UNIVERSIDADE ESTADUAL DE CAMPINAS

FACULDADE DE ODONTOLOGIA DE PIRACICABA

LADY PAOLA ARISTIZABAL ARBOLEDA

DISTRIBUIÇÃO DEMOGRÁFICA E CLINICOPATOLÓGICA DOS TUMORES MALIGNOS DE CABEÇA E PESCOÇO EM PACIENTES PEDIÁTRICOS DE UMA INSTITUIÇÃO BRASILEIRA: ESTUDO RETROSPECTIVO

DEMOGRAPHIC AND CLINICOPATHOLOGIC DISTRIBUTION OF HEAD AND NECK MALIGNANT TUMORS IN PEDIATRIC PATIENTS FROM A BRAZILIAN INSTITUTION: A RETROSPECTIVE STUDY.

Piracicaba

2018

LADY PAOLA ARISTIZABAL ARBOLEDA

DISTRIBUIÇÃO DEMOGRÁFICA E CLINICOPATOLÓGICA DOS TUMORES MALIGNOS DE CABEÇA E PESCOÇO EM PACIENTES PEDIÁTRICOS DE UMA INSTITUIÇÃO BRASILEIRA: ESTUDO RETROSPECTIVO

DEMOGRAPHIC AND CLINICOPATHOLOGIC DISTRIBUTION OF HEAD AND NECK MALIGNANT TUMORS IN PEDIATRIC PATIENTS FROM A BRAZILIAN INSTITUTION: A RETROSPECTIVE STUDY

Dissertação apresentada à Faculdade de Odontologia de Piracicaba da Universidade Estadual de Campinas como parte dos requisitos exigidos para a obtenção do título de Mestra em Estomatopatologia, na Área de Patologia.

Dissertation presented to the Piracicaba Dental School of the University of Campinas in partial fulfillment of the requirements for the degree of Master in Stomatopathology, in Pathology area.

Orientador: Prof. Dr. Alan Roger dos Santos Silva

Este exemplar corresponde a versão final da dissertação defendida pela aluna Lady Paola Aristizabal Arboleda e orientada pelo Prof. Dr. Alan Roger dos Santos Silva

Piracicaba

2018

Agência(s) de fomento e nº(s) de processo(s): CAPES, 33003033009P4

Ficha catalográfica
Universidade Estadual de Campinas
Biblioteca da Faculdade de Odontologia de Piracicaba
Marilene Girello - CRB 8/6159

Ar45d

Aristizabal-Arboleda, Lady Paola, 1992-
Distribuição demográfica e clinicopatológica dos tumores malignos de cabeça e pescoço em pacientes pediátricos de uma instituição brasileira : estudo retrospectivo / Lady Paola Aristizabal Arboleda. – Piracicaba, SP : [s.n.], 2018.

Orientador: Alan Roger dos Santos Silva.
Dissertação (mestrado) – Universidade Estadual de Campinas, Faculdade de Odontologia de Piracicaba.

1. Neoplasias de cabeça e pescoço. 2. Câncer em crianças. 3. Câncer. 4. Adolescentes. I. Santos-Silva, Alan Roger, 1981-. II. Universidade Estadual de Campinas. Faculdade de Odontologia de Piracicaba. III. Título.

Informações para Biblioteca Digital

Título em outro idioma: Demographic and clinicopathologic distribution of head and neck malignant tumors in pediatric patients from a brazilian institution : a retrospective study
Palavras-chave em inglês:
Head and neck neoplasms
Cancer in children
Cancer
Adolescents
Área de concentração: Patologia
Titulação: Mestra em Estomatopatologia
Banca examinadora:
Alan Roger dos Santos Silva [Orientador]
Fábio de Abreu Alves
Regina Maria Holanda de Mendonça
Data de defesa: 22-02-2018
Programa de Pós-Graduação: Estomatopatologia

UNIVERSIDADE ESTADUAL DE CAMPINAS
Faculdade de Odontologia de Piracicaba

A Comissão Julgadora dos trabalhos de Defesa de Dissertação de Mestrado, em sessão pública realizada em 22 de Fevereiro de 2018, considerou a candidata LADY PAOLA ARISTIZABAL ARBOLEDA aprovada.

PROF. DR. ALAN ROGER DOS SANTOS SILVA

PROF. DR. FÁBIO DE ABREU ALVES

PROFª. DRª. REGINA MARIA HOLANDA DE MENDONÇA

A Ata da defesa com as respectivas assinaturas dos membros encontra-se no processo de vida acadêmica do aluno.

“Come, my friends, ‘tis not too late to seek a newer world. We are not now that strength which in old days moved earth and heaven; that which we are, we are; one equal temper of heroic hearts, made weak by time and fate, but strong in will to strive, to seek, to find, and not to yield.”

Alfred Lord Tennyson

DEDICATÓRIA

Dedico este trabalho aos meus pais, Ezequiel Aristizabal e Marleny Arboleda pelo apoio e o amor incondicional. Obrigada por me dar a força e inspiração diária. À minha irmã Maria Fernanda, por ser a pessoa que me motiva cada dia, obrigada por tanto amor e paciência.

AGRADECIMENTOS

À Deus, por todas bênçãos concedidas diariamente, por guiar-me e por colocar pessoas tão especiais no meu caminho.

À Universidade Estadual de Campinas, na pessoa do Magnífico Reitor, Prof. Dr. Marcelo Knobel.

À Faculdade de Odontologia de Piracicaba, na pessoa de seu Diretor, Prof. Dr. Guilherme Elias Pessanha Henriques e seu Diretor Associado, Prof. Dr. Francisco Haiter Neto.

À Profa. Dra. Cínthia Pereira Machado Tabchoury, Coordenadora Geral da Pós-Graduação da Faculdade de Odontologia de Piracicaba.

Ao Coordenador do Programa de Pós-Graduação em Estomatopatologia, Prof. Dr. Marcio Ajudarte Lopes.

Ao CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior) pela concessão da bolsa para a realização dessa dissertação de Mestrado.

Ao meu orientador, Prof. Dr. Alan Roger dos Santos Silva, por sua ajuda, paciência e ensinamentos. Admiro muito sua competência, sua dedicação e comprometimento com meu crescimento profissional. Fico muito feliz e grata de ter tido a oportunidade de trabalhar e aprender com o senhor. Obrigada por se preocupar sempre pelo bem-estar dos estudantes e estar presente sempre que precisei.

À Dra. Regina Holanda de Mendonça, obrigada por me receber no Boldrini, fico muito feliz de ter tido a oportunidade de compartilhar e aprender com a senhora, admiro muito você como ser humano e profissional, já que além dos conhecimentos, você trabalha com muito amor. Obrigada por sua paciência, disponibilidade, ensinamentos e confiança no trabalho.

Á Dra. Iva Loureiro Hoffmann, por sua orientação, ensinamentos e ajuda, a senhora foi essencial para o desenvolvimento do trabalho. Obrigada por seu valioso tempo e por estar sempre presente quando precisei da senhora.

Ao equipe do SAME do Centro Infantil Boldrini que me proporcionou ajuda com a busca e fornecimento dos prontuários.

Ao Prof. Dr. Oslei Paes de Almeida, pelas oportunidades concedidas e por me motivar sempre a aprender. O senhor é um grande exemplo como profissional e como ser humano. Sempre serei muito grata por todo o apoio e os ensinamentos.

À Dra. Eliana Muñoz, por ser a pessoa que me motivou em continuar meu caminho profissional, pelos conselhos e ensinamentos. Obrigada por estar sempre presente nesta etapa acadêmica e pela confiança.

Ao professor Fábio Abreu Alves por aceitar ser membro da banca e se dispor a avaliar o nosso trabalho.

Aos Profs. Drs. das Áreas de Semiologia e Patologia da Faculdade de Odontologia de Piracicaba: Prof. Dr. Oslei Paes de Almeida, Márcio Ajudarte Lopes, Pablo Agustin Vargas, Ricardo Della Coletta, Edgard Graner e Jacks Jorge Júnior pelos ensinamentos durante esses dois anos de mestrado.

A todos os meus colegas de pós-graduação, cada um de vocês aportaram positivamente de maneira profissional e pessoal nestes dois anos de mestrado. Quero agradecer especialmente a Natália Palmier, Cristian Madrid, e Anna Araújo pelo apoio, disponibilidade, ensinamentos e ajuda no trabalho, vocês são pessoas especiais que admiro muito.

Agradeço aos meus amigos do Brasil e aos amigos estrangeiros, por estarem sempre presentes quando precisei, pelos ensinamentos profissionais e acadêmicos, por tornarem meus dias mais felizes, pelo apoio e momentos compartilhados. São coisas que lembrarei sempre com muito carinho. Fico muito grata e feliz por ter tido a oportunidade de conhecer cada um de vocês.

Agradeço aos meus amigos da Colômbia, vocês foram um grande apoio nesta etapa da minha vida, obrigada por todos os seus conselhos, a motivação e o amor. Quero agradecer especialmente à Katherine Gómez pelo apoio incondicional neste processo da minha vida e à Gloria Carmenza Alzate por suas sábias palavras e ensinamentos.

Agradeço, de forma especial, à Celeste Sanchez Romero. As palavras não são suficientes para expressar toda a minha gratidão. Você tornou-se como uma irmã para mim. Agradeço muito todos os ensinamentos acadêmicos, a motivação, o tempo compartilhado, a paciência e sua ajuda nesses dois anos. Admiro muito você e tenho certeza que todos os seus caminhos e planos serão abençoados. Você e o André são pessoas muito especiais para mim e serei eternamente grata por tudo.

Às minhas amigas Marisol Miranda e Florence Cuadra, admiro muito vocês como profissionais e, além disso, são pessoas de um coração gigante. Obrigada por estarem sempre presentes quando precisei de vocês, pela ajuda acadêmica, pelos conselhos e orientações. Sem dúvida aprendi muito com vocês. Desejo sempre muito sucesso e bênçãos.

A minha família, Ezequiel Aristizabal, Marleny Arboleda e Maria Fernanda Aristizabal, vocês são minha inspiração e minha força para continuar cada dia realizando meus sonhos. Apesar de estarmos tão longe, vocês sempre estão no meu coração. Fico eternamente grata por todo a apoio, amor, os ensinamentos, e a motivação que vocês me brindam. Amo muito vocês e tenho certeza que todo o esforço, a paciência e a dedicação terão sua recompensa. Todas as minhas conquistas são suas. Muito obrigada por tudo.

RESUMO

Mundialmente, o câncer representa uma das principais causas de morte entre crianças. A despeito do aprimoramento das modalidades de tratamentos do câncer, sua incidência continua a aumentar no âmbito da pediatria. Neste contexto, estudos demostraram que o câncer de cabeça e pescoço (CCP) corresponde a 12% dos casos; representado uma das topografias mais frequentemente afetadas pelo câncer pediátrico. Ademais, a literatura internacional relata que a região de cabeça e pescoço de pacientes pediátricos pode ser acometida por uma miríade de tumores malignos incluindo linfomas, rabdomiossarcomas, neuroblastomas, carcinomas de tireoide e de nasofaringe. Embora se reconheça que a frequência do CCP é influenciada por uma série de variáveis demográficas dos pacientes pediátricos, estudos epidemiológicos sobre o perfil clinicopatológico dos pacientes afetados por CCP na infância são escassos e, até o momento, não existem dados publicados em veículos científicos internacionais sobre esta problemática em pacientes da América Latina. Portanto, o objetivo deste estudo foi descrever a distribuição demográfica e clinicopatológica dos tumores malignos de cabeça e pescoço em pacientes de um centro brasileiro de referência no diagnóstico e tratamento do câncer infantil. Com essa finalidade, foram revisados retrospectivamente os prontuários médicos dos pacientes pediátricos (0 a 19 anos) diagnosticados com tumores malignos na região de cabeça e pescoço no Centro Infantil Boldrini, em Campinas (SP), registrados no período entre 1986 a 2016. Os diagnósticos anatomopatológicos e a localização dos tumores; o gênero, a idade e a raça dos pacientes foram as variáveis analisadas. Retinoblastomas e tumores do sistema nervoso central foram excluídos das análises deste estudo. No período de 30 anos, o CCP representou 5,11% de todas as malignidades; os tipos de câncer mais comuns foram linfomas, seguido de carcinomas e sarcomas. O linfoma de Burkitt, o linfoma de Hodgkin clássico tipo esclerose nodular, o carcinoma nasofaríngeo e o rabdomiossarcoma foram os diagnósticos histopatológicos mais comuns. Os principais sítios anatômicos afetados foram a região cervical e linfonodos, a nasofaringe e a glândula tireoide. A média de idade dos pacientes no momento do diagnóstico foi de 9,35 anos e os pacientes na faixa etária entre 10 a 14 anos apresentaram maior prevalência de tumores malignos. Foi identificada predominância pelo gênero masculino (65,67%) e pela raça branca (73,02%). Em suma, o presente estudo apresenta dados originais acerca do perfil demográfico e clinicopatológico de pacientes brasileiros pediátricos com CCP e sugere que os linfomas foram mais frequentes do que carcinomas e sarcomas.

Palavras-chave: câncer cabeça e pescoço, crianças, neoplasias, malignidades

ABSTRACT

Worldwide, cancer represents one of the main causes of death among children. Despite the improvement in cancer treatments modalities, its incidence continues to increase in the pediatric field. In this context, some studies showed that head and neck cancer (HNC) corresponds to 12% of cases; representing one of the most frequently topographies affected by pediatric cancer. In addition, the international literature reports that the head and neck region in pediatric patients may be affected by a myriad of malignant tumors including lymphomas, rhabdomyosarcomas, neuroblastomas, thyroid carcinoma and nasopharyngeal carcinomas. Although it is known that the HNC frequency is influenced by a series of demographic variables in pediatric patients, epidemiological studies on the clinicopathological profile of HNC patients in childhood are scarce and, to date, there are no published data in the international literature regarding Latin American patients. Therefore, the aim of this study was to describe the demographic and clinicopathological distribution of malignant head and neck tumors in patients from a Brazilian reference center in the diagnosis and treatment of childhood cancer. Hence, the medical records of pediatric patients (0 to 19 years old) diagnosed with malignant tumors in the head and neck region of the Boldrini Children's Center, Campinas (SP), were registered retrospectively between 1986 and 2016. Variables such as histopathological diagnoses and the location of the tumors; gender, age and patient race were analyzed. Retinoblastomas and tumors of the central nervous system were excluded from analysis of the current study. In a 30 years period, the HNC represented 5.11% of all malignancies; lymphomas were the most common type of cancer, followed by carcinomas and sarcomas. Burkitt lymphoma, nodular sclerosis Hodgkin lymphoma, nasopharyngeal carcinoma, and rhabdomyosarcoma were the most common histopathological diagnoses. The main anatomical sites affected were the cervical region and lymph nodes, the nasopharynx and the thyroid gland. At the moment of diagnosis, the mean age of the patients was 9.35 years, and the group aged from 10 to 14 years had a higher prevalence of malignant tumors. It was identified a slight predominance on male (65.67%) and white (73.02%) patients. In summary, the present study showed original data about the demographic and clinicopathological profile of Brazilian pediatric patients with HNC, and suggested that lymphomas are more frequent than carcinomas and sarcomas.

Key words: head and neck cancer, children, tumors, malignancies

SUMÁRIO

1. INTRODUÇÃO..... 13

2. ARTIGO: DEMOGRAPHIC AND CLINICOPATHOLOGIC DISTRIBUTION OF HEAD AND NECK MALIGNANT TUMORS IN PEDIATRIC PATIENTS FROM A BRAZILIAN POPULATION: A RETROSPECTIVE STUDY……...……. 17

3. CONCLUSÃO…….....…...…… 41

REFERENCIAS*…… 42

ANEXO 1 – Certificado do Comitê de Ética em Pesquisa..... 46

ANEXO 2 – Certificado de submissão do artigo 49

1. INTRODUÇÃO

O câncer representa a segunda causa mais frequente de óbito entre crianças nos Estados Unidos, superada apenas pelos acidentes (Siegel et al., 2017). Neste campo, o avanço das terapias antineoplásicas permitiu observar aumentos substanciais nas taxas de sobrevida para a maioria dos tipos de câncer pediátrico (Linabery et al., 2008), fato que foi validado por análises realizadas nos períodos de tempo entre os anos de 1975 a 1977 e 2007 a 2010, onde constatou-se que a mortalidade global diminuiu 52% entre os pacientes pediátricos com câncer; com declínio significativo demonstrado para vários tipos de câncer. Apesar disso, aproximadamente 2.000 mortes por câncer ainda ocorrem anualmente entre crianças nos Estados Unidos (Siegel et al., 2017). A diminuição da mortalidade não está, contudo, relacionada com a incidência, uma vez que vários estudos epidemiológicos demostraram o aumento do número de tumores malignos neste segmento da população (Ries et al., 1999 ; Ward et al., 2014 ; Smith et al., 2014; Siegel et al., 2017). A título de exemplo, um estudo retrospectivo apontou aumento de 38% na incidência dos tumores malignos em crianças menores de 15 anos comparando dois períodos de tempo ; 1973-1975 e 2007-2009 (Schwartz et al., 2015).

Dados epidemiológicos relacionados ao Brasil apresentaram resultados similares, sendo o câncer pediátrico a principal doença relacionada a óbitos em crianças. No ano de 2013, o Instituto Nacional do Câncer (INCA) estimou a ocorrência de 2.800 óbitos por câncer em crianças. Para o ano de 2016, as estimativas do INCA para ocorrência de novos casos de câncer em crianças foram de 12.600 casos (INCA, 2016). Aparentemente, países desenvolvidos apresentam melhores taxas de sobrevida para os pacientes pediátricos com câncer quando comparados com os países em desenvolvimento (Braga et al., 2002; Howell et al., 2007).

O câncer pediátrico é considerado uma doença que possui grandes diferenças em termos de fatores de risco e biologia tumoral. Portanto, é imperioso estudar a problemática do câncer em crianças de modo independente do câncer em adultos, sobretudo, para poder levar em consideração as peculiaridades das neoplasias nesta faixa etária, já que eles apresentam uma grande variação no comportamento clínico (agressividade), fisiopatológico e, consequentemente, nos padrões de resposta ao tratamento oncológico (INCA, 2008).

A Classificação Internacional do Câncer na Infância (CICI), divide por categorias os diferentes tipos de câncer que ocorrem nos pacientes pediátricos tomando por base a

histopatologia, a topografia acometida pelo tumor e o comportamento clínico do tumor. Neste sistema, os tumores malignos da infância são classificados em leucemias, doenças mieloproliferativas e mielodisplásicas; linfomas e neoplasias reticuloendoteliais; tumores do sistema nervoso central (SNC), miscelânea de neoplasias intracranianas e intraespinhais; neuroblastomas e outros tumores de células nervosas periféricas; retinoblastoma; tumores renais; tumores hepáticos; tumores ósseos; tumores de tecidos mole e outros sarcomas extra-ósseos; tumores de células germinativas, tumores trofoblásticos, e neoplasias gonadais; outras neoplasias epiteliais e melanomas; e outras neoplasias malignas não especificadas (Steliarova-Foucher et al., 2005).

Nos Estados Unidos, um estudo baseado no programa de Vigilância, Epidemiologia e Resultados (SEER) aponta que as leucemias representam –em termos gerais– o tipo de câncer mais comum (29%), seguido dos tumores do SNC (26%) e linfomas (11%). Quando separado por grupo de idades, para as crianças entre 0-14 anos as neoplasias mais frequentes são leucemias, tumores do SNC, linfomas, sarcomas de tecido mole, neuroblastoma e tumores renais. Nos pacientes de 15-19 anos, os linfomas representam as neoplasias mais frequentes, seguido de tumores do SNC, leucemia, tumores de células germinativas, câncer de tireoide e melanoma (Siegel et al., 2017). De modo semelhante, no Brasil, apesar do baixo número de estudos nesta linha, o tipo de câncer mais comum em crianças é representado pelas leucemias (18-41%), linfomas (13-24%), e tumores do SNC (7-17%) (Reis et al., 2007; De Camargo et al., 2010).

Vários fatores genéticos e ambientais têm sido estabelecidos no desenvolvimento do câncer pediátrico, entretanto, a etiologia de muitos tipos de câncer da infância ainda permanece desconhecida (Stiller, 2004). Neste sentido, o conhecimento da prevalência de neoplasias associadas às características demográficas como idade, gênero e raça numa população determinada, pode auxiliar na busca de possíveis fatores de risco para o câncer. A título de exemplo, vários estudos relataram que a incidência do carcinoma de tireoide aumenta em crianças do sexo feminino após os 12 anos de idade (Albright et al., 2002; Siegel et al., 2014), dado que pode direcionar investigações clínicas (busca ativa) e pesquisas específicas acerca da etiologia desta malignidade nesta subpopulação pediátrica. Adicionalmente, as diferenças raciais podem representar fatores importantes na incidência dos tumores pediátricos (Gurney et al., 1995; Cesmebasi et al., 2014).

O câncer de cabeça e pescoço (CCP) é considerado a sexta neoplasia maligna mais comum na população mundial e refere-se a um grupo de tumores que acomete uma série

de estruturas ou tecidos de regiões anatômicas como a cavidade oral (lábios, mucosas jugais, língua, assoalho bucal, palato duro, gengivas e trígonos retromolares); a faringe (orofaringe, nasofaringe e hipofaringe); a laringe (laringe supraglótica, cordas vocais e laringe subglótica); a cavidade nasal e os seios paranasais (seios maxilares, seio etmoidal, seio esfenoidal e seios frontais); e as glândulas salivares maiores (submentonianas, submandibulares e parótidas) e menores, entre outros. Contudo, casos de tumores extensos tornam-se complexos de serem classificados devido ao acometimento simultâneo de diferentes topografias (Huber & Terezhalmy, 2003; Duvvuri & Myers, 2009; Matzinger et al., 2009).

Estima-se que 10% dos tumores malignos da população pediátrica se desenvolva na região de cabeça e pescoço. Interessantemente, evidências científicas demostraram aumento da frequência do CCP na infância quando comparado a tumores malignos de outras topografias do corpo. Os autores que publicaram os resultados supramencionados identificaram um aumento de 35% na prevalência de casos de câncer pediátrico de cabeça e pescoço (CPCP) durante o período de tempo compreendido entre os anos de 1975 e 1996 (Albright, 2002). Schwartz et al., (2015) também constataram que a prevalência do CPCP aumentou de modo significativo nos períodos de tempo entre os anos de 1973-1975 e 2007-2009.

A despeito da carência de estudos delineando o perfil demográfico e clinicopatológico dos pacientes diagnosticados com CPCP, a maior parte dos trabalhos já publicados neste contexto sugere que os linfomas representam o tipo de câncer mais prevalente (incluindo linfomas não Hodgkin e linfomas Hodgkin), seguido por rabdomiossarcomas (RMS), carcinomas de tireoide, carcinomas de nasofaringe, carcinoma de glândulas salivares, e neuroblastomas (Jaffe et al., 1973; Cunningham et al., 1987; Robinson et al., 1988; Albright et al., 2002; Gosepath J et al., 2007; Sengupta et al., 2009; Khademi et al., 2009; Das et al., 2011; Omoregie et al., 2014; Schwartz et al., 2015). Adicionalmente, estudos no campo do CPCP sugeriram que as topografias mais frequentemente afetadas foram a região cervical, a glândula tireoide, os seios paranasais, a mandíbula, a nasofaringe, a glândula parótida, a língua, as glândulas salivares menores, e a órbita. Os sítios primários mais raramente afetados pelo CPCP foram o ouvido médio, o ouvido externo, a laringe, e o espaço parafaríngeo (Rapidis et al., 1988; Albright et al., 2002; Ajayi et al., 2007; Khademi et al., 2009; Cesmebasi et al., 2014; Levi et al., 2017).

Tendo em vista o conteúdo exposto, existe uma notória preocupação com o aumento do número de casos de câncer na infância, sobretudo, dos casos de CPCP. Este

cenário se torna ainda mais complexo pelo fato do diagnóstico precoce representar um dos maiores desafios no contexto do tratamento e da sobrevida das crianças com câncer. Por consequência, uma série de políticas internacionais em saúde pública foi desenvolvida a fim de alertar profissionais da saúde e familiares quanto aos sinais e sintomas mais frequentemente associados ao desenvolvimento do câncer infantil (Ward et al., 2014).

Portanto, o objetivo deste estudo foi descrever a distribuição demográfica dos pacientes diagnosticados com CPCP e o perfil clinicopatológico dos tumores malignos de cabeça e pescoço em pacientes de um centro brasileiro de referência no diagnóstico e tratamento do câncer infantil.

2. ARTIGO: Demographic and clinicopathologic distribution of head and neck malignant tumors in pediatric patients from a Brazilian population: a retrospective study

Artigo submetido ao periódico Journal of Oral Pathology & Medicine (Anexo 2)

Authors: Lady Paola Aristizabal Arboleda[1], Iva Loureiro Hoffmann[2], Izilda Aparecida Cardinalli[2], Alan Roger Santos-Silva[1], Regina Maria Holanda de Mendonça[1,2]

Affiliation: (1) Department of Oral Diagnosis, Piracicaba Dental School, University of Campinas, Brazil; (2) Boldrini Children's Center, Brazil.

Short Title: Pediatric head and neck cancer distribution

Key Words: Children; Malignancies; Neoplasms, Head and Neck

Corresponding Author:

Alan Roger Santos-Silva

Oral Diagnosis Department

Piracicaba Dental School, University of Campinas (UNICAMP)

Av. Limeira, 901. Areão, Piracicaba, São Paulo – Brazil

Postal code: 13414- 903

Phone number: +55 (19) 2106 5320

E-mail: alan@unicamp.br

Abstract

Background: The incidence of pediatric head and neck cancer (PHNC) is increasing worldwide, especially when compared with childhood cancer in general. However, there is still a lack of knowledge about the demographic profile of such patients across the globe. Therefore, the aim of this study was to describe demographic, topographic and histopathological features of pediatric head and neck cancer patients from a single Brazilian institution. **Methods:** Medical records were retrospectively reviewed for all cancer cases diagnosed from 1986 to 2016 affecting patients aged 19-years and younger. The demographic variables (age, gender, race), topographic aspects of primary tumors, and histopathological diagnoses were collected and analyzed by descriptive statistics. **Results:** three hundred and sixty-seven (5.11%) head and neck malignant tumors were found among 7,181 pediatric cancers diagnosed in this period. Mean age at diagnosis was 9.35 years with male (65.67%) predominance. Patients between the age group of 10 to 14 years presented the higher prevalence of malignant tumors. In terms of race, 73.02% of the patients were white and 9.54% were black. The main affected anatomical site was the neck and lymph nodes (41.42%), followed by nasopharynx (22.89%) and thyroid gland (6.54%). The most common cancer type was lymphoma (52.86%), followed by carcinoma (22.89%), and sarcoma (19.07%). Burkitt lymphoma, nodular sclerosis Hodgkin lymphoma, nasopharyngeal carcinoma, and rhabdomyosarcoma were the most common histopathological diagnoses (16.62%, 13.08%, 12.81% and 12.81%, respectively). **Conclusion:** The current study originally demonstrated that lymphomas may be more frequent than carcinomas and sarcomas in Brazilian PHNC patients.

Keywords: Children; Malignancies; Neoplasms; Head and Neck

Introduction

Cancer represents a significant cause of mortality in children worldwide.[1] Head and neck cancer (HNC) is the sixth most common type of cancer around the world,[2-3] and represents up to 12% of all malignant tumors that affect pediatric population.[4] Currently, the survival rates have increased due to treatments improvement,[5] as well as easier access to health services and awareness of the need of treatment. Nevertheless, the incidence of pediatric head and neck cancer (PHNC) is increasing significantly overall when compared with childhood cancer in general,[4] which should alert health service professionals. However, Schwartz et al.[6] provided an update on the epidemiology of PHNC in USA, offering a direct comparison of current trends with those reported by Albright et al.[4] They demonstrated that despite the increased incidence between 1973 and 2009, the proportion of HNC cancers to all cancers in the pediatric population has remained stable.[6]

A review of the English-language literature about PHNC suggests that the most common types of cancer were lymphomas [including non-Hodgkin lymphomas (NHL) and Hodgkin lymphomas (HL)], followed by rhabdomyosarcomas (RMS), thyroid carcinoma (TC), nasopharyngeal carcinoma (NC), salivary gland malignancies (SGM), and neuroblastomas.[4,7-9]

Only very limited data are available in the literature regarding the incidence of PHNC worldwide.[9] In Brazil, there are epidemiological studies regarding pediatric general cancer showing that the most prevalent types are leukemia, followed by lymphoma and central nervous system (CNS) tumors.[10] To date, only a few studies of cancer distribution were performed for certain specific head and neck topographies, such as the oral cavity and maxillofacial tumors[11,12] however, the clinicopathological distribution of PHNC is largely unknown in Latin American patients. Hence, a deeper comprehension of this issue will serve

as a base to adopt a faster and earlier diagnose, which might improve access to prompt treatment, quality of life and survival rates among PHNC patients.

Therefore, the aim of this study was to describe demographic characteristics and the clinicopathologic distribution of head and neck malignant tumors in pediatric patients from a Brazilian population.

Material and Methods

This study was approved by the ethics committee of Boldrini Center (protocol number 1.947.295). The medical records of the Boldrini Children's Center, Campinas, São Paulo, Brazil, were reviewed for all primary head and neck malignant tumors diagnosed in pediatrics patients from January 1986 to December 2016. The demographic variables (age, gender and race), topographic location of tumors, and histopathologic diagnosis were collected. The age cut of 19 years was used following the definition of childhood provided by the World Health Organization (WHO),[13] and then it was categorized into five groups: < 1 year, 1 to 4 years, 5 to 9 years, 10 to 14 years and 15 to 19 years.[9] In addition, patient's race was classified as white, black and other (brown, yellow).

All tumors were grouped and classified according to the 4th edition of the World Health Organization (WHO) Classification of Head and Neck Tumours[14] and the following categories were considered: nasal cavity, paranasal sinuses and skull base; nasopharynx; parapharyngeal space; oral cavity and mobile tongue; oropharynx (base of tongue, tonsils, adenoids); neck and lymph nodes; salivary glands; odontogenic and maxillofacial bone; and the ear. Tumors of the skin, thyroid gland and orbit were also included in this study.

Inclusion criteria included primary solid tumors in the head and neck region diagnosed in patients 19-years-old and younger presenting complete medical records with confirmed histopathological diagnoses. Benign tumors, malignant tumors diagnosed outside

the head and neck region, second primary tumors and metastases affecting the head and neck region, tumors diagnosed in patients older than 19 years old, and patients with incomplete medical records were excluded from the analyses. Tumors affecting the central nervous system (CNS) and retinoblastomas were also excluded specifically.[9]

Data were collected in a datasheet, systematically organized in Microsoft Office Excel 2013 software (Microsoft Corporation, Redmond, Washington, USA) and further analyzed by descriptive statistics by using absolute numbers, percentages, mean values and standard deviations.

Results

During a 30-year period (from 1986 to 2016), 7,181 malignant tumors were diagnosed at Boldrini Children's Center among patients younger than 19 years, of which 367 (5.11%) were located in the head and neck region. Twenty patients with incomplete medical records were excluded from the analyses. Nine hundred and twenty-nine (12.94%) cases of CNS tumors and 251 (3.50%) retinoblastomas were diagnosed in this period and excluded from analyses. The mean age at diagnosis was 9.35 ± 4.78 years. Analysis by gender showed that 241 (65.67%) patients were males whereas 126 (34.33%) were females. **Figure 1** shows patterns of gender distribution according to age groups in studied PHNC patients. In terms of race, 268 (73.02%) were white, 59 (16.08%) were 'other races', 35 (9.54%) were black, and 5 (1.36%) were not available. PHNC cases were most frequently diagnosed among patients between 10 to 14 years [131 (35.69%)], followed by patients aged 5 to 9 years [106 (28.88%)]; 1 to 4 years [64 (17.44%)]; 15 to 19 years [55 (14.99%)], and younger than 1 year [11 (3.00%)].

The most common cancer type was lymphomas [194 (52.86%)], followed by carcinomas [84 (22.89%)], and sarcomas [70 (19.07%)]. The less frequent cases were

embryonal malignant tumors [10 (2.72%)], melanomas [5 (1.36%)], and germ cells malignant tumors [3 (0.82%)]. Burkitt lymphoma (BL) [61 (16.62%)], nodular sclerosis HL [48 (13.08%)], NC [47 (12.81%)], and RMS [47 (12.81%)], were the most common histopathological diagnoses. Mixed cellularity HL [25 (6.81%)], papillary thyroid carcinoma (PTC) [17 (4.63%)], and diffuse large B-cell lymphoma (DLBCL) [17 (4.63%)] were also prevalent cancers among studied patients. **Table 1** shows main data regarding age, gender, tumor type and histopathological subtypes distribution.

The neck and lymph nodes was the leading site category [152 (41.42%)], with nodular sclerosis HL [45 (12.26%)], mixed cellularity HL [25 (6.81%)] and BL [24 (6.24%)] representing the most common tumor subtypes that affected this topography. Nasopharynx was the second most frequently affected topographic site [84 (22.89%)], where NC [47 (12.81%)] and RMS [16 (4.36%)] were the most prevalent diagnoses. Tumors located in the thyroid gland represented the third most affected topography site [24 (6.54%)], in which PTC [17 (4.63%)] and follicular carcinoma [4 (1.09%)] were the most frequently tumors. Tumors of the parapharyngeal space [5 (1.36%)], ear [4 (1.09%)] and skin attachments (scalp) [3 (0.82%)] constituted less frequently affected topographies. The topographic distribution of PHNC is summarized in **table 2.**

Table 3 shows the histopathological subtypes distribution per tumor topography. RMS was the tumor subtype that presented the largest distribution in terms of topography, affecting the nasopharynx [16 (4.36%)], the nasal cavity and maxillary sinuses [7 (1.9%)], orbit [4 (1.09%)] and parapharyngeal space [4 (1.09%)] more often. Cervical region [3 (0.82%)], ear [3 (0.82%)], and oral cavity and mobile tongue [2 (0.54%)] constituted less frequently affected topographies by RMS.

Table 4 shows the most common head and neck malignancies per age group. The group of patients younger than 1-year-old was more affected by malignant embryonal tumors

and sarcomas, among them, neuroblastoma [2 (0.54%)], undifferentiated sarcoma [2 (0.54%)], and infantile fibrosarcoma [1 (0.27%)] were the most common. Patients aged 1 to 4 years were more frequently affected by RMS [21 (5.72%)], followed by BL [16 (4.36%)], and nodular sclerosis HL [5 (1.36%)]. Patients aged 5 to 9 years were more frequently affected by BL [22 (5.99%)], nodular sclerosis HL [15 (4.09%)], and RMS [14 (3.81%)]. In the group aged 10 to 14 years, NC [23 (6.27%)] was the most common tumor followed by nodular sclerosis HL [22 (5.99%)], and BL [17 (4.63%)]. In patients among 15 to 19 years, NC corresponded to the leading diagnosis [15 (4.09%)], followed by BL [6 (1.63%)] and nodular sclerosis HL [6 (1.63%)].

Discussion

This seems to be the first study in the English-related literature describing demographic and clinicopathologic patterns of HNC in pediatric patients from a Latin American population. In the current study, PHNC accounted for 5.11% of all malignancies diagnosed in a period of 30 years, which represents a relatively low prevalence when compared to similar previously published studies.[4,6,9,15] Other retrospective studies performed in single institutions from Iran, Nigeria and USA[8,16-17] presented lower percentages to ours **(Table 5)**. Likewise, Levi et al.[18] conducted a large study through the National Cancer Registry databases in Israel, where they found a percentage of 2.6% over a 41-years period, showing that despite the difference in number of cases and time studied, the results showed a low prevalence.

The present study was composed of children from 0 to 19 years old and the mean age at the time of HNC diagnosis was 9.35 years, similarly to several other studies, which used the same age group and found mean ages ranging from 10 to 11 years.[4,19-20] The main reason for classifying patients in five age groups in this and other published studies was the known

prevalence of specific tumors at certain ages.[9] In this sense, patients between the ages of 10 to 14 years were more affected by HNC (35,69%); similar percentages in this age group were found in another study, nonetheless, for them the peak incidence was observed in children from 15 to 19 years (34.2%).[15] The lack of standardization with respect to the age cut among previously published studies on PHNC limited more accurate discussion of our results.

In terms of association between age groups and the histopathologic diagnoses, we observed similar results to others studies. All neuroblastomas from the current study affected patients younger than one year, which differs to other series where it was more frequent in the group of 1 to 4 years and between 5 to 9 years;[21-23] however, they were not found in patients in the second decade, which suggests a higher incidence in younger patients. We observed that the highest frequency of RMS was diagnosed in patients with 1 to 4 years (5.72%), which is in accordance with other studies.[20,22] BL was the leading histopathologic diagnoses in the group of 5 to 9 years (5.99%), similarly to the results of Ajayi et al.[16] Nodular sclerosis HL was found with a high percentage (5.99%) in the group of 10 to 14 years, which is in agreement with other studies demonstrating that this tumor is more prevalent in patients older than 10 years.[1,4] Carcinomas were rarely diagnosed in patients in the first decade of life, however, as the age increased they became more frequent, being NC and PTC predominantly seen in patients aged between 10 to 14 and 15 to 19 years - these results are in accordance with previous published studies.[11,16-17,21]

Overall, pediatric male patients presented a higher prevalence of HNC than female patients (65.67% *versus* 34,33%, respectively); this finding was also reported in most of the previously published studies.[4,7,9,16,22,24-25] Male patients were most affected in the group of 10 to 14 years, especially due to the high prevalence of lymphomas, nevertheless, similarly to Gosepath et al.[9], we found that females were more affected by thyroid carcinoma in this same age group.

PHNC was most prevalent among white patients, probably because our study was performed in a geographic region where the white population predominates. This result was similar to other published studies[26-27]; nonetheless, one of these studies noted that NC showed a strong prevalence in black patients and other ethnic populations[26], which was not the case of the present study.

Lymphomas represented the most common PHNC type in the present sample. Remarkably, our study is in line with most of the pertinent results found in the literature, in which lymphomas showed high prevalence among PHNC patients.[7,8,15-16,18-19,22,24-25] Most of these studies were performed in Asiatic and African countries where genetic and geographic factors may be attributed to the higher incidence of lymphomas,[19] however, other studies conducted in USA also showed that lymphomas were the most common type of PHNC.[17,21,23]

Although carcinomas are mostly seen in adults, they represented the second most common PHNC type in the current study, which is considered uncommon but was also observed in two other published studies on pediatric cancer patients.[7,28] Sarcomas, in turn, constituted the third most frequently PHNC, which differs from Gosepath et al.[9] who observed this as the major type of PHNC.

NHL, specifically BL, was the main histopathological subtype of cancer in the present study, followed by nodular sclerosis HL, NC and RMS. In agreement with our results, other studies showed that NHL are more common than HL in the head and neck region of pediatric patients, indicating that BL may be the most frequent histopathological subtype of pediatric lymphomas.[7,15,19,24-25] Conversely, three studies conducted in the USA showed that HL may represent the main PHNC.[17,21,23] NC was observed in three previously published studies among the 'top 3' PHNC, which means it's a frequent diagnosis.[7,24,28] Similarly to the present results, RMS was among the first three tumor subtypes in several studies, including two publications suggesting that they corresponded to the main cancer subtype.[9,20] These

results confirmed that RMS continues to be one of the most prevalent PHNC types worldwide, affecting several head and neck topographies.

There is controversy and lack of standardization to define which anatomic topographies should be included in HNC studies, which difficult the comparison among published results. In order to minimize this complex scenario, the sample of the present study was classified according to the most recent edition (4th) of the WHO Classification of Head and Neck Tumours.[14] The neck and lymph nodes represented the main (41.42%) affected topography in the current study, where lymphomas were the most common tumor types, which is in accordance with previously published studies[8,15,17,21,22,24] Moreover, other studies also reported RMS, neuroblastoma and squamous cell carcinoma (SCC) in the neck region of children.[7,8,22,23] Some other studies considered the neck and its adjacent structures, such as the thyroid gland, as one topographic category; for this reason they observed higher percentages of cancer in this particular anatomic site.[4,21]

The second most affected topography was nasopharynx (22.89%), where NC, RMS and BL were the most common tumor types, which is in accordance with two previously published studies.[18,23] In other PHNC studies, nasopharyngeal malignancies represented the second and the third most commonly affected sites.[4,9,15,17,21,28]

In the current series, the thyroid gland was the third most affected topography (6.54%), which was considerably less involved than the studies of Albright et al.[4] (22.06%), Gosepath et al.[9] (28.2%) and Das et al.[28] (29.4%). The PTC represented the most common histopathological subtype in all of the above-mentioned studies, including ours.[4,9,28]

The main limitation of the present study, apart from its retrospective nature, is the fact that it was based on the experience of a single Brazilian institution, in São Paulo State. However, these results may accurately represent other states of the country and should be considered representative, at the national level, in terms of the epidemiological reality of the

entire country, especially because ‘Boldrini Children’s Center’ is the biggest pediatric onco-hematology hospital in Brazil, providing medical assistance for patients of the entire country.

In summary, this study is considered original in the context of Latin American pediatric cancer patients. Remarkably, it demonstrated a low prevalence of HNC and great diversities in terms of demographic and clinicopathologic aspects. Lymphomas, most specifically NHL, were the most common type of HNC among Brazilian pediatric patients. Considering that cancer represents one of the main causes of pediatric mortality worldwide, and that the incidence of this disease seems to be increasing in the head and neck region[29], the knowledge provided by the current study may be key to guide future studies on PHNC and to generate new strategies in terms of health policies for pediatric populations.

References

1. Ward E, DeSantis C, Robbins A, Kohler B, Jemal A. Childhood and adolescent cancer statistics, 2014. CA Cancer J Clin. 2014;64(2):83-103.

2. Huber MA, Terezhalmy GT. The head and neck radiation oncology patient. Quintessence Int. 2003;34(9):693-717.

3. Duvvuri U, Myers JN. In Brief. Current Problems in Surgery. 2009;46(2):114-117.

4. Albright JT, Topham AK, Reilly JS. Pediatric head and neck malignancies: US incidence and trends over 2 decades. Arch Otolaryngol Head Neck Surg. 2002;128(6):655-9.

5. Linabery AM, Ross JA. Childhood and adolescent cancer survival in the US by race and ethnicity for the diagnostic period 1975-1999. Cancer. 2008;113(9):2575-2596.

6. Schwartz I, Hughes C, Brigger MT. Pediatric head and neck malignancies: incidence and trends, 1973-2010. Otolaryngol Head Neck Surg. 2015;152(6):1127-1132.

7. Sengupta S, Pal R, Saha S, Bera SP, Pal I, Tuli IP. Spectrum of head and neck cancer in children. J Indian Assoc Pediatr Surg. 2009;14(4):200-3.

8. Fattahi S, Vosoughhosseini S, Moradzadeh Khiavi M, Mahmoudi SM, Emamverdizadeh P, Noorazar SG, et al. Prevalence of Head and Neck Tumors in Children under 12 Years of Age Referred to the Pathology Department of Children's Hospital in Tabriz during a 10-year Period. J Dent Res Dent Clin Dent Prospects. 2015;9(2):96-100.

9. Gosepath J, Spix C, Talebloo B, Blettner M, Mann WJ. Incidence of childhood

cancer of the head and neck in Germany. Ann Oncol. 2007; 18(10):1716-1721.

10. de Camargo B, de Oliveira Santos M, Rebelo MS, de Souza Reis R, Ferman S, Noronha CP, Pombo-de-Oliveira MS. Cancer incidence among children and adolescents in Brazil: first report of 14 population-based cancer registries. Int J Cancer. 2010;126(3):715-720.

11. Almeida JA, Oliveira LV, Alves CN, Frenzel L, Carvalho A, Costac NL, et al. A multicenter study of malignant oral and maxillofacial lesions in children and adolescents. Oral Oncology. 2017;75:39-45.

12. Ataíde AP, Fonseca FP, Santos Silva AR, Jorge Júnior J, Lopes MA, Vargas PA. Distribution of oral and maxillofacial lesions in pediatric patients from a Brazilian southeastern population. Int J Pediatr Otorhinolaryngol. 2016; 90:241-244.

13. Diane S, Sheri F, Eudice G, Norman G, Karen ML, Douglas M et al. Age limits and adolescents. Paediatr Child Heal. 2003; 8(9):577.

14. El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ. WHO Classification of Head and Neck Tumours. WHO/IARC Classification of Tumours; 2017.

15. Khademi B, Taraghi A, Mohammadianpanah M. Anatomical and histopathological profile of head and neck neoplasms in Persian pediatric and adolescent population. Int J Pediatr Otorhinolaryngol. 2009; 73(9):1249-1253.

16. Ajayi OF, Adeyemo WL, Ladeinde AL, Ogunlewe MO, Omitola OG, Effiom OA, et al. Malignant orofacial neoplasms in children and adolescents: A clinicopathologic review of cases in a Nigerian tertiary hospital. Int J Pediatr Otorhinolaryngol. 2007; 71(6):959-963.

17. Rapidis AD, Economidis J, Goumas PD, Langdon JD, Skordalakis A, Tzortzatou F, Anagnostopoulos D, Matsaniotis N. Tumours of the head and neck in children. A clinico-pathological analysis of 1,007 cases. J Craniomaxillofac Surg. 1988;16(6):279-286.

18. Levi S, Zini A, Fischman S, Czerninski R. Epidemiology of oral, salivary gland and pharyngeal cancer in children and adolescents between 1970 and 2011. Oral Oncol. 2017; 67:89-94.

19. Aregbesola SB, Ugboko VI, Akinwande JA, Arole GF, Fagade OO. Orofacial tumours in suburban Nigerian children and adolescents. Br J Oral Maxillofac Surg. 2005;43(3):226-231.

20. Al-Khateeb T, Al-Hadi Hamasha A, Almasri NM. Oral and maxillofacial tumours in north Jordanian children and adolescents: a retrospective analysis over 10 years. Int J Oral Maxillofac Surg. 2003;32(1):78-83.

21. Cunningham MJ, Myers EN, Bluestone CD. Malignant tumors of the head and neck in children: a twenty-year review. Int J Pediatr Otorhinolaryngol. 1987; 13(3):279-292

22. Robinson LD, Smith RJ, Rightmire J, Torpy JM, Fernbach DJ. Head and neck malignancies in children: an age-incidence study. Laryngoscope. 1988;98(1):11-13.

23. Jaffe BF. Pediatric head and neck tumors: a study of 178 cases. Laryngoscope. 1973;83(10):1644-1651.

24. Abdulai AE, Nuamah IK, Gyasi R. Head and neck tumours in Ghanaian children. A 20 year review. Int J Oral Maxillofac Surg. 2012;41(11):1378-1382.

25. Elarbi M, El-Gehani R, Subhashraj K, Orafi M. Orofacial tumors in Libyan children and adolescents. A descriptive study of 213 cases. Int J Pediatr Otorhinolaryngol. 2009; 73(2):237-242.

26. Cesmebasi A, Gabriel A, Niku D, Bukala K, Donnelly J, Fields PJ, Tubbs RS, Loukas M. Pediatric head and neck tumors: an intra-demographic analysis using the SEER* database. Med Sci Monit. 2014; 20:2536-2542.

27. Gurney JG, Severson RK, Davis S, Robison LL. Incidence of cancer in children in the United States. Sex-, race-, and 1-year age-specific rates by histologic type. Cancer. 1995;75(8):2186-2195.

28. Das K, Jain S, Chichra A, Gupta H, Kapoor G. Non-hematological tumors of head and neck region in the pediatric age group in a tertiary care cancer center. Pediatr Surg Int. 2011; 27(9):919-923.

29. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin. 2017;67(1):7-30.

30. Omoregie FO, Akpata O. Paediatric orofacial tumours: new oral health concern in paediatric patients. Ghana Med J. 2014;48(1):14-19.

Table 1. Demographic and clinicopathologic distribution of head and neck malignancies in pediatric patients.

Histologic characteristics	Total		Male		Female		Mean	±SD*
	No.	(%)	No.	(%)	No.	(%)	age	
Lymphomas	194	(52.86)	146	(39.78)	48	(13.08)	9.54	4.32
Non-Hodgkin lymphoma	104	(28.34)	74	(20.16)	30	(8.17)	9.34	4.48
Burkitt lymphoma	61	(16.62)	51	(13.90)	10	(2.72)	8.34	4.52
Diffuse large B-cell lymphoma	17	(4.63)	9	(2.45)	8	(2.18)	10.88	4.18
Lymphoblastic lymphoma	13	(3.54)	8	(2.18)	5	(1.36)	10.69	-
Anaplastic large cell lymphoma	7	(1.91)	4	(1.09)	3	(0.82)	9.43	3.91
Non-Hodgkin lymphoma, NOS	3	(0.82)	1	(0.27)	2	(0.54)	12.5	4.95
Follicular lymphoma	2	(0.54)	1	(0.27)	1	(0.27)	9	1.41
Peripheral T-cell lymphoma	1	(0.27)	-	(0.00)	1	(0.27)	-	-
Hodgkin Lymphoma	90	(24.52)	72	(19.62)	18	(4.90)	9.79	4.14
Nodular sclerosis	48	(13,08)	34	(9,26)	14	(3,81)	10.21	4.18
Mixed cellularity	25	(6,81)	22	(5,99)	3	(0,82)	8.04	3.51
Nodular lymphocyte predominant	12	(3,27)	12	(3,27)	-	(0,00)	11	4.13
Classical Hodgkin lymphoma	3	(0,82)	2	(0,54)	1	(0,27)	12.33	5.03
Hodgkin lymphoma, NOS	2	(0,54)	2	(0,54)	-	(0,00)	10.5	4.95
Carcinomas	84	(22.89)	42	(11.44)	42	(11.44)	11.70	3.93
Nasopharyngeal Carcinoma	47	(12.81)	26	(7.08)	21	(5.72)	12.36	3.49
Thyroid carcinoma	23	(6.27)	9	(2.45)	14	(3.81)	11.57	3.80
Papillary thyroid carcinoma	17	(4.63)	7	(1.91)	10	(2.72)	11.18	3.83
Follicular thyroid carcinoma	4	(1.09)	-	(0.00)	4	(1.09)	12.50	4.65
Medullary thyroid carcinoma	2	(0.54)	2	(0.54)	-	(0.00)	13	2.83
Salivary gland carcinoma	11	(3.00)	5	(1.36)	6	(1.63)	8.82	4.75
Mucoepidermoid carcinoma	5	(1.36)	2	(0.54)	3	(0.82)	12	3.81
Acinic Cell Carcinoma	2	(0.54)	-	(0.00)	2	(0.54)	10	1.41
Sebaceous Adenocarcinoma	1	(0.27)	1	(0.27)	-	(0.00)	6	-
Adenoid Cystic Carcinoma	1	(0.27)	1	(0.27)	-	(0.00)	0	-
Epithelial-Myoepithelial Carcinoma	1	(0.27)	-	(0.00)	1	(0.27)	7	-
Adenocarcinoma, NOS	1	(0.27)	1	(0.27)	-	(0.00)	4	-
Squamous Cell Carcinoma	1	(0.27)	1	(0.27)	-	(0.00)	8	-
Embryonal Carcinoma	1	(0.27)	-	(0.00)	1	(0.27)	12	-
Teratocarcinoma	1	(0.27)	1	(0.27)	-	(0.00)	19	-
Sarcomas	70	(19.07)	40	(10.90)	30	(8.17)	7.41	5.05
Soft tissue sarcomas	54	(14.71)	30	(8.17)	24	(6.54)	6.50	4.77
Rhabdomyosarcoma	47	(12.81)	27	(7.36)	20	(5.45)	6.79	6.61
Infantile fibrosarcoma	2	(0.54)	-	(0.00)	2	(0.54)	0.50	0.71
Rhabdoid sarcoma	2	(0.54)	1	(0.27)	1	(0.27)	2	1.41
Myxoid liposarcoma	1	(0.27)	1	(0.27)	-	(0.00)	13	-
Infantile Myofibrosarcoma	1	(0.27)	1	(0.27)	-	(0.00)	2	-
Synovial sarcoma	1	(0.27)	-	(0.00)	1	(0.27)	13	-
Bone sarcomas	13	(3.54)	8	(2.18)	5	(1.36)	12	3.08
PNET/EWS	6	(1.63)	4	(1.09)	2	(0.54)	13.83	2.71
Chondrosarcoma	5	(1.36)	4	(1.09)	1	(0.27)	10.20	3.03
Osteosarcoma	2	(0.54)	-	(0.00)	2	(0.54)	11	1.41
Other sarcomas	3	(0.82)	2	(0.54)	1	(0.27)	2.67	4.62
Undifferentiated sarcoma	2	(0.54)	1	(0.27)	1	(0.27)	-	-
Sarcoma, NOS	1	(0.27)	1	(0.27)	-	(0.00)	8	-
Embryonal tumours	10	(2.72)	6	(1.63)	4	(1.09)	4.40	5.48
PNET/EWS	5	(1.36)	4	(1.09)	1	(0.27)	6.80	5.76
Olfactory neuroblastoma	2	(0.54)	1	(0.27)	1	(0.27)	5	7.07

Neuroblastoma	2	(0.54)	-	(0.00)	2	(0.54)	5	5.66
Atypical teratoid/rabdoid tumour	1	(0.27)	1	(0.27)	-	(0.00)	-	-
Melanomas	5	(1.36)	4	(1.09)	1	(0.27)	9	6.60
Germ cells	3	(0.82)	2	(0.54)	1	(0.27)	1	1
Immature teratoma	2	(0.54)	2	(0.54)	-	(0.00)	1.50	0.71
Endodermal sinus tumor	1	(0.27)	-	(0.00)	1	(0.27)	-	-
Ameloblastic carcinoma	1	(0.27)	1	(0.27)	-	(0.00)	3	-
TOTAL	**367**	**(100.00)**	**241**	**(65.67)**	**126**	**(34.33)**	**9.35**	**4.78**

SD: standard deviation; PNET/EWS: Primitive neuroectodermal tumor/Ewing sarcoma; NOS: No other specification

Table 2. Topographic distribution of pediatric head and neck malignant tumors.

Anatomic site	Total		Male		Female	
	No.	(%)	No.	(%)	No.	(%)
Neck and lymph nodes	152	(41.42)	113	(30.79)	39	(10.63)
Cervical region	16	(4.36)	9	(2.45)	7	(1.91)
Lymph Nodes	136	(64.31)	104	(28.34)	32	(8.72)
Nasopharynx	84	(22.89)	51	(13.90)	33	(8.99)
Thyroid gland	24	(6.54)	9	(2.45)	15	(4.09)
Nasal cavity, paranasal sinuses and skull base	21	(5.72)	11	(3.00)	10	(2.72)
Nasal cavity	12	(3.27)	6	(1.63)	6	(1.63)
Maxillary sinus	7	(1.91)	4	(1.09)	3	(0.82)
Skull base	2	(0.54)	1	(0.27)	1	(0.27)
Oropharynx (base of tongue, tonsils, adenoids)	21	(5.72)	14	(3.81)	7	(1.91)
Tonsils	19	(5.18)	13	(3.54)	6	(1.63)
Base of tongue	2	(0.54)	1	(0.27)	1	(0.27)
Odontogenic and maxillofacial bone	21	(5.72)	17	(4.63)	4	(1.09)
Mandible	9	(2.45)	7	(1.91)	2	(0.54)
Temporal region	3	(0.00)	2	(0.54)	1	(0.27)
Occipital region	3	(0.82)	3	(0.82)	-	(0.00)
Retroorbital region	1	(0.27)	1	(0.27)	-	(0.00)
Skullcap	1	(0.27)	1	(0.27)	-	(0.00)
Malar region	2	(0.54)	2	(0.54)	-	(0.00)
Zygomatic region	1	(0.27)	-	(0.00)	1	(0.27)
Salivary glands	17	(4.63)	9	(2.45)	8	(2.18)
Parotid gland	11	(3.00)	7	(1.91)	4	(1.09)
Submandibular gland	2	(0.54)	-	(0.00)	2	(0.54)
Minor salivary glands (palate)	2	(0.54)	1	(0.27)	1	(0.27)
Sublingual gland	1	(0.27)	-	(0.00)	1	(0.27)
Other (Unidentified)	1	(0.27)	1	(0.27)	-	(0.00)
Orbit	9	(2.45)	4	(1.09)	5	(1.36)
Oral cavity and mobile tongue	6	(1.63)	5	(1.36)	1	(0.27)
Buccal mucosa	3	(0.82)	3	(0.82)	-	(0.00)
Palate	2	(0.54)	2	(0.54)	-	(0.00)
Nasolabial region	1	(0.27)	-	(0.00)	1	(0.27)
Parapharyngeal space	5	(1.36)	3	(0.82)	2	(0.54)
Ear	4	(1.09)	2	(0.54)	2	(0.54)
Skin attachments (scalp)	3	(0.82)	3	(0.82)	-	(0.00)
TOTAL	**367**	**(100.00)**	**241**	**(65.67)**	**126**	**(34.33)**

Table 3. Histopathological subtypes distribution per tumor topography.

Topography	Sub-Region	Tumor type	No.	(%)
Neck and lymph nodes	Neck	Rhabdomyosarcoma	3	(0.82)
		Infantile fibrosarcoma	2	(0.54)
		Immature teratoma	2	(0.54)
		Neuroblastoma	2	(0.54)
		Embryonal Carcinoma	1	(0.27)
		Myxoid liposarcoma	1	(0.27)
		Rhabdoid sarcoma	1	(0.27)
		Synovial sarcoma	1	(0.27)
		PNET/EWS	1	(0.27)
		Atypical teratoid / rabdoid tumour	1	(0.27)
		PNET/EWS	1	(0.27)
	Lymph nodes	Nodular sclerosis HL	45	(12.26)
		Mixed cellularity HL	25	(6.81)
		Burkitt lymphoma	24	(6.54)
		Nodular lymphocyte predominant HL	11	(3.00)
		Lymphoblastic lymphoma	9	(2.45)
		Diffuse large B-cell lymphoma	8	(2.18)
		Anaplastic large cell lymphoma	6	(1.63)
		Classical Hodgkin lymphoma	3	(0.82)
		Hodgkin lymphoma, NOS	2	(0.54)
		Follicular lymphoma	2	(0.54)
		Non-Hodgkin lymphoma, NOS	1	(0.27)
Nasopharynx		Nasopharyngeal Carcinoma	47	(12.81)
		Rhabdomyosarcoma	16	(4.36)
		Burkitt lymphoma	14	(3.81)
		PNET/EWS	2	(0.54)
		Chondrosarcoma	1	(0.27)
		PNET/EWS	1	(0.27)
		Non-Hodgkin lymphoma, NOS	1	(0.27)
		Endodermal sinus tumor	1	(0.27)
Thyroid gland		Papillary carcinoma	17	(4.63)
		Follicular carcinoma	4	(1.09)
		Medullary thyroid carcinoma	2	(0.54)
		Burkitt lymphoma	1	(0.27)
Nasal cavity. paranasal sinuses and skull base	Nasal cavity	Rhabdomyosarcoma	5	(1.36)
		Chondrosarcoma	2	(0.54)
		Teratocarcinoma	1	(0.27)
		Olfactory neuroblastoma	1	(0.27)
		Diffuse large B-cell lymphoma	1	(0.27)
		Peripheral T-cell lymphoma	1	(0.27)
		Non-Hodgkin lymphoma, NOS	1	(0.27)
	Maxillary sinus	Rhabdomyosarcoma	2	(0.54)
		Burkitt lymphoma	2	(0.54)
		Diffuse large B-cell lymphoma	1	(0.27)
		Rhabdoid sarcoma	1	(0.27)
		Olfactory neuroblastoma	1	(0.27)
	Skull base	Osteosarcoma	1	(0.27)
		PNET/EWS	1	(0.27)
Odontogenic and maxillofacial bone	Mandible	Rhabdomyosarcoma	2	(0.54)
		PNET/EWS	2	(0.54)
		Burkitt lymphoma	2	(0.54)
		Ameloblastic carcinoma	1	(0.27)

		Infantile Myofibrosarcoma	1	(0.27)
		Osteosarcoma	1	(0.27)
	Maxilla	Burkitt lymphoma	3	(0.82)
	Temporal region	Chondrosarcoma	1	(0.27)
		Burkitt lymphoma	1	(0.27)
		Rhabdomyosarcoma	1	(0.27)
	Occipital region	Chondrosarcoma	1	(0.27)
	Retroorbital region	PNET/EWS	1	(0.27)
	Skullcap	PNET/EWS	1	(0.27)
		Lymphoblastic lymphoma	1	(0.27)
	Zygomatic region	Undifferentiated sarcoma	1	(0.27)
	Malar region	Rhabdomyosarcoma	1	(0.27)
Oropharynx (base of tongue. tonsils. adenoids)	Tonsils	Burkitt lymphoma	11	(3.00)
		Diffuse large B-cell lymphoma	4	(1.09)
		Nodular sclerosis HL	3	(0.82)
		Nodular lymphocyte predominant	1	(0.27)
	Base of tongue	Rhabdomyosarcoma	1	(0.27)
		Undifferentiated sarcoma	1	(0.27)
Salivary glands	Parotid gland	Mucoepidermoid carcinoma	3	(0.82)
		Rhabdomyosarcoma	2	(0.54)
		Acinic Cell Carcinoma	1	(0.27)
		Sebaceous Adenocarcinoma	1	(0.27)
		PNET/EWS	1	(0.27)
		Burkitt lymphoma	1	(0.27)
		Lymphoblastic lymphoma	1	(0.27)
		Adenoid Cystic Carcinoma	1	(0.27)
	Submandibular gland	Acinic Cell Carcinoma	1	(0.27)
		Epithelial-Myoepithelial Carcinoma	1	(0.27)
	Minor salivary glands (palate)	Mucoepidermoid carcinoma	2	(0.54)
	Sublingual gland	Rhabdomyosarcoma	1	(0.27)
	Other (Unidentified)	Adenocarcinoma, NOS	1	(0.27)
Orbit		Rhabdomyosarcoma	4	(1.09)
		Melanoma	4	(1.09)
		Diffuse large B-cell lymphoma	1	(0.27)
Oral cavity and mobile tongue	Buccal mucosa	Anaplastic large cell lymphoma	1	(0.27)
		Rhabdomyosarcoma	1	(0.27)
		Burkitt lymphoma	1	(0.27)
	Palate	Sarcoma, NOS	1	(0.27)
		Diffuse large B-cell lymphoma	1	(0.27)
	Nasolabial region	Rhabdomyosarcoma	1	(0.27)
Parapharyngeal space		Rhabdomyosarcoma	4	(1.09)
		Burkitt lymphoma	1	(0.27)
Ear		Rhabdomyosarcoma	3	(0.82)
		Lymphoblastic lymphoma	1	(0.27)
Skin attachments (scalp)		Melanoma	1	(0.27)
		Lymphoblastic lymphoma	1	(0.27)
		Squamous Cell Carcinoma	1	(0.27)
TOTAL			**367**	(100.00)

PNET/EWS: primitive neuroectodermal tumor/Ewing sarcoma; NOS: No other specification

Table 4. Head and neck malignancies distribution per age group*.

< 1 year	1-4 years	5-9 years	10-14 years	15-19 years
Neuroblastoma (0.54%)	Rhabdomyosarcoma (5.72%)	Burkitt lymphoma (5.99%)	Nasopharyngeal Carcinoma (6.27%)	Nasopharyngeal Carcinoma (4.09%)
Undifferentiated sarcoma (0.54%)	Burkitt lymphoma (4.36%)	Nodular sclerosis HL (4.09%)	Nodular sclerosis HL (5.99%)	Burkitt lymphoma (1.63%)
Infantile fibrosarcoma (0.27%)	Nodular sclerosis HL (1.36%)	Rhabdomyosarcoma (3.81%)	Burkitt lymphoma (4.63%)	Nodular sclerosis HL (1.63%)
Rhabdomyosarcoma (0.27%)	Immature teratoma (0.54%)	Nasopharyngeal Carcinoma (2.18%)	Papillary thyroid carcinoma (2.72%)	Rhabdomyosarcoma (1.09%)
Olfactory neuroblastoma (0.27%)	PNET/EWS (0.54%)	Diffuse larg B-cell lymphoma (2.18)	Rhabdomyosarcoma (1.91%)	Papillary thyroid carcinoma (0.82%)

*Age groups according to Gosepath et al.[9] PNET/EWS: Primitive neuroectodermal tumor/Ewing sarcoma.

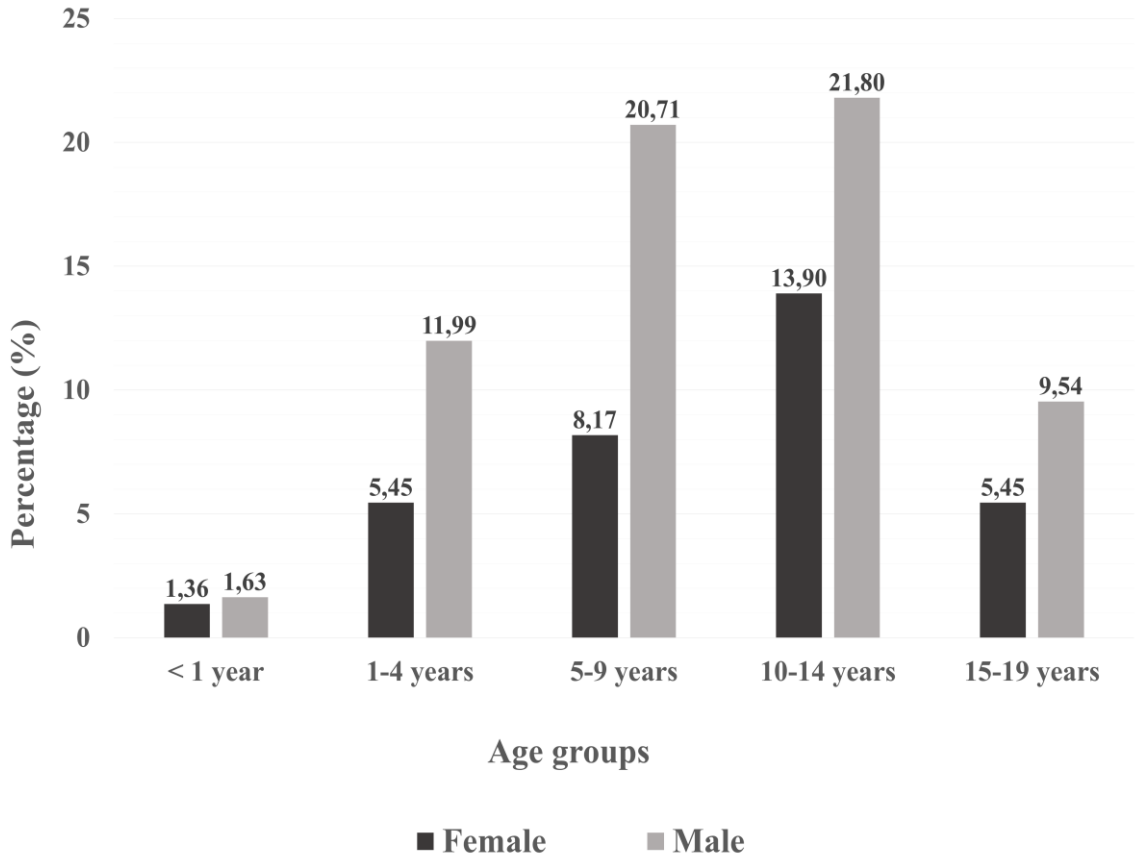
Table 5. Previously published demographic, clinicopathologic and topographic patterns of head and neck malignancies in pediatric patients.

Country	Age (years)	% HNC	Topographic HNC	%	Histologic type	%	Histologic subtype	%
Brazil (present study)	≤19	5.11	Neck and lymph nodes	41.42	L	52.86	HL	24.52
			Nasopharynx	22.89	C	22.89	BL	16.62
			Thyroid gland	6.54	S	19.07	NC	12.81
India[7]	≤12	0.25	-	-	L	43.39	NHL	26.41
			-	-	C	28.3	RMS	20.75
			-	-	S	20.75	NC	15.09
India[28]	≤18	-	Thyroid gland	29.4	C	47.5	PTC	29.4
			Salivary glands	26.9	S	8.9	NC	16.7
			Nasopharynx	16.7	N	2.5	RMS	8.9
Iran[8]	≤12	2.36	Neck	41.0	L	50.0	NHL	27.0
			Head	8.1	N	17.0	HL	23.0
			Nose	6.2	S	5.0	N	17.0
Israel[18]	≤19	2.6	Nasopharynx	42.3	L	20.7	BL	10.4
			Salivary glands	20.5	C	19.9	MEC	8.1
			Tonsils	13.4	S	11.2	SCC	8.1
Iran[15]	≤ 19	8.94	Lymph nodes	42.0	L	55.0	NHL	33.08
			Nasopharynx	12.5	C	20.0	HL	37.94
			Paranasal sinuses	8.0	S	10.5	SSC	9.55
USA[22]	≤ 21	-	Cervical lymph nodes	-	L	42.17	L	42.17
			Orbital/periorbital	-	S	6.23	RMS	6.23
			-	-	N	2.15	N	2.15
USA[23]	≤ 21	-	Nasopharynx	8.9	L	55.0	HL	24.7
			Cheek	5.0	S	20.0	RMS	11.2
			Skull	3.9	C	9.5	FS	6.1
USA[4]	≤ 19	12	Thyroid gland	22,06	C	29.0	PTC	18.0
			Orbit	20.22	L	27.0	HL	17.0
			Nasopharynx	4.68	NT	23.0	NHL	10.0
USA[21]	≤ 19	-	Neck	70.0	L	59.0	HL	35.0
			Nasopharynx	16.0	S	17.5	NHL	24.0
			Orbit	6.0	C	17.5	RMS	13.0
USA[17]	-	2.39	Neck	58.5	L	52.0	HL	26.62
			Nasopharynx	11.4	S	26.5	NHL	25.32
			Ear	9.7	C	6.7	RMS	22.07
USA[6]	≤ 14	11.93	-	-	C	33.4	PTC	23.3
			-	-	L	23.8	HL	13.8
			-	-	NT	19.2	NHL	10.0
Germany[9]	≤ 15	7.3	Thyroid	28.2	S	39.7	RMS	70.0
			Orbit	21.4	C	33.8	TC	27.0
			Nasopharynx	15.4	L	21.4	NHL	16.2

C: Carcinoma; S: Sarcoma; L: Lymphoma; N: Neuroblastoma; NT: Neural tumors; OS: Osteosarcoma; RMS: Rhabdomyosarcoma; NC: Nasopharyngeal carcinoma; PTC: papillary thyroid carcinoma; HL: Hodgkin lymphoma; NHL: Non-Hodgkin lymphoma; BL: Burkitt lymphoma; MEC: Mucoepidermoid carcinoma; SCC: Squamous cell carcinoma; EWS: Ewing sarcoma; TC: Thyroid carcinoma

Figure legends

Figure 1. Gender distribution according to age groups* in head and neck malignancies in pediatric patients.



*Age groups according to Gosepath et al.[9]

Conflict of interest:

We, authors of this manuscript, declare that there is none financial relationship with any commercial associations, current and within the past five years, that might pose a potential, perceived or real conflict of interest. These include grants, patent licensing arrangements, consultancies, stock or other equity ownership, advisory board memberships, or payments for conducting or publicizing our study. The authors also state the material is original, has not been published elsewhere, and is being submitted only to the Journal of Oral Pathology & Medicine

Acknowledgement

This study was supported by the Brazilian Coordination of Higher Education (CAPES-Brazil).

3 CONCLUSÃO

No período de 30 anos, o CCP representou 5,11% de todas as malignidades.

A média de idade dos pacientes no momento do diagnóstico foi de 9,35 anos e os pacientes na faixa etária entre 10 a 14 anos apresentaram maior prevalência de tumores malignos. Foi identificada discreta predominância pelo gênero masculino (65,67%) e pela raça branca (73,02%).

Os tipos de câncer mais comuns na população pediátrica alvo deste estudo foram os linfomas seguido de carcinomas, e sarcomas. O linfoma de Burkitt, o linfoma de Hodgkin clássico tipo esclerose nodular, o carcinoma nasofaríngeo e o RMS foram os diagnósticos histopatológicos mais comuns.

Os principais sítios anatômicos afetados foram a região cervical e linfonodos, a nasofaringe, e a glândula tireoide.

REFERÊNCIAS*[1]

Ajayi OF, Adeyemo WL, Ladeinde AL, Ogunlewe MO, Omitola OG, Effiom OA, et al. Malignant orofacial neoplasms in children and adolescents: A clinicopathologic review of cases in a Nigerian tertiary hospital. Int J Pediatr Otorhinolaryngol. 2007; 71(6): 959-963.

Albright JT, Topham AK, Reilly JS. Pediatric head and neck malignancies: US incidence and trends over 2 decades. Arch Otolaryngol Head Neck Surg. 2002; 128(6): 655-659.

Braga P, Latorre M, Curado M. Câncer na infância: análise comparativa da incidência, mortalidade e sobrevida em Goiânia (Brasil) e outros países. Cadernos de saúde pública. 2002; 18(1): 33-44.

Cesmebasi A, Gabriel A, Niku D, Bukala K, Donnelly J, Fields PJ, Tubbs RS, Loukas M. Pediatric head and neck tumors: an intra-demographic analysis using the SEER* database. Med Sci Monit. 2014; 20: 2536-2542.

Cunningham MJ, Myers EN, Bluestone CD. Malignant tumors of the head and neck in children: a twenty-year review. Int J Pediatr Otorhinolaryngol. 1987; 13(3): 279-292.

Das K, Jain S, Chichra A, Gupta H, Kapoor G. Non-hematological tumors of head and neck region in the pediatric age group in a tertiary care cancer center. Pediatr Surg Int. 2011; 27(9): 919-923.

de Camargo B, de Oliveira Santos M, Rebelo MS, de Souza Reis R, Ferman S, Noronha CP, Pombo-de-Oliveira MS. Cancer incidence among children and adolescents in Brazil: first report of 14 population-based cancer registries. Int J Cancer. 2010; 126(3): 715-720.

Duvvuri U, Myers JN. In Brief. Current Problems in Surgery. 2009; 46(2): 114-117.

Gosepath J, Spix C, Talebloo B, Blettner M, Mann WJ. Incidence of childhood cancer of the head and neck in Germany. Ann Oncol. 2007; 18(10): 1716-1721.

[1] * De acordo com as normas da UNICAMP/FOP, baseadas na padronização do International Committee of Medical Journal Editors - Vancouver Group. Abreviatura dos periódicos em conformidade com o PubMed.

Gurney JG, Severson RK, Davis S, Robison LL. Incidence of cancer in children in the United States. Sex-, race-, and 1-year age-specific rates by histologic type. Cancer. 1995; 75(8): 2186-2195.

Howell DL, Ward KC, Austin HD, Young JL, Woods WG. Access to pediatric cancer care by age, race, and diagnosis, and outcomes of cancer treatment in pediatric and adolescent patients in the state of Georgia. Journal of clinical oncology original. 2007; 25(29): 4610-4615.

Huber MA, Terezhalmy GT. The head and neck radiation oncology patient. Quintessence Int. 2003; 34(9): 693-717.

INCA. Coordenação de Prevenção e Vigilância de Câncer. Câncer da criança e adolescente no Brasil: dados dos registros de base populacional e de mortalidade [Digital]. Rio de Janeiro: Instituto Nacional do Câncer; 2008.

INCA. Estimativas 2016: Incidência de Câncer no Brasil [Digital]. Rio de Janeiro: Instituto Nacional do Câncer; 2016.

Jaffe BF. Pediatric head and neck tumors: a study of 178 cases. Laryngoscope. 1973; 83(10): 1644-1651.

Khademi B, Taraghi A, Mohammadianpanah M. Anatomical and histopathological profile of head and neck neoplasms in Persian pediatric and adolescent population. Int J Pediatr Otorhinolaryngol. 2009; 73(9): 1249-1253.

Levi S, Zini A, Fischman S, Czerninski R. Epidemiology of oral, salivary gland and pharyngeal cancer in children and adolescents between 1970 and 2011. Oral Oncol. 2017; 67: 89-94.

Linabery AM, Ross JA. Childhood and adolescent cancer survival in the US by race and ethnicity for the diagnostic period 1975-1999. Cancer. 2008; 113(9): 2575-2596.

Matzinger O, Zouhair A, Mirimanoff RO, Ozsahin M. Radiochemotherapy in Locally Advanced Squamous Cell Carcinomas of the Head and Neck. Clinical Oncology. 2009; 21(7): 525-531.

Omoregie FO, Akpata O. Paediatric orofacial tumours: new oral health concern in

paediatric patients. Ghana Med J. 2014; 48(1): 14-19.

Rapidis AD, Economidis J, Goumas PD, Langdon JD, Skordalakis A, Tzortzatou F, Anagnostopoulos D, Matsaniotis N. Tumours of the head and neck in children. A clinico-pathological analysis of 1,007 cases. J Craniomaxillofac Surg. 1988; 16(6): 279-286.

Robinson LD, Smith RJ, Rightmire J, Torpy JM, Fernbach DJ. Head and neck malignancies in children: an age-incidence study. Laryngoscope. 1988; 98(1): 11-13.

Reis RS, Santos MO,Thuler LCS. Incidência de tumores pediátricos no Brasil. Revista Brasileira de Cancerologia. 2007; 53(1): 5-15.

Ries LAG, Smith MA, Gurney JG, Linet M, Tamra T, Young JL, Bunin GR (eds). Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975-1995 [Digital]. Maryland: National Cancer Institute; 1999.

Schwartz I, Hughes C, Brigger MT. Pediatric head and neck malignancies: incidence and trends, 1973-2010. Otolaryngol Head Neck Surg. 2015; 152(6): 1127-1132.

Sengupta S, Pal R, Saha S, Bera SP, Pal I, Tuli IP. Spectrum of head and neck cancer in children. J Indian Assoc Pediatr Surg. 2009; 14(4): 200-203.

Siegel DA, King J, Tai E, Buchanan N, Ajani UA, Li J. Cancer incidence rates and trends among children and adolescents in the United States, 2001-2009. Pediatrics. 2014; 134(4): 945-955.

Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin. 2017; 67(1): 7-30.

Smith MA, Altekruse SF, Adamson PC, Reaman GH, Seibel NL. Declining childhood and adolescent cancer mortality. Cancer. 2014; 120(16): 2497-2506.

Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International Classification of Childhood Cancer, third edition. Cancer. 2005; 103(7): 1457-1467.

Stiller CA. Epidemiology and genetics of childhood cancer. Oncogene. 2004; 23(38): 6429-6444.

Ward E, Desantis C, Robbins A, Kohler B, Jemal A. Childhood and Adolescent Cancer Statistics, 2014. CA: A Cancer Journal for Clinicians. 2014; 64(2): 83-103.

ANEXO 1- Certificado do Comitê de Ética em Pesquisa

Certificado do Comitê de Ética em Pesquisa

CENTRO INFANTIL DE INVESTIGAÇÕES HEMATOLÓGICAS DR.

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: TUMORES MALIGNOS DE CABEÇA E PESCOÇO EM CRIANÇAS E ADOLESCENTES: ANÁLISE RETROSPECTIVA EM UMA INSTITUIÇÃO

Pesquisador: Regina Maria Holanda de Mendonça

Área Temática:

Versão: 1

CAAE: 64034217.5.0000.5376

Instituição Proponente: Centro Infantil de Investigações Hematológicas Dr.Domingos A Boldrini

Patrocinador Principal: FUND COORD DE APERFEICOAMENTO DE PESSOAL DE NIVEL SUP

DADOS DO PARECER

Número do Parecer: 1.947.205

Apresentação do Projeto:

A proposta do trabalho é de fazer um estudo retrospectivo de 150 pacientes com tumores de cabeça e pescoço diagnosticados e tratados no período de 1990 a 2017.

Objetivo da Pesquisa:

Revisar os prontuários dos pacientes atendidos e avaliar os dados epidemiológicos referentes ao CCP na população infanto-juvenil de um centro de referencia hospitalar brasileiro especializado em oncologia e hematologia pediátrica.

Avaliação dos Riscos e Benefícios:

Riscos são baixos e os benefícios futuros relevantes.

Comentários e Considerações sobre a Pesquisa:

Inexistentes.

Considerações sobre os Termos de apresentação obrigatória:

Todos os termos e documentos anexados cumprem os requisitos da pesquisa.

Recomendações:

Inexistentes.

Endereço: Rua Dr. Gabriel Porto, 1270 Cidade Universitária
Bairro: Barão Geraldo **CEP:** 13.083-210
UF: SP **Município:** CAMPINAS
Telefone: (19)3787-5001 **Fax:** (19)3289-3571 **E-mail:** cep@boldrini.org.br

CENTRO INFANTIL DE INVESTIGAÇÕES HEMATOLÓGICAS DR.

Continuação do Parecer: 1.947.205

Conclusões ou Pendências e Lista de Inadequações:
O projeto foi apresentado à plenária do CEP e aprovado.

Considerações Finais a critério do CEP:

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_826673.pdf	24/01/2017 19:37:24		Aceito
Outros	CartaAoCEPBoldriniPaola.pdf	24/01/2017 19:32:20	Regina Maria Holanda de Mendonça	Aceito
Outros	CartaAoCEPBoldriniAlan.pdf	24/01/2017 19:30:35	Regina Maria Holanda de Mendonça	Aceito
Projeto Detalhado / Brochura Investigador	PROJETODEPESQUISA.pdf	24/01/2017 19:28:28	Regina Maria Holanda de Mendonça	Aceito
Folha de Rosto	FolhaDeRosto.pdf	28/11/2016 19:20:47	Regina Maria Holanda de Mendonça	Aceito
Outros	PARECER2.pdf	20/11/2016 16:22:57	Regina Maria Holanda de Mendonça	Aceito
Outros	PARECER1.pdf	20/11/2016 16:22:03	Regina Maria Holanda de Mendonça	Aceito
Outros	TERMODECONSENTIMENTO.pdf	20/11/2016 16:20:40	Regina Maria Holanda de Mendonça	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TermoDeSigilo.pdf	20/11/2016 16:15:59	Regina Maria Holanda de Mendonça	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

Endereço: Rua Dr. Gabriel Porto, 1270 Cidade Universitária
Bairro: Barão Geraldo **CEP:** 13.083-210
UF: SP **Município:** CAMPINAS
Telefone: (19)3787-5001 **Fax:** (19)3289-3571 **E-mail:** cep@boldrini.org.br

CENTRO INFANTIL DE INVESTIGAÇÕES HEMATOLÓGICAS DR.

Continuação do Parecer: 1.947.205

CAMPINAS, 03 de Março de 2017

Assinado por:
Francisco Benedito Teixeira Pessine
(Coordenador)

MINISTÉRIO DA SAÚDE - Conselho Nacional de Saúde - Comissão Nacional de Ética em Pesquisa – CONEP
PROJETO DE PESQUISA ENVOLVENDO SERES HUMANOS

Projeto de Pesquisa:	TUMORES MALIGNOS DE CABEÇA E PESCOÇO EM CRIANÇAS E ADOLESCENTES: ANÁLISE RETROSPECTIVA EM UMA INSTITUIÇÃO BRASILEIRA.

Informações Preliminares

Responsável Principal

CPF/Documento: 739.535.636-53	Nome: Regina Maria Holanda de Mendonça
Telefone: (19) 3365-2600	E-mail: reginamhm@gmail.com

Instituição Proponente

CNPJ: 50.046.887/0001-27	Nome da Instituição: Centro Infantil de Investigações Hematológicas Dr.Domingos A Boldrini

É um estudo internacional? Não

Equipe de Pesquisa

CPF/Documento	Nome
222.243.428-96	Alan Roger dos Santos Silva
Lady Paola Aristizabal Arboleda	Lady Paola Aristizabal Arboleda

Área de Estudo

Grandes Áreas do Conhecimento (CNPq)

- Grande Área 4. Ciências da Saúde

Propósito Principal do Estudo (OMS)

- Outros

Título Público da Pesquisa: TUMORES MALIGNOS DE CABEÇA E PESCOÇO EM CRIANÇAS E ADOLESCENTES: ANÁLISE RETROSPECTIVA EM UMA INSTITUIÇÃO BRASILEIRA.

Contato Público

CPF/Documento	Nome	Telefone	E-mail
739.535.636-53	Regina Maria Holanda de Mendonça	(19) 3365-2600	reginamhm@gmail.com

Contato Regina Maria Holanda de Mendonça

ANEXO 2 – Certificado de submissão do artigo

Journal of Oral Pathology & Medicine

Submission Confirmation

Thank you for your submission

Submitted to	Journal of Oral Pathology and Medicine
Manuscript ID	JOPM-01-18-OA-4725
Title	Demographic and clinicopathologic distribution of head and neck malignant tumors in pediatric patients from a Brazilian population: a retrospective
Authors	Arboleda, Lady Paola Hoffmann, Iva Cardinalli, Izilda Santos-Silva, Alan Roger Mendonça, Regina Maria Holanda de
Date Submitted	15-Jan-2018