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Impact of gestational diabetes and other maternal factors on neonatal body composition in the first week of life: a case-control study

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ABSTRACT

Objectives: Newborns of diabetic mothers are at increased risk of abnormal nutritional status at birth, thus developing metabolic disorders. The aim of this study was to evaluate the anthropometric measurements and body composition of newborns born to mothers with gestational diabetes in comparison to newborns born to mothers with normal glucose tolerance in pregnancy, in the first week of their life. Maternal factors affecting the gestational period were also evaluated.

Material and methods: The study included 70 participants: neonates born to mothers with gestational diabetes (GDM) and neonates born to healthy mothers (non-GDM). A set of statistical methods (*e.g.*, ANOVA, Kruskal-Wallis test, Chi-square test, regression, cluster analysis) was used to compare data between the study groups and to find their association with maternal factors.

Results: Our approach resulted in statistically significant classification ($p < 0.05$) by maternal history of hypothyroidism, weight gain during pregnancy and diagnosis of GDM. Newborns of mothers diagnosed with both GDM and hypothyroidism had lower birth weight and fat mass than newborns of mothers without GDM nor hypothyroidism ($p < 0.05$), however this finding might be associated with high incidence of excessive gestational weight gain among

healthy mothers. No differences in body composition were found between the study groups on account of maternal GDM only ($p > 0.05$).

Conclusions: Thus, well-controlled gestational diabetes mellitus as an individual factor does not significantly affect neonatal anthropometric measurements and body composition.

Key words: gestational diabetes; hypothyroidism; body composition; newborn; bioelectrical impedance

INTRODUCTION

Based on the theory of nutritional programming, a child's nutritional status in the first 1,000 days after conception has a significant impact on the neurological development, mental health throughout the life, and the risk of developing obesity, hypertension and diabetes [1, 2]. During this period, especially in prenatal life, nutritional programming largely depends on the quality of the mother's diet and her comorbidities, which affect the supply of nutrients for the fetus [1]. Moreover, events in prenatal life (*e.g.*, maternal comorbidities or nutritional status, maternal stress) altogether with genetic and environmental factors influence the determination of a certain pattern of physiological processes (Barker hypothesis) resulting in long-term adaptive changes in the developing fetus. These adaptive changes are initially favorable, because they adapt the fetus to cover the current needs, however they can have a detrimental effect in the long-term and enhance the risk of development of non-communicable diseases in the adulthood [2].

It has conclusively been shown that disturbances in the physical development of the fetus and an increased risk of postnatal metabolic complications constitute a typical clinical picture of an infant of a diabetic mother. Currently, it is estimated that gestational diabetes affects approximately 5.4% of women in Europe and 3.4% of women in Poland [3].

The newborns of diabetic mothers are observed with increased incidence of macrosomia, polyhydramnios, stillbirths, perinatal injuries and surgical deliveries. In the long term, maternal diabetes during pregnancy increases the risk of obesity, impaired glucose tolerance and diabetes in offspring, and in the case of uncontrolled diabetes, also neurological development disorders. Nevertheless, most of the above-mentioned complications result from overnutrition and fetal macrosomia, the primary source of which are maternal disorders of glucose and fat metabolism during pregnancy. Therefore, gestational diabetes requires special attention mainly for early diagnosis, appropriate treatment and metabolic control.

Consequently, newborns born by mothers with gestational diabetes require special care and increased observation [4–6].

Body composition disturbances in early life, including the prenatal period, might play a key role in the programming of a variety of health disorders in the future, including hypertension, type 2 diabetes and obesity [6, 7]. It is known that changes in fat mass (FBM) are associated with changes in total body water volume (TBW), mainly extracellular water volume (ECW) and extracellular water to intracellular water ratio (E/I ratio). So far, it has been shown that obesity is associated with a disturbed ratio of individual water compartments in the body, which is not normalized by weight reduction, probably due to primary alteration in haemodynamics and fluid regulation [8, 9].

Objectives

The aim of this study was to evaluate the anthropometric measurements and body composition of neonates born to mothers with gestational diabetes in comparison to neonates born to mothers with normal glucose tolerance in pregnancy, in the first week of their life. In the present paper we also aimed to find maternal factors affecting the gestational period that might have influence on newborns' body composition.

MATERIAL AND METHODS

All 70 participants came from Poland (Wroclaw University Hospital) and were enrolled in prospective, observational case-control study after birth. Inclusion criteria for the case and control groups were: mother's age 18 – 45 years; delivery at term (≥ 37 + 0/7 weeks of gestation) or near term (from 35 + 0/7 to 36 + 6/7 weeks of gestation), both by vaginal delivery and by caesarean section; single pregnancy; good condition of the child after birth (vigorous, cardiovascularly and respiratorily stable neonate, who did not require assistance in transition to extrauterine life), rated > 7 points on the Apgar score after the 1st minute of life; exclusive or predominant breastfeeding. Exclusion criteria were any clinical condition of the mother and/or the newborn that may negatively affect the nutritional status of the newborn (IUGR, lack of medical care during pregnancy, maternal addictions to alcohol or other psychoactive substances, nicotinism in pregnancy); uncontrolled asthma in the mother; metabolic diseases in the mother or newborn).

The results of assessment of body composition and anthropometric measurements of the newborn, clinical data on the course of pregnancy and maternal pregestational medical history, childbirth, puerperium (interview from mother) in the period of postnatal

hospitalization of the newborn in the Department of Neonatology, before discharge from the hospital (up to 7 days of age) were collected.

Maternal body weight changes during the pregnancy were analysed based on medical documentation. As gestational weight gain guidelines, that are based on prepregnancy body mass index (BMI), ranges for underweight, normal weight, overweight, and obese women, the categories of maternal gestational weight gain (below, within or above recommendations) were set in reference to American College of Obstetricians and Gynecologists Committee Opinion, that was approved by Polish Society of Gynaecologists and Obstetricians [3, 10].

Criteria for diagnosis of gestational diabetes (according to World Health Organization and American Diabetes Association, adopted by Polish Society of Gynaecologists and Obstetricians) based on Oral Glucose Tolerance Test (OGTT) with the use of 75 g of glucose state as follows and only one of them is enough to meet: 1) fasting blood glucose 92–125 mg/dL, 2) glycemia in 1 h OGTT ≥ 180 mg/dL, 3) blood glucose level in 2 h OGTT 153–199 mg/dL [3, 11, 12].

Management of maternal thyroid disorders and hypertension during pregnancy was consistent with international guidelines and recommendations, adopted in Poland [13–15]

Study groups

The 70 participants were being enrolled from December 2019 to February 2021. Study group was divided into 50 neonates born to mothers with Gestational Diabetes, treated with diet (GDM G1) or treated with insulin (GDM G2). The control group included 20 randomly assigned neonates of healthy non-diabetic mothers (non-GDM), born at similar gestational age, who met the eligibility criteria.

Based on the medical documentation and interview, none of the 70 mothers were diagnosed with chronic pregestational diabetes nor insulin resistance before the pregnancy. All the GDM mothers received regular medical control. A total of 20 mothers were diagnosed with chronic hypothyroidism and 13 mothers were diagnosed with gestational hypothyroidism — all of them were successfully treated with levothyroxine, which resulted in TSH level ≤ 2.5 mIU/L. Considering hypertension, it was chronic in 6 mothers and pregnancy — induced in 8 mothers — all women were treated with methyldopa. Nicotinism before pregnancy was found in 22 mothers — all of them claimed to quit smoking before the conception.

Ethical issues

The study was approved by the Bioethics Committee at the Medical University in Wroclaw (No. KB 773/2019, 35/2020, 407/2020). The written and informed consents were obtained from the mothers. The presented research results were carried out within the project registered in Clinical Trials (https://clinicaltrials.gov/), NCT04937348.

Anthropometric measurements

Anthropometric measurements were taken twice — after birth and just before the body composition analysis. On the day of body composition assessment, each newborn infant was weighed naked to the nearest 10 g on an electronic baby scale (RADWAG type WPT 6 / 15D). Crown-heel length (measured in recumbent position) and occipito-frontal circumference were measured to the nearest 0.5 cm by a standard disposable non-stretchy tape. The measurements taken before body composition analysis were made by the same investigator (K.K).

Body composition assessment

Neonatal body composition was evaluated using a noninvasive method of bioimpedance analysis (BIA), which determines particular body compartments based on electrical properties of human tissues [16]. As body tissues differ in electrical conductivity due to their various hydration, a low-level electrical current sent through the body during measurement is impeded and passes through tissues with various speeds. The device measures the signal, thus determines the resistance of the electrical current, estimates body water and based on equations calculates fat mass and lean mass. This method was chosen as it is easily available, portable, noninvasive and quick in use. Based on available literature, BIA appears to be an effective and reliable technique of body composition estimations as a single use method in infants and young children [17, 18].

The measurements were made with Body Composition Monitor (BCM, Fresenius Medical Care, Germany) and dedicated disposable electrodes BCM-FMC (< 25 kg). The measurements were made at 50 frequencies over a range from 5 to 1000 kHz, with amplitude of the electric current 0.8 mA. The measurements were performed in accordance with the manufacturer's instructions, by the same investigator (K.K.). During the examination the patients were undressed, lying in a supine position. Electrodes were attached at least two minutes before measurement to the dorsal sides of one hand and one foot, with two electrodes on each extremity, providing the most possible distal location and ensuring at least 2 cm distance between the electrodes. In each patient, the electrodes were placed on the right side

of the body, in similar locations — as the precision and reproducibility of electrodes placement was found important [19]. The placement of electrodes applied in the study is presented in Figure 1. The body composition assessment was made during the newborn's sleep, at least 1.5 hour after the last feeding.

Statistical analysis

For computations Microsoft Excel for Office 365 (Microsoft, Redmond, WA, USA), Statistica 13.3 (StatSoft, Inc., Tulsa, OK, USA) and R version 3.6.2 (R Core Team, 2013. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/.) [20–22] were used.

The data are presented as: mean and standard deviation (SD), or median and interquartile range (IQR), or number of cases and percentage, where applicable.

The level of significance in statistical analysis was set at $\alpha = 0.05$. Comparisons of demographic and clinical data between study groups were made with one-way ANOVA, Kruskal–Wallis test and Chi-square test, depending on the type of data and their distribution. Univariate regression (generalized linear model) was used to assess the impact of selected maternal factors on the studied neonatal anthropometric parameters and body composition. As the next step, a cluster analysis was performed using the Marczewski-Steinhaus' taxonomic approach (M–S) [23] and the dendrogram was built. The type effect was studied using one-way ANOVA. The verification of the taxonomic method was made using expectation-maximization (E–M) algorithm [24].

RESULTS

The overall characteristics of the newborns is presented in Table 1. There were 21 newborns in GDM G1 group, 29 newborns in GDM G2 group and 20 newborns in non-GDM group. In the whole study population median of gestational age at birth was 39.0 (IQR 2.0) weeks (range 37 41 weeks), with no significant differences between the study groups [$H (2, N = 70) = 3.246$, $p > 0.05$]. Approximately 71% (50/70) of the newborns were born by the cesarean section (main indications for cesarean section were previous cesarean section and lack of progress in labour) and 55.7% were girls — there were no significant differences in terms of sex [$\chi2 (2, N = 70) = 0.620$, $p > 0.05$] and mode of delivery [$\chi2 (2, N = 70) = 0.533$, $p > 0.05$] between the study groups. In the whole study population mean birth weight was 3.23 (± 0.45) kg (range 2.02–4.3 kg), mean length 53.2 (± 2.7) cm (range 47–61 cm), mean head circumference 34.7 (± 1.5) cm (range 31–38 cm). Also, these anthropometric

measurements taken after birth were comparable between newborns of diabetic and non-diabetic mothers [respectively birth weight $F(2, 67) = 2.633$ $p > 0.05$; length $F(2, 67) = 0.266$ $p > 0.05$; head circumference $F(2, 67) = 0.12$ $p > 0.05$]. There were no significant differences in prevalence of maternal hypothyroidism [$\chi 2(2, N = 70) = 6.343$, $p > 0.05$], hypertension [$\chi 2(2, N = 70) = 3.498$, $p > 0.05$] and nicotinism before pregnancy [$\chi 2(2, N = 70) = 1.032$, $p > 0.05$] between study groups. However, the mothers differed in BMI before pregnancy [$H(2, N = 70) = 8.537$, $p < 0.05$], with the highest values in GDM G2 group; and weight gain during pregnancy [$F(2, 67) = 12.923$, $p < 0.001$], with the highest values in non-GDM group.

Body composition and anthropometrics

The measurements were made between 2nd and 7th day of the neonate's life, with mode equal to 3 days of life. The newborns in each of the study groups had similar current body weight [$F(2, 67) = 2.894$, $p > 0.05$], length [$F(2, 67) = 0.266$, $p > 0.05$], and head circumference [$F(2, 67) = 0.12$, $p > 0.05$], as well as BMI [$F(2, 67) = 1.859$, $p > 0.05$] and PI [$F(2, 67) = 2.792$, $p > 0.05$]. No significant differences were found in body water compartments: TBW [$F(2, 67) = 1.038$, $p > 0.05$], TBW% [$F(2, 67) = 1.440$, $p > 0.05$], ECW [$H(2, 70) = 2.903$, $p > 0.05$], ICW [$F(2, 67) = 1.053$, $p > 0.05$], E/I [$H(2, N = 70) = 1.077$, $p > 0.05$]; body fat: FBM [$F(2, 67) = 2.758$, $p > 0.05$], FBM% [$F(2, 67) = 1.610$, $p > 0.05$]; and fat-free mass: LBM [$F(2, 67) = 2.071$, $p > 0.05$], LBM% [$F(2, 67) = 2.174$, $p > 0.05$]. The detailed results are summarized in Table 2.

Maternal factors

To assess the impact of maternal factors on neonatal birth weight, TBW and FBM, an univariate regression (generalized linear model) was performed. The analysis considered the study group (equal to the level of disturbances in glucose metabolism), maternal age, parity, gravidity, BMI before the pregnancy, weight gain during the pregnancy, and medical history of hypothyroidism, hypertension, nicotinism. Among all factors: belonging to a particular study group and maternal history of hypothyroidism were found significant. Based on AIC values, the following factors: belonging to a particular study group and maternal history of hypothyroidism, maternal weight gain during the pregnancy were chosen as best-fitting predictors of neonatal anthropometrics and body composition. The results are presented in Supplemental Table 1.

Cluster analysis

Based on the identified three factors: belonging to a particular study group, maternal history of hypothyroidism and weight gain during pregnancy, a classification tree of patients was created (Suppl. Fig. 1.) The dendrogram presents four types of patients — the characteristics of identified types of patients are presented in Table 3. ‘Cluster 1’ included newborns of mothers diagnosed with gestational diabetes, without any thyroid disfunctions. ‘Cluster 2’ included newborns of mothers diagnosed both with gestational diabetes and hypothyroidism. ‘Cluster 3’ included newborns of healthy mothers, without any diabetic nor thyroid disorders. ‘Cluster 4’ included newborns of non-diabetic mothers with concomitant hypothyroidism. The highest maternal weight gain was observed in ‘Cluster 2’. The post-hoc Turkey-Kramer test revealed differences in maternal weight gain in pregnancy between clusters, as follows: ‘Cluster 1’ — ’Cluster 2’ $p = 0.999$; ‘Cluster 1’ — ’Cluster 3’ $p < 0.001$; ‘Cluster 1’ — ’Cluster 4’ $p = 0.057$; ‘Cluster 2’ — ’Cluster 3’ $p < 0.001$; ‘Cluster 2’ — ’Cluster 4’ $p = 0.047$; ’Cluster 3’ — ’Cluster 4’ $p = 0.983$. Chi-square analysis revealed a non-significant difference between clusters in maternal weight gain during pregnancy in reference to pre-gestational BMI [$\chi 2$ (6, N = 70) = 11.12, $p = 0.08$]. In ‘Cluster 3’, weight gain above recommendations was found in 10/14 mothers (71.4%), while in ‘Cluster 1’ — in 5/23 mothers (21.7%), in ‘Cluster 2’ — in 8/27 mothers (29.6%) and in ‘Cluster 4’ — in 3/6 mothers (50.0%). Weight gain within recommendations was achieved by 11/23 (47.8%) mothers in ‘Cluster 1’, 10/27 (37.0%) in ‘Cluster 2’, 3/14 (21.4%) in ‘Cluster 3’, and 2/6 (33.3%) in ‘Cluster 4.’ The remaining mothers in each of the clusters had weight gain below recommendations.

From the statistical comparison of clusters, which is presented in Table 4., we can see those newborns in ‘Cluster 2’ and ‘Cluster 3’ differed significantly in terms of: birth weight and FBM. Although, there were no other significant differences between the clusters of newborns, several differences in general results of anthropometric and body composition measurements can be observed. Mean (SD) newborns' birth weight in each of the clusters was: ‘Cluster 1’ 3.39 (± 0.49) kg, ‘Cluster 2’ 3.35 (± 0.51) kg, ‘Cluster 3’ 3.77 (± 0.41) kg, ‘Cluster 4’ 3.39 (± 0.22) kg. Considering total body water and body water compartments, mean (SD) values were found as follows: ‘Cluster 1’: TBW 2.6 (± 0.4) l, TBW% 83.4 (± 6.7)%, ECW 0.9 (± 0.2) l, ICW 1.8 (± 0.2) l, E/I 0.5 (±0.1); ‘Cluster 2’: TBW 2.6 (± 0.4) l, TBW% 81.6 (± 5.9)%, ECW 0.9 (± 0.2) l, ICW 1.7 (± 0.3) l, E/I 0.5 (±0.1); ‘Cluster 3’: TBW 2.9 (± 0.4) l, TBW% 81.9 (± 6.9)%, ECW 1.0 (± 0.2), ICW 1.9 (± 0.3), E/I 0.5 (± 0.1); ‘Cluster 4’: TBW 2.5 (± 0.2) l, TBW% 76.6 (± 4.4)%, ECW 0.8 (± 0.1) l, ICW 1.6 (± 0.2) l,

E/I 0.5 (± 0.1). Concerning FBM and FBM%, means (SD) were: ‘Cluster 1’ FBM 0.26 (± 0.1) kg, FBM% 7.9 (± 2.3)%; ‘Cluster 2’ FBM 0.25 (± 0.1) kg, FBM% 7.9 (± 2.3)%; ‘Cluster 3’ FBM 0.34 (± 0.1) kg, FBM% 9.6 (± 2.0)%; ‘Cluster 4’ FBM 0.22 (± 0.1) kg, FBM% 7.0 (± 2.1)%. The visual comparison of results obtained in clusters is illustrated in Figure 2.

DISCUSSION

It is already well-known that severity of metabolic disorders during pregnancy and the increase in mother's weight determine the nutritional status of the newborn. Based on the literature, maternal weight gain is a significant factor that might modify influence of other maternal conditions (e.g., thyroid disorders, glucose metabolic disorder, pregestational obesity or undernutrition) on fetal growth and neonatal nutritional status at birth (including body anthropometrics and fat tissue mass). Maayan-Metzger et al. [25] showed that newborns of mothers whose weight gain exceeded the recommended norms had higher birth weight and were more likely to be born by caesarean section. Moreover, these mothers were diagnosed with gestational diabetes requiring insulin therapy. Similar research results were obtained by Wang et al. [26] — among the studied women with diagnosed gestational diabetes, excessive gestational weight gain was a significant risk factor for fetal macrosomia [OR 2.884, 95% CI 1.385–6.004]. A significant effect on the development of the fetus was also demonstrated regarding high fasting blood glucose [OR 1.933, 95% CI 1.126–3.316] and elevated serum triglycerides in the third trimester of pregnancy [OR 1.235, 95% CI 1.053–1.449]. In the study conducted by Abreu et al. [27], newborns of diabetic mothers had higher body fat content than newborns from healthy mothers. However, the main predictors of fat mass were maternal BMI before pregnancy [OR 6.75; 95% CI 2.36–11.1] and pregnancy weight gain [OR 5.64; 95% CI 1.16-10.1].

Considering hypothyroidism, Zhang et al. [28] found that persistently low levels of maternal fT3 and fT4 during the pregnancy increase a risk of large for gestational age (LGA) birth weight in a newborn, but the role of TSH level is unclear. It was also observed that adequate treatment with levothyroxine reduced a risk of fetal and neonatal macrosomia. Similar results were obtained by Turunen et al. [29] — the higher prevalence of LGA newborn was found in hypothyroid mothers than in euthyroid mothers (OR 1.14, 95% CI 1.06–1.22). Moreover, in the studied population, maternal hypothyroidism was associated with higher risk of developing gestational diabetes and LGA in newborns, but this risk was not altered by regular levothyroxine treatment.

The results of our study seem to be consistent with the abovementioned results. In general, the biggest mean values of birth weight, TBW, ICW, FBM, FBM% were found in ‘Cluster 3’ including newborns of non-GDM mothers without hypothyroidism, but with the highest weight gain in pregnancy and the highest rate of weight gain above recommendations in reference to pre-gestational BMI among the whole group. Whereas the lowest mean values of birth weight, TBW, TBW%, ICW, FBM, FBM% were found in ‘Cluster 4’ including newborns born of non-GDM mothers diagnosed with hypothyroidism, whose mean weight gain in pregnancy was lower than in ‘Cluster 3’ but higher than in ‘Cluster 1’ and ‘Cluster 2’. Values of ECW and E/I were comparable between all clusters.

The mothers participating in the study had well-controlled diabetes and regularly treated hypothyroidism. Hence, the influence of glucose disorders and hypothyroidism may not be as pronounced. However, the effect of maternal weight gain during pregnancy is clearly visible — newborns of mothers with excessive weight gain in pregnancy (‘Cluster 3’) were found with higher birth weight and FBM than the other newborns. On the other hand, when mean maternal weight gain was higher than in other groups, but within ranges recommended for pre-gestational BMI, its effect on neonatal body composition was not prominent (‘Cluster 4’ vs ‘Cluster 1’ or ‘Cluster 2’). Furthermore, mothers diagnosed with GDM had the highest mean pre-gestational BMI, but their gestational weight gain was within normal ranges, and their newborns were generally smaller than newborns of non-GDM mothers. Thus, the results of the study indicate that maternal weight gain in pregnancy has higher impact on neonatal body composition than maternal pre-gestational BMI.

Considering the diagnosis of hypothyroidism, the mean results were comparable between newborns of GDM mothers with vs without hypothyroidism (‘Cluster 2’ vs ‘Cluster 1’), whereas among newborns of non-GDM mothers, those born out of mothers without hypothyroidism (but highest weight gain, often exceeding recommendations) had higher values of birth weight, TBW, TBW%, ICW, FBM and FBM% (‘Cluster 3’ vs ‘Cluster 4’). Considering the diagnosis of GDM, among newborns of mothers without hypothyroidism, those in non-GDM group had higher values of birth weight, TBW, ICW, FBM, FBM% (‘Cluster 3’ vs ‘Cluster 1’) and comparable TBW%, ECW, E/I, but also in this group maternal weight gain was significantly higher (16.5 ± 5.9 kg vs 11.2 ± 5.7 kg). In the groups of newborns of mothers diagnosed with hypothyroidism, apart from TBW% and FBM% that were moderately lower in non-GDM newborns, all mean results were found comparable (‘Cluster 4’ vs ‘Cluster 2).

In authors' opinion, the abovementioned results and similarities between groups of patients, thus limited influence of gestational diabetes and hypothyroidism on neonatal anthropometrics in the first days of life might result from appropriate maternal treatment and good compliance with medical recommendations. However, cluster abundance is the study limitation and continuation on a larger population is necessary to clarify these results.

It needs to be emphasized that the application of taxonomic analysis has enabled us to identify significant groups of patients, based on the results of a combination of several risk factors. This approach might be helpful in explicating the pathophysiology of fetal growth and neonatal outcomes in context of maternal comorbidities.

CONCLUSIONS

Neonatal anthropometrics and body composition in the first week of life are affected by a combination of maternal factors, with prominent effects of modifiable factors such as: glycemic control in gestational diabetes, sufficient supplementation of levothyroxine in hypothyroidism and gestational weight gain. Well-controlled GDM as an individual factor did not significantly affect neonatal nutritional status. Maternal weight gain during pregnancy, with reference to recommendations based on pregestational BMI, seems to be the most important determinant of neonatal birth weight, adiposity and body water distribution. Further research is needed, as newborn body composition is likely to be an important determinant of long-term health status.

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Conflict of interest

The authors declare no conflict of interest.

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Table 1. Characteristics of the study population (n = 70)

	All newborns (n = 70)	**GDM G1 (n = 21)**	**GDM G2 (n = 29)**	**non-GDM (n = 20)**	**p value**
Gestational age [weeks], Median (IQR)	39.0 (2.0)	39.0 (2.0)	38.0 (1.0)	39.0 (2.0)	0.197[a]
Sex, N (%)					
Boys	28 (40.0)	7 (33.3)	12 (41.4)	9 (45.0)	0.733[c]
Girls	52 (60.0)	14 (66.7)	17 (58.6)	11 (55.0)	
Mode of delivery, n (%)					
Vaginal birth	20 (28.6)	7 (33.3)	7 (24.1)	6 (30.0)	0.766[c]
Cesarean section	50 (71.4)	14 (66.7)	22 (75.9)	14 (70.0)	
Birth weight [kg], Mean (SD)	3.45 (0.48)	3.41 (0.57)	3.34 (0.44)	3.65 (0.4)	0.079[b]
Length [cm], Mean (SD)	53.2 (2.8)	53.0 (3.5)	53.1 (2.5)	53.6 (2.3)	0.767[b]
Head circumference [cm], Mean (SD)	34.7 (1.5)	34.5 (1.6)	34.8 (1.6)	34.7 (1.6)	0.887[b]
Maternal age [years], Mean (SD)	32.7 (4.5)	33.9 (4.9)	32.1 (4.6)	32.5 (3.9)	0.363[b]
Gravidity, Median (IQR)	2.0 (1.0)	2.0 (2.0)	2.0 (1.0)	2.0 (1.0)	0.520[a]
Parity, Median (IQR)	2.0 (1.0)	1.0 (1.0)	1.0 (1.0)	2.0 (1.0)	0.395[a]
Maternal BMI before pregnancy, Median (IQR)	24.17 (6.40)	23.34 (3.48)	28.04 (6.80)	22.96 (2.83)	0.014[a]
Maternal BMI before pregnancy, n (%)					
Normal	40 (57.1)	14 (66.7)	9 (31.0)	17 (85.0)	0.004[c]
Overweight	16 (22.9)	4 (19.0)	11 (38.0)	1 (5.0)	
Obese	14 (20.0)	3 (14.3)	9 (31.0)	2 (10.0)	
Maternal weight gain during pregnancy [kg], Mean (SD)	11.5 (5.7)	10.2 (3.5)	9.2 (5.4)	16.2 (5.4)	< 0.001[b]
Maternal weight gain during pregnancy in reference to pre-gestational BMI,					

n (%)					
Below recommendations	18 (25.8)	7 (33.3)	9 (31.0)	2 (10.0)	
Within recommendations	26 (37.1)	10 (47.7)	11 (38.0)	5 (25.0)	0.033[c]
Above recommendations	26 (37.1)	4 (19.0)	9 (31.0)	13 (65.0)	
Maternal history of hypertension, n (%)					
Chronic (onset before the pregnancy)	6 (8.6)	1 (4.8)	5 (17.2)	0	
Pregnancy induced	8 (11.4)	2 (9.5)	5 (17.2)	1 (5.0)	0.478[c]
None	56 (80.0)	18 (85.7)	19 (65.6)	19 (95.0)	
Maternal history of hypothyroidism, n (%)					
Chronic (onset before the pregnancy)	20 (28.6)	6 (28.6)	12 (41.4)	2 (10.0)	
Gestational (onset during the pregnancy)	13 (18.6)	5 (23.8)	4 (13.8)	4 (20.0)	0.175[c]
None	37 (52.9)	10 (47.6)	13 (44.8)	14 (70.0)	
Nicotinism before pregnancy, n (%)	22 (31.4)	6 (28.6)	11 (37.9)	5 (25.0)	0.597[c]

a — Kruskal-Wallis test; b — one-way ANOVA; SD — standard deviation; IQR — interquartile range; BMI — body mass index

Table 2. Results of the anthropometric measurements and body composition analysis in newborns (n = 70)

	GDM G1 (n = 21)	**GDM G2 (n = 29)**	**non-GDM (n = 20)**	**p value**
Chronological age [days], Median (IQR)	3.0 (1.0)	4.0 (1.0)	3.0 (0.5)	0.253[a]
Current weight [kg], Mean (SD)	3.21 (0.53)	3.12 (0.41)	3.42 (0.35)	0.062[b]
Length [cm], Mean (SD)	53.0 (3.5)	53.1 (2.5)	53.6 (2.3)	0.767[b]
Head circumference [cm], Mean (SD)	34.5 (1.6)	34.8 (1.6)	34.7 (1.6)	0.887[b]

BMI [kg/m^2], Mean (SD)	11.36 (1.21)	11.09 (1.18)	11.93 (1.21)	0.164[b]
PI [kg/m^3], Mean (SD)	2.16 (0.27)	2.09 (0.25)	2.24 (0.28)	0.058[b]
TBW [l], Mean (SD)	2.6 (0.5)	2.6 (0.4)	2.7 (0.4)	0.360[b]
TBW%, Mean (SD)	81.2 (4.7)	82.67 (6.77)	80.31 (6.63)	0.244[b]
ECW [l], Median (IQR)	0.8 (0.3)	0.9 (0.1)	0.9 (0.2)	0.234[a]
ICW [l], Mean (SD)	1.7 (0.3)	1.7 (0.3)	1.8 (0.3)	0.355[b]
E/I, Median (IQR)	0.4 (0.1)	0.5 (0.1)	0.5 (0.1)	0.584[a]
FBM [kg], Mean (SD)	0.27 (0.1)	0.24 (0.1)	0.31 (0.1)	0.071[b]
FBM%, Mean (SD)	8.32 (2.24)	7.5 (2.55)	9.19 (2.21)	0.208[b]
FFM [kg], Mean (SD)	2.93 (0.46)	2.89 (0.36)	3.11 (0.3)	0.142[b]
FFM%, Mean (SD)	91.62 (2.29)	92.51 (2.54)	90.96 (2.56)	0.122[b]

a — Kruskal-Wallis test; b — one-way ANOVA; SD — standard deviation; IQR — interquartile range; BMI — body mass index; PI — ponderal index; TBW — total body water; ECW — extracellular water; ICW — intracellular water; E/I — extracellular/intracellular water ratio; FBM — fat mass; FFM — fat-free mass

Table 3. Characteristics of newborns in clusters, following one-way ANOVA

Cluster	**n**	**Study group**			**History of hypothyroidism**			**Weight gain during pregnancy [kg] (Mean ± SD)**
		GDM G1 (n)	**GDM G2 (n)**	**Non-GDM (n)**	**Chronic (n)**	**Gestational (n)**	**None (n)**	
1	23	10	13	0	0	0	23	11.1 ± 5.7
2	27	11	16	0	18	9	0	11.2 ± 5.7
3	14	0	0	14	0	0	14	16.5 ± 5.9
4	6	0	0	6	2	4	0	15.6 ± 1.7
F statistic	-	n/a			n/a			8.31
p value	-	n/a			n/a			< 0.001

n/a — non applicable

Table 4. Multiple comparisons between clusters (post-hoc Turkey-Kramer and Dunn's test p values) for selected parameters of neonatal anthropometrics and body composition

Difference between	Birth	TBW [l]	TBW%	ECW	ICW [l]	E/I	FBM	FBM%

clusters	weight [kg]			[l]			[kg]	
1–2	0.987	0.833	0.761	1.0	0.821	1.0	0.978	1.0
1–3	0.099	0.298	0.905	0.605	0.267	1.0	0.061	0.135
1–4	1.0	0.678	0.104	0.524	0.599	1.0	0.859	0.815
2–3	0.043*	0.062	0.999	1.0	0.050	1.0	0.021*	0.109
2–4	0.998	0.929	0.312	1.0	0.888	1.0	0.946	0.823
3–4	0.348	0.113	0.327	1.0	0.078	1.0	0.067	0.097

* — statistically significant (α = 0.05)

TBW — total body water, ECW — extracellular water, ICW — intracellular water, E/I — extracellular/intracellular water ratio, FBM — fat mass

Figure 1. Placement of the electrodes during body bioimpedance analysis

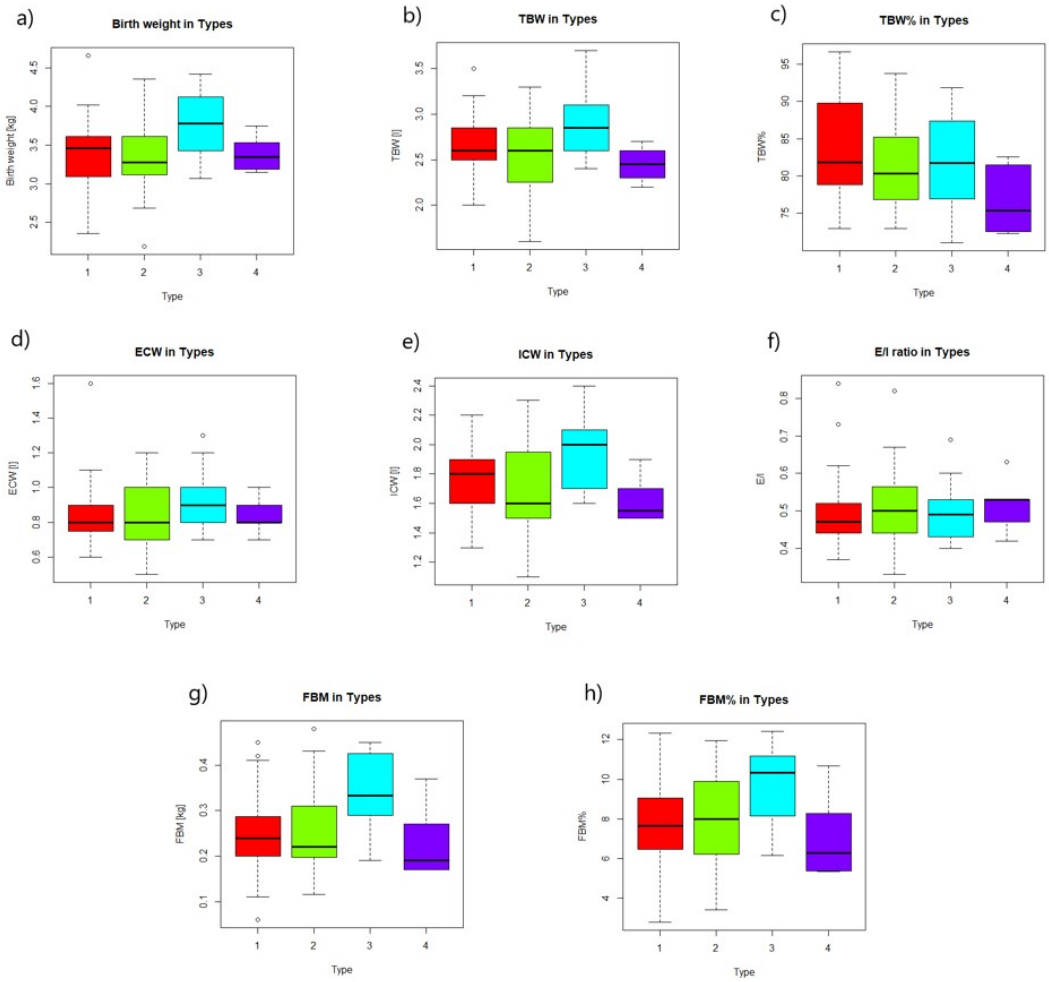

Figure 2. Plot of mean selected parameters of neonatal anthropometrics and body composition in types (clusters): **A.** birth weight; **B.** total body water [kg]; **C.** total body water percentage; **D.** extracellular water [l]; **E.** intracellular water [l]; **F.** extra/intracellular water ratio; **G.** fat mass [kg]; **H.** fat mass percentage. The horizontal axis presents numbers of clusters matching each of the box plots: ‘Cluster 1’ — GDM without hypothyroidism, ‘Cluster 2’ — GDM with hypothyroidism, ‘Cluster 3’ — non-GDM without hypothyroidism, ‘Cluster 4’ — non-GDM with hypothyroidism; notice the maternal gestational weight gain differed in clusters — details in text and in Table 3. Newborns in ‘Cluster 2’ and ‘Cluster 3’ differed significantly in terms of: birth weight and FBM

SUPPLEMENTAL FILES

Supplemental Table 1. Results of univariate regression analysis

Variable	Coefficient	p value	AIC
Birth weight			
Study group	–0.149	0.032*	97.38**
Maternal age	–0.004	0.723	102.03
Parity	0.062	0.355	101.27
Gravidity	0.069	0.213	100.55
Maternal BMI before the pregnancy	0.017	0.112	99.53
Maternal weight gain during the pregnancy	0.019	0.059	98.48**
Medical history of hypothyroidism	–0.114	0.088	99.13**
Medical history of hypertension	0.083	0.512	100.94
Medical history of nicotinism	–0.127	0.279	101.71
TBW			
Study group	–0.073	0.211	73.42
Maternal age	–0.011	0.315	73.99
Parity	0.082	0.135	72.73
Gravidity	0.075	0.101	72.26
Maternal BMI before the pregnancy	0.009	0.286	73.86
Maternal weight gain during the pregnancy	0.015	0.085	71.98**
Medical history of hypothyroidism	–0.123	0.013*	69.42**
Medical history of hypertension	0.007	0.943	75.04
Medical history of nicotinism	0.145	0.159	72.99
FBM			
Study group	0.033	0.021*	–126.33**
Maternal age	<0.001	0.850	–120.83
Parity	0.004	0.772	–120.88
Gravidity	0.004	0.755	–120.89

Maternal BMI before the pregnancy	0.002	0.374	–121.61
Maternal weight gain during the pregnancy	0.002	0.352	–121.69
Medical history of hypothyroidism	–0.024	0.075	–124.08**
Medical history of hypertension	–0.026	0.286	–121.97
Medical history of nicotinism	–0.001	0.967	–120.79

*— significant at $p < 0.05$; ** — best–fitting variables according to AIC values; TBW — total body water; FBM — fat mass; BMI — body mass index; AIC — Akaike information criterion

Supplemental Figure 1. Dendrogram of the newborns. The y–axis (height) shows the value of distance metric (dissimilarity) between clusters. Horizontal bars indicate the points where clusters are merged. P identifies each of the 70 patients