THE INCIDENCE RATE AND RISK FACTORS ASSOCIATED WITH EARLY AGE ACUTE LEUKAEMIA

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INTRODUCTION

- World-wide childhood leukemia is the most common malignancy diagnosed in children < 5years of age. The acute lymphoblastic leukemia (ALL) incidence rate has a sharp peak between 2-4 years of age at the diagnosis and, frequently the disease affects more boys than girls;
- The etiology of childhood leukemia remains a challenge, although a premises that early-age leukemia (EAL) arising from somatic clonal cells originated during fetal life, encourage the researches toward risk factors associated with environmental exposures.
- Some per natal characteristics, as birth weight, birth order, mode of delivery, maternal age and maternal occupational exposures have been associated with childhood leukemia;
- Because of classic case-control study can be inefficient in rare diseases such as EAL (≤ 2years of life), methodological alternative is to combine one case-control study in a cohort.
- The population-based registries (PBCR and Information System on Live Births-SINASC in Brazil) have information that enables us to test risk factors associated with leukemia in early age.

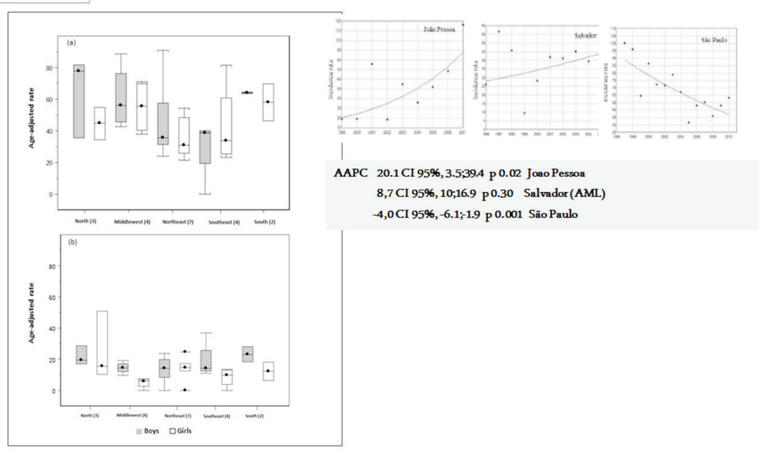
AIM

- To re-visit whether the incidence rate of acute leukemia in children under 5 years of age differ according to Brazil regions;
- To investigate maternal and birth characteristics associated with EAL risk factors using case-cohort model.

MATERIAL AND METHODS

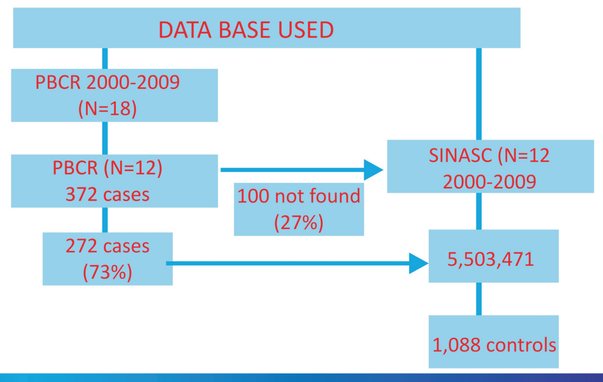
1st. Incidence rate of EAL (≤5yrs of age); n, 18 PBCR located in major cities of Brazil

Region	RCBP (Period)	Ratio (M/F)	Ratio (ALL/NALL)	ALL CR	NALL CR	ALL together AAIR
North						
	Belém (1999-2003)	1,63	3,7	60,74	16,67	77,03
	Manaus (2001-2005)	1,74	3,51	67,84	19,38	87,19
Northest						
	Aracaju (2004-2008)	2,73	-	45,73	0,00	45,39
	Fortaleza (2002-2006)	1,68	2,73	45,31	19,03	64,34
	João Pessoa (2003-2007)	0,78	2,56	46,77	17,99	64,76
	Natal (2001-2005)	0,96	1,67	29,79	17,88	47,67
	Recife (2003-2007)	0,62	3,00	44,80	14,93	59,74
	Salvador (2001-2005)	1,08	2,27	31,07	13,71	44,74
	Teresina (2000-2002)	0,96	1,00	28,43	28,43	56,86
Central						
	Campo Grande (2000-2003)	0,75	5,78	48,93	8,15	57,08
	Cuiabá (2002-2006)	1,10	8,11	70,55	8,47	79,01
	Distrito Federal (1999-2002)	1,07	5,41	39,31	7,37	46,68
	Goiânia (2005-2009)	1,44	6,39	82,66	12,72	95,37
Sudeste						
	Belo Horizonte (2001-2005)	1,01	3,48	38,03	10,87	48,90
	Grande Vitória (2004-2008)	1,56	2,08	31,85	15,23	47,09
	São Paulo (2006-2010)	1,31	3,39	34,47	14,28	48,74
Sul						
	Curitiba (2004-2008)	0,88	3,59	72,66	19,68	92,34
	Porto Alegre (2002-2006)	2,14	2,53	55,62	22,25	77,86
Median		1,09	3,00	45,52	15,08	58,41



AAPC 20.1 CI 95%, 3.5;39.4 p 0.02 Joao Pessoa
8,7 CI 95%, 10;16.9 p 0.30 Salvador (AML)
-4,0 CI 95%, -6.1;-1.9 p 0.001 São Paulo

2nd. Case-cohort study to identify EAL risk factors



- Birth Characteristics; Birth order; Congenital syndrome
- Maternal age ; Maternal education
- Delivery Labour type
- Maternal occupation

RESULTS AND CONCLUSION

- The overall IR of EAL varied according to Brazilian regions; the lowest IR in the Northeast region (37.00/million). Increased IR were observed in eight cities, mainly in the Northeast; João Pessoa city showed a significant increase AAPC=20.11%;CI95%:3.5;39.4 per/annum (10 years period). The median IR is increasing and directly proportional to age in childhood AL.
- For the second analysis, 1,215 children being 272 cases and 1,088 controls were randomly selected. There was null association with socioeconomic indicators in the PBCR dataset. The risk of EAL were associated with Males (adjOR 1.25, 95% CI, 0.93-1.66), birth defects (adjOR 3.62, 95% CI, 1.19-11.00) and maternal occupational exposure to chemicals (adjOR 2.18, p 0.002). Birth weight every 500g and 1000g of additional weight had a null effect whereas delivery labor as cesarean section a low association (adjOR, 1.28 CI,0.95-1.73).
- The sum up of this study with the identification of CL risk factors in population-based design,strengthens the exchange of knowledge and improvement of databases, and contributes to investigations on leukemia causation around the world.

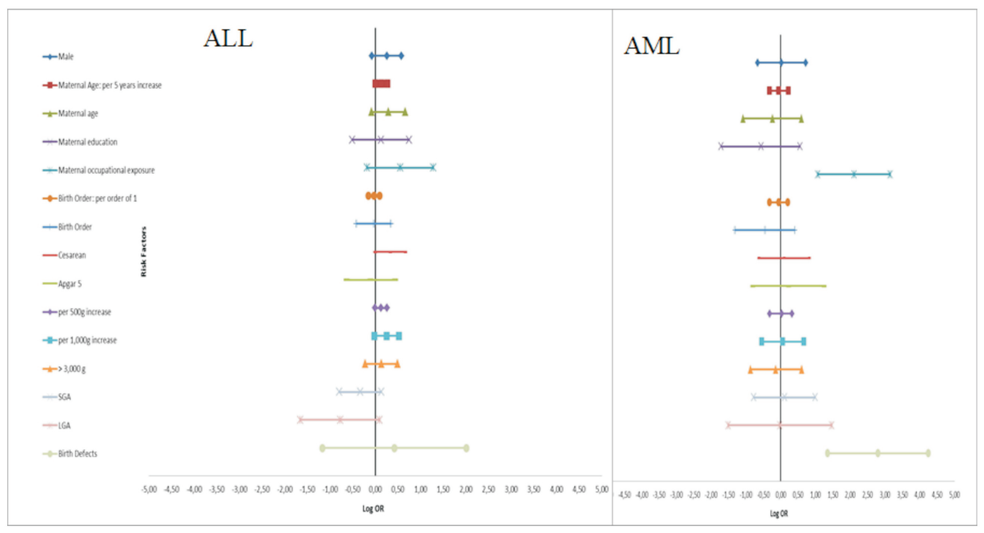
The frequencies distributions of maternal and per natal characteristics for cases and controls, Brazil, 2000-2009

		Controls (%)	Cases (%)	*p* value	ALL (%)	*p* value	AML (%)	*p* value	NOS (%)	*p* value
		1.088	272		207		41		24	
Gender										
	Female	532 (48.9)	117 (43.0)		87 (42.0)		19 (46.3)		11 (45.8)	
	Male	555 (51.0)	155 (57.0)		120 (58.0)		22 (53.7)		13 (54.2)	
	Missing	1 (0.1)	-	0.191	-	0.172	-	0.930	-	0.945
Race										
	White	465 (42.7)	1215 (46.0)		87 (42.0)		21 (51.2)		17 (70.8)	
	Non-white	509 (46.8)	140 (51.5)		114 (55.1)		20 (48.8)		6 (25.0)	
	Missing	114 (10.5)	7 (2.6)	<0.001	6 (2.9)	0.001	-	0.083	1 (4.2)	0.023
Maternal age (years)										
	< 30	818 (75.2)	189 (69.5)		141 (68.1)		29 (70.7)		19 (79.2)	
	≥ 30	270 (24.8)	83 (30.5)		66 (31.9)		12 (29.3)		5 (20.8)	
	Missing	-	-	0.063	-	0.038	-	0.581	-	0.803
Maternal education (years)										
	≤3	94 (8.6)	25 (9.2)		16 (7.7)		4 (9.8)		5 (20.8)	
	≥ 4	954 (87.7)	240 (88.2)		185 (89.4)		37 (90.2)		18 (75.0)	
	Missing	40 (3.7)	7 (2.6)	0.654	6 (2.9)	0.770	-	0.451	1 (4.2)	0.113
Maternal occupational exposure										
	Not workers	646 (59.4)	158 (58.1)		121 (58.5)		19 (46.3)		18 (75.0)	
	Chemical*	30 (2.9)	18 (6.6)		12 (5.8)		6 (14.6)		-	
	Others	335 (30.8)	77 (27.2)		57 (27.5)		13 (31.7)		4 (16.7)	
	Missing	77 (7.1)	22 (8.1)	0.015	17 (8.2)	0.117	3 (7.3)	<0.001	2 (8.3)	0.360
Birth order										
	First	363 (33.4)	90 (33.1)		70 (33.8)		11 (26.8)		9 (37.5)	
	Two or higer	521 (47.9)	137 (50.4)		105 (50.7)		21 (51.2)		11 (45.8)	
	Missing	204 (18.8)	45 (16.5)	0.650	32 (15.5)	0.503	9 (22.0)	0.665	4 (16.7)	0.907
Mode of delivery										
	Vaginal	594 (54.6)	132 (48.5)		98 (47.3)		20 (48.8)		14 (58.3	
	Cesarean	493 (45.3)	139 (51.5)		108 (52.2)		21 (51.2)		10 (41.7)	
	Missing	1 (0.1)	1 (0.4)	0.123	1 (0.5)	0.074	-	0.746	-	0.927
Gestacional age (weeks)										
	< 37	75 (6.9)	17 (6.3)		12 (5.8)		4 (9.8)		1 (4.2)	
	37-41	1001 (92.0)	254 (93.4)		194 (93.7)		37 (90.2)		23 (95.8)	
	> 41	12 (1.1)	1 (0.4)		1 (0.5)		-		-	
	Missing	-	-	0.494	-	0.597	-	0.629	-	0.757
5 minute APGAR										
	≤ 8	118 (10.8)	30 (11.0)		21 (10.1)		5 (12.2)		4 (16.7)	
	> 8	938 (86.2)	223 (82.0)		170 (82.1)		33 (80.5)		20 (83.3)	
	Missing	32 (2.9)	19 (7.0)	0.007	16 (7.7)	0.004	3 (7.3)	0.265	-	0.483
Birth weight										
	≤ 3.000 g	341 (31.3)	80 (29.4)		56 (27.1)		14 (34.1)		10 (41.7)	
	> 3.000 g	745 (68.5)	191 (70.2)		150 (72.5)		27 (65.9)		14 (58.3)	
	Missing	32 (2.9)	1 (0.4)	0.708	1 (0.5)	0.347	-	0.899	-	0.501
Fetal growth										
	SGA	177 (16.3)	38 (14.0)		26 (12.6)		8 (19.5)		4 (16.7)	
	AGA	839 (77.1)	220 (80.9)		170 (82.1)		31 (75.6)		19 (79.2)	
	LGA	69 (6.3)	13 (4.8)		10 (4.8)		2 (4.9)		1 (4.2)	
	Missing	3 (0.3)	1 (0.4)	0.559	1 (0.5)	0.395	-	0.916	-	0.968
Birth defects										
	No	1,026 (94.3)	250 (91.9)		192 (92.8)		35 (85.4)		23 (95.8)	
	Yes	7 (0.6)	7 (2.6)		3 (1.4)		3 (7.3)		1 (4.2)	
	Missing	55 (5.1)	15 (5.5)	0.017	12 (5.4)	0.429	3 (7.3)	<0.001	-	0.072

Association between maternal and perinatal characteristics and Early-age acute leukemia, Brazil, 2000-2009

	Crude OR (95% CI)	*p-value*	Adjusted OR (95% CI)	*p-value*
Gender				
Female	1		1	
Male	1.27 (0.97 - 1.66)	0.08	1.25 (0.93 - 1.66)	0.137
Maternal age (years)				
per 5 years increase	1.11 (1.00 - 1.22)	0.048	1.08 (0.96 - 1.21)	0.209
< 30	1		1	
≥ 30	1.33 (0.99 - 1.78)	0.056	1.21 (0.86 - 1.44)	0.271
Maternal education (years)				
≤3	1		1	
≥ 4	0.95 (0.60 - 1.50)	0.81	0.86 (0.52 - 1.44)	0.571
Maternal occupational expousure				
Not workers	1		1	
Chemical*	2.45 (1.33 - 4.51)	0.004	2.18 (1.16 - 4.10)	0.002
Others	0.90 (0.66 - 1.23)	0.514	0.77 (0.55 - 1.07)	0.123
Birth order				
per order of 1	1.02 (0.93 - 1.13)	0.621	0.99 (0.89 - 1.10)	0.820
First	0.94 (0.7 - 1.27)	0.699	0.96 (0.68 - 1.34)	0.799
Two or higer	1		1	
Mode of delivery				
Vaginal	1		1	
Cesarean	1.27 (0.97 - 1.66)	0.08	1.28 (0.95 - 1.73)	0.104
Gestacional age (weeks)				
< 37	0.89 (0.52 - 1.54)	0.893	0.79 (0.43 - 1.46)	0.457
37-41	1		1	
> 41	0.33 (0.40 - 2,54)	0.328	-	-
5 minute APGAR				
≤ 8	1.07 (0.70 - 1.64)	0.758	0.96 (0.60 - 1.52)	0.861
> 8	1		1	
Birth weight				
per 500 g increased	1.09 (0.96 - 1.24)		1.09 (0.95 - 1.25)	
per 1000 g incresed	1.19 (0.93 - 1.54)	0.167	1.19 (0.91 - 1.56)	0.196
≤ 3.000 g	1		1	
> 3.000 g	1.09 (0.82 - 1.46)	0.550	1.05 (0.77 - 1.44)	0.747
Fetal growth				
SGA	0.82 (0.56 - 1.20)	0.303	0.79 (0.53 - 1.19)	0.261
AGA	1		1	
LGA	0.72 (0.39 - 0.289)	0.289	0.56 (0.27 - 1.15)	0.111
Birth defects				
no	1		1	
yes	4.10 (1.42 - 11.81)	0.009	3.62 (1.19 - 11.00)	0.023

Association between maternal and perinatal characteristics and Acute Lymphoblastic Leukemia (ALL) and myeloblastic (AML)



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