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Prevalence and Prognostic Factors of Thrombocytopenia in Pediatric Oncology at CHUD-Ouémé from 2022 to 2024 (Benin)

Gilles Bognon[1], Yévèdo Tohodjede[2], Mohamed Ladjouan[1], Romaric Massi[3], Annabella Hountondji[1], Michée Assogba[1], Roméo Dah Bolinon[1]

[1]Service d'Oncologie Pédiatrique du CHU Départemental Ouémé (CHUD-O), Porto-Novo, Benin
[2]Clinique Universitaire de Pédiatrie et Génétique Médicale du CNHU Hubert Koutoucou Maga, Cotonou, Benin
[3]Unité d'hématologie du Service de Médecine du CHU Départemental Ouémé (CHUD-O), Porto-Novo, Benin
Email: bognongilles@yahoo.fr

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Abstract

Introduction: thrombocytopenia is a common and serious hematologic complication in pediatric oncology, for which data remain limited in Benin. The objective of this study was to determine the prevalence and prognostic factors of thrombocytopenia in the pediatric oncology department at CHUD-O from 2022 to 2024. **Methodology:** this was a descriptive and analytical cross-sectional study with prospective data collection. It included all cases of thrombocytopenia (platelet count < 150 G/L) among hospitalized children being treated for cancer in the pediatric oncology department of CHUD-O between May 1, 2022, and December 31, 2024. A multivariate analysis was performed to identify prognostic factors, with a significance threshold of $p < 0.05$. **Results:** the in-hospital prevalence was 21.0%. The mean age was 7.9 ± 4.8 years, and 36.8% of the children were between 6 and 12 years old; the sex ratio was 1.7. The main underlying cancers were acute leukemia (36.8%), lymphomas (23.5%), nephroblastoma (11.8%), and retinoblastoma (7.4%). Thrombocytopenia was severe in 45.6% of cases and asymptomatic in 55.9%. The main hemorrhagic signs were epistaxis (13.2%), gingival bleeding (13.2%), and hematemesis (8.8%). The two main causes were chemotherapy-induced bone marrow aplasia (50%) and bone marrow infiltration by malignant hematologic disorders (41.18%). The platelet concentrate availability rate of 28.9%. The case-fatality rate was 58.8%. Factors associated with death were the presence of hemorrhage ($OR = 10.3$ [3.3 - 32.1], $p < 0.0001$), the severity of thrombocytopenia ($OR = 12.5$ [1.4 - 110], $p = 0.01$), bone marrow involvement ($OR = 4.1$ [1.5 - 11.4], $p = 0.006$), the use of fresh frozen plasma ($OR = 4$ [1.4 - 11.4], $p = 0.008$), and iatrogenic bone marrow aplasia ($OR = 0.3$ [0.1 - 0.8], $p = 0.01$). **Conclusion:** thrombocytopenia is com-

mon in pediatric oncology at CHUD-Ouémé and is associated with a high mortality rate. Reducing this mortality rate will require taking the identified prognostic factors into account.

Keywords

Thrombocytopenia, Pediatric Oncology, Chemotherapy, Platelet Transfusion, CHUD-Ouémé

1. Introduction

Thrombocytopenia represents major hematological emergencies in pediatric oncology and is associated with considerable morbidity and mortality [1] [2]. In children with cancer, the vulnerability of primary hemostasis—exacerbated by central bone marrow failure or the iatrogenic toxicity of antimitotic treatments—exposes patients to a high risk of severe hemorrhagic events [2] [3]. In sub-Saharan Africa, the frequency of cytopenias and hemorrhagic manifestations during hematologic malignancies and chemotherapy protocols remains particularly high [4] [5]. Diagnosis is based on rapid clinical evaluation of hemostasis, biological confirmation through a complete blood count (CBC with platelet count < 150 G/L) combined with peripheral blood smear analysis, and bone marrow examination (myelogram) when indicated [1] [6]. Clinical manifestations are dominated by cutaneous-mucosal bleeding (purpura, petechiae, ecchymoses, epistaxis, and gingival bleeding), but may progress to life-threatening visceral involvement (gastrointestinal, urinary, or cerebro-meningeal) [2] [7]. The etiologies are multifactorial [1]. They primarily include chemotherapy- and radiotherapy-induced bone marrow aplasia, bone marrow infiltration by hematologic malignancies (acute leukemias, lymphomas) or metastases from solid tumors (nephroblastoma, neuroblastoma), as well as peripheral mechanisms such as consumption (severe sepsis, DIC) or immune-mediated destruction [1]-[3] [8]-[10]. Therapeutic management requires prompt preventive and curative medical and surgical interventions [6]. It includes platelet and red blood cell transfusions in cases of anemia due to blood loss, pharmacological control of bleeding, adjustment or postponement of chemotherapy cycles, and treatment of aggravating factors such as infections [3]-[6] [8] [11]. However, in low-resource countries, limited access to platelet concentrates and the scarcity of apheresis facilities remain major barriers to optimal care [11] [12]. Without adequate and immediate management, the outcome may be complicated by severe events, primarily hemorrhagic shock and death [2] [12].

In Benin, although the Pediatric Oncology Unit at CHUD-O is part of the Franco-African Pediatric Oncology Group (GFAOP) network and follows standardized treatment protocols, the management of hematological emergencies continues to face significant structural constraints [12]-[15]. Among these, severe thrombocytopenia and its hemorrhagic complications are a major cause of mor-

bidity and unplanned interruptions of chemotherapy [3] [12]. However, local data on the profile of thrombocytopenia in children with cancer remain limited and insufficiently documented [12] [14]. While restricted access to platelet concentrates and apheresis platforms is known to affect prognosis, no local study has yet identified the specific determinants and predictive factors of unfavorable or fatal outcomes. The present study was therefore conducted to determine the prevalence and prognostic factors of thrombocytopenia in the pediatric oncology department, with the aim of improving survival and quality of life in treated children.

2. Methods

This was a descriptive and analytical prospective cohort study including all cases of thrombocytopenia (one or more episodes) in patients under 18 years of age, either hospitalized or managed on an outpatient basis for confirmed cancer in the pediatric oncology department of CHUD-O between May 1, 2022, and December 31, 2024. Thrombocytopenia was defined as a blood platelet count below 150.109/L on the complete blood count (CBC) without platelet clumping (confirmed by peripheral blood smear examination) and was graded according to the Common Terminology Criteria for Adverse Events (CTCAE) classification grid (**Table 1**), whereas the severity of the hemorrhagic syndrome was evaluated using the WHO scale (Grades 1 to 4) (**Table 2**) [13] [14]. Any child receiving anticoagulant or antiplatelet therapy upon admission was excluded. The dependent variable was the occurrence of thrombocytopenia-related death, defined as any death resulting directly from a severe hemorrhagic syndrome (WHO Grade 3 or 4, such as intracranial, massive gastrointestinal, or pulmonary hemorrhage) or uncontrolled hemorrhagic shock, with causality collegially assigned by the medical team based on longitudinal clinical and laboratory data (non-hemorrhagic terminal causes of death, such as refractory septic shock or disease progression without major bleeding, were classified as non-thrombocytopenia-related). Independent variables included sociodemographic (age, sex, socioeconomic status, and parental education level) and anthropometric characteristics (weight-for-height Z-scores, BMI-for-age, mid-upper arm circumference), underlying cancer type (hematologic malignancy or solid tumor), time elapsed since diagnosis, characteristics of the hemorrhagic syndrome (site, WHO severity grade), laboratory findings (depth of thrombocytopenia, hemoglobin level, leukocyte count, coagulation profile, presence of pancytopenia defined as the combination of anemia, neutropenia, and thrombocytopenia), identified etiologies (chemotherapy toxicity, bone marrow infiltration, infection/sepsis, disseminated intravascular coagulation) established through a bundle of chronological, clinical, and microbiological evidence, as well as therapeutic modalities (type of chemotherapy protocol, duration of exposure to antineoplastic agents, corticosteroid therapy, antifibrinolytics, antibiotic therapy), transfusion support, and outcome (resolution of clinical signs, occurrence of complications, or death). A death was considered thrombocytopenia-related when it occurred as a direct consequence of a major hemorrhagic syndrome (according to

the WHO scale) not exclusively attributable to another cause of terminal failure (such as refractory septic shock or terminal disease progression without symptomatic bleeding), following analysis of the clinical and laboratory course recorded in the medical chart. Causality was collegially assigned by the department's medical team based on longitudinal clinical and laboratory data. The platelet concentrate availability rate was calculated as the ratio of the number of platelet units issued to the number of units prescribed. Data were collected using a pretested structured questionnaire, combining medical record reviews, clinical examination findings, and face-to-face interviews with parents or guardians. Data analysis was performed using SPSS software (version 25) and RStudio (version 4.3.2). Qualitative variables were expressed as frequencies and percentages, while quantitative variables were presented as means with their standard deviations (SD) or as medians with their interquartile ranges (IQR). To identify independent risk factors associated with death, a multivariable logistic regression analysis was performed. Candidate variables were selected based on a bivariate significance threshold of $p < 0.20$ and their clinical relevance. To account for the limited number of events (deaths) and to prevent model overfitting, a parsimonious selection procedure was applied using backward stepwise elimination based on the Akaike Information Criterion (AIC). Results of the multivariable model are reported as adjusted Odds Ratios (aOR) with their 95% Confidence Intervals (95% CI). Missing data (<5%) were handled using complete-case analysis. Statistical significance was set at $p < 0.05$.

The study protocol received institutional approval from the Faculty of Health Sciences (FSS) and administrative authorization from the management of CHUD-O (Ref. 0109/MS/DDS-O/CHUD-0/DG/DAF/SRH/SA). Free and informed consent from the parents or legal guardians of all included children was systematically obtained prior to enrollment, strictly guaranteeing data anonymity and absolute confidentiality.

3. Results

Of the 324 admissions to the Pediatric Oncology Department of CHUD-Ouémé during the study period, 68 cases of thrombocytopenia were recruited, representing a cumulative prevalence of 21%. The mean age was 7.9 ± 4.8 years, with 36.8% of children aged between 6 and 12 years. The sex ratio was 1.7. Hematologic malignancies were the most common cancers (60.3%) (**Figure 1**). Approximately seven out of ten parents or guardians (69.1%) had a primary school education level. Thrombocytopenia was symptomatic in 44.1% of cases. The main hemorrhagic signs were epistaxis (13.2%), gingival bleeding (13.2%), hematemesis (8.8%), and melena (8.8%) (**Table 3**). According to the WHO classification, bleeding was grade 1 (10%), grade 2 (26.6%), grade 3 (43.3%), and grade 4 (20%). Thrombocytopenia was mild, moderate, and severe in 14.7%, 39.7%, and 45.6% of cases, respectively. It was associated with anemia and leukopenia in 95.6% and 36.8% of cases, respectively. The underlying causes included chemotherapy-induced bone marrow apla-

sia (50%), bone marrow infiltration by hematologic malignancies (41.2%), disseminated intravascular coagulation (4.4%), and bacterial or parasitic infections (4.4%). Therapeutically, transfusions of packed red blood cells (77.9%), fresh frozen plasma (35.3%), and platelet concentrates (32.4%) were administered. Of the 76 requests for platelet concentrates, only 22 were fulfilled, corresponding to the platelet concentrate availability rate of 28.9%. Dose reduction or postponement of chemotherapy was carried out in 85.3% of cases with severe or moderate thrombocytopenia. The clinical outcome was favorable, with improvement of hemorrhagic signs and thrombocytopenia in 41.2% of children. The case fatality rate was 58.8%. Deaths were due to catastrophic and cerebral hemorrhages.

In bivariate analysis, factors associated with death included the presence of hemorrhagic signs ($p < 0.0001$), grade 4 thrombocytopenia ($p = 0.01$), hematologic malignancies ($p = 0.006$), and transfusion of fresh frozen plasma ($p = 0.008$). In multivariate logistic regression analysis, factors that increased the risk of death were the presence of hemorrhage (OR = 10.3 [3.3 - 32.1], $p < 0.0001$), severity of thrombocytopenia (OR = 12.5 [1.4 - 110], $p = 0.01$), bone marrow infiltration by hematologic malignancy (OR = 4.1 [1.5 - 11.4], $p = 0.006$), and the use of fresh frozen plasma (OR = 4 [1.4 - 11.4], $p = 0.008$). The presence of chemotherapy-induced bone marrow aplasia reduced the risk of death (OR = 0.3 [0.1 - 0.8], $p = 0.01$) (Table 4).

Table 1. CTCAE v5.0 classification grid for thrombocytopenia.

CTCAE Grade	Platelet Count (G/L ou × 10^9/L)	Value in/mm³
Grade 1 (Mild)	<LNN – 75 G/L	<LNN – 75,000
Grade 2 (Moderate)	50 G/L ≤ Platelets < 75 G/L	50,000 ≤ Platelets < 75,000
Grade 3 (Severe)	25 G/L ≤ Platelets < 50 G/L	25,000 ≤ Platelets < 50,000
Grade 4 (Life-threatening)	<25 G/L	<25,000

*LNN = Laboratory Lower Limit of Normal (generally 150 G/L).

Table 2. WHO classification of bleeding severity in thrombocytopenic patients.

	Grade	Main Clinical Manifestations
Grade 0	**No bleeding**	No clinical or biological bleeding
Grade 1	**Minor bleeding**	P Cutaneous or mucosal petechiae; purpura ≤ 2.5 cm; minor ecchymoses/hematomas; epistaxis or oropharyngeal bleeding ≤ 30 min/24 h; occult blood in stools; microscopic hematuria or hemoglobinuria; vaginal spotting
Grade 2	**Moderate bleeding**	Epistaxis > 30 min/24 h; purpura > 2.5 cm; macroscopic hematuria; melena; hematemesis; hemoptysis; hematochezia; joint bleeding; vaginal bleeding greater than simple spotting; visible blood in a body cavity; retinal bleeding without visual impairment; bleeding at an invasive site
Grade 3	**Major bleeding**	Bleeding requiring red blood cell transfusion beyond usual transfusion needs and/or associated with moderate hemodynamic instability
Grade 4	**Life-threatening bleeding**	Bleeding associated with severe hemodynamic instability; central nervous system hemorrhage; fatal hemorrhage

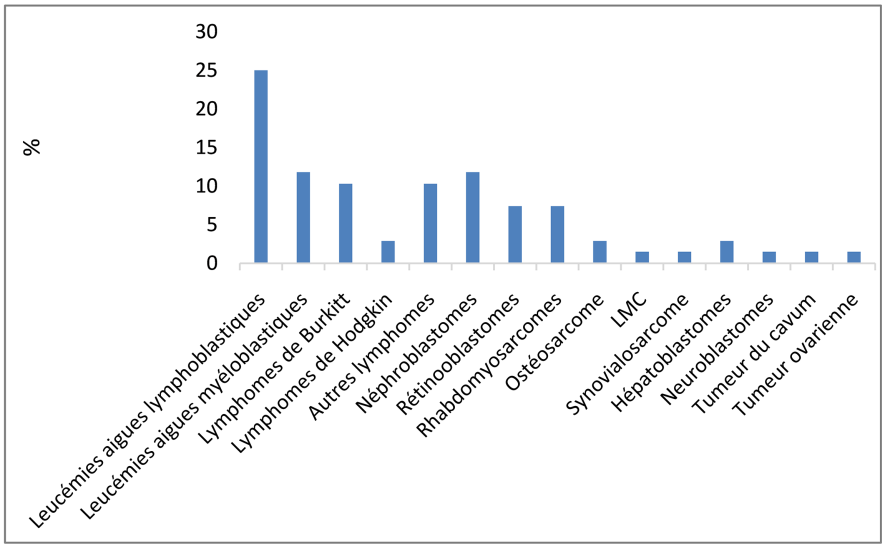

Figure 1. Distribution of different cancers observed in children with thrombocytopenia.

Table 3. Distribution of children according to the hemorrhagic signs observed.

Hemorrhagic Sign	Number of Cases	Percentage (%)
Epistaxis	9	13.2
Gingival bleeding	9	13.2
Hematemesis	6	8.8
Melena	6	8.8
Hematochezia	5	7.4
Hematuria	5	7.4
Purpura	4	5.9
Ecchymoses	3	4.4
Hematoma	3	4.4
Mucosal hemorrhages	3	4.4
Petechiae	2	2.9
Hemorrhagic bullae	2	2.9
Hemoglobinuria	2	2.9
Hemoptysis	2	2.9
Conjunctival hemorrhage	2	2.9
Cerebral hemorrhage	1	1.5
Otorrhagia	1	1.5

Table 4. Distribution of factors associated with an unfavorable outcome of thrombocytopenia.

Variable	Death		p-value	OR	95% CI [OR]
	Yes	No			
Presence of symptoms					
No	7	31		1	
Yes	21	9	**<0.0001**	10.3	3.3 - 32.1

Continued

Bleeding severity (n = 27)					
Stage 0 - 2	7	4	0.3	1	
Stage 3 - 4	13	3		2.5	0.4 - 14.3
Thrombocytopenia					
Mild thrombocytopenia	1	9		1	
Moderate thrombocytopenia	9	18	0.01	4.5	0.5 - 41.2
Severe thrombocytopenia	18	13	**0.01**	12.5	1.4 - 110
Etiology of thrombocytopenia					
Bone marrow infiltration (hematologic malignancies)	17	11	**0.006**	4.1	1.5 - 11.4
Chemotherapy-induced bone marrow aplasia	9	25	**0.01**	0.3	0.1 - 0.8
Disseminated intravascular coagulation	2	1	0.3	3	0.3 - 34.8
Bacterial infections	0	2	0.2	1.3	0.8 - 2.2
Parasitic infections	0	1	0.4	1.3	0.8 - 2.1
Treatment					
Packed red blood cell transfusion	24	29	0.2	2.3	0.6 - 8
Fresh frozen plasma transfusion	15	9	**0.008**	4	1.4 - 11.4
Platelet concentrate transfusion	11	11	0.3	1.7	0.6 - 4.8
Chemotherapy dose reduction	0	1	0.4	0.2	0.01 - 1.3

4. Discussion

This original work has provided evidence-based data on thrombocytopenia in the pediatric oncology setting in our working context. This study has certain limitations related to local technical facility constraints. First, qualitative platelet function (aggregometry) could not be evaluated, with diagnosis relying solely on quantitative counts and the WHO bleeding scale. Second, specific micronutrient assays (vitamin B12, folate) were not routinely performed to assess their contribution to cytopenias, although anthropometric assessment and management of malnutrition were routinely integrated into clinical care. The hospital prevalence of thrombocytopenia found in this study falls within the 10% - 35% range reported in the literature [1] [2] [8] [15] [16]. Indeed, the prevalence of thrombocytopenia in pediatric oncology units varies according to the timing and location of case recruitment (before and/or after the start of chemotherapy) and the level of development of the country. The prevalence estimated in our working context is probably related to the delay in the diagnosis of pediatric cancers, the frequent bone marrow infiltration by leukemias (the main underlying hematologic malignancy in this study), and the severity of comorbidities, particularly infections [1] [5] [9] [17]-[19]. The distribution of thrombocytopenia cases according to the age and sex of the children is consistent with epidemiological data from sub-Saharan Africa, where hematologic malignancies predominate in school-age boys [17] [20]. The low educational level among the majority of parents of the included children, combined with socioeconomic vulnerability, constitutes a major determinant of de-

layed consultation, which therefore limits early detection of clinical and biological warning symptoms during chemotherapy [18] [19]. The various underlying tumor pathologies reported in this work are consistent with data from the Franco-African Pediatric Oncology Group network [17] [20]. From an etiopathogenic perspective, the central mechanisms responsible for thrombocytopenia—namely iatrogenic bone marrow aplasia induced by chemotherapy resulting from the direct marrow toxicity of antimitotic agents (alkylating agents, antimetabolites, anthracyclines) on megakaryocyte precursors, and bone marrow invasion or infiltration by the malignant disease, particularly observed in acute leukemias and disseminated forms of non-Hodgkin lymphomas—are consistent with findings in the literature [1] [3] [8] [9]. Indeed, in solid tumors, thrombocytopenia is due to chemotherapy or bone marrow infiltration, whereas in acute leukemias it is linked to central bone marrow failure caused by blast cell suffocation [1] [8]. The association of anemia and leukopenia with thrombocytopenia exacerbates tissue hypoxia and microvascular fragility, thereby increasing the risk of hemorrhagic events [4] [7]. Epistaxis was also the main hemorrhagic sign reported by Lukamba Mbuli *et al.* in Lubumbashi in 2023 [15]. The occurrence of gastrointestinal bleeding in one-quarter of our patients reflects the severity of mucosal involvement, often exacerbated by post-chemotherapy mucositis [5] [19]. According to the CTCAE classification, the majority of thrombocytopenia cases were severe to life-threatening [13]. A platelet drop below the critical threshold of 20 - 25 G/L exposes patients to spontaneous bleeding and intracranial hemorrhage, the leading cause of immediate mortality [6] [7]. Management was hindered by major therapeutic constraints. Indeed, chemotherapy adjustment (suspension, postponement, or dose reduction) was required in 85.3% of children. While these measures protect against worsening hemorrhage, they expose patients to tumor relapse [3] [8]. The low platelet concentrate availability rate in our setting is explained by the absence of apheresis cell separators in most sub-Saharan hospitals, the short shelf life of platelet concentrates (5 days), and the high cost of these products [11] [12]. Inaccessibility to alternative therapies, particularly thrombopoietin receptor agonists such as romiplostim or eltrombopag, further increases the risk of fatal outcomes due to uncontrolled bleeding [21] [22]. The particularly high case fatality rate observed in this study, mainly caused by catastrophic and cerebral hemorrhages, is consistent with data from low- and middle-income countries but contrasts sharply with those from high-income countries (<2% - 5%) [2] [12] [15] [17] [23]. The four factors that significantly increased the risk of death—namely the presence of hemorrhagic signs, severity of thrombocytopenia, bone marrow infiltration by an underlying hematologic malignancy, and the need for fresh frozen plasma transfusion—have also been reported by other authors [1] [7] [12]. Other prognostic factors for thrombocytopenia in pediatric oncology, such as the stage of the underlying disease, delays in care, and socioeconomic vulnerability, have also been described [17]-[19]. The reduced risk of death associated with iatrogenic bone marrow aplasia may be explained by the fact that suspending or

postponing chemotherapy cycles or reducing antimitotic doses helped limit the worsening of thrombocytopenia and, consequently, the risk of hemorrhage. However, this study may have confounding biases regarding the exclusive responsibility of thrombocytopenia in the occurrence of deaths in children suffering from severe conditions such as hematologic malignancies. Nevertheless, multivariate logistic regression analysis allowed identification of the true prognostic factors on which targeted interventions can be implemented to reduce this high mortality rate.

5. Conclusion

Thrombocytopenia is a major hematological emergency that is common among children with cancer at CHUD-Ouémé and is associated with a very high mortality rate. The predictive factors for mortality identified were the severity of thrombocytopenia, the presence of hemorrhagic signs, an underlying hematologic malignancy, and the need for fresh frozen plasma transfusion. The platelet transfusion satisfaction rate remains low. Improving the survival of these children will require urgent strengthening of the transfusion chain, particularly through the development of platelet apheresis, reduction of diagnostic delays, and optimization of hematological supportive care.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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