




ORIGINAL ARTICLE

CLINICAL DETERIORATION OF THE ONCOLOGY CHILD: RELIABILITY OF A NEW TOOL ADAPTED FROM THE BRIGHTON PEDIATRIC EARLY WARNING SCORE*

HIGHLIGHTS

1. Early detection of clinical deterioration in pediatric oncology.
2. Evaluation of predictors of clinical deterioration in children with cancer.
3. Inter-judge reliability of the modified alertness scale for pediatric oncology.

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ABSTRACT

Objective: To measure the degree of reliability of the construction of new items and the adaptation of the Brighton Pediatric Early Warning Score for children with cancer. **Method:** Methodological study to analyze the equivalence of inter-judge content regarding the inclusion of items in the scale to detect early clinical deterioration in children with cancer: signs of bleeding, changes in temperature, and presence of grade III/IV mucositis. The Intraclass Correlation Coefficient and Cronbach's Alpha were used for analysis, considering a value ≥ 0.750 . **Results:** Based on the judges' feedback, the items proposed for inclusion were retained, with minor adjustments to the scores. Thirty nurses (86.1%) and six doctors (13.9%) from Brazil evaluated the scale, resulting in an intraclass correlation coefficient of 0.823. **Conclusion:** The instrument proved suitable, with theoretical relevance and practical application, for early detection of clinical deterioration in children with cancer. To this end, it contributes to timely identification by the team, minimizing unfavorable outcomes.

DESCRIPTORS: Medical Oncology; Clinical Deterioration; Pediatrics; Hospitalization; Methodological Studies.

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INTRODUCTION

Advances in the treatment of childhood cancer offer greater chances of remission and cure but also a more significant occurrence of adverse events¹. Febrile neutropenia and sepsis are the most frequent events, with sepsis being responsible for most ICU referrals and deaths in pediatric oncology and the fever being one of the central warning signs¹⁻². There is evidence that children who died in the first 24 hours of poor perfusion, in addition to neutropenia, also had respiratory, hematological, and neurological alterations³.

The mortality rate for these patients is up to 35%, which is very high compared to children in general (5%)¹. As a result, around 38% will need an ICU at some point during their cancer treatment¹, with the risk of severe sepsis increasing fourfold when there is associated mucositis and febrile neutropenia².

One way of detecting these alterations early is through assessment scales such as the Pediatric Early Warning Score (PEWS), which use quick and simple resources and do not depend on more complex equipment or tests⁴. In pediatrics, more than 30 scales are being used and adapted worldwide; however, the Brighton Pediatric Early Warning Score (BPEWS) was the first PEWS published and is the scale translated and validated for the Brazilian context (BPEWS-Br)⁴. The authors of the BPEWS-Br also developed the Pediatric Early Warning Score (EPA, in Portuguese), adding temperature, diuresis, and other modifications⁴. However, although essential for oncology, we understand that diuresis can generate subjectivity during assessment and interfere with the patient's score.

A study adapted the Bedside Pews scale for pediatric oncology in the Netherlands with the addition of temperature¹. However, it is longer and requires a blood pressure cuff for each age group, which could make it unfeasible to use routinely in many centers. We couldn't find any scales aimed at the child oncology population that covered the main adverse events, and considering the above, the BPEWS-Br scale turned out to be the most appropriate for this adaptation.

This study aimed to measure the degree of reliability of the construction of new items and the adaptation of the Brighton Paediatric Early Warning Score (BPEWS-Br) for Pediatric oncology.

METHOD

This is a two-stage methodological study. The present study reports on the first phase, in which the items applied to oncology children admitted to pediatric units were developed and validated by expert judges regarding adapting the BPEWS-Br scale, which aims to detect early clinical deterioration during hospitalization for cancer treatment.

Data was collected from May 1 to September 13, 2022, by sending a form via email or the multiplatform messaging application WhatsApp® using the Google Forms® link. When accessing the form, the first page contained the Free and Informed Consent Form, which the participant could only continue with if they accepted.

At this stage, the judges individually analyzed the BPEWS-Br scale and the new proposal, including items constructed specifically for the clinical deterioration of hospitalized cancer children. They assigned a degree of importance from 0 (not important) to 10 (totally important) to one decimal place after the comma. The reliability of the inter-judge agreement was measured by the Intraclass Correlation Coefficient (ICC).

The inclusion criteria were meticulously designed to ensure the participation of professionals with a degree in nursing or medicine and at least one year's experience with children with cancer, either in hospital clinical practice or in teaching and research. To reach the desired number of professionals, the number suggested by Gwet⁵ was adopted, which would be at least 35 subjects selected randomly from a larger population of subjects with similar characteristics when the bilateral randomization method is recommended.

The aim was to choose a profile of judges representative of the field of care work so that the data from the study could be generalized and applied to the care of children with cancer. 83 professionals (doctors and nurses) from Brazil were randomly invited⁵ after consulting their Lattes curriculum vitae. Of these, 37 participated in the study and thoroughly answered the adapted BPEWS-Br scale for Pediatric oncology.

This scale was developed based on the original scale translated and adapted for use in Brazil, the BPEWS-Br, as well as the scientific evidence from the literature on pediatric oncology and the main emergencies that affect this population^{2,6-7}, especially while they are undergoing treatment or monitoring the disease during hospitalization.

Items for hematological evaluation and "complementary states" were included. The presence of mucositis was added to the scale based on the mucositis scale proposed by the World Health Organization (WHO) at the time of the nurse's evaluation⁸ (Chart 1).

Chart 1 - Brighton Pediatric Early Warning Score (BPEWS-Br) for Pediatric oncology adapted⁹. Londrina, PR, Brazil, 2022

Components	Score				Score
	0	1	2	3	
Neurological Status (Original Scale)	Active	Sleepy/ hypoactive	Irritate	Lethargic/ obnubilated or reduced response to pain	
Cardiovascular (Original Scale)	Blushed or TEC 1-2 seconds (sec.)	Pale or 3 sec CRT for HR above the upper limit for age	Moted or CRT 4 sec. or HR ≥20 bpm above upper limit for age	Grayish/cyanotic or CRT ≥5 sec. or HR ≥30 bpm above the upper limit for age or bradycardia for age	
Respiratory (Original Scale)	Typical RR for age, no retraction	RR above the upper limit for age or use of accessory muscles or FiO ₂ ≥30% or 4 liters/minute of O ₂	RR ≥20 rpm above the upper limit for age or subcostal, intercostal, and furcula retractions or FiO ₂ ≥40%	RR ≤5 rpm below the lower limit for age or subcostal, intercostal, furcula, sternum and twining retractions or FiO ₂ ≥50% or 8 liters/minute of O ₂	
Hematology (Adaptation for Oncology)	No signs of bleeding	Petechiae / bruising	Bleeding gums / epistaxis	Hematemesis/ enterorrhagia	
Complementary states	Add 2 extra points (Original Scale)				
	The patient received a nebulizer until 15 minutes ago				
	Persistent vomiting after surgery				
	Add 1 extra point (Adaptation for Oncology)				
	Axillary body temperature <36°C or ≥37.8°C (during chemotherapy or up to 14 days after)				
	Mucositis grade III or IV				
Final score					

Source: The authors (2024).

The survey form for the experts consisted of three parts: sociodemographic characterization (age, length of training, length of time working at the institution, length of time working at the institution and profession); the adapted BPEWS-Br scale for Pediatric oncology (Figure 1); and the question in which the judge scored (from zero to 10) the importance of the scale for assisting children with cancer during hospitalization, as well as an open question for them to add comments to improve the scale. It is worth noting that the original scale has a total score of 13 points. The new scale adapted for Pediatric oncology now scores 18 points.

The data were entered into Microsoft Excel® and analyzed using the Statistical Package for the Social Science, v.26 (SPSS)®. Reliability analysis was carried out using the ICC, with bilateral randomization, and the homogeneity of the judges' judgments using Cronbach's alpha to demonstrate equivalence between the judges/evaluators¹⁰. A minimum ICC value of ≥ 0.750 was considered adequate to attest to the reliability between the experts¹¹.

The research project for this study was authorized by the research department of the study institution and approved by the Research Ethics Committee, opinion no. 4.562.827. It is worth noting that the authors' authorization was previously obtained from BPEWS-Br in October 2020.

RESULTS

According to Table 1, of the five Brazilian regions, three had some professional taking part in the survey: the south with thirty (83.3%), followed by the southeast with five (13.9%), and the northeast with one (2.8%).

Of the experts, 30 were nurses (83.3%) and six were doctors (16.7%). The age ranged from 20 and 40 to 31 (86.1%) and fifteen (58.3%) had worked in pediatrics or Pediatric oncology for up to three years. All the doctors had a specialization/residency in oncology, while only half the nurses (15) reported having a specialization in the area (Table 1).

Table 1 - Sociodemographic characterization of the Brazilian experts participating in the study. Londrina, PR, Brazil, 2022

Variables	n	%
	36	100
Region		
South	30	83.3
Southeast	5	13.9
Northeast	1	2.8
Professional		
Category	30	83.3
Nurse	6	16.7
Age range		
20 to 30 years	14	38.9
31 to 40 years	17	47.2
≥41 years	5	13.9
Time working in pediatric oncology		
1 to 3 years	21	58.3
4 to 6 years	6	16.7
7 to 10 years	5	13.9
≥11 years	4	11.2
Specialization/residency in pediatric oncology		
No training in the area	15	41.7
≤ 2 years	8	22.2
3 to 5 years	6	16.7
6 to 10 years	3	8.3
≥10 years	4	11.1

Source: The authors (2024).

Clinical observations

Contributions scored by 19 experts refer mainly to cardiovascular and neurological assessment, temperature, and mucositis. About cardiovascular alterations, the caveat was skin pallor since children with cancer tend to be paler because of the pathology and the treatment, and this is not necessarily a clinical risk.

However, others pointed out that, although it is a common characteristic in children with cancer, it is an essential clinical sign to consider, even though it is a subjective alteration since it is related to the gaze of the person assessing it. As the original scale has already validated this item, keeping it in the scale adapted for pediatric oncology was essential.

As for the neurological state, the observation was in the item drowsiness/hypoactivity and irritability, with the suggestion to invert the score of both, considering that the former may represent greater severity than the latter and, therefore, could have a higher score. However, it is not an item exclusive to children with cancer and, as validated in the translation and cross-cultural adaptation of the original scale, the decision was to keep it.

The items "temperature" and "mucositis" scores were suggested to increase from 1 to 2 points, as these are essential alterations in children with cancer and can impact the early detection of clinical deterioration. As temperature is part of the hospitalized patient's daily assessment and has well-defined parameters for alteration and normality, it was moved from a complementary state to a component in the leading score.

Another expert suggestion was to indicate on the scale whether the child is undergoing chemotherapy or in a period corresponding to NADIR¹², which ranges from 7 to 14 days after the start of chemotherapy. Therefore, the experts' suggestions were accepted for inclusion in the final version of the scale.

With regard to the clinical sign "persistent vomiting after surgery", the expression "after surgery" was removed and replaced with "after chemotherapy". The clinical sign "diarrhea" was added, as it is an alteration frequently present in children undergoing chemotherapy, as is "vomiting". As a result, the final scale was configured as shown in Chart 2 below.

It should be noted that the version sent to the experts scored 18 points, and after suggestions, the final version of the BPEWS-Br scale adapted for pediatric oncology was changed to a score of 20 points.

Chart 2 - Adapted Brighton Pediatric Early Warning Score (BPEWS-Br) for pediatric oncology. Londrina, PR, Brazil, 2022

Components	Score				Score
	0	1	2	3	
Neurological Status (Original Scale)	Active	Sleepy/ hypoactive	Irritate	Lethargic/obnubilated or reduced response to pain	
Cardiovascular (Original Scale)	Blushed or CRT 1-2 seconds (sec.)	Pale or 3 sec CRT for HR above the upper limit for age	Moted or TEC 4 sec. or HR ≥20 bpm above the upper limit for age	Grayish/cyanotic or TEC ≥5 sec. or HR ≥30 bpm above the upper limit for age or bradycardia for age	
Respiratory (Original Scale)	Typical RR for age, no retraction	RR above the upper limit for age or use of accessory muscles or FiO ₂ ≥30% or 4 liters/ minute of O ₂ .	RR ≥20 rpm above the upper limit for age or subcostal, intercostal, and furcula retractions or FiO ₂ ≥40%.	RR ≤5 rpm below the lower limit for age or subcostal, intercostal, furcula, sternum and twining retractions or FiO ₂ ≥50% or 8 liters/minute of O ₂ .	
Hematology (Adaptation for Oncology)	No signs of bleeding	Petechiae / bruising	Bleeding gums / epistaxis	Hematemesis/ enterorrhagia	
Axillary Temperature During chemotherapy or up to 14 days after (Adaptation for Oncology)	≥36°C or ≤37,8°C		<36°C or ≥37,8°C		
Complementary states	Add 2 extra points				
	Patient received nebulizer up to 15 minutes before assessment				
	Persistent vomiting /diarrhea after chemotherapy				
	Mucositis grade III or IV				
Final score					

Source: The authors (2024).

As for the experts' assessment (0 to 10) of the importance of the BPEWS-Br scale for pediatric oncology, with an emphasis on clinical practice in pediatric oncology units, an average of 9.36 was obtained.

Inter-judge reliability

The reliability test of the BPEWS-Br scale for pediatric oncology, which 37 experts answered, resulted in a reliability of 0.78. However, based on the analysis of the homogeneity of the judges¹⁰, it was possible to detect that expert E17 had a heterogeneous score compared to the others. When he was excluded from the analysis, the result changed to 0.82, with a lower limit of 0.71 and an upper limit of 0.91. Therefore, this study excluded E17, keeping the other 36 (Table 2).

Table 2 - Homogeneity of the judges by Cronbach's alpha. Londrina, PR, Brazil, 2023

Experts	Scale average if the item is excluded	Scale variance if the item is excluded	Corrected total item correlation	Cronbach's alpha if the item is excluded
E1	331.40	200.66	0.00	0.82
E2	333.44	188.36	0.09	0.84
E3	331.80	187.37	0.30	0.82
E4	332.04	200.73	-0.05	0.83
E5	332.16	198.39	0.13	0.82
E6	331.63	196.20	0.44	0.82
E7	331.72	182.51	0.71	0.81
E8	331.44	199.98	0.17	0.82
E9	331.44	196.71	0.70	0.82
E10	331.56	187.65	0.84	0.81
E11	332.12	193.80	0.24	0.82
E12	331.92	189.56	0.46	0.81
E13	331.88	164.97	0.70	0.80
E14	333.20	181.85	0.40	0.81
E15	333.08	190.99	0.17	0.82
E16	332.67	183.33	0.67	0.81
E18	332.62	197.08	0.08	0.82
E19	332.36	187.47	0.63	0.81
E20	331.40	200.66	0.00	0.82
E21	331.40	200.66	0.00	0.82
E22	331.56	186.41	0.81	0.81
E23	331.84	195.69	0.33	0.82
E24	331.56	193.83	0.64	0.82
E25	331.68	189.43	0.49	0.81
E26	331.48	195.49	0.45	0.82
E27	332.68	168.50	0.49	0.81
E28	331.48	201.17	-0.05	0.82
E29	331.40	200.66	0.00	0.82
E30	331.68	195.74	0.37	0.82
E31	331.48	192.84	0.70	0.81
E32	333.08	144.22	0.73	0.80
E33	331.40	200.66	0.00	0.82
E34	331.68	189.41	0.34	0.82
E35	331.60	193.04	0.45	0.82
E36	331.72	185.85	0.65	0.81
E37	331.40	200.66	0.00	0.82
	Intraclass correlation	Lower limit	Upper limit	N of items
Average measurements	0.82	0.71	0.91	36

Source: The authors (2024).

DISCUSSION

Regarding the evaluation of the experts in this study and considering the interpretation standards for the use of the ICC, that an ICC >0.75 indicates good inter-judge reliability¹¹, the results obtained after excluding one of the experts for a Cronbach's Alpha score of 0.82 showed greater homogeneity in the inter-judge judgment regarding the inclusion of items in the scale for detecting clinical deterioration in hospitalized oncology children. Using Cronbach's alpha score to assess the homogeneity of inter-judge judgment is characterized as a skillful and innovative strategy to complement this stage in validation studies¹⁰.

According to the results of this study, most of the experts belonged to the category of nurses, and some had no specific training in pediatric oncology. One study¹³ corroborates the findings of this study, in which most of the experts had no specialization in their field. On the contrary, doctors must hold a specialist qualification, as determined by the Federal Council of Medicine, for pediatric oncology training after specializing in pediatrics, clinical oncology, or hematology/chemotherapy¹⁴.

It is worth noting that nurses are trained to work more generally, focusing on humanistic, critical, and reflective guidelines based on scientific rigor, with the capacity for an intellectual and ethical outlook. Thus, on this basis, professionals often establish their work and care in oncology, even though it is challenging¹⁵.

Although the medical team and other healthcare team members are essential inpatient care, nurses play a leading role in applying scales to the early detection of clinical deterioration in adults and children. They are professionals in full-time contact with patients, with adequate clinical judgment to reliably and assertively recognize the presence of signs and symptoms suggestive of clinical worsening¹⁶, which justifies the fact that most of the experts are nurses.

Regarding the theoretical relevance and practical application of the items included to assess children with cancer, bleeding stands out as one of the main oncological emergencies in pediatrics. It is mainly related to the effects of chemotherapy on the bone medulla, with a decrease in platelet production. Its severity is characterized by mucosal bleeding/epistaxis and is due to thrombocytopenia, evidenced in laboratory tests by a drop in the platelet count¹⁷⁻¹⁸.

When considering the inclusion of temperature as a warning sign in hospitalized oncology children, we considered three critical issues that permeate the phases of chemotherapy treatment: NADIR, febrile neutropenia, and sepsis. NADIR is the period that comprises the phase with the lowest hematological count and, therefore, with the most excellent chance of infections by various types of microorganisms and opportunistic diseases, which makes this the phase with the most amazing chance of severe clinical deterioration in children with cancer undergoing treatment. This period usually occurs between the 7th and 14th day after chemotherapy infusion and requires constant care and monitoring¹².

Febrile neutropenia is one of the main concerns in children with cancer, especially during the period between chemotherapy infusions, which is often linked to the NADIR period. Children diagnosed with lymphomas and leukemias are more likely to develop febrile neutropenia than children with solid tumors due to the more aggressive chemotherapy treatment¹⁹.

This alteration refers to a low neutrophil count, which are the defense cells, added to the presence of hyperthermia, which leads to an imminent risk of infections and requires the immediate administration of antibiotics because, if not detected and treated early, it can become a severe clinical condition and potentially fatal, thus characterizing it as one of the main oncological emergencies in pediatrics¹⁹⁻²⁰.

To characterize the diagnosis of febrile neutropenia, neutrophil values of less than 500 μ L or less than 1000 μ L with a predicted drop in 48 hours are considered, in addition to the presence of fever. Although some studies consider neutropenia fever when the axillary temperature is equal to or greater than 38°C, for the present study, fever was considered when values were equal to or greater than 37.8°C, as recommended by the Brazilian Society of Pediatrics^{19,21}. However, some patients may present in hypothermia and, therefore, any sign of clinical deterioration in the presence of neutropenia should be considered for treatment, even if empirical, to avoid a poor prognosis¹⁹.

Fever is also frequently related to Systemic Inflammatory Response Syndrome (SIRS), which can occur precisely because of the low immune response in neutropenia. If it is not possible to quantify leukocytes, in addition to temperature changes, heart or respiratory rate variations outside the normal range for each age group should be considered²². In addition, the new Phoenix sepsis criteria include four organ dysfunctions (respiratory, cardiovascular, coagulation, and neurological). The SIRS criteria were not included but continue to have value in clinical practice for assessing the presence of infection²³.

Many patients (around 80%) experience some episode of fever while they are suffering from neutropenia, and even after starting antibiotic treatment, around 10% can still die. Furthermore, the longer a child remains in febrile neutropenia, the greater the risk of clinical worsening and worsening of the condition. For this reason, early detection and intervention can help ensure a faster and more effective recovery²⁴.

Another critical alteration, mucositis, is one of the most common oral manifestations in patients undergoing chemotherapy or radiotherapy, and the younger the child, the greater the chances of developing it in the severe form induced by chemotherapy²². Its presence can be a determining factor for interrupting treatment, which implies a risk of disease progression with the advance of cancer cell proliferation and a worsening prognosis. In addition, severe mucositis results in limited food and fluid intake, which leads to malnutrition and dehydration, as well as the risk of bacteremia and sepsis, mainly when associated with neutropenia, since it can affect the oral mucosa and the entire gastrointestinal tract, with the risk of death²⁵.

To evaluate and monitor mucositis, the World Health Organization (WHO) has developed an instrument that evaluates severity based on the signs of the lesion and the ability to swallow water and food. It is divided into grades I, II, III, and IV, with grades III and IV considered severe mucositis⁸.

Vomiting and diarrhea are common adverse reactions in chemotherapy treatment; however, even if they are expected, they can have a direct impact on the child's clinical condition and treatment, resulting in dehydration, malnutrition, and treatment interruption if there is no monitoring and early intervention^{7,26}. For evaluation purposes, persistent vomiting or diarrhea, that is, more than three episodes a day, is considered to be critical for the child's clinical deterioration^{9,27}.

The study's limitations were the low number of pediatric medical professionals with experience in caring for children with cancer and experts working exclusively in the field of pediatric oncology, making it necessary to expand to pediatric areas that had experience or work in oncology.

CONCLUSION

The study indicated good inter-judge reliability when new elements were added to the scale, allowing us to infer that the new tool will be a good resource for the care team, especially nurses, to identify early warning signs of clinical deterioration in children with cancer, thus minimizing late actions and unfavorable outcomes.

In addition, the method of selecting the judges applied to the study, how it was analyzed, and the profile of the participating judges conferred the degree of generalization of the tool to the national territory. From then on, the BPEWS-Br scale, adapted to detect clinical deterioration in children affected by cancer, proved valid for use in hospital units and was renamed BPEWS-Br for pediatric oncology.

After reliability testing, the scale developed and validated by experts is recommended to be applied to a sample of the target audience to guarantee its applicability and effectiveness in clinical practice so that it can be instituted as a scale for detecting early clinical deterioration in children with cancer in hospital units.

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