

Epstein–Barr virus in paediatric sporadic Burkitt lymphoma: real-world experience from a Peruvian national referral centre

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Abstract

Introduction: Burkitt lymphoma (BL) is an aggressive B-cell lymphoma, representing 30%–40% of childhood non-Hodgkin lymphomas globally. In Peru, Epstein–Barr virus (EBV) is highly prevalent in lymphomas, yet its role in paediatric BL remains underexplored.

Objective: This study evaluates the clinical and epidemiological characteristics of paediatric BL at the National Institute of Neoplastic Diseases, focusing on EBV-positive cases, pathological features, treatment response and prognostic factors, within the real-world setting of a lower-middle-income country (LMIC).

Materials and methods: From 2009 to 2021, 187 aggressive B-cell lymphomas were diagnosed in children, from which 34 high-grade B-cell lymphomas underwent central pathology review, yielding 23 molecularly confirmed sporadic BL cases. Inclusion criteria comprised age <15 years, availability of tumour tissue for immunohistochemical analysis and available clinical records.

Results: EBV infection was detected using EBV-encoded RNA (EBER) in situ hybridisation, and MYC translocation (8q24) was identified via FISH. Among the subset, 61% were EBV-positive, with males comprising 65% and a mean age of 6.7 years. EBV-positive status and younger age were associated with inferior survival in univariate analyses (log-rank $p=0.012$ and $p=0.009$, respectively). The association with EBV was attenuated after exploratory adjustment (HR, 3.69; 95% CI, 0.35–38.98; $p=0.278$).

Conclusion: In this cohort, 61% of paediatric sporadic BL cases were EBV-positive, associated with younger age ($p=0.01$) and inferior survival in univariate analysis (log-rank

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$p = 0.012$). The independent prognostic contribution of EBV could not be established. These LMIC findings support expanded molecular diagnostics and larger multicentre studies.

Keywords: lymphoma, B-cell, Burkitt lymphoma, infections, Epstein–Barr virus, oncogenic viruses, Latin America, Peru

Introduction

Every year, ~400,000 children and adolescents aged 0 to 19 years are affected by cancer worldwide [1,2]. In low- and middle-income countries, 4.6% of cancer cases occur in children aged 0 to 14 years, leading to a higher mortality rate compared to high-income countries, where childhood cancers constitute only 0.5% of all cases [3]. In developed nations, 80% of childhood cancers are successfully treated, with haematological malignancies showing the highest incidence rates [1]. In Peru, lymphoma and leukaemia have age-standardised incidence rates of 9.9 and 7.6 per 100,000, respectively, and haematological neoplasms account for 60% of childhood cancers [4,5]. Furthermore, the incidence of cancer-related infections in low- and middle-income regions ranges between 15% and 30% [6], highlighting an important, preventable cause of cancer.

Non-Hodgkin lymphoma (NHL) encompasses diverse subtypes with distinct morphological, genetic and clinical features, and its aetiology involves both infectious agents and genetic predispositions [7].

The Epstein–Barr virus (EBV), the first oncogenic virus identified over 56 years ago by Dr. Anthony Epstein and Dr. Yvonne Barr, was originally associated with Burkitt lymphoma (BL) in equatorial Africa [8,9]. EBV encodes around 100 viral proteins, with only five oncoproteins (latent membrane protein 1, latent membrane protein 2A, latent membrane protein 2B, Epstein–Barr nuclear antigen 1 and Epstein–Barr nuclear antigen 2) required to transform primary B cells into proliferating lymphoblastoid cell lines. Notably, in BL, the virus typically adopts Latency I, expressing only EBNA1 and EBV-encoded RNAs (EBERs) [10]. BL, an aggressive B-cell lymphoma common in paediatric populations, represents ~30% to 40% of childhood NHL worldwide [11–13]. It manifests in three clinical forms: sporadic BL; endemic BL, which is associated with *Plasmodium falciparum* malaria in equatorial Africa; and immunodeficiency-associated BL (i.e. HIV-associated BL) [14–16]. Peru has the highest incidence of EBV-positive diffuse large B-cell lymphoma, not otherwise specified (DLBCL NOS) and classic Hodgkin lymphoma (HL) in Latin America, with EBV presence confirmed in tumour tissues through immunological or molecular techniques.

BL is marked by characteristic cytogenetic translocations, specifically t(8;14), t(2;8) and t(8;22), which activate the MYC gene and drive cell proliferation [17,18]. EBV is detected in 20% to 30% of sporadic BL cases globally; however, few studies have focused on EBV-positive sporadic BL.

Moreover, there is a notably high prevalence of T-cell EBV-associated lymphoproliferative disorders and NK/T-cell lymphomas, reinforcing EBV's role as a significant etiological factor in Peru [19–21]. BL remains a major cause of paediatric cancer in the country, and this study investigates its epidemiological and pathological features, along with relevant risk factors. From 2009 to 2021, 187 cases of mature aggressive B-cell lymphomas were diagnosed in children at the National Institute of Neoplastic Diseases. Our study focuses on 23 cases of sporadic BL unrelated to HIV, treated at Instituto Nacional de Enfermedades Neoplásicas (INEN) in Lima, Peru. In this work, we present a comprehensive analysis of the clinical and epidemiological characteristics of paediatric sporadic BL at INEN, including EBV prevalence, pathological diagnosis, treatment response and prognostic factors.

Materials and methods

Tissue samples and case characterisation

This was a retrospective single-centre cohort study. Between 2009 and 2021, 187 children with mature aggressive B-cell lymphomas were diagnosed at INEN. From this cohort, 34 cases of high-grade B-cell lymphoma with a germinal centre phenotype were selected for central pathological review based on the following inclusion criteria: availability of pathological material for immunohistochemical analysis, patient age below 15 years and available clinical records. Of these, 24 cases were MYC-FISH-positive; one lacked an available clinical record, leaving 23 cases that constitute the final study cohort.

To detect chromosomal rearrangements involving the MYC gene located on chromosome 8q24, a MYC-FISH translocation assay was performed during central review. In instances where BCL2 immunohistochemistry results were inconclusive, BCL2-FISH testing was conducted ($n = 3$). All cases tested negative for BCL2 rearrangements, effectively ruling out double-hit high-grade lymphoma. Additionally, in four cases that were negative for MYC rearrangement, the presence of 11q aberrations was assessed using a FISH method, with one case confirming the aberration ($n = 1/4$).

This study adhered to confidentiality and anonymity principles according to the Declaration of Helsinki and its amendments. Approval was granted by the Ethics Committee and the INEN Scientific Council (INEN 543-2020).

Statistical analysis

A retrospective cohort analysis was performed on 187 cases of mature aggressive B-cell lymphomas, including 23 patients diagnosed with BL at the INEN in Lima, Peru. Categorical variables were analysed using the chi-square and Fisher's exact tests, while continuous variables were compared using Student's *t*-test. Missing data were reported as not available and were not imputed. Overall survival was calculated from the date of diagnosis to death from any cause or last follow-up, with patients alive at last follow-up censored. Follow-up was administratively truncated at 36 months. Survival probabilities were estimated by the Kaplan–Meier method, with survival distributions compared using the log-rank test and median follow-up estimated using the reverse Kaplan–Meier method. Univariable Cox regression was used to report hazard ratios (HRs) and 95% confidence intervals (CIs). An exploratory Cox model included EBV status, age group and treatment documentation; proportional hazards were assessed using Schoenfeld residuals. EBER status was analysed as positive or negative. A *p*-value of < 0.05 was deemed statistically significant. All analyses were conducted with R software environment version 4.6.1 (R Core Team), Stata software version 17.0 (StataCorp) and QGIS software version 3.14 (QGIS Development Team).

Immunohistochemistry

Immunohistochemical staining for CD20, BCL6, CD10, BCL2, Ki67, MUM1, TDT and MYC was reviewed by three experienced pathologists, with results reported as positive, negative or by expression percentage. Consensus from at least two pathologists was required for reporting.

In situ hybridisation for EBER

The presence of EBV RNA was detected by EBER in situ hybridisation. EBER results were classified as positive or negative.

Fluorescence in situ hybridisation

The MYC translocation was confirmed in all 23 BL cases using FISH analysis.

Results

Epidemiological, demographic and clinical features

The cohort of mature aggressive B-cell lymphomas in children from the INEN diagnosed between 2009 and 2021 ($N = 187$) included 106 BL (57%) and 81 (43%) DLBCL NOS cases. Patients diagnosed with BL were generally younger (7.25 years; SD, 4.5) than DLBCL NOS patients (11.4 years; SD, 5.2), with a greater proportion of males and a higher representation from the coastal region (Table 1). BL cases tended to be in a more advanced stage, with a majority in stage III, compared to DLBCL NOS cases, where there is a more even distribution across different stages.

Table 1. Baseline socio-demographic and clinical characteristics of aggressive mature B-cell lymphoma cases at INEN (2009–2021).

	BL	DLBCL
Characteristics	<i>n</i> = 106	<i>n</i> = 81
Age (years)		
Mean $\pm$ SD	7.25 $\pm$ 4.5	11.48 $\pm$ 5.2
Median	5.5	13
Q1–Q3	[4–10]	[6–15]
Interquartile range	6	9
Age (<i>n</i> , %)		
1–6	61 (58%)	21 (26%)
7–12	27 (25%)	18 (22%)
>12	18 (17%)	42 (52%)
Sex (%)		
Female	25 (24%)	26 (32%)
Male	81 (76%)	55 (68%)
Sub-region		
Coast	72 (68%)	51 (63%)
Highland	21 (20%)	18 (22%)
Jungle	13 (12 %)	12 (15%)
Stage		
I	0	3 (4%)
IB	0	1 (1%)
II	9 (8%)	17 (21%)
IIB	1 (1%)	3 (4%)
III	65 (61%)	39 (48%)
IV	28 (26%)	10 (12%)

This table summarises baseline socio-demographic and clinical data for patients with aggressive mature B-cell lymphomas treated at INEN from 2009 to 2021, including age, sex, disease stage and comorbidities.

BL, Burkitt lymphoma; DLBCL, diffuse large B-cell lymphoma; *N* = 187.

In our review of 34 cases of high-grade B-cell lymphoma, 23 were confirmed as BL. The 11 excluded cases comprised eight MYC-FISH-negative cases, one case with 11q aberration, one case with unconfirmed MYC status and one MYC-FISH-positive case without an available clinical record ([Figure 1](#)). The median age of the patients included in the review was 5 years, and the mean was 6.7 ± 3.6 SD (range between 1 and 15 years); most of them were males (65%), and 48% were from the Peruvian coastal region ([Figure 2](#)). The positivity for infection by EBV was 61%, predominantly among males and in the 4–6 years group ([Table 2](#)). Similarly, most patients with EBV-negative status were male and aged between 7 and 10 years (*n* = 4). The mean age of infected patients was significantly younger than that of non-infected patients (5.2 years $\pm$ 2.8 SD versus 9 years $\pm$ 3.6 SD, respectively, *p* = 0.01); most patients (48%) came from the Peruvian coastal region, and 65% were male. The abdominal visceral region primary compromise accounted for 78% of instances, followed by the head and neck with 17% of cases, and the thorax with a single case accounting for the remaining 4% of patients. At diagnosis, all our cases were in advanced stages (III–IV) ([Table 3](#)).

Study flow diagram

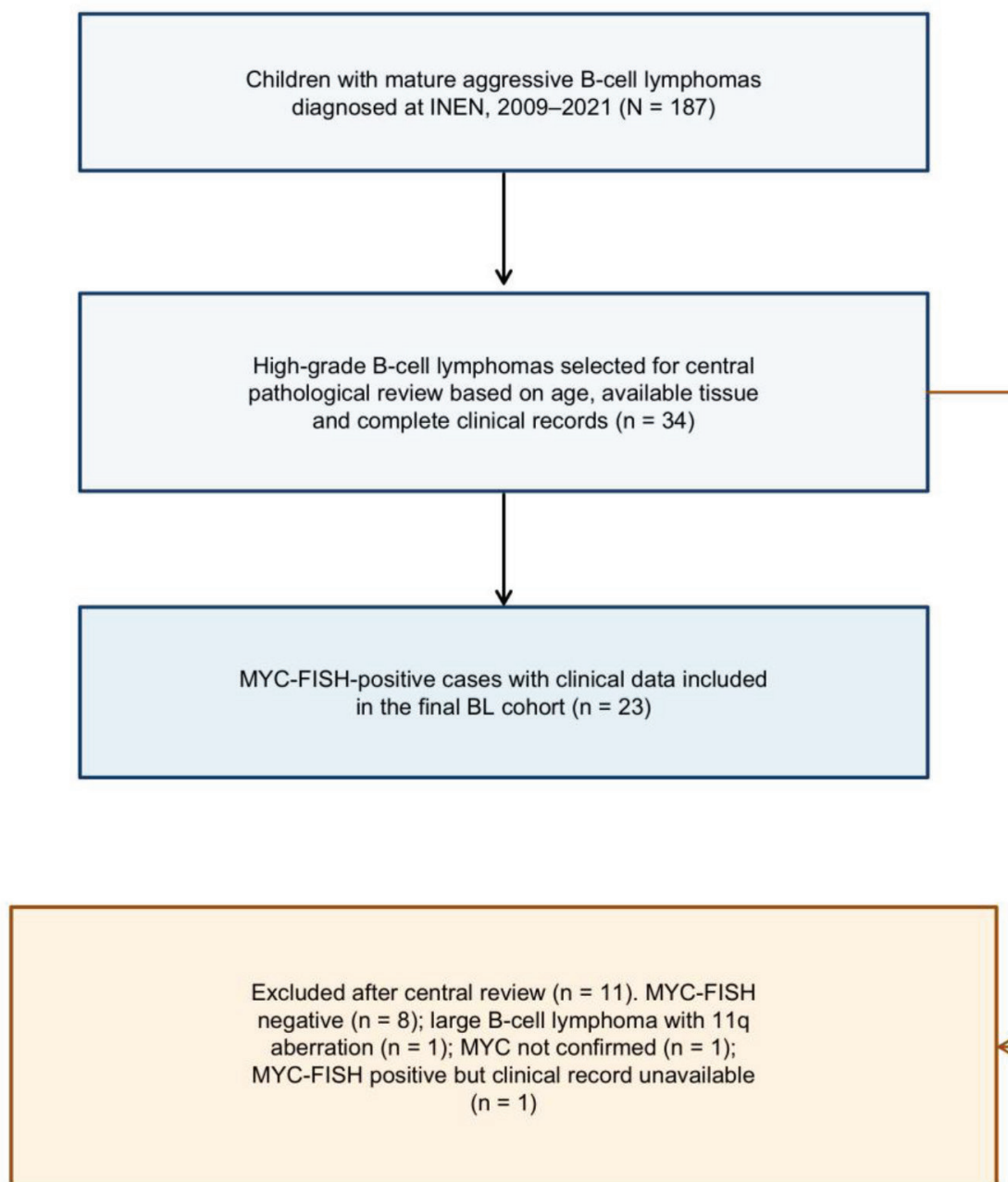


Figure 1. Study flow diagram showing the derivation of the final molecularly confirmed Burkitt lymphoma cohort.

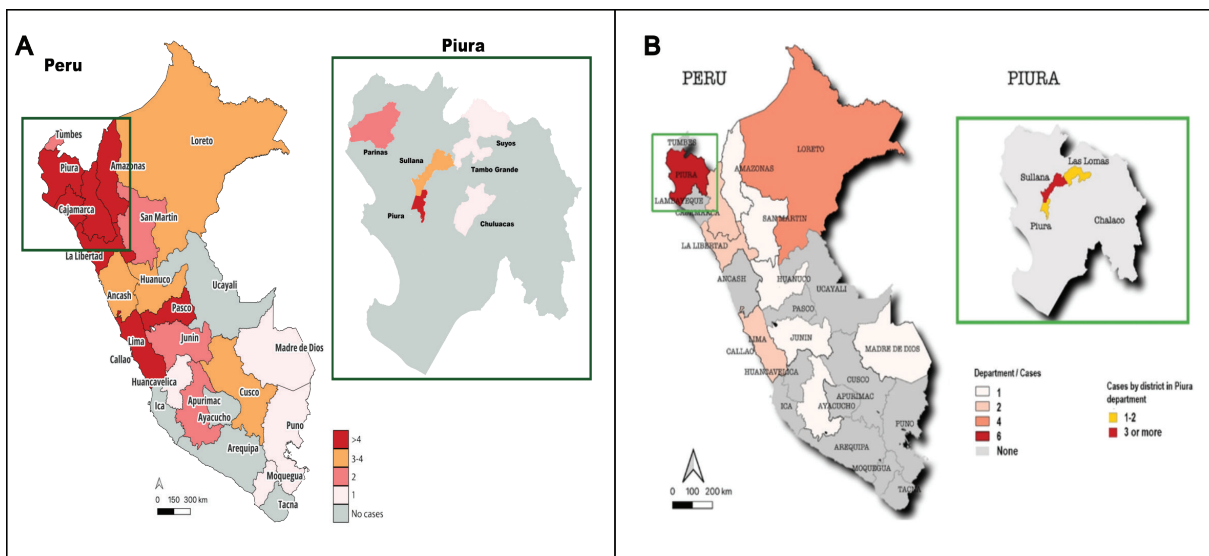


Figure 2. Geographic distribution of Burkitt lymphoma cases. **A.** The geographic distribution of Burkitt lymphoma cases. The magnified section in the upper right highlights an unusual increase in cases reported across several districts within the department of Piura, indicating a potential regional concentration that warrants further investigation. **B.** The geographic distribution of 23 Burkitt lymphoma cases with confirmed MYC translocation, based on place of birth. An unusual concentration of cases is observed in the district of Sullana, Piura.

Table 2. General socio-demographic and clinical characteristics of 23 cases with molecular diagnosis of MYC translocation and EBV status.

Features	N = 23
Age (years)	
Mean ± SD	6.7 ± 3.6
Median	5
Q1–Q3	[4–9]
Interquartile range	5
Age (n, %)	
>5 years	9 (39%)
≤ 5 years	14 (61%)
Sex (%)	
Female	8 (35%)
Male	15 (65%)
EBV status (n, %)	
Positive	14 (61%)
Negative	9 (39%)
Sub-region	
Coast	11 (48%)

Table 2. General socio-demographic and clinical characteristics of 23 cases with molecular diagnosis of MYC translocation and EBV status.

Features	N = 23
Jungle	7 (30%)
Highlands	5 (22 %)
Stage	
I	0
II	0
III	19 (83%)
IV	4 (17%)
MYC 8q24	
Positive	23 (100%)
Negative	0
Therapy	
CHOP	15 (65%)
NA	8 (35%)
Response to therapy (n, %)	
Complete	9 (39%)
Partial	6 (26%)
NA	8 (35%)
Tumour location (n, %)	
Abdominal	18 (78%)
Head and neck	4 (17%)
Thoracic	1 (4%)
Bone marrow compromise	
Yes	3 (13%)
No	20 (87%)
B symptoms (n, %)	
Yes	9 (39%)
No	14 (61%)
Survival status (%)	
Alive	13 (57%)
Deceased	10 (43%)

This table summarises the general socio-demographic and clinical characteristics of 23 reviewed cases, each confirmed with a molecular diagnosis of MYC translocation and evaluated for EBV status.

Cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) was documented as first-line therapy in 15 patients (65%), and none received rituximab. Treatment information was not recorded for eight patients (35%); this does not necessarily indicate that they were untreated. Among the 15 patients with documented CHOP, 9 (60%) had a complete response and 6 (40%) had a partial response ([Table 4](#)). The total clinical-socio-demographic characteristics are presented in [Table 3](#).

Table 3. Clinical and socio-demographic characteristics of patients with Epstein–Barr virus infection.

Features	Total	EBV-	EBV+	p value
Cohort	23	9 (39%)	14 (61%)	
Age (years)				0.01
Mean ± SD	6.7 ± 3.6	9 ± 3.6	5.2 ± 2.8	
Median	5	8	4.5	
Q1–Q3	[4–9]	[8–12]	[4–5]	
Interquartile range	5	4	1	
Sex				1
Female	8 (35 %)	3 (33%)	5 (36%)	
Male	15 (65%)	6 (67%)	9 (64%)	
Age (years)				0.003
0–3	3 (13%)	1 (11%)	2 (14%)	
4–6	11 (48%)	1 (11%)	10 (72%)	
7–10	4 (17%)	4 (45%)	0	
>10	5 (22%)	3 (33%)	2 (14%)	
Sub-region				0.1
Coast	11 (48%)	7 (78%)	4 (29%)	
Highland	5 (22%)	1 (11%)	4 (29%)	
Jungle	7 (30%)	1 (11%)	6 (42%)	
Clinical stage				1
I	0	0	0	
II	0	0	0	
III	19 (83%)	8 (89%)	11 (79%)	
IV	4 (17%)	1 (11%)	3 (21%)	
Tumour location				0.7563
Head, neck and thorax	5 (22%)	2 (22%)	3 (21%)	
Abdominal	18 (78%)	7 (78%)	11 (79%)	
Bone marrow involvement				1
Negative	20 (87%)	8 (89%)	12 (86%)	
Positive	3 (13%)	1 (11%)	2 (14%)	
Response to therapy				0.3
Complete	9 (60 %)	6 (75%)	3 (43%)	
Partial	6 (40%)	2 (25%)	4 (57%)	
B-symptoms				0.4
No	14 (61%)	4 (44%)	10 (71%)	
Yes	9 (39%)	5 (56%)	4 (29%)	

Student's t test, Fisher's exact test; EBER CICH test for EBV. Bold values indicate statistical significance ($p < 0.05$)

Table 4. Clinical and socio-demographic features versus response to therapy (CHOP).

Features	Response to therapy (CHOP)			p value
	Total	Complete	Partial	
Cohort	15 (100%)	9 (60%)	6 (40%)	
Age (years)				0.5
Mean $\pm$ SD	7.6 $\pm$ 3.7	8.1 $\pm$ 4	6.8 $\pm$ 3.3	
Median	8	8	6.5	
Q1–Q3	[5–11]	[5–12]	[4–10]	
Interquartile range	6	7	6	
Sex				0.2
Female	4 (27%)	1 (11%)	3 (50%)	
Male	11 (73%)	8 (89%)	3 (50%)	
EBV				0.3
Negative	8 (53%)	6 (67%)	2 (33%)	
Positive	7 (47%)	3 (33%)	4 (67%)	
Clinical stage				1
I	0	0	0	
II	0	0	0	
III	13 (87%)	8 (89%)	5 (83%)	
IV	2 (13%)	1 (11%)	1 (17%)	
Tumour location				0.2
Head, neck and thorax	3 (20%)	3 (33%)	0	
Abdominal	12 (80%)	6 (67%)	6 (100%)	
Bone marrow involvement				1
Negative	14 (93%)	8 (89%)	6 (100%)	
Positive	1 (7%)	1 (11%)	0	
B-symptoms				0.3
No	9 (60%)	4 (44%)	5 (83%)	
Yes	6 (40%)	5 (56%)	1 (17%)	

Statistical tests: Student's *t*-test and Fisher's exact test.

Pathological features

Pathological analysis of the 23 BL cases revealed characteristic immunohistochemical profiles, demonstrating positive staining for CD20, BCL6 and CD10, while TDT, BCL2 and MUM1 were consistently negative. Ki67 was available for 20 cases, with a median value of 98.5% (range, 70%–100%); 19 of 20 cases had Ki67 values of at least 95%. Fluorescence in situ hybridisation (FISH) analysis confirmed the presence of MYC translocation (8q24-positive) in all BL cases (Figure 3). Among these, EBER was positive in 14 cases and negative in nine.

In the MYC-negative group of high-grade B-cell lymphomas, FISH analysis detected an 11q aberration in one case. The study also identified 10 cases of DLBCL NOS.

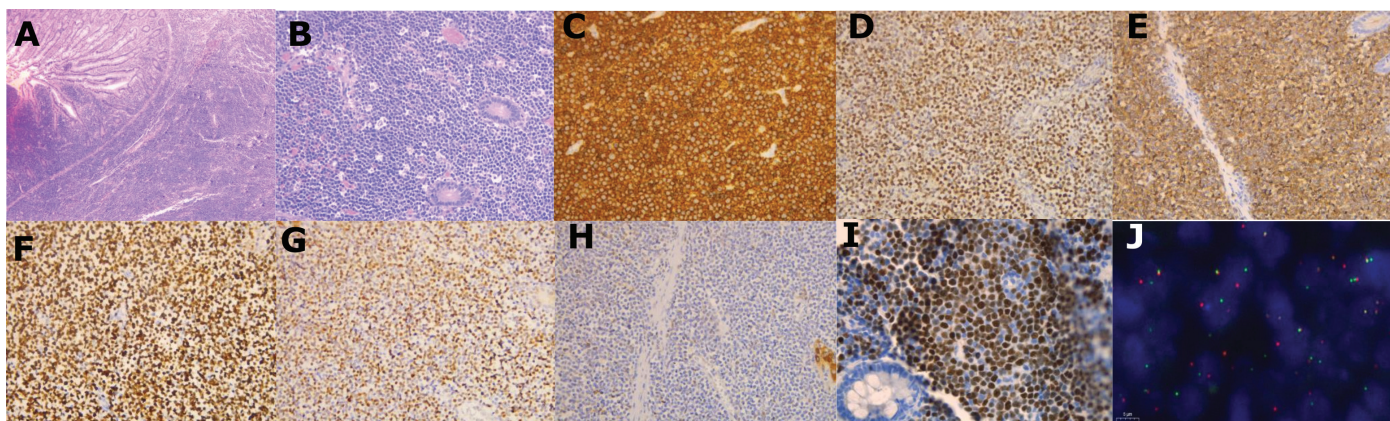


Figure 3. Ileocecal mucosal involvement in Burkitt lymphoma. (A) Hematoxylin and eosin (H&E) staining, panoramic view (5x), showing infiltration of the ileocecal mucosa by Burkitt lymphoma. (B) Higher magnification (10x) demonstrating the classic 'starry sky' pattern characteristic of Burkitt lymphoma. (C) CD20 immunostaining at 20x, highlighting predominantly membranous positivity. (D) BCL6 immunostaining with nuclear expression at 20x magnification. (E) CD10 immunostaining showing positive cytoplasmic expression at 20x. (F) Ki67 immunostaining indicating a proliferative index approaching 100% with nuclear expression at 20x magnification. (G) MYC immunostaining positive for nuclear expression at 20x. (H) MUM1 immunostaining negative at 20x magnification. (I) Chromogenic in situ hybridization (CISH) for Epstein–Barr virus (EBV) with positive nuclear brown staining (40x). (J) Fluorescence in situ hybridization (FISH) test MYC (100x) for 8q24 translocation detection.

Survival-related factors

Of the 23 patients included in this study, 10 (43%) died. With follow-up administratively truncated at 36 months, the median follow-up estimated by reverse Kaplan–Meier was 36 months (observed range, 0.3–36 months). Kaplan–Meier overall survival was 67.2% (95% CI, 43.1–82.8) at 6 months and 52.3% (95% CI, 29.5–71.0) at 12 months (Figure 4). Survival differed according to age (log-rank $p = 0.009$) and EBV status (log-rank $p = 0.012$). In univariable Cox analysis, EBV-positive status was associated with inferior survival (HR, 9.20; 95% CI, 1.15–73.58; $p = 0.036$), as was age ≤ 5 years (HR, 9.88; 95% CI, 1.22–79.93; $p = 0.032$). Documentation of CHOP was also associated with survival (HR, 0.19; 95% CI, 0.05–0.68; $p = 0.011$), but this comparison should not be interpreted as a treatment effect because missing treatment records do not indicate absence of treatment (Supplementary Figure 1). In the exploratory model including EBV status, age and treatment documentation, EBV was no longer statistically significant (adjusted HR, 3.69; 95% CI, 0.35–38.98; $p = 0.278$). The total survival estimates are presented in Table 5.

Bivariate analysis revealed that, in this series of patients, age ($p = 0.01$) was a factor associated with EBV infection. When stratified by age group, the presence of the virus was more frequent in the 4–6-year-old group (Table 3). In particular, there was a significant association with patients under 5 years of age. Most of the patients with the infection came from the jungle region of Peru. The complete results are presented in Table 3.

Discussion

In our review of 34 cases of high-grade B-cell lymphoma, 23 MYC-FISH-positive cases with clinical data were included as BL, one additional MYC-FISH-positive case lacked an available clinical record, one case was identified as large B-cell lymphoma with 11q aberration and nine cases were not molecularly confirmed as BL. This highlights the importance of molecular testing to confirm specific alterations within the diverse group of aggressive high-grade lymphomas.

Of the BL cases, 61% (14 of 23) were EBV-positive, consistent with rates reported across Latin America (29%–87%) [22]. With follow-up administratively truncated at 36 months, the observed mortality rate of 43% in our cohort is substantially higher than that reported in high-income countries, where paediatric treatment success rates are typically over 90%.

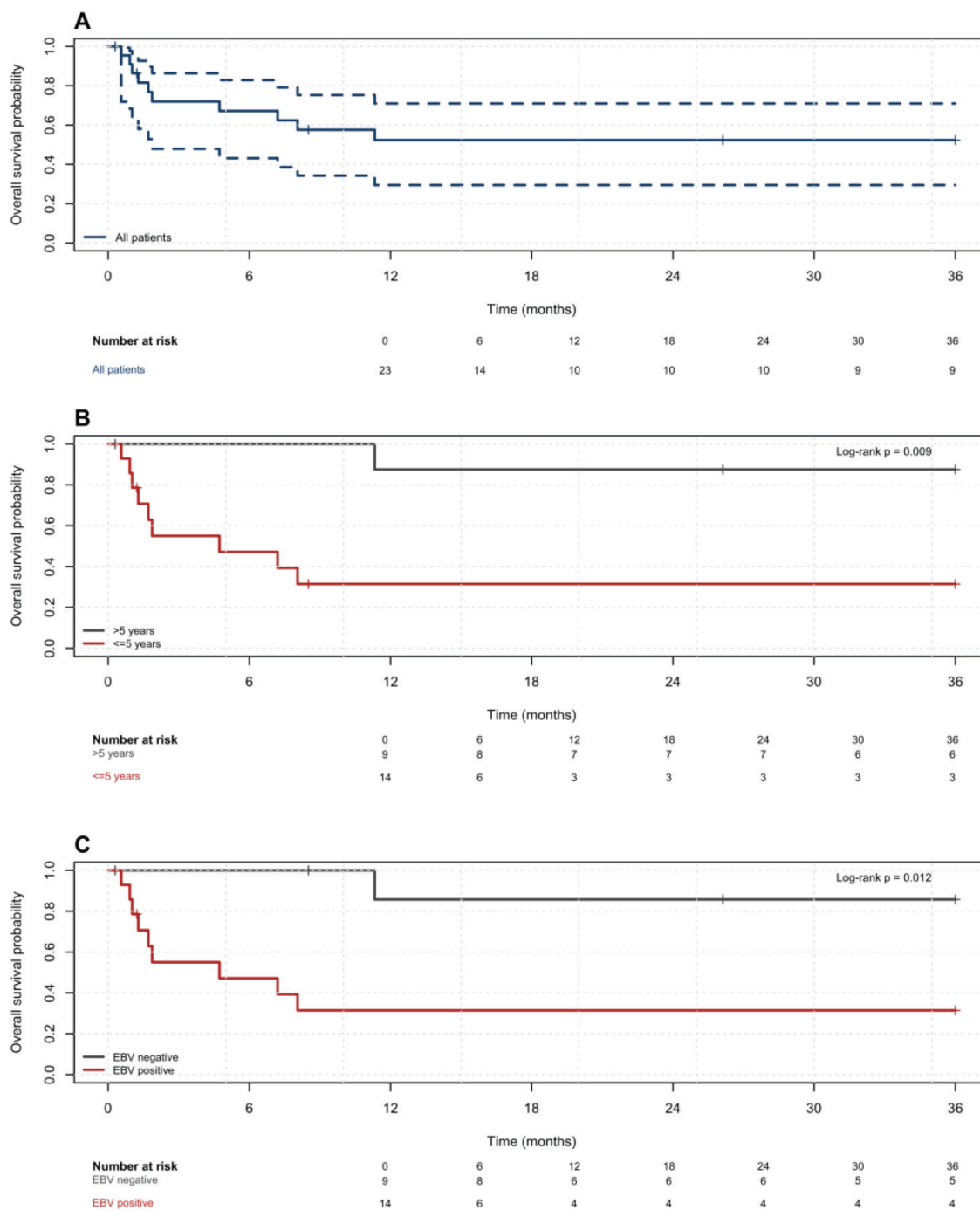


Figure 4. Kaplan–Meier curves for overall survival (A), age groups (B) and EBV status (C), with numbers at risk. Follow-up was administratively truncated at 36 months.

Table 5. Kaplan–Meier overall survival estimates according to clinical factors.

	Log-rank test <i>p</i>	KM 6 months (%)	KM 12 months (%)
Patients (N = 23)		67.2	52.3
Age	0.009		
>5 years old		100.0	87.5
≤ 5 years old		47.1	31.4
Sex	0.214		
Female		57.1	28.6
Male		72.7	65.5
EBV	0.012		
Positive		47.1	31.4
Negative		100.0	85.7
Tumour location	0.344		
Abdominal		63.3	49.9
Head, neck and thorax		100.0	75.0

Kaplan–Meier estimates were calculated after administrative truncation at 36 months. One patient with missing tumour location was excluded from the location comparison.

Survival outcomes were poorer among younger patients (log-rank $p = 0.009$) and in those with EBV-positive status (log-rank $p = 0.012$), with bivariate analysis further indicating a correlation between younger age and EBV positivity ($p = 0.01$). However, the EBV association was attenuated and was no longer statistically significant after exploratory adjustment for age and treatment documentation. In contrast to the findings of Richter *et al* [23], who associated EBV positivity in sporadic BL with older age [23], our study did not reveal significant associations between clinical or socio-demographic factors and treatment response. The small sample size, wide confidence intervals and incomplete treatment information limit the generalisability of these findings and do not allow EBV to be considered an independent prognostic factor.

Recent studies by Thomas *et al* [24] suggest that EBV status may be a stronger molecular predictor of BL prognosis than age alone [24]. EBV-positive cases have been linked to unique genetic features, including somatic hypermutation-mediated breakpoints and mutations in genes such as FOXO1 and BCR, which could contribute to distinct clinical behaviours warranting further investigation [24–26].

Phylogenetic analyses reveal geographical variations in EBV strains, with distinct sequence patterns observed in African, Asian and European lineages [27]. In Peru, where over 80% of the ancestry of the population has Indigenous traces, further research is needed to explore the co-evolution of EBV with host factors, particularly in high-prevalence areas like the jungle. In our cohort, an apparent concentration of sporadic BL cases was observed in the Piura region, specifically in Sullana. Environmental factors such as pesticide exposure, immunosuppression and malaria were not measured in this study, and their possible relationship with this concentration may warrant future investigation [28,29].

While the role of EBV infection in oncogenesis is established, the interaction between viral and host factors in BL development remains complex and not fully understood [30]. Clarifying the prevalence and impact of EBV in paediatric BL, particularly within Latin American populations, is essential for the development of targeted therapies that address viral oncogenic mechanisms and modulate immune responses to EBV-infected cells. This research represents a promising direction for improving outcomes in paediatric BL patients in EBV-endemic regions.

This study has several limitations. It was retrospective and conducted at a single referral centre, and the final cohort was small, with 23 patients and 10 deaths. Selection for central review depended on the availability of tissue and clinical records, which may have introduced selection bias. The low number of events, the association between EBV status and age, and incomplete treatment information limited the adjusted analysis. Treatment was not standardised, rituximab was not administered and information on treatment abandonment, treatment-related mortality and salvage therapy was incomplete. The technical details of EBER testing, the MYC-IHC threshold and the classification framework were not available in the records reviewed. Therefore, the survival findings should be considered exploratory.

Conclusion

In this Peruvian paediatric cohort of sporadic BL with molecular confirmation ($N = 23$), EBV-positive status was present in 61% of cases and was associated with younger age ($p = 0.01$) and inferior overall survival in univariate analysis (log-rank $p = 0.012$). Given the correlation between age and EBV status, incomplete treatment information and the limited sample size, the independent prognostic contribution of EBV could not be established, and these findings should be interpreted as exploratory. Our results support the need to strengthen access to standardised molecular diagnostics (EBER and MYC testing) and to conduct larger multicentre studies in Latin America to clarify the contribution of EBV and related factors to outcome.

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Conflicts of interest

The authors declare no conflicts of interest.

Author contributions

Conceptualisation: SCZ, JM, RDC, SB; Methodology: JH, RLP, JCG; Validation: JPC, CB, TV; Formal Analysis CL, JH, RLP, JBM; Data Curation JH, JCM; Writing – Original Draft Preparation: SCZ, JM, RDC, RLP; Writing – Review & Editing: CB, TV, JCM, SB; Visualisation: JH, JBM, JCM; Supervision: SCZ, SB; Project Administration: SCZ, SB; Funding Acquisition: SCZ, SB.

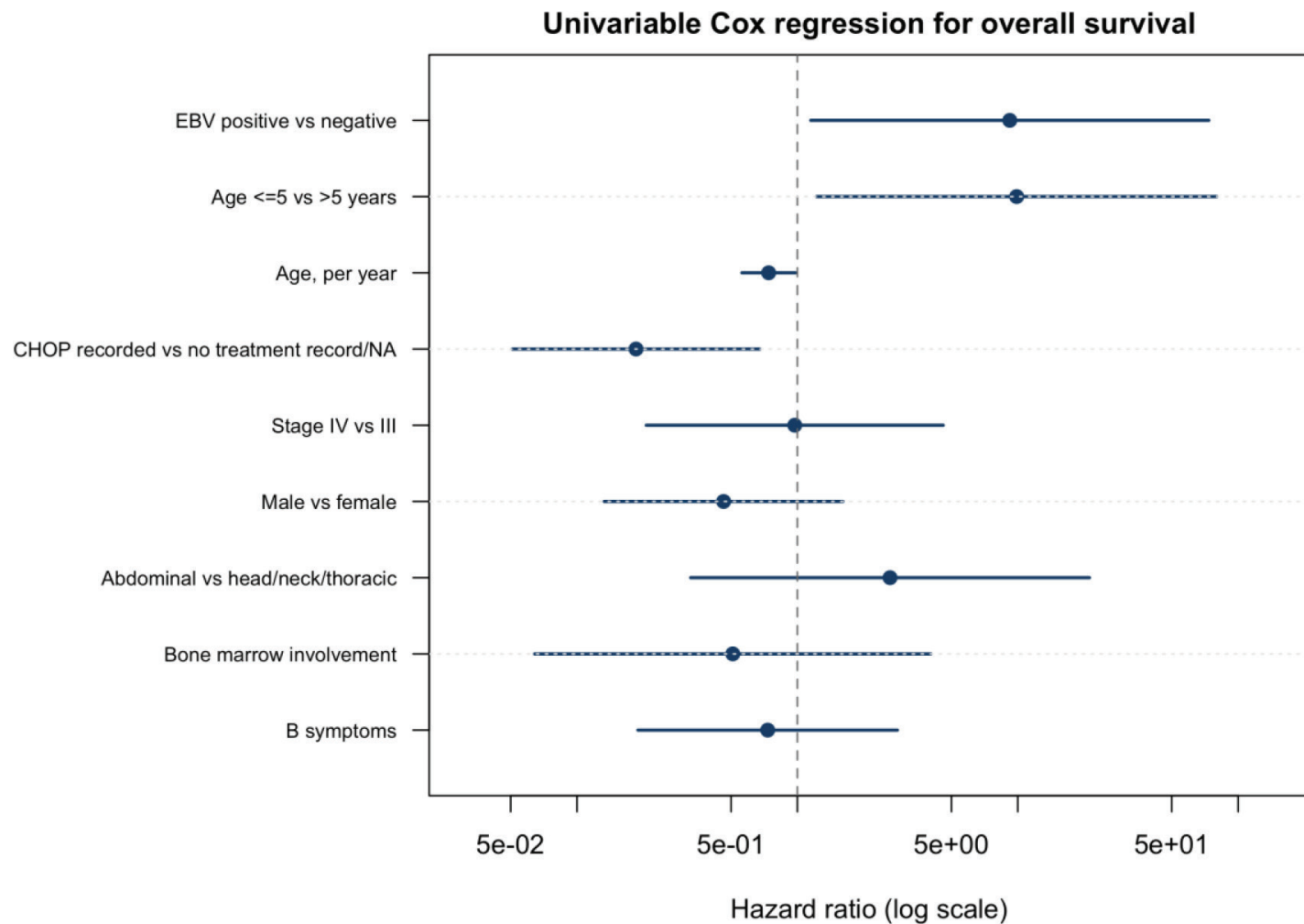
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Supplementary figure



Supplementary Figure 1. Univariable Cox regression for overall survival. Hazard ratios are presented with 95% confidence intervals; estimates are exploratory because of the small cohort and low number of events. Epstein–Barr virus in paediatric sporadic Burkitt lymphoma: real-world experience from a Peruvian national referral centre