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S.O. Ostafiichuk, P.M. Prudnikov, P.R. Volosovskiy, N.I. Henyk
Ivano-Frankivsk National Medical University, Ivano-Frankivsk

CARBOHYDRATE AND LIPID METABOLISMS IN PREGNANT WOMEN WITH EXCESSIVE GESTATIONAL WEIGHT GAIN

e-mail: svitlana.ostafijchuk@gmail.com

During pregnancy, the changes in carbohydrate and lipid metabolisms are determined by the level of gestational weight gain independent of the prepregnancy weight. In excessive weight gain women's insulin concentration and insulin resistance index in the third trimester were higher compared to the early terms ($p<0.05$), while the insulin resistance index 1.8–fold ($p<0.05$) exceeded the similar index with normal gestational weight gain. There were hyperlipoproteinemia ($p<0.05$) in the second trimester and increased dyslipidemia in late pregnancy. The level of triglycerides at the end of pregnancy in 1.4–fold ($p<0.05$) exceeded this indicator with the recommended gestational weight gain patients. A significant association between the high levels of atherogenic lipids in the middle of pregnancy and an excessive increase in the percentage of body fat mass in late terms was found. Consequently, excessive gestational weight gain can be considered as the marker of disruption of adaptive metabolic changes in conditions of increased energy demand, with the risk of weight retention, development of obesity and metabolic syndrome after delivery.

Key words: pregnancy, weight gain, insulin, lipids.

С.О. Остафійчук, П.М. Прудніков, П.Р. Волосовський, Н.І. Геник

СТАН ВУГЛЕВОДНОГО ТА ЛІПІДНОГО ОБМІНІВ У ВАГІТНИХ З НАДЛИШКОВИМ ГЕСТАЦІЙНИМ ЗБІЛЬШЕННЯМ МАСИ ТІЛА

Під час вагітності зміни у вуглеводному і жировому обмінах визначаються рівнем гестаційного збільшення маси тіла незалежно від прегравідарної ваги. При надлишковій надбавці у вазі в третьому триместрі концентрація інсуліну та індексу інсулінорезистентності були вищими порівняно з ранніми термінами ($p<0,05$), а індекс HOMO-IR в 1,8 разів ($p<0,05$) перевищував аналогічний показник при нормальному ГЗМТ. Характерна гіперліпопротеїнемія ($p<0,05$) вже в другому триместрі та посилення дисліпідемії до кінця вагітності. Рівень тригліцеридів в кінці вагітності в 1,4 рази ($p<0,05$) перевищував даний показник при рекомендованому ГЗМТ. Відмічена достовірна залежність між високими рівнями атерогенних ліпідів в середині вагітності і надлишковим зростанням відсотку жирової маси тіла наприкінці вагітності. Отже, надлишкове гестаційне збільшення маси тіла може слугувати маркером зриву адаптаційних змін метаболізму в умовах підвищеної енергетичної потреби з подальшою затримкою редукції ваги, розвитком ожиріння і метаболічного синдрому після пологів.

Ключові слова: вагітність, приріст маси тіла, інсулін, ліпіди.

The study is a fragment of the research project "Creation of diagnostic tactics and pathogenetic justification of effective methods of preservation and restoration of reproductive potential and improvement of parameters of quality of life of the woman with obstetric and gynecological pathology", state registration No. 0121U109269.

Pregnancy is a unique physiological state which characterized by profound changes in metabolism that ensure the adaptation of the maternal organism to the growing needs of the fetus. The continuous process of energy supply to the fetus is supported by interrelated changes in carbohydrate and fat metabolisms by the influence of placental hormones [5]. From early pregnancy, elevated serum steroid hormone levels cause pancreatic β-cell hyperplasia, leading to increased insulin secretion to improve tissue glucose uptake. In the second trimester, elevated insulin level and the insulin resistance index, which are responsible for hypertriglyceridemia during pregnancy, continue to increase. Hormones such as estrogen, progesterone, placental lactogen, human chorionic somatotropin cause the increased fat synthesis in the liver, hypertrophy of fat cells, decreased lipolysis, which is manifested in an increased fat depot in the first half of pregnancy. The maximum elevation of the concentration of high-density lipoproteins in the second trimester is aimed at reducing insulin resistance [7]. Total cholesterol is used by the placenta to synthesize steroid hormones, and fatty acids are used to form its membranes. Increased lipolysis in the third trimester of pregnancy leads to an increase of fatty acids in the serum and their penetration through the placenta to form fat deposits in the fetus, provide energy and adequate metabolism. Very low-density lipoproteins (VLDL) increase in the second half of pregnancy due to decreased activity of endothelial lipoprotein lipase, an enzyme that breaks down triglycerides in VLDL in adipose tissue and liver and is the major transport form of triglycerides. They do not cross the placenta and are actively used for the maternal metabolic needs, storing glucose for the fetus [11]. After delivery in women with the recommended gestational weight gain (GWG), the fat mass corresponds to the pre-pregnancy level. However, excessive weight gain leads to excessive accumulation of adipose tissue, slow postpartum reduction with the high risk of development of obesity and metabolic syndrome [6].

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The problem of excessive GWG is very actual in terms of prediction of obstetric and perinatal complications: high risk of macrosomia, impaired glucose tolerance, gestational diabetes, hypertension, operative delivery [15]. Nowadays, in vast majority of studies, changes in carbohydrate and fat metabolisms were studied in physiological gestation [11], pregnancy and metabolic disorders – obesity [14], diabetes mellitus [5]. However, the dynamics of components of metabolism in pregnant women with excessive GWG is not fully covered.

The purpose of the study was to determine the state of carbohydrate and lipid metabolisms in pregnant women depending on the level of weight gain during pregnancy.

Materials and methods. A total of 130 pregnant women, who visited the antenatal clinics in Ivano-Frankivsk, Ukraine, were enrolled from April 2016 until December 2021. Inclusion criteria to the study were: age 18 years and older, singleton pregnancy, delivery at 37 weeks or more, the absence of severe extragenital diseases. Patients under 18 years old, diagnosed with multiple pregnancies, severe chronic diseases, overweight, obesity and diabetes mellitus were excluded from the study. All women have signed "Informed consent to participate in the study". The research design was approved by the Ethics Committee of the Ivano-Frankivsk National Medical University (No. 93/16 from 01.12.2016).

75 out of 130 (57.7 %) of the examined patients were nulliparous and 55 (42.3 %) were multiparous women. In all women, delivery took place in full-term pregnancy (39.1±1.3 weeks (95 % CI 38.9–39.3)).

The mean age of patients on the onset of examination was 29.4±4.8 (95 % CI 28.6–30.2) kg. The mean height of the patients was 165.7±5.9 cm (95 % CI 164.7–165.7). Pre-pregnancy weight was 64.5±14.8 kg (95 % CI 62.0–67.0), pre-pregnancy body mass index (BMI) 23.5±5.1 kg/m^2 (95 % CI 22.6–24.4). The recommended GWG was diagnosed in 56 (43.1 %) and excessive in 74 (56.9 %) patients due to the Order of the ministry of health of Ukraine № 417 [2]. There was no significant difference in age, height, body weight before pregnancy in the studied groups of women ($p>0.05$) (tabl. 1).

Table 1

Characteristics of women with normal and excessive GWG (x±SD)

Indices	Recommended GWG (n=56)	Excessive GWG (n=74)	p
Weight, years	28.7±5.2	29.9±4.4	>0.05
Parity, n			
- nulliparous	31 (55.4 %)	44 (59.5 %)	>0.05
- multiparous	25 (44.6 %)	30 (40.5 %)	>0.05
Height, kg	166.5±5.6	165±6.1	>0.05
Prepregnancy weight, kg	64.0±17.8	64.8±11.9	>0.05
Prepregnancy BMI, kg/m^2	23.0±5.5	23.9±4.8	>0.05
Number of women, n			
- BMI 18.5–24.9 kg/m^2	33 (58.9 %)	45 (60.8 %)	>0.05
- BMI<18.5 kg/m^2	8 (14.3 %)	–	
- BMI≥25.0 kg/m^2	15 (26.8 %)	29 (39.2 %)	>0.05
GWG, kg	11.5±2.7	16.9±3.7	>0.05

Anthropometry was performed at the first prenatal visit (9.8±1.4 weeks (95 % CI 9.6–10.1)), at 22–24 weeks, and before the delivery. Patients were weighed with the electronic scale to the nearest 0.1 kg. Height was measured using a digital stadiometer with an accuracy of 1.0 cm. GWG was evaluated by the difference between the weight before delivery and pre-pregnancy. Pre-pregnancy weight status of patients was assessed with BMI (kilogram/meter^2) calculated from pre-pregnancy weight and height. Information on the body weight of women before pregnancy was obtained by interviewing patients and medical records. The results were compared to the recommended weight gain according to the national recommendations [2].

Lipid profile was found on the basis of the laboratory determination of the concentration of triglycerides (TG) (Triglycerides SpL (SpinLab LLC, Ukraine)), total cholesterol (TC) (Cholesterol SPL (LLC SpinLab, Ukraine)), high-density lipoproteins, low-density lipoproteins and very low-density lipoproteins (HDL, LDL, VLDL) ("HDL-Cholesterol SPL" (LLC "SpinLab", Ukraine)). Insulin concentration at baseline were measured by the immunoassay method (Insulin Test System-2425–300 (Monobind Inc., USA)). Insulin resistance index was calculated by the formula for the homeostasis model assessment (HOMO-IR): fasting glucose (mmol/l) x fasting insulin (μU/ml)/22.5. Biochemical analyses were performed in according to standard methods [1] in the centralized clinical and diagnostic laboratory of the Regional Perinatal Centre (Ivano-Frankivsk). Percentage of body fat mass was determined using spectral bioimpedansometry (with the use of "Diamant-aist" analyzer KM-AP-01) connected to a computer [13].

Antenatal care with nutrition and physical activity recommendations was carried out in accordance with existing Ukrainian guidelines [2].

The results were statistically analyzed using Statistica 6.0 program pack (StatSoft Inc.,USA) and the Microsoft Excel statistical analysis package, parametric methods of analysis were used. The parameters are presented as mean arithmetic value, mean standard deviation (x±SD). To represent the accuracy of the calculated arithmetic mean odds ratio (OR), 95 % confidence interval (CI), and p–value were obtained. Pearson's correlation-regression analysis method (r) was used to determine the presence, strength, and direction of the relationship between the parameters. The differences between the selections were considered statistically reliable at $p<0.05$ (Tukey's test).

Results of the study and their discussion. Analysis of carbohydrate metabolism in the examined women has showed a significant positive association between the value of GWG and glucose level (r=0.44, p=0.000; r=0.67, p=0.000), insulin level (r=0.74, p=0.000; r=0.84, p=0.000) та HOMO-IR (r=0.72, p=0.000; r=0.81, p=0,000) respectively in the second and third trimesters of pregnancy. However, the dynamics of these indicators during the gestational period differed in groups (fig. 1 a-c).

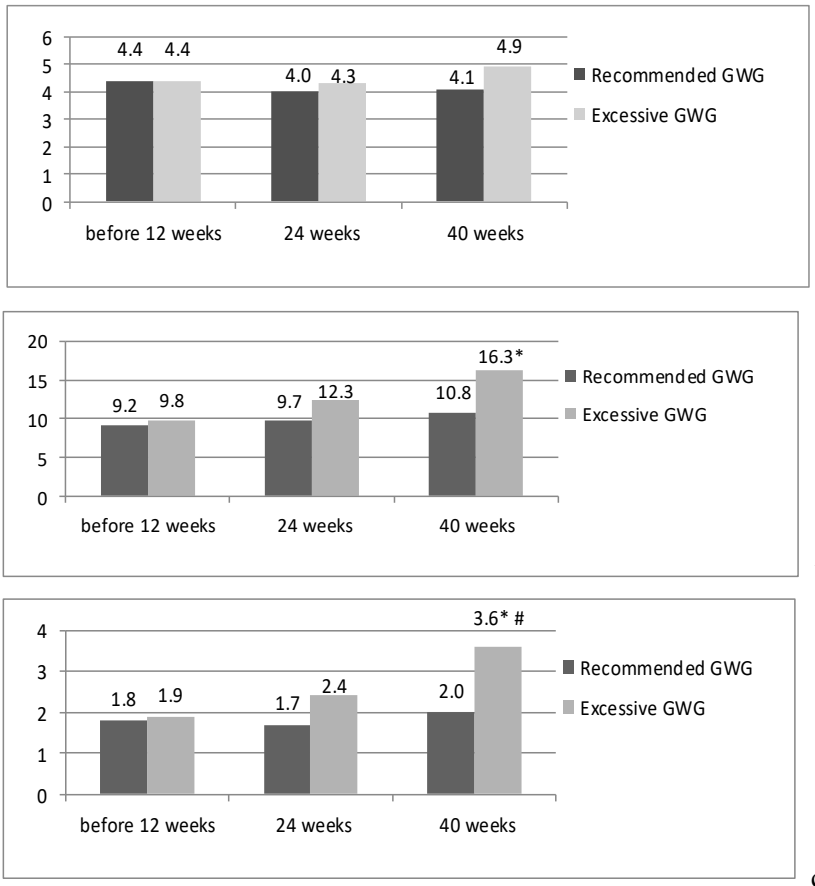

Fig. 1. Dynamics of carbohydrate metabolism in recommended and excessive GWG groups of women: a – glucose concentration, mmol/l; b – insulin, μIU/ml; c – HOMO-IR; * – compared to the indices of the first trimester ($p<0.05$), # – compared to the indices of the recommended GWG group of women ($p<0.05$)

Thus, in recommended GWG group of women there was no significant dynamics of blood glucose level during pregnancy ($p>0.05$). We have seen elevation of insulin concentration in early pregnancy compared to the reference values of non-pregnant women (0.7–9.0 μIU/ml) and an increase until the end of pregnancy, but these changes were not statistically significant ($p>0.05$). Women in this group no significant dynamics of HOMO-IR during pregnancy were diagnosed.

In excessive weight gain women insulin level and HOMO-IR have been shown to increase gradually during pregnancy. In the third trimester, the insulin concentration 1.7–fold ($p<0.05$), HOMO-IR 1.9–fold ($p<0.05$) were higher than in the early terms. At the end of pregnancy HOMO-IR was 1.8–fold ($p<0.05$) significantly higher compared to normal GWG patients and exceeded the reference values (0–2.7) ($p<0.05$).

The results of the study of lipid metabolism have shown that the concentration of atherogenic lipoproteins increased during pregnancy, regardless of the category of GWG and reflected the body weight gain due to the fat component. Detailed analysis in the groups has showed a significant increase of TG levels 1.8–fold ($p<0.05$), LDL 1.3–fold ($p<0.05$) in the third trimester compared to early terms and the absence of significant changes in the levels of TC, HDL, VLDL during pregnancy in normal GWG women ($p>0.05$) (fig. 2 a – e).

In excessive weight gain women, we have found a statistically significant increase in certain indicators in the second trimester and dyslipidemia at the end of pregnancy. Thus, the concentration of TG 2.0–fold ($p<0.01$), TC 1.3–fold ($p<0.01$), LDL 2.2–fold ($p<0.05$), VLDL 1.8–fold ($p<0.05$) were significantly higher in the second trimester and 2.3–fold ($p<0.001$), 1.2–fold ($p<0.05$), 1.4–fold ($p<0.02$) and 3.0–fold ($p<0.001$), respectively, in the third trimester compared to early pregnancy. It should be noted, that TG level at the end of pregnancy in excessive GWG women was significantly 1.4–fold ($p<0.05$) higher than in recommended weight gain women. TG are the main source of the mother's metabolic needs, and their excessive accumulation before delivery indicates a high risk of overweight in the postpartum period.

We've investigated that hyperlipoproteinemia was correlated with GWG: TG (r=0.19, p=0.016; r=0.59, p=0.000), VLDL (r=0.33, p=0.000; r=0.51, p=0.000) in the second and third trimesters, respectively, regardless of the final level of weight gain. At the end of pregnancy, there was a direct relationship between weight gain and levels of TG (r=0.47, p=0.000), LDL (r=0.34, p=0.000) and inverse with HDL (r=0.54, p=0.000). It was important to identify a significant association between high concentrations of TG (r=0.34, p=0.000), TC (r=0.51, p=0.000), HDL (r=0.20, p=0.011), LDL (r=0.35, p=0.000), VLDL (r=0.33, p=0.000) in mid-pregnancy and GWG in late pregnancy.

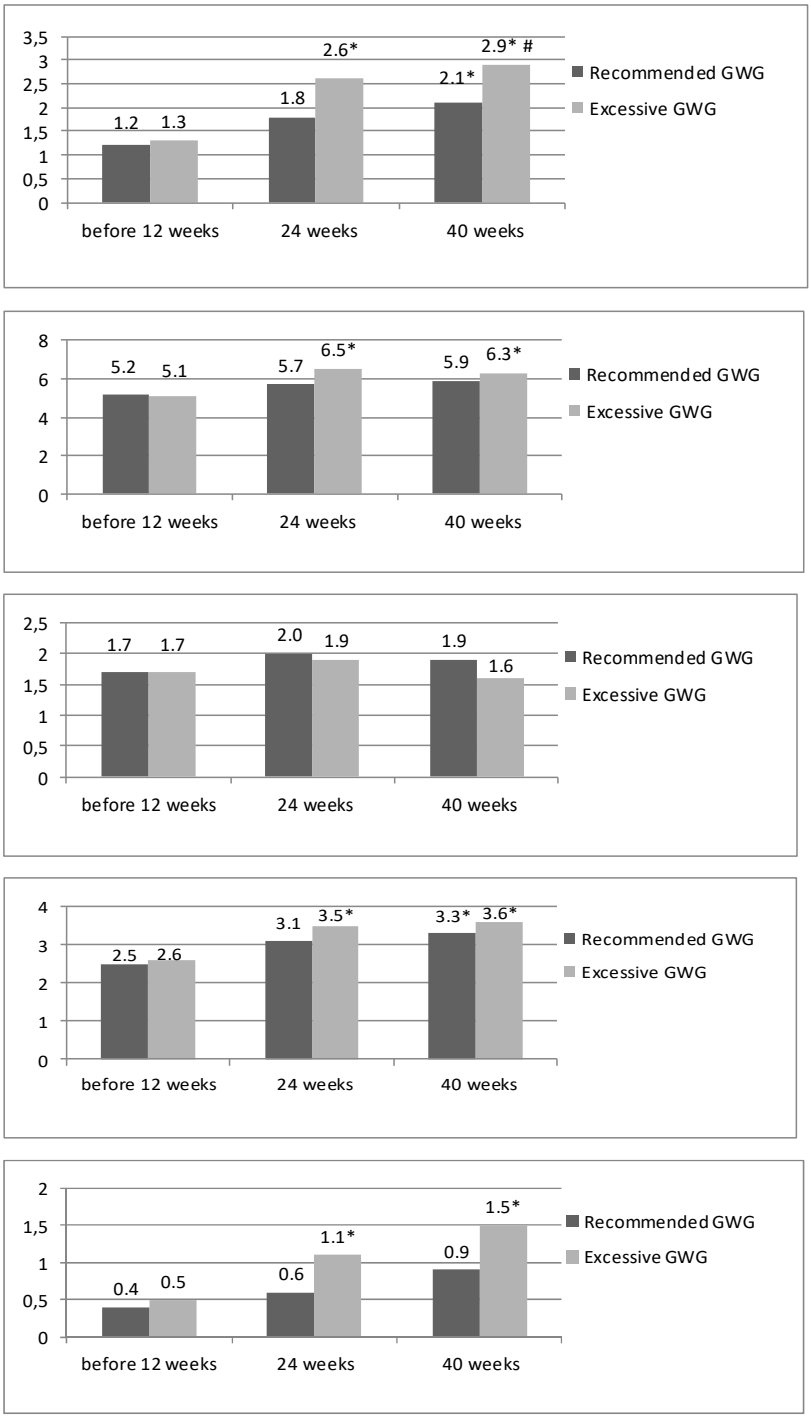

Fig. 2. Dynamics of lipid metabolism in normal and excessive GWG groups of women: a – concentration of TG, mmol/l; b – TC, mmol/l; c – HDL, mmol/l; d – LDL, mmol/l; e – VLDL, mmol/l; * – compared to the indices of the first trimester ($p<0.05$), # – compared to the indices of recommended GWG group of women ($p<0.05$)

Analysis of the association between fat mass, the main component of pathological weight gain, with lipid profile levels indicated a significant correlation of high levels of atherogenic lipids in mid-pregnancy with an excessive increase in the percentage of body fat mass: TG (r=0.65, p=0.000; r=0.64 , p=0.000), TC (r=0.46, p=0.000; r=0.61, p=0.000), HDL (r=0.32, p=0.0002; r=0.40, p=0.000), LDL (r=0.36, p=0.000; r=0.53, p=0.000), VLDL (r=0.79, p=0.000; r=0.84, p=0.000) in both the second and third trimesters, respectively. In the middle of pregnancy there was a positive relationship between the concentration of TG (r=0.74, p=0.000), TC (r=0.61, p=0.000), LDL (r=0.45, p=0.000), VLDL (r=0.75, p=0.000) and inverse correlation of HDL (r=0.26, p=0.001) with the percentage of body fat mass at the end of pregnancy. This may indicate that the excessive accumulation of fat mass in late pregnancy is a clinical manifestation of hyperlipoproteinemia at the earlier terms.

According to modern knowledge, weight gain in non-pregnant women is associated with the development of obesity, insulin resistance and type 2 diabetes mellitus. It is considered, that such mechanisms of body weight is the basis of changes in glucose metabolism during pregnancy. Changes in carbohydrate and lipid metabolisms during normal pregnancy initiate the accumulation of maternal fat stores in the first half of pregnancy and increase mobilization in the late stages, regardless of pre-pregnancy body weight. We have proved in our work that recommended weight gain during pregnancy is accompanied with compensated hyperinsulinemia on the background of

normal HOMO-IR, which indicates the activation of compensatory mechanisms of the body to maintain tissue sensitivity to insulin for adequate energy supply to cells.

In excessive GWG pregnant, we've found significant hyperinsulinemia and an increased HOMO-IR in late pregnancy, which indicate the development of insulin resistance, which leads to impaired glucose uptake into insulin-dependent tissues: muscle, fat, liver. The studies of Kampmann U. et al. [8], Sonagra AD. et al. [12] also showed the state of hyperinsulinemia and insulin resistance during pregnancy, however, they did not take into account the difference in GWG, and compare the results with non-pregnant women. Moyce BL. et al. [9] and Powe CE. et al. [10] demonstrated an enhanced insulin response during a normal pregnancy, but suggested that excessive GWG, pre-pregnancy obesity, and genetic predisposition may cause beta-cell adaptation failure. In a current study (2020) Alvarado FL. et al. noted that the rate of insulin sensitivity before pregnancy is a strong determinant of changes in gestational glucose metabolism [4].

It is known, that the leading etiopathogenetic mechanisms of excessive weight are associated with energy imbalance – more energy intake from food against loss, which affects the synthesis of triglycerides and their increased deposition in fat depots [3]. Improper eating behavior of pregnant women with excessive amounts of calories, sedentary lifestyle, reduced physical activity lead to reduced energy consumption and play a leading role in the excessive GWG. Hypertriglyceridemia, hyperlipoproteinemia, inhibited glucose uptake into the tissues due to the progression of insulin resistance are observed in excessive GWG women, are the pathogenetic basis of energy deficiency that reduced adaptive capacity of the maternal organism to gestation.

Conclusion

During pregnancy the changers in carbohydrate and lipid metabolisms are determined by the level of gestational weight gain. Pathological pre-pregnancy body weight is an aggravating factor, but not significant. Excessive weight gain is associated with the development of pathological insulin resistance and dyslipidemia, regardless of weight before pregnancy. Pathological weight gain diagnosed in the second and third trimesters of pregnancy is a clinical manifestation of impaired carbohydrate and fat metabolisms at an earlier terms with progressing to the end of pregnancy. Consequently, excessive gestational weight gain can be considered as the marker of disruption of adaptive metabolic changes in conditions of increased energy demand, with the risk of weight retention, development of obesity and metabolic syndrome after delivery.

References

1. Klinicheskaya laboratornaya diagnostika. Natsionalnoye rukovodstvo. Za red. V.V. Dolgova v 2 tomakh. Tom 1.2013; 934. [in Russian]
2. Nakaz MOZ Ukrayini № 417 vid 15.07.2011 "Metodychni rekomendatsiyi shchodo orhanizatsiyi ambulatornoyi akushersko-hinekolohichnoyi dopomohy". [in Ukrainian]
3. Shevchenko YuS, Mamontova TV, Baranova AF, Vesnina LE, Kaydashev IP. Mekhanizmy rozvytku pidvyshchenoyi masy tila u molodykh osib. Problemy ekolohiyi ta medytsyny. 2014; 18(5–6):44–9. [in Ukrainian]
4. Alvarado FL, O'Tierney-Ginn P, Catalano P. Contribution of gestational weight gain on maternal glucose metabolism in women with GDM and normal glucose tolerance. J Endocr Soc. 2020; 5(2):bvaa195. Published 2020 Dec 31. doi:10.1210/jendso/bvaa195
5. Castillo-Castrejon M, Powell TL. Placental nutrient transport in gestational diabetic pregnancies. Front. Endocrinol. 2017;8:306. doi: 10.3389/fendo.2017.00306.
6. Farpour-Lambert NJ, Ells LJ, Martinez de Tejada B, Scott C. Obesity and weight gain in pregnancy and postpartum: an evidence review of lifestyle interventions to inform maternal and child health policies. Front. Endocrinol. 2018; 9:546. doi: 10.3389/fendo.2018.00546.
7. Gaccioli F. Lager S. Placental nutrient transport and intrauterine growth restriction. Front. Physiol. 2016; 7:40. doi: 10.3389/fphys.2016.00040.
8. Kampmann U, Knorr S, Fuglsang J, Ovesen P. Determinants of maternal insulin resistance during pregnancy: an updated overview. Journal of Diabetes Research. 2019;:9. doi: 10.1155/2019/5320156.
9. Moyce BL, Dolinsky VW. Maternal β-cell adaptations in pregnancy and placental signalling: implications for gestational diabetes. Int J Mol Sci. 2018; 19(11). doi:10.3390/ijms19113467
10. Powe CE, Huston PLP, Locascio JJ, Catalano PM. Augmented insulin secretory response in early pregnancy. Diabetologia. 2019; 62(8):1445–52.
11. Pusukuru R., Shenoi A.S., Kyada P.K., Ghodke B., Mehta V., Bhuta K. Evaluation of lipid profile in second and third trimester of pregnancy. Journal of Clinical and Diagnostic Research. 2016 Mar;10(3):12–6. doi:10.7860/JCDR/ 2016/17598.7436.
12. Sonagra AD, Biradar SM, Dattatreya R, Murthy JDS. Normal pregnancy-a state of insulin resistance. J of Clin and Diagn Res. 2014 Nov; 8(11):1–3. doi:10.7860/JCDR/2014/10068.5081.
13. Staelens AS, Vonck S, Molenberghs G, Malbraine MLNG, Gyselaersa W. Maternal body fluid composition in uncomplicated pregnancies and preeclampsia: a bioelectrical impedance analysis. The European J of Obstet & Gynecol and Reprod Biol. 2016; 204:69–73. doi: https://doi.org/10.1016/ j.ejogrb.2016.07. 502.
14. Vernini JM, Moreli JB, Araújo Costa RA, Negrato CA, Cunha Rudge MV, Paranhos Calderon IM. Maternal adipokines and insulin as biomarkers of pregnancies complicated by overweight and obesity. Diabetology & Metabolic Syndrome. 2016; 8:68. doi:10.1186/s13098-016-0184-y.
15. Wu Y, Wan S, Gu S, Mou Z, Dong L. Gestational weight gain and adverse pregnancy outcomes: a prospective cohort study. BMJ Open. 2020; 10:e038187. doi:10.1136/ bmjopen-2020-038187.

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