Case-Control Study: Birth Weight and Risk of Childhood Acute Lymphoblastic Leukemia

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BACKGROUND:

Case-control and cohort studies among European populations have repeatedly implicated high birth weight as a risk factor for childhood leukemia
State-level studies in the United States, however have not always confirmed this finding
Studies in the United States have not always matched on race or adjusted for race
We used linked cancer-registry and birth-certificate data from Arizona, Kentucky, and Illinois to conduct a case-control study, matching on demographic factors

METHODS:

Cases of acute lymphoblastic leukemia (ALL) diagnosed among children under five years of age were abstracted from the cancer registries of three states: Arizona, Kentucky, and Illinois.
Birth certificate data were abstracted for each case, and for a set of control birth certificates matched on sex, race, ethnicity, county of birth, and date of birth.
The matching ratio (number of controls per case) ranged from 4:1 in Kentucky and Illinois to 6:1 in Arizona.

Using normal birth weight (2500-4000 grams) as the referent group, the odds ratios (OR) and 95% confidence intervals (CI) for childhood ALL among lighter and heavier newborns were calculated by conditional logistic regression (matched-sets analysis) using SAS PROC LOGISTIC.

RESULTS:

Compared with children of normal birthweight (2500-4000 grams), children whose birthweight exceeded 4000 grams had an elevated risk of acute lymphoblastic leukemia in the first five years of life [OR=1.314; 95% CI=(1.041-1.650)].

The excess risk in the entire population was driven by the substantial excess risk among non-Hispanic white children [OR=1.831; 95% CI=(1.106-2.568)]; within this ethnic group, the excess risk was observed among both boys [OR=1.623; 95% CI=(1.039-2.535)] and girls [OR=2.179; 95% CI=(1.299-3.656)].

No such excess risk was observed among Hispanic children [OR=1.101; 95% CI=(0.684-1.772)] nor among African-American children [OR=1.030; 95% CI=(0.553-1.918)], nor among "other" children [OR=0.810; 95% CI=(0.426-1.504)].

Low birthweight was associated with a non-significantly reduced risk of childhood ALL among children of all races [OR=0.778; 95% CI=(0.541-1.119)], and among non-Hispanic white [OR=0.943; 95% CI=(0.569-1.562)], Hispanic [OR=0.906; 95% CI=(0.452-1.815)], African-American [OR=0.831; 95% CI=(0.177-1.534)], and "other" [OR=0.381; 95% CI=(0.115-1.306)] children.

When the data for children of all races were stratified by sex, low birthweight was statistically significantly associated with reduced risk among girls [OR=0.545; 95% CI=(0.305-0.965)], but not among boys [OR=1.0403; 95% CI=(0.651-1.670)].

DISCUSSION:

This study confirms the elevated risk of childhood ALL previously reported by other studies in children of European ancestry.
The few studies that did not find such an association were conducted in more diverse populations, and either did not stratify by race or did not adequately adjust for it.

Matched-Pairs Odds Ratios (OR) for Acute Lymphoblastic Leukemia (ALL), with 95% Confidence Intervals (CI), by Conditional Logistic Regression:

All Races, Both Sexes, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	8	148	21
Birth	2500-4000	189	2315	312
Weight (g)	>4000	25	434	63
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		1.341	(1.041, 1.650)	
2500-4000 g		1.000	(referent)	
>4000 g		0.778	(0.541, 1.119)	

N.H. Whites, Both Sexes, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	6	81	8
Birth	2500-4000	85	1038	126
Weight (g)	>4000	14	236	30
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		0.943	(0.569, 1.562)	
2500-4000 g		1.000	(referent)	
>4000 g		1.831	(1.306, 2.568)	

Blacks, Both Sexes, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	1	14	1
Birth	2500-4000	26	287	47
Weight (g)	>4000	4	48	10
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		0.521	(0.177, 1.534)	
2500-4000 g		1.000	(referent)	
>4000 g		1.030	(0.553, 1.918)	

Hispanics, Both Sexes, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	0	42	10
Birth	2500-4000	52	611	86
Weight (g)	>4000	4	109	15
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		0.906	(0.452, 1.805)	
2500-4000 g		1.000	(referent)	
>4000 g		1.101	(0.684, 1.772)	

Other Races, Both Sexes, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	1	11	2
Birth	2500-4000	26	379	53
Weight (g)	>4000	3	41	8
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		0.388	(0.115, 1.306)	
2500-4000 g		1.000	(referent)	
>4000 g		0.810	(0.426, 1.504)	

All Races, Males, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	4	88	16
Birth	2500-4000	87	1200	213
Weight (g)	>4000	20	300	48
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		1.043	(0.651, 1.670)	
2500-4000 g		1.000	(referent)	
>4000 g		1.352	(1.018, 1.795)	

N.H. White Males, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	2	36	6
Birth	2500-4000	40	509	79
Weight (g)	>4000	10	133	21
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		1.012	(0.496, 2.064)	
2500-4000 g		1.000	(referent)	
>4000 g		1.623	(1.039, 2.535)	

Black Males, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	1	11	0
Birth	2500-4000	11	156	35
Weight (g)	>4000	4	39	7
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		0.843	(0.233, 3.054)	
2500-4000 g		1.000	(referent)	
>4000 g		1.196	(0.590, 2.424)	

Hispanic Males, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	0	30	8
Birth	2500-4000	24	320	62
Weight (g)	>4000	3	98	13
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		1.466	(0.611, 3.519)	
2500-4000 g		1.000	(referent)	
>4000 g		1.417	(0.834, 2.406)	

Other Races, Males, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	1	11	2
Birth	2500-4000	12	215	37
Weight (g)	>4000	3	30	7
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		0.788	(0.222, 2.802)	
2500-4000 g		1.000	(referent)	
>4000 g		0.897	(0.425, 1.893)	

All Races, Females, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	4	60	5
Birth	2500-4000	102	1115	99
Weight (g)	>4000	5	134	15
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		0.542	(0.305, 0.965)	
2500-4000 g		1.000	(referent)	
>4000 g		1.255	(0.831, 1.895)	

N.H. White Females, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	4	45	2
Birth	2500-4000	45	529	47
Weight (g)	>4000	4	103	9
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		0.877	(0.429, 1.793)	
2500-4000 g		1.000	(referent)	
>4000 g		2.179	(1.299, 3.656)	

Black Females, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	0	3	1
Birth	2500-4000	15	131	12
Weight (g)	>4000	0	9	3
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		0.228	(0.029, 1.804)	
2500-4000 g		1.000	(referent)	
>4000 g		0.642	(0.170, 2.427)	

Hispanic Females, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	0	12	2
Birth	2500-4000	28	291	24
Weight (g)	>4000	1	11	2
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		0.475	(0.142, 1.587)	
2500-4000 g		1.000	(referent)	
>4000 g		0.445	(0.131, 1.516)	

Other Races, Females, Arizona, Illinois, & Kentucky		Control Birth Weight (g)		
		<2500	2500-4000	>4000
Case	<2500	0	0	0
Birth	2500-4000	14	164	16
Weight (g)	>4000	0	11	1
Birth Weight:		Odds Ratio:	95% Confidence Interval	
<2500 g		OR and 95% CI not calculated		
2500-4000 g		1.000	(referent)	
>4000 g		0.618	(0.172, 2.221)	