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Effects of delivery on maternal & neonatal irisin levels in normal and preeclamptic pregnant women

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ABSTRACT

Study objective: The aim of this work was to measure the irisin levels in maternal and umbilical cord serums at cesarean section and vaginal delivery.
Study design: This is a case-control study conducted at the Obstetric Department of the Mansoura University Hospital, Mansoura University, Egypt.
Material and methods: The 150 nulliparous cases were divided into three groups.
Main outcome measure: Serum irisin concentrations were assayed by enzyme-linked immunosorbent assay (ELISA) method.
Statistical analysis: Unpaired *t*-test and correlation were done by using the Statistical Package for Social Scientists (SPSS).
Results: The maternal irisin levels in cases with mild preeclampsia were found to be significantly lower than that of the normal cases. In cases with mild preeclampsia, the maternal irisin levels early in labor for vaginal deliveries were significantly higher than that during cesarean section. The maternal irisin levels after vaginal deliveries were significantly higher than the levels early in labor.

The maternal serum irisin was a significantly correlated with the duration of the first stage. The umbilical cord serum irisin levels were significantly correlated with the neonatal weight and with the duration of the first stage of labor.
Major conclusion: Labor is a strong stimulus to the release of irisin into the maternal and fetal circulations. Neonatal serum irisin levels are positively correlated with the birth weight and with the duration of the first stage. The neonatal birth weight and the duration of the first stage of labor are positively correlated with the umbilical cord serum irisin levels.

1. Introduction

Bostrom and colleagues [1] identified a new peptide that comes from skeletal muscle to other parts of the body, which they named irisin, capable of promoting brown adipose tissue differentiation [1]. Irisin is encoded by the fibronectin type III domain-containing protein 5 (FNDC5) precursor gene and its' expression is stimulated in conditions of muscle activity, the extracellular N-terminal part of FNDC5 is supposed to be cleaved and released as irisin [1].

Irisin staining, in male rats, revealed that irisin was associated with secretory organs such as adipose tissue, testis, pancreatic islets, liver, spleen, stomach, brain, bone, placenta, and ovary. Also, cardiac tissues and fetal skeletal muscle cells produce irisin [2].

Garcés et al. [3] found that irisin precursor FNDC5 is expressed in human placenta and its serum levels were higher during the entire pregnancy when compared to non-pregnant women [3]. They suggested that the increased maternal serum irisin during pregnancy may be explained by placental production, or it may be a compensatory-response caused by an irisin resistance during gestation, as already established for leptin [4] or insulin [5].

One of the maternal adaptations during pregnancy involves temperature regulation, with two predominant sources of heat production: an increased basal metabolic rate and the energy released by the fetus and utero-placental unit [6]. A lower temperature in pregnant women at the end of pregnancy may be due to decreased irisin sensitivity in late pregnancy in spite of high irisin levels [7]. It was reported by Garcés et al. [3] that irisin levels were higher in eumenorrheic women in the luteal than in the follicular phase, suggesting that irisin might play a key role in the regulation of the core body temperature during the menstrual cycle.

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Studies in obese patients found that the circulating irisin is positively correlated with insulin sensitivity [8], insulin levels and with Homeostatic Model Assessment-Insulin Resistance (HOMA-IR) [9].

Labor is considered as an extreme degree of stress resulting in an endocrinal response which might be involved in the mechanism of maternal and fetal adaptation to such a stressful condition [10].

The purpose of the article was to determine the irisin levels in mild and in severe preeclampsia, as well as the effects of vaginal delivery and cesarean section (C/S) on the levels of irisin in maternal plasma and umbilical cord plasma in normotensive pregnant cases and in cases with preeclampsia.

2. Material and methods

2.1. Participants

In this case-control study, 150 nulliparous cases were recruited from the Obstetric Department of the Mansoura University Hospital, Mansoura, Egypt, during the period between September 2015 and April 2017, in accordance with the inclusion and exclusion criteria.

The study was approved by the IRB committee of Faculty of Medicine, Mansoura University, Egypt [Code number; R/15.08.62, Date: 7/9/2015]. Informed written consent was taken from the participants.

2.1.1. Inclusion criteria

The cases had no history of hypertension before pregnancy and had documented normal blood pressure in the first trimester.

Preeclampsia (PE) is defined as de novo hypertension (> 140/90 mm Hg) and proteinuria (> 0.3 g per 24 h) after 20 weeks of gestation [11].

2.1.2. Exclusion criteria

All pregnant females with chronic hypertension, heart disease, thyroid disorders, diabetes mellitus, and multi-fetal gestation.

The cases were subdivided into three groups:

Group 1: included 50 nulliparous cases with normal pregnancies near term for vaginal delivery after spontaneous onset of labor.
Group- 2: included 50 nulliparous cases with mild preeclampsia for vaginal deliveries after spontaneous onset of labor.
Group-3: included 50 nulliparous cases with mild preeclampsia for elective cesarean section.

Cases in groups 1 & 2 were early selected in cases attending for vaginal delivery with spontaneous onset of labor.

2.2. Sampling

In cases attending for delivery, three ml of maternal venous blood were withdrawn at the beginning of the first stage of labor (as a control sample) and the second maternal blood sample was withdrawn after fetal delivery. In cases performing cesarean section, the control sample was taken before performing the operation (as a control sample), and the second blood sample was withdrawn after fetal delivery. In all cases, three ml of umbilical cord blood were withdrawn just after delivery of the fetus.

All samples were collected in a vacutainer tube with gel, and then the serum was stored at -80 °C until the time of assay.

2.3. Methods of assay

Serum irisin concentrations were measured with enzyme-linked immunosorbent assay (ELISA) by using commercial Human Irisin ELISA Kits supplied by BioVendor, according to the method recommended by the manufacturer.

2.3.1. Principle of irisin assay

This assay is a specific competitive Enzyme Linked-Immuno-Sorbent Assay (ELIZA) for quantitative determination of irisin in human biological fluids. A polyclonal antibody recognizing native irisin reacts with a series of predetermined recombinant irisin standard proteins n the irisin coated plate. Their relative reactivity is plotted with that of the standard proteins. The color was measured at OD 450 in an ELIZA reader within 30 min. Generate the standard curve by plotting the average absorbance obtained by each standard concentration on vertical (Y) axis vs the corresponding irisin concentration on the horizontal axis. Calculate the irisin concentrations by interpolation of the regression curve formula. If the test samples were diluted, multiply the interpolated values by the dilution factor to calculate the concentration of irisin in the sample.

2.3.2. Sensitivity

The lowest level of irisin that can be detected by this assay is 1 ng/ml.

The assay range is 1 ng/ml to 5000 ng/ml.

2.4. Statistical analysis

Means and standard deviations were used to describe data. Unpaired *t*-test was used to test for significant change in quantitative data between two groups. Pearson product moment correlation was used to test for the linear relationship between quantitative variables. P value was considered significant if less than 0.05. Statistical Package for Social Scientists (SPSS) for Windows 7 (SPSS Inc., Chicago, IL, USA) was used to analyze the results.

3. Results

Table 1 shows the mean arterial blood pressure (MABP), duration of first stage & second stage of labor, and cervical dilatation of the studied groups.

Table 2 shows the levels of maternal serum irisin early in labor and after delivery.

Table 3 represents the value of significance (P value) on comparing the irisin levels during labor and after delivery in-between groups.

On comparing the irisin levels during vaginal deliveries, the mean of maternal serum irisin level in group 1 was significantly higher than the level in group 2 at the start of labor for vaginal deliveries (P = .000).

The maternal serum irisin levels after vaginal delivery were significantly higher than the levels during labor, in both normal pregnancy (P = .008) and mild preeclamptic cases (P = .000).

On comparing the irisin levels at the start of labor for vaginal deliveries with that before performing cesarean section (CS), the levels of mild preeclampsia (PE) during early vaginal deliveries were significantly higher than the levels in mild PE during CS [P = .004].

Table 1
Clinical parameters of the studied groups (mean ± SD).

Affecting Factors		Group 1	Group 2	Group 3
MABP (mm Hg)	*Mean*	**92.1**	**106.89**	**106.51**
	± *SD*	± 1.23	± 1.7	± 1.49
Cervical dilatation (cm)	*Mean*	10	10	–
	± *SD*	0	0	–
1st stage duration (h)	*Mean*	14.4	14.36	–
	± *SD*	± 1.38	± 1.33	–
2nd stage duration (min)	*Mean*	29.67	28.27	–
	± *SD*	± 6.29	± 6.11	–
Neonatal birth weight (g)	*Mean*	3403.3	3330.0	3368.5
	± *SD*	182.39	111.11	136.84

Bold values denotes the mean values.