IS INSULIN RESISTANCE MORE FREQUENT IN CHILDREN BORN SGA?

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Abstract

Introduction: Rapid increase in weight during early childhood, "catch-up growth" phenomenon, in children born small for gestational age (SGA) has been strongly linked with insulin resistance (IR), which may be a risk factor for type 2 diabetes mellitus and cardiovascular disease. IR occurred in the prenatal period has a protective role, that of intrauterine survival in conditions of malnutrition. In the postnatal period, early onset IR becomes a risk factor for metabolic syndrome and its components correlated with normal (or excessive) nutritional intake. ***Material and methods:*** A retrospective observational study was carried out on long-term metabolic complications in children born SGA, which were admitted to our hospital over a 5 year period from 2007 to 2011. 517 patients (mean age 12 years±0.6, aged between 6 - 18 years) were divided in two study groups, following the statistical processing of data sheets, as follows: 410 obese patients that were born appropriate for gestational age (AGA) (79,30 %) and 107 obese patients that were born SGA (29,69 %). Baseline glucose and insulin levels of the patients were measured and IR index was assessed by homeostasis model assessment (HOMA). A cut-off HOMA level of >2.5 in the prepubertal period and of > 3.5 for adolescents was used to identify an IR status. ***Results:*** IR was found in 20% of obese AGA children and 25,3% of obese SGA. Rate of IR in patients born SGA was greater compared to obese children born AGA and had a significant statistical difference (P = 0.03, mean 2,95229 AGA versus 3,72778 SGA group and SD 1,7 versus 2,6).***Conclusion:*** Increased prevalence of IR patients born SGA compared to AGA indicates that being born SGA appears to be an additional risk factor in the developement of IR. IR met in a high percentage among obese patients born SGA, allows us to affirm that the cardiovascular risk in these patients as well as the risk of developing type 2 diabetes is higher. Monitoring, periodic evaluation and appropriate dietary therapy in the case of obese children born SGA is crucial in preventing early onset cardiovascular disease.

Key words: Small for gestational age, obesity, insulinresistance

Introduction:

About 3-5% of neonates are born small for gestational age (SGA). 85-90% of them recover weight up to 2 years of age, majority of which become obese up to 4 years of age, later on developing components of the metabolic syndrome (MetS).The rapid “catch up” growth during the cell division period up to 2 years of age leads to hyperplastic obesity (1,2). These children have a high risk of developing MetS with all its components: obesity, impaired glucose tolerance, insulin resistance with subsequent development of diabetes, arterial hypertension, dyslipidemia. There is also a risk of developing adrenocortical pathology and reproductive pathology (3,4,5,6).

Rapid increase in weight during early childhood, "catch-up growth" phenomenon, in children born small for gestational age (SGA) has been strongly linked with insulin resistance (IR), which may be a risk factor for type 2 diabetes mellitus and cardiovascular disease. IR occurred in the prenatal period has a protective role, that of intrauterine survival in conditions of malnutrition. In the postnatal period, early onset IR becomes a risk factor for metabolic syndrome and its components correlated with normal (or excessive) nutritional intake. (7,8,9,10)

Whilst several epidemiological surveys have confirmed the association between metabolic disturbances in adulthood and low birth size, few and conflicting data exist for childhood . The potential impact of the early recognition of altered insulin sensitivity in clinical practice is high, because it might prompt the establishment of appropriate hormone-, diet-, or lifestyle-based strategies to prevent the long-term metabolic consequences of intrauterine growth retardation.

Material and methods:

A retrospective descriptive study was conducted over a period of five years, between January 2007 and December 2011, on cases of obesity in children diagnosed at the Emergency Hospital for Children "Louis Ţurcanu" Timişoara in the departments of Diabetes and Nutritional Diseases, Endocrinology and Cardiology.

Children were considered obese on the basis of age specific BMI reference guidelines from Centers for Disease Control and Prevention Child Growth Standards 2000 (above 95th percentile).(11) When defining SGA, growth nomograms and charts proposed by Niklasson (12) are being used; newborns weighing less than 2 standard deviations (SD) from the average for gestational age, we considered as being SGA.

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Antropometric and metabolic characteristic of the study group

	AGA						SGA					
total number	410						107					
	prepubertal		pubertal		adolescents		prepubertal		pubertal		adolescents	
total number	165		150		95		42		46		19	
residence urban/rural	95(57%)/70(43%)		106(70%)/44(30%)		56(59%)/39(41%)		23 (55%)/19 (45%)		28(60%)/18(40%)		12(63%)/7(27%)	
gender male/female	105(64%)/60(36%)		90(60%)/60(40%)		38(40%)/57(60%)		23 (55%)/19 (45%)		19(41%)/27(59%)		7 (37%)/12(63%)	
	Mean ± standard deviation	range	Mean± standard deviation	range	Mean± standard deviation	range	Mean± standard deviation	range	Mean± standard deviation	range	Mean± standard deviation	range
Age (years)	7.35±1.922	5 10	12.35±1.04	11 14	16.25±1.2	15 18	7.45±1.867	5 10	12.28±1.096	11 14	15.79±0.83	15-18
Anthropometric data												
Weight (kg)	39.34±14.5	10.3 82	66.72±16.63	45-112	84.57±20.3	49-142	36.5±18.63	10.5-105	63.64±17.9	41-105	73.9±26.95	53-143
Height (cm)	126±0.2	67-164	155.7±0.09	127-177.5	166.28±10.35	150-190	129.5±18.29	90-145	152.82±10.8	131.2-180	157.41±15.43	116-177.5
BMI (kg/m2)	23.88±6.3	14-34	27.23±5.37	16-48.9	30.44±6.29	19.5-44.9	38±2.96	13.4-120	26.9±5.557	19-43	29.31±8.3	19-54
Biological data												
Baseline glucose (mmol/l)	4.55±0.533	2.91-5.75	4.55±0.71	3.9-5.5	4.667±0.63	3.9-6.21	4.8±0.6	3.6-5.6	4.65±0.533	3.9-5.5	4.4±0.22	3.9 - 5.1
Baseline insulin (uui/l)	10.29±6.62	2 35	15.57±9.41	2-45.1	18.62±15.7	3.3-88.5	12.6±8.64	1.86-35.3	21.7±17.13	2-74.9	13.45±9.16	2-37.3
HOMA	2.4±1.57	0.34-8.2	3.6±3.17	0.38-23	3±2.28	0.4-9.2	3.32±1.65	0.66-7.31	4.57±3	0.39-11.78	4.22±3.35	0.72-20.82

Table 1. Antropometric and metabolic characteristic of the study group

		Prepubertal		Pubertal		Adolescents		Total	
		AGA	SGA	AGA	SGA	AGA	SGA	AGA	SGA
IR+	No(%)	27 (16.3%)	8(19%)	32(21.33%)	14 (30%)	22(23%)	5(26.3%)	81 (20%)	27(25.3%)
IR-	No(%)	138(83.6%)	34(81%)	118(78.66%)	32(70%)	73(77%)	14(73.6%)	329(80%)	80(74.7%)

Tabel 2- Presence of IR in AGA and SGA children according to age: prepubertal, pubertal, adolescents

Basal glucose and insulin levels of the patients were measured and IR index was assessed by homeostasis model assessment (HOMA- fasting glucose in mmol/l multiplied by baseline insulin in microunits per milliliter, divided by 22.5). A cut-off HOMA level above 2.5 in the prepubertal period and of > 3.5 for adolescents was used to define an IR status.

Exclusion criteria were evidenced for syndromal, chromosomal, or infectious etiology of low birth weight;endocrine or syndromal disorders, systemic disease or acute illness.

Thus, the result was an extended batch of 517 patients diagnosed with obesity, including 410 patients AGA and 107 patients SGA. Obese AGA and SGA patients were distributed into subgroups by age, namely prepubertal (5-10 years), pubertal (11-14 years) and adolescent (15-18 years). We divided children into two categories according to their HOMA values: children with IR (IR+) and children without IR(IR-).

The data are expressed as means± standard deviation pr as frequencies. We used the unpaired t test (with a confidence interval of 95 percent) to evaluate the differences between the two groups SGA vs. AGA.

Results

Clinical and metabolic characteristics of the study groups are shown in Table 1.

The study group has been homogeneous regarding BMI with one exception prepubertal AGA subgroup comparing to prepubertal SGA subgroup (mean 23.88±6.3 vs. 38±2.96).

The distribution of the 517 patients from the original study group according to gestational age, resulting in two

groups, obese AGA patients and obese SGA patients is shown in Figure 1. As expected, it appears that the SGA group is smaller than the AGA group, representing about a third of it:AGA-410 (79%), SGA-107 (21%).

The presence of IR among AGA and SGA are illustrated in Table 2. IR was found in 20% of obese AGA children and 25,3% of obese SGA. IR increases by age: prepubertal group 16.3% in AGA group and 19% in SGA group adolescent group: 23% AGA group and 26.3% SGA group. We found a higher prevalence IR in the pubertal SGA group 30%. Figure 2a, 2b, 3.

Discussions:

Rate of IR in patients born SGA was greater compared to obese children born AGA and had a significant statistical difference (P = 0.03, mean 2, 95229 AGA versus 3,72778 SGA group and SD 1,7 versus 2,6).

Baseline glucose levels were almost similar in all the 6 subgroups. A difference in baseline insulin has been noticed. Higher levels of insulin have been observed in the patients born SGA (table 2) in all the three subgroups prepubertal, pubertal, adolescents. We speculated that an early phase of increased insulin level during childhood might precede the onset of insulin resistance in young adult SGA subjects.

Several reports suggest reduced insulin sensitivity in SGA children, to date very few strict case-control studies have been carried out. Gray and colleagues studied 100 premature and/or small for gestational age infants (age range: 1-65 days). Fasting and postprandial glucose and insulin levels were measured. SGA neonates had higher 60-minute insulin levels than AGA neonates despite similar glucose levels.(13)Yanjnik and colleagues performed a glucose tolerance test in 379 4-year-old low birth weight Indian children. 30 minutes after an oral glucose load, subjects with lower birth weights had higher plasma glucose and insulin levels, irrespective of their current size.(14). Those findings coincide with the conclusions drawn in the present study.

As far as we know, our study is the first study in obese children analyzing the impact of former SGA status in order to set up the prevalence of IR. We consider important establishing an appropriate period for screening the former SGA to prevent cardiovascular disease.

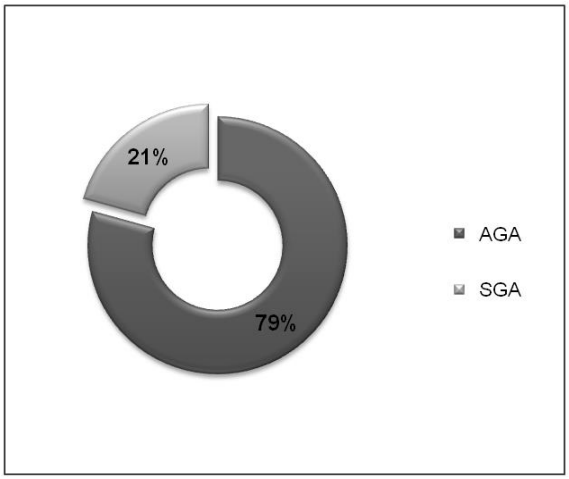
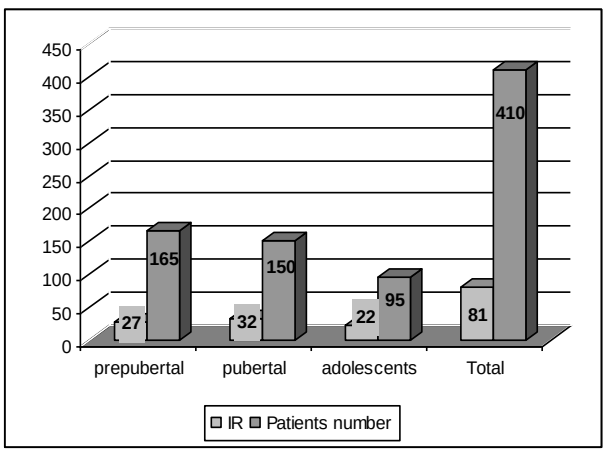
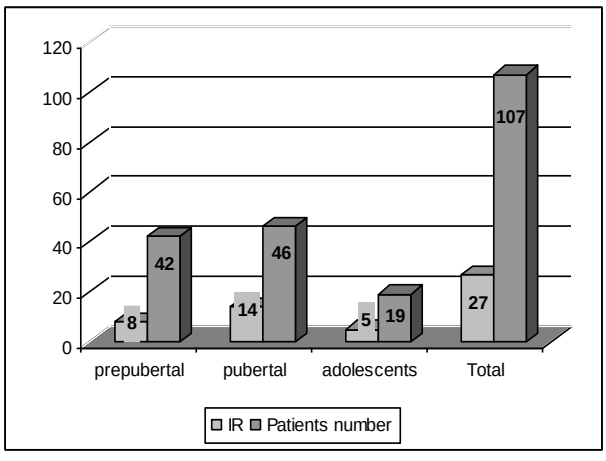


Figure 1: Percentage distribution of study groups according to gestational age

AGA=appropriate for gestational age, SGA=small for



a. AGA group



b. SGA group

Figure 2- Distribution of IR in a. AGA group and b. SGA group according to age

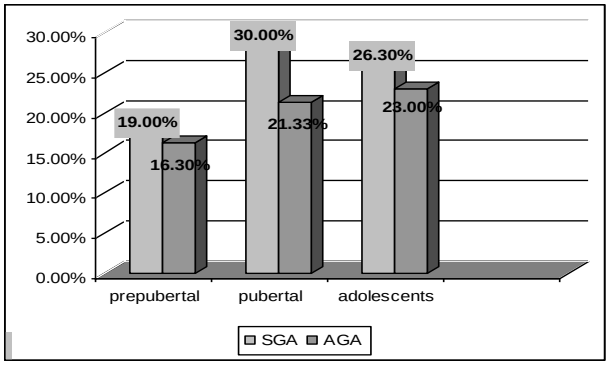


Figure 3 Percentage distribution of IR in AGA vs. SGA group according to age

Conclusions:

Metabolic impairment in SGA children is amplified by weight gain and influenced by fetal programming; developing intrauterine IR as a prenatal surviving mechanism is a risk factor for postnatal MetS and cardiovascular disease. Influence of SGA on developing IR increases gradually with age.

Increased prevalence of IR patients born SGA compared to AGA indicates that being born SGA appears to be an additional risk factor in the developement of IR. IR met in a high percentage among obese patients born SGA, allows us to affirm that the cardiovascular risk in these patients as well as the risk of developing type 2 diabetes is higher. Monitoring, periodic evaluation and appropriate dietary therapy in the case of obese children born SGA is crucial in **preventing early onset cardiovascular disease**.

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