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Glucose Intolerance in Survivors of Childhood Hematologic Disorders

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Introduction and objectives

To investigate overall characteristics of glucose intolerance in childhood survivors of hematologic diseases and suggest potential risk factors which increase A1c (glycated hemoglobin) level.

Methods

Based on a retrospective review of 394 children who were diagnosed with acute leukemia or aplastic anemia between 2015 and 2016 under the age of 15, glucose intolerance was observed in 14 patients. A definition of glucose intolerance was A1c above 5.7 %. Auxological and biochemical profiles as well as therapeutic factors were compared.

Table 1. Clinical and biochemical profiles at diagnosis of glucose intolerance

	AL (n=7)	AA (n=7)
Age (years)	16.1 (4.1 – 21.1)	12.2 (8.3 – 16.6)
A1c (%)	6.4 (5.7 – 9.4)	6.6 (5.7 – 7.8)
FBS (mg/dL)	174.0 (81.0 -400.0)	240.0 (97.0 – 29.0)
Fasting insulin (μU/mL)	25.7 (1.2 – 58.2)	31.2 (9.9 – 97.6)
Fasting c-peptide (ng/mL)	5.2 (1.1 – 7.5)	5.3 (2.1 – 14.4)
HOMA-IR	13.5 (0.2 – 25.4)	15.1 (4.4- 69.9)
RBC counts (10^{12}/L)	4.3 (2.6 – 4.8)	2.6 (1.9-4.9)
MCV(10^{-15}/L)	95.3 (70.3 – 100.5)	91.7 (80.6 – 100.5)

Table 2. Clinical profiles of the fourteen patients with glucose intolerance

ID	Gender	Diagnosis	Transplant	GvHD		A1c	FBS (mg/dL)	GC dose (mg)	TF volume (mL)	Possible trigger	Treatment
				Type	Lesion						
1	F	ALL	Allo-CBT	Acute	Skin	9.4	292.0 [2]‡	46649.2 [1]	36660.0 [1]	Glucocorticoid	Insulin
2	M	AA	FMM-PBSCT	Chronic	Skin, liver	7.8	290.0 [3]	31265.0 [2]	14650.0 [2]	Glucocorticoid	Insulin
3	F	ALL	-	-	-	7.5	400.0 [1]	26455.6 [3]	11600.0 [3]	Glucocorticoid	None
4	F	AA	Allo-PBSCT	Chronic	Skin, eye, lung, liver	7.4	240.0 [7]	19105.0 [4]	11010.0 [4]	Glucocorticoid	None
5	M	AA	Allo-PBSCT	Acute	Skin	7.2	274.0 [4]	13397.6 [5]	9300.0 [5]	Glucocorticoid	Insulin Biguanide
6	F	AML	MSD-PBSCT	Chronic	Skin, oral, lung, liver	6.8	270.0 [5]	13308.5 [6]	4920.0 [9]	Glucocorticoid	None
7	M	FA	Allo-PBSCT	Acute	Skin	6.6	249.0 [6]	6853.9 [7]	3000.0 [11]	Glucocorticoid	None
8	F	FA	-	-	-	6.5	150.0 [9]	5611.8 [8]	2300.0 [12]	Hemochromatosis	Insulin
9	F	AML	MSD-PBSCT	Chronic	Skin, eye, oral, lung, liver	6.4	85.0 [13]	4185.0 [10]	2110.0 [13]	Glucocorticoid	Biguanide
10	M	JMML	FMM-PBSCT	Chronic	Skin, eye, lung	6.2	81.0 [14]	4178.1 [11]	5310.0 [8]	Glucocorticoid	None
11	F	AA	Allo-BMT	Acute	Upper GI	5.8	102.0 [10]	3666.6 [12]	4300.0 [10]	Glucocorticoid	None
12	M	ALL	MSD-PBSCT	Acute	Engraftment syndrome	5.7	174.0 [8]	1559.0 [14]	6550.0 [6]	Glucocorticoid	Insulin
13	F	ALL	Allo-PBSCT	Acute	Skin, oral	5.7	94.0 [12]	2800.0 [13]	5440.0 [7]	Glucocorticoid	None
14	M	AA	FMM-PBSCT	Acute	Skin	5.7	97.0 [11]	5611.8 [8]	1090.0 [14]	Glucocorticoid	None

Abbreviations: A1c, glycated hemoglobin; AA; aplastic anemia; AL, acute leukemia; BMT, bone marrow transplant; CBT, cord blood transplant; FBS, fasting blood glucose; FMM, family mismatched; GC, glucocorticoid; GvHD; graft-versus-host disease; HOMA-IR, homeostatic model assessment of insulin resistance; MCV, mean corpuscular volume; MSD, matched sibling donor; PBSCT, peripheral blood stem cell transplant; RBC, red blood cell; TF, transfusion

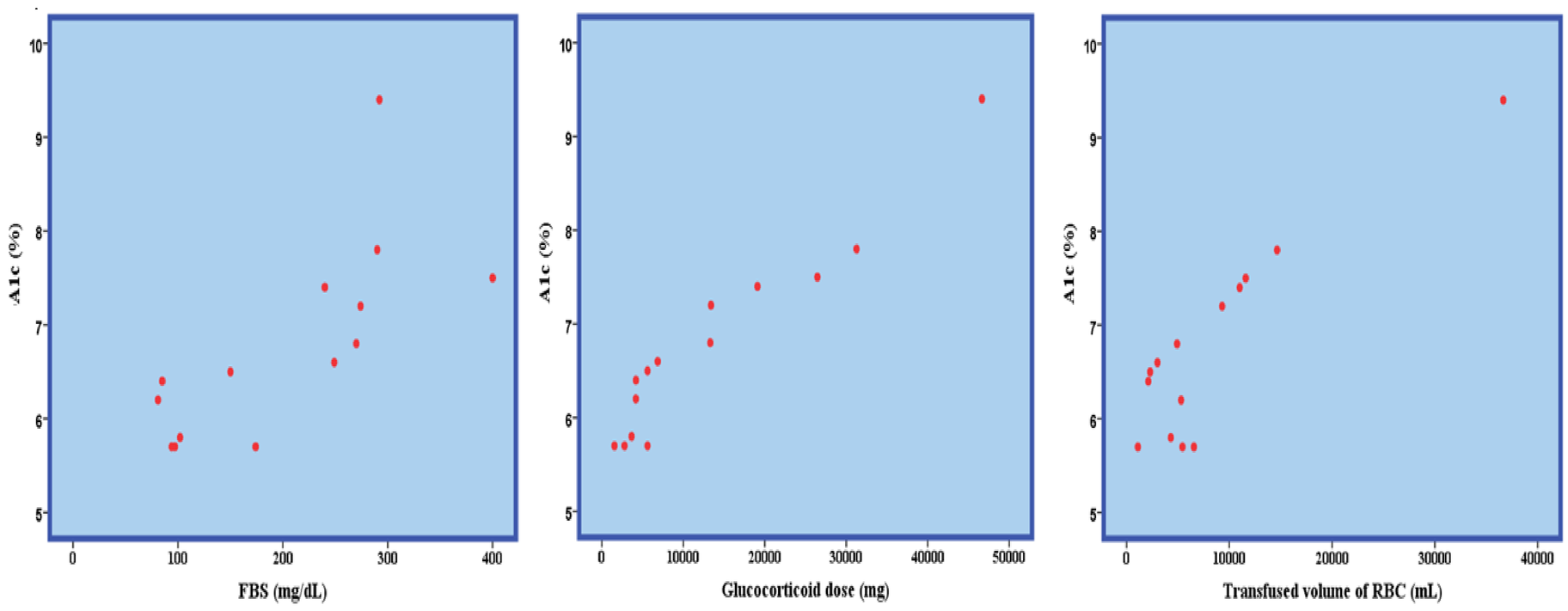

Fig. Clinical factors affecting the A1c at diagnosis of glucose intolerance

Results

Among 14 children (3.5 %) with glucose intolerance, 7 (50.0 %) patients were diagnosed with leukemia and 7 with aplastic anemia. Eight patients (57.1 %) were diabetic (A1c ≥ 6.5 %, fasting blood glucose ≥ 126.0 mg/dL with clinical presentation of polyuria, polydipsia or weight loss) whereas 6 (42.9 %) were prediabetic (A1c in between 5.7 – 6.4 %). By univariate regression, fasting blood glucose (R^2=0.538, *P=0.003*), glucocorticoid dose (R^2=0.920, *P<0.001*) and volume of transfused red blood cell (R^2=0.789, *P<0.001*) were positively correlated with A1c. Multiple regression analysis suggested accumulated glucocorticoid dose (R^2=0.920, *P=0.019*) as a strong risk factor of glucose intolerance.

Conclusion

In young survivors after treatment completion of hematologic diseases, several clinical and biochemical factors could influence serum A1c and cause glucose intolerance. Among them, glucocorticoid dose might significantly trigger newly diagnosed diabetes.

The authors have no conflict to interest to disclose.