

## Investigating the Association of Cord Blood Resistin and Birth Weight in Term and Preterm Neonates

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### Abstract

#### Background

Resistin is reported as an antagonistic hormone of insulin and in the literature. Nowadays, importance of resistin is being more highlighted in the metabolism of mother and fetus during pregnancy. This study aimed to assess the level of resistin in the umbilical cord and blood sugar at birth and evaluate the association of resistin and neonatal birth weight.

#### Materials and Methods

This case-control study included 80 term and 80 preterm neonates. 5ml blood sample for measurement of resistin and glucose was obtained from cord blood. Neonatal birth weight was measured by standard method. Association of resistin and neonatal birth weight was evaluated.

#### Results

Cord blood resistin was  $27.1 \pm 32.2$  and  $21.9 \pm 9.8$  ng/ml in preterm and term neonates, respectively. There was not a significant differences between Resistin and birth weight ( $P > 0.05$ ). Blood sugar was  $78.1 \pm 23.6$  and  $79.5 \pm 19.8$  mg/dl in preterm and term neonates, respectively. Cord blood Resistin and blood sugar did not differ in term and preterm neonates ( $P = 0.158$  and  $P = 0.165$ , respectively).

#### Conclusion

The present study did not reveal any significant differences in resistin level between the term and preterm neonates. Blood glucose was nearly the same in both groups, and resistin did not show any significant correlation with birth weight.

**Key Words:** Birth weight, Preterm newborn, Resistin, Term newborn, Umbilical cord blood.

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## 1- INTRODUCTION

Preterm neonates defined as whom delivered before the completion of 37-week gestation, are one of the high risk groups for morbidity and mortality among infants worldwide. These morbidities could be due to the underdeveloped lung tissue, sepsis, necrotizing enterocolitis, intraventricular hemorrhage, periventricular leukomalacia, cerebral palsy, and retinopathy of prematurity (1). Despite advances in neonatal care, it still imposes a high burden on health services, families and caregivers (2). This is due to the fact that preterm birth is a multifactorial event, and it might be due to either maternal pathological conditions (placental abruption, placenta previa, severe preeclampsia, eclampsia, etc.); or fetal conditions (fetal distress, fetal growth restriction, fetal malformations, etc.). Therefore, studies to identify its causes or risk factors during pregnancy could help us to prevent its morbidities (3).

Some studies revealed that fetal growth has an association with insulin like growth factor 1 (IGF1) and insulin like growth factor 2 (IGF2), presenting in the fetal plasma since the 15<sup>th</sup> week of gestation (4, 5). Another important suggested fetal growth factor is adipokines which is secreted from adipose tissue (6, 7). They consist of hormone-like factors, cytokines and several chemokines which exert important functions on inflammation, immunity and adipogenesis (6, 8).

One of the most noted factors secreted from the adipose tissue is resistin. It is an antagonistic hormone of insulin and its function interferes with glucose homeostasis (9). This cysteine rich protein, discovered in 2001, is also secreted from the mononuclear cells of human body and seems to play a substantial role in fetal growth (9-12). Trophoblastic cells of the placenta seem to be the other source of resistin secretion (9). Resistin in

association with leptin and also their correlation with gestational age and anthropometric indices have been revealed in some investigations (13). In addition to resistin, leptin and adiponectin influence the insulin resistance, fetal growth and property of fat resources (14, 15). The positive correlation between resistin level and insulin resistance has been observed in some investigations (16). Also, a reduction in the insulin sensitivity has been reported more prevalently in small for gestational age (SGA) neonates (17). On the other hand, energy metabolism is altered during pregnancy and many of the placental hormones are suggested to have the maternal insulin-resistance effect by an unknown mechanism probably due to providing adequate energy and nutrient to the fetus (18). Resistin is supposed to play a role as a source of energy in metabolism of pregnant women (17).

Moreover, the positive correlation between gestational age and resistin level may only demonstrate more hormone production due to the greater mass of fat in the advanced stages of pregnancy (17). This adipokine is suggested to play a role in fetal development due to its high level demonstration in the umbilical blood cord in recent studies. However, its role in fat synthesis and glucose homeostasis is not yet firmly demonstrated (19-21). Resistin level in term and preterm neonates seems to show differences in some studies. For instance, higher levels of resistin in term infants compared with preterm neonates have been reported in Pak-Cheng et al.'s investigation (13). On the other hand, lower amounts of resistin was discovered in term neonates compared with preterm neonates in Martos-Moreno et al.'s study (22). This study aimed: to assess the level of Resistin and blood sugar in the umbilical blood cord at birth, and also to illustrate the probable association of Resistin in determining neonatal birth weight.

## 2- MATERIALS AND METHODS

### 2-1. Population

This case-control study has been conducted on 160 neonates delivered in Hafez hospital affiliated with Shiraz University of Medical Sciences from April 2015 to January 2016. Eighty term neonates were enrolled as the case group. Eighty age and sex matched pre-term neonates were selected randomly as the control group.

Exclusion criteria were: 1) Maternal diseases including kidney transplantation, systemic lupus erythematosus, Rheumatoid arthritis, chronic diabetic mellitus, chorioamnionitis, intra uterine infections, the history of medication use in recent pregnancy and prolonged rupture of membrane (PROM) and 2) Neonatal complications consisting of chromosomal disorders, asphyxia chromosome, congenital anomalies (microphthalmia, hepatosplenomegaly, and cataract).

### 2-2. Anthropometric measurements

Gestational age was verified by sonography, physical examination and new Ballard scoring in the first trimester. Anthropometric indices of the mothers and neonates were evaluated by an expert physician. Salter spring balance was applied for birth weight measurement. Head circumference of the neonates was measured by a fiber glass tape (CMS Instruments, London, UK). Harpenden infant stadiometer (CMS instruments, London, UK) was used to measure the birth length. The mother's height was measured while standing without shoes on the floor with a standard-mounted meter and rounded to the nearest 0.5 cm. A standard scale (Seca, Germany) was applied to measure the mothers' weight, while they were wearing a light cloth and no shoes. The following formula was used to demonstrate the Body Mass Index (BMI) calculation:

$$\text{BMI (Kg/m}^2\text{)} = \text{Weight (Kg)} / [\text{height (m)}]^2$$

### 2-3. Biochemical study

Blood samples 5 ml cord blood sample was collected from the umbilical vein after delivery of the infant. Resistin in the cord blood was measured by Bender Med systems (Vienna, Austria) and by using primary and secondary antibodies by standard enzyme-linked immunosorbent assay (ELISA) method. Neonatal blood sugar was assessed by ACCU-CHEK glucometer device (made in Germany).

### 2-4. Statistical analysis

SPSS.18 software was applied for analysis of data. Sample size was calculated according to previous report (17) and through this formula:

$$(Z_{1-\alpha/2} + Z_{1-\beta})^2 (S_1^2 + S_2^2) / (\mu_1 - \mu_2)^2$$

Where,  $\alpha = 0.01$ ,  $\beta = 0.05$  (power =  $1 - \beta = 0.95$ ),  $s_1 = 180$ ,  $s_2 = 537$  and  $\mu_1 - \mu_2 = 689$ . It was calculated 12; however, for increasing the power of significance we include 80 samples in each group. Qualitative variables between groups were compared by Chi-square test and Student T-test was employed for quantitative variables; P value less than 0.05 was considered as significant.

### 2-5. Ethical consideration

Ethics committee approval for this study was issued by ethic committee of Pediatric Health Research Center and Research Vice Chancellor of Shiraz University of Medical Sciences with grant no. 93.01.01.8997. Written informed consent form was signed by all the parents.

## 3- RESULTS

160 neonates including 80 preterm ones (as case group) and 80 term neonates (as control group) were enrolled in this study. The route of delivery was caesarean section in 13 neonates (16.2%) of control and 17 neonates (21%) of case group. Thirty nine neonates (48%) in the term group and 35 neonates (43%) in the

preterm group, were female (p=0.396). Mean gestational age was different between the two groups (P=0.001). A significant difference between the birth length was demonstrated between two groups according to definition (P=0.001). The mean maternal age was the same in the term and preterm groups (P=0.210).

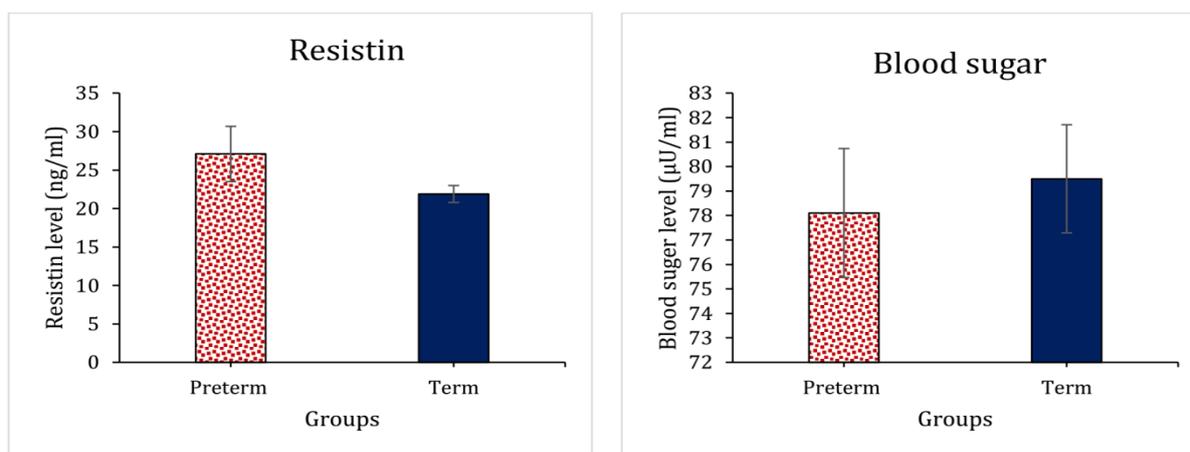
The mean maternal BMI was the same in both (P=0.147). **Table.1** summarized the general characteristics of neonates. Head circumferences in term group was more than the preterm ones (P<0.001). The mean cord blood sugar didn't differ significantly between the two groups (79.5 ± 19.8 in the term and 78.1 ± 23.6 in the preterm group) (P=0.165). The neonates' birth weight differed in both groups

(2663.6 ± 566.5 in the term group and 1513.9 ± 530.5 in the preterm group) (P<0.001). **Figure.1**, shows the mean cord blood parameters.

Results showed that there was not any significant association between the umbilical cord resistin level and type of delivery (P=0.567), and neonate's gender (P=0.984). We also didn't found any significant correlation between resistin and birth weight (P= 0.956). Also, there was not any significant association between blood sugar and birth weight (P=0.177). There was no significant association between cord blood resistin and blood sugar in term and preterm neonates (P =0.175, and P=0.675), respectively.

**Table-1:** General characteristics of neonates

Characteristics	Preterm neonates (n=80)	Term neonates (n=80)	P- value
<b>Route of delivery</b>			
Caesarean section	17 (21%)	13 (16.2%)	0.476
Normal Vaginal Delivery	63 (79%)	67 (83.8%)	0.468
<b>Gender</b>			
Girls	35 (43%)	39 (48%)	0.396
Boys	46(57%)	42 (52%)	0.401
Gestational age (week)	32.0±3.0	38.0±1.1	<0.001
Birth length (cm)	40.5±6.1	47.9±3.4	<0.001
Head circumferences (cm)	28.9±3.7	33.3±1.8	<0.001
Birth weight (g)	1513±530	2663±566	<0.001
Maternal age (years)	29.3±5.4	28.0±5.1	0.111
Maternal BMI (kg/cm2)	30.1±5.5	29.0±4.2	0.143
Resistin (ng/ml)	27.1±32.2	21.9±9.8	0.175
Blood sugar (mg/dl)	78.1±23.6	79.5±19.8	0.675



**Fig.1:** Resistin and sugar in the blood umbilical cord (data are presented as mean and standard error)

#### 4- DISCUSSION

The present study did not reveal any significant differences in Resistin level between the term and preterm neonates. Blood glucose was nearly the same in both groups, and Resistin did not show any significant correlation with birth weight.

On the contrary, a significant positive correlation between the resistin level and anthropometric indices at birth (gestational age and birth weight) was observed in the evaluation of Pak-Cheng NG et al. conducted on the two groups of term and preterm neonates. Unlike our study, higher plasma Resistin level in normal vaginal delivery infants compared with neonates who were born by caesarean section was observed in the mentioned investigation (13). On the other hand, in the study performed by Davarifarid et al., resistin level showed a reverse correlation with birth weight in term new-borns and its amounts did not show any significant differences between normal vaginal delivery (NVD) and cesarean section (C-S) neonates (17).

Maturity and birth weight might have some different effect on cord blood resistin (even opposite effects) that could result in controversies in previous reports. We propose that future studies could analysis the level of resistin specifically in SGA-term, Appropriate for gestational age (AGA)- term to find out the independent effect of resistin on birth weight. Although the mechanism by which insulin resistance appears during pregnancy is still unknown, placental hormones are supposed to cause insulin resistance (23). resistin is one of the placental hormones which seemingly has a substantial role in the homeostasis of pregnancy and fetal development. However, there is insufficient data revealing the role of resistin in this regard (17). Similarly, the umbilical serum resistin level demonstrated an inverse correlation with neonatal birth weight in the Cho et al.'s and Wang et al.'s studies,

thus suggesting the role of resistin in determining the neonate's birth weight (24, 25). The level of resistin has not shown a definitive pattern in term and preterm neonates until now. Lower levels of resistin have been observed in preterm neonates compared with term newborns in the Pak-Cheng et al.'s investigation (13, 26). On the contrary, higher levels of resistin were found in the preterm newborns in the study of Martos-Moreno et al. compared with term neonates (22).

##### 4-1. Limitations of the study

Lack of data on preterm neonates and subsequent resistin measurement in neonatal period was one of our limitations. In addition, the roles of resistin in inflammation and its impression on glucose hemostasis and fetal growth affected our study results. So, subsequent studies with less limitations and larger sample size may reveal more obvious results in the field of resistin's association with fetal growth.

#### 5. CONCLUSION

The present study did not reveal any significant differences in resistin level between the term and preterm neonates. Blood glucose was nearly the same in both groups, and resistin did not show any significant correlation with birth weight. Future studies with larger sample size and considering small for gestational infants could help us to understand the role of resistin in neonatal growth.

#### 6- CONFLICT OF INTEREST

The authors had not any financial or personal relationships with other people or organizations during the study. So there was no conflict of interests in this article.

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