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THE IMPACT OBESITY HAS ON EARLY PERINATAL OUTCOMES AND NEONATAL MORBIDITIES IN PREMATURE INFANTS

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In an epidemiological retrospective study, which included 4.874 women, the frequency of obesity of various degrees among pregnant women, increased risks of adverse pregnancy complications and obstetric outcomes, in particular hypertension disorders, preeclampsia, uterine inertia, use of emergency cesarean section, excessive fetal growth. At the same time among women with stage III obesity compared to women of the stage I, the risks of having hypertensive conditions are 3.5 times higher, the uterine inertia is twice as high, preeclampsia is 56.8 % and excessive fetal growth is 21.3 %. It has been shown that there is no impact of obesity on the premature birth of babies. Large-for-gestational-age babies born prematurely to obese (non-diabetic) mothers have been shown to have an increased risk of jaundice (RR 3.08) and neonatal hypoglycemia (RR 9.11) and no such risk compared with those of normal weight regarding the occurrence of other diseases (intraventricular hemorrhages, birth asphyxia, respiratory distress, hemodynamic significance patent ductus arteriosus, retinopathy). No significant differences were noted between the children of both groups in the frequency of noninvasive/invasive ventilatory support, oxygen support, and parenteral nutrition.

Key words: pregnant, maternal obesity, perinatal outcomes, premature, large for gestational age, morbidity.

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ВПЛИВ ОЖИРІННЯ НА РАННІ ПЕРИНАТАЛЬНІ НАСЛІДКИ У ЖІНОК ТА ЗАХВОРЮВАНІСТЬ ЇХ ПЕРЕДЧАСНО НАРОДЖЕНИХ ДІТЕЙ

В епідеміологічному ретроспективному дослідженні, що включало 4874 жінок, встановлено частоту ожиріння різних ступенів серед вагітних, підвищені ризики виникнення несприятливих ускладнень вагітності та акушерських наслідків, зокрема гіпертонічні стани, прееклампсії, слабкості пологів, застосування екстренного кесаревого розтину, надлишкового росту плода, при цьому у жінок з ожирінням ІІІ ст. порівняно з жінками І ступеня ризики мати гіпертензивні розлади є вищими в 3,5 рази, слабкість пологів – вдвічі, прееклампсію – на 56,8 %, надлишковий ріст плода – на 21,3 %. Показано відсутність впливу ожиріння на передчасне народження немовлят. У немовлят завеликих до гестаційного віку, народжених передчасно від матерів з ожирінням (без діабету), порівняно з такими дітьми, маса яких відповідала гестаційному віку, показано підвищені ризики розвитку жовтяниці (RR 3.08) і неонатальної гіпоглікемії (RR 9.11) та відсутність таких ризиків щодо виникнення інших захворювань (внутрішньошлуночкових крововиливів, асфіксії при народженні, дихального дистресу, значущої відкритої артеріальної протоки, ретинопатії). Не відмічено достовірних відмінностей між дітьми обох груп у частоті застосування штучної вентиляції легень, кисневої терапії та парентерального харчування.

Ключові слова: вагітні, ожиріння, перинатальні наслідки, передчасно народжені, завеликі до гестаційного віку, захворюваність.

The study is a fragment of the research project “To develop clinical and laboratory criteria, methods of prediction and prevention of metabolic disorders in young children”, state registration No. 0120U102856.

Prevention of obesity among women of reproductive age is a global public health priority, as today there are convincing data on the connection of obesity during pregnancy with early and long-term adverse outcomes for both the woman and her child [2]. Obese pregnant women have higher risks of early pregnancy loss, spontaneous and medically indicated premature birth, gestational diabetes and preeclampsia, which are associated with long-term postpartum morbidity, and higher risks of developing

fetal malformations, delivery of large for gestational age infants, etc. [9] Failure to diagnose fetal size before delivery is associated with adverse outcomes such as fetal asphyxia, stillbirth, and neonatal cerebral hemorrhage [15].

Large-for-gestational-age babies (LGA) are worrisome in terms of both long-term and short-term outcomes. A lot of examinations have been devoted to the study of the risks of increased morbidity among full-term babies who are too large for GA, which shows that such children may have an increased risk for short-term outcomes, such as shoulder dystocia, neonatal hypoglycemia, and prolonged hospital stay [3]. However, most of these studies were about cohorts of full-term babies, while there is a scarce number of them examining adverse outcomes among preterm ones.

As for long-term consequences, systematic reviews and meta-analyses show that excess weight at birth is associated with increased overweight risk during childhood and adulthood [13]. Epidemiological studies demonstrate a strong association between the birth of a child too large for gestational age (LGA) and adverse metabolic and cardiovascular outcomes at a later age [14].

Our previous studies have identified risk factors for having a baby that is too large for GA, but this was for full-term babies and women with metabolic syndrome [1]. At the same time, little attention has been paid to the study of perinatal outcomes among obese women without concomitant diabetes and the short-term outcomes her prematurely born baby has.

The purpose of the study was to determine the rates of adverse pregnancy and obstetric outcomes among women depending on their body mass index and compare the risk of morbidities in large-for-gestational-age babies premature infants with those of appropriate for gestational age infants.

Materials and methods. A retrospective cohort study was conducted, which assessed the frequency of perinatal complications among women with different BMIs. All women who gave birth during 1–7 months of 2021 in obstetric hospitals of the Poltava region are included in the study. The data of the electronic health care system became the information base of the study. Pregnancy complications and obstetric outcomes were studied among non-obese women – 4427 women with BMI<30 kg/m^2, and among obese women – 447 women with BMI≥30 kg/m^2. The latter were divided into 3 groups depending on BMI: the first group included 308 women with the degree I obesity BMI≥30 kg/m^2 to ≤ 34.99 kg/m2 (Diagnoses according to ICD-10: E66.91_E66.11); in the second group – 96 women with degree II obesity – BMI≥35 kg/m^2 to ≤ 39.99 kg/m2 (Diagnoses according to ICD-10: E66.92; E66.12); in the third group – 43 women with degree III obesity – BMI≥40 kg/m^2 (Diagnoses according to ICD-10: E66.93).

The subject of the study was: hypertensive conditions (codes O10, O13); anemia (codes O99.0-4); preeclampsia (codes O14.-, O15.-), premature rupture of membranes (codes O42.-), uterine inertia (codes O62.0, 1O62.1, O62.2); fetal stress (codes O68.-, O36.3); injuries – codes (O70.2, O70.3, O70.9, O71.-), emergency cesarean section (codes 16520.-), medical induction and stimulation (codes 90465.-), premature birth – duration of pregnancy 33-37 weeks (code O09.5), and excessive fetal growth (code O36.6).

At the second stage of the study, the risks of early morbidity were studied among preterm, LGA children born to obese (non-diabetic) women, compared with AGA infants. The study included 288 babies who were born at a gestation period of 34^{+0}–36^{+6} weeks with a birth weight of 1500-2500 g and who were hospitalized at neonatal units of obstetric institutions and children's hospitals of the Poltava region. The first group included LGA babies (n=22), the second group included 266 AGA. The criteria for exclusion from the study were too low weight for GA, birth from twins, the presence of a congenital anomaly.

Children with weight more than 90 percentile were considered to be LGA (code according to ICD-10 P08.1), children with weight that corresponded to 10-90 percentile according to the WHO tables – AGA babies.

The research design was discussed and approved by the medical ethics committee (Extract from the minutes of the meeting of the committee on biomedical ethics of the Ukrainian Medical and Dental Academy No. 170 dated January 24, 2019). All parents consented to the examination of their children.

Statistical processing of the obtained results was carried out using the package of application programs EXCEL-2003® and STATA version 11 for Windows (StataCorp, Texas, USA). With a normal distribution, the central tendency was determined using the mean value (M) and standard error (m), comparison – by the two-sample Student's t-test (t).

Comparison of relative or percentage values was carried out using the Pearson test. We calculated the risk ratio (RR – Risk ratio), their 95 % confidence intervals (95 % CI), Pearson's test. Values of $p<0.05$ were considered statistically significant.

Results of the study and their discussion. In the examined cohort of women, obesity was found with 9.17 % of women (447 women out of 4874), while the share of women from the stage I of obesity was 68.9 % (308 out of 447), the share of women from the stage II – 21.5 % (96 out of 447) and the share of women from the stage III – 9.6 % (43 out of 447) (table 1).

Table 1

Frequency of pregnancy complications and obstetric complications among women of research groups

	Obese pregnant women				Women without obesity (n=4427)
	Group 1 (n=308) abs/% RR (95 % CI) p	**Group 2** (n=96) abs/% RR (95 % CI) p	**Group 3** (n=43) abs/% RR (95 % CI) p	**All** (n=447) abs/% RR (95 % CI) p	
Hypertensive conditions	21/6.8 2.88 (1.952–4.32) <0.001	19/19.8 9.45 (5.93–15.08) <0.001	11/25.6 14.01 (7.26–27.055) <0.001	51/11.4 4.14 (3.25–5.27) <0.001	96/2.2
Anemia	86/27.9 1.27 (0.99–1.61) 0.0537	26/27.1 1.23 (0.79–1.91) 0.361	8/18.6 0.76 (0.35–1.64) 0.485	120/26.8 1.19 (0.98–1.46) 0.0755	1023/23.1
Preeclampsia	56/18.2 3.73 (2.87–4.85) <0.001	19/19.8 4.62 (2.85–7.51) <0.001	10/23.3 5.85 (2.92–11.72) <0.001	85/19.0 3.64 (2.97–4.47) <0.001	210/4.7
PRAM	43/14.0 0.99 (0.73–1.36) 0.982	14/14.6 1.04 (0.59–1.83) 0.871	12/27.9 2.35 (1.21–4.56) 0.009	69/15.4 1.1 (0.86–1.41) 0.407	620/14.0
Uterine inertia	28/9.1 1.72 (1.19–2.49) 0.004	11/11.4 2.28 (1.24–4.23) 0.007	7/16.3 3.45 (1.55–7.68) 0.0013	46/10.3 1.9 (1.44–2.51) <0.001	231/5.2
Fetal distress	22/7.1 1.06 (0.7–1.61) 0.768	6/6.3 0.93 (0.41–2.10) 0.858	2/4.7 0.68 (0.16–2.79) 0.590	30/6.7 1.0 (0.7–1.42) 0.998	297/6.7
Obstetric trauma	16/5.2 0.44 (0.27–0.73) <0.001	4/4.2 0.35 (0.3–0.94) 0.028	4/9.3 0.81 (0.29–2.25) 0,684	24/5.4 0.47 (0.31–0.70) 0.001	499/11.3
Emergency cesarean section	49/15.9 1.25 (0.93–1.68) 0.133	17/17.7 1.43 (0.85–2.41) 0.167	9/20.9 1.77 (0.85–3.67) 0.120	75/16.8 1.31 (1.04–1.66) 0.022	572/12.9
Medical induction and stimulation	26/8.4 1.41 (0.96–2.07) 0.082	8/8.3 1.41 (0.69–2.89) 0.339	3/7.0 1.18 (0.37–3.77) 0.785	37/8.3 1.36 (0.99–1.87) 0.055	265/6.0
Preterm birth	20/6.5 1.52 (0.99–2.34) 0.056	6/6.3 1.5 (0.66–3.39) 0.324	1/2.3 0.54 (0.07–3.94) 0.541	27/6.0 1.41 (0.97–2.02) 0.069	186/4.2
Excessive fetal growth	32/10.4 2.21 (1.57–3.11) <0.001	10/10.4 2.34 (1.23–4.44) 0.008	5/11.6 2.68 (1.06–6.74) 0.030	47/10.5 2.43 (1.7–3.4) <0.001	204/4.6

Note. PRAM – premature rupture of the amniotic membrane.

The analysis of demographic characteristics showed that the average age of women without obesity (28.5±0.08 years old) was significantly lower ($p<0.001$ for all groups) than women with obesity of the first degree (29.9±0.32 years old), for women with second-degree obesity (30.9±0.63 years old) and for women with third-degree obesity (31.4±0.84 years old). Obesity is reliably associated with hypertensive conditions (HD), preeclampsia, uterine inertia, and the use of emergency cesarean section (ESC). A more detailed analysis in groups of obese women showed that with an increase in BMI, the risk of having hypertensive conditions increases more than 3.5 times (from 2.88 among women with obesity of the first degree to 14.01 among women with obesity of the third degree), preeclampsia – by 56.8 % (corresponding RRs from 3.73 to 5.85), uterine inertia – twice (corresponding RRs 1.72 and 3.45), excessive fetal growth – by 21.3 % (corresponding RRs 2.21 and 2.68). It should be noted that there are no reliable risks regarding premature rupture of membranes (PRAM) among women with obesity of the first and second stages and double the risk among women with third-degree obesity (RR 2.35). We obtained a reliable more frequent use of

emergency caesarean section with obese women than with non-obese women. However, conducting such an analysis in separate groups did not show reliable differences, which is due, in our opinion, to a smaller sample of women in these groups. Therefore, the clarification of differences in the frequency of emergency caesarean section in particular needs further study.

Regarding preterm babies, we found no significant differences between preterm LGA babies and AGA infants at delivery by caesarean section (4.5 % [1 of 22] vs. 3.5 % [8 out of 266], p=0.690) and the number of cases of hypertensive conditions the mother had (4.5 % [1 out of 22] vs. 13.7 % [31 out of 266], p=0.308). In addition, the groups of babies were identical in distribution by gender (40.9 % [9 out of 22] girls and 56.2 % [127 out of 266] girls, p=0.537).

In the groups of preterm babies, included in the study, there were no statistical differences as for the frequency of intraventricular hemorrhage (IVH), asphyxia, respiratory distress, hemodynamic significance patent ductus arteriosus, retinopathy, use of noninvasive/invasive ventilatory support, oxygen respiratory support, use of parenteral nutrition (table 2).

Table 2

Morbidity risks among premature born babies included in the study

	Infants LGA (n=22)	Infants AGA (n=266)	RR (95% CI)	P
Intraventricular hemorrhages	2 (9.1)	24 (9.0)	0.99 (0.88–1.12)	0.991
Birth asphyxia	2 (9.1)	27 (10.2)	0.89 (0.21–3.62)	0.874
Jaundice	17 (77.3)	134 (50.4)	3.08 (1.16–8.13)	0.015
Neonatal hypoglycaemia	8 (36.4)	9 (3.4)	9.11 (4.44–18.66)	<0.001
Respiratory distress	7 (31.8)	115 (43.2)	0.63 (0.27–1.51)	0.298
Hemodynamic significance patent ductus arteriosus	5 (22.7)	40 (15.0)	1.59 (0.62–4.08)	0.339
Retinopathy	1 (4.5)	11 (4.1)	1.09 (0.16–7.48)	0.926
Noninvasive/invasive ventilatory support	6 (27.3)	92 (34.6)	0.73 (0.29–1.79)	0.486
Oxygen support	5 (22.7)	76 (28.6)	0.75 (0.29–1.97)	0.557
Catheterization of the umbilical vein	9 (40.9)	115 (43.2)	0.91 (0.40–2.07)	0.832
Parenteral nutrition	7 (31.8)	57 (21.4)	1.63 (0.69–3.83)	0.260

At the same time, a significantly higher number of cases of jaundice and neonatal hypoglycemia were found among preterm LGA infants than preterm AGA babies.

In our epidemiological study, the proportion of obese women is 9.2 %. At the same time, according to the US National Health and Nutrition Examination Survey (NHANES), the prevalence of obesity among women aged 20–39 in the United States was 31.8 % [7], according to the European Peristat Database and WHO data, the highest prevalence obesity in Europe is observed in Great Britain (25.2 %) and the lowest – in Poland (7.1 %) [10]. Attention is drawn to the rapid growth of obesity among pregnant women in European countries, therefore, in our opinion, we should expect an increase in the number of obese mothers in Ukraine as well.

According to our data, the share of women from the I obesity stage was 68.9%, the share of women from the obesity stage II – 21.5 % and the share of women from the obesity stage III – 9.6 %. In other scientific works, a slightly different distribution of women according to the degree of obesity is given, in particular, in the work of Ogden CL and co-authors, it is shown that about half of obese women belonged to the stage I, but a quarter – to the stage II and another quarter to the stage III [8].

Our study showed that women with a BMI more than 30 kg/m^2 have a high risk of developing both pregnancy complications and adverse obstetric outcomes, including hypertensive conditions, preeclampsia, uterine inertia, and the use of ECS.

Systematic reviews indicate a 3- to 10-fold increased risk of preeclampsia in a general cohort of obese women compared to non-obese women [12]. It should be noted that our study examined the risk of preeclampsia depending on the degree of obesity among pregnant women. In particular, it was shown that the risk increased by 56.8 % among women from the stage III obesity compared to women from the stage I obesity.

According to our data, obesity during pregnancy doubles the risk of developing weakness at childbirth, while women with third-degree obesity have twice the risk of weak childbirth than obese women of the stage I. Taking this into account, obese women were significantly more likely to receive ECS (RR 1.31, p=0.022), although the systematic review by Poobalan AS with co-authors, who studied indicated higher risks of using this intervention – 2.26 (95 % CI 2. 0–2.51) for women of obesity stage I and 3.38 (2.49–4.57) for women of obesity stage II and III relative to women of normal weight [4].

Our study shows that obesity is not associated with preterm birth, although other researchers have reported increased risks of spontaneous preterm birth in a cohort of preterm infants. A 2015 systematic review

showed that preterm birth is associated with obesity among pregnant women, but reported that with more mature preterm babies, maternal obesity does not affect or even has a protective role for spontaneous preterm birth, thus supporting the view that maternal obesity plays a role in very low birth weight preterm babies.

LGA babies are more often born to pregnant women complicated by obesity than to women with a normal weight. Maternal obesity is associated with a more than two-fold increase in the risk of giving birth to LGA babies relative to women with normal weight, while the risk among women with obesity of the 3rd degree is higher than among women with obesity of the 1st degree. Increases by almost 13 % when the reference group is women of normal weight. Although in the works of other scientists it is said about a 30 % increase in risks. Other studies have shown that women with a BMI ≥40 kg/m^2 have a higher chance of having a LGA baby, for example, a retrospective cohort study by Australian scientists showed that the risks for women of this weight category of Asian origin were 9.92 for having a LGA baby, and for women of Australian origin – 2.66 [11], which is close to our data (2.68).

In our comparative study of the risks of increased morbidity among preterm LGA babies and preterm AGA infants, no statistical differences were found in the number of cases of asphyxia, respiratory distress, hemodynamic significance patent ductus arteriosus, retinopathy, as well as the need for Noninvasive/invasive ventilatory support, oxygen support, and parenteral nutrition. In our research we didn't obtain reliable differences in the frequency of respiratory distress, although according to scientist such differences were obtained, but in the cohort of full term newborns. At the same time, in premature LGA infants significantly higher risks of developing jaundice (RR 95 % CI 3.08 (1.16–8.13)) and neonatal hypoglycemia (RR (95 % CI 9.11 (4.44-18.66).

Hypoglycemia can occur in LGA infants when the placental supply of glucose is interrupted at birth, even in the absence of maternal diabetes. Groenedaal and colleagues used the Netherlands Perinatal Registry data from 1997 to 2002 to evaluate the relationship between LGA birth weight (>90th percentile) and neonatal hypoglycemia in infants without other risk factors for hypoglycemia [6]. Among LGA infants of women without diabetes, hypoglycemia occurred in 10.5 % of these infants, in our study – 36.4 %. In another large case series of 887 LGA infants (birth weight of >90th percentile) born to women without diabetes, 16 % had hypoglycemia during the first 24 hours of life. But our study included premature babies born to obese mothers, that's why we consider the number of cases of neonatal hypoglycemia is higher [5].

Our data highlight the importance of routine postdelivery glucose monitoring in preterm infants with LGA birth weight.

We acknowledge that there are several limitations to this study. First, because it was a retrospective study, maternal and neonatal complications were defined before the study. Second, because the number of preterm LGA infants born to mothers with obesity was small and information on the impact of maternal obesity on LGA infants was lacking, we could not draw definitive conclusions from morbidities.

Conclusion

Obese pregnant women have an increased risk of developing adverse obstetric outcomes, including HD, preeclampsia, labor weakness, the use of emergency cesarean section, and excessive fetal growth. Premature infants large to gestational age born to obese (non-diabetic) mothers, compared to such children whose weight appropriate to gestational age, have been shown to have increased risks of developing jaundice and neonatal hypoglycemia, and the absence of such risks for other diseases.

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BIOMECHANICAL ASPECTS OF POSTURAL CONTROL OF THE HUMAN BODY

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The uterus is a muscle-elastic-collagen system of levers involved in stabilizing a woman's posture during pregnancy; being in an unusual state due to changes in the connective tissue elements of both the uterus and extrauterine structures. With the increase of the uterus during pregnancy, the recovery of the typical posture changes due to changes in its muscular and elastic apparatus and in elastic-collagen connections with the bones of the pelvis. It is important that the dense area of the ligaments is a collagen structure and is the least elastic component of this chain. The uterus is attached to the pelvis from the inside. In contrast, the areas of the external spiroid dynamic muscle chains are attached from the outside, thus entwining the body both homolaterally and heterolaterally. Based on the above, we hypothesize that these are synergistic and mutually competing biomechanical structures. Disturbance in the balance of these structures can lead to a suboptimal condition of the pregnant woman's body in statics and dynamics.
Key words: postural control, diaphragm, uterus, center of gravity, muscle spirals, biomechanics.

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БІОМЕХАНІЧНІ АСПЕКТИ ПОСТУРАЛЬНОГО КОНТРОЛЮ ТІЛА ЛЮДИНИ

Матка являє собою м'язово-еластично-колагенову систему важелів, що беруть участь у стабілізації пози жінки під час вагітності, перебуваючи в нехарактерному стані внаслідок змін сполучнотканинних елементів як матки, так позаматкових структур. При збільшенні матки під час вагітності змінюється відновлення типової постави за рахунок змін в її м'язово-еластичному апараті, а також в еластично-коллагенових зв'язках з кістками таза. Важливо, що щільна ділянка зв'язок є колагеновою структурою і є найменш еластичним компонентом цього ланцюга. Матка прикріплюється до малого тазу зсередини, а ділянки зовнішніх спіроїдних динамічних м'язових ланцюгів прикріплюються ззовні, обплітаючи тіло як гомолатерально, так і гетеролатерально. Виходячи з вищесказаного, ми припускаємо, що це синергетичні та взаємоконкуруючі біомеханічні структури. Порушення балансу цих структур може призвести до неоптимального стану організму вагітної в статиці та динаміці.
Ключові слова: постуральний контроль, діафрагма, матка, центр ваги, м'язові спіралі, біомеханіка.

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Postural control is the most important component of the static and dynamic balance of the human body [13]. The biomechanical explanation of the center of gravity is applied in the field of physical rehabilitation for the construction of dynamic models; in the choice of the optimum protocol of physical therapy; in determining the stability and angular acceleration of equipment used by people in various postural manifestations; in designing the aircraft seats; in the study of muscle biomechanics, etc [2, 11, 15].