

Serum AFP was recorded at diagnosis and after neoadjuvant chemotherapy, in ng/mL. The concentration categories used in the analysis were <100, 100–1,000,

and >1,000 ng/mL, with both boundaries included in the middle category. These were analytical concentration bands, not stand-alone classifications of clinical risk, remission, or chemotherapy resistance. The primary comparison used postchemotherapy AFP because baseline AFP was >1,000 ng/mL in every included patient.

Baseline hepatic involvement was classified into PRETEXT groups I–IV from the diagnostic imaging records. Group I indicates three adjoining tumor-free hepatic sections; group II indicates two adjoining tumor-free sections but not three; group III indicates one tumor-free section or two nonadjoining tumor-free sections; and group IV indicates no tumor-free section [5,6]. The analysis used the baseline PRETEXT group throughout. Pulmonary metastasis at diagnosis was recorded as present or absent from the clinical and imaging records. Age was summarized using the recorded groups of <1 year and 1–5 years, and sex as female or male.

Data collection and quality control

A structured case report form was used to extract demographic information, laboratory results, imaging classifications, and pulmonary metastasis status. Its content was reviewed by a general pediatrician and a pediatric oncology subspecialist. Following institutional authorization, medical charts, laboratory findings, and tomographic reports were reviewed, and the extracted data were organized in Microsoft Excel. Patient identifiers were replaced with numerical codes. Frequencies, denominators, and marginal totals were checked across all five tables before the final analysis.

Statistical Analysis

Categorical variables were summarized as counts and percentages rounded to one decimal place. Descriptive percentages used 30 patients as the denominator. The AFP-by-PRETEXT table used percentages within each postchemotherapy AFP category; its total row described the PRETEXT distribution in the entire sample. No association test was applied to baseline AFP because it had no variation across the selected categories.

The primary association analysis used the two-sided Fisher–Freeman–Halton exact test for the 3 × 4 contingency table. The exact p-value was obtained by enumerating all tables with the observed row and column margins and summing probabilities no greater than that of the observed table. This approach was selected because ten of the twelve expected cell frequencies were below five, including three below one. Pearson chi-square with six degrees of freedom was additionally reported, and Cramér's V was calculated as $V = \sqrt{[\chi^2/\{N \times \min(r-1, c-1)\}]}$, where r and c are the numbers of rows and columns. Cramér's V was treated as a descriptive measure of nominal association. Tests were unadjusted, with statistical significance set at $p < 0.05$. The statistical workflow used IBM SPSS Statistics, version 29, and reproducible calculations in Python with SciPy and exact integer enumeration.

Ethical considerations

The research protocol was approved by the institutional research ethics committee under Decision No. 238-CEI-EPM-UCV-2024. The committee waived informed consent because the study involved retrospective review of clinical records. The research followed the ethical principles of the Declaration of Helsinki [10]. Institutional authorization was obtained before accessing records, identifiers were replaced with numerical codes, and information was handled confidentially. Results are presented in aggregate, and access to clinical information remains subject to institutional privacy safeguards.

Results

Thirty of the 37 identified patients were included in the analysis. The five tables summarize demographic characteristics, AFP measurements, baseline PRETEXT groups, pulmonary metastasis, and the association between postchemotherapy AFP and baseline PRETEXT (Tables 1–5).

Twenty-one patients (70.0%) were in the 1–5-year age group and nine (30.0%) were younger than one year. There were 18 male and 12 female patients, corresponding to a male-to-female ratio of 1.5:1 (Table 1).

Table 1. Age and sex of children with hepatoblastoma

Characteristic	n	%
Age group		
<1 year	9	30.0
1–5 years	21	70.0
Sex		
Female	12	40.0
Male	18	60.0
Total	30	100.0

N = 30. Percentages were calculated separately within each characteristic. Age categories follow the study classification.

All 30 patients had AFP >1,000 ng/mL at diagnosis. After neoadjuvant chemotherapy, 17 (56.7%) had AFP <100 ng/mL, three (10.0%) had AFP of 100–1,000 ng/mL, and ten (33.3%) remained in the >1,000 ng/mL category. Thus, 20 patients (66.7%) moved to a lower concentration category (Table 2).

Table 2. Serum AFP categories at diagnosis and after neoadjuvant chemotherapy

AFP concentration	At diagnosis		After chemotherapy	
	n	%	n	%
<100 ng/mL	0	0.0	17	56.7
100–1,000 ng/mL	0	0.0	3	10.0
>1,000 ng/mL	30	100.0	10	33.3
Total	30	100.0	30	100.0

AFP: alpha-fetoprotein. Percentages use 30 patients at each assessment. The 100–1,000 ng/mL category includes both endpoints. Concentration bands describe the laboratory findings and do not independently define treatment response.

PRETEXT IV was the most frequent baseline group, comprising 12 patients (40.0%), followed by PRETEXT III with nine (30.0%). Together, groups III and IV accounted for 21 patients (70.0%) (Table 3).

Table 3. Baseline hepatic involvement according to PRETEXT group

Baseline PRETEXT group	n	%
PRETEXT I	3	10.0
PRETEXT II	6	20.0
PRETEXT III	9	30.0
PRETEXT IV	12	40.0
Total	30	100.0

N = 30. **PRETEXT:** pretreatment extent of tumor. Groups describe the distribution of tumor-free hepatic sections at diagnosis; definitions are provided in Methods.

Pulmonary metastasis was documented at diagnosis in 14 patients (46.7%); the remaining 16 (53.3%) had no documented pulmonary metastasis (Table 4).

Table 4. Pulmonary metastasis at initial diagnosis

Pulmonary metastasis	n	%
Present	14	46.7
Absent	16	53.3
Total	30	100.0

N = 30. Percentages refer to the full analytical sample. Metastasis status corresponds to the initial diagnostic assessment.

Among the 17 patients with postchemotherapy AFP <100 ng/mL, eight (47.1%) had been classified as PRETEXT IV at diagnosis. Of the ten patients with AFP >1,000 ng/mL, two had baseline PRETEXT II, four PRETEXT III, and four PRETEXT IV. The exact test did not identify a statistically significant association between postchemotherapy AFP category and baseline PRETEXT group ($p = 0.287$). The Pearson comparison also did not reach statistical significance ($p = 0.229$), and Cramér's V was 0.368 (Table 5).

Discussion

The principal finding was that postchemotherapy AFP categories were not significantly associated with baseline PRETEXT groups in this series of 30 children. The exact p-value was 0.287, while the Pearson analysis yielded $p = 0.229$ and Cramér's $V = 0.368$. The effect-size estimate describes the observed contingency table but does not establish a clinically validated relationship. The descriptive findings were nevertheless informative: all patients initially had AFP >1,000 ng/mL, more than half had AFP <100 ng/mL after chemotherapy, and 70.0% had baseline PRETEXT III or IV.

The age distribution and male predominance were consistent with the usual presentation of hepatoblastoma in early childhood. Zhi et al. described 192 boys and 124 girls among 316 children younger than three years, with a median age of 1.45 years [7]. Differences in eligibility and referral patterns should be considered when comparing these series. The present distribution describes the children treated in one hospital and does not estimate the incidence or demographic risk of hepatoblastoma in Peru.

The change in AFP categories after chemotherapy indicates that a biochemical decrease occurred in many patients. Because every baseline value exceeded 1,000 ng/mL, the 20 patients whose subsequent values were at or below that threshold necessarily moved to a lower band. The ten remaining above 1,000 ng/mL could also have experienced a decrease within that broad band. A category alone therefore does not distinguish the magnitude or rate of AFP decline. This matters when comparing the present analysis with the study by Jeong et al., which evaluated AFP after a specified fourth chemotherapy cycle, imaging changes, and event-free survival in 73 patients [4]. Their prognostic analysis addressed a different question from the distributional association examined here.

Table 5. Postchemotherapy AFP categories by baseline PRETEXT group

AFP after chemotherapy	PRETEXT I	PRETEXT II	PRETEXT III	PRETEXT IV	Total	Exact p-value
<100 ng/mL	3 (17.6)	2 (11.8)	4 (23.5)	8 (47.1)	17 (100.0)	
100–1,000 ng/mL	0 (0.0)	2 (66.7)	1 (33.3)	0 (0.0)	3 (100.0)	0.287
>1,000 ng/mL	0 (0.0)	2 (20.0)	4 (40.0)	4 (40.0)	10 (100.0)	
Total	3 (10.0)	6 (20.0)	9 (30.0)	12 (40.0)	30 (100.0)	—

AFP: alpha-fetoprotein; **PRETEXT:** pretreatment extent of tumor. Values are n (%). Percentages are calculated within AFP rows; percentages in the total row use N = 30. Row sums may differ from 100.0% by 0.1% because of rounding. The exact p-value refers to the entire 3 × 4 table. Pearson $\chi^2 = 8.131$; degrees of freedom = 6; asymptotic p = 0.229. Cramér's V = 0.368.

Treatment context also helps explain why baseline anatomical extent and subsequent AFP need not correspond closely. Prospective Japanese studies evaluated different regimens in carefully selected groups: JPLT3-S investigated cisplatin monotherapy in young children with localized standard-risk disease, whereas JPLT3-H examined dose-dense therapy in high-risk patients with pulmonary metastases [11,12]. Their findings support interpreting biomarker measurements alongside treatment exposure and risk characteristics. Neither a postchemotherapy value below 100 ng/mL nor one above 1,000 ng/mL, by itself, establishes complete remission or resistance.

The timing of the imaging classification is equally important. Eight patients with baseline PRETEXT IV subsequently had AFP <100 ng/mL. This observation is compatible with a biochemical decrease after treatment in children whose initial disease involved all four hepatic sections; it does not describe their post-treatment anatomical extent. Contemporary imaging guidance uses POSTTEXT for reassessment after chemotherapy [6]. The Children's Oncology Group AHEP0731 surgical analysis also incorporated imaging at diagnosis and after successive treatment cycles when examining the timing of resection and transplant referral [13]. Serial anatomical assessment and biochemical measurements therefore provide different information for multidisciplinary care.

Pulmonary metastasis at diagnosis was common in this referral series. Zhi et al. likewise reported substantial metastatic disease in their tertiary-center cohort, with the lung being the predominant metastatic site [7]. However, the proportion with pulmonary metastasis here should not be directly equated with their proportion with metastasis at any distant site. The concentration of PRETEXT III–IV disease and pulmonary metastases warrants attention to referral and care pathways, but these cross-sectional descriptions do not demonstrate that diagnostic delay caused the observed disease distribution.

Baseline and post-treatment AFP thresholds must also remain conceptually separate. Recent CHIC analyses showed that historical associations between very low baseline AFP or small-cell undifferentiated histology and poor outcome were affected by the inclusion of rhabdoid tumors [14]. The AHEP0731 pathology analysis similarly found that a small-cell undifferentiated component did not independently confer an adverse outcome in the studied hepatoblastomas [15]. Consequently, high baseline AFP cannot exclude a histological component, and a low concentration after chemotherapy cannot be interpreted through the same framework as low AFP at diagnosis. Histopathological classification remains necessary.

The clinical implication is to evaluate AFP alongside imaging, pathology, and the broader treatment course. International data comparing upfront and delayed surgery in resectable hepatoblastoma illustrate that treatment choices depend on anatomical and clinical eligibility, rather than an isolated biomarker category [16]. Studies of advanced disease similarly emphasize individualized selection for resection or transplantation [17,18]. The present findings provide a local description of these routinely assessed features; they do not support changing treatment pathways on the basis of the observed Cramér's V.

Long-term prognosis is a distinct question. Studies of recurrence after remission and of relapsed hepatoblastoma have evaluated PRETEXT, metastatic disease, surgical factors, and follow-up outcomes [19,20]. AFP surveillance can contribute to detecting recurrence, although its interpretation may require additional clinical and imaging information [3]. Future

multicenter work could combine serial AFP measurements, PRETEXT and POSTTEXT, standardized histopathology, treatment exposure, and survival endpoints. The international consensus dataset for hepatoblastoma pathology reporting provides a framework for more consistent collection of relevant tumor characteristics [21].

Strengths of this study include histopathological confirmation, inclusion of both diagnostic and postchemotherapy AFP assessments, and preservation of the full AFP-by-PRETEXT distribution. Exact inference was appropriate for the small category counts. The single-center retrospective design and convenience sample limit generalizability and remain susceptible to selection and documentation biases. The small sample also limits precision and adjusted analysis, while categorization reduces the detail available from continuous AFP measurements. These considerations support a descriptive and exploratory interpretation rather than a conclusion about causal effects or prognostic accuracy.

Conclusions

In this series of 30 children with hepatoblastoma, all had baseline AFP >1,000 ng/mL and 56.7% had AFP <100 ng/mL after neoadjuvant chemotherapy. Baseline PRETEXT III–IV accounted for 70.0% of patients, and pulmonary metastasis was documented in 46.7%. Postchemotherapy AFP category was not significantly associated with baseline PRETEXT group in the exact analysis ($p = 0.287$). The observed biochemical and anatomical distributions provide local clinical characterization, but do not establish prognostic performance or support using either assessment as a substitute for the other.

Author Contributions Statement (CrediT)

LLC: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization, and Project administration. **JFQ:** Conceptualization, Methodology, Validation, Writing – review and editing, and Supervision. All authors critically reviewed the intellectual content and approved the final version of the manuscript for publication.

Acknowledgments

The authors thank the oncology and medical-records personnel of the participating hospital for facilitating authorized access to clinical documentation, and the academic team for support during the study.

Funding

The research was self-funded by the authors and received no external grants or sponsorship from public, commercial, or nonprofit organizations.

Conflict of Interest

The authors declare no financial, personal, or professional conflicts of interest related to this study.

Data Availability

The aggregate findings are presented in the tables. Requests for de-identified study data may be addressed to the corresponding author for reasonable academic purposes, subject to institutional authorization and the privacy protections applicable to pediatric clinical records.

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