

## Quality of life of cancer children-adolescents with and without fatigue

Qualidade de vida da população infantojuvenil oncológica com e sem fadiga

Calidad de vida de la población infantojuvenil oncológica con y sin fatiga

Michele Darezzi Rodrigues Nunes<sup>1</sup>  <https://orcid.org/0000-0001-7685-342X>Eufemia Jacob<sup>2</sup>  <https://orcid.org/0000-0002-6294-9508>Luís Carlos Lopes-Júnior<sup>3</sup>  <https://orcid.org/0000-0002-2424-6510>Ana Carolina Andrade Biaggi Leite<sup>4</sup>  <https://orcid.org/0000-0003-0262-0441>Regina Aparecida Garcia de Lima<sup>4</sup>  <https://orcid.org/0000-0002-0611-5621>Lucila Castanheira Nascimento<sup>4</sup>  <https://orcid.org/0000-0002-7900-7111>

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## Corresponding author

Michelle Darezzi Rodrigues Nunes  
Email: mid13@hotmail.com

## Associate Editor (Peer review process):

Camila Takao Lopes  
(<https://orcid.org/0000-0002-6243-6497>)  
Escola Paulista de Enfermagem, Universidade Federal de São Paulo, SP, Brazil

## Abstract

**Objective:** To compare the health-related quality of life (HRQoL) scores of children and adolescents hospitalized with cancer who had and did not have fatigue and to correlate fatigue and HRQoL.

**Method:** This is a cross-sectional study carried out for 48 months in the onco-hematology sector of a public hospital located in the interior of São Paulo, with 63 children and adolescents with cancer. To measure fatigue and HRQoL, participants completed the instruments Pediatric Quality of Life Inventory™ Multidimensional Fatigue Scale and Pediatric Quality of Life Inventory™ Pediatric Quality of Life Inventory - acute version - in the generic module and cancer module. Data were analyzed using descriptive, bivariate and multivariate statistics.

**Results:** The means of the total fatigue scores (61.2±16.3) and HRQoL (generic: 61.5±20.5; cancer: 61.2±16.3) were low, demonstrating that children and adolescents with cancer are fatigued (p=0.000) and with low quality of life (p=0.000). In the regression model, fatigue could be explained in 61.25% by the variables emotional functioning (p=0.0110), school functioning (p=0.0004) and cognitive difficulties (p=0.0017). Participants without fatigue had better mean HRQoL score when compared to the group with fatigue.

**Conclusion:** Children and adolescents hospitalized with cancer have a low quality of life and high levels of fatigue. Furthermore, the relationship between some HRQoL dimensions and fatigue is positive, indicating that the worse the school and emotional functioning and the greater the cognitive difficulties, the greater the fatigue.

## Resumo

**Objetivo:** Comparar os escores de qualidade de vida relacionada à saúde (QVRS) de crianças e adolescentes hospitalizados com câncer que apresentaram e não apresentaram fadiga e correlacionar fadiga e QVRS.

**Método:** Estudo transversal realizado durante 48 meses no setor de onco-hematologia de hospital público localizado no interior paulista, com 63 crianças e adolescentes com câncer. Para mensurar a fadiga e a QVRS, os participantes preencheram, respectivamente, os instrumentos *Pediatric Quality of Life Inventory*™ Escala Multidimensional do Cansaço e *Pediatric Quality of Life Inventory*™ Inventário Pediátrico de Qualidade de Vida, versão *aguda*, no módulo genérico e módulo câncer. Os dados foram analisados por meio de estatística descritiva, bivariada e multivariada.

**Resultados:** As médias dos escores total de fadiga (61,2±16,3) e QVRS (genérica: 61,5±20,5; câncer: 61,2±16,3) foram baixas, demonstrando que as crianças e os adolescentes com câncer se apresentam fatigados (p=0,000) e com baixa qualidade de vida (p=0,000). No modelo de regressão, a fadiga pôde

<sup>1</sup>Universidade do Estado do Rio de Janeiro, Rio de Janeiro, RJ, Brazil.

<sup>2</sup>University of California Los Angeles, School of Nursing, Los Angeles, CA, USA.

<sup>3</sup>Universidade Federal do Espírito Santo, Vitória, ES, Brazil.

<sup>4</sup>Escola de Enfermagem de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.

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ser explicada em 61,25% pelas variáveis funcionamento emocional ( $p=0,0110$ ), funcionamento escolar ( $p=0,0004$ ) e dificuldades cognitivas ( $p=0,0017$ ). Participantes sem fadiga apresentaram melhor escore médio de QVRS quando comparado ao grupo com fadiga.

**Conclusão:** Crianças e adolescentes hospitalizados com câncer apresentam baixa qualidade de vida e altos níveis de fadiga. Ainda, é positiva a relação entre algumas dimensões da QVRS com a fadiga, indicando que, quanto pior for o funcionamento escolar e emocional e maiores forem as dificuldades cognitivas, maior também será a fadiga.

## Resumen

**Objetivo:** Comparar las puntuaciones de calidad de vida relacionadas con la salud (CVRS) de niños y de adolescentes hospitalizados con cáncer que presentaron y que no presentaron fatiga y correlacionar la fatiga y la CVRS.

**Métodos:** Estudio transversal realizado durante 48 meses en el sector de oncohematología de un hospital público ubicado en el interior del estado de São Paulo, con 63 niños y adolescentes con cáncer. Para medir la fatiga y la CVRS, los participantes rellenaron, respectivamente, los instrumentos *Pediatric Quality of Life Inventory™* Escala Multidimensional del Cansancio y *Pediatric Quality of Life Inventory™* Cuestionario de Calidad de Vida Pediátrica, versión *aguda*, en el módulo genérico y en el módulo cáncer. Los datos fueron analizados por medio de estadística descriptiva, bivariada y multivariada.

**Resultados:** Los promedios de las puntuaciones total de fatiga ( $61,2\pm 16,3$ ) y CVRS (genérica:  $61,5\pm 20,5$ ; cáncer:  $61,2\pm 16,3$ ) fueron bajas, demostrando que los niños y los adolescentes con cáncer se muestran fatigados ( $p=0,000$ ) y con baja calidad de vida ( $p=0,000$ ). En el modelo de regresión, se puede explicar la fatiga en el 61,25 % por las variables funcionamiento emocional ( $p=0,0110$ ), funcionamiento escolar ( $p=0,0004$ ) y dificultades cognitivas ( $p=0,0017$ ). Participantes sin fatiga presentaron mejor puntuación promedio de CVRS al compararlos con el grupo sin fatiga.

**Conclusión:** Niños y adolescentes hospitalizados con cáncer presentan baja calidad de vida y altos niveles de fatiga. Aun así, es positiva la relación entre algunas dimensiones de la CVRS con la fatiga, indicando que, cuanto peor sea el funcionamiento escolar y emocional y mayores sean las dificultades cognitivas, mayor será también la fatiga.

## Introduction

Global estimates by GLOBOCAN 2020 of cancer incidence and mortality, focusing on geographic variability in 185 countries, indicated, for the year 2020, about 19.3 million new cases of cancer and 10 million deaths.<sup>(1)</sup> More than 15,000 new cases of cancer are diagnosed in children and adolescents annually, resulting in 1,960 deaths.<sup>(2-5)</sup> For pediatric patients aged one to 19 years in the United States of America, cancer is the leading cause of death from disease.<sup>(5)</sup>

In the Brazilian context, the *Instituto Nacional de Câncer José Alencar Gomes da Silva* (INCA) estimates the occurrence of 625,000 new cases of cancer for each year of the 2020-2022 triennium.<sup>(6)</sup> Specifically for juvenile neoplasms (between 0 and 19 years old), INCA estimates for Brazil, in each year of the triennium, the incidence of 4,310 cases for males and 4,150 for females, corresponding to a risk of 134.87 per million in males and 139.04 per million in females. Pediatric cancer in boys will have a higher incidence in southeastern Brazil, with 158.15/million, and in the group of girls it will be more frequent in the South Region, with 173.55/million.<sup>(6)</sup>

Notably, advances in cancer treatment over the past four decades have improved the 5-year survival rate from 10% to approximately 90% in children.<sup>(3,5)</sup>

However, childhood cancer incidence rates have continuously increased since 1975.<sup>(3)</sup>

Among the most common types, in children and adolescents, are leukemias, central nervous system tumors and lymphomas.<sup>(6)</sup> Symptoms related to diagnosis and treatment are common and the most frequent for this population is fatigue,<sup>(7,8)</sup> followed by nausea, lack of appetite and pain.<sup>(8)</sup>

Cancer-related fatigue (CRF) is a subjective sensation of patients, which can be considered a distressing, persistent feeling such as physical, emotional or cognitive exhaustion.<sup>(9)</sup> It can be related to the diagnosis of cancer or be induced by treatments such as chemotherapy and radiotherapy.<sup>(9,10)</sup> Still, children and adolescents suffer when they experience CRF together with other uncontrolled symptoms that occur simultaneously, forming clusters of cancer symptoms.<sup>(11,12)</sup> Evidence suggests a direct relationship between CRF and quality of life and how this symptom affects different dimensions of the lives of children and adolescents with cancer.<sup>(13,14)</sup>

Previous studies report symptoms of children and adolescents with cancer, including CRF and psychological stress as dependent variables.<sup>(15,16)</sup> However, this knowledge is still incipient, especially when considering CRF and quality of life as primary outcomes, particularly in the Brazilian pediatric population.<sup>(17)</sup> CRF is a multifactorial and complex

symptom to be reported by children and adolescents with cancer, due to age and clinical factors.<sup>(11)</sup>

CRF typically increases during cancer treatment, particularly during chemotherapy, radiotherapy, hormone therapy, and targeted therapies.<sup>(18)</sup> CRF prevalence estimates during treatment range from 25% to 99%, depending on the patient population, type of treatment received and method of assessment.<sup>(19)</sup> In children and adolescents with cancer, CRF is the most prevalent symptom, occurring in 35.6% to 93% of cases, with a higher level experienced by those undergoing chemotherapy.<sup>(9)</sup> CRF generally improves within the year after treatment is completed, although a significant minority of patients continue to experience fatigue for months or years after successful treatment.<sup>(20)</sup> Studies of long-term cancer survivors suggest that about 25% to 33% experience persistent fatigue for up to 10 years after cancer diagnosis.<sup>(21)</sup> CRF pathogenesis is not fully elucidated and a variety of mechanisms may contribute to its development,<sup>(20)</sup> such as dysregulation of cytokine levels, hypothalamic-pituitary-adrenal axis activity, dysregulation of circadian rhythm, dysregulation of neurotransmitter 5-hydroxytryptophan (5-HT) and alterations in adenosine triphosphate (ATP) metabolism.<sup>(20,22)</sup>

In the context of cancer, it is well established that tumors and the treatments used to eradicate them can activate the pro-inflammatory cytokine network, leading to fatigue symptoms through cytokine signaling in the central nervous system.<sup>(20,23)</sup> In the pre-treatment period, the tumor itself can be a source of pro-inflammatory cytokines, while during treatment, cytokines can be produced in response to tissue damage from radiation or chemotherapy.<sup>(20,23)</sup> The inflammatory response may persist after completion of treatment, as well as during the course of treatment when patients deal with persistent pathogens, infections, and changes in homeostasis.<sup>(20)</sup>

Human studies examining the relationships between inflammation and CRF in patients before, during, and after cancer treatment showed strong associations between a range of inflammatory markers.<sup>(18,24)</sup> Chemotherapy and radiation therapy are two of the most common types of can-

cer treatment; both are associated with increases in fatigue and elevations in certain inflammatory markers, especially in pro-inflammatory cytokines such as IL-1 $\beta$ , TNF- $\alpha$  and IL-6.<sup>(18,24)</sup>

Particularly in the pediatric oncology population, a recent literature review<sup>(25)</sup> reinforces the lack of studies to assess symptoms in this population and illustrates the lack of consensus among studies on fatigue measurement. Regarding the influence of diagnosis and treatment, the review included studies that demonstrated a decrease in fatigue during treatment in children with acute lymphoid leukemia, with leukemia and lymphoma, and with mixed diagnoses, while in another it remained unchanged in children with solid tumors and central nervous system. Contrary to these findings, another study identified increased fatigue over a 10-month follow-up period, in all age groups and associated with hospitalization. Regarding the chemotherapy cycle, fatigue reached its peak in the first two to four days after the beginning of the cycle.<sup>(25)</sup>

It is noteworthy that studies exploring the CRF symptom in hospitalized Brazilian children and adolescents and its relationship with HRQoL are still limited in the scientific literature, which has minimized the possibilities of successful strategies and interventions in the management of this symptom in pediatric oncology. In this sense, the present investigation aimed to compare the HRQoL scores of children and adolescents hospitalized with cancer who presented and did not present fatigue and to correlate fatigue and HRQoL.

## Methods

This is a cross-sectional study, conducted in a pediatric onco-hematology sector of a public university hospital in the countryside of São Paulo, which had nine beds dedicated to the care of children and adolescents with cancer.

Children and adolescents aged 8 between 18 years old, who were hospitalized, diagnosed and undergoing cancer treatment (chemotherapy, radiotherapy or surgery) during the period of data collection and who presented cognitive conditions to

participate in the study were included. This assessment was carried out by the researchers, through observation, together with information provided by health professionals in the sector, as well as by analyzing the electronic medical record. Children and adolescents with cancer in palliative care, in the immediate postoperative period, i.e., less than 5 days, and who underwent concomitant chemotherapy and radiotherapy were excluded from the sample. The collection took place over a period of 48 months, from January 2013 to December 2016 and included 63 children and adolescents. The criterion for interrupting data collection was based on the period established for this stage of the research.

The primary outcomes of the present investigation were fatigue and quality of life (dependent variables). To measure fatigue, the Pediatric Quality of Life Inventory™ (PedsQL™) - Multidimensional Fatigue Scale was used.<sup>(26)</sup> This is a multidimensional scale, used in the acute version, which assesses three dimensions of fatigue: general fatigue, fatigue related to sleep/rest and mental fatigue during the last week. To measure the HRQoL, the generic module and the cancer module of the Pediatric Quality of Life Inventory (PedsQL™) were used, which has four dimensions: physical, emotional, social and school functioning. Both inventories are validated for the Brazilian context<sup>(27–29)</sup> with specific versions for age group (8 to 12 years old and 13 to 18 years old). They are five-point Likert-type scales, with scores that are converted to a scale from zero to one hundred, and values are inversely proportional, i.e., the higher the value, the lower the fatigue or the better the HRQoL.<sup>(26)</sup> Children and adolescents with fatigue were considered as those with a score below 75, i.e., those who responded that fatigue is ‘often’ or ‘almost always’ a problem for them; and ‘without fatigue’ those with scores equal to or above 75, i.e., those who answered that fatigue is a problem: ‘never’, ‘almost never’ or ‘sometimes’.<sup>(10)</sup>

The authors of the scales granted authorization for the researchers to use the instruments in this study. This research was approved by ‘parent and co-participant institutions’ Institutional Review Board (opinion 1390/2011).

After obtaining parental Informed Consent Form, children and adolescents were approached. The study was explained to obtain Child Assent, then the children were approached. Child and adolescent self-report versions of the PedsQL™ Multidimensional Fatigue Scale and the PedsQL™ Pediatric Quality of Life Inventory generic module version 4.0 and cancer module 3.0 were used. Thus, the participants themselves responded to the instruments using a clipboard and pen. If a child or adolescent was unable to use the arm to mark the answers, the interviewer read the sentences and the answer options and marked the one that the participant chose. Information regarding the clinical and sociodemographic data of participants and their guardian was collected through interviews with the person in charge and a direct search in the medical record, having been recorded in an instrument constructed by the researchers and widely used in the research group.

To quantify fatigue and HRQoL, descriptive statistics were used, through mean and standard deviation, minimum and maximum values of the respective scores. After verifying data normality by the Shapiro-Wilk test for all variables, we identified that some of them obeyed the Gaussian distribution and others did not. To describe the relationship between fatigue and HRQoL, Pearson’s or Spearman’s correlation was used, depending on whether the analyzed variables followed the normal distribution or not. Values were considered weak when less than 0.40, moderate if between 0.41 and 0.60, good or substantial if between 0.61 and 0.80, and almost perfect or very good if above 0.81.<sup>(30)</sup> Data were processed using the software IBM Statistical Package for Social Science (SPSS), version 24.

For the correlations found, linear regression was also used, considering fatigue as a dependent variable. To perform the linear regression test, the R 3.3.0 program was used. Access to this program was made directly through website <http://www.R-project.org/>.<sup>(31)</sup> The significance level used in the research was 0.05.

## Results

Sixty-three children and adolescents participated in this study, and 52.4% (n=33) were children aged 8

to 12 years, with a mean age of  $12.1 \pm 2.7$ . The majority (41; 65.1%) were male, had white skin color and studied between 5 and 9 years.

Regarding diagnosis, the most frequent were leukemia/lymphoma (36.5%) and sarcomas (28.6%). Only 7.9% of the sample (n=5) reported recurrent neoplasia. With regard to treatment, 57.1% (n=36) underwent chemotherapy; 15.5% (n=11) surgical procedures and chemotherapy; 9.5% (n=6) underwent chemotherapy, radiotherapy and surgery during treatment; 7.9% (n=5) underwent only surgical procedures; 4.8% (n=3) underwent chemotherapy and radiotherapy; 3.2% (n=2) had already undergone chemotherapy and/or surgical treatment and were waiting for the definition of therapeutic treatment for recurrence.

During data collection, 39.7% (n=25) of children and adolescents were undergoing chemotherapy in a period of less than 1 month, 27% (n=17) were undergoing chemotherapy between 1 and 3 months and only 11, 1% (n=7) did not undergo chemotherapy.

The majority (n=31; 49.2%) of participants were hospitalized for chemotherapy and 22.2% (n=14) due to neutropenia and signs and symptoms of infection.

Participants and their guardians came, for the most part (n=46; 73%), from the city itself or from nearby cities (<100km) from the collection site; 15.9% (n=10) were from cities located between 100 and 500km from the collection site; 11.1% (n=7) lived in distant cities (>500km). Most families (n=22; 34.9%) had an income between R\$701.00 and R\$1,400.00 (about US\$120 and US\$240, respectively). When asked about the number of siblings, 41.3% (n=26) reported having one and 19% (n=12), two.

According to data obtained through the PedsQL™ Multidimensional Fatigue Scale, the mean total fatigue was  $61.2 \pm 16.3$ , which meant that fatigue was “often or almost always a problem”, with a minimum score of 20.3 and maximum of 91.6. The lowest score (8.3) occurred in the dimension of mental fatigue. The mean scores for the dimensions were  $65.1 \pm 19.6$  for general fatigue,  $58.7 \pm 21.3$  for fatigue related to sleep and  $66.1 \pm 23.1$  for mental fatigue.

Table 1 presents the comparison between HRQoL cancer module scores and their dimensions according to a group of children and adolescents with and without fatigue. In all HRQoL dimensions, children with fatigue had significantly worse scores.

**Table 1.** Comparison between health-related quality of life scores module cancer and its dimensions according to a group of children and adolescents with and without fatigue

Group	Mean	Standard deviation	p-value
Total HRQoL (cancer module)*			
Without fatigue (19)	73.2	11.0	0.000
With fatigue (44)	56.0	15.5	
Pain and bruises†			
Without fatigue (19)	90.7	12.3	0.000
With fatigue (44)	63.5	27.0	
Nausea*			
Without fatigue (19)	63.9	19.5	0.045
With fatigue (44)	51.5	22.8	
Anxiety to procedures†			
Without fatigue (19)	77.6	21.3	0.010
With fatigue (44)	55.8	31.8	
Anxiety to treatment †			
Without fatigue (19)	78.9	22.8	0.028
With fatigue (44)	61.9	28.9	
Concerns †			
Without fatigue (19)	54.8	28.6	0.089
With fatigue (44)	40.7	31.5	
Cognitive difficulties*			
Without fatigue (18)	81.9	14.0	0.000
With fatigue (43)	59.3	22.8	
Physical appearance†			
Without fatigue (18)	79.6	20.4	0.069
With fatigue (43)	65.3	26.7	
Communication†			
Without fatigue (18)	78.7	21.0	0.026
With fatigue (43)	62.0	28.1	

\*Variables in which parametric tests were used (t-test); † variables in which nonparametric tests were used (Mann-Whitney U test). HRQoL - health-related quality of life

In order to verify the adequacy of the use of linear regression analysis, the Shapiro-Wilk normality test was applied in the dependent variable (fatigue), which presented normality ( $p=0.41$ ), confirming the adequacy of the use of linear regression analysis. The generic module and cancer module HRQoL dimensions were considered as independent variables that brought the possible explanatory factors for fatigue (Table 2).

In this model, fatigue could be explained in 61.25% by the variables emotional functioning ( $p=0.0110$ ), school functioning ( $p=0.0004$ ) and

**Table 2.** Linear regression

	Estimate	Standard deviation	Statistics	p-value
(Intercept)	13.35	2.39	5.566	0.0198
Emotional functioning	0.22	2.62	0.086	0.0110
School functioning	0.30	3.79	0.081	0.0004
Cognitive difficulties	0.27	3.30	0.084	0.0017

Multiple R-square: 0.6124; adjusted R-square: 0.5916; Statistics F: 29.4910 in 3 and 56 DF; p-value: 0.0000

cognitive difficulties ( $p=0.0017$ ). Thus, these variables had a positive relationship with fatigue, i.e., the worse the school and emotional functioning and the greater the cognitive difficulties, the greater the fatigue.

## Discussion

Our findings showed that the main diagnoses of most participants in this research were leukemia and lymphoma (36.5%). These results are in line with worldwide epidemiological data which indicate that, among the most common cancers in children and adolescents, are leukemia with 25% to 35%, followed by central nervous system (CNS) tumors and lymphomas.<sup>(3-5)</sup>

Regarding the data obtained through the PedsQL™ - Multidimensional Fatigue Scale, the mean total fatigue was  $61.2\pm 16.3$ , indicating that fatigue was “often or almost always a problem”. Our findings are consistent with those reported in a study that assessed the different dimensions of fatigue (general, sleep/rest, cognitive), HRQoL (physical, emotional, cognitive and social) and relationships between fatigue and HRQoL in children and adolescents hospitalized with cancer, finding the mean PedsQL™ score in the generic module to be  $61.1\pm 17.0$ .<sup>(14)</sup>

Slightly different findings were reported in a recent quasi-experimental study, which verified the effect of an intervention involving the art of clown theater on levels of psychological stress and cancer-related fatigue in pediatric cancer patients undergoing chemotherapy, showing a baseline mean general fatigue score of  $66.3\pm 19.6$  (pre-intervention).<sup>(15)</sup> In contrast, a pre/post-test quasi-experimental pilot study that examined the longitudinal viability of psychophysiological parameters of cancer-related stress and fatigue, including cortisol,

salivary alpha-amylase, pro- and anti-inflammatory cytokines, and metalloproteinase-9 of matrix dosed via saliva in pediatric patients with osteosarcoma hospitalized for chemotherapy undergoing non-pharmacological intervention, it showed a baseline mean general fatigue score of  $73.7\pm 15.1$ .<sup>(16)</sup> Probably, the difference in the results obtained in these two quasi-experimental studies may be related to the non-pharmacological intervention to which patients were submitted, playing an important modulating role of this type of intervention in the management of this symptom.

When comparing the cancer module HRQoL scores and their dimensions, according to the group of children and adolescents with and without fatigue, the group without fatigue had a mean score of  $73\pm 11$ , while the group with fatigue had  $56\pm 15.5$ , and this difference was statistically significant ( $p=0.000$ ). A previous study conducted with children and adolescents with cancer whose outcomes were fatigue and quality of life identified that the mean total HRQoL score (generic) was  $61.1\pm 17.0$  and the mean total HRQoL (cancer module) was of  $59.1\pm 16.7$  for the fatigued. Moreover, the authors reported lower scores in the dimensions of school functioning, emotional and physical functioning.<sup>(14)</sup> These literature data support those identified in the present linear regression model, in which fatigue can be explained in 61.25% by the variables emotional functioning ( $p=0.0110$ ), school functioning ( $p=0.0004$ ) and cognitive difficulties ( $p=0.0017$ ). According to the findings of this study, children with cancer in other countries also reported low HRQoL scores,<sup>(13,32)</sup> compared to healthy children.<sup>(29)</sup>

Interestingly, participants in this research showed more problems in emotional functioning and school functioning, in addition to cognitive difficulties. Additionally, disease- and treatment-related effects negatively affected HRQoL physically, psychologically and emotionally.<sup>(33)</sup> In line with the findings of this study, lower scores on general HRQoL, cognitive difficulties, and school functioning are reported in children with cancer undergoing chemotherapy compared to healthy children.<sup>(32)</sup> Thus, these variables have a positive relationship with fatigue, i.e.,

the worse the school and emotional functioning and the greater the cognitive difficulties, the greater the fatigue.

Furthermore, the findings of this study, with regard to the mean total fatigue scores reported by pediatric cancer patients, are consistent with the PedsQL™ Multidimensional Fatigue Scale scores reported during hospitalization of children and adolescents with cancer in other countries.<sup>(13,34)</sup> It is possible that, considering the socioeconomic and cultural differences of each country, fatigue continues to be a problem, because the characteristics and symptoms related to the disease, the treatment protocols and the effects related to the therapy were comparable.

Non-pharmacological interventions, such as physical exercise, leisure activities during hospitalization, therapeutic touch, and aerobic exercise after hospital discharge, have been consistently reported in the literature as effective strategies for managing fatigue.<sup>(12,15,35,36)</sup> Therefore, it is essential that the health team is sensitive to identify, assess and intervene in the fatigue of children and adolescents hospitalized with cancer and, consequently, improve the quality of life of these patients.<sup>(37,38)</sup>

It should be noted that cancer-related fatigue is often neglected by health professionals and family members. An exploratory study with a qualitative approach, carried out with 53 health professionals (33 nursing assistants, ten nurses, three doctors, three nutritionists, two psychologists and two physiotherapists), which aimed to investigate what knowledge health professionals had about knowledge, assessment and intervention on fatigue in children and adolescents with cancer, pointed out limited knowledge of healthcare professionals about fatigue, as well as little investment in continuing education and continuing education.<sup>(37)</sup>

The importance of understanding healthcare professionals' experiences regarding knowledge, assessment and intervention on fatigue in hospitalized children and adolescents with cancer can greatly contribute to specialized care.<sup>(37,39)</sup> The nursing team and other healthcare professionals can provide family-centered care, identifying the individual

needs of its members and working with interventions and instruments to meet them.

We recognize the study limitations as follows: the inclusion only of hospitalized children and adolescents did not make it possible to identify how fatigue and quality of life behave in life contexts outside the hospital; the cross-sectional design of this study allows only the punctual identification of variables, without establishing precise relationships on cause-effect; data collection period length and a small sample size, which even though it was developed in a reference hospital for the care of children and adolescents with cancer diagnosis, has a limited number of beds; recall bias in instrument responses may have affected the results; generalization of the results of this study to other contexts should be carried out with caution; the inclusion of participants diagnosed with different types of cancer, established therapies and clinical-social variables, which were not assessed in this study, may have influenced fatigue and HRQoL scores.

## Conclusion

Children and adolescents hospitalized with cancer have a low quality of life and high levels of CRF. Furthermore, the relationship between some dimensions of HRQoL and CRF is positive, indicating that the worse the school and emotional functioning and the greater the cognitive difficulties, the greater the CRF. With regard to the group of children and adolescents with or without fatigue, the results of this study demonstrate a statistically significant difference in HRQoL scores. This indicates that the group without fatigue has better HRQoL scores.

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## Collaborations

Nunes MDR, Jacob E, Lopes-Júnior LC, Leite ACAB, Lima RAG and Nascimento LC contributed to the project design, data analysis and interpretation, article writing, relevant critical review of the intellectual content and approval of the final version to be published.

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