Risk of childhood leukaemia in relation to birth month: case-control study based on data from Italian National Childhood Cancer Register

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Introduction

Seasonal variation of month of birth suggests that exposures acting close to birth are etiologically relevant (Boland et al, 2015). In order to investigate the association between childhood leukaemia and exposure to infectious factors in the first years of life, numerous studies have used the month or the birth season as an indicator of neonatal infection (Goujon-Bellec et al, 2113; Marcotte et al, 2014). In this case-control study we evaluated the childhood leukaemia (CL) risk and in particular the acute lymphoblastic leukaemia (ALL) risk compared to the children month birth.

Methods

Through the Italian National Childhood Cancer Register we have identified all diagnosed cases of childhood leukaemia between 1998-2013 in Modena and Reggio Emilia provinces. We selected a control population of 4 children paired by gender, year of birth and province of residence. Through conditional logistic regression we calculated the ALL odds ratio (OR) and the respective 95% confidence interval (95% CI), adopting December as reference month since it is allocated just before the beginning of the winter influence peak.

	CL (N=138)			ALL (N=110)		
	OR	IC 95%	*P*	OR	IC 95%	*P*
January	2.84	(0.89 - 9.12)	*0.079*	2.66	(0.69 - 10.16)	*0.154*
February	3.94	(1.21 - 12.80)	*0.022*	5.84	(1.54 - 22.09)	*0.009*
March	1.83	(0.49 - 6.87)	*0.370*	1.96	(0.44 - 8.76)	*0.379*
April	5.55	(1.79 - 17.17)	*0.003*	5.55	(1.52 - 20.23)	*0.009*
May	3.51	(1.08 - 11.42)	*0.037*	3.18	(0.82 - 12.30)	*0.094*
June	2.34	(0.67 - 8.13)	*0.181*	3.11	(0.77 - 12.56)	*0.111*
July	1.46	(0.39 - 5.50)	*0.575*	1.76	(0.39 - 7.90)	*0.458*
August	4.05	(1.19 - 13.72)	*0.025*	3.77	(0.93 - 15.22)	*0.062*
September	3.24	(0.93 - 11.30)	*0.065*	3.18	(0.75 - 13.47)	*0.117*
October	3.06	(0.93 - 10.10)	*0.067*	3.19	(0.81 - 12.57)	*0.098*
November	2.72	(0.83 - 8.93)	*0.100*	3.38	(0.89 - 12.78)	*0.073*
December	Ref.	-		Ref.	-	

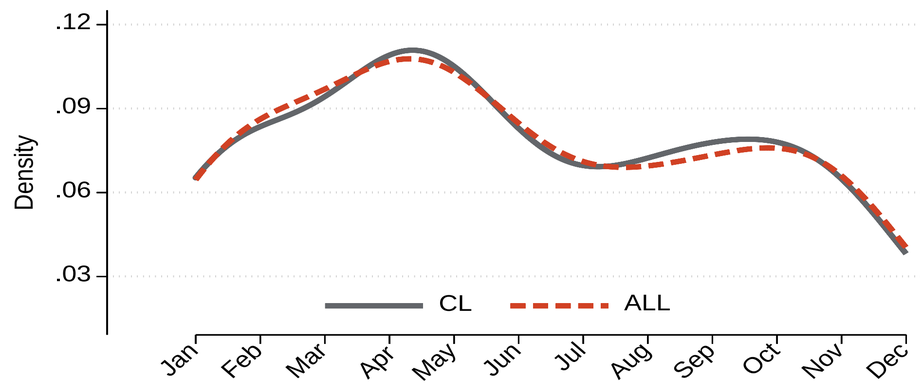
Table 1. Leukaemia risk based on birth month for between 1998-2013, for all children and only for ALL cases.

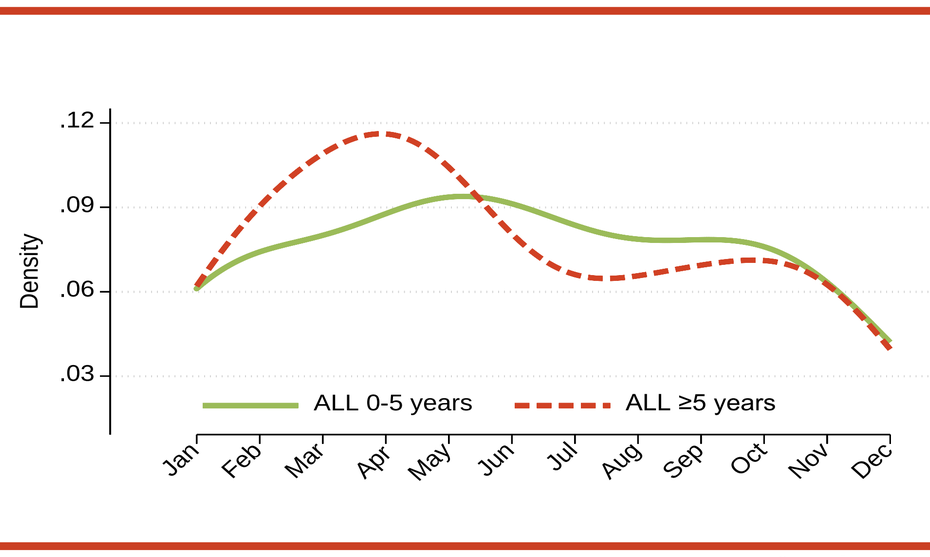
	ALL 0-5 years (N=44)			ALL ≥5 years (N=66)		
	OR	IC 95%	*P*	OR	IC 95%	*P*
January	1.36	(0.24 - 7.74)	*0.726*	5.14	(0.56 - 46.90)	*0.146*
February	6.40	(0.94 - 43.55)	*0.058*	8.17	(0.96 - 69.41)	*0.054*
March	-			7.42	(0.81 - 68.31)	*0.077*
April	3.22	(0.53 - 19.47)	*0.202*	9.39	(1.15 - 76.56)	*0.036*
May	1.30	(0.20 - 8.70)	*0.784*	6.90	(0.79 - 60.01)	*0.080*
June	2.11	(0.34 - 13.10)	*0.422*	4.43	(0.46 - 42.79)	*0.199*
July	1.65	(0.23 - 11.70)	*0.619*	2.11	(0.18 - 24.58)	*0.550*
August	2.30	(0.31 - 16.91)	*0.412*	6.31	(0.70 - 56.77)	*0.101*
September	1.59	(0.22 - 11.46)	*0.644*	5.76	(0.58 - 56.94)	*0.134*
October	2.98	(0.51 - 17.46)	*0.226*	3.82	(0.40 - 36.55)	*0.245*
November	1.38	(0.20 - 9.35)	*0.742*	7.37	(0.88 - 61.64)	*0.065*
December	Ref.			Ref.		

Table 2. Risk of childhood leukaemia based on birth month between 1998-2013 for ALL of stratified by age at diagnosis before and after 5 years.

Results

We have identified 138 CL cases and 552 controls, including 110 cases of ALL. Density distribution showed a bimodal trend for the CL cases, as well as for ALL, with a first peak in the months of February-April and a second less extensive peak in September-October. Corresponding estimates showed an increased risk for children born in February with OR of 3.94 (95% CI 1.21 - 12.80) for CL and 5.84 (1.54 -22.09) for ALL, while the OR for those born in April was 5.55 (1.79 - 17.17) for CL, 5.55 (1.52 - 20.23) per ALL.





Figures. Density distribution based on the birth month of childhood leukaemia cases. Above all cases of CL and ALL. Below only the ALL cases stratified by age at diagnosis.

Conclusions

In the present study we have assessed seasonal variation in leukaemia risk by month of birth. Despite the imprecision of such estimates, due to the low number of included cases and the inability to assess the infectious history of children, the results suggest an influence of birth month on childhood leukaemia risk, with particular reference to ALL subtype and February-April period.

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