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Gestational obesity and subclinical inflammation

The pathway from simple assessment to complex outcome (*STROBE-compliant article*)

Cosmin Rugină, MD[a], Cristina Oana Mărginean, MD, PhD[a,*], Lorena Elena Meliţ, MD, PhD[a], Adina Huţanu, MD, PhD[b], Dana Valentina Ghiga, MD, PhD[c], Viviana Modi, MD[d], Claudiu Mărginean, MD[d]

Abstract

Maternal obesity and excessive gestational weight gain (GWG) are associated with pregnancy-related complications, poor birth outcomes, and increased birth weight (BW).

The aims of this study were to assess the relationship between excessive GWG and gestational inflammatory status in terms of blood parameters, as well as its influence on newborn's outcomes.

We performed a prospective study on 176 pregnant women divided into 2 groups depending on the GWG: group 1—normal GWG, 80 cases; and group 2—high GWG, 96 cases. The statistical analysis was performed using the GraphPad Prism program, trial variant. We performed a thorough anamnesis and clinical examination in all mothers and their newborns, as well as an assessment of multiple laboratory parameters.

The levels of both platelets and triglycerides were significantly higher in pregnant women from high GWG group ($P = .0165$/$P = .0247$). The newborns whose mothers presented an excessive GWG were found with a significantly higher BW as compared to those with normal GWG mothers ($P = .0023$). We obtained a positive correlation between the mothers' and newborns' values for hemoglobin, high-density lipoprotein, leucocytes, and platelets/lymphocytes ratio ($P = .0002$/$P = .0313$/$P = .0137$). Moreover, a significant positive correlation was found between GWG and BW ($r = 0.2049$, 95% CI: 0.0588–0.3425, $P = .0064$).

Our findings sustain the hypothesis that maternal obesity is a risk factor for macrosomia and childhood obesity since we found a positive correlation between GWG and BW. Women with high GWG expressed significantly higher levels of platelets and triglycerides suggesting a subclinical inflammation associated to excessive fat accumulation. The inflammation transfer from mother to fetus in our study was suggested by the positive correlations between maternal and neonatal leukocytes and platelets/lymphocytes ratio.

Abbreviations: BMI = body mass index, BW = birth weight, CBC = complete cellular blood count, CI = confidence interval, CRP = C reactive protein, ESR = erythrocyte sedimentation rate, GWG = gestational weight gain, HDL = high-density lipoprotein, Hgb = hemoglobin, NLR = neutrophils/lymphocytes, PLR = platelets/lymphocytes ratio, *r* = relative risk, statistical significance ($P < .05$).

Keywords: birth weight, gestational inflammatory status, gestational obesity, gestational weight gain

1. Introduction

Obesity has become a pandemic condition of the 21st century, presenting a persistent increasing incidence irrespectively of the age. This nutritional imbalance is defined as a multifactorial disorder triggered by the interaction between obesogenic factors, that is, behavioral and environmental factors, and genetic susceptibility.[1] Maternal nutritional status and weight gain during pregnancy express a great impact on birth and neonatal outcomes being proved that maternal obesity and excessive gestational weight gain (GWG) are associated with pregnancy-

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[a] Department of Pediatrics, [b] Research Laboratory, Center for Advanced Medical and Pharmaceutical Research, [c] Department of Medical Scientific Research Methodology, [d] Department of Obstetrics and Gynecology, "George Emil Palade" University of Medicine, Pharmacy, Sciences and Technology, Târgu Mureş, Romania.

[*] Correspondence: Cristina Oana Mărginean, Department of Pediatrics, "George Emil Palade" University of Medicine, Pharmacy, Sciences and Technology, Gheorghe Marinescu Street No. 38, Târgu Mureş 540136, Romania (e-mail: marginean.oana@gmail.com).

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related complications, poor birth outcomes and increased birth weight (BW).[2–5] Furthermore, it was underlined that childhood obesity originates from the intrauterine life, BW being an important predictor for child's future proper development, weight gain, and general wellbeing.[6–8] Moreover, multiple gene polymorphisms were found to express an increased risk for excessive GWG and increased BW, among which matrix metalloproteinase 9, alfa 2 adrenergic receptors, melanocortin receptor 4, nucleotide pyrophosphatase/phosphodiesterase, and others.[9–11]

Multiple recent studies have focused on assessing the systemic low-grade inflammatory status associated to obesity and its impact on short- and long-term complications related to this condition, such as cardiovascular disorders, metabolic syndrome, type 2 diabetes mellitus, and nonalcoholic steatohepatitis.[12,13] The noninvasive or minimally invasive detection of obesity-associated systemic inflammation or its related complications is of major importance in clinical practice taking into account the patient's comfort and the current medical trends for developing and approaching these diagnostic tools in daily practice.[8,14,15] Thus, multiple serum biomarkers were proposed as potential diagnostic tools for this subclinical inflammatory status, among which were complete blood cellular (CBC) parameters, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), or the ratios neutrophils/lymphocytes (NLR) and platelets/lymphocytes (PLR), respectively.[8,16,17] Moreover, red blood cell distribution width is another CBC parameter, whose utility was recently proved in patients with stroke.[18] Both NLR and PLR are simple, noninvasive markers, computed based on a routine CBC count and their utility has been proven in multiple medical fields, such as gastroenterology,[19,20] cardiology,[21] and oncology,[22] their elevated levels being underlined as both diagnostic and prognostic markers not only in the setting of sepsis,[23] but also in a wide-spectrum of pathologies. Moreover, baseline NLR level seems to be useful in predicting the clinical outcome of both ischemic and hemorrhagic stroke.[24] In terms of pregnancy, these markers were proven to be reliable indicators of certain pregnancy-related complications, among which were preeclampsia, HELLP syndrome, preterm delivery, hyperemesis gravidarum, or ectopic pregnancy.[25] Considering the increased incidence of maternal obesity and its negative impact on birth outcomes, the assessment of blood parameters in detecting the gestational and neonatal inflammatory status would be extremely useful for preventing further complications.

The aims of this study were to assess the relationship between excessive GWG and gestational inflammatory status in terms of blood parameters, as well as its influence on newborn's outcomes.

2. Material and methods

2.1. Study design

We performed a prospective study on 176 pregnant women from Romania between July 2017 and October 2019, who were divided into 2 groups according to GWG: group 1—normal GWG, 80 cases; and group 2—high GWG, 96 cases. The GWG represented the difference between the weight at the time of delivery and the pre-pregnancy weight. The Institute of Medicine[26] recommends the following criteria in terms of GWG taking into account the pre-pregnancy weight: for underweight women (body mass index [BMI] $<18.5\,kg/m^2$), the recommended GWG is 12.5 to 18 kg; for normal-weight women (BMI = 18.5–24.9 kg/m^2), the recommended GWG is 11.5 to 16 kg; regarding overweight women (BMI = 25–29.9 kg/m^2), the recommended GWG is 7.00 to 11.5 kg; whereas for obese ones (BMI $>30\,kg/m^2$), the recommended GWG is 5 to 9 kg.[26]

2.2. Subjects

We included in the study all pregnant women that presented for the first trimester ultrasound, with a gestational age of approximately 12 to 13 weeks. The exclusion criteria consisted of preterm delivery with insufficient GWG, maternal chronic disorders, incomplete anamnesis, and pregnant women who refused to sign the informed consent form. Of 245 pregnant women aged between 20 and 41 years, who presented for the routine ultrasound during pregnancy, only 180 pregnant women agreed to sign the informed consent before the inclusion in the study. After applying the exclusion criteria, our final sample consisted of 176 pregnant women.

2.3. Laboratory parameters

All mothers and their newborns underwent a thorough anamnesis and clinical examination. We also assessed the following blood parameters in mothers–newborns couples: CBC, mean corpuscular hemoglobin concentration), **mean corpuscular volume**, CRP, ESR, iron, total proteins, as well as lipid parameters (low-density lipoprotein, high density lipoprotein [HDL], cholesterol, triglycerides). NLR and PLR were calculated by dividing the neutrophil count and platelet count, respectively, to the lymphocyte count. The laboratory parameters were assessed using a Cobas Integra 400 plus automated analyzer (Roche Diagnostics GmbH, Mannheim, Germany.

2.4. Informed consent

The study was approved by the Ethics Committee of the University of Medicine, Pharmacy, Sciences and Technology from Târgu Mureş (No 138/05.07.2017).

All pregnant women signed the informed consent for themselves and their newborns before the inclusion in the study.

2.5. Statistical analysis

The statistical analysis comprised both descriptive statistics elements (mean, median, standard deviation, correlation coefficient, and a confidence interval of 95%), and inferential statistics elements. The Shapiro-Wilk test was applied to determine the series distributions of the analyzed data. We used *t* Student test for Gaussian distribution to compare the means of the analyzed variables values, whereas for non-Gaussian distribution of data series, Mann–Whitney test was applied to determine whether there was a statistically significant difference between the median values of the studied variables. Pearson test was applied for identifying possible correlations. The significance threshold was established at a *P* value of .05. The statistical analysis was performed using the GraphPad Prism program, trial variant.

3. Results

3.1. Descriptive analysis of pregnant women

Among the 176 pregnant women included in the study, the mean age for those with high GWG was 29.22 ± 4.496 years, whereas for pregnant women with normal GWG, we found a mean age of

Table 1

The descriptive analysis of the blood parameters in the 2 groups of pregnant women.

Laboratory parameters	Normal GWG group (n = 80), mean ± SD	High GWG group (n = 96), mean ± SD	P
Age	29.41 ± 4.090	29.22 ± 4.496	.7672
Pre-pregnancy weight, kg	59.55 ± 12.15	67.74 ± 13.30	*<.0001
Leukocytes (/μL)	10404 ± 2521	10746 ± 2150	*.1188
Lymphocytes (/μL)	1967 ± 523.0	2108 ± 671.2	*.2601
Platelets (/μL)	230090 ± 56911	251919 ± 61696	**.0165**
Hgb, g/dL	11.76 ± 1.129	11.83 ± 1.081	.6756
MCHC (%)	33.77 ± 0.9096	33.59 ± 1.206	.2549
MCV, fL	85.38 ± 5.149	85.21 ± 5.690	*.7292
Cholesterol, mg/dL	245.6 ± 47.39	247.4 ± 55.36	*.7857
Triglycerides, mg/dL	206.5 ± 74.76	239.0 ± 103.2	***.0247**
Iron, mg/dL	83.28 ± 53.29	82.70 ± 77.64	*.2848
LDL (mg/dl)	159.3 ± 44.64	157.9 ± 53.64	*.4934
HDL, mg/dL	69.03 ± 17.13	72.33 ± 30.06	*.5785
Total proteins, g/dL	6.182 ± 0.6041	6.157 ± 0.5482	*.7812
CRP, mg/dL	38.72 ± 49.52	37.63 ± 48.12	*.6873
ESR, mmHg	38.68 ± 15.97	39.53 ± 15.31	*.5999
NLR	4.184 ± 2.503	4.071 ± 1.906	*.8329
PLR	124.7 ± 45.49	129.4 ± 51.17	*.6883

CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, GWG = gestational weight gain, HDL = high-density lipoprotein, Hgb = hemoglobin, LDL = low-density lipoprotein, MCHC = mean corpuscular hemoglobin concentration, MCV = mean corpuscular volume, n = number, NLR = neutrophil/ lymphocyte ratio, PLR = platelets/lymphocyte ratio, SD = standard deviation.
* Mann–Whitney test was used.

Table 2

The descriptive analysis of the newborns' blood parameters.

Laboratory parameters	Newborns of the pregnant women with normal GWG (n = 80), mean ± SD	Newborns of the pregnant women with high GWG (n = 96), mean ± SD	P
Birth weight, g	3227 ± 406.6	3409 ± 372.7	**.0023**
Leukocytes (/μL)	17,914 ± 6073	18130 ± 6163	.8159
Lymphocytes (/μL)	4382 ± 1320	4427 ± 1227	*.4813
Platelets (/μL)	274,185 ± 58,509	275,354 ± 59,636	*.6282
Hgb, g/dL	15.93 ± 1.620	15.91 ± 1.420	*.5743
MCHC (%)	35.15 ± 1.043	35.03 ± 0.8295	*.7391
MCV, fL	101.1 ± 4.912	102.5 ± 4.917	*.1263
Cholesterol, mg/dL	5.202 ± 0.3932	5.195 ± 0.4145	*.9007
Triglyceride, mg/dL	71.57 ± 16.43	71.12 ± 19.46	*.8445
Iron, mg/dL	29.11 ± 12.32	30.09 ± 14.69	*.9858
LDL, mg/dL	25.40 ± 8.419	23.89 ± 7.192	*.2855
HDL, mg/dL	100.1 ± 38.93	105.7 ± 37.16	*.2226
Total proteins, g/dL	47.09 ± 18.32	47.73 ± 18.58	*.8469
CRP, mg/dL	3.425 ± 4.282	4.771 ± 7.724	*.6473
NLR	2.586 ± 1.296	2.570 ± 1.480	*.8329
PLR	67.56 ± 22.55	68.66 ± 33.14	*.6883
Birth week, wk	38.73 ± 1.441	39.16 ± 1.069	*.0595
Apgar score	8.538 ± 1.055	8.667 ± 0.7632	*.4154
Male	40	48	
Female	40	48	

CRP = C-reactive protein, GWG = gestational weight gain, HDL = high-density lipoprotein, Hgb = hemoglobin, LDL = low-density lipoprotein, MCHC = mean corpuscular hemoglobin concentration, MCV = mean corpuscular volume, n = number, NLR = neutrophil/ lymphocyte ratio, PLR = platelets/ lymphocyte ratio, SD = standard deviation.
* Mann–Whitney test was used.

29.41 ± 4.090 years ($P = .7672$). We encountered a significantly higher pre-pregnancy weight in high GWG group (67.74 ± 13.30 kg) versus control group (59.55 ± 12.15 kg) ($P < .0001$). Among the blood parameters, we found significantly higher levels of platelets ($P = .0165$) and triglycerides ($P = .0247$) in pregnant women included in the high GWG group in contrast to the women with normal GWG. All the assessed parameters were detailed in Table 1.

3.2. Descriptive analysis of the newborns' parameters

The newborn's birth weight whose mothers were included in the high GWG group was found to be significantly higher (3409 ± 372.7 g) as compared to those whose mothers had a normal GWG (3227 ± 406.6 g) ($P = .0023$) (Table 2). In terms of laboratory parameters, we found no significant differences between the newborns from mothers with high GWG versus those with normal GWG mothers. All the assessed parameters in newborns were described in Table 2.

3.3. The relationship between maternal and neonatal parameters

Analyzing the relationship between maternal and neonatal parameters, we obtained a significant positive correlation between the mothers' and newborns' values for hemoglobin ($r = 0.2762$, 95% CI: 0.1337–0.4075, $P = .0002$), HDL ($r = 0.2267$, 95% CI: 0.08153–0.3625, $P = .0025$), leucocytes ($r = 0.1624$, 95% CI: 0.01478–0.3031, $P = .0313$) and PLR ($r = 0.1855$, 95% CI: 0.03862–0.3246, $P = .0137$) (Table 3, Fig. 1). All parameters were provided in Table 3.

Table 3

Correlations between mothers' parameters and their newborns.

Laboratory parameters in newborns (n = 176)	r coefficient	95% Confidence Interval	P
Hgb in mothers			
Hgb, g/dL	0.2762	0.1337 to 0.4075	**.0002**
Total proteins in mothers			
Total proteins, g/dL	−0.0630	−0.2090 to 0.08574	.4060
Cholesterol in mothers			
Cholesterol, mg/dL	0.0772	−0.07158 to 0.2226	.3085
LDL in mothers			
LDL, mg/dL	0.0528	−0.09584 to 0.1993	.4859
HDL in mothers			
HDL, mg/dL	0.2267	0.08153 to 0.3625	**.0025**
Triglyceride in mothers			
Triglyceride, mg/dL	−0.0448	−0.1915 to 0.1039	.5551
Iron in mothers			
Iron, mg/dL	0.0001	−0.1479 to 0.1480	.9994
CRP in mothers			
CRP, mg/dL	0.0909	−0.05789 to 0.2356	.2305
Leukocytes in mothers			
Leukocytes (/μL)	0.1624	0.01478 to 0.3031	**.0313**
Lymphocytes in mothers			
Lymphocytes (/μL)	0.1352	−0.01298 to 0.2776	.0735
Platelets in mothers			
Platelets (/μL)	0.0796	−0.06915 to 0.2249	.2935
Neutrophils in mothers			
Neutrophils (/μL)	0.0029	−0.1451 to 0.1508	.9693
MCV in mothers			
MCV, fL	0.0888	−0.05991 to 0.2337	.2410
MCHC in mothers			
MCHC (%)	0.1144	−0.03409 to 0.2580	.1304
NLR in mothers			
NLR	0.0818	−0.06696 to 0.2270	.2804
PLR in mothers			
PLR	0.1855	0.03862 to 0.3246	**.0137**

CRP = C-reactive protein, HDL = high-density lipoprotein, Hgb = hemoglobin, LDL = low-density lipoprotein, MCHC = mean corpuscular hemoglobin concentration, MCV = mean corpuscular volume, n = number, NLR = neutrophil/ lymphocyte ratio, PLR = platelets/lymphocyte ratio, r = relative risk.

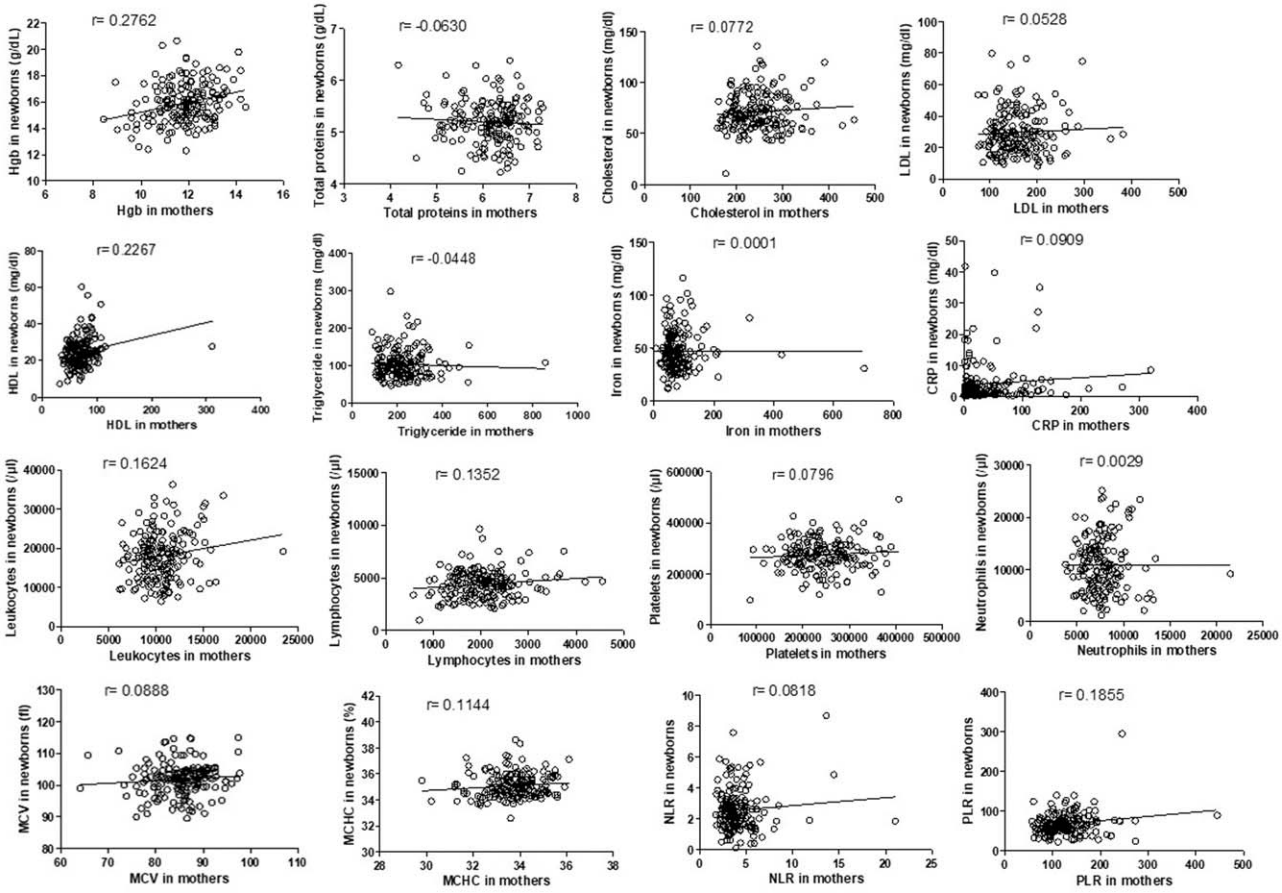

Figure 1. The correlations between maternal and neonatal parameters.

3.4. The impact of GWG and on mothers' and newborns' laboratory parameters

Analyzing the impact of GWG on the newborns' laboratory parameters we found a positive significant correlation between GWG and birth weight ($r=0.2049$, 95% CI: 0.0588–0.3425, $P=.0064$) and a negative significant correlation between GWG and newborns' mean corpuscular hemoglobin concentration ($r=-0.1659$, 95% CI: −0.3063 to −0.0184, $P=.0278$) (Fig. 2). Nevertheless, in terms of GWG and maternal parameters, we found no significant correlation (Fig. 3). We detailed our results in Table 4.

4. Discussions

The adipose tissue has been proven to express an essential role in both the initiation and maintenance of low-grade systemic inflammation.[27,28] Studies performed on otherwise healthy overweight or obese subjects underlined that the peripheral blood parameters of these subjects prove the presence of a low-grade inflammation.[29] Taking into account the secretion and storage functions of the adipose tissue, certain hormones, among which leptin, resistine or adiponectin, or different proinflammatory cytokines, such as interleukin 6, interleukin 1β, or tumor necrosis factor alpha, might also be useful in detecting the inflammatory status associated to obesity.[14,30,31] It is a well stated fact that the incidence of overweight and obesity is increasing in the general population, but maternal obesity and excessive GWG represent a particular concern since their negative impact reflects on both their wellbeing and newborn's outcome. Thus, excessive GWG results in multiple short-term complications such as increased risk of cesarean section, gestational diabetes, gestational arterial hypertension, or macrosomia.[3,32] Moreover, the long-term consequences of excessive GWG are definitely increasing the obesity rates among the general population being proved that it leads to maternal weight retention and excessive adiposity in newborn.[8,33] Our study also identified a higher number of pregnant women with GWG above the recommended limits as compared to those with adequate GWG. In terms of macrosomia, our study sustained the above-mentioned findings since we also encountered a significant higher BW in newborns whose mothers were included in the high GWG in comparison to those from normal GWG mothers. Thus, we might definitely state that excessive GWG has a negative impact on the outcomes of mother–newborn couples. Based on the analysis of the Pregnancy Risk Assessment Monitoring System performed in 9 states, the prevalence of obesity in women of childbearing age almost doubled since 1993 to 2003 suggesting that pre-pregnancy BMI might be used as a risk indicator for excessive GWG.[34] These findings were sustained also by other studies performed by American or Romanian childbearing age women.[4,5,9,10,35] The present study also identified a significant higher pre-pregnancy weight in the study group versus control one.

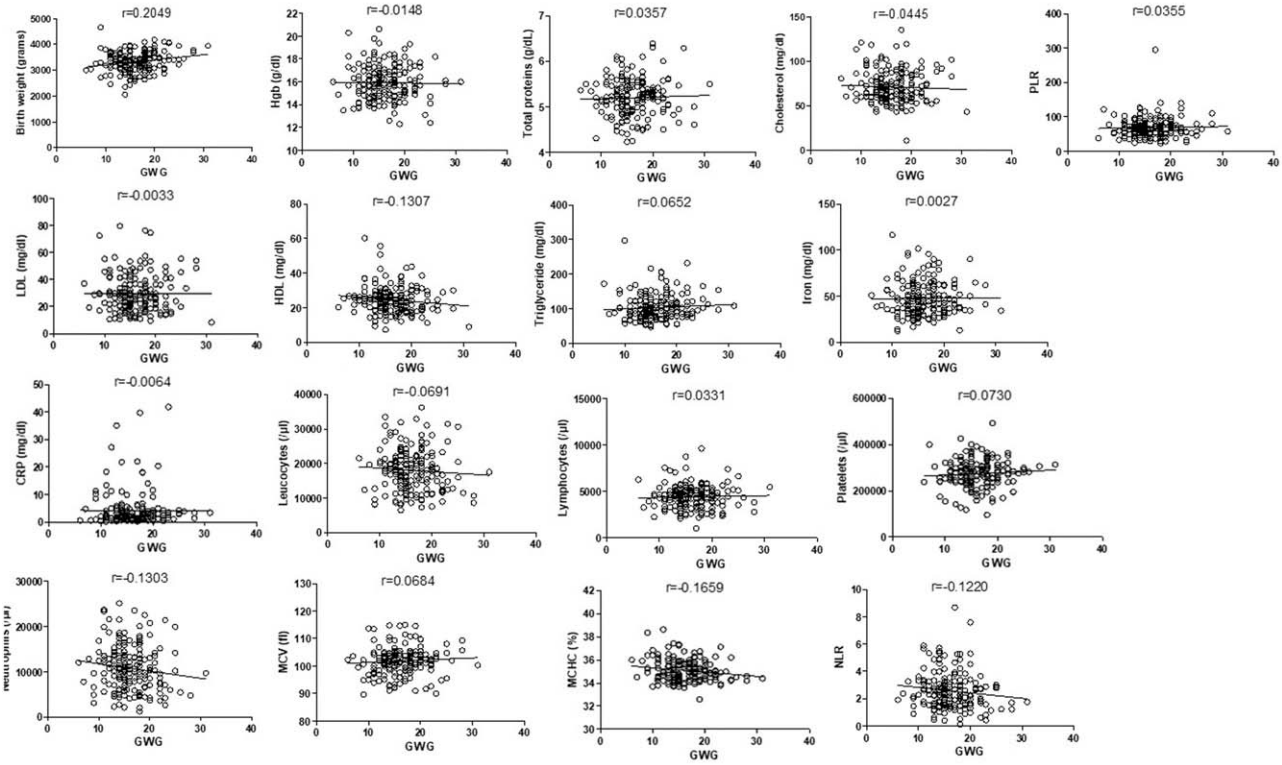

Figure 2. The relationship among gestational weight gain and newborns' laboratory parameters.

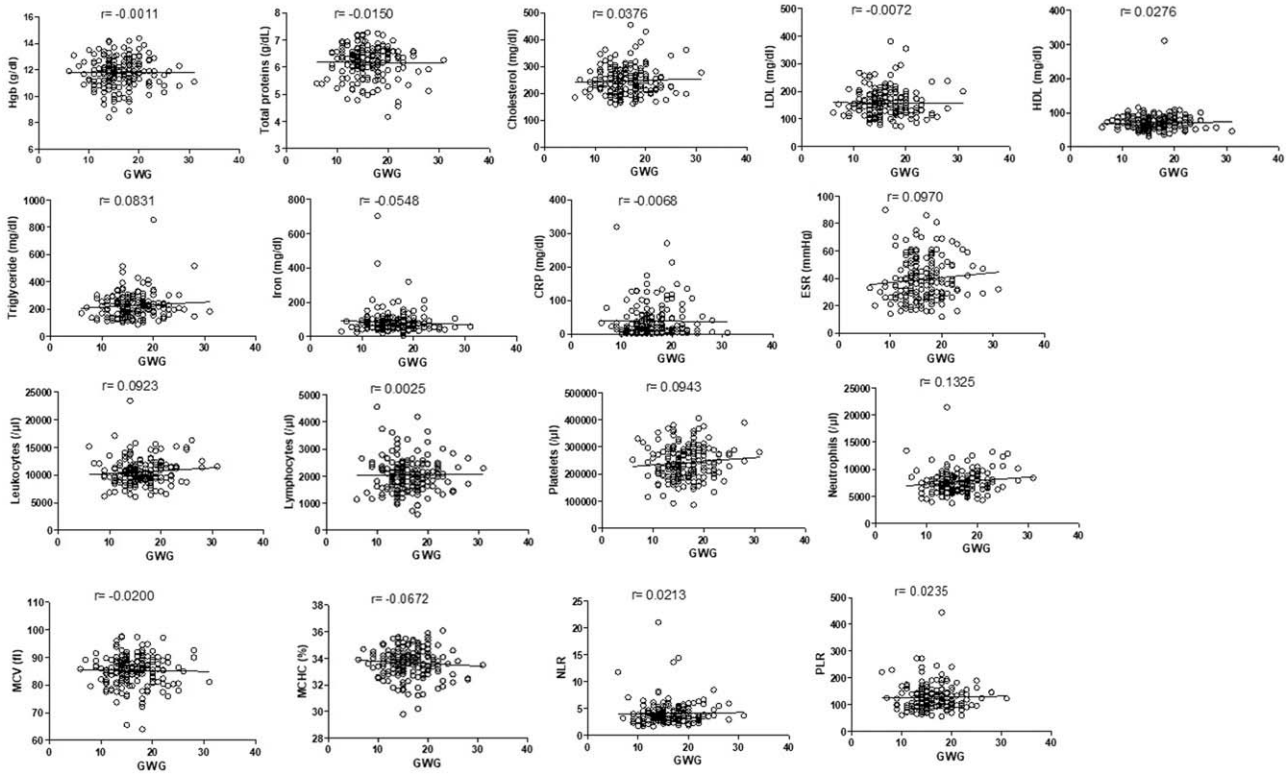

Figure 3. The relationship among gestational weight gain and mothers' laboratory parameters.

Table 4

Correlations between GWG and on mothers' and newborn's laboratory parameters.

Newborn's variables (n = 176)	GWG		
	r coefficient	95% Confidence Interval	*P*
Birth weight, g	0.2049	0.0588 to 0.3425	.0064
Hgb, g/dL	−0.0148	−0.1623 to 0.1335	.8460
Total proteins, g/dL	0.0357	−0.1128 to 0.1827	.6379
Cholesterol, mg/dL	−0.0445	−0.1912 to 0.1041	.5575
LDL, mg/dL	−0.0033	−0.1511 to 0.1448	.9658
HDL, mg/dL	−0.1307	−0.2734 to 0.0176	.0837
Triglyceride, mg/dL	0.0652	−0.0835 to 0.2112	.3896
Iron, mg/dL	0.0027	−0.1453 to 0.1506	.9712
CRP, mg/dL	−0.0064	−0.1542 to 0.1417	.9325
Leucocytes (/μL)	−0.0691	−0.2149 to 0.0797	.3621
Lymphocytes (/μL)	0.0331	−0.1154 to 0.1802	.6627
Platelets (/μL)	0.0730	−0.0758 to 0.2186	.3358
Neutrophils (/μL)	−0.1303	−0.2730 to 0.0180	.0847
MCV, fL	0.0684	−0.0804 to 0.2142	.3672
MCHC (%)	−0.1659	−0.3063 to −0.0184	**.0278**
NLR	−0.1220	−0.2652 to 0.0264	.1066
PLR	0.0355	−0.1130 to 0.1825	.6399
Mothers' variables (n = 176)	**GWG**		
	***r* coefficient**	**95% Confidence Interval**	***P***
Hgb, g/dL	−0.0011	−0.1491 to 0.1469	.9882
Total proteins, g/dL	−0.0150	−0.1627 to 0.1332	.8426
Cholesterol, mg/dL	0.0376	−0.1110 to 0.1845	.6202
LDL, mg/dL	−0.0072	−0.1549 to 0.1410	.9249
HDL, mg/dL	0.0276	−0.1209 to 0.1748	.7166
Triglyceride, mg/dL	0.0831	−0.0657 to 0.2282	.2730
Iron, mg/dL	−0.0548	−0.2011 to 0.0940	.4704
CRP, mg/dL	−0.0068	−0.1546 to 0.1413	.9290
ESR, mmHg	0.0970	−0.0517 to 0.2415	.2005
Leukocytes (/μL)	0.0923	−0.0565 to 0.2370	.2232
Lymphocytes (/μL)	0.0025	−0.1455 to 0.1504	.9737
Platelets (/μL)	0.0943	−0.0544 to 0.2389	.2133
Neutrophils (/μL)	0.1325	−0.0158 to 0.2750	.0797
MCV, fL	−0.0200	−0.1675 to 0.1283	.7917
MCHC (%)	−0.0672	−0.2131 to 0.0816	.3754
NLR	0.0213	−0.1270 to 0.1688	.7786
PLR	0.0235	−0.1249 to 0.1709	.7565

CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, GWG = gestational weight gain, HDL = high-density lipoprotein, Hgb = hemoglobin, LDL = low-density lipoprotein, MCHC = mean corpuscular hemoglobin concentration, MCV = mean corpuscular volume, n = number, NLR = neutrophil/ lymphocyte ratio, PLR = platelets/lymphocyte ratio, r = relative risk.

Previous studies performed on both adult and pediatric patients with obesity proved that this nutritional disorder is associated with a low-grade systemic inflammation suggesting that a wide range of laboratory parameters might be useful in assessing the presence of this inflammatory status, such as leukocytes, lymphocytes, neutrophils, platelets, mean platelet volume, NLR, PLR, or acute phase reactants, CRP or ESR.[8,13,14,27,29] In terms of pregnancy, it was emphasized that this subclinical inflammatory status might occur in the setting of excessive GWG. Thus, a large recent study comprising 671 pregnant women, which assessed the relationship between pregnant woman's diet, GWG, and certain inflammatory biomarkers proved that mainly-based animal protein diet and excessive GWG are associated with increased levels of inflammatory markers, such as CRP and serum amyloid suggesting the presence of a gestational inflammatory status as a result of GWG above the recommended limits.[36] Moreover, a large study including 6700 individuals showed that waist circumference is positively correlated with leukocytes, neutrophils, platelets, and medium platelet volume.[16] Furthermore, it was hypothesized that neutrophil count is directly related to the inflammatory status reflecting the degree of obesity, whereas the lymphocyte one is a better indicator of nutritional status and general stress.[37] Inflammation is a well-known trigger for thrombosis resulting in megakaryocytic proliferation and relative thrombocytosis. Therefore, elevated platelet count and low lymphocytes one were proven to be risk indicators due to their involvement in both aggregation and inflammation.[38] Similarly, our findings revealed a significantly higher platelet count among women from high GWG as compared to those with normal GWG suggesting most-likely only the initial phase of obesity-associated inflammatory status. The lack of significant differences in terms of the remaining laboratory parameters is probably related to the insufficient amount of time required for their alteration.

The negative impact of maternal obesity on newborns was emphasized by multiple studies. Thus, it was underlined that the transfer of inflammation from mother to fetus and consequently to newborn might occur directly through placenta, as well as indirectly as a result of excessive lipid transfer from mother to offspring leading to the fetal secretion of proinflammatory cytokines.[39] Another recent study proved that maternal obesity influences the child's long-term risk for developing obesity and metabolic syndrome.[40] Similarly, in terms of relationship between maternal and neonatal parameters, our study revealed a significant positive correlation between leukocytes and PLR emphasizing clearly the above stated inflammation transfer from mother to fetus in the setting of excessive GWG. Contrariwise, our findings pointed out also a positive aspect of mother–newborn couple in terms of HDL significant positive correlation suggesting that a proper maternal health status improves the newborn's outcome.

Multiple studies focused on assessing the role of PLR and NLR in different pregnancy related complications. Thus, a recent study underlined that both parameters seem to be related to gestational diabetes mellitus suggesting a systemic inflammatory status in the setting of this condition.[41] Additionally, Biyik et al[42] reported higher values of these parameters in pregnant women whose pregnancy ended in missed abortion. In terms of preeclampsia, several studies assessed mostly the role of NLR, but the findings are inconsistent. Thus, recent case–control studies proved that this marker is increased during the first and second trimester of pregnancy representing a reliable risk indicator for preeclampsia.[43,44] Nevertheless, Mannaerts et al[45] performed a study a large sample and found no correlation between either NLR or PLR and preeclampsia. Except of pregnancy related complications, the study of Akgun et al[46] assessed the relationship between the inflammatory biomarkers and BW suggesting that maternal NLR and PLR are negatively correlated with gestational week at delivery time and newborn's BW. Our findings revealed a significant positive correlation between mother's and newborn's PLR emphasizing once more the alarming transfer of inflammation from mother to fetus.

The *limitations* of this study consist of the relatively small sample size; the fact that we did not assess other factors that might have contributed to the excessive GWG like dietary habits or physical activity; the assessment of mother-newborn couple from a single geographic area of Romania; as well as the lack of

determination of other laboratory parameters that might have proved the presence of inflammatory status associated to high GWG or the fact that we did not followed these couples prospectively to monitor the postpartum maternal weight retention or the child's development. Nevertheless, this is the first study in our country and among the few worldwide, if not the first that assessed the usefulness of a wide-spectrum of laboratory parameters in detecting the low-grade systemic inflammatory status associated to excessive weight gain during pregnancy and its influence on newborn's wellbeing.

5. Conclusions

Gestational inflammatory status related to excessive weight gain during pregnancy represents a real concern for birth outcome. Our findings pointed out that an increased pre-pregnancy weight was significantly associated with high GWG resulting also in a significantly higher BW. Moreover, the peripheral blood of the pregnant women with high GWG expressed a significantly higher platelet count and elevated levels of triglycerides as compared to those with an adequate GWG. The inflammation transfer from mother to fetus in our study was underlined by the significant positive correlations between maternal and neonatal leukocytes and PLR. Nevertheless, further studies on bigger samples involving also other factors related to gestational inflammatory status and birth outcomes are necessary to clearly define the role of blood parameters in assessing this topic.

Author contributions

Dr Rugină Cosmin, Prof Cristina Oana Mărginean, Dr Lorena Elena Meliţ, Dr Viviana Modi and Dr Mărginean Claudiu conceptualized and designed the study, drafted the initial manuscript, and revised the manuscript.
Dr. Adina Huţanu performed the laboratory analysis
Dr Dana Valentina Ghiga performed the statistical analysis.
All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.
Conceptualization: Cosmin Rugină, Cristina Oana Marginean, Lorena Elena Meliţ, Claudiu Mărginean.
Formal analysis: Cosmin Rugină, Cristina Oana Marginean.
Investigation: Cosmin Rugină, Adina Huţanu, Viviana Modi, Claudiu Mărginean.
Methodology: Adina Huţanu, Dana Valentina Ghiga, Claudiu Mărginean.
Resources: Cosmin Rugină, Cristina Oana Marginean.
Software: Dana Valentina Ghiga.
Supervision: Cristina Oana Marginean, Claudiu Mărginean.
Validation: Cristina Oana Marginean, Claudiu Mărginean.
Visualization: Cosmin Rugină, Cristina Oana Marginean, Claudiu Mărginean.
Writing – original draft: Cosmin Rugină, Cristina Oana Marginean, Lorena Elena Meliţ, Claudiu Mărginean.
Writing – review & editing: Cosmin Rugină, Cristina Oana Marginean, Lorena Elena Meliţ, Claudiu Mărginean.

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