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Leptin/SFRP5 ratio as a potential predictor of postpartum weight retention. A prospective pilot study

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ABSTRACT

Excessive gestational weight gain (EGWG) and failure to lose weight within 6 months from delivery are important and identifiable predictors of the long-term obesity. The aim of the study was to verify clinical usefulness of several substances that had been proved to play a significant role in metabolism and body mass regulation, *i.e.*, leptin, ghrelin, fatty acid binding protein 4 (FABP4), secreted frizzled-related protein 5 (SFRP5), and vaspin, in relation to certain laboratory results, body composition and hydration status of females in the early postpartum period. The main goal was to determine a potential marker, which assessed as early as 48 hours after delivery, could predict serious difficulties in achieving pre pregnancy body mass of women with EGWG six months afterwards. The same inclusion criteria applied to the study group (women with EGWG) as well as the control group (women with appropriate body mass gain in pregnancy). These included normal pre-pregnancy BMI, absence of any diseases prior, during pregnancy and after delivery, 6-month long breastfeeding. Postpartum weight retention (PPWR) depended positively on gestational weight gain as well as the leptin/SFRP5 ratio assessed 48 hours after delivery. Both obstetricians and midwives should pay special attention to proper nutrition of pregnant women. The assessment of biophysical and biochemical parameters in the early postpartum

period, when the mothers are usually hospitalized, seems to allow to predict the risk of greater body weight retention. Future research will help to determine to what extent the circulating concentrations of leptin and SFRP5 in the early puerperium are important for prediction of maternal PPWR and obesity.

Key words: adipokines; leptin; secreted frizzled-related protein 5; excessive gestational weight gain; bioelectrical impedance analysis; postpartum weight retention

INTRODUCTION

Pregnancy is likely to result in overweight and obesity of many females in later life. Postpartum weight retention (PPWR) is a well-known risk factor of cardiovascular diseases and metabolic disorders such as diabetes [1]. Nowadays more and more emphasis are put on new medical challenges dealing with pregnancy such as excessive gestational weight gain (EGWG) and PPWR. This is undoubtedly due to the fact that these conditions have been confirmed to affect health of both mothers and their children.

According to Farpour-Lambert and coauthors [2] women who gain too much weight in pregnancy were found to be more prone to overweight and obesity as demonstrated at 21 years from delivery — odds 2.15 (95% CI: 1.64–2.82) and 4.49 (95% CI; 3.42–5.89), respectively. A similar observation with regard to offspring obesity was also reported [2]. Excess weight gain and failure to lose weight by 6 months postpartum are important and identifiable predictors of the long-term obesity. Breastfeeding and exercise may be beneficial to control long-term weight.

The pro-inflammatory biomolecules secreted by the adipose tissue include, among others, leptin, tumor necrosis factor (TNF), interleukin 6 (IL-6), resistin, retinol binding protein 4 (RBP4) and fatty acid binding protein 4 (FABP4) [3–6]. In addition to numerous pro-inflammatory adipokines, the adipose tissue also secretes a smaller number of anti-inflammatory factors. These factors include adiponectin, which has been subjected to painstaking investigation, as well as secreted frizzled-related protein 5 (SFRP5), which has been recently identified as an adipokine with anti-inflammatory properties [3, 4, 7]. Any imbalance between the two types of adipokines brings about an abnormal expansion of the adipose tissue, the leading cause of obesity, and triggers local and systemic inflammation [3, 4]. Whilst the adipose tissue depots differ from one another, depending on their relative levels of adipokine production, obesity will generally favor the production of pro-inflammatory

adipokines regardless of the depot site location [4]. Excessive adiposity and adipocyte dysfunction are strongly associated with metabolic diseases such as obesity and type 2 diabetes mellitus (T2DM) [3].

Leptin is widely engaged in the energy homeostasis [8]. It has been shown to play an important role in the pathogenesis of atherosclerosis, cardiovascular disease, inflammation, obesity and T2DM. The biological role of leptin is to regulate energy homeostasis, insulin resistance and lipid metabolism [9]. It regulates blood glucose via the action on peripheral target tissues in addition to the effect on the central nervous system. Its concentration depends on the quantity of body fat whereas the role that it plays in the central nervous system significantly affects food intake as demonstrated by Izquierdo et al. in obese children with hyperphagia who were deprived of leptin [8]. For instance, leptin accommodates the blood glucose by downregulating the cytokines which promote lipogenesis, altering the glucagon concentration and activating the adenosine monophosphate-activated protein kinase (AMPK) pathway in hepatocytes. Moreover, it has been shown that a high leptin standard indicates a succedent development of T2DM [9]. Taking into consideration the fact that leptin is seriously involved in the pathogenesis of obesity and effectively suppresses appetite, still much research focuses on this attractive and promising molecule. Obese subjects have in fact the increased concentrations of leptin and yet they do not lose weight, which reflects the metabolic state of certain inadequate sensitivity to this hormone. Accordingly, treatments targeting the leptin resistance could potentially result in improved control of excessive body mass gain [8].

Objectives

For the abovementioned reasons it appears highly probable that EGWG could result in both maternal and fetal programming, which will potentially affect health of a fetus and its mother but also determine to a certain extent future medical problems of other children born by such predisposed females. Bearing in mind the potential for some disturbances, including changes in the body composition and hydration status, we intended to implement into the clinical use post-partum serum concentrations of leptin, ghrelin, FABP4, SFRP5, and vaspin as factors of proven or highly probable significance to metabolism and body mass regulation.

The aim of this research was to investigate a potential novel early puerperium biomarker (or an index based on two other parameters) for the prediction and the early

diagnosis of failure to recover the pre-pregnancy body mass within 6 months from delivery in women, especially with EGWG.

MATERIAL AND METHODS

The studied group comprised Caucasian women in a singleton term pregnancy (after 37 weeks of gestation) and were hospitalized at the Chair and Department of Obstetrics and Perinatology, at the Medical University of Lublin, Poland. The subjects of the study were divided into two groups: Group I consisted of 28 healthy controls, i.e., women free of metabolic disorders who had three normal results of 2-hour-75 gram-oral glucose tolerance test (OGTT) at 24–28 weeks of gestation. The pregnant women in this group had no comorbidities, were given merely vitamin-iron supplements and exhibited normal values of pre-pregnancy body mass index (BMI) (i.e., between 18.5 and 24.99 kg/m^2), normal gestational weight gain (*i.e.*, 11.5–16 kg) [10, 11] and proper gestational age.

Group II consisted of 38 patients with EGWG with normal pre-pregnancy BMI (*i.e.*, between 18.5 and 24.99 kg/m^2), three normal results of the OGTT at 24-26 weeks of gestation and gestational weight gain of at least 20 kg.

Multiparas, women with chronic infectious diseases or abnormal laboratory results (*e.g.*, the complete blood count, urine test, creatinine, glomerular filtration rate (GFR) findings) were excluded from the study. Other exclusion criteria encompassed metabolic disorders (such as polycystic ovarian syndrome; except those listed in the inclusion criteria for the studied groups), mental illness, cancer, liver diseases, cardiovascular disorders, fetal malformation, premature membrane rupture, intrauterine growth retardation, the presence of metallic prostheses, and pacemakers or cardioverter-defibrillators.

In the early postpartum period (*i.e.*, 48 hours after delivery) and following a 6-hour fasting, anthropometric measurements as well as sampling performed. The bioelectrical impedance analysis (BIA) method and body composition monitor (BCM) (Fresenius Medical Care) were used to evaluate the maternal body composition and hydration status, whereas the serum levels of albumin, hemoglobin A1c and lipid profile were measured by a certified laboratory. Following centrifugation, all of the serum specimens were stored at –80 °C. The concentrations of SFRP5, ghrelin (Wuhan EIAab Science Co., Wuhan, China), leptin, FABP4 (R and D Systems, Inc., Minneapolis, MN, USA), and vaspin (MyBioSource.com, San Diego, CA, USA) in the studied materials were determined with the use of commercially available kits and remained in compliance with the manufacturer’s instructions via traditional

enzyme-linked immunosorbent assay (ELISA). The procedure was duplicated for each patient.

In the second part of this study, based on a telephone survey conducted 6 months after delivery, we obtained information about our patients` body weight. Five women out of 66 (*i.e.*, 2 from the 28 EGWG group and 3 from the 38 healthy controls` group) were excluded from further analyses due to:

— the duration of breastfeeding was shorter than 6 months (3 cases),

— treatment of postpartum depression (1 case),

— unsuccessful contact to obtain six-month-postpartum data (1 case).

PPWR was calculated by subtracting the maternal pre-pregnancy weight from the six-month postpartum weight [12].

Having received information about the study protocol, each study subject gave a written consent to participate in the study.

Stages of the study methodology was presented in Figure 1.

All of the values were reported as the median (interquartile range 25–75%). The differences between the studied groups were tested for significance using the Mann–Whitney U test. The Spearman's coefficient test was used for the correlation analyses. The multiple linear regression model was used to adjust the covariates and examine the associations between PPWR and the selected maternal biophysical and biochemical parameters (i.e., gestational weight gain, leptin/SFRP5 ratio, fat tissue index, the serum concentrations of ghrelin and vaspin).

All of the analyses were performed using the Statistical Package for the Social Sciences software (version 19; SPSS Inc., Chicago, IL, USA). A p value of < 0.05 was considered statistically significant.

RESULTS

We observed significant differences in several variables assessed 48 hours after delivery between the healthy study subjects and EGWG women (Tab. 1). We found significant differences, *inter alia*, in the serum concentrations of SFRP5 as well as vaspin in these two study groups; significantly lower serum SFRP5 and vaspin levels were observed in the EGWG group, *i.e.*, 2.7 ng/mL vs 3.1 ng/mL and 670.4 pg/mL vs 871.5 pg/mL, respectively (Tab. 1).

The greatest statistical significance (*i.e.*, p = 0.000002) was observed in case of the ratio of serum leptin levels to those of SFRP5 (*i.e.*, the leptin/SFRP5 ratio) in the EGWG women when compared to the healthy subjects (Fig. 2).
We noticed that PPWR was significantly higher in the EGWG group than in the women with normal gestational weight gain [10 kg (8–12) vs 4 kg (0–6)] (Fig. 3).

Correlation coefficients between PPWR at 6 months after delivery and clinical as well as laboratory parameters in the control and EGWG groups are presented in Table 2. We observed that PPWR correlated positively with gestational weight gain, BMI values at delivery, BMI gain in the period from pre-pregnancy to 48 h after delivery (*i.e.*, BMI), fat tissue index, and leptin/SFRP5 ratio in the EGWG group as well as in all subjects (Tab. 2). The scatterplot diagram with a positive correlation between the leptin/SFRP5 ratio and PPWR in all subjects (*i.e.*, from the control and healthy groups) is shown in Figure 4. A negative correlation occurred between PPWR and the serum SFRP5 level both in the EGWG and all women (Tab. 2).

In the multiple linear regression models, after adjustments for gestational weight gain, leptin/SFRP5 ratio, fat tissue index, the serum concentrations of ghrelin and vaspin, PPWR depended positively on the gestational weight gain and the leptin/SFRP5 ratio (Tab. 3).

DISCUSSION

Nowadays, pre-pregnancy obesity and EGWG are perceived as independent risk factors which account for pregnant and postpartum complications both in the mother and child [13, 14], thereby increasing their risk of developing chronic diseases later in life. PPWR defined as a failure to return to pre-pregnancy weight within 6 months following delivery is associated with the long-term obesity and adverse health outcomes [15]. The cause of PPWR is multifaceted; however, it has been proposed that one potential pathway is through EGWG [16, 17].

The assessment of ratio of concentrations of different biologically active substances has a well-documented significant impact in many clinical situations. The authors predominantly tend to concentrate on the proportion of serum concentrations of leptin and adiponectin at different stages of life with regard to body mass, BMI change or the increased risk of certain metabolic disorders [18, 19]. In the available literature some emphasis is also placed on the leptin/ghrelin index [20]. There is some evidence to suggest different patterns of

the central response to adipokine signaling depending on the weight rebound. The research carried out by Crujeiras et al. [21] pointed out that leptin and ghrelin concentrations were not identical in subjects who differently responded to intentional body mass reduction. This observation is in line with some other reports regarding leptin and ghrelin concentrations in normal weight individuals and those obese ones. It seems that weight regain may be associated with some central or peripheral resistance to these both hormones [21].

BIA is used to assess the body composition and hydration status. This technique represents a non-invasive, reliable, and fast clinical approach, which is well tolerated by patients. A segmental impedance measurement might be advantageous in pregnant women, particularly in late pregnancy. It seems that BIA has a better prognostic potential for gestational and post-partum outcomes than body mass index. The BIA method can be successfully used to study the effect of excessive gestational weight gain in pregnancy on the development of obstetric complications [22].

We have concentrated on leptin and SFRP5 as potential biomarkers for the prediction and early diagnosis of PPWR. SFRP5 has been suggested a promising novel adipokine to be used in calculations with leptin [23, 24]. In our previous research [23] we pointed out that SFR5/leptin ratio could be successfully used as a metabolic index in women diagnosed with gestational diabetes mellitus in the early puerperium. In the present study, however, our team focused on the attempt to identify the leptin/SFRP5 ratio, which would reflect and predict the risk of PPWR at 6 months following the delivery. This parameter was calculated on the basis of the laboratory findings made 48 hours after delivery, which is when the placenta — representing an endocrine organ — has no further effect on the maternal metabolism. On the other hand, such an assessment to be performed two days after birth, which is usually before discharge, can be effectively and safely made in hospital. Puerperal women after delivery, even a physiological one, are closely monitored and accordingly spend a few days in the ward entering the early postpartum period.

It was not without a reason why SFRP5 was chosen by us out of several new biomolecules to evaluate concentrations in the serum of women with EGWG in the early postpartum period in comparison with the healthy mothers. SFRP5 is a recently defined adipokine with highly probable anti-inflammatory features, which appears to protect against insulin resistance, obesity, hepatic steatosis, fibrosis, and metabolic syndrome [3, 4, 25]. The secreted frizzled-related protein (SFRP) family consists of five identified secreted glycoproteins. SFRPs have been identified as negative modulators of the wingless-type MMTV integration site family member (Wnt) signaling transduction pathway which is known

to be involved in pancreatic development, β-cell proliferation, adiposity, insulin resistance and inflammation [3, 7, 26, 27]. As functional antagonists, both the Wnt family and SFRPs, control multiple biological processes, including embryonic development, inflammation and immunity [28]. Additionally, Wnt signaling is engaged in placental vascularization and angiogenesis as well as in extraembryonic development [25]. Furthermore, Canivell et al. [29] reported significantly increased levels of the serum SFRP5 in the patients previously treated for T2DM who presented optimal glycemic control [29]. It appears that the circulating SFRP5 concentrations may depend on the metabolic disease severity and the effectiveness of treatment. Nevertheless, Schulte et al. [24] showed that circulating SFRP5 levels were not influenced by obesity but they increased with caloric restriction in very obese individuals. Ouchi et al. [7] also reported that after being put on a high-fat diet, genetically engineered SFRP5-lacking mice showed greater insulin resistance and adipose tissue inflammation due to an unrestrained wingless type MMTV integration site family member 5a (Wnt5a) activity. Interestingly, overexpression of SFRP5 in the adipocytes of these animals blocked the Wnt5a activity so that an inflammatory and insulin-resistant state could have been prevented [7]. As a result, the authors concluded that in the setting of an obese animal model, the SFRP5 secretion by adipocytes exerts salutary effects on metabolic dysfunction with anti-inflammatory properties within the adipose tissue [7].

There is very limited data regarding the SFRP5 concentrations in pregnant and puerperal women [23, 25, 30]. Our previous research revealed that in the gestational diabetes mellitus (GDM) group serum and urine SFRP5 levels correlated positively [30]. In the present study significant differences were found in the serum SFRP5 concentrations between the healthy study subjects and EGWG women. SFRP5 levels were decreased in the serum of the EGWG mothers at 48 hours after delivery. This vantage point seems to be important for understanding the current data and future findings regarding the serum SFRP5 in pregnant, delivering and puerperal women. Pregnancy is by necessity a period of relative metabolic plasticity during which physiological changes need to occur in order for the body to accommodate shifting nutritional needs. These adaptations are achieved through a variety of mechanisms, including hormonal, metabolic and immunological alterations. Meanwhile, due to the normal body mass and BMIs before pregnancy and with normal OGTT results at 24–26 weeks of pregnancy, the patients in the EGWG group were not under accurate dietary control throughout their pregnancy. EGWG is currently considered the first step in the vicious circle and is arguably the most perilous implication of pregnancy affecting the future health of the mother [17]. Nowadays, many authors emphasize that EGWG is closely associated with the

post-partum obesity [15, 31, 32]. It was observed that a high-fat diet during gestation causes the long-term post-partum obesity due to adverse programming of long-term post-partum energy metabolism by epigenetically reducing estrogen signaling in the white and brown adipose tissue in mice [32].

However, we reveal negative correlations between the serum SFRP5 levels at 48 hours after delivery and the values of PPWR in the EGWG mothers as well as in all subjects. Moreover, we were also able to point out that the PPWR was positively dependent on the serum leptin/SFRP5 ratio. Each 0.021 of increase in the leptin/SFRP5 ratio on the second day after delivery was associated with a 1-kilogram increase in the PPWR value 6 months after delivery. Interestingly, we found that the PPWR was also directly dependent on the gestational weight gain. An increase in gestational weight gain by 0.912 kilograms was associated with an increase in the PPWR value by 1 kilogram 6 months after delivery.

On the basis of the obtained results, we conclude that calculation of gestational weight gain and the ratio of serum concentrations of leptin and SFRP5 seem indeed to be very useful clinical parameters. They enable the early diagnosis and prediction of the mentioned maternal malnutrition in later life and in a majority of cases this assessment could be performed prior to discharge from hospital.

CONCLUSIONS

Both obstetricians and midwives should pay special attention to proper nutrition of pregnant women. Their education regarding the optimal gestational weight gain during the first pregnancy check-ups will pay dividends in the maternal programming for future diseases, such as dyslipidemia, insulin resistance, T2DM, overweight, obesity and metabolic syndrome.

The assessment of biophysical and biochemical parameters (*i.e.*, serum leptin and SFRP5 concentrations as well as gestational weight gain) in the early postpartum period, when the mothers are usually hospitalized, seems to allow to predict the risk of greater body weight retention. The rate of weight loss after delivery as well as return to pre-pregnancy BMI values seem to be important for the maternal future health and prevention of metabolic complications. Excessive weight gain during pregnancy is the primary factor for PPWR.

The calculation of leptin/SFRP5 ratio based on the quotient formula of serum concentrations of these two differently metabolically oriented adipokines appears a very useful clinical parameter. The early diagnosis of the anticipated problem with restoring the pre-pregnancy body mass can be initiated soon after delivery in hospital prior to discharge.

Undoubtedly, future research is required in order to confirm whether serum concentrations of leptin and SFRP5 in the early puerperium can indeed effectively predict maternal PPWR and obesity.

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Institutional review board statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Bioethics Committee of the Medical University of Lublin (no. KE-0254/221/2015 [25th June, 2015] and no. KE-0254/348/2016 [15th December, 2016]).

Conflicts of interest

All authors declare no conflict of interest.

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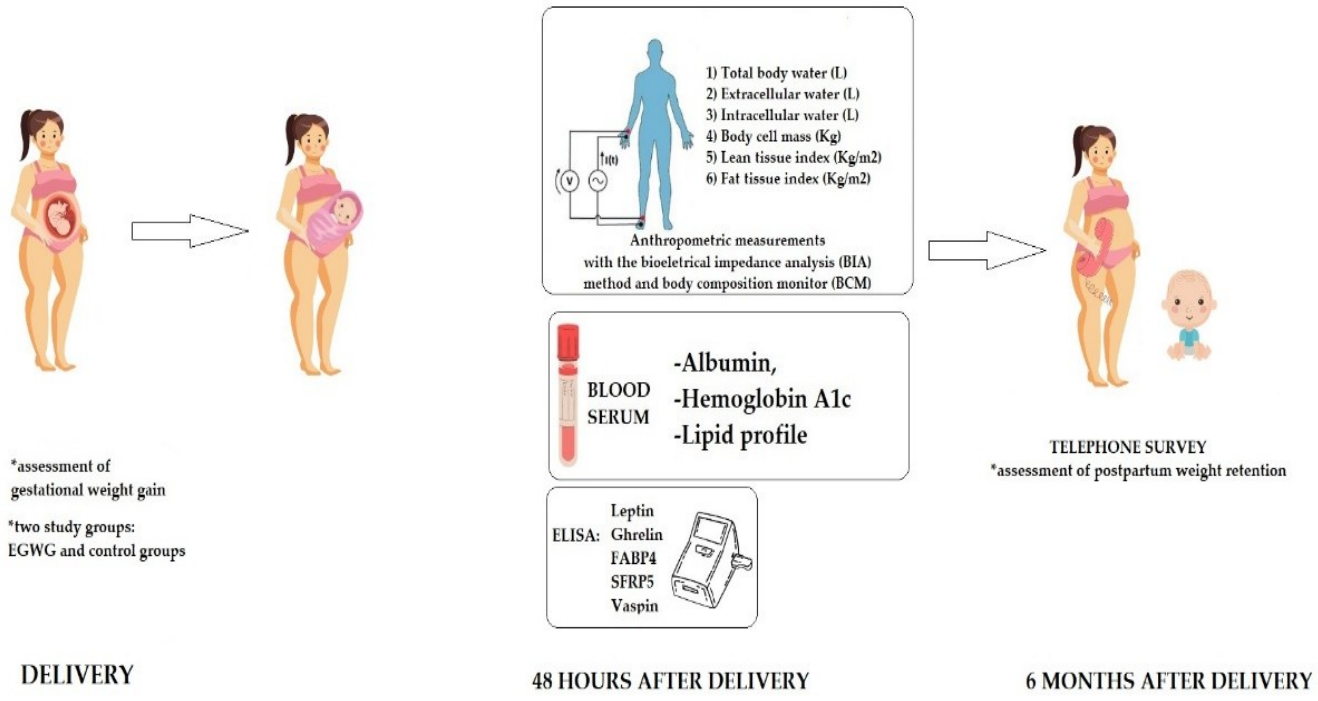

Figure 1. Stages of the study methodology

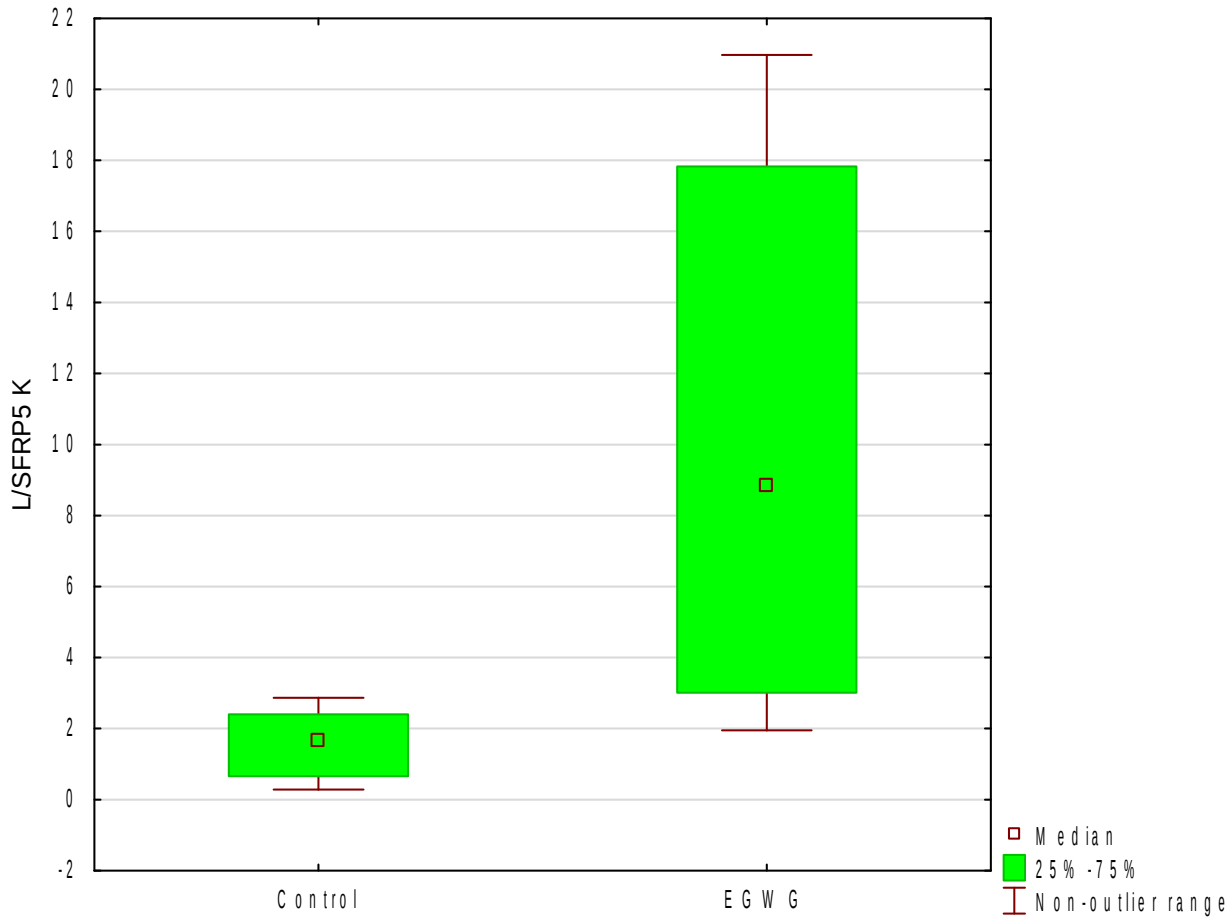

Figure 2. Ratio of serum leptin and SFRP5 concentrations in the control and excessive gestational weight gain (EGWG) groups, *** $p < 0.001$; —median; boxes — 25th to 75th percentiles; whiskers — non-outlier range

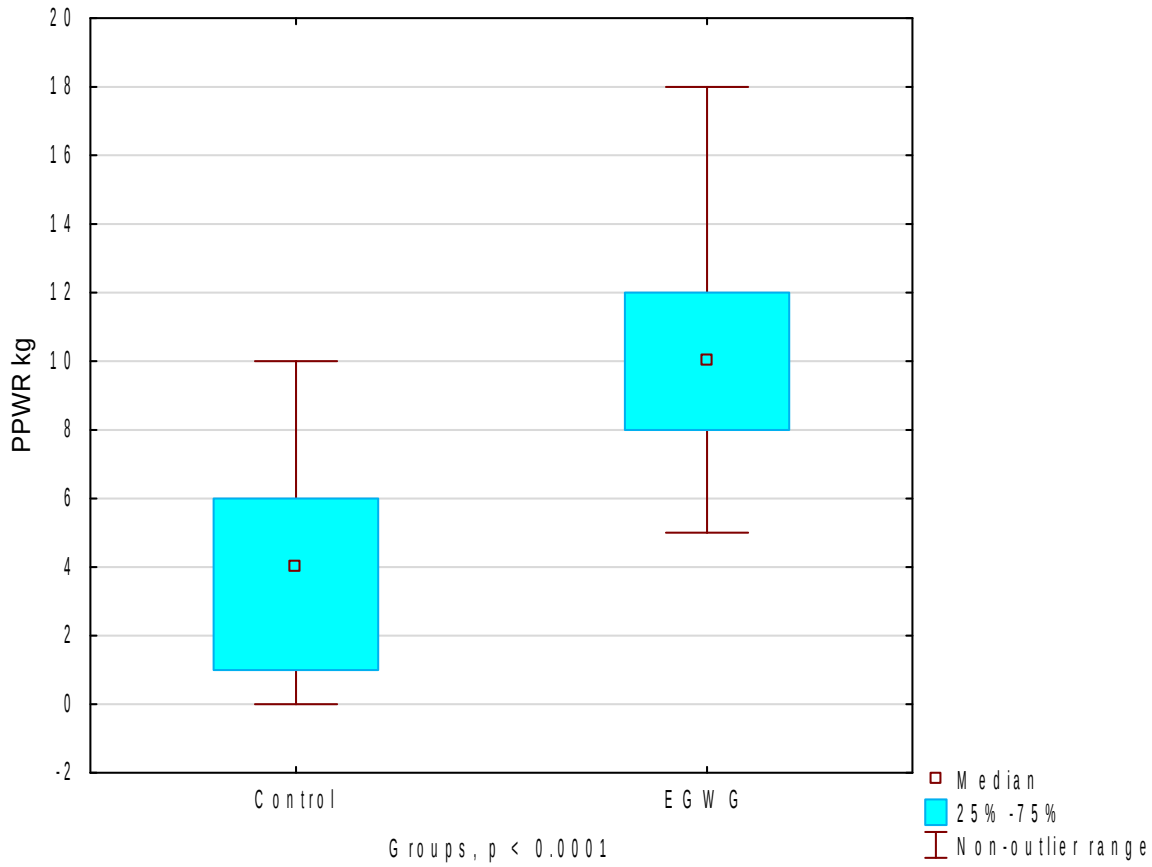

Figure 3. The PPWR in the control and EGWG groups

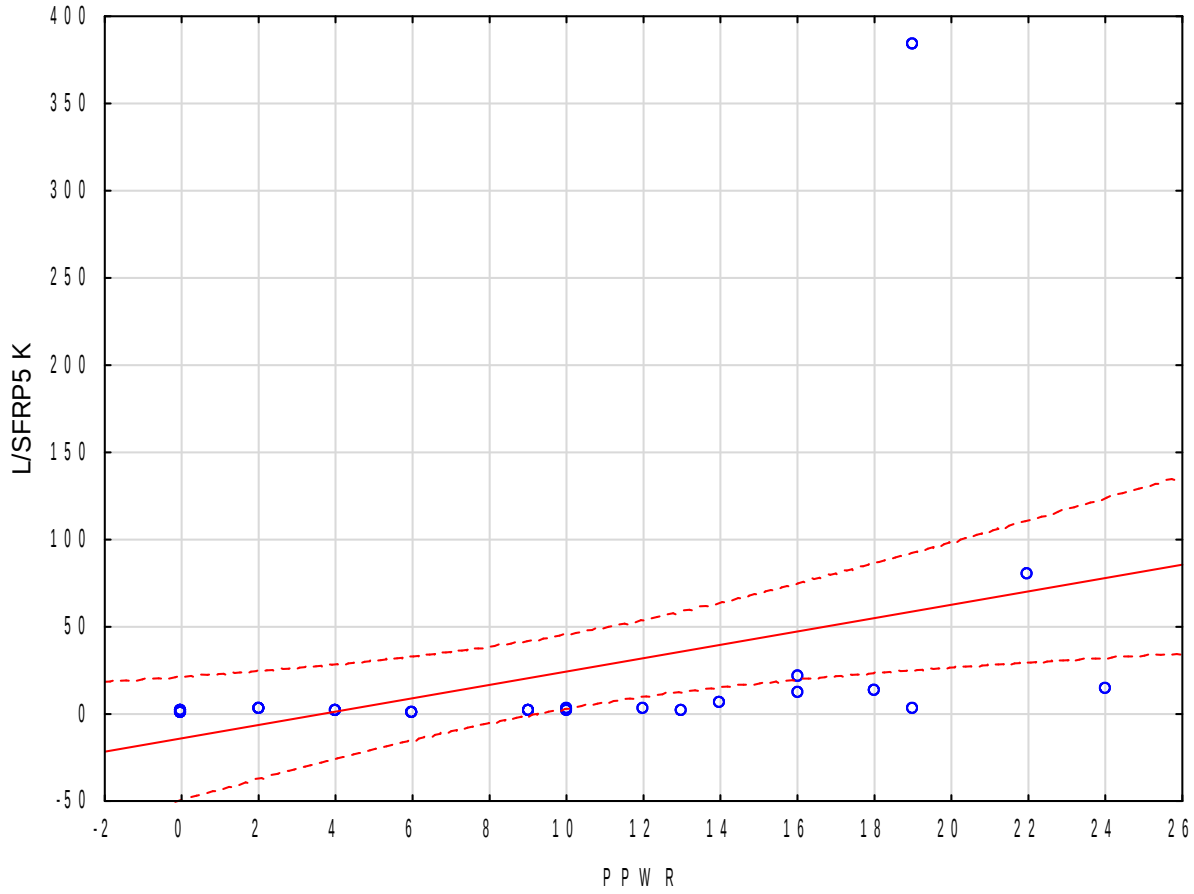

Figure 4. A scatterplot diagram showing a positive correlation between the ratio of serum leptin and SFRP5 concentrations and PPWR in all subjects (*i.e.*, from the control and healthy groups)

Table 1. Comparison of characteristics of the study subjects

Variables	**Control Group (n = 26)**	**EGWG Group (n = 35)**	**p**
age, years	30 (28–32)	29 (26–38)	NS
pre-pregnancy BMI, kg/m^2	21.6 (19.5–24.4)	23.1 (21.6–24.7)	NS
Day of Delivery			
fasting blood glucose, mg/dL			
Gestational weight gain, kg	14.5 (11.8–15.6)	24.2 (21.3–25.5)	< **0.001**

Variables	Control Group (n = 26)	EGWG Group (n = 35)	p
Gestational BMI gain, kg/m^2	5.6 (3.2–5.8)	8.3 (7.3–9.4)	**0.00001**
BMI at delivery, kg/m^2	23.4 (23.8–29.1)	31.4 (29.9–32.1)	**0.00001**
Cesarean delivery, %	26	16	NS
2nd Day of Postpartum Period			
BMI after delivery, kg/m^2	21.9 (21.1 – 24.3)	28.3 (26.2–29.6)	**0.00001**
BMI loss after delivery, kg/m^2	2.4 (2.1 – 4.2)	2.8 (2.1–3.2)	NS
ΔBMI, kg/m^2	0.86 (0.36–2.8)	5.6 (4.4–4.9)	**< 0.001**
Albumin, g/dL	3.5 (3.3–3.7)	3.6 (3.4–3.7)	NS
Hemoglobin A1c, %	5.2 (4.6–5.4)	5.5 (5–5.5)	**< 0.05**
Total cholesterol, mg/dL	246 (188–287)	215 (197–249)	NS
HDL, mg/dL	78.4 (75–82)	72 (59–79)	**< 0.05**
LDL, mg/dL	129 (93–152)	112 (87–128)	NS
Triglycerides, mg/dL	174 (152–254)	209 (179–258)	**< 0.05**
Leptin, ng/mL	10.4 (6.2–15)	14.6 (12.4–47.6)	NS
Ghrelin, ng/mL	0.8 (0.6–1.2)	1.2 (0.4–2.4)	NS
FABP4, ng/mL	11.1 (10.8–11.6)	11.9 (10.3–15.5)	NS
SFRP5, ng/mL	3.4 (2.6–7.9)	2.5 (1.2–5)	**< 0.05**
Vaspin, pg/mL	1750.5 (519.6–1135.5)	499.9 (371.4–687.4)	**< 0.05**
Total body water, L	30.3 (25.6–34.2)	34.9 (33.7–41)	**< 0.001**
Extracellular water, L	14.7 (13.2–15.7)	16.8 (15.5–19.7)	**< 0.001**
Intracellular water, L	15.8 (13.5–17.6)	18.9 (17.5–20)	**< 0.001**
Body cell mass, kg	15.3 (12.8–19.1)	19.4 (16.6–21.1)	**< 0.01**
Lean tissue index, kg/m^2	10.6 (9.4–13.2)	12.9 (11.4–13.9)	**< 0.01**
Fat tissue index, kg/m^2	10.2 (9.1–13.7)	14.5 (13.3–17.2)	**<0.001**
Leptin/HDL	0,1 (0.07–0.2)	0.2 (0.2–0.8)	**0.0002**
Leptin/LDL	0.08 (0.04–0.1)	0.2 (0.1–0.5)	**0.00002**
Leptin/triglycerides	0.05 (0.04–0.07)	0.1 (0.1–0.2)	**0.002**

Variables	Control Group (n = 26)	EGWG Group (n = 35)	p
Leptin/hemoglobin A1c	1.9 (1.2–2.8)	2.7 (2.4–8.6)	< **0.05**
Leptin/ghrelin	6.1 (2.8–22.9)	40.8 (6–52.5)	**0.003**
Leptin/FABP4	0.6 (0.6–1.3)	1.4 (0.9–4.2)	< **0.05**
Leptin/vaspin	17.2 (5.4–30.4)	36.3 (18.2–40.8)	**0.003**
Leptin/SFRP5	1.7 (0.7–2.4)	8.9 (3–17.9)	**0.000002**
Leptin/extracellular water	0.7 (0.4–1)	1 (0.8–2.2)	< **0.05**
Leptin/intracellular water	0.6 (0.4–0.9)	0.9 (0.7–2.2)	< **0.05**
Leptin/lean tissue index	0.8 (0.6–1.5)	1.3 (0.9–3.4)	< **0.05**
Leptin/fat tissue index	0.8 (0.6–1.1)	1.1 (1–2.8)	**0.001**
Leptin/body cell mass	0.6 (0.4–1)	0.9 (0.6–2.1)	< **0.05**
Six months after Delivery			
PPWR, kg	10.2 (8.1–12)	4.6 (0–5.6)	**0.0006**

The results are shown as the median (interquartile range: 25–75%). Statistically significant values are given in bold. BMI — body mass index; ΔBMI — BMI gain in the period from pre-pregnancy to 48h after delivery; EGWG — excessive gestational weight gain; FABP4 — fatty acid binding protein 4; HDL — high-density lipoprotein cholesterol; LDL — low-density lipoprotein cholesterol; PPWR — postpartum weight retention; SFRP5 — secreted frizzled-related protein 5

Table 2. Correlation coefficient between PPWR at 6 months after delivery and clinical and laboratory parameters in the EGWG group and in all subjects

Variables	EGWG Group	All
Pre-pregnancy BMI	–0.182	0.039
Gestational weight gain	**0.871*** **	**0.444***
BMI at delivery	**0.674*** **	**0.552****
2nd Day of Postpartum Period		
ΔBMI	**0.874*** **	**0.639*** **
Albumin	0.033	0.002
Total cholesterol	0.246	–0.158
HDL	**0.327***	–0.191
LDL	–0.005	–**0.266***
Triglycerides	–0.199	0.168
Hemoglobin A1c	–**0.433***	0.177

Leptin	–0.197	**0.658*** **
Ghrelin	**0.418***	0.244
FABP4	–0.13	–0.149
Vaspin	–0.151	–**0.436***
SFRP5	**-0.812*** **	–**0.679*** **
Total body water	**0.349***	0.248
Extracellular water	**0.492***	0.232
Intracellular water	**0.361***	0.163
Lean tissue index	0.053	0.336
Fat tissue index	**0.598****	**0.367***
Leptin/HDL	0.394	**0.718*** **
Leptin/LDL	**0.474***	0.287
Leptin/triglycerides	0.383	**0.389***
Leptin/hemoglobin A1c	**0.489***	0.136
Leptin/ghrelin	–0.232	0.232
Leptin/FABP4	**0.439***	0.298
Leptin/vaspin	**0.45***	0.297
Leptin/SFRP5	**0.773*** **	**0.71*** **
Leptin/extracellular water	0.216	**0.516****
Leptin/intracellular water	**0.45***	0.254
Leptin/lean tissue index	0.282	**0.482***
Leptin/fat tissue index	0.327	0.267
Leptin/body cell mass	**0.467***	0.159

Statistically significant values are given in the bold type. *p < 0.05; **p < 0.001; ***p < 0.0001. BMI — body mass index; ΔBMI — BMI gain in the period from pre-pregnancy to 48h after delivery; EGWG — excessive gestational weight gain; FABP4 — fatty acid-binding protein 4; HDL — high-density lipoprotein cholesterol; LDL — low-density lipoprotein cholesterol; PPWR — postpartum weight retention; SFRP5 — secreted frizzled-related protein 5

Table 3. Multiple linear regression analyses for the PPWR

Variables	**B**	***β***	**95% CI**	**p**
Gestational weight	0.912	0.766	–0.712	**< 0.001**
Gain	–0.021	0.216	1.112	**< 0.05**
Leptin/SFRP5			–0.005	
			0.037	

Adjusted for the gestational weight gain, leptin/SFRP5 ratio, fat tissue index, the serum concentrations of ghrelin and vaspin. Unstandardized *β* coefficients with 95% confidence interval and B linear regression coefficients are shown. Statistically significant values are

presented. PPWR — postpartum weight retention; SFRP5 — secreted frizzled-related protein 5