Characterization and Risk Factors of Hyperglycaemia During Treatment Of Childhood Hematologic Malignancies

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ESPE 2021 The 59th Annual Meeting Online 22-26 September 2021

INTRODUCTION AND AIM

Secondary forms of diabetes mellitus are underdiagnosed in children and adolescents with cancer. Despite the whole body of evidence that asparaginase, steroids and total body irradiation increase the risk of developing diabetes, risk factors are missing and – asides from treatments – understudied (e.g., pre-existing obesity, sex, age, ethnicity, family history of diabetes). The objectives of our study were to study the incidence and associated risk factors of hyperglycaemia in leukaemia and lymphoma patients.

METHODS

We retrospectively collected 15 years of data from paediatric patients aged 0 to 18 years treated in Cliniques universitaires Saint-Luc (CUSL, Brussels) for acute lymphoblastic leukaemia (ALL), Hodgkin's lymphoma (HL), and non-Hodgkin's lymphoma (NHL) immediately at cancer diagnosis.

According to guidelines of the American Diabetes Association, patients developed hyperglycaemia when random glucose levels exceeded 11 mmol/L, for at least two measurements separated by 24 hours.

The variables were compared according to the occurrence or not of hyperglycaemia using Student t test or Mann-Whitney test (as appropriate) for continuous variables and Fisher exact test for discrete variables. A binary logistic regression analysis was performed to predict hyperglycaemia occurrence from all potential predictors available by estimating odds ratios and their 95% confidence intervals. All covariates with a p-value less than 0.10 in univariate analysis were introduced into a multivariate model (Wald Chi-Square).

RESULTS: INCIDENCE, EVOLUTION AND RISK FACTORS OF HYPERGLYCAEMIA

INCIDENCE OF HYPERGLYCAEMIA

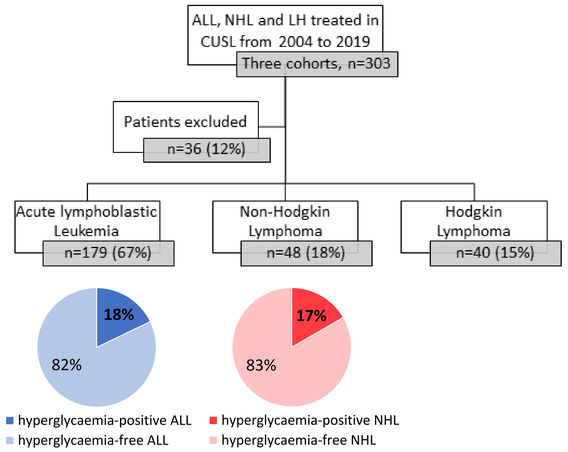

Figure 1. Our study cohort included 267 patients corresponding to 179 patients with ALL, 48 with NHL and 40 with HL. Eighteen percent of ALL patients (32/179) and 17% of NHL patients (8/48) developed hyperglycaemia. No hyperglycaemia was observed in HL patients.

ONSET OF HYPERGLYCAEMIA

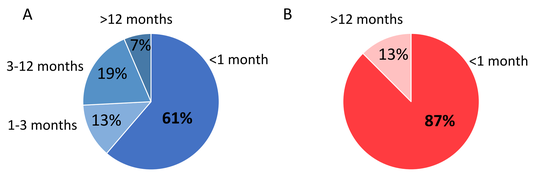

Figure 2. The majority of ALL (A, 61%) and NHL (B, 87%) patients developed hyperglycaemia within the first month of chemotherapy, corresponding to pre- and induction phases that are the most aggressive in terms of steroid doses.

PROBABILITIES OF REMAINING FREE OF HYPERGLYCAEMIA

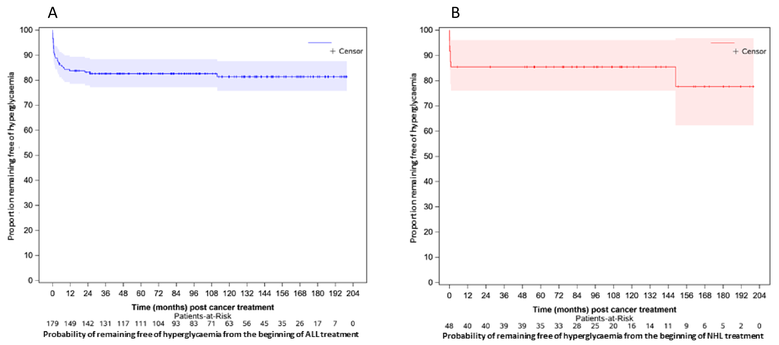

Figure 3. Kaplan-Meier estimates of the probability of remaining free of hyperglycaemia in acute lymphoblastic leukaemia (ALL) and non-Hodgkin lymphoma (NHL) paediatric cohorts.

(A) At 12 months post ALL treatment, the probability of remaining free of hyperglycaemia was 83.8% and remained relatively unchanged thereafter. (B) In the NHL group this probability remained unchanged at 85.4% after one month of cancer treatment.

RISK FACTORS OF HYPERGLYCAEMIA

Table 1. Univariate (Likelihood Ratio) and multivariate (Wald Chi-Square) logistic regression analyzes of factors leading to hyperglycaemia occurrence for ALL and NHL cohorts.

		Univariate Analysis		Multivariate Analysis	
ALL predictors	N	p-value	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)
History of overweight at cancer diagnosis	179	0.008	4.293 (1.464-12.588)	0.046	3.793 (1.026-14.022)
Tanner staging ≥2	179	<0.001	4.880 (2.159-11.032)	0.002	4.269 (1.676-10.875)
Steroid-resistant disease	179	0.014	3.204 (1.265-8.113)	0.032	3.445 (1.114-10.657)
HSCT	179	0.002	5.111 (1.795-14.553)	0.037	4.754 (1.099-20.554)
NHL predictors					
Cancer treatment risk higher vs lower	48	0.038	5.667 (1.104-29.073)		

ALL=Acute Lymphoblastic Leukemia; NHL=Non-Hodgkin Lymphoma; CI=Confidence Interval; BMI=Body Mass Index; SDS=Standard Deviation Score; HSCT=Hematopoietic Stem Cell Transplantation.

Table 1. Multivariate analysis showed that ALL patients with history of obesity/overweight (OR 3.793), a pubertal stage equal to or greater than 2 (OR 4.269) at cancer diagnosis, a presence of steroid-resistant disease (OR 3.445,) and a hematopoietic stem cell transplant (OR 4.754) were associated with a higher risk of developing hyperglycaemia.

CONCLUSIONS

In our cohort, 18% of patients with ALL or NHL developed early-onset hyperglycaemia after chemotherapy/radiotherapy. Our findings may help clinicians to identify patients with acute lymphoblastic leukaemia at risk of early onset of hyperglycaemia, by considering BMI and pubertal stage as potential markers and by monitoring blood glucose levels closely during treatment intensification for steroids-resistant disease or relapse, especially when total body irradiation and stem cell transplantation are required.

ACKNOWLEDGEMENTS

The study was funded by Université Catholique de Louvain (Action de Recherche Concertée) and by Fondation Saint Luc (Prix Cancérologie – Institut Roi Albert II).

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