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Chorionic thickness and PlGF concentrations as early predictors of small-for-gestational age birth weight in a low risk population

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ABSTRACT

Objectives: SGA is associated with higher incidence of postnatal complications, including suboptimal neurodevelopment and increased cardiovascular risk. Screening for SGA, carried out at 11–13 (+ 6d) gestational weeks enables to reduce or completely eliminate the above mentioned complications. The aim of this study was to assess the correlation between chorionic thickness, concentration of PlGF protein and foetal birth weight in a single low-risk pregnancy.

Material and methods: The study included 76 patients at 11–13 (+ 6d) gestational weeks, monitored throughout pregnancy. Ultrasound examinations identified the location and thickness of the chorion by measuring it in its central part at its widest point in a sagittal section. Additionally, at each visit venous blood was collected to determine the level of PlGF, PAPP-A, and BhCG.

Results: A significant positive correlation (r = 0.37) was found between the foetal weight and chorionic thickness. This correlation was affected by the location of the chorion and a significant negative correlation was observed between the level of PLGF, FHR, weight and length of the newborn. Maternal early-pregnancy BMI did not affect neonatal weight and body length, FHR, chorionic thickness, and the levels of PlGF, PAPP-A, and BhCG.

Conclusions: The preliminary analysis indicates an association between chorionic thickness assessed during ultrasound at 11–13 (+ 6d) gestational weeks, PlGF levels assayed at the same time and birth weight. Increasing chorion thickness was accompanied by increasing foetal birth weight. PlGF level showed an inversely proportional effect on the foetal weight. This correlation was significant for the posterior location of the chorion.

Key words: SGA, chorion thickness, newborn birth weight, ultrasound

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INTRODUCTION

The term 'small for gestational age' (SGA) has been coined to denote foetuses unable to reach normal body weight (defined as the 10th percentile in a growth chart) [1]. Although normal umbilical blood flow has been shown in SGA foetuses towards the end of pregnancy, the low birth

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weight is associated with numerous postnatal complications. These include abnormal neuromotor development and increased cardiovascular risk, as compared to normal birth weight neonates [2].

Proper identification of pregnant women at risk of intrauterine hypotrophy enables increased pregnancy monitoring in selected cases, early treatment of potential maternal conditions, which increase the risk of abnormal foetal development, in order to reduce or eliminate the previously mentioned complications. The contemporary model of antenatal care aims at performing all risk assessments, including the risk of complications, such as abnormal foetal development, during the first trimester. Plethora of research carried out in order to determine high sensitivity screening test for SGA is based on the findings of ultrasound assessment at 11–13 (+ 6d) gestational weeks and maternal serum biomarkers assayed at the same time.

The chorion, followed by the placenta at later stages of pregnancy, plays the key role in supplying the growing foetus with oxygen and nutrients, thus ensuring its normal development. Abnormal cytotrophoblast invasion (implantation) leads to the decreased placental blood flow, which is one of secondary causes of abnormal foetal development. Size, shape and maturity of the placenta strongly correlate with the birth weight [3–6]. Currently, the only standard element of ultrasound-based assessment of the chorion (placenta) includes determining its location relative to the internal cervical os [3–6]. In recent years, though, studies have been published, which suggest correlation between chorionic volume and intrauterine hypotrophy.

Until recently, the narrow laboratory test panel for the first trimester included maternal serum PAPP-A and BhCG assays only. Nowadays, though, the research has focused on extending it by additional biomarkers, such as P13, PTX-3 , sFLT-1,VEGF-1, sP-selectin and fibronectin, which may help assess the risk of developing an individual clinical condition later in pregnancy. In recent years, some attention has been paid to the placental growth factor (PlGF), which is one of the vascular endothelial growth factors (VEGF). Produced by trophoblast cells, PlGF is essential for normal placental development. Low serum free PlGF levels were seen in the first and second trimester of pregnancy in women presenting subsequently with preeclampsia [7–10]. Low urinary PlGF levels were seen at 25–28 gestational weeks in women presenting subsequently with late-onset preeclampsia. Furthermore, its predictive value in Down Syndrome and other chromosomal disorders has been established [11].

OBJECTIVES

The aim of the research was to determine the association between chorionic thickness, PlGF levels and ultimate birth weight in a single low-risk pregnancy.

MATERIAL AND METHODS

The study included 76 patients of the Antenatal Clinic of the Podhalański Specialist Hospital in Nowy Targ. Their gestational age on enrolment was 11 to 13 (+ 6d) weeks.

All patients were informed about the purpose and scope of the research, and gave their informed consent to participate.

The mean patient age was 28.3 years. The cohort consisted of 34 primigravida and 42 multigravida. The mean maternal BMI was 24.4 (kg/m^2). Comorbidities were present in three females: one case of factor V Leiden thrombophilia, hyperlipidaemia and polycystic kidney disease, respectively. All analysed pregnancies ended in term live birth (at or after 37 gestational weeks) with caesarean section performed in 18 cases, as compared to 57 cases of vaginal delivery. The lowest birth weight was 1900 g (at 37 gestational weeks) and the highest birth weight was 4600 g (at 41 gestational weeks). The standard ultrasound assessment at 11–13 (+ 6d) gestational weeks demonstrated the location of the chorion on the anterior uterine wall in 44 cases and on the posterior uterine wall in 32 cases (Tab. 1).

Survey-based history was taken from all enrolled patients. It included such data as:

- maternal age,
- maternal education level,
- gravidity and parity,
- comorbidities,
- complications in previous pregnancies *(in multigravida only),
- smoking status,
- use of contraception before pregnancy
- barrier, vs. hormone.

The antenatal ultrasound performed at 11–13 (+ 6d) gestational weeks aimed at assessing the following:

- foetal anatomy and chromosomal aberration biomarkers, in line with assessment standards set out by the Ultrasound Section of the Polish Society of Gynaecology (foetal biometry: CRL, BPD, and chromosomal aberration biomarkers: NT, NB, DV),
- uterine artery blood flow,
- chorionic thickness, measured centrally at the widest point in sagittal view, perpendicularly to chorionic-uterine interface.

During the study visit, a blood sample was collected in each patient for the following tests: PAPP-A, B-hCG and PlGF. The collected venous blood samples were maintained at room temperature for 30–40 minutes, until clotted. The serum was separated within 24 hours following sample collection. The preprocessed blood samples were frozen at –20°C. Next, the samples were transported under storage conditions determined by DHL, by special courier delivery to the Central Laboratory, Gynaecology and Obstetrics

Table 1. Characteristics of the research material		
Maternal age [years] mean ± SD (min-max)		28.3 + 4.9 (19–41)
Maternal body weight [kg] mean ± SD (min-max)		65.7 + 12.6 (44.6–99)
Maternal body height [cm] mean ± SD (min-max)		164.5 + 6.1 (150–176)
Maternal body mass index [kg/m^2] mean ± SD (min-max)		24.4 + 4.8 (17.6–39)
BMI-based nutritional status assessment	Underweight n (%)	6 (7.9%)
	Normal n (%)	42 (55.3%)
	Overweight n (%)	15 (19.7%)
	Obese n (%)	13 (17.1%)
Pregnancy duration — mean ± SD (min-max)		39.3 + 1.2 (37–41)
Delivery method	Caesarean section n (%)	18 (24%)
	Vaginal delivery n (%)	58 (76%)
Birth weight [g] mean ± SD (min-max)		3342 ± 454 (1900–4600)
Birth length [g] mean ± SD (min-max)		55 ± 2 (47–61)
Number of pregnancies	Primigravida n (%)	34 (44.7%)
	Multigravida n (%)	42 (55.3%)
Use of contraceptives	No n (%)	70 (92.1%)
	Hormone n (%)	5 (6.6%)
	Barrier n (%)	1 (1.3%)
Location of the chorion	Anterior wall n (%)	44 (57.9%)
	Posterior wall n (%)	32 (42.1%)

University Hospital of K. Marcinkowski Poznań University of Medical Sciences, where PlGF, PAPP-A and BhCG levels were determined in ISO9000-certified laboratory facilities.

The PlGF level was determined using the immunofluorometric assay on DELFIA Xpress analyser. The method involves coating the surface of the reaction cup with the specific IgG capture antibody targeting the respective determinant of the PlGF molecule present in the serum. The labelled non-specific, detection antibody is applied to target another determinant of the molecule. It is followed by the 20-minute incubation at +35°, when the antibodies bind to their target determinants. Next, the reaction cup is washed in order to remove excess unbound antibodies, so that the reaction mix contains only analyte antibody complexes. Subsequently, an inducer is added to the mix. It releases the label from the 'sandwich' complex and induces its fluorescence. The fluorescence is measured at 612 nm, and its intensity is directly proportional to the PlGF level.

PAPP-A — Pregnancy Associated Placental Protein is a metalloproteinase derivative synthesized in the syncytiotrophoblast, which cleaves the IGF-binding proteins and ensures appropriate trophoblast implantation [12]. The PAPP-A levels were determined using immunofluorometric assay on DELFIA Xpress analyzer, which involves coating the surface of the reaction cup with the specific IgG capture antibody targeting the respective determinant of the PAPP-A/proMBP complex present in the serum. The Europium-labelled non-specific, detection antibody is applied to target another determinant of the molecule. It is followed by the 20-minute incubation at +35°, when the antibodies bind to their target determinants. Next, the reaction cup is washed in order to remove excess unbound antibodies, so that the reaction mix contains only analyte antibody complexes. Subsequently, an inducer is added to the mix. It releases the label from the 'sandwich' complex and induces its fluorescence. The fluorescence is measured at 612 nm, and its intensity is directly proportional to the PAPP-A level.

Human chorionic gonadotropin (hCG) is a glycoprotein hormone (molecular weight of ~37 kDa) consisting of two noncovalently bound dissimilar subunits, designated α and β (molecular weight of ~15 and 22 kDa, respectively). HCG is secreted by trophoblast cells in the placenta and its role involves maintaining the corpus luteum over the early weeks of pregnancy. Additionally, it is known to regulate steroid production [13, 14]. The β-hCG assay, measuring the level of its free β subunit, is a multi-step process. The first stage involves incubation. The 10 µL sandwich complex sample contains biotinylated, monoclonal βhCG-specific antibody and a ruthenylated, βhCG-specific antibody. After

streptavidin coated microparticles are applied, the complex binds to the solid phase via biotin — streptavidin affinity-mediated interactions. The reaction mix is then transferred to a measuring cell, where the microparticles are magnetically captured onto the surface of the electrode. The unbound particles are removed using the ProCell/ProCell M washing reagents. Afterwards, the electrochemiluminescence reaction and photon emission are induced by applying a voltage to the electrode and measured using the photomultiplier. The results are determined via a calibration curve which is instrument-specifically generated by a 2-point calibration and a master curve provided via the reagent barcode.

Statistical analysis included univariate and bivariate ANOVA as well as Pearson linear correlation. The p value ≤ 0.05 was considered statistically significant. Distribution normality for all analysed parameters in the entire cohort and the identified subgroups was assessed using the Shapiro-Wilk test.

RESULTS

The correlation analysis revealed a significant positive correlation (r = 0.37) between the birth weight and chorionic thickness in the first trimester in the entire cohort. Similarly, a statistically significant correlation (r = 0.42) was demonstrated in the arm with the chorion located on the anterior uterine wall. In the arm with the chorion located on the posterior uterine wall, a statistically insignificant trend towards the positive correlation (r = 0.33, p = 0.06) between chorionic thickness and ultimate birth weight was noticed. However, a statistically significant positive correlation (r = 0.35) between the birth length and chorionic thickness in the first trimester was demonstrated in this arm (Tab. 2, Fig. 1).

A statistically significant negative correlation was demonstrated in the study cohort between the maternal serum PIGF levels, foetal heart rate (FHR), birth weight and length, which was not confirmed in the arm with the chorion located on the anterior uterine wall. In the arm with the location of chorion at the posterior uterine wall, a statistically

Table 2.The correlation between the level of proteins in maternal serum, chorionic thickness in the first trimester, foetal heart rate in the first trimester and the ultimate birth parameters

Group		Chorionic thickness [mm]	PIGF [mU/L]	PAPP-A [mU/L]	BhCG [ng/mL]
Total	FHR [min]	r = 0.0632	r = –0.4577	r = –0.2158	r = 0.2833
		n = 76	n = 65	n = 75	n = 75
		p = 0.587	p = 0.000	p = 0.063	p = 0.014
	Birth weight [g]	r = 0.3687	r = –0.2641	r= –0.1493	r = –0.0195
		n = 76	n = 65	n = 75	n = 75
		p =0.001	p = 0.034	p = 0.201	p = 0.868
	Birth lenght [cm]	r = 0.2199	r = –0.2683	r= –0.0378	r = 0.0918
		n = 76	n = 65	n = 75	n = 75
		p = 0.056	p = 0.031	p = 0.748	p = 0.434

r — Pearson linear correlation coefficient; n — number of cases; p — statistical significance level

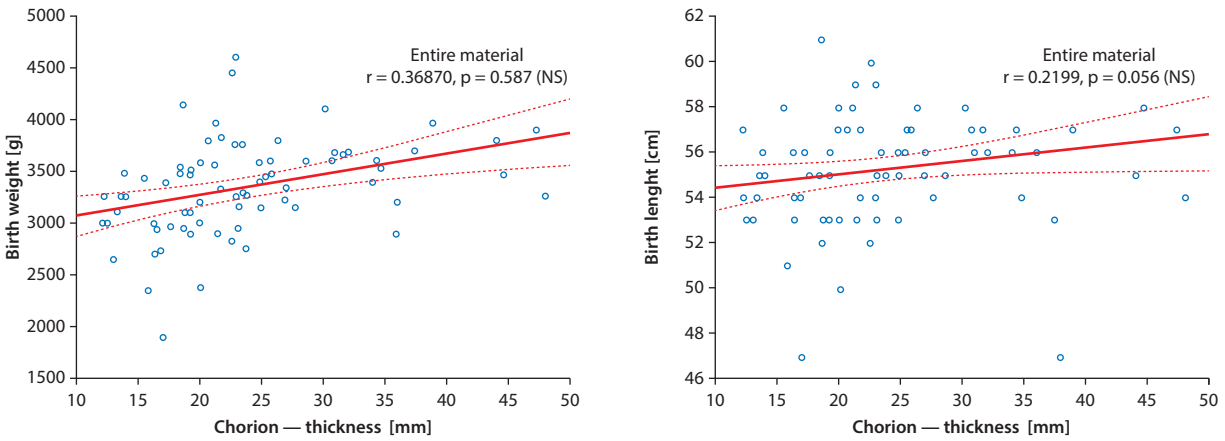

Figure 1. The correlations between chorionic thickness, measured at 11–13 (+ 6d) gestational weeks and ultimate birth parameters

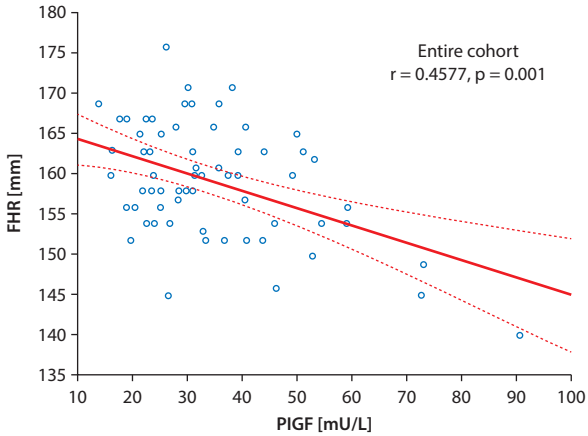

Figure 2. The correlations between FHR measured at 11–13 (+ 6d) gestational weeks and the level of PIGF determined in maternal serum during the first trimester of pregnancy

significant, negative correlation was demonstrated between PIGF levels and FHR, birth weight and length, as well as between PAPP-A levels and FHR.

Furthermore, a statistically significant positive correlation was perceived between BhCG levels and FHR, in the entire cohort and in its arm with location of the chorion on the posterior uterine wall (Fig. 2, Fig. 3).

Finally, the maternal body mass index (BMI) at the beginning of pregnancy was shown not to affect the birth weight and length, FHR, chorionic thickness and maternal serum PIGF, PAPP-A and BhCG levels.

Then, the cohort was divided into 3 groups, by birth weight assessed using the growth chart. Subgroup I included newborns with birth weight below the 25th percentile, group II included newborns with birth weight between

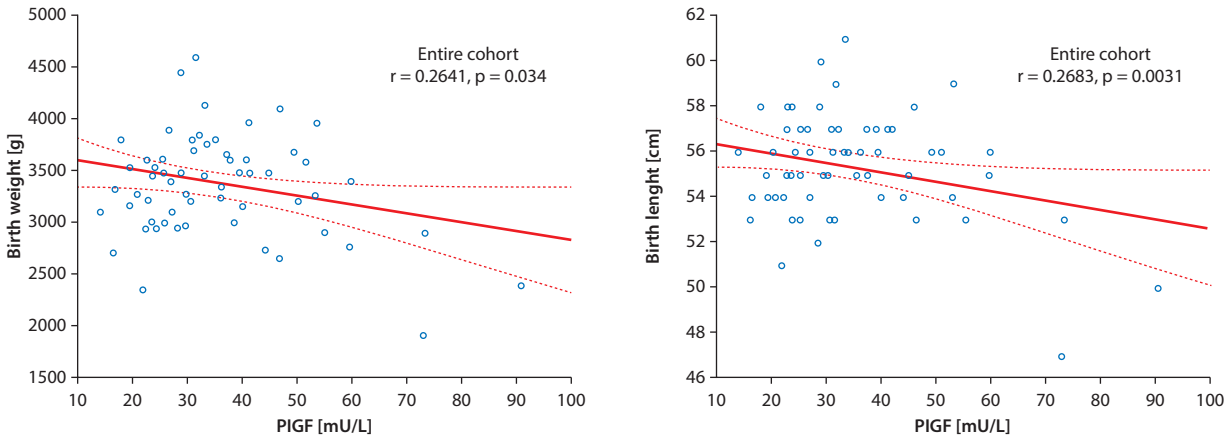

Figure 3. The correlations between ultimate birth parameters and the level of PIGF determined in maternal serum during the first trimester of pregnancy

Table 3. The analysis of average chorionic thickness measured at 11–13 (+ 6d) gestational weeks in 3 classes of birth weight

Group	Birth weight	n	Chorionic thickness [mm]					ANOVA
			Mean	SD	Me	Min	Max	
Total	1900–3000	20	18.93	5.19	18.15	12.2	35.9	p < 0.001
	3100–3590	35	23.23	8.2	21.7	12.2	48	
	3600–4600	21	29.13	7.86	28.6	18.6	47.3	
Location of the chorion on the anterior uterine wall	1900–3000	13	17.22	3.33	16.8	12.2	22.5	p = 0.001
	3100–3590	18	23.42	7.67	21.55	13.9	44.6	
	3600–4600	13	27.29	7.49	23.4	18.6	44	
Location of the chorion on the posterior uterine wall	1900–3000	7	22.11	6.7	20.1	16.3	35.9	p = 0.033
	3100–3590	17	23.02	8.95	21.7	12.2	48	
	3600–4600	8	32.13	7.99	30.85	22.9	47.3	

the 25th and 75th percentile, whereas group III included newborns with birth weight above the 75th percentile. The univariate analysis of variance (ANOVA) was used to compare chorionic thickness measured during the ultrasound assessment at 11–13 (+ 6d) gestational weeks between the three subgroups. A significant correlation between birth weight and chorionic thickness was demonstrated for the three subgroups, measured for both the entire cohort, and its respective arms with location of the chorion on the anterior or posterior uterine wall. The increase of chorionic thickness with the ultimate birth weight was consistently seen in all subgroups (Tab. 3, Fig. 4).

The results obtained using the univariate ANOVA were replicated in subsequent bivariate analysis of birth weight variance, which showed statistically significant association between birth weight and chorionic thickness (p = 0.003) and a non-significant association between birth weight and PIGF levels (p = 0.045).

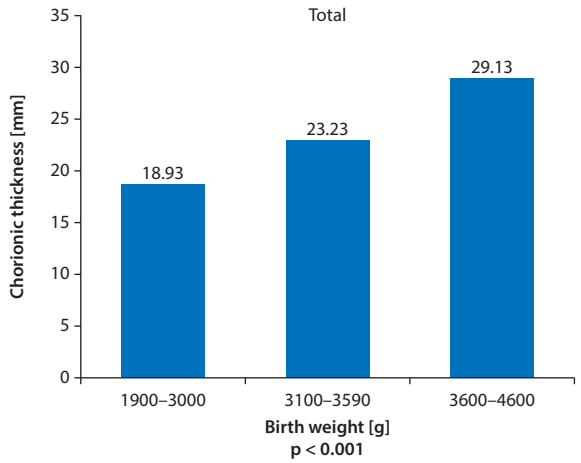

Figure 4. The average chorionic thickness measured at 11–13 (+ 6d) gestational weeks in 3 classes of birth weight

The analysis of variance did not demonstrate a significant correlation between chorionic thickness, PIGF levels and birth weight (Tab. 4, Fig. 5). However, as shown in Figure 8 the birth weight to PIGF level variance between subgroups with low (below 25th percentile) and medium (25–75th percentile) PIGF levels tended to follow the trend previously seen in groups with low, medium and large chorionic thickness. The lowest birth weight was shown in subgroups where low and medium PIGF levels coexisted with low chorionic thickness. In cases with medium chorionic thickness (27–75th percentile), the birth weight slightly increased in both subgroups, whereas in cases with large chorionic thickness, the birth weight did not virtually differ between the subgroups of low and medium PIGF levels. In a subgroup with high PIGF levels (> 75th percentile), though, the birth weight variance followed a completely different pattern. When chorionic thickness was analysed as a predictor variable, the mean birth weight in subjects with low chorionic thickness and high PIGF levels was 2960 g, increasing to 3137 g in subjects with medium chorionic thickness and high PIGF levels. However, the highest birth weight was seen in subjects with consistently high values of both chorionic thickness and PIGF level. This association may prove significant when tested in a bigger sample.

The mean birth weight in a subgroup with low chorionic thickness (below 25th percentile) was only 2988 g. It increased significantly to 3379 g in the subgroup with medium chorionic thickness (25–75th percentile) to reach 3523 g in the group with large chorionic thickness (above 75th percentile). The observed effect was statistically significant (p = 0.0026). While the difference in birth weight between the subgroups with low and medium chorionic thickness was significant and amounted to 391 g, there was only slight birth weight increase of 144g between the subgroups with medium and large chorionic thickness (Tab. 5, Fig. 6).

Table 4. The average level of PIGF determined in the first trimester of pregnancy in 3 groups of birth weight

Group	Birth weight	n	PIGF [mU/L]					ANOVA
			Mean	SD	Me	Min	Max	
PIGF [mU/L]	1900–3000	16	41.62	22.59	33.65	15.9	90.8	NS
	3100–3590	29	30.71	12.02	26.6	13.6	59.4	
	3600–4600	20	33.89	8.84	32.15	17.4	53.1	
PIGF [mU/L]	1900–3000	11	35.62	17.45	29.2	15.9	73.2	NS
	3100–3590	16	28.93	11.83	24.9	13.6	59.4	
	3600–4600	12	34.78	8.28	32.15	24.9	53.1	
PIGF [mU/L]	1900–3000	5	54.84	28.9	59.18	23.6	90.8	p = 0.036
	3100–3590	13	32.91	12.36	29.5	16.2	52.8	
	3600–4600	8	32.55	10.06	33.9	17.4	46.2	

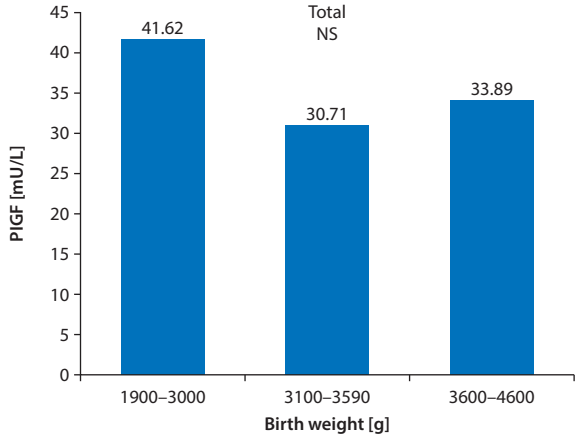

Figure 5. The average level of PIGF determined in the first trimester of pregnancy in 3 groups of birth weight

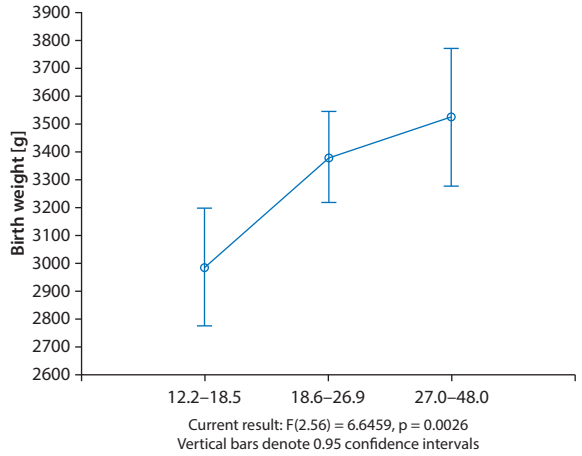

Figure 6. The birth weight and chorionic thickness in 3 groups — below 25th, 25–75th, and above 75th percentile

Table 5. Mean birth weight calculated for intervals adopted for chorionic thickness measured at 11–13 (+ 6d) gestational weeks

Chorionic thickness [mm]	Birth weight [g]				N
	Mean	Standard error	95% confidence interval		
12.2–18.5	2988	104.20	2779	3196	17
18.6–26.9	3379	81.14	3216	3542	29
27.0–48.0	3523	121.25	3280	3765	19

Table 6. The mean birth weight calculated for the adopted ranges of PIGF level determined in the first trimester of pregnancy

PIGF [mU/L]	Birth weight [g]				N
	Mean	Standard error	95% confidence interval		
13.6–23.3	3275	122.07	3031	3520	17
23.4–40.5	3471	79.90	3311	3632	31
40.6–90.8	3142	104.20	2934	3351	17

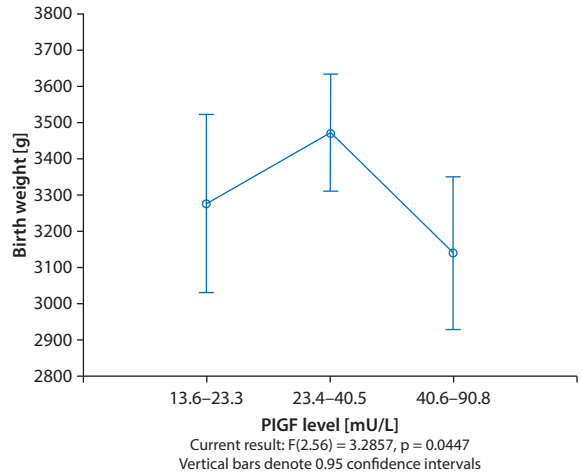

Figure 7. The birth weight and PLGF level in 3 groups — below 25th, 25–75th, and above 75th percentile

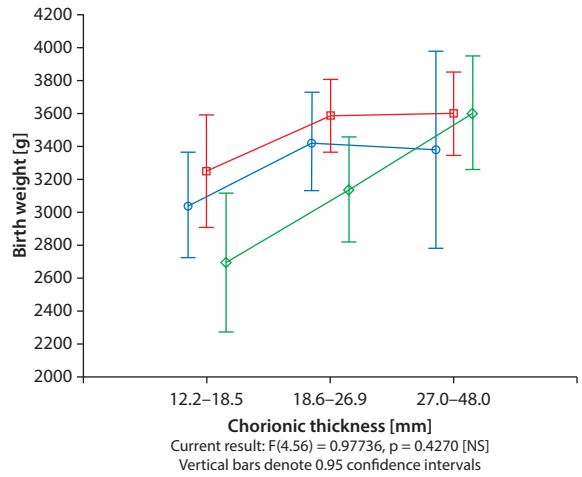

Figure 8. The birth weight and the interaction between chorionic thickness and PIGF level

The mean birth weight in the subgroup with low PIGF level (below 25th percentile) was 3275 g. It increased slightly to 3471 g in the subgroup with medium PIGF levels (25–75th percentile), but in cases with large chorionic thickness (above 75th percentile) it dropped to only 3142 g, below the level seen in the subgroup with low PIGF levels. The observed effect was trending towards statistical significance (Tab. 6, 7 Fig. 7).

DISCUSSION

Our research focused on clinical utility of structural (thickness) and functional (PIGF) placental parameters as low birth weight predictors.

Table 7. The mean birth weight calculated for the adopted intervals of PlGF level, determined in the first trimester of pregnancy, and chorionic thickness measured at 11–13 (+ 6d) gestational weeks

Chorionic thickness [mm]	PlGF [mU/L]	Birth weight [g]				N
		Mean	Standard error	95% confidence interval		
12.2–18.5	13.6–23.3	3031	157.96	2715	3348	7
	23.4–40.5	3242	170.61	2.900	3583	6
	40.6–90.8	2690	208.96	2271	3109	4
18.6–26.9	13.6–23.3	3420	147.76	3124	3716	8
	23.4–40.5	3580	111.69	3356	3804	14
	40.6–90.8	3137	157.96	2821	3454	7
27.0–48.0	13.6–23.3	3375	295.51	2783	3967	2
	23.4–40.5	3593	126.01	3340	3845	11
	40.6–90.8	3600	170.61	3258	3942	6

Our findings indicate the relationship between PlGF levels, chorionic thickness and ultimate birth weight. The location of the chorion on the anterior vs. the posterior uterine wall appears to significantly affect the discussed correlation. In the arm with the location of chorion at the posterior uterine wall, a statistically significant, negative correlation was demonstrated between PlGF levels and FHR, birth weight and length. Furthermore, the location of chorion affects the correlation between PAPP-A levels and FHR, which was statistically significant and negative in the arm with the location of chorion at the posterior uterine wall. This correlation was not confirmed in the arm with the location of chorion on the anterior uterine wall or in the entire cohort.

Additionally, we demonstrated high PlGF levels in mothers of low birth weight newborns. A positive correlation was shown between the birth weight and chorionic thickness assessed with the 2D ultrasound at 11–13 (+ 6d) gestational weeks. The effect of maternal age and BMI on the birth weight was not statistically significant. However, it should be noted that our cohort consisted of females with normal body mass index, which additionally emphasizes the obstetric uniqueness of obese women, in whom the association between maternal BMI and the risk of intrauterine hypertrophy was confirmed.

The literature review for the research of SGA reveals that finding the optimum diagnostic algorithm based on thorough medical history, ultrasound findings from the first trimester and maternal serum protein levels has been the main focus of recent studies. Such diagnostic algorithm is intended to serve as screening for SGA and IUGR.

The SGA prediction model proposed by Schwarz et al. is based on serum PlGF and PP13 levels as well as chorionic assessment in 3D ultrasound in the first trimester. They found that patients with SGA had significantly lower PlGF levels ($p = 0.02$). Additionally, they demonstrated that patient age, BMI and nulliparity did not affect SGA. However, according to their analyses, there was a statistically significant association between such factors as non-white race, concomitant chronic hypertension or smoking and SGA. The chorion was assessed using 3D ultrasound (VOCAL). It was asserted that all chorionic thickness values in SGA were significantly lower as compared to those in normal birth weight newborns and that the flatter chorions of larger surface area were associated with foetal growth abnormalities. Finally, they concluded that the 2D ultrasound-based chorionic assessment had a similar predictive value to the one of 3D ultrasound-based one, while being much easier and quicker to perform [15]. Other researchers developed the so-called placental profile, which combines two chorionic dimensions (i.e. its length and thickness). Along with serum biomarkers, it offered an excellent predictive value [16–20]. However, as the study was done in extremely high-risk pregnancy cases, high rates of unfavourable outcomes were reported.

In 2015, a paper was published that compared the 2D and 3D ultrasound-based assessment of chorionic volume, as a part of larger SGA screening in the first trimester. The study was conducted in 139 patients. It demonstrated low compliance of both methods, which was attributed to heterogeneous chorionic structure at this stage of pregnancy [21].

The effect of chorionic thickness on the ultimate birth weight was also assessed in the second trimester, with a 3D ultrasound performed at 17–20 gestational weeks [22]. The placental volume was shown to be significantly lower in SGA group as compared to the average birth weight group ($p = 0.015$).

CONCLUSIONS

The preliminary analysis of presented data indicates an association between chorionic thickness assessed during the antenatal ultrasound at 11–13 (+ 6d) gestational weeks, PlGF levels assayed at the same time and birth weight. Chorionic thickness significantly affects birth weight. The ultimate birth weight increases with chorionic thickness. An inverse correlation was demonstrated between PlGF level and birth weight. It was statistically significant only in patients with chorion located on the posterior uterine wall. Chorion location on the posterior uterine wall affects both the inverse correlation between PAPP-A and birth weight, as well as the positive correlation between BhCG levels and birth weight. Change in chorionic thickness from 12.2 to 26.9 mm significantly affects the ultimate birth weight. However, its further increase over 27 mm does not have a significant effect on birth weight. In terms of PlGF levels, the highest birth weight was seen in cases with PlGF level ranging between 23.4 and 40.5uU/L and it was lower in cases with PlGF levels below or above this range.

The birth weight in cases with PlGF levels ranging between 40.5 and 90.8 uU/L can be expected to increase linearly with chorionic thickness. On the other hand, no interaction effect was demonstrated between PlGF level and chorionic thickness in cases with low or medium PlGF levels. Nevertheless, it should be emphasized that our results were obtained from a small cohort study. Therefore, it appears legitimate to design a prospective observational study in a larger cohort, in order to replicate our results and further specify PlGF ranges.

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