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Incidence and Geographic Distribution of Renal Tumors in Brazilian Children (2013-2022)

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Authors' contributions

This work was carried out in collaboration among all authors. Authors BDCE, RME, HDHS and EBSR designed the study, managed the literature searches, performed the statistical analysis, and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Aims: To analyze the incidence geographical distribution and therapeutic modalities of renal tumors in Brazil on children aged 0 to 14 years from 2013 to 2022.
Methods: Data on malignant neoplasms (ICD-10 groups C64-C68) for individuals aged 0 to 14 years from 2013 to 2022 were obtained from the Ministry of Health's oncology panel. Incidence rates were calculated per year, state of residence, and age group. Statistical analyses included the

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Kruskal-Wallis test with Dunn's post-hoc test and Pearson's chi-square test. Data extraction, processing, and analysis were conducted using R software version 4.3.2.
Results: During the study period, 2,728 cancer cases were reported, predominantly in children aged 0 to 4 years. Females were slightly more affected. Most treatments occurred outside the municipality of residence, with chemotherapy being the primary treatment. An average incidence rate of 0.60 new cases per 100,000 inhabitants was observed, with a 30% increase over the period. The incidence was highest in the 0 to 4 years age group (1.13 per 100,000), followed by 5 to 9 years and 10 to 14 years. Fourteen states had incidence rates above the national average, with the highest rates in the Federal District, Santa Catarina, and Alagoas.
Conclusion: These findings can inform health policies and prevention programs to improve clinical outcomes and quality of life through early diagnosis and individualized treatment strategies.

Keywords: Wilms tumor; kidney cancer; embryonal neoplasms; chemotherapy; pediatrics.

1. INTRODUCTION

Childhood cancer is a significant global health concern and represents a distinct set of malignancies that fundamentally differ from the cancers that typically bother adults. The physiological [1] and immunological [2,3] disparities between children and adults significantly influence the pathogenesis and progression of cancer. While pediatric cancers typically result from genetic alterations that occur early in development, often before birth and associated with developmental syndromes, adult cancers are more commonly linked to accumulated genetic mutations resulting from environmental exposures and lifestyle factors [4]. The immature immune system of children may be less effective in recognizing and eliminating malignant cells, whereas adult immune responses to tumors can both protect and promote tumor growth. Moreover, the rapid growth and heightened metabolism of childhood cancers can lead to more aggressive tumor behavior, and children's developing organs are particularly susceptible to tumorigenesis. For these reasons, therapeutic approaches to pediatric and adult cancers must be adjusted to account for these fundamental biological differences [2,3].

Unlike adult cancers, which are often linked to lifestyle and environmental risk factors, childhood cancers are primarily driven by genetic changes that occur early in the development of cells [5]. These genetic alterations can include mutations, deletions, and translocations, which disrupt the normal growth and development of cells [6]. Additionally, congenital abnormalities or developmental defects can predispose children to certain types of cancer [7]. This contrast between the genetic basis of childhood cancers and the multifactorial etiology of adult cancers features as challenges and opportunities in the prevention and treatment of pediatric malignancies. Children with cancer require specialized treatment approaches that consider their unique physiological characteristics [1]. Due to their immature immune systems and developing bodies, children may be more susceptible to the side effects of traditional cancer treatments, such as chemotherapy and radiation therapy [8]. Therefore, pediatric oncologists carefully select treatment regimens that balance the need for effective cancer control with the preservation of the child's overall health and well-being. This often involves a multidisciplinary approach, incorporating surgery, chemotherapy, radiation therapy, targeted therapies, and stem cell transplantation, customized to the specific type of cancer, stage of disease, and individual patient factors [8]. Additionally, supportive care measures, such as pain management, nutrition counseling, and psychological support, play a crucial role in improving the quality of life for children with cancer. While advancements in medical care have improved treatment outcomes, the overall burden of childhood cancer remains high, especially in developing countries where access to specialized care is limited [9].

According to Global Cancer Statistics data (GLOBOCAN), in 2020, the incidence of cancer among children and adolescents (0-19 years) worldwide is significant, with over 275,000 new cases diagnosed annually. In terms of mortality, more than 105,000 children and adolescents die from cancer each year [10]. The current global incidence rate of childhood cancer is estimated at about 400,000 new cases per year for children and adolescents aged 0-19 years. This translates to roughly 150 cases per million children annually. Although the specific data on the

number of deaths among children and adolescents aged 1 to 19 years in Brazil were not detailed in the research, cancer remains one of the leading causes of mortality in this age group in the country. National Cancer Institute estimates that for the 2023-2025 triennium, each year during this period, 7,930 new cases of cancer will be diagnosed in children and adolescents aged 0 to 19 in Brazil [11].

Despite the etiology and risk factors of childhood cancer are not fully understood, research suggests that certain demographic and socioeconomic factors may play a role in disease incidence and outcomes [12].

Wilms tumors, also known as nephroblastoma, is a rare form of kidney cancer that primarily affects children and typically occurs between 3 and 4 years of age, being rare in older children and adults. Most cases are diagnosed before the age of 5. The tumor originates from the primitive embryonic kidney tissue known as the metanephric blastema, which is the precursor to the fully developed renal structures [13]. The exact mechanisms behind the development of Wilms tumor are not fully understood, but research suggests that genetic and environmental factors may play a role in its pathogenesis [14-16] The estimated rate is approximately 1 case per 10,000 children [17], regardless of gender distribution or geographic location, as well as the factors that shape its diagnosis, prognosis and the socioeconomic conditions that influence its prevalence and outcomes potentially due to factors such as reduced access to healthcare and early detection [18]. The diagnosis of Wilms tumors often involves a combination of imaging techniques, such as ultrasound, CT scans, and MRI, to accurately assess the size, location, and extent of the tumor [19].

In Brazil, the epidemiology of Wilms tumor is not well-documented, with limited data available on the precise incidence and prevalence of the disease [20].

The study aims to analyze the incidence and epidemiological profile of childhood renal tumors in Brazil, focusing on children aged 0 to 14 years from 2013 to 2022, to understand their clinical characteristics, geographical distribution, diagnostic patterns, therapeutic modalities, and temporal changes.

2. METHODS

The cases were obtained from the oncology panel of the Brazilian Unified Health System Data System (DATASUS) server. Individuals aged 0 to 14 years, diagnosed with malignant neoplasms belonging to ICD-10 groups C64, C65, C66, C67, and C68 between 2013 and 2022 were included in the sample. Population data for the respective year of diagnosis, state of residence, and age group were also collected from the DATASUS server using Brazilian Institute of Geography and Statistics (IBGE) projections.

Incidence rates were calculated per year, state of residence, and age group, multiplied by 100,000 inhabitants. The percentage variation was calculated by dividing the difference between the incidence rate at the end of the trend and the incidence rate at the beginning of the trend by the initial rate, and then multiplying by 100. Median rates were compared by age group using the Kruskal-Wallis test with Dunn's post-hoc test. Pearson's chi-square test was used to evaluate the association between categorical variables.

R software version 4.3.2 (R Core Team, Vienna, Austria) was used for data extraction, processing, and analysis. The script developed for this study is available in a public access repository (https://gist,github,com/datahoffmann/ac70955af5dba16eafb54f4f39a7c1d9). For inferential statistics, a significance level of 5% was considered.

3. RESULTS AND DISCUSSION

During the study period, there were a total of 2.728 cancer cases. with the majority occurring in children aged 0 to 4 years. Females were the most prevalent sex. Most treatments had to be conducted in a municipality different from the municipality of residence. The main treatment was chemotherapy, stage 0 was the most prevalent, and the most frequent diagnosis was malignant neoplasm of the kidneys, with most cases waiting up to 6 days between diagnosis and the start of treatment (Table 1).

There was an average of 0.60 new cases per 100,000 inhabitants aged 0 to 14 years, with an increasing trend and a positive percentage change of 30% in the incidence rate over the study period (Fig. 1).

As shown in Fig. 2, the population aged 0 to 4 years had an average incidence rate of 1.13 cases per 100,000 people, followed by those aged 5 to 9 years, with an average rate of 0.61 cases per 100,000 people, and finally, individuals aged 10 to 14 years, with an average of 0.11 cases per 100,000 people. This difference was statistically significant ($p<0.001$). The percentage change in the incidence rate was positive across all age groups, demonstrating a growth trend with varying intensities: 200% in the population aged 10 to 14 years, 50% in the population aged 5 to 9 years, and 9% in the population aged 0 to 4 years.

A total of 14 (51.85%) states had an average incidence rate per 100,000 people aged 0 to 14 years above the national average. In descending order, they were: Federal District (0.90), Santa Catarina (0.86), Alagoas (0.84), Paraná (0.83), Mato Grosso do Sul (0.77), Acre (0.73), Paraíba (0.71), Espírito Santo (0.70), Rio Grande do Sul (0.70), Piauí (0.69), Goiás (0.68), Mato Grosso (0.65), Sergipe (0.63), and Minas Gerais (0.61) (Fig. 3).

Table 1. Distribution of Demographic, Clinical, and Treatment Variables Among Pediatric Renal Cancer Patients in Brazil, 2013-2022

Variables	N (%)
Age Group	
0-4 years	1617 (59.27)
5-9 years	930 (34.09)
10-14 years	181 (6.63)
Sex	
Female	1399 (51.28)
Male	1329 (48.72)
Treatment Facility	
Same municipality	727 (29.76)
Other municipality	1716 (70.24)
Not reported	285
Treatment Received	
Surgery	242 (8.87)
Chemotherapy + Radiotherapy	8 (0.29)
Chemotherapy	2100 (76.98)
Radiotherapy	93 (3.41)
Not informed	285 (10.45)
Stage	
0	669 (27.42)
I	424 (17.38)
II	339 (13.89)
III	391 (16.02)
IV	375 (15.37)
Not applicable	242 (9.92)
Not reported	288
Diagnosis	
Bladder	93 (3.41)
Other organs	11 (0.40)
Renal pelvis	100 (3.67)
Kidneys	2509 (91.97)
Ureters	15 (0.55)
Time until treatment onset	
0-6 years	1187 (50.21)
7-14 years	487 (20.60)
15-30 years	321 (13.58)
31-60 years	153 (6.47)
61 ou years	216 (9.14)
Not reported	364

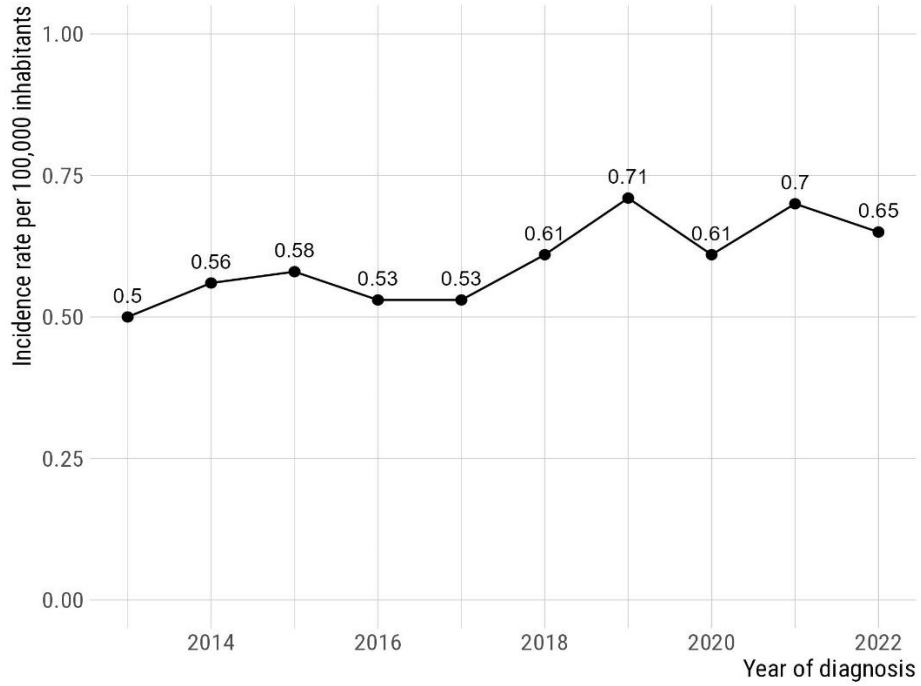

Fig. 1. Temporal trend of renal cancer incidence in Brazilian children and adolescents

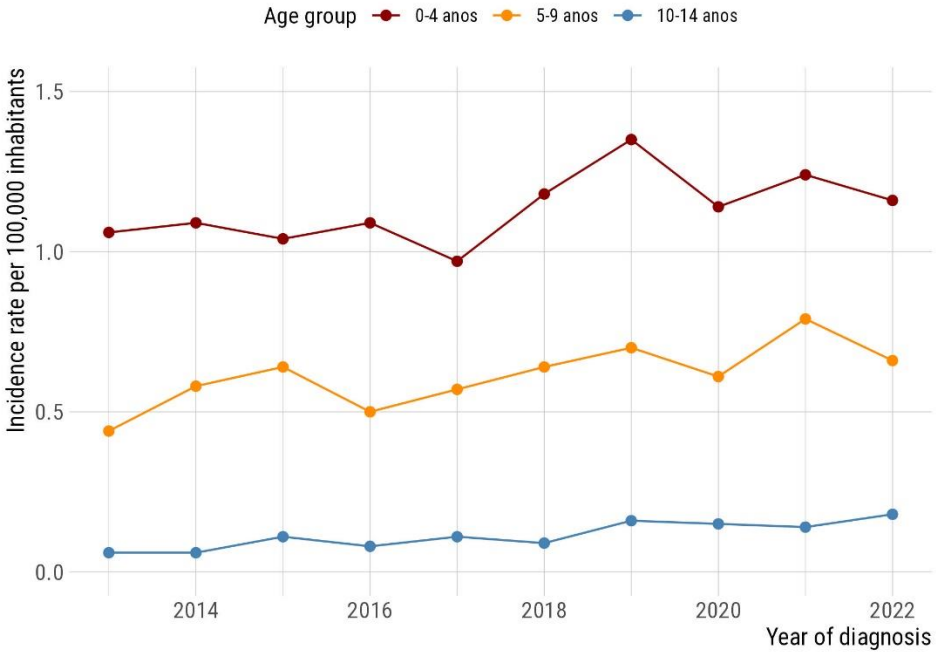

Fig. 2. Temporal trend of renal malignancy incidence rate among individuals aged 0 to 14 years in Brazil by age group

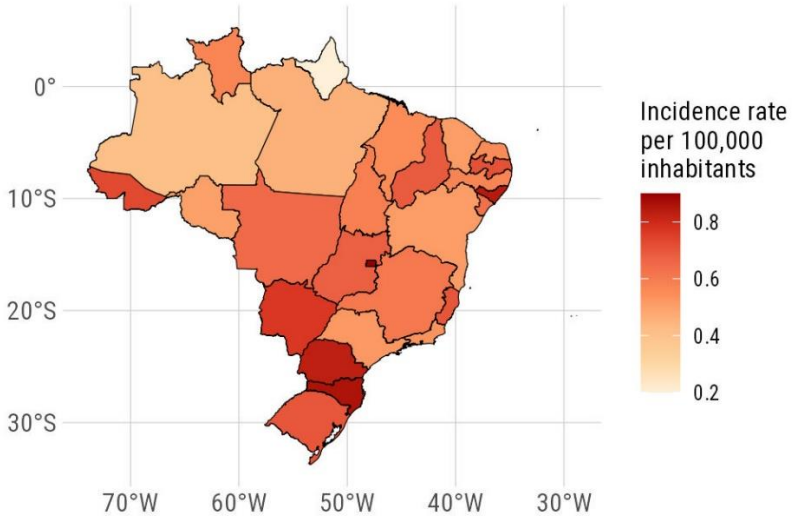

Fig. 3. Geographical distribution of renal malignancy incidence rate among individuals aged 0 to 14 years in Brazil between 2013 and 2022

There was a statistically significant difference in the proportion of treatment types concerning the diagnosis of malignant neoplasms (Fig. 4). Malignant neoplasms of the kidneys and bladder were mostly treated with chemotherapy, the ureters were mainly treated surgically, and for other organs of the genitourinary system, radiotherapy was the preferred treatment (Fig. 4).

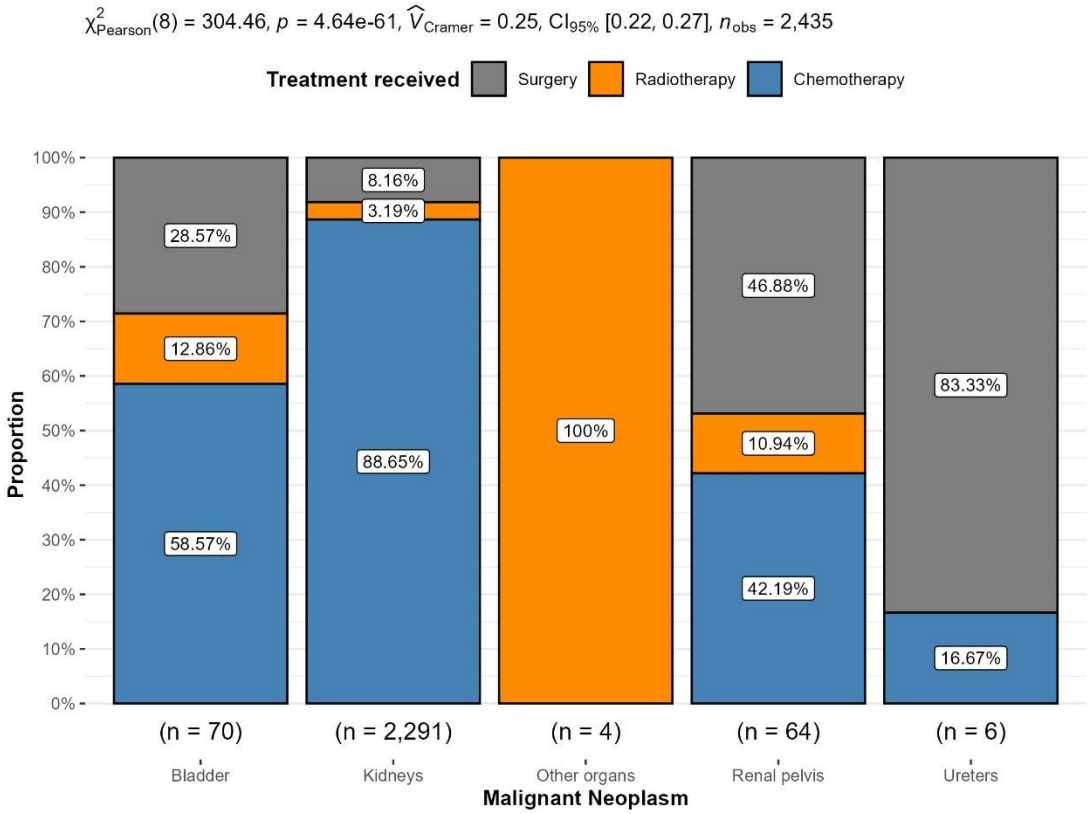

Fig. 4. Distribution of treatment types by diagnosis of malignant neoplasms

3.1 Discussion

This study identified an average incidence rate of 0.60 new cases of renal cancer per 100,000 inhabitants among children aged 0 to 14 years in Brazil from 2013 to 2022. In comparison, the international study conducted in 2020 reported an age-standardized incidence rate (ASR) of 8.3 per million for renal tumors in children, demonstrating a significantly lower rate within the Brazilian context [21]. More recently, a global study on Pediatric Renal Tumor Epidemiology indicated that the ASR for renal tumors in Brazil has risen to 8.4 per million, aligning closely with the global average of 8.3 per million. Although this figure reflects a 30% increase over the analyzed period, it remains lower than the rates reported in North America and Europe (9.1–9.8 per million each). The data also show that Central and South America and the Caribbean have an ASR of 6.7, while regions in Asia report lower rates of 4.1–5.4 [22]. The higher incidence observed in children aged 0 to 4 years (1.13 per 100,000) corroborates the international literature, which points to this age group as the most affected [22]. The gradual decline in incidence in subsequent age groups also aligns with the findings suggesting a decreasing risk throughout childhood [22].

Gender analysis revealed a slight predominance of cases in girls (51.28%), a finding that diverges from a recent study, which found no significant difference between the sexes [23]. This discrepancy may be due to factors such as differences in the genetic composition of the studied population or variations in diagnostic protocols. Chemotherapy was the treatment of choice, in line with international guidelines. The trend of increasing incidence rates across all age groups, with the highest increase observed in the 10 to 14-year age group, followed by the 5 to 9-year and 0 to 4-year groups, can be attributed to improvements in diagnostic practices and reporting, as well as a possible increase in underlying risk factors. These observations are consistent with statistics from the American Cancer Society, which also indicate an overall increase in pediatric renal cancer incidence, partially attributable to advances in imaging technologies and diagnostic methods that enable early and accurate detection of renal tumors in children [24]. These findings align with those presented in studies which also observe an increase in pediatric renal tumor incidence due to advances in imaging technologies, improved diagnostic methods, and more rigorous reporting protocols [22]. However, the possibility of a real increase in incidence, possibly related to yet not fully understood risk factors, cannot be ruled out. Comparing our findings with international literature, we observe that the highest incidence of pediatric renal cancer generally occurs in children under 5 years old. While our study also identified a significant number of cases in this age group, the most significant percentage increase was observed in older children. This discrepancy may be related to specific factors of the Brazilian population or changes in risk factor exposure patterns over time. The detection of 27.42% of cases in stage 0 indicates an advancement in diagnostic systems and greater access to healthcare services, allowing for early diagnosis and better prognosis. This rate is higher than that observed in the international study [22], suggesting that the early screening and diagnosis protocols implemented in Brazil may be effective. The distribution of disease stages, although relatively homogeneous, diverges in some aspects from international data, which may reflect differences in clinical presentation or staging practices. There was a significant difference in treatment types based on the diagnosis of malignant neoplasms. Chemotherapy was the main treatment for malignant neoplasms of the kidneys and bladder, while surgical treatment was preferred for ureters, and radiotherapy was used for other organs of the genitourinary system. The choice of treatment depends on several factors, including the type and stage of the cancer, the patient's age, the region of diagnosis, and the need for travel to treatment centers [25,26]. These factors also impact prognosis, quality of life, and the burden on families who must travel for extended treatment periods. Most treatments were conducted in municipalities different from the patients' places of residence. This reflects disparities in healthcare infrastructure and the availability of specialized oncology centers across different regions. Demographic and socioeconomic factors likely contribute to these disparities, affecting the timely diagnosis and treatment of pediatric cancer patients [22]. The need to travel for treatment in specialized centers, often located in other cities or states, imposes logistical, financial, and social challenges that compromise the patients' ability to follow the prescribed therapeutic plan. Difficulties in accessing transportation, high costs associated with treatment, and the reorganization of family routines are factors that contribute to reduced adherence. Consequently, non-

adherence to treatment can lead to severe consequences for the patient's prognosis, such as disease progression, increased mortality, and greater demand on the healthcare system. Studies have shown that limited access to specialized care can negatively impact prognosis, particularly in low- and middle-income countries [27]. Socioeconomic status significantly impacts the survival of children with cancer, with limited access to specialized care compromising prognosis, particularly in regions with lower socioeconomic development [26].

The data from this study indicate that fourteen Brazilian states had average incidence rates above the national average, with the highest rates observed in the Federal District, Santa Catarina, and Alagoas. Regional variations may be influenced by factors such as the Human Development Index (HDI), the availability of specialized diagnostic centers, and environmental risk factors. States with higher HDIs and better healthcare infrastructure may report higher incidence rates due to better diagnostic capabilities. The variation in renal cancer incidence among Brazilian states may be related to exposure to different environmental factors, such as pesticides, air pollutants, and water contamination, as discussed in studies on prenatal environmental exposure and the risk of Wilms' tumor in children aged 0 to 5 years [28] The higher rates observed in the Federal District and Santa Catarina may reflect better access to healthcare services, early diagnosis, and more complete cancer registries, while the lower rates in some northeastern states may be attributed to socioeconomic inequalities [27], limited access to specialized care, and underreporting. Additionally, systematic reviews on somatic, genetic, and epigenetic changes in nephrogenic rests and their transformation into Wilms' tumors suggest that environmental exposures and parental habits during the perinatal period can play a significant role in the etiology of these tumors [28-31].

Limitations of this study include the possibility of underreporting cases and the absence of data on the histological type of the tumor. Despite these limitations, our results contribute to the knowledge of the epidemiology of pediatric renal cancer in Brazil and highlight the need for additional studies to investigate the risk factors and mechanisms involved in the etiology of this disease.

4. CONCLUSION

This study provides a comprehensive overview of malignant renal neoplasms in children in Brazil, highlighting not only incidence but also demographic factors and treatment patterns. This information can guide and inform health policies and prevention programs aimed at improving clinical outcomes and quality of life for these pediatric patients through early diagnosis and individualized treatment strategies. It is important to consider the epidemiological variations in the geographic distribution of this disease due to socio-environmental factors, which necessitate specific approaches for different regions of the country. Based on the information obtained in this study and the analysis of the clinical and epidemiological profile of children and adolescents diagnosed with cancer nationwide, it was observed that the data highlight the importance of the health profile of infants in the diagnosis of neoplasms to assist in the development of protocols, care flows, and strategies that can effectively meet real needs. This contributes to the qualification of pediatric care.

Since these epidemiological analyses are part of the construction of public policies directed at this age group, it is crucial to intensify investment in the training of health professionals to recognize risk factors and early warning signs of these diseases' severity. Additionally, it is important that new studies similar to this one be carried out to strengthen the epidemiological basis of these diseases, their incidences, characteristics, and particularities. In this way, it is expected that specific actions can reduce indicators associated with hospitalizations and pediatric mortality related to the conditions studied.

Some limitations of this study should be considered, such as the interpretation of the results and the lack of comparison of the period of highest incidence of COVID-19 with other periods, which may present different health indicators due to the pandemic context.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

According to Brazilian National Health Council Resolution No. 510/2016, the data used in this study were considered public access and did not require submission to the Research Ethics Committee. The data were presented in aggregate form, without allowing the identification of individual participants, ensuring privacy and confidentiality.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Kattner P, Strobel H, Khoshnevis N, et al. Compare and contrast: Pediatric cancer versus adult malignancies. Cancer Metastasis Rev. 2019;38(4):673-682.
2. Pandya PH, Murray ME, Pollok KE, Renbarger JL. The Immune System in Cancer Pathogenesis: Potential Therapeutic Approaches. J Immunol Res. 2016;2016:4273943.
3. Pathania AS. Immune Microenvironment in Childhood Cancers: Characteristics and Therapeutic Challenges. Cancers. 2024;16(12):2201.
4. Bahrami H, Tafrihi M. Global trends of cancer: The role of diet, lifestyle, and environmental factors. Cancer Innovation. 2023;2(4):290-301.
5. Dangoni GD, Teixeira ACB, da Costa SS, Scliar MO, Carvalho LML, Silva LN, et al. Germline mutations in cancer predisposition genes among pediatric patients with cancer and congenital anomalies. Pediatric Research. 2024;95(5):1346-1355.
6. Dean SJ, Farmer M. Pediatric cancer genetics. Current Opinion in Pediatrics. 2017;29(6):629-633.
7. Beck P, Selle B, Madenach L, et al. The genomic landscape of pediatric renal cell carcinomas. iScience. 2022;25(4):104167.
8. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Health Care Services; Committee on Childhood Cancers and Disability. Childhood cancer and functional impacts across the care continuum. Aiuppa L, Cartaxo T, Spicer CM, et al., editors. Washington (DC): National Academies Press (US) Chapter 3, Treatment Modalities for Childhood Cancers; 2020 Dec 9. Available:https://www.ncbi.nlm.nih.gov/books/NBK569416/
9. Haileamlak A. The Challenge of Childhood Cancer in Developing Countries. Ethiopian Journal of Health Sciences. 2016;26(3): 199.
10. 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: A Cancer Journal for Clinicians. 2021;71(3):209-249.
11. Ministério da Saúde IN de C (INCA). Estimativa 2023: Incidência de câncer no Brasil. Rio de Janeiro. 2022;160. Available:http://controlecancer.bvs.br/
12. Beltrami A, Hilliard A, Green AL. Demographic and socioeconomic disparities in pediatric cancer in the United States: Current knowledge, deepening understanding, and expanding intervention. Cancer Epidemiol. 2022;76: 102082.
13. Spreafico F, Fernandez CV, Brok J, et al. Wilms tumour. Nat Rev Dis Primers. 2021;7(1):75.
14. Murphy AJ, Cheng C, Williams J, Shaw TI, Pinto EM, Dieseldorff-Jones K, et al. Genetic and epigenetic features of bilateral Wilms tumor predisposition in patients from the Children's Oncology Group AREN18B5-Q. Nature Communications. 2023;14(1):8006.
15. Khan A, Feulefack J, Sergi CM. Exposure to pesticides and pediatric Wilms' tumor. A meta-analysis on pre-conception and pregnancy parental exposure with an IARC/WHO commentary. Human and Experimental Toxicology. 2022;41: 9603271221136211.
16. Shrestha A, Ritz B, Wilhelm M, Qiu J, Cockburn M, Heck JE. Prenatal exposure to air toxics and risk of wilms' tumor in 0- to 5-year-old children. Journal of Occupational and Environmental Medicine. 2014;56(6):573-8.
17. American Cancer Society. Key Statistics for Wilms Tumors; 2020.

Available:https://www.cancer.org/cancer/wilms-tumor/about/key-statistics.html.

18. Chalfant V, Riveros C, Stec AA. Effect of social disparities on 10 year survival in pediatric patients with Wilms' tumor. Cancer Medicine. 2023;12(3):3452-3459.
19. Kister K, Laskowski J, Bronst P, Mazur M, Małolepsza A, Zach-Źródlak M, et al. Update on Wilms tumor. Journal of Education, Health and Sport. 2023; 46(1):453-467. eISSN2391-8306.
20. Lima MF de S, Silva AMTC, Silva TVM, Bertazzi LC, Neto EBC, Hanauer B, et al. Análise Epidemiológica em 10 Anos de Tumor de Wilms na Infância na Cidade de Goiânia, Goiás. Brazilian Journal of Development. 2020;6(10):78147–78153.
21. Nakata K, Colombet M, Stiller CA, Pritchard-Jones K, Steliarova-Foucher E; IICC-3 Contributors. Incidence of childhood renal tumours: An international population-based study. Int J Cancer. 2020;147(12):3313-3327.
22. Libes J, Hol J, Neto JCA, et al. Pediatric renal tumor epidemiology: Global perspectives, progress, and challenges. Pediatr Blood Cancer. 2023;70(1):e30006.
23. de Aguirre-Neto JC, de Camargo B, van Tinteren H, Bergeron C, Brok J, Ramírez-Villar G, et al. International Comparisons of Clinical Demographics and Outcomes in the International Society of Pediatric Oncology Wilms Tumor 2001 Trial and Study. JCO Glob Oncol. 2022;(8): e2100425.
24. American Cancer Society. 2020. Key Statistics for Wilms Tumors. Available:https://www.cancer.org/cancer/wilms-tumor/about/key-statistics.html.
25. Leslie SW, Sajjad H, Murphy PB. Wilms Tumor. In: StatPearls. Treasure Island (FL): StatPearls Publishing; May 30, 2023.
26. Gupta S, Howard SC, Hunger SP, et al. Treating Childhood Cancer in Low- and Middle-Income Countries. In: Gelband H, Jha P, Sankaranarayanan R, et al., editors. Cancer: Disease Control Priorities, Third Edition (Volume 3). Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2015 Nov 1. Chapter 7.
27. Oncoguia. Desigualdades socioeconômicas limitam o acesso a novas terapias contra o câncer. Available:https://www.oncoguia.org.br/conteudo/desigualdades-socioeconomicas-limitam-o-acesso-a-novas-terapias-contra-o-cancer/17003/7/
28. Shrestha A, Ritz B, Wilhelm M, Qiu J, Cockburn M, Heck JE. Prenatal exposure to air toxics and risk of wilms' tumor in 0- to 5-year-old children. J Occup Environ Med. 2014;56(6) :573-8.
29. Bánki T, Drost J, van den Heuvel-Eibrink MM, Mavinkurve-Groothuis AMC, de Krijger RR. Somatic, Genetic and Epigenetic Changes in Nephrogenic Rests and Their Role in the Transformation to Wilms Tumors, a Systematic Review. Cancers. 2023;15(5):1363.
30. Chu A, Heck JE, Ribeiro KB, et al. Wilms' tumour: A systematic review of risk factors and meta-analysis. Paediatr Perinat Epidemiol. 2010;24(5):449-469.
31. Khan A, Feulefack J, Sergi CM. Exposure to pesticides and pediatric Wilms' tumor. A meta-analysis on pre-conception and pregnancy parental exposure with an IARC/WHO commentary. Hum Exp Toxicol. 2022;41:9603271221136211.

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