Correlation of Serum Adiponectin and Leptin Concentrations with Anthropometric Parameters in Newborns

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SUMMARY

Introduction It has been shown that some adipocytokines and their mutual relationship can be indicators of fetal and neonatal growth. Physiological role of leptin and adiponectin in fetal and neonatal growth is not well established.

Objectives The aim of this study was to assess the correlation of the anthropometrics parameters and serum concentration of leptin and adiponectin levels in healthy newborns.

Methods A cohort of 110 neonates, born after uncomplicated singleton pregnancies at term, were classified as AGA (n=60), SGA (n=30) and LGA (n=20) according to the Lubchenco curves. Anthropometric parameters of the neonates: birth weight (BW), birth length (BL), body weight/body length ratio (BW/BL), Body Mass Index (BMI) and Ponderal Index (PI) were recorded after birth.

Results Mean serum leptin and adiponectin levels in both sexes were not significantly different (male: 1.85±0.75; 29.51±22.89 and female: 2.06±0.99; 31.60±23.51 ng/mL). There was a significant difference between leptin levels in AGA and LGA newborns (1.93±0.84 vs. 3.12±1.50 ng/mL) ($p<0.05$), and in adiponectin levels between AGA and LGA compared to SGA newborns (32.8±23.29 and 43.40±31.24 vs. 12.67±2.43 ng/mL, respectivel; $p<0.05$; $p<0.05$). Leptin and adiponectin levels were positively correlated with BW ($r=0.63$ and $r=0.41$), BL ($r=0.63$, $r=0.42$), BW/BL ($r=0.61$, $r=0.41$), BMI ($r=0.54$, $r=0.35$), and PI ($r=0.47$, $r=0.29$, ($p<0.01$).

Conclusion Significantly higher adiponectin levels were found in AGA neonates compared to SGA neonates. Leptin and adiponectine levels were positively correlated with birth weight. These findings suggest that these adipocytokines may be involved in fetal growth regulation.

Keywords: leptin; adiponektin; anthropometric parameters; newborn

INTRODUCTION

Fetal growth is determined by many factors, including genetic factors, placental flow, and comorbidities. It has been generally accepted that the growth of the fetus is not dependent on growth hormone, but other growth factors such as insulin and other insulin growth factors – IGF1, IGF2, etc [1]. Recently it has been shown that some adipocytokines and their mutual relationship can be indicators of fetal and neonatal growth.

Leptin and adiponectin are proteins secreted mostly by adipose tissues, and in minor proportion, by some other tissues. Leptin is a regulating protein that is involved in balance between energy intake and expenditure. High levels of leptin are noticed in overweight neonates, leading to conclusion that they are markers of growth [2]. Like in adults, higher concentrations of fetal leptin leads to higher fetal fat, leading to the conclusion that the fetal fat is capable of producing leptin accordingly [3, 4]. The mechanism and factors that produce leptin in fetus are still unknown. In addition, placental secretion of leptin has been also confirmed in order to maintain the pregnancy and feto-maternal adaptation, and therefore has a role in the fetal growth [5].

Adiponectin is produced by fat tissue only, and has a role in glucose and lipid metabolism. Therefore, it is an important predictor of metabolic disease, diabetes, hyperlipidemia. Little is known about the level of adiponectin in fetus and its significance for further neonatal development. However, Tsai et al. [6] postulated that large neonates have higher level of adiponectin than those with appropriate weight. Sivan et al. [7] confirmed that adiponectin was present in cord blood at significantly higher levels than those measured in blood of older children.

It has been well known that children have higher levels of leptin according to the total body fat mass, and they vary in different age and gender [8, 9]. Studies in neonatal cohorts were made including comparisons with different parameters – birth weight, gestation, maternal BMI [10]. However, data about the levels of adipocytokines in healthy neonates are still not well defined, as well as its significance of their levels in future weight gain of a child.

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OBJECTIVE

The aim of this study was to assess the correlation of the anthropometrics parameters with leptin and adiponectin levels in healthy newborns.

METHODS

A cohort of 110 (61 female and 49 male) neonates, born from uncomplicated, singleton pregnancies at term i.e., between 37 and 42 gestational weeks was evaluated in the study. Neonates with risk factors (maternal diabetes, stressful delivery, infection, etc.), were excluded from the study.

Anthropometric measurements were made at birth, including length, weight and head circumference, body weight/body length. Because a single standard anthropometrics factor (BW; BL) cannot assess the nutritional status of newborn properly, we also used combinations of two anthropometric factors: Ponderal index (PI), and Body Mass Index (BMI). PI and BMI are expressed by the following formulas: PI= body weight (g)/ [body length (cm)] 3x100 and BMI= body weight (kg)/birth length 2 (m).

The neonates were categorized in three groups according to the Lubchenco [11]; curves as: appropriate for gestational age (AGA – birth weight between 10th and 90th percentiles), large for gestational age (LGA – birth weight more than 90th percentile) and small for gestational age (SGA – birth weight lower than 10th percentile). Gestational age at birth was calculated from the last menstrual period, supported by ultrasound measurements and confirmed by Dubowitz scoring [12].

Serum levels of leptin and adiponectin in fasting state were determined from a blood sample at regular control visit from each neonate. Blood samples were taken at least 48 hours after delivery (and not from cord blood) with the purpose of avoiding any bias of hormones deriving from maternal tissues [13]. The blood samples were immediately centrifuged and stored at -20°C until assayed.

Serum adiponectin and leptin concentrations were measured by the ELISA method (Human DRG Instruments GmbH, Germany). The limit of sensitivity of adiponectin assay was 0.78 ng/ml. and the intra- and inter-assay coefficient of variations (CV%) were 0.9-7.4 and 2.4-8.4 ng/mL respectively. The sensitivity of the DRG Leptin ELISA was 1.0 ng/mL, and the intra- and inter- assay CV % ranged from 5.9 5-6.91 and 8.66-11.55, respectively.

Correlation between the anthropometric parameters and adiponectin and leptin were statistically analyzed using STATISTICA program, one way ANOVA, LSD test and Spearmen rank correlations.

The study was reviewed and approved by the Institutional Rewired Board of the hospital. Informed consent was obtained from all mothers before blood samples were taken and inclusion of their infants in the study.

RESULTS

The neonates' anthropometric data, leptin and adiponectin serum concentrations are presented in Table 1. Mean birth weight of the newborns classified as AGA (n=60), SGA (n=30) and LGA (n=20) was 3443±338 g, 4604±484 g and 2409±295 g, respectively. Mean birth length, and birth weight/birth length ratio were 50.65±2.1 cm (68.00±6.28 g/cm) for AGA, 52.70±4.45 cm (87.88±11.41 g/cm) for LGA and 46.69±2.00 cm (51.50±4.79 g/cm) for SGA, respectively. These marked differences between above mentioned anthropometric values were transposed also to the ponderal and body mass index values of the groups stressing the difference between LGA (3.30±1.23; 16.94±3.87) compared to AGA (2.67±0.46; 13.46±1.6) and SGA (2.37±0.21; 11.03±0.86), respectively.

No marked differences were observed in anthropometric data of both sexes.

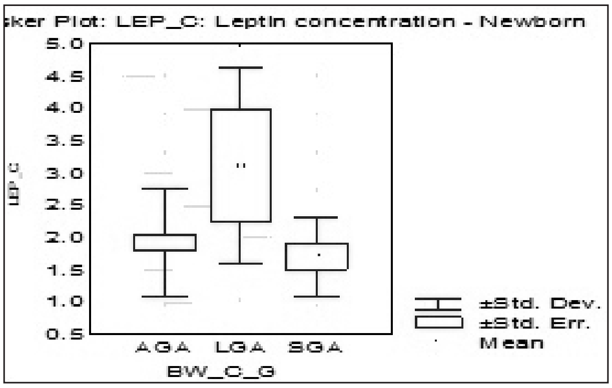
Significantly higher level of leptin concentration was observed in LGA (3.12±1.50) compared to AGA and SGA. On the other side the leptin concentration in AGA (1.93±0.84) and SGA (1.71±0.61) group did not differ significantly.

Adiponectin levels in SGA group were significantly lower compared to AGA and LGA groups (12.67±2.43 vs. 32.80±23.29 and 43.40±31.24), respectively. No significant difference in adiponectine levels between AGA and SGA groups were monitored (Graphs 1 and 2).

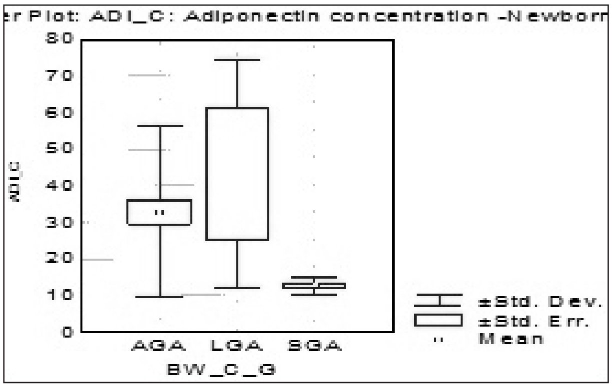
Table 1. Clinical characteristics of newborns, leptin and adiponectin concentration in newborn's serum

Parameter	AGA	LGA	SGA	Total
Birth weight (kg)	3.44±0.33	4.60±0.48	2.40±29.5	3.48±0.37
Birth length (cm)	49.65±2.1	52.7±04.45	46.69±2.09	50.02±2.88
Birth weight/Body Length ratio (g/cm)	68.00±6.28	87.88±11.41	51.50±4.79	69.13±0.49
Ponderal (Rohrer) Index	2.67±0.46	3.30±1.23	2.37±0.21	2.78±0.64
Body Mass Index	13,46±1.6	16.94±3.87	11.03±0.86	13.81±2.11
Leptin concentration (ng/mL)	1.93±0.84^{a}	3.12±1.50^{a,b}	1.71±0.61^{b}	1.96±0.88
Adiponectin concentration (ng/mL)	32.80±23.29^{a}	43.40±31.24^{b}	12.67±2.43^{a,b}	30.61±23.04

^{a,b} Values with same superscript are significantly different (p<0.05).



Graph 1. Whisker plots for leptin concentrations in different groups



Graph 2. Whisker Plots for adiponectin concentrations in different groups

Table 2. Spearman Rank Order Correlations (r) between nthropometric data, leptin and adiponectin concentrations

Parameter	BMI	PI	BW	BW/BL	BL
Leptin	0.5492	0.4746	0.6359	0.6153	0.6331
Adiponectin	0.3507	0.2952	0.4360	0.4155	0.4266

All correlation coeficients were statistically significant (p<0.001).

Neither leptin nor adiponectin levels were significantly different in males compared to female newborns; therefore no additional adjustment for gender was performed during the analysis. These findings support the thesis that other factors influence leptin and adiponectin serum concentration in this starting growth period of the newborn [7, 14, 15].

Considering the analyzed newborns as one population, leptin and adiponectin levels were strongly correlated with all anthropometric variables (p<0.001) as can be seen in Table 2.

DISCUSSION

The correlation between maternal weight and fetal measurements (weight, length, ponderal index) is still poorly understood. Maternal diabetes and genetic factors (height and weight of the parents) are the only known factors so far that are positively correlated with the increased neonatal weight. It is known that there is not always correlation between BMI of mothers with the weight of the neonate. Therefore other mechanisms are still to be evaluated. Recently several studies about the levels of some adipokines and neonatal size were conducted especially leptin and adiponectin [8, 10, 16, 17, 18]. However, some other adipokines were studied trying to explain this correlation, i.e. resistin [19], vaspin, amylin [20], etc. As it can be seen, neonatal weight and length depend on many factors that can mutually interact.

Leptin is a product of gene, and serves as a regulator between the amount of adipose tissue and energy expenditure through influence on satiety centers in hypothalamus [21]. Since the fetus cannot have satiety response to the energy taken by the placenta, the reason for leptin levels in newborn is still unknown. Several studies in different populations showed that leptin level was positively correlated with the newborn's weight [8, 16]. Our data confirm these data in our population including all ethnicity groups – Macedonian, Albanian or Roma babies. One way ANOVA analysis revealed that leptin levels in LGA babies were significantly elevated compared to AGA and SGA. On the contrary, no significant difference in leptin levels was observed between sexes. Leptin levels were positively correlated with birth weight, birth length, body weight/body length which is a good parameter of fat content in the newborn. It is still not known why leptin levels are more elevated in newborns than in other age groups (prepubertal children, adults) in comparison to fetal mass in these groups, and remains to be clarified. Placental production of leptin, and therefore initiation for the beginning of birth could be the cause.

The role of adiponectin is more complicated, since it has been shown that it has negatively correlated with the body fat in adults, especially in obesity [22]. Few studies made in newborns have shown that adiponectin levels are decreased in newborns of mothers with diabetes or insulin resistance [23]. There was no correlation between adiponectin levels and weight in neonates of normal mothers in this study. However, in several other studies a positive correlation between neonatal size and adiponectine levels in blood cord, unlike the studies in adults, were found [6, 7, 15]. Our study also showed a positive correlation between neonatal weight and adiponectine levels, without detected significance between two genders. In the group of SGA significantly lower values of adiponectin levels were found, such as in studies of Martos-Moreno et al. [24].

CONCLUSION

Most of the studies in the literature were made on the umbilical cord sampling. The importance of this study is that these data for above mentioned correlations are confirmed in neonatal blood sampling as well. This study confirms that these adipocytokines may be involved in fetal growth regulation. A significantly higher adiponectin levels were found in the AGA neonates compared to lower values in the SGA neonates. Leptin and adiponectine levels positively correlate with birth weight.

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doi: 10.2298/SARH1210595P

Корелација нивоа адипонектина и лептина у серуму с антропометријским параметрима код новорођенчади

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КРАТАК САДРЖАЈ

Увод Показано је да неки адипоцитокини и њихови узајамни односи могу бити индикатори раста фетуса и новорођенчета. Физиолошки утицај нивоа лептина и адипонектина на овај раст није довољно разјашњен.

Циљ рада Циљ студије била је процена корелације антропометријских параметара и концентрације лептина и адипонектина у серуму здраве новорођенчади.

Методе рада Група од 110 новорођенчади рођене из некомпликованих појединачних терминских трудноћа подељена је, на основу Љубченкових кривуља, на три мање групе: новорођену децу оптималног раста и развоја за гестациони узраст (*AGA*), коју је чинило 60 деце, децу малу за гестациони узраст (*SGA*) са 30 деце и новорођенчад велику за гестациони узраст (*LGA*), у којој је било 20 деце. Антропометријски параметри новорођенчади (тежина и дужина на рођењу, однос телесне тежине и дужине, индекс телесне масе и пондерални индекс) забележени су после порођаја.

Резултати Средњи ниво лептина и адипонектина у серуму беба оба пола није се значајно разликовао (дечаци: 1,85±0,75 и 29,51±22,89 *ng/ml*; девојчице: 2,06±0,99 и 31,60±23,51 *ng/ml*). Забележена је значајна разлика у нивоу лептина између *AGA* и *LGA* новорођенчади (1,93±0,84 према 3,12±1,50 *ng/ml*; $p<0,05$), и у нивоу адипонектина између *AGA* и *LGA* у поређењу са *SGA* новорођенчади (32,8±23,29 и 43,40±31,24 према 12,67±2,43 *ng/ml*, редом; $p<0,05$; $p<0,05$). Нивои лептина и адипонектина били су у позитивној корелацији с тежином на рођењу ($r=0,63$; $r=0,41$), дужином на рођењу ($r=0,63$; $r=0,42$), односом ова два параметра ($r=0,61$; $r=0,41$), индексом телесне масе ($r=0,54$; $r=0,35$) и пондералним индексом ($r=0,47$; $r=0,29$, ($p<0,01$).

Закључак Значајно више концентрације адипонектина у серуму утврђене су код *AGA* новорођенчади у поређењу са *SGA* децом. Лептин и адипонектин били су у позитивној корелацији с тежином на рођењу. Овакви налази указују на то да ови адипоцитокини играју улогу у регулацији раста фетуса.

Кључне речи: лептин; адипонектин; антропометријски параметри; новорођенчад

Примљен • Received: 20/02/2012 **Прихваћен • Accepted:** 03/07/2012