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Non-chromosomal congenital anomalies and risk of childhood leukaemia: an Italian population-based case-control study

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Introduction

Several studies have evaluated the association between birth defects and childhood leukaemia (Carrozza et al, 2012; Norwood et al, 2017). Although the association between chromosomal conditions such as Down syndrome and increased childhood leukaemia risk is well established, associations between non-chromosomal birth defects and the disease are far less clear (Fischer et al, 2012; Von Behren et al, 2017). We conducted a population-based case-control study in two provinces of Northern Italy to evaluate childhood leukaemia risk in children born with non-chromosomal anomalies.

Methods

We identified all leukaemia cases diagnosed from 1998 to 2013 in children <15 years old in the Modena and Reggio-Emilia provinces (1,2 million inhabitants) through the Italian National Childhood Cancer Register. For each case, we randomly selected four population controls matched by age, sex, province of residence and calendar year. Through the Emilia-Romagna Region population-based Birth Defects Registry, linked to the European Surveillance of Congenital Anomalies network EUROCAT, we retrieved information about occurrence and type of congenital malformations for all study participants. We computed the odds ratio (OR) of leukaemia for children affected by non-chromosomal birth defects in a multivariable conditional logistic regression analysis. We adjusted the risk estimates for parental age, family income, residential exposure to benzene from vehicular traffic and electromagnetic field from high voltage power lines.

Table 1. Baseline characteristics of study population.

	Cases		Controls	
	N	(%)	N	(%)
Study subjects	132	(100)	528	(100)
Congenital anomalies	2	(1.53)	3	(0.57)
	Median	(IQR)[a]	Median	(IQR)[a]
Maternal age	31	(27 - 35)	30	(27 - 34)
Paternal age	34	(30 - 38)	33	(30 - 37)
Family income[b]	42	(22 - 69)	35	(19 - 53)
Outdoor benzene (μg/m³)	0.29	(0.11 - 0.74)	0.25	(0.10 - 0.57)
Electro-magnetic field (>0.1 μT)	2	(1.16)	1	(0.20)

[a]Interquartile range; [b]In thousands of euros a year.

Data sources

AIEOP
ASSOCIAZIONE ITALIANA EMATOLOGIA ONCOLOGIA PEDIATRICA

Italian National Childhood Cancer Register

Registro IMER

Emilia-Romagna Region Birth Defects Registry

eurolinkcat
Establishing a linked European Cohort of Children with Congenital Anomalies

Results

We included in the study 132 cases and 528 controls, 5 of which (2 cases and 3 controls) were affected by a non-chromosomal congenital malformation. We found an increased risk of leukaemia in children born with non-chromosomal anomalies, with an OR of 2.7 (95% confidence interval 0.4–16.0) and 7.2 (95% confidence interval 0.4–143.6) in the crude and fully adjusted regression models, respectively.

Table 2. Non-chromosomal congenital anomalies affecting children including in study.

	ICD9-codes	Congenital anomalies
Cases	742.2 & 756.41	Reduction deformities of brain & chondrodystrophy
	759.8	Unspecified congenital anomalies (including anomalies of heart, face and skin)
Controls	753.2	Obstructive defects of renal pelvis and ureter
	749.21	Cheilopalatoschisis
	745.4 & 746.9	Ventricular septal defect & unspecified anomaly of heart

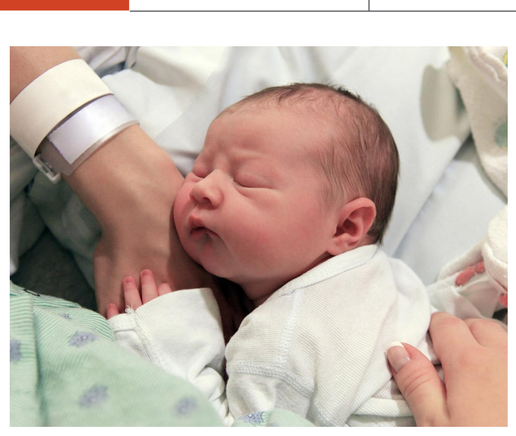

Table 3. Risk of leukaemia for children affected by non-chromosomal birth defects: *odds ratio* (OR) and 95% confidence interval (CI) calculated through crude and multivariate models of conditional logistic regression analysis (matched for sex, age and province of residence).

	Case/Controls	OR	95% CI
Crude model	132/528	2.7	0.4 - 16.0
Multivariate model[a]	132/528	7.2	0.4 - 143.6

[a]Adjusted for parental age, family income, residential exposure to benzene from vehicular traffic and electro-magnetic field from high voltage power lines

Conclusions

Despite the limited stability of the risk estimates and the risk of unmeasured confounding, our study appears to suggest an association between non-chromosomal birth defects and risk of childhood leukaemia.

References

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