Maternal pregestational diabetes and risk of childhood leukaemia in the offspring: a population-based study in Northern Italy

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Introduction

Acute lymphoblastic leukemia (ALL) is an aggressive neoplasia characterized by the uncontrolled proliferation of aberrant lymphocytes, and represents the most common cancer in children under 15 years of age. Although the aetiology of ALL is not well understood, the typically early onset suggests that genetic, prenatal and perinatal factors, such as maternal diabetes, may be involved (Wiemels, 2015). The aim of the study is to examine the influence of maternal pregestational diabetes on ALL risk in the offspring.

Methods

All children born in Bologna and Reggio Emilia, two provinces in Northern Italy, between 1998–2010 (n=161,804) were followed from birth until first cancer diagnosis, age 15 years, or December 31, 2017. Data on newborns, maternal diabetes and covariates (maternal age and ethnicity) were obtained from hospital discharge records, data on ALL cases from the National Childhood Cancer Register of the Italian Association of paediatric haematology and oncology (AIEOP). We calculated annual incidence rate of ALL per 100,000 person-years, and Hazard Ratio (HR) with 95% confidence interval (CI) by using Cox regression adjusted for maternal age and nationality.

Results

We observed 97 cases of ALL, with annual incidence rate of 16.3 (95% CI: 4.1–65.2) per 100,000 newborns among children born to women with pregestational diabetes and 4.6 (95% CI: 3.8–5.6) among those born to women without pregestational diabetes. Annual incidence rate of ALL per 100,000 newborns was slightly higher in children born to Italian mother than foreigners (4.8 vs 4.1) and in children born to a mother with ≥35 years at the time of delivery (4.9 vs 4.6) [Table 1]. In multivariable analysis [Table 2], maternal pregestational diabetes was associated with higher risk of ALL in the offspring (adjusted HR [95% CI]: 3.5 [0.8–14.1]).

Table 2. Association between childhood acute lymphoblastic leukemia and maternal pregestational diabetes among children born in Bologna and Reggio Emilia between 1998-2010.

	Acute lymphoblastic leukemia			
	Crude HR	95% CI	Adjusted HR*	95% CI
Maternal PGD				
No	Ref.		Ref.	
Yes	3.3	0.8-13.6	3.5	0.8-14.1

*Adjusted for maternal age at delivery and ethnicity. PGD=pregestational diabetes; HR=hazard ratio.

Table 1. Childhood acute lymphoblastic leukemia incidence rate per 100,000 newborns in Bologna and Reggio Emilia, according to maternal demographic characteristics and diabetes status.

		N	Annual incidence rate	95% CI
Maternal ethnicity				
Italian (n=132,345)	1,732,592	83	4.8	3.9-5.9
Other (n=29,459)	342,522	14	4.1	2.4-7.0
Maternal age				
<35 (115,342)	1,504,483	69	4.6	3.6-5.8
≥35 (46,462)	570,632	28	4.9	3.4-7.1
Maternal PGD				
No (160,767)	2,062,860	95	4.6	3.8-5.6
Yes (1,037)	12,254	2	16.3	4.1-65.2
Total (161,804)	2,075,115	97	4.7	3.8-5.7

PGD=pregestational diabetes.

Conclusions

In this population-based cohort study, we estimated higher risk of ALL among offspring of women with pregestational diabetes. These results are consistent with previous findings (Contreras et al, 2016; Deleskog et al, 2017; Søegaard et al, 2017) and they are compatible with a role of prenatal and perinatal glycaemic environment in childhood cancer aetiology. Since the overall rarity of both maternal diabetes and childhood leukemia, studying their association is challenging. Further studies, including larger cohorts of newborns, are needed to refine our understanding of this association and to identify biological mechanisms underlying childhood ALL.

References

Contreras et al, (2016) Cancer Caus Cont 27:1273–1285
Deleskog et al, (2017) Clin Epidemiol 9: 633 – 642
Søegaard et al, (2018) Br J Cancer 118: 117 – 120
Wiemels (2015) Eur J Epidemiol 30: 1225 – 1227

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