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INTERNATIONAL EXPERIENCE IN APPLYING THE SYSTEM OF PEDIATRIC EARLY WARNING SIGNS OF CRITICAL CONDITIONS IN ONCOLOGICAL CHILDREN: A LITERATURE REVIEW

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ABSTRACT

Relevance: *Oncological diseases remain the main cause of death in children, increasing the need for intensive care. Hospitalized children suffering from oncological diseases are at high risk for sudden deterioration of their condition, both for the underlying disease and due to infectious complications and the toxic effects of medications. This review highlights information on the Pediatric Early Warning Signs (PEWS) system in oncological patients to detect clinical deterioration promptly.*

The study aimed to *analyze international literature on using pediatric early warning signs (PEWS) for clinical deterioration in pediatric oncology.*

Methods: *Current literature on using the PEWS of clinical deterioration in pediatric oncology was studied.*

Results: *The published data show the critical role of using the PEWS system in cancer patients for early detection of deterioration of the condition with subsequent provision of emergency medical care.*

Conclusion: *The analysis of international experience has shown that using the PEWS system in children with oncological diseases is an effective method of early recognition of signs of clinical deterioration, which, in turn, allows the timely initiation of complex intensive therapy.*

Keywords: *oncology, hematology, PEWS, clinical deterioration, children, intensive care.*

Introduction: Pediatric oncology studies tumors and develops practical recommendations for prevention, diagnosis, and complex therapy. Approximately 10% of all pediatric cancer patients have a genetic predisposition to cancer [1].

Due to the opportunity of obtaining high-quality medical services, more than 80% of pediatric cancer patients are cured in high-income countries. Pediatric cancer patients in low- and middle-income countries are cured in less than 30% of cases [2]. A modern approach to therapy in pediatric oncology is the creation of interdisciplinary teams with the participation of pediatric hematologists, oncologists, infection control specialists, anesthesiologists, resuscitators, transfusiologists, pediatricians, pediatric surgeons, neurosurgeons, vascular surgeons, neurologists, gynecologists, endocrinologists and other specialists necessary for patients at different stages of the path to recovery [3].

The global burden of pediatric oncology is disproportionately shifting towards low- and middle-income countries. Countries with limited resources account for about 80% of childhood cancer morbidity and about 90% of cancer mortality in children [4]. Hospitalized children suffering from oncological diseases are in a high-risk group since frequent life-threatening complications can deteriorate their conditions. The most common childhood oncological diseases include leukemia, malignant brain tumors, lymphomas, and solid tumors such as neuroblastoma and nephroblastoma [5].

Timely early diagnosis of various complications aimed at improving survival rates in oncological diseases [6-8]. Medical personnel needs clear criteria and algorithms to prevent critical conditions, allowing timely identification and provision of necessary, complete, and urgent care, which is particularly important in hospitals with limited resources [9]. During inpatient treatment, inadequate initial assessment of the general condition, lack of constant monitoring of vital signs, and inadequate therapy lead to undesirable results, partly due to the lack of systems that detect clinical deterioration in patients [10]. As a result, several severity assessment systems have been developed and tested to

improve the identification of patients in the pediatric population with a higher risk who need complex intensive care [11-13].

Pediatric Early Warning Signs (PEWS) system is a tool for the clinical assessment of the patient's condition, taking into account vital signs and symptoms of the oncological patients to detect clinical deterioration promptly [14]. The use and implementation of the PEWS system in children's hospitals showed a decrease in the frequency of cardiopulmonary arrest outside the intensive care unit (ICU), unscheduled transfers to the ICU, and general hospital mortality [15].

The study aimed to analyze international literature on using pediatric early warning signs (PEWS) for clinical deterioration in pediatric oncology.

Materials and methods: We searched using keywords like oncology, hematology, PEWS, clinical deterioration, and children in the databases PubMed, MEDLINE, EMBASE, Web of Science, and Cochrane Library. To compile the review, we studied all publications on this topic in open access, the search depth was ten years, and the original language is English. The analysis included the results of original clinical and comparative studies in pediatric oncology hospitals, as well as case studies in the field of pediatric oncology. The exclusion criteria were abstracts not in English, summaries of materials, and personal messages that did not contain the primary significance.

Results: This review includes 50 studies published over the past ten years evaluating the results of the introduction and impact of PEWS in clinical practice in cancer patients. The parameters used in the PEWS system include neurological problems, heart rate, capillary filling time, respiratory rate, participation of auxiliary muscles, oxygen therapy, and body temperature.

In recent decades, against the background of complex therapy, there has been a noticeable increase in the overall survival of children with hematological diseases. However, some cancer patients need treatment that includes hematopoietic stem cell transplantation, and these patients still represent a group with a higher mortality risk. In addition, we have learned that ventilation and cardiovascular support, along with renal replacement therapy, can benefit pediatric patients with hematological diseases if these procedures are started promptly [16].

In an international multicenter study, Parshuram C.S. et al. conducted a case-control study in hospitalized children with the participation of three clinics from Canada and one from the UK (n=2074 patients). In the case of clinical deterioration, patients experienced either immediate referral to the intensive care unit or urgent hospitalization in the ICU. No events were recorded in the control patients. The overall scores on the Bedside PEWS system were different; the assessment was carried out 24 hours before the event of clinical deterioration. The median (interquartile range) of the leading indicators of Bedside PEWS for 12 hours ending 1 hour before clinical deterioration was 8 (from 5 to 12) in patients receiving treatment and 2 (from 1 to 4) in patients of the control group (P<0.0001). The Area Under Curve Receiver Operator Characteristic (AUCROC) curve (95% confidence interval) was 0.87 (from 0.85 to 0.89). In patients who received treatment, the average scores were 5.3 for 20-24 hours and 8.4 for 0-4 hours before the event (P<0.0001). The AUCROC curve (95% CI) of retrospective nurse evaluations was 0.83 (0.81 to 0.86). Assessment of Bedside PEWS allows us to distinguish "sick" from "healthy" hospitalized patients. These data suggest that the PEWS assessment can help doctors identify children at risk of immediate and actual cardiac arrest [17].

In the following retrospective study, before and after introducing the PEWS tool with an appropriate algorithm for interdisciplinary actions in the department of Hematology, it is reported that barriers between departments that prevented the timely transfer of children with clinical deterioration requiring urgent care were eliminated. The introduction of the PEWS system improved the interaction between multidisciplinary teams, which helped ensure that the necessary assistance was received in the right place and at the right time [18]. Finally, the study mainly focuses on implementing the system itself.

At Kamuzu Central Hospital, a large specialty hospital in Lilongwe, Malawi, with over 15,000 hospitalizations of children per year, the introduction of the PEWS system reduced the inpatient mortality rate in study phases A, B, and C: from Phase A (9.3%) to Phases B (5.7%) and C (6.9%) [19].

In an observational study by Sefton G. et al. before and after the introduction of the PEWS system in a pediatric hospital, the median infant mortality index (PIM2) decreased from 0.60 to 0.44 ($p < 0.001$). For fewer hospitalizations, invasive lung ventilation was required – 62.7% versus 75.2% ($p = 0.015$); its average duration decreased from 4 to 2 days. The average length of stay in the ICU decreased from 5 to 3 days ($p = 0.002$). In addition, there was a slight decrease in mortality ($p= 0.47$) [20].

The study by Agulnik A. et al., introducing the PEWS system in the Pediatric Cancer Hospital in Guatemala (Unidad Nacional de Oncologia Pediatrica), has reduced unplanned ICU transfers. The results of a study published in 2016 show that hospital investments in PEWS can improve the quality of pediatric cancer care, optimize the use of ICU and reduce costs [21].

A 2017 publication highlighting the results after the successful implementation of PEWS in a children's cancer hospital with limited resources in Guatemala reported a significant reduction in unplanned transfers to the

ICU, a decrease in the length of stay in the ICU and a decrease in the frequency of severe sepsis or septic shock when transferring to the ICU [22].

The same author shows that the PEWS assessment largely correlates with the need for unplanned transfer to the ICU in patients with oncology after hematopoietic stem cell transplantation. In addition, it is reported that the PEWS system correctly identified most patients who needed ICU care [23].

According to the St. Jude Research Hospital, patients after hematopoietic cell transplants have a worsening condition requiring ICU transfer. As a rule, critical deterioration is preceded by a long period of abnormal vital signs, which makes it potentially preventable by earlier recognition of the precursors of critical conditions; PEWS appropriately identified hospitalized patients who needed to be transferred to a higher level of treatment [24].

At Alder Hey Children's Hospital, a top-level pediatric facility in Liverpool, United Kingdom, parents of children were invited to participate in semi-structured telephone interviews. Recruitment was conducted in the period from February 2020 to February 2021. There is data on parents' experience and perception of the acceptability of a hospital-wide active electronic system for early warning of complications in children. Parents reacted positively and welcomed the use of new technologies to support the care of their children [25].

Dylan G. et al . described the algorithmic approach to care used in Guatemala and the United States, showing that PEWS improves interdisciplinary communication, expanding the capabilities of medical professionals [26]. PEWS also improves communication between attending physicians and families by enhancing interaction, which once again demonstrates the importance of PEWS for improving the quality of medical care in conditions with both high and limited resources [27].

In turn, there are clinical and organizational risk factors for mortality with deterioration among patients with pediatric oncology. Thus, in Latin America, a multicenter prospective study involving 16 centers registered 553 critical impairments in patients from 11,536 hospitalizations and 119,414 days of hospital stay. Event mortality was 29% but varied greatly by the center (11-79%). In addition, cases with organ dysfunction and high disease severity had higher mortality. According to the researchers, early detection of complications and timely transfer to the ICU can improve the prognosis [28].

After introducing PEWS in 29 pediatric cancer centers in Latin America, an anonymous survey among medical staff showed a high ability to maintain the PEWS system [29].

A qualitative study involving five pediatric oncology centers with limited resources in 4 Latin American countries assessed barriers and factors contributing to introducing an early warning system for complications. The survey involved 71 employees (70% women), including 32 doctors (45%), 32 nurses (45%), and seven administrators (10%). Many obstacles to implementing PEWS have been identified, including insufficient resources and staff resistance to change. In addition, the survey participants highlighted barriers at the level of clinical staff, hospital, and external factors. The survey (research) result showed that many barriers are not unchangeable and can be transformed into factors contributing to the implementation process [30].

The Dutch Children's Oncology Hospital conducted a prospective cohort study, where all national pediatric oncology care is centralized and which is directly connected to a 22-bed general ICU, the results of which may provide additional evidence of the benefits of using the PEWS system in hospitalized patients with pediatric oncology or indicate that PEWS needs optimization (modification) in children with oncological diseases [31].

Discussion: Regular assessment, monitoring, and registration of the vital signs of the child are critical components of monitoring the patient's condition, fundamental for early detection of clinical deterioration and provision of high-quality medical care [32, 33]. Clinical deterioration in a patient not recognized in time becomes a source of the critical condition [34]. It can lead to extended hospitalization, unplanned hospitalization in the ICU, cardiac arrest, or death [35, 36]. Many children who die unexpectedly or whose condition worsens in the hospital have noticeable signs before the severity of their condition is recognized [37]. Untimely recognition of clinical deterioration is an urgent patient safety problem, necessitating the introduction of PEWS systems in the care of children in the hospital [38]. Using PEWS to stratify the risk of clinically deteriorating patients can also help solve the problem of the burden on medical institutions that lack resources [39, 40]. The assessment of the condition is calculated manually or electronically, while each component is evaluated, taking into account its deviation from the norm [41-43]. The data indicate that electronic assessment has advantages over paper assessment [44].

During the night shift, one doctor on duty serves all departments. Given the potential burden of many patients for whom a doctor may be responsible, the PEWS system can provide an objective triage tool to effectively assess the risk of clinical deterioration, leading to more efficient use of resources. However, we should note that many patients do not require interventions after the PEWS assessment. Moreover, it could create an unintended burden on the department's medical staff. There are also contradictory data on the effectiveness of the PEWS system, reflecting the complexity of using and evaluating measurement results [45].

Hospitalized children suffering from oncological diseases are at high risk for sudden deterioration of their condition. However, as access to pediatric cancer therapy expands in resource-constrained settings, there is a need for effective and inexpensive methods to improve the care of cancer patients, as a lack of infrastructure and a shortage of staff can lead to late detection of PEWS.

During the long therapy process, it is necessary to maintain a dialogue between doctors, nursing staff, the child, and his parents. It is paramount for optimizing the care of children with complex diseases and changing medical status. After all, the life of parents whose child needs intensive care in an ICU is turned upside down; many compare it to "riding a roller coaster" [46]. In addition, some parents of children with severe and long-term illnesses become "experts" in vital indicators of their child's health status and can recognize changes in their condition [47]. In addition, there is evidence that parents are reliable partners in expanding care [48].

According to the analyzed publications, many positive results are reported, but there are also contradictory data on using PEWS. In this regard, it is necessary to evaluate the effectiveness in the long term.

Conclusion: The lack of early diagnosis of complications, infections, erroneous interpretation of the observed symptoms, and late referral to specialists – all these factors are crucial concerning the outcome of the disease [49]. Deterioration of the child's condition can develop at any stage of program polychemotherapy [50]. Therefore, special qualification of medical staff is required for timely recognition of early signs of clinical deterioration and provision of comprehensive, intensive care.

Implementing the PEWS assessment system in the Department of Pediatric Hematology/Oncology is feasible. It can contribute to an adequate assessment of the patient's condition by increasing the frequency of collecting vital signs in real time.

We want to emphasize the need for early diagnosis of clinical deterioration before, during, and after program therapy in children with oncological diseases to promptly provide the necessary complex intensive therapy. Thus, unified approaches to early precursors of critical conditions in children with oncological diseases are necessary to prevent critical conditions and reduce adverse disease outcomes.

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АҢДАТПА

ОНКОЛОГИЯЛЫҚ БАЛАЛАРДАҒЫ АУЫР ЖАҒДАЙЛАРДЫҢ ЕРТЕ АЛДЫН АЛУДЫҢ ПЕДИАТРИЯЛЫҚ БЕЛГІЛЕРІ ЖҮЙЕСІН ҚОЛДАНУДЫҢ ХАЛЫҚАРАЛЫҚ ТӘЖІРИБЕСІ: ӘДЕБИЕТКЕ ШОЛУ

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Өзектілігі: *Онкологиялық аурулар ісік балалар өлімінің басты себебі болып қала береді, нәтижесінде қарқынды терапия жүргізу қажеттілігі артуда. Онкологиялық аурулармен ауыратын ауруханаға жатқызылған балалар негізгі ауру бойынша да, жүқпалы асқынуларға және дәрілік препараттардың уытты әсеріне байланысты да жағдайдың кенеттен нашарлауы бойынша жоғары тәуекел тобына жатады. Бұл шолуда клиникалық нашарлауды уақтылы анықтау мақсатында онкологиялық науқастарда ерте ескертудің педиатриялық белгілері (Pediatric Early Warning Signs, PEWS) жүйесі туралы мәліметтер қамтылған.*

Зерттеудің мақсаты *– балалар онкологиясындағы клиникалық нашарлаудың ерте алдын алудың педиатриялық белгілері жүйесін қолдану туралы өзекті әдеби деректерге шолу.*

Әдістері: *онкологиялық балаларда PEWS жүйесін қолдану бойынша интернет-ресурстарда жарияланған зерттеулерге шолу жасалды.*

Нәтижелері: *жарияланған деректер бойынша онкологиялық науқастарда PEWS жүйесін қолдану маңызды рөл көрсетеді, ол клиникалық жағдайдың нашарлауын ерте анықтау үшін және уақытылы шұғыл медициналық көмек көрсету үшін қажет.*

Қорытынды: *Халықаралық тәжірибеге жүргізілген талдау көрсеткендей онкологиялық аурулары бар балаларда PEWS жүйесін қолдану халықаралық тәжірибеде клиникалық нашарлау белгілерін ерте танудың тиімді әдісін ұсынады, бұл өз кезегінде кешенді қарқынды терапияны уақтылы қосуға мүмкіндік береді.*

Түйінді сөздер: *онкология, гематология, pews, клиникалық нашарлау, балалар, қарқынды терапия.*

АННОТАЦИЯ

МЕЖДУНАРОДНЫЙ ОПЫТ ПРИМЕНЕНИЯ СИСТЕМЫ ПЕДИАТРИЧЕСКИХ ПРИЗНАКОВ РАННЕГО ПРЕДУПРЕЖДЕНИЯ КРИТИЧЕСКИХ СОСТОЯНИЙ У ОНКОЛОГИЧЕСКИХ ДЕТЕЙ: ОБЗОР ЛИТЕРАТУРЫ

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Актуальность: *Онкологические заболевания остаются основной причиной смерти у детей, в результате потребность в проведении интенсивной терапии возрастает. Госпитализированные дети, страдающие онкологическими заболеваниями, находятся в группе*

высокого риска по внезапному ухудшению состояния, как по основному заболеванию, так и в связи с инфекционными осложнениями и токсичными действиями лекарственных препаратов. В этом обзоре освещаются сведения по системе педиатрические признаки раннего предупреждения (Pediatric Early Warning Signs, PEWS) у онкологических пациентов, с целью своевременного выявления клинического ухудшения.

***Цель исследования** – изучение актуальных литературных данных о применении системы педиатрических признаков раннего предупреждения клинического ухудшения в детской онкологии.*

***Методы:** Был проведен обзор опубликованных исследований по применению системы PEWS у онкологических детей.*

***Результаты:** Опубликованные данные показывают важную роль использования PEWS у онкологических пациентов для раннего выявления ухудшения состояния с последующим оказанием интенсивной помощи.*

***Заключение:** Проведенный анализ международного опыта показал, что применение системы PEWS у детей с онкологическими заболеваниями является эффективным методом раннего распознавания признаков клинического ухудшения, что, в свою очередь, позволяет своевременно подключить комплексную интенсивную терапию.*

***Ключевые слова:** онкология, гематология, педиатрические признаки раннего предупреждения (Pediatric Early Warning Signs, PEWS), клиническое ухудшение, дети.*

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