Scientific Research Publishing

Open Journal of Pediatrics, 2026, 16(6), 832-839
https://www.scirp.org/journal/ojped
ISSN Online: 2160-8776
ISSN Print: 2160-8741

Hyperglycemia during Induction Therapy in Pediatric Acute Lymphoblastic Leukemia at Chud-Ouémé (CHUD-O)

Gilles Modeste Alain Bognon[1*], Chakirou Mohamed Ladjouan[1], Yévèdo Tohodjèdé[2], Romaric Massi[3], Annabella Hountondji[1], Roméo Dah Bolinon[1], Michée Assogba[1]

[1]Pediatric Oncology Department, Departmental University Teaching Hospital of Ouémé, Porto-Novo, Benin
[2]Clinic of Pediatrics and Medical Genetics, Hubert Koutoucou Maga National University Teaching Hospital, Cotonou, Benin
[3]Hematology Unit, Departmental University Teaching Hospital of Ouémé, Porto-Novo, Benin
Email: *bognongilles@yahoo.fr

How to cite this paper: Bognon, G.M.A., Ladjouan, C.M., Tohodjèdé, Y., Massi, R., Hountondji, A., Dah Bolinon, R. and Assogba, M. (2026) Hyperglycemia during Induction Therapy in Pediatric Acute Lymphoblastic Leukemia at Chud-Ouémé (CHUD-O). *Open Journal of Pediatrics*, **16**, 832-839.
https://doi.org/10.4236/ojped.2026.166080

Received: October 20, 2026
Accepted: November 21, 2026
Published: November 24, 2026

Copyright © 2026 by author(s) and Scientific Research Publishing Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/

Open Access

Abstract

Introduction: Iatrogenic hyperglycemia during the induction phase of pediatric acute lymphoblastic leukemia (ALL) is a frequent but poorly documented complication in Sub-Saharan Africa. The objective of this study was to evaluate hyperglycemia in children treated for ALL at CHUD-O. **Methods:** This was a retrospective cohort study conducted from May 2022 to May 2026 in the Pediatric Oncology Department of CHUD-O. Of the 78 children screened, 62 children who met the inclusion criteria (aged 1 to 18 years and treated for acute lymphoblastic leukemia according to the Marall 2006 protocol) were included. Induction hyperglycemia was defined as the occurrence of at least two fasting blood glucose levels ≥ 180 mg/dL or one random blood glucose level ≥ 250 mg/dL between Day 1 and Day 33. Data analysis was performed using SPSS software, with a significance threshold set at $p < 0.05$. **Results:** The overall prevalence of induction hyperglycemia was 38.7% (n = 24/62), including 25.8% (n = 16/62) of cases of chemotherapy-induced diabetes. The median age was 5.8 years. The median time to onset of hyperglycemia was 9 days, with a median peak blood glucose level of 298 mg/dL. In multivariate analysis, factors associated with the development of hyperglycemia included age > 10 years (OR = 4.1; p = 0.004), family history of diabetes (p = 0.02), and exposure to dexamethasone compared with prednisone (p = 0.04). Prognostically, children who developed hyperglycemia had a significantly higher risk of infections (54.1% vs. 23.7%; p = 0.02), prolonged neutropenia > 10 days (66.7% vs. 34.2%; p = 0.013), and delays in L-asparaginase administration (50.0% vs. 10.5%; p = 0.00054). A non-significant trend toward increased mortality during induction was also observed (25.0% vs. 7.9%; p = 0.08). **Conclusion:** Hyperglycemia

affects more than one in three children during ALL induction at CHUD-O. Associated with increased infectious morbidity and chemotherapy delays, it highlights the need for routine blood glucose monitoring and standardized management protocols.

Keywords

Acute Lymphoblastic Leukemia, Iatrogenic Hyperglycemia, Pediatric Oncology, Dexamethasone

1. Introduction

Acute lymphoblastic leukemia (ALL) is the most common hematologic malignancy in children [1]. Thanks to major advances in therapeutic stratification, intensification of chemotherapy regimens, and improvements in supportive care, overall survival for children with ALL now exceeds 80% - 90% in high-income countries [2] [3]. The induction phase, a cornerstone of treatment protocols, aims to achieve complete remission through a combination of high-dose corticosteroids (prednisone or dexamethasone), L-asparaginase, vincristine, and anthracyclines [3] [4]. However, this phase is associated with significant acute toxicities, including metabolic disorders and, in particular, iatrogenic hyperglycemia [4] [5]. Corticosteroids induce peripheral insulin resistance and increase hepatic gluconeogenesis, while L-asparaginase impairs insulin synthesis and secretion by pancreatic beta cells [4] [6]. The synergistic effect of these agents promotes glucose intolerance that may progress to chemotherapy-induced diabetes [6] [7].

In the international literature, the prevalence of hyperglycemia during induction therapy ranges from 10% to 45%, depending on the diagnostic criteria and corticosteroid protocols used [5] [7] [8]. This metabolic complication has been associated with an increased risk of severe infections, delayed wound healing, prolonged hospitalization, and undesirable adjustments in chemotherapy dosing [5] [9].

In sub-Saharan Africa, and particularly in Benin, epidemiological data on metabolic complications of chemotherapy in children remain extremely limited [10]. Due to local diagnostic and therapeutic constraints, this condition is often underrecognized [10]. It is in this context that the present study was conducted in the Pediatric Oncology Department of the Centre Hospitalier Universitaire Départemental de l'Ouémé (CHUD-O), with the objective of investigating hyperglycemia during induction therapy for acute lymphoblastic leukemia.

2. Methods

This was a retrospective cohort study with descriptive and analytical objectives, conducted from May 1, 2022, to May 31, 2026, in the Pediatric Oncology Department (SOP) in collaboration with the Hematology Unit of CHUD-O in Porto-

Novo. During the study period, 78 children aged 1 to 18 years were diagnosed with confirmed acute lymphoblastic leukemia (ALL) and received induction therapy. Sixteen children were excluded due to incomplete medical records or insufficient glycemic monitoring (more than 48 consecutive hours without glucose measurements). Thus, 62 children who completed the induction phase were included. Glycemic monitoring consisted of systematic twice-daily measurements (every 12 hours) from Day 1 to Day 33.

Induction hyperglycemia was defined as the occurrence of at least two fasting blood glucose levels ≥ 180 mg/dL (10.0 mmol/L) or at least one random blood glucose level ≥ 250 mg/dL (13.9 mmol/L) measured between Day 1 (D1) and Day 33 (D33) of induction therapy [5] [7].

Chemotherapy-induced diabetes was defined as hyperglycemia requiring insulin therapy or associated with marked clinical signs of hyperglycemia (polyuria, polydipsia, weight loss) during corticosteroid treatment [7] [11].

The Marall 2006 protocol was used for leukemia management [10].

Corticosteroid therapy consisted of either prednisone (60 mg/m^2/day orally) or dexamethasone (6 mg/m^2/day orally or intravenously) for 28 consecutive days. The choice of corticosteroid was determined by the protocol's risk stratification guidelines and drug availability at the institution during the study period. L-asparaginase was administered intramuscularly at a dose of 6000 IU/m^2 per dose, according to a schedule of 6 to 8 injections during the induction phase (on Days 8, 10, 12, 14, 17, 20, 23, and 26).

The time to onset was defined as the number of days between the initiation of corticosteroid therapy (Day 1) and the first episode of hyperglycemia meeting the study definition [7]. Data were collected from medical records, clinical monitoring sheets, and hospitalization registers using a standardized digital data extraction form. Collected variables included sociodemographic and anthropometric data (age, sex, family history of diabetes mellitus), oncologic and therapeutic data (type of corticosteroid administered—dexamethasone or prednisone—cumulative doses, and L-asparaginase administration), metabolic monitoring data (fasting and random capillary and/or plasma glucose values, time to onset of hyperglycemia, and maximum recorded glucose level), and outcome and prognostic data (occurrence of infectious complications, duration of neutropenia, delays or dose modifications of L-asparaginase, and death during the induction phase).

Statistical analysis was performed using SPSS version 25.0. Qualitative variables were expressed as frequencies and percentages. Quantitative variables were presented as medians with interquartile ranges according to data distribution. Proportions were compared using Pearson's chi-square test or Fisher's exact test when expected frequencies were less than 5. Median comparisons were performed using appropriate non-parametric tests.

A multivariate logistic regression analysis was conducted to identify independent factors associated with the occurrence of hyperglycemia, calculating adjusted odds ratios (aOR) and their 95% confidence intervals (95% CI). To limit model

overfitting given the 24 observed hyperglycemia events (in accordance with the events-per-variable rule), the complexity of the multivariate logistic regression model was strictly limited to a maximum of three prespecified clinical covariates (age, type of corticosteroid, and family history of diabetes). Candidate variables were selected based on clinical relevance and their association in univariate analysis ($p < 0.20$). The statistical significance threshold was set at $p < 0.05$.

The study was conducted in strict compliance with medical ethics guidelines, ensuring confidentiality and anonymity of data following administrative authorization from CHUD-O. As this was a retrospective study using anonymized medical records, a waiver of individual informed consent was granted by the ethics committee, in accordance with national ethical guidelines and the Declaration of Helsinki.

3. Results

A total of 62 children meeting the inclusion criteria were included in the study. The median age of the patients was 5.8 years (range: 1 - 18 years). The sex ratio was 1.21.

During the induction phase, 24 children developed hyperglycemia, representing an overall prevalence of 38.7% (24/62). Among these patients, 16 children met the criteria for chemotherapy-induced diabetes, corresponding to a frequency of 25.8% in the entire study population. Nearly two-thirds (62.5%; n = 15) of these children were older than 10 years. A family history of diabetes in a first- or second-degree relative was noted in 41.7% of them. Corticosteroid therapy consisted of dexamethasone in 70.8% (n = 17) of the children and prednisone in 29.2% (n = 7). The median time to onset of hyperglycemia after initiation of induction corticosteroid therapy was 9 days (range: 4 - 17 days). The median maximum blood glucose level recorded in hyperglycemic patients was 298 mg/dL (range: 250 - 520 mg/dL).

Table 1. Factors associated with the occurrence of induction hyperglycemia in multivariate analysis.

Variable	Hyperglycemia (n = 24)	Normoglycemia (n = 38)	Adjusted OR (IC 95%)	p
Age group				
≤10 years	9 (37.5%)	29 (76.3%)	1.0	
>10 years	15 (62.5%)	9 (23.7%)	4.1 [1.5 - 11.2]	0.004
Family history of diabetes				
No	14 (58.3%)	33 (86.8%)	1.0	
Yes	10 (41.7%)	5 (13.2%)	3.2 [1.1 - 9.4]	0.02
Corticosteroid therapy				
Prednisone	7 (29.2%)	22 (57.9%)	1.0	
Dexamethasone	17 (70.8%)	16 (42.1%)	2.8 [1.0 - 7.6]	0.04

In multivariate logistic regression analysis, three major risk factors were identi-

fied (Table 1). Children older than 10 years had a fourfold increased risk of developing hyperglycemia compared with younger children (OR = 4.1; 95% CI: [1.5 - 11.2]; p = 0.004). In addition, a parental history of diabetes was significantly associated with hyperglycemia (p = 0.02). Finally, exposure to dexamethasone conferred a significantly higher risk of hyperglycemia than prednisone (p = 0.04).

On the prognostic level, the occurrence of hyperglycemia during induction was associated with increased morbidity and disruptions in the continuation of anticancer treatment (Table 2).

Table 2. Distribution of complications, prognostic events, and therapeutic consequences in the entire cohort (N = 62).

Event	Number (n)	Proportion (%)
Overall infectious complications	**22**	**35.5%**
Sepsis	10	16.1%
Pneumonia	7	11.3%
Febrile mucositis	5	8.1%
Prolonged neutropenia (>10 days)	**29**	**46.8%**
Delay in L-asparaginase administration	**16**	**25.8%**
Early mortality during induction	**9**	**14.5%**

Infectious complications were significantly more frequent in hyperglycemic children than in normoglycemic children (54.1% vs. 23.7%; p = 0.02). Similarly, prolonged neutropenia exceeding 10 days was observed in 66.7% of hyperglycemic patients compared with 34.2% in the normoglycemic group (p = 0.03). Regarding the impact on chemotherapy, a delay in L-asparaginase administration was required in half of the children in the hyperglycemic group, compared with only 10.5% in the normoglycemic group (p = 0.008). Finally, regarding early mortality, the death rate during the induction phase showed a trend toward increase in the hyperglycemic group (25.0% vs. 7.9%), although it did not reach statistical significance (p = 0.08). Table 3 presents the events occurring during the induction phase according to the children's glycemic status.

Table 3. Prognostic impact and complications during the induction phase according to glycemic status.

Event	Hyperglycemia (n = 24)	Normoglycemia (n = 38)	p-value
Infectious complications	13 (54.1%)	9 (23.7%)	0.02
Prolonged neutropenia (>10 days)	16 (66.7%)	13 (34.2%)	0.013
Delay in L-asparaginase administration	12 (50.0%)	4 (10.5%)	0.00054
Mortality during induction	6 (25.0%)	3 (8.5%)	0.08

4. Discussion

This retrospective cohort study provides the first documented data on hyperglycemia

during induction therapy for pediatric acute lymphoblastic leukemia in Benin [10]. In our series, more than one in three children (38.7%) developed hyperglycemia, and one in four (25.8%) presented with chemotherapy-induced diabetes [5] [7]. These figures fall within the range reported in the international literature, which describes overall incidences between 10% and 45% depending on the diagnostic criteria used [5] [7] [8] [12]. The high frequency observed at CHUD-Ouémé may be explained by delayed screening in our setting [10].

The median time to onset of 9 days after treatment initiation corresponds to the period of peak action of induction corticosteroid therapy combined with the first administrations of L-asparaginase [6] [7]. This finding is consistent with observations from several North American and European teams, which highlight that the first two weeks of induction constitute a high-risk window for metabolic complications [5] [7] [12].

The risk factors identified in our multivariate analysis align closely with known pathophysiological mechanisms [4] [7]. Age greater than 10 years emerged as a major predictive factor (OR = 4.1; p = 0.004) [5] [7] [8]. During adolescence, physiological insulin resistance associated with pubertal maturation, under the influence of growth hormone and sex steroids, creates a particularly vulnerable substrate for the diabetogenic effects of corticosteroids [4] [13]. Similarly, the presence of a family history of diabetes (p = 0.02) suggests an underlying genetic predisposition revealed by the pharmacological stress of anticancer agents [7] [13].

Regarding the corticosteroid protocol, our study demonstrates that dexamethasone is associated with a significantly higher risk of hyperglycemia than prednisone (p = 0.04) [4] [14]. Dexamethasone has markedly greater anti-inflammatory potency and a longer biological half-life than prednisone, resulting in stronger inhibition of glucose uptake in skeletal muscle and adipose tissue, as well as increased stimulation of hepatic gluconeogenesis [4] [14]. Although dexamethasone provides superior central nervous system control in acute lymphoblastic leukemia, its metabolic side effects require heightened vigilance [2] [4].

From a prognostic standpoint, induction hyperglycemia was found to be detrimental [5] [9]. The significant association with infectious complications (54.1% vs. 23.7%; p = 0.02) can be explained by the impairment of leukocyte functions (chemotaxis and phagocytosis) induced by acute hyperglycemia [5] [9]. This combined immunosuppressive state (chemotherapy-induced and metabolic) promotes the development of severe sepsis and prolongs the duration of neutropenia (p = 0.03) [5] [9] [15]. In addition, glucose intolerance necessitated a delay in L-asparaginase administration in half of the affected children (p = 0.008) [6] [11]. Given that L-asparaginase is a critical component for achieving durable complete remission, even temporary interruption of its administration may compromise long-term oncologic control [3] [6]. Finally, the observed trend toward higher mortality during induction in hyperglycemic children (25% vs. 8.5%; p = 0.08) underscores the potential severity of these metabolic disorders in a setting where pediatric intensive care resources remain limited [5] [10].

Our results demonstrate a significant association between induction hyperglycemia and increased rates of infectious complications, prolonged neutropenia, and chemotherapy delays. However, due to the retrospective nature of the study, these outcome comparisons are unadjusted, and a direct causal relationship cannot be definitively established. In particular, uncertainty regarding the chronology of events does not allow us to exclude reverse causality, in which subclinical or overt intercurrent infections may have triggered or worsened glycemic dysregulation rather than resulting from it. Furthermore, the observed difference in induction mortality between groups did not reach statistical significance and remains inconclusive.

This study has several limitations. First, its retrospective, single-center design and the relatively small sample size (N = 62) limit the statistical power for multivariate adjustments and subgroup analyses. Second, biological assays such as C-peptide or insulin levels were not available to distinguish between insulin resistance and pancreatic beta-cell dysfunction.

5. Conclusion

At CHUD-O, induction hyperglycemia affects nearly four out of ten children treated for acute lymphoblastic leukemia. Favored by age over 10 years, family history, and the use of dexamethasone, it increases infectious morbidity and disrupts the chemotherapy schedule. To address this, it is essential to generalize twice-daily glycemic monitoring, establish a standardized insulin therapy protocol, and strengthen collaborative management with endocrinologists and diabetologists.

Conflicts of Interest

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

References

[1] Pui, C. and Evans, W.E. (2006) Treatment of Acute Lymphoblastic Leukemia. *New England Journal of Medicine*, **354**, 166-178. https://doi.org/10.1056/nejmra052603

[2] Inaba, H., Greaves, M. and Mullighan, C.G. (2013) Acute Lymphoblastic Leukaemia. *The Lancet*, **381**, 1943-1955. https://doi.org/10.1016/s0140-6736(12)62187-4

[3] Hunger, S.P. and Mullighan, C.G. (2015) Acute Lymphoblastic Leukemia in Children. *New England Journal of Medicine*, **373**, 1541-1552. https://doi.org/10.1056/nejmra1400972

[4] Inaba, H. and Pui, C. (2010) Glucocorticoid Use in Acute Lymphoblastic Leukaemia. *The Lancet Oncology*, **11**, 1096-1106. https://doi.org/10.1016/s1470-2045(10)70114-5

[5] Sonabend, R.Y., McKay, S.V., Okcu, M.F., Yan, J., Haymond, M.W. and Margolin, J.F. (2008) Hyperglycemia during Induction Therapy Is Associated with Increased Infectious Complications in Childhood Acute Lymphocytic Leukemia. *Pediatric Blood & Cancer*, **51**, 387-392. https://doi.org/10.1002/pbc.21624

[6] Hijiya, N. and van der Sluis, I.M. (2015) Asparaginase-Associated Toxicity in Chil-

dren with Acute Lymphoblastic Leukemia. *Leukemia & Lymphoma*, **57**, 748-757. https://doi.org/10.3109/10428194.2015.1101098

[7] Roberson, J.R., Spraker, H.L., Shelso, J., Zhou, Y., Inaba, H., Metzger, M.L., *et al.* (2008) Clinical Consequences of Hyperglycemia during Remission Induction Therapy for Pediatric Acute Lymphoblastic Leukemia. *Leukemia*, **23**, 245-250. https://doi.org/10.1038/leu.2008.289

[8] Lowas, S.R., Marks, D. and Malempati, S. (2009) Prevalence of Transient Hyperglycemia during Induction Chemotherapy for Pediatric Acute Lymphoblastic Leukemia. *Pediatric Blood & Cancer*, **52**, 814-818. https://doi.org/10.1002/pbc.21980

[9] Koltin, D., Sung, L., Naqvi, A. and Urbach, S.L. (2011) Medication Induced Diabetes during Induction in Pediatric Acute Lymphoblastic Leukemia: Prevalence, Risk Factors and Characteristics. *Supportive Care in Cancer*, **20**, 2009-2015. https://doi.org/10.1007/s00520-011-1307-5

[10] Harif, M., Mallon, B., Patte, C., Bey, P., Chalvon-Demersay, C., Omer-Decugis, L., *et al.* (2021) Improving Care for Children with Cancer in Africa: Two Decades of Experience of the French African Pediatric Oncology Group. *JCO Global Oncology*, **7**, 1509-1512. https://doi.org/10.1200/go.21.00239

[11] Gatzioura, I., Papakonstantinou, E., Dimitriadou, M., Kourti, M., Sidi, V., Triantafyllou, P., *et al.* (2016) Glucose Levels before the Onset of Asparaginase Predicts Transient Hyperglycemia in Children with Acute Lymphoblastic Leukemia. *Pediatric Blood & Cancer*, **63**, 1181-1184. https://doi.org/10.1002/pbc.25956

[12] Taher, Y.Y., Lehmann, L., Zamzam, M., Mona Atteya, H., Reda, H., Abuelhassan, A.A., *et al.* (2025) Risk Factors and Clinical Implications of Hyperglycemia during Induction Therapy in Pediatric Acute Lymphoblastic Leukemia. *International Journal of Cancer*, **158**, 163-171. https://doi.org/10.1002/ijc.70084

[13] Moran, A., Jacobs, D.R., Steinberger, J., Hong, C.P., Prineas, R., Luepker, R., *et al.* (1999) Insulin Resistance during Puberty: Results from Clamp Studies in 357 Children. *Diabetes*, **48**, 2039-2044. https://doi.org/10.2337/diabetes.48.10.2039

[14] Möricke, A., Zimmermann, M., Valsecchi, M.G., Stanulla, M., Biondi, A., Mann, G., *et al.* (2016) Dexamethasone vs Prednisone in Induction Treatment of Pediatric ALL: Results of the Randomized Trial AIEOP-BFM ALL 2000. *Blood*, **127**, 2101-2112. https://doi.org/10.1182/blood-2015-09-670729

[15] Inaba, H., Pei, D., Wolf, J., Howard, S.C., Hayden, R.T., Go, M., *et al.* (2017) Infection-Related Complications during Treatment for Childhood Acute Lymphoblastic Leukemia. *Annals of Oncology*, **28**, 386-392. https://doi.org/10.1093/annonc/mdw557