RESEARCH ARTICLE

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Mortality by Childhood Acute Lymphoblastic Leukemia: A Regional Analysis in Peru and Ecuador

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Abstract

Background: Acute lymphoblastic leukemia (ALL) is the most common malignant neoplasm in children representing the leading cause of death in pediatric oncology. However, studies in the Latin American and Caribbean region are scarce. The objective of this study was to determine the childhood ALL-mortality rates of Ecuador and Peru from 2005 to 2020. Methods: We retrieved ALL deaths from the mortality databases of Ecuador and Peru. Age-standardized mortality rates per 100,000 person-years were estimated. Mortality trends were evaluated by country, and sex, between 2005 and 2020 with Joinpoint regression analyses. Results: Between 2016 and 2020, Ecuador and Peru reported a mortality rate of 1.7 for boys and 1.2 for girls 0-14 years of age. The Coastal region had the highest mortality rate in this period for both age groups, and the Rainforest had the lowest rates. Only Peru showed a significant increase in both sexes, with large increases for boys in the Highlands (+17.6% annually) and girls in Lima (+13.3% annually). Conclusion: Our findings suggest considerable increases in ALL mortality in Peru. It is important to implement public health strategies for early diagnosis and timely treatment of children with ALL in Peru.

Keywords: Leukemia- children Peru- Ecuador

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Introduction

Childhood leukemia emerges as the primary neoplasm among children aged 0-14 years, occupying the foremost position in the incidence (32.5% of all cancers) and mortality (31.3% of all cancers) in this population. Moreover, the number of cases and deaths continues to significantly increase in several countries worldwide, mainly in middle- and low-income countries [1, 2]. GLOBOCAN 2020 reported about 67,000 new cases (rate: 3.4 per 100,000) and 25,000 deaths (rate: 1.3 per 100,000) by childhood leukemia affecting more boys than girls [1].

Latin America and the Caribbean has the highest mortality rates by childhood leukemia [1, 3-6]. Within of this region, Venezuela, Ecuador, Mexico and Peru present the highest mortality rates (above 2 deaths per 100,000 for boys, and above 1.4 deaths per 100,000 for girls) [3]. Whereas other countries like Chile, Argentina, Paraguay, Brazil, and Uruguay reported the lowest mortality rates (below 1.7 deaths per 100,000 for boys, and below 1.4

deaths per 100,000 for girls) [3].

Acute lymphoblastic leukemia (ALL) is the most common form of childhood leukemia, representing 25% of pediatric malignancies and serving as the leading cause of disease-related deaths among children [4, 7]. Despite its significance, studies within the Latin America and Caribbean are notably scarce, with the few available reports primarily addressing leukemia in a global context [8, 3]. Unfortunately, specific reports dedicated to ALL within our region are still scarce.

The scenario of ALL mortality trends in Peru and Ecuador is not known. For this reason, the objective of this study was to analyze ALL mortality rates in these countries by sex, age group and natural regions.

Materials and Methods

Design and study setting

We conducted an ecological study, based on a secondary data analysis using the mortality database of the

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Peruvian Ministry of Health (https://www.minsa.gob.pe/portada/transparencia/solicitud/) and the National Institute of Census and Statistics (INEC) databases (https://www.ecuadorencifras.gob.ec/defunciones-generales/) of Ecuador. We used code C91 from the International Code of Diseases 10th edition (ICD-10) to identify data for ALL deaths from 2005 to 2020. Data on the number of deaths by ALL was classified into 3 age groups (0-4, 5-9, 10-14 years), according to the place of residence.

Peru and Ecuador are characterized by diverse geographical landscapes, each comprising several provinces distributed across distinct natural regions. In Peru, the country is divided into 25 provinces situated within three primary natural zones delineated by the imposing Andes mountains: the coast, highlands, and rainforest. Whereas Ecuador boasts 24 provinces spanning four unique natural regions: the coast, highlands, rainforest, and the island territory of the Galápagos Islands.

The coast region of both countries stands out as the most densely populated area. In Peru, it is home to 56.3% of the total population, occupying 11.7% of the national territory, with Lima housing 30% of Peru's total inhabitants. Meanwhile, in Ecuador, the coastal region accommodates 50.08% of the populace and covers 26.28% of the country's landmass.

Moving inland, the highlands present a mix of rural and urban settlements nestled amidst the Andean peaks. In Peru, the highlands cover 27.9% of the national territory, accommodating 29.7% of the population. Similarly, in Ecuador, the highlands encompass 24.97% of the territory and are inhabited by 44.63% of the total population.

Venturing further into the depths of the rainforest, also known as the Peruvian Amazon, vast expanses of lush greenery dominate the landscape. This region covers 60.3% of Peru's territory, hosting 14.0% of the population. In Ecuador, the rainforest territory spans 45.62% of the nation's land area, with 5.12% of the population calling it home.

Moreover, in Ecuador, the Galápagos Islands form a distinct island region, renowned for its unique biodiversity. Though sparsely populated, with only 0.17% of the total population, these islands hold ecological significance. They comprise a mere 3.13% of Ecuador's surface area, however for this analysis, the island region was excluded due to insufficient case data. Yet similar, differences in the healthcare systems contrast Peru and Ecuador. The Peruvian healthcare system is more fragmented than the Ecuadorian one, with the former encompassing the public, social security, and private sectors, each with multiple forms of financing. Conversely, Ecuador's system emphasizes greater coverage in the public sector [9]. According to the World Bank, universal health service coverage has been increasing for both Peru and Ecuador, as indicated by the Coverage Index for Essential Health Services, rising from an index of 48 and 51 in the year 2000, to 71 and 77 by 2021, respectively [10].

Peruvian total population estimates were obtained from census data conducted by the National Institute of Statistics and Informatics (INEI), which is the central and governing body of statistics reporting in Peru. The demographic data for Ecuador was retrieved from the population projections issued by the National Institute of Statistics and Census (INEC), as publicly accessible through the official website of the National Planning Secretariat.

It is well known that mortality statistics are an important source of information for population health monitoring, priority setting and planning. However, the quality of data is poor. However, Peru has made efforts in the last decade to implement new programs to improve these data. One of these programs is National Death Information System (Sistema Informático Nacional de Defunciones, SINADEF), which was implemented to improve death notification and certification processes [11]. This system also improved data quality by eliminating the effect of illegible handwriting; reducing the use of illdefined conditions; and reducing the use of abbreviations. Whereas Ecuador has established a National Tumor Registry by the Society for the Fight Against Cancer (Sociedad de Lucha Contra el Cáncer, SOLCA), which gathers and integrates data on incidence, mortality, and trends from SOLCA's registry nationwide.

Data analysis

Age-standardized mortality rate (ASMR) were estimated using the direct method and SEGI world standard population per 100,000 person-years [12]. ALL mortality trends were analyzed for children aged 0 to 14 years between 2005 and 2020. Moreover, we performed further analyses to determine the average mortality rates for the last 5 years (2016-2020).

Joinpoint regression analysis was performed to examine the mortality trends using the Joinpoint regression program version 4.7.0 [13]. We calculated the estimated annual percentage change (APC) and considered an APC to be statistically significant with p-values <0.05. For this analysis we selected the permutation test method with an allowed number of permutations of 4499 and an overall significance level of 0.05. The APCs followed a parametric method. The minimum number of joinpoints was zero and the maximum was two [14]. The significance levels used are based on the Monte Carlo permutation method using the logarithm of the ratio [13, 15].

Ethical considerations

This manuscript is based on administrative databases and does not use any identifiable personal information.

Results

During the 5-year period from 2016 to 2020, Peru reported a mortality rate of 1.7 for boys, and 1.2 for girls. According to regions, the Coastal region reported the highest mortality rate with 1.9 for boys, and 1.5 for girls. Lima (the capital) reported a mortality rate of 2.6 for boys and 1.9 for girls. On the other hand, Ecuador reported a mortality rate of 1.7 for boys and 1.2 for girls. Similar to Peru, the coast also had the highest mortality rate by region (2.0 for boys, and 1.2 for girls), whereas Pichincha (Quito - the capital) had a mortality rate of 1.6 for boys, and 0.8 for girls (Figure 1).

Table 1. Annual Percentage Change	in Mortality by Acute	Lymphoblastic Leukemia i	n Children Aged 0-14 Years in
Ecuador and Peru		-	_

Geographical		Male			Fe	male	Ratio 2005 (M/F)	Ratio 2020 (M/F)
area	2005	2020	APC (95% CI)	2005	2020	APC (95% CI)		
Peru	0.46	2.09	11.1*(9.4,12.9)	0.28	1.45	11.6*(9.8,13.5)	1.6	1.4
Coastal	0.7	2.18	8.5*(6.6,10.4)	0.34	1.8	11.8*(8.8,14.8)	2.1	1.2
Highlands	0.14	2.42	17.6*(12.8,22.6)	0.28	1.32	9.5*(4.4,14.9)	0.5	1.8
Rainforest	0.19	0.92	11.7*(6.4,17.4)	0	0.36	NA	NA	2.6
Lima	0.73	2.58	9.0*(5.8,12.2)	0.32	1.91	13.3*(9.5,17.2)	2.3	1.4
Ecuador	1.42	1.59	1.8 (-0.3, 3.9)	0.9	0.72	1.8 (-0.9, 4.7)	1.6	2.2
Coastal	1.43	2.05	2.3*(0.5,4.1)	0.91	0.68	3.3(-0.5, 7.2)	1.6	3
Highlands	1.62	1.05	0.8 (-3.1, 4.9)	1.02	0.61	0.3 (-4.1, 4.8)	1.6	1.7
Rainforest	0	1.61	NA	0	1.66	NA	0	1
Pichincha	2.19	1.11	-0.8 (-4.5, 3.6)	1.7	0.45	-5.1 (-10.5, 0.6)	1.3	2.5

APC, Annual percentage change; * p value <0.05. NA, Not applicable; CI, confidence interval

Between the study period (2005-2020), we report higher mortality rates in males compared to females. Peru and its regions (coastal and highlands) reported the highest mortality rates in the last years. Consequently, Lima had the highest mortality rate in 2018 for boys (3.2 per 100,000), and in 2019 for girls (2.6 per 100,000) (Figure 2). On the other hand, Ecuador had the highest mortality rate in 2015 for boys (2 per 100,000) and in 2012 for girls (1.7 per 100,000), whereas the mortality estimates in the coastal and highlands regions increased in the last years. Notably, Pichincha reported heterogeneity with respect to its mortality rates, with the highest rate for boys in 2017 (2.2 per 100,000), and for girls in 2008 (2.7 per 100,000) (Figure 3).

For children aged 0-14 years, Peru reported a significant increase in mortality in both sexes from 2005 to 2020, rising from 0.46 to 2.09 for boys (+11.1% annually) and from 0.28 to 1.45 for girls (+11.6% annually). Regional analysis demonstrated the Highlands showed the greatest increase compared to the Coast and Rainforest. The mortality rates in the Coastal region significantly increased from 0.70 to 2.18 for boys (+ 8.5% annually) and from 0.34 to 1.80 for girls (+11.8% % annually). Moreover, mortality rates in the Highlands increased from 0.14 to 2.42 for boys (+17.6% annually), and from 0.28 to 1.32 for girls (+11.8% annually). In the Rainforest region, the mortality rates in boys increased from 0.18 in 2007 to 0.92 in 2020 (+11.7% annually), with no deaths in 2006.

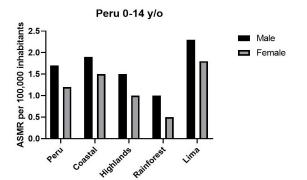
On the other hand, there were not registered deaths among girls for several years of the study period, and therefore, it was impossible to determine the changes in mortality. Lima reported a significant increase from 0.73 in 2005 to 2.58 in 2020 (+9% annually) for boys and from 0.32 in 2005 to 1.91 in 2020 (+13.3% annually) for girls (Table 1).

Ecuador reported an increase in the mortality rates by ALL from 1.42 in 2005 to 1.59 in 2020 for boys, and from 1.42 in 2005 to 1.59 in 2020 for girls, however, annual changes were not significant. The coastal region of Ecuador reported a significant increase from 1.43 in 2005 to 2.30 in 2020 (+2.3% annually) for boys (Table 1).

Table 2 reported the mortality rates by specific age, where it was observed that in Peru and its regions there was an increase in the mortality rate in the different age groups analyzed. While in Ecuador and its regions there were differences in the evolution of the mortality rate according to age group.

Discussion

The present study marks a pioneering endeavor in assessing mortality rates spanning a 15-year period for ALL in two Latin American countries with the highest mortality rates. Our analysis revealed a noteworthy increase in mortality rates from 2005 to 2020 in both of the countries of our study. Particularly in Peru, we observed a significant rise in mortality rates across various



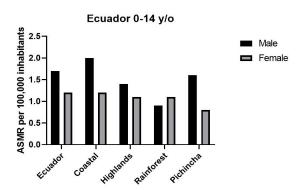


Figure 1. Mortality Rates for Acute Lymphoblastic Leukemia from Peru and Ecuador, 2016-2020.

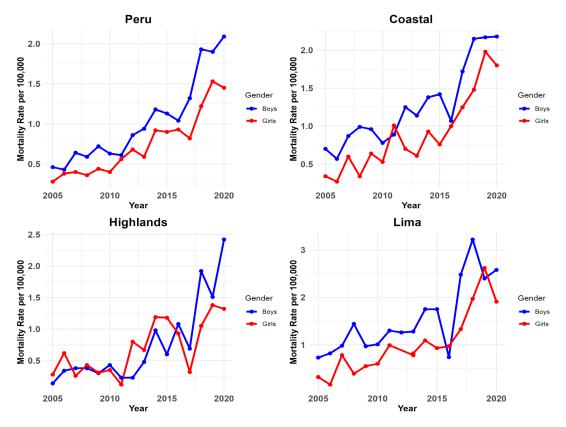


Figure 2. Mortality Rates for Acute Lymphoblastic Leukemia from Peru and Its Geographical Areas, 2005-2020.

demographic parameters, including age group, sex, and geographical region. Conversely, in Ecuador, a statistically significant increment was detected solely among boys residing in the Coastal region.

Peru and Ecuador, along with their respective geographic regions reported mortality rates of approximately 2 deaths per 100,000. However, in the last years, Peru increased its mortality rates. Conversely,

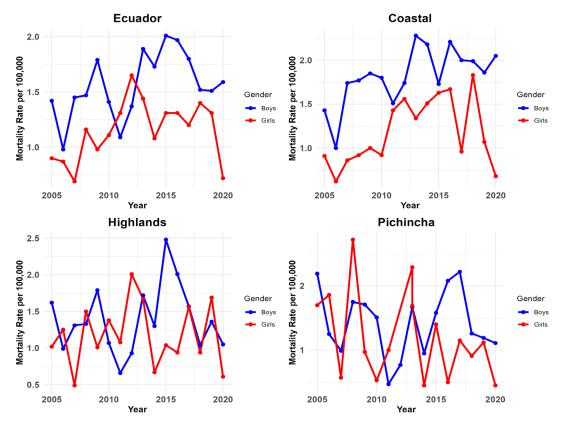


Figure 3. Mortality Rates for Acute Lymphoblastic Leukemia from Ecuador and Its Geographical Areas, 2005-2020.

Table 2. Age- Standardized Mortality Rates per 100.000 Person-Years from ALL in Peru and Regions According to Age Groups

C			lren aged 0-4	years		E	1-		
Geographical Areas	20	Ma 005)20	Female 2005 2020				
	Deaths	ASMR	Deaths	ASMR	Deaths	ASMR	Deaths	ASMR	
Country	Deaths	7 ISMIT	Deaths	TISIVIIC	Deaths	TISIVIIC	Deaths	TISIVIIC	
Peru	6	0.4	22	1.54	2	0.14	18	1.32	
Ecuador	9	1.13	4	0.48	8	1.03	5	0.62	
Peru Regions									
Coast	6	0.71	14	1.63	1	0.14	14	1.98	
Highlands	0	0	8	2.04	1	0.18	4	0.83	
Rainforest	0	0	0	0	0	0	0	0	
Ecuador Regions									
Coast	3	0.74	3	0.72	4	1.03	4	1.01	
Highlands	6	1.75	1	0.28	4	1.17	1	0.28	
Rainforest	0	0	0	0	0	0	0	0	
		Child	ren aged 5-9	years					
Geographical Areas		Male			Female				
	20	005	20)20	2005		20	20	
	Deaths	ASMR	Deaths	ASMR	Deaths	ASMR	Deaths	ASMR	
Country									
Peru	10	0,67	29	2,22	4	0,28	23	1,79	
Ecuador	13	1.7	24	2.85	8	1.07	4	0.49	
Peru Regions									
Coast	7	0,81	20	2,64	2	0,28	15	2,30	
Highlands	2	0,42	7	1,81	2	0,35	8	1,68	
Rainforest	1	0,60	2	1,21	0	0	0	0	
Ecuador Regions									
Coast	8	2.07	17	4.01	4	1.08	1	0.25	
Highlands	5	1.51	5	1.4	4	1.2	2	0.56	
Rainforest	0	0	2	3.41	0	0	1	1.81	
		Childr	en aged 10-1	4 years					
Geographical Areas		Ma	ale		Female				
	20	2005		2020		2005		2020	
	Deaths	ASMR	Deaths	ASMR	Deaths	ASMR	Deaths	ASMR	
Country									
Peru	5	0,32	37	2,69	7	0,47	17	1,25	
Ecuador	11	1.51	14	1.66	4	0.56	9	1.1	
Peru Regions									
Coast	5	0,56	19	2,38	5	0,67	7	1,01	
Highlands	0	0	15	3,62	2	0,34	8	1,58	
Rainforest	0	0	3	1,81	0	0	2	1,24	
Ecuador Regions									
Coast	6	1.63	7	1.63	2	0.56	3	0.73	
Highlands	5	1.56	7	1.69	2	0.62	4	1.12	
Rainforest	0	0	1	1.76	0	0	2	3.73	

Southern-Eastern European countries have experienced significant declines in its mortality rates over recent decades [16]. For example, within the European Union,

childhood cancer mortality rates decreased by 2.8% annually between 1990 and 2015 [17]. This downwards trends could be attributed to enhanced access to treatment

and advanced technologies for ALL management in European countries, which contrasts with the limited therapeutic options available in countries such as Peru and Ecuador.

Comparisons with similar low- and middle-income countries (LMICs) reinforce the urgency of addressing the rising mortality burden from childhood ALL in Peru and Ecuador. For instance, data from El Salvador and Guatemala show mortality rates exceeding 2.5 per 100,000 children in some years, similar to the highest rates observed in Peru [8]. In Southeast Asia, Indonesia reported mortality rates of approximately 2.2 per 100,000 among boys and 2.0 per 100,000 among girls during certain periods, which are comparable to the figures found in our study [18]. In Africa, countries like Egypt and Nigeria have reported elevated childhood leukemia mortality rates attributed to delayed diagnosis and limited treatment availability [19-21], factors which mirror the challenges faced in Peru and Ecuador. These comparisons highlight shared barriers among LMICs, such as resource constraints, limited specialized care, and unequal access to early diagnosis, and call for regional cooperation and investment in pediatric oncology.

Some studies conducted within the Latin America reported significant reductions in childhood leukemia mortality rates in Argentina, Brazil, Chile, and Mexico [22, 23]. These reductions could be related to technology transfer and more economic investment in the healthcare access and novel therapeutics installment. Also, could be attributed to socioeconomic factors, including technology transfer and increased investment in healthcare infrastructure and novel therapeutic interventions. On the other hand, Peru has not shown these reductions; on the contrary, it has had significant increases in mortality in recent years. In fact, In fact, in 2022, GLOBOCAN reported Peru as one of the countries with the highest mortality from childhood leukemia worldwide [1]. Some studies in Peru have reported low survival in childhood leukemia [24]. This probably due to a poor treatment adherence, a phenomenon seemingly more prevalent in developing nations, with reported rates reaching up to 64% [25]. The problems identified in the care process of ALL in Peru include delays in diagnosis and treatment initiation, shortage of facilities with the capacity to treat these patients, the lack of a consensus treatment protocol across Peruvian hospitals until 2017, the high percentage of treatment abandonment (mainly due to economic barriers as well as social and/or cultural factors) and medications needed to treat ALL are not always available [26]. Thus, the promotion of health programs featuring comprehensive medical coverage is crucial, as they have been shown to significantly reduce treatment abandonment and refusal rates. Such programs ensure adherence to complete treatment protocols and provide vital social, economic, and educational support to the families of patients afflicted with this disease [27].

In Ecuador, however, comprehensive data on overall survival (OS) or progression-free survival (PFS) for pediatric patients is unavailable. Nonetheless, concerning adult ALL patients, a study conducted in a coastal city (Guayaquil) reported a 5-year overall survival rate of

20%, with a median survival around of 8 months [28]. The OS documented appear notably diminished, likely attributable to elevated early mortality rates, which may stem from treatment-related complications or early disease relapse. Furthermore, the limited number of patients who underwent specialized treatment could also contribute to these lower survival rates.

This trend in Ecuador correlates with technical reports from SOLCA, an institution in Guayaquil, indicating a sustained upward trajectory in mortality cases in recent years, predominantly affecting males. However, further investigation is warranted, especially considering advancements in diagnostic techniques and therapeutic alternatives. Additionally, gender disparities in mortality trends are apparent, particularly in the rates of potential years of life lost attributable to ALL, notably pronounced in children aged 5 to 9 years [29].

We observed a higher mortality rate from ALL in boys compared to girls, a trend consistent with previous studies indicating a greater incidence and mortality of leukemia in boys [3, 8, 30, 7, 6]. A comprehensive meta-analysis investigating gender disparities in ALL occurrence and mortality rates among Indonesian children from 1997 to 2017 revealed a higher incidence rate among males compared to females (2.45 per 100,000 for boys vs. 2.05 per 100,000 for girls) [18]. Furthermore, multiple studies have reported elevated mortality rates from ALL in children. Data from The Surveillance, Epidemiology, and End Results (SEER) program indicated a mortality ratio of 1.2:1 in boys compared to girls [31]. Similarly, in Mexico, a significant increase in mortality rates per 100,000 boys compared to girls was observed between 1998 and 2018, with figures of 0.6 and 0.3, respectively [32]. These findings emphasize the need for further research and targeted interventions to address genderbased disparities in ALL incidence and mortality rates.

The economic burden of ALL treatment significantly affects mortality rates, particularly in lower-income countries [33-35]. In the United States, the average 3-year treatment costs for ALL exceed \$500,000, with approximately \$300,000 allocated to the initial 8 months of treatment [36]. Limited research has been conducted to evaluate the cost of treatment in Latin America. For instance, according to the National Institute of Neoplastic Diseases (INEN) of Peru, only the annual cost of Clofarabine-based treatment amounts to approximately \$49,000 [37]. Likewise, in Colombia, the estimated total cost of treatment is approximately \$450,000. Hence, there is a pressing necessity for additional research exploring treatment expenses across various regions, especially within lower-income countries. Such investigations are vital to enhancing the formulation of cost-effective interventions aimed at alleviating the financial strain on both patients and healthcare systems.

More than 40% of the total costs associated with ALL treatment can be attributed to inpatient beds, while medication costs account for approximately 25% [38]. Therefore, there is an urgent need for strategies to reduce treatment cost, especially in developing nations. Addressing this challenge demands a collective effort involving pharmaceutical companies, international

organizations, and governments. Introducing outpatient treatment approaches could potentially yield significant cost reductions, which may have positive effects on mortality rates and treatment adherence. However, it is important to note that the reduction in risks associated with infections caused by multi-resistant bacteria has not been considered thus far [39]. Evaluating the feasibility and potential benefits of outpatient care, considering the associated infection risks, could provide valuable insights for optimizing ALL treatment strategies and improving patient outcomes.

In 2020, Ecuador embarked on a significant endeavor to enhance the quality and capacity of cancer care by establishing a partnership agreement with the renowned St. Jude Children's Research Hospital in the United States [40]. Due to the impact of the pandemic and administrative procedures, this collaboration officially took effect in 2021. The primary objective of this partnership is to elevate the standards of oncopediatric hospitals in Ecuador. The proposal aims to create a regional network of medical assistance, facilitating access to pediatric oncology medications and providing technical support and training. However, the applicability of these protocols, diagnostic methods, medications, and appropriate evaluation methodologies for implementation in the country requires analysis by the Ecuadorian Health Authority in accordance with current regulations [41].

These rates may have worsened due to the COVID-19 pandemic with a subsequent rise in mortality rates. A study conducted in 2020 at INEN reported that treatment was delayed in 51.6% of patients and 30.6% of patients were unable to make an appointment with a cancer specialist after the initial diagnosis and referral. In addition, patients with hematological malignancies who become infected with COVID-19 have a four-fold higher probability of dying compared to patients with solid tumors [42]. However, there are no studies in our country that comprehensively detail the picture of childhood leukemia mortality during the pandemic.

Currently, Ecuador enjoys the presence of the SOLCA, which serves as the national specialized center for cancer treatment. SOLCA operates branches in Guayaquil, Quito, Cuenca, Loja, Portoviejo, and Machala, with the overarching goal of delivering comprehensive coverage to the entire Ecuadorian population. The establishment of dedicated and specialized cancer treatment centers holds significant promise for enhancing treatment outcomes, lowering mortality rates, and fostering advancements in the field of oncology across Ecuador. Likewise, since 2012 Peru has also implemented a program called "Plan Esperanza" to reduce mortality and morbidity by cancer by improving access to cancer health services, including promotion, prevention, early detection, diagnosis, staging, treatment, and palliative care [43]. From 2012 to 2014, approximately 2400 leukemia patients under 18 years of age benefited from the program [44]. In addition, in 2017, the national plan for comprehensive care of ALL patients aged 1 to 21 years was also approved to establish strategic actions that contribute to improving access and comprehensive and timely patient care. Nonetheless, despite these efforts, not all aspects of the national cancer plan could be achieved, and therefore, the National Plan for Comprehensive Cancer Care (2020-2024) was initiated [26, 45].

Although both Peru and Ecuador are middle-income countries with historical limitations in mortality data quality, substantial progress has been made in recent years. In Peru, the implementation of the National Death Information System (SINADEF) has significantly improved death certification by reducing the frequency of ill-defined causes, minimizing human error from handwritten forms, and standardizing electronic reporting [46, 47]. Ecuador, on the other hand, operates through SOLCA, which manages a national tumor registry integrating mortality and incidence data from multiple provinces. While independent validations of the completeness of mortality reporting in children remain scarce, these institutional improvements enhance the accuracy and reliability of the datasets. Nevertheless, we acknowledge that some underreporting or misclassification may still exist, especially in rural or low-resource regions.

Limitations

Our study recognizes the inherent limitations commonly encountered in cancer registry analyses utilizing secondary databases, including concerns regarding the accuracy and reliability of death certifications, as well as the scarcity of detailed individual-level information. Moreover, the constrained number of cases presents challenges in conducting comprehensive incidence analyses and gaining a thorough understanding of ALL dynamics within each country. Nevertheless, the strengths of our study, as previously highlighted, are its pioneering nature as the first to report on ALL mortality rates within two countries characterized by notably high leukemia mortality rates. Additionally, this research offers a comprehensive examination of ALL mortality trends spanning over a decade across various regions of Peru and Ecuador. It is noteworthy that the calculations in this study relied on nationally available databases obtained from governmental institutions for both case identification and population statistics, thereby underscoring the robustness and validity of the data utilized.

In conclusion, Ecuador and Peru display worrisome mortality rates linked to ALL in their pediatric populations. Moreover, recent data underscores a notable escalation in ALL-related mortality rates among Peruvian children. Consequently, immediate action is imperative to implement robust interventions focused on early detection and swift initiation of treatment for children diagnosed with ALL. Such measures aim to improve prognosis and alleviate the burden of this disease, thereby safeguarding the health and well-being of pediatric patients in these regions.

Author Contribution Statement

Conceived and designed the idea: KSR, JSTR. Had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis: KSR, JSRT. Contributed to the writing of the manuscript: All authors. Contributed to the statistical

analysis: JSTR, DJM, CQV, JG. Critical revision of the manuscript: JSTR, JAP, JMA. Approval of the submitted and final version: All authors.

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Availability of data and materials

The datasets generated and/or analysed during the current study are available in the following links: https://www.minsa.gob.pe/portada/transparencia/solicitud/. https://www.ecuadorencifras.gob.ec/defuncionesgenerales/.

Competing interests

The author(s) declare that they have no competing interests.

References

- 1. Ferlay J, Ervik M, Lam f, Colombet M, Mery L, Piñeros M, et al. Global cancer observatory: Cancer today. Lyon, france: International agency for research on cancer. 2020. [cited 11 march, 2023]. Available from: Https://gco.Iarc.Fr/today.
- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49. https://doi.org/10.3322/caac.21660.
- Torres-Roman JS, Valcarcel B, Guerra-Canchari P, Santos CAD, Barbosa IR, La Vecchia C, et al. Leukemia mortality in children from latin america: Trends and predictions to 2030. BMC Pediatr. 2020;20(1):511. https://doi.org/10.1186/ s12887-020-02408-y.
- 4. Shoag JM, Barredo JC, Lossos IS, Pinheiro PS. Acute lymphoblastic leukemia mortality in hispanic americans. Leuk Lymphoma. 2020;61(11):2674-81. https://doi.org/10.1080/10428194.2020.1779260.
- 5. Silva FF, Zandonade E, Zouain-Figueiredo GP. Analysis of childhood leukemia mortality trends in brazil, from 1980 to 2010. J Pediatr (Rio J). 2014;90(6):587-92. https://doi.org/10.1016/j.jped.2013.12.013.
- 6. Chatenoud L, Bertuccio P, Bosetti C, Levi F, Negri E, La Vecchia C. Childhood cancer mortality in america, asia, and oceania, 1970 through 2007. Cancer. 2010;116(21):5063-74. https://doi.org/10.1002/cncr.25406.
- Miranda-Filho A, Pineros M, Ferlay J, Soerjomataram I, Monnereau A, Bray F. Epidemiological patterns of leukaemia in 184 countries: A population-based study. Lancet Haematol. 2018;5(1):e14-e24. https://doi.org/10.1016/ S2352-3026(17)30232-6.
- Curado MP, Pontes T, Guerra-Yi ME, Cancela Mde C. Leukemia mortality trends among children, adolescents, and young adults in latin america. Rev Panam Salud Publica. 2011;29(2):96-102. https://doi.org/10.1590/s1020-49892011000200004.
- Carrillo-Larco RM, Guzman-Vilca WC, Leon-Velarde F, Bernabe-Ortiz A, Jimenez MM, Penny ME, et al. Peruprogress in health and sciences in 200 years of independence. Lancet Regional Health–Americas. 2022;7:100148. https:// doi.org/10.1016/j.lana.2021.100148
- World Health Organization. Tracking universal health coverage: 2023 global monitoring report. World Health

- Organization; 2023 Nov 7.
- 11. Miki J, Rampatige R, Richards N, Adair T, Cortez-Escalante J, Vargas-Herrera J. Saving lives through certifying deaths: Assessing the impact of two interventions to improve cause of death data in peru. BMC Public Health. 2018;18(1):1329. https://doi.org/10.1186/s12889-018-6264-1.
- World Health Organization. Age standardization of rates: a new WHO standard. Geneva: WHO. 2021. Available from:// www.emro. who.int/ncd/publications/WHO_pop_standard. pdf. Acceso el. 2001;25.
- 13. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med. 2000;19(3):335-51. https://doi.org/10.1002/(sici)1097-0258(20000215)19:3<335::aid-sim336>3.0.co;2-z.
- 14. National cancer institute. Number of joinpoints. [cited february 14,2024]. Available from: Https://surveillance. Cancer.Gov/help/joinpoint/setting-parameters/method-and-parameters-tab/number-of-joinpoints.
- 15. Kim HJ, Fay MP, Yu B, Barrett MJ, Feuer EJ. Comparability of segmented line regression models. Biometrics. 2004;60(4):1005-14. https://doi.org/10.1111/j.0006-341X.2004.00256.x.
- 16. Petridou ET, Dimitrova N, Eser S, Kachanov D, Karakilinc H, Varfolomeeva S, et al. Childhood leukemia and lymphoma: Time trends and factors affecting survival in five southern and eastern european cancer registries. Cancer Causes Control. 2013;24(6):1111-8. https://doi.org/10.1007/s10552-013-0188-y.
- 17. Bertuccio P, Alicandro G, Malvezzi M, Carioli G, Boffetta P, Levi F, et al. Childhood cancer mortality trends in europe, 1990-2017, with focus on geographic differences. Cancer Epidemiol. 2020;67:101768. https://doi.org/10.1016/j.canep.2020.101768.
- 18. Garniasih D, Susanah S, Sribudiani Y, Hilmanto D. The incidence and mortality of childhood acute lymphoblastic leukemia in indonesia: A systematic review and meta-analysis. PLoS One. 2022;17(6):e0269706. https://doi.org/10.1371/journal.pone.0269706.
- Soliman RM, Elhaddad A, Oke J, Eweida W, Sidhom I, Ahmed S, et al. Temporal trends in childhood cancer survival in egypt, 2007 to 2017: A large retrospective study of 14 808 children with cancer from the children's cancer hospital egypt. Int J Cancer. 2021;148(7):1562-74. https://doi.org/10.1002/ijc.33321.
- 20. Farrag A, Osman AM, Ghazaly MH. Pediatric cancer mortality: Analyzing early deaths and fatalities in a resource-limited tertiary care context. PLoS One. 2024;19(10):e0312663. https://doi.org/10.1371/journal.pone.0312663.
- Ochicha O, Gwarzo AK, Gwarzo D. Pediatric malignancies in kano, northern nigeria. World J Pediatr. 2012;8(3):235-9. https://doi.org/10.1007/s12519-012-0363-3.
- 22. Couto AC, Ferreira JD, Koifman RJ, Monteiro GT, Pombo-de-Oliveira MS, Koifman S. Trends in childhood leukemia mortality over a 25-year period. J Pediatr (Rio J). 2010;86(5):405-10. https://doi.org/10.2223/JPED.2027.
- Malvezzi M, Santucci C, Alicandro G, Carioli G, Boffetta P, Ribeiro KB, et al. Childhood cancer mortality trends in the americas and australasia: An update to 2017. Cancer. 2021;127(18):3445-56. https://doi.org/10.1002/cncr.33642.
- Castro-Arechaga S, Ronceros-Salas L, Vega-Centeno S, Moreno M, Soto A. Global and disease-free survival in a peruvian cohort of patients with acute lymphoblastic leukemia. Rev Peru Med Exp Salud Publica. 2018;35(3):416-25. https://doi.org/10.17843/rpmesp.2018.353.2947.
- 25. Klünder-Klünder M, Miranda-Lora AL, Dorantes-Acosta E, Zapata-Tarrés M, Carranco-Hernández T, Escamilla-Núñez A, et al. Treatment abandonment in pediatric patients with

- acute lymphoblastic leukemia. Bol méd Hosp Infant México. 2012;69(3):226-32.
- 26. Ministerio de salud. Rm. 383 2017/minsa. Plan nacional para la atencion integral de la leucemia linfatica aguda en pacientes de 1 a 21 años: Ministry of Health. Rm. 383 - 2017/minsa. National plan for comprehensive care of acute lymphocytic leukemia in patients aged 1 to 21 years. Available from: Http://bvs.Minsa.Gob.Pe/local/minsa/4233.
- 27. Schrappe M, Hunger SP, Pui CH, Saha V, Gaynon PS, Baruchel A, et al. Outcomes after induction failure in childhood acute lymphoblastic leukemia. N Engl J Med. 2012;366(15):1371-81. https://doi.org/10.1056/ NEJMoa1110169.
- 28. Sabando B, Orquera A, Navarrete D, Ramirez J, Chisesi T, Oliveros-Alvear J, et al. Pb1734: Survival of adults with acute lymphoblastic leukemia in ecuador. An analysis of the real world. HemaSphere. 2023;7(S3):e64113c3. https://doi. org/10.1097/01.HS9.0000973796.64113.c3
- 29. Departamento de bioestadísitca solca-guayaquil. Leucemias en niños de 0-19 años en la ciudad de guayaquil. Periodo 2009-2018: Department of Biostatistics, Solca, Guayaquil. Leukemia in children aged 0–19 years in the city of Guayaquil. Period 2009–2018. [cited 10 february, 2024]. Available from: Http://www.Estadisticas.Med.Ec/publicaciones/8%20 leucemias%20poblaci%c3%b3n%20infantil%202019.Pdf
- 30. Mejia-Arangure JM, Bonilla M, Lorenzana R, Juarez-Ocana S, de Reyes G, Perez-Saldivar ML, et al. Incidence of leukemias in children from el salvador and mexico city between 1996 and 2000: Population-based data. BMC Cancer. 2005;5:33. https://doi.org/10.1186/1471-2407-5-33.
- 31. Holmes L, Jr., Hossain J, Desvignes-Kendrick M, Opara F. Sex variability in pediatric leukemia survival: Large cohort evidence. ISRN Oncol. 2012;2012:439070. https://doi. org/10.5402/2012/439070.
- 32. Munoz-Aguirre P, Zapata-Tarres M, Espinosa-Tamez P, Sanchez-Blas H, Brochier M, Lamadrid-Figueroa H. Childhood acute lymphoblastic leukemia in mexico: Mortality trend analysis, 1998-2018. Salud Publica Mex. 2022;64(1):26-34. https://doi.org/10.21149/13210.
- 33. Mostert S, Sitaresmi MN, Gundy CM, Janes V, Sutaryo, Veerman AJ. Comparing childhood leukaemia treatment before and after the introduction of a parental education programme in indonesia. Arch Dis Child. 2010;95(1):20-5. https://doi.org/10.1136/adc.2008.154138.
- 34. Mostert S, Sitaresmi MN, Gundy CM, Sutaryo, Veerman AJ. Influence of socioeconomic status on childhood acute lymphoblastic leukemia treatment in indonesia. Pediatrics. 2006;118(6):e1600-6. https://doi.org/10.1542/peds.2005-3015.
- 35. Ribeiro RC, Steliarova-Foucher E, Magrath I, Lemerle J, Eden T, Forget C, et al. Baseline status of paediatric oncology care in ten low-income or mid-income countries receiving my child matters support: A descriptive study. Lancet Oncol. 2008;9(8):721-9. https://doi.org/10.1016/ S1470-2045(08)70194-3.
- 36. Turcotte LM, Hocutt C, Messinger YH, Gilchrist L, Watson D, Finch M. Cost of pediatric acute lymphoblastic leukemia care in the current treatment era. Blood. 2021;138:663. https://doi.org/10.1182/blood-2021-146621
- 37. National Institute of Neoplastic Diseases. Health Technology Assessment. Efficacy and safety of clofarabine with chemotherapy for relapsed/refractory acute lymphoblastic leukemia or acute myeloid leukemia in patients under 21 years of age, as a bridge to treatment before hematopoietic progenitor cell transplantation.
- 38. Hayati H, Kebriaeezadeh A, Ehsani M-A, Nikfar S. Cost-

- analysis of treatment of childhood acute lymphoblastic leukemia based on ukall protocol. Iran J Pediatr. 2018;28(6):e7985. https://doi.org/10.5812/ijp.7985
- 39. Colunga-Pedraza JE, Gonzalez-Llano O, Gonzalez-Martinez CE, Gomez-Almaguer D, Yanez-Reyes JM, Jimenez-Antolinez V, et al. Outpatient low toxic regimen with bortezomib in relapsed/refractory acute lymphoblastic leukemia in pediatrics and aya patients: Single-center mexican experience. Pediatr Blood Cancer. 2020;67(5):e28241. https://doi.org/10.1002/pbc.28241.
- 40. Government of the Republic of Ecuador. Ecuador signs an agreement with St. Jude Children's Research Hospital in the United States for healthcare, research, and innovation in the treatment of children with cancer within the public health network.
- 41. Gobiero de la republica del ecuador. Ecuador implementará protocolo para tratamiento de cáncer infantil: Government of the Republic of Ecuador. Ecuador implements protocol for treating childhood cancer.
- 42. Valdiviezo N, Alcarraz C, Castro D, Salas R, Begazo-Mollo V, Galvez-Villanueva M, et al. Oncological care during first peruvian national emergency covid-19 pandemic: A multicentric descriptive study. Cancer Manag Res. 2022;14:1075-85. https://doi.org/10.2147/CMAR.S350038.
- 43. Vidaurre T, Santos C, Gomez H, Sarria G, Amorin E, Lopez M, et al. The implementation of the plan esperanza and response to the impact review. Lancet Oncol. 2017;18(10):e595-e606. https://doi.org/10.1016/S1470-2045(17)30598-3.
- 44. Ministerio de salud. Gracias al plan esperanza se financiaron a más de 2,400 pacientes con leucemia. [cited 30 june, 2023]: Ministry of Health. Thanks to the Hope Plan, more than 2,400 leukemia patients received funding. [cited June 30, 2023]. Available from: Https://www.Gob.Pe/institucion/ minsa/noticias/32175-gracias-al-plan-esperanza-sefinanciaron-a-mas-de-2-400-pacientes-con-leucemia.
- 45. Ministerio de salud. Plan nacional de cuidados integrales del cáncer (2020 - 2024): Ministry of Health. National Comprehensive Cancer Care Plan (2020-2024). Available from: Http://bvs.Minsa.Gob.Pe/local/minsa/5341.Pdf.
- 46. Mikkelsen L, Phillips DE, AbouZahr C, Setel PW, de Savigny D, Lozano R, et al. A global assessment of civil registration and vital statistics systems: Monitoring data quality and progress. Lancet. 2015;386(10001):1395-406. https://doi. org/10.1016/S0140-6736(15)60171-4.
- 47. Miki J, Rampatige R, Richards N, Adair T, Cortez-Escalante J, Vargas-Herrera J. Saving lives through certifying deaths: Assessing the impact of two interventions to improve cause of death data in perú. BMC Public Health. 2018;18:1-11. https://doi.org/10.1186/s12889-018-6264-1



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