# 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 (CL) (Carrozza et al, 2012; Norwood et al, 2017). Although the association between chromosomal conditions such as Down syndrome and increased CL 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 CL 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) |
| 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) |
| Electromagnetic field (>0.1 µT) | 2 | (1.16) | 1 | (0.20) |

[a]Interquartile range; [b]Thousands of euros / 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

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## 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 |

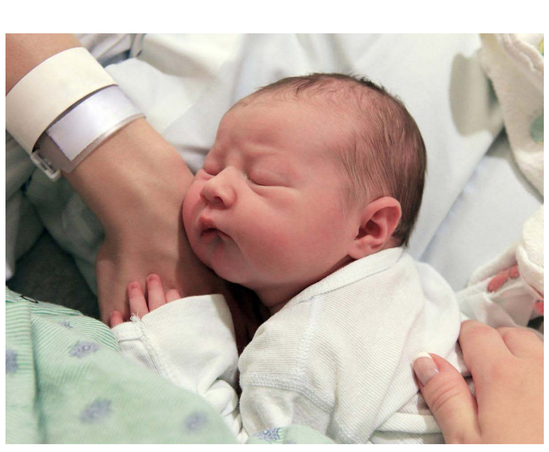

**Table 3.** Risk of leukaemia for children affected by non-chromosomal birth defects: *odds ratio* (OR) and 95% confidence interval (CI) calculated through crude and multivariate models of conditional logistic regression analysis (matched for sex, age and province of residence)

| | 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

Carrozza SE, Langlois PH, Miller EA *et al*, (2012) Am J of Epidemiol 175: 1217 – 24
Fischer PG, Reynolds P, Von Behren J *et al*, (2012) J Pediatr 160: 978 – 83
Norwood MS, Lupo PJ, Chow EJ *et al*, (2017) PLoS One 12: e0179006
Von Behren J, Fisher PG, Carmichael SL *et al*, (2017) J Pediatr 185: 237 – 40

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