



Platelet Indices before Vaginal Delivery in Healthy Teenage Pregnant Women Compared to Healthy Adult Pregnant Women

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Authors' contributions

This work was carried out in collaboration among all authors. Author RC designed the study and performed data curation. Author DS performed supervision and wrote the final manuscript. Author IP managed the literature searches and wrote the first draft of the manuscript. Author AC performed data curation and wrote the first draft of the manuscript. Author LVB performed the statistical analysis and wrote the first draft of the manuscript. Author RS managed the analysis of the study and wrote the final manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Aims: This work aimed to study whether there are any differences in platelet indices of the teenagers compared to adult pregnant women, differences that could be used for the benefit of the patients.

Study Design: Prospective study.

Place and Duration of Study: This study included all consecutive patients admitted for delivery between July 2019 and December 2019 in the Elena Doamna Obstetrics and Gynecology University Hospital, Iasi, Romania, who met the inclusion criteria.

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Methodology: There were 167 patients (ranged between 14-46 years old). Complete blood count just before vaginal delivery was analyzed.

Results: A statistical difference ($P=0.043$) was found between plateletcrit values of healthy adolescents compared with healthy adult pregnant patients. No statistical difference was found between plateletcrit values in the 4 consecutive age groups. No pregnant patient had abnormal plateletcrit value. The neutrophil-to-lymphocyte ratios were significantly higher ($P=0.024$) in adolescents versus the over 40 age group; moreover, the teenage median values were slightly over the normal limits. The NLR values were significantly higher ($P=0.013$) in adolescent patients versus adult pregnant patients.

Conclusion: Even if plateletcrit or NLR values in teenage pregnant patients may be slightly higher than in adults, this was normal to happen in healthy patients, and required no therapeutic measures.

Keywords: Platelet indices; pregnancy; teenagers; vaginal delivery.

ABBREVIATIONS

PLT : Platelet count,
MPV : Mean platelet volume,
PDW : Platelet derived width,
PCT : Plateletcrit,
P-LCR : Platelet large cell ratio,
NLR : Neutrophil to lymphocyte ratio,
PLR : Platelet to lymphocyte ratio,
IQR : Interquartile range

1. INTRODUCTION

Teen pregnancy represents a huge challenge for pregnant patients, for their families, and for the health care system. Yee et al. [1] correlated higher social vulnerability with higher teen birth rates. Sedgh et al. [2] reported that among the 21 countries with complete statistics, the pregnancy rate among 15- to 19-year-olds was highest in the United States (57 pregnancies per 1000 women), and the lowest rate was in Switzerland (8 pregnancies per 1000 women). Darroch et al [3] noted that adolescent childbearing was more common in the United States (22%), than in Great Britain (15%), Canada (11%), France (6%), and Sweden (4%). Socolov et al [4] reported 8.3% of teenage singleton pregnancies per 1000 women who delivered in a university hospital in Romania, between 2014 and 2017.

Teen pregnancies are more likely to be associated with health risks than adult pregnancies are. Younger adolescents have an increased risk of maternal anemia, postpartum hemorrhage, preeclampsia or hemolysis, and low platelet syndrome, whereas older adolescents have an increased risk of maternal anemia and blood transfusion [5]. Ganchimeg et al [6] observed that adolescent mothers, compared with mothers aged 20-24 years old, had higher

risk of eclampsia, puerperal endometritis, systemic infections, low birthweight preterm delivery, and severe neonatal conditions. At the same time, coverage of prophylactic ureterotonics, prophylactic antibiotics for cesarean delivery, and antenatal corticosteroids for preterm delivery was significantly lower among adolescent mothers. Suci et al. [7] noticed that adolescent mothers, versus adult mothers, were more likely to deliver vaginally, and their newborns were more likely to have low birth weight. The adolescent mothers were more likely single, living in a rural area, and living with extended family. Jolly et al. [8] concluded that pregnant patients less than 18 years old were more likely to deliver preterm than older patients were. Dimitriu et al. [9] reported a high percentage of caesarean deliveries in teen mothers, particularly in patients aged over 17 years, whereas the percentage of caesarean deliveries for their second pregnancy was even higher compared with the primipara adolescent mothers.

Pregnancy is associated with platelet adaptation. Moser et al. [10] highlighted that, during pregnancy, platelet count decreases gradually from the first to the third trimester, due to hemodilution and platelet consumption in the placenta, but exaggerated activation of platelets at the maternal-fetal interface can generate a systemic inflammatory response in the mother. Oğlak [11] showed that the neutrophil to lymphocyte ratio and the platelet to lymphocyte ratio were significantly higher in early pregnancy loss patients than in healthy patients. Swanepoel et al. [12] showed changes in the platelet ultrastructure associated with healthy pregnancy, which generate the hypercoagulable state: internal granules modified number, more numerous α - and lysosomal granules, and less

numerous dense granules and mitochondria, compared with that in the nonpregnant group. Szklanna et al. [13] identified, in the platelet releasate, numerous proteins to be differentially released from platelets in pregnancy, including proteins only expressed in pregnancy (pregnancy-specific glycoproteins and human placental lactogen).

Platelets progressively change with increasing age. Tian et al. [14] demonstrated, using transmission electron microscopy, that, with ageing, the platelet membrane becomes more irregular in shape, not smooth, and multiple platelet membrane ruptures were observed, pseudopodia and protuberances became more numerous, and the number of α -granules was significantly reduced. Cowman et al. [15] showed on digital-image microscopy that aging resulted in a significant decrease in the number of platelet tracks, translocating platelets and unstable platelet interactions with human von Willebrand Factor, and that these changes were more profound in women than in men. Vasquez-Santiago et al. [16] showed that platelet counts and plateletcrit decrease with increasing age, whereas mean platelet volume, platelet distribution width, and platelet-large cell ratio increase with age.

Because no one studied the differences generated by age in platelet indices in pregnant women, and because, in a previous study et al [17], we showed that there were some differences in the coagulation factors in healthy adolescents versus healthy adult pregnant women before vaginal birth, we further investigated the platelet indices in pregnant women to see if there are any differences between healthy adolescents versus healthy adults.

2. MATERIALS AND METHODS

We prospectively studied all the pregnant patients admitted for delivery between July 2019 and December 2019 in an obstetrics and gynecology university hospital. The total number of patients was 260. Standard hospital protocol included the harvesting of blood for complete blood count just before delivery, no matter whether they delivered vaginally or by cesarean delivery. Some of these patients (n=93) were removed from the study because they required cesarean delivery, because they were pregnant for less than 37 weeks, or because their data were incomplete. Therefore, the remaining

patients (n=167), who delivered vaginally, at term, were assumed healthy, so that they were studied in this work.

Inclusion criteria were: patients who delivered vaginally, at term, in our hospital. Patients who delivered at home, or on the way to our hospital; patients who were admitted during labor; patients who had no data about the blood count before delivery, or data came from another healthcare establishment, with a different laboratory unit; or patients who delivered before 37 weeks of pregnancy were excluded from this study. Hospital policy requires that patients with systemic disorders, with known chronic diseases, with immune thrombocytopenic purpura or other thrombocyte-related diseases will deliver by cesarean section, so that they were removed from the study.

Thirty-seven patients were teenagers (under 20 years), 88 were between 20-29 years old, 35 were between 30-39 years old, and only 7 patients were over 40 years old. Mean gestational age was: 39.06; 38.76; 39.13 and 38.66 respectively. Mean birth weight of the neonates was: 3.27; 3.29; 3.54 and 3.02 respectively.

The following data were considered for this study: platelet count (PLT), mean platelet volume (MPV), platelet-derived width (PDW), plateletcrit (PCT), platelet-large cell ratio (P-LCR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to lymphocyte ratio (PLR).

We used RAYTO 2201C laboratory installation in order to determine the complete blood count.

There was a small number of patients ≥ 40 years old (n=7), a lack of normal data distribution, therefore we studied the median values, being more fitted as compared to mean values.

We used SPSS version 18 (PASW Statistics for Windows, Chicago: SPSS Inc.) for statistical analysis. We calculated the median value and the interquartile range. The Kruskal-Wallis 1-way ANOVA nonparametric test was used for multiple group comparison. The Bonferroni correction for multiple post-hoc tests was involved in adjustments of significance values. We also used the Mann Whitney-U test, for 2 sets. *P* of 0.05 was considered statistically significant. The box-plot charts showed the distribution within the group. Though the small number of patients in one particular group imply reduced statistical

power, there was a close shape distribution in the age groups, and the nonparametric tests reveal the differences between median values. The more powerful Kruskal-Wallis test was preferred versus the median.

3. RESULTS

Primary outcomes showed that plateletcrit values were significantly higher ($P=0.043$) in the teenage group of pregnant patients than in adult pregnant patients, but they were in normal ranges. Neutrophil-to-lymphocyte ratio was also significantly higher ($P=0.013$) in teenage pregnant patients versus adults, and even a little bit higher than normal. There was no significant difference between PLT, MPV, PDW, P-LCR, and PLR values, in the healthy adolescents compared with adults. (Tables 1,2). Secondary outcomes showed that these values did not affect the capacity of patients to deliver vaginally.

There was no difference ($P=0.18$) between platelet count values in the four age groups, and the median values were normal. Platelet count was not significantly different ($P=0.216$) in healthy adolescents versus adults. There was no difference ($P=0.133$) between mean platelet volumes in the 4 age groups. No teenage patient had an abnormal MPV value. There was no difference ($P=0.104$) between the mean platelet volumes of pregnant adolescents versus adults. There was no difference ($P=0.364$) between platelet derived width values in the 4 age groups. No teenage pregnant patient had decreased PDW value; however, of the 130 adult pregnant patients, 4 (3.07%) had decreased PDW values. There was no difference ($P=0.131$) between the platelet derived width of pregnant patients <20 years old compared with patients >20 years old. There was no difference ($P=0.119$) between plateletcrit percents in the 4 consecutive age groups. No pregnant patient, either teenage or adult, had abnormal plateletcrit values. A statistical difference ($P=0.043$) existed between plateletcrit value of teenagers as compared to adults.

No significant difference ($P=0.258$) occurred between P-LCR ratios in the 4 age groups. Only the 20-29 age group displayed abnormal P-LCR values: 2 patients (1.19% of the total pregnant patients) had elevated P-LCR values (46.33% and 55.17%, respectively) whereas 5 patients

(2.99%) had decreased P-LCR values (ranging from 2.21% in a 25-year-old pregnant patient to 11.72% in a 27-year-old patient). No teenage pregnant patient had abnormal P-LCR values, but of the 130 adult pregnant patients, 7 (5.38%) had abnormal, elevated, or decreased P-LCR values. No statistical difference ($P=0.2$) was found between the P-LCR values of teenagers versus adults.

The values of neutrophil-to-lymphocyte ratio were significantly higher ($P=0.024$) in teenage pregnant patients compared with the over 40 years age group (Table 3); moreover, the teenage median values were slightly over the normal limits. There were 44 patients (26.34%) who had elevated NLR values: 15 (8.98%) teenage patients (range, 3.61-10.4), 21 (12.57%) pregnant patients between 20-29 years old (range, 3.63-8.94), 8 (4.79%) pregnant patients between 30-39 years old (range, 3.95-6.7), and no (0%) patient over 40 years old had an elevated NLR value. Of the 37 teenage pregnant patients, 15 (40.54%) had elevated NLR values. Of the 88 pregnant patients between 20-29 years old, 21 (23.86%) had elevated NLR values. Of the 35 pregnant patients between 30-39 years old, 8 (22.85%) had elevated NLR values. There was only 1 (0.59%) pregnant patient, aged 24, who had a decreased NLR value (0.58). The NLR values were significantly higher ($P=0.013$) in teenage pregnant patients compared with adult pregnant patients (Fig. 1).

No significant difference ($P=0.287$) was found between the platelet-to-lymphocyte ratio values of the 4 pregnant patient age groups, but value was slightly higher in teenage patients compared with the other age groups. There were 13 patients (7.78%) with elevated PLR values: 5 patients (2.99%) were under 20 years old (PLR range, 165.19-210.34), 7 patients (4.19%) were between 20-29 years old, and 1 (0.59%) was between 30-39 years old. There were no over 40-year-old pregnant patients with elevated PLR values. Eleven pregnant patients had (6.58%) decreased PLR values: 1 (0.59%, PLR=62.5) under 20 years, 8 (4.79%) between 20-29 years old (PLR range, 52.07-67.79), 2 (1.19%) between 30-39 years old (range, 46.68-64.66), and 0 over 40 years old. PLR values were not significantly ($P=0.073$) different in the teenagers as compared to adults.

Table 1. Platelet indices in different age groups of pregnant patients

Platelet indices (units)	<20 years (37)	20-29 years (88)	30-39 years (35)	>40 years (7)	P
PLT (*10 ³ /μL)	270.00 (94)	257.00 (96)	244.00 (70)	287.00 (149)	.18
MPV (fL)	7.99 (.78)	7.87 (1.04)	7.92 (1.07)	7.47 (1.37)	.133
PDW (%)	17.23 (2.59)	17.65 (3.77)	17.46 (3.75)	17.66 (5.83)	.364
PCT (%)	.22 (.08)	.20 (.06)	.20 (.06)	.20 (.09)	.119
P-LCR (%)	23.03 (5.88)	22.15 (8.17)	23.23 (7.99)	17.55 (9.24)	.258
NLR	3.60 (2.3)	2.59 (1.57)	2.85 (1.24)	1.86 (1.19)	.024
PLR	111.33 (51.78)	101.80 (41.8)	104.69 (48.97)	109.45 (37.16)	.287

Median values and interquartile range for platelet indices for the four different age groups of healthy pregnant patients just before vaginal delivery. P≤.05 was considered significant. PLT= platelet count, MPV=mean platelet volume, PDW=platelet derived width, PCT=plateletcrit, P-LCR=platelet large cell ratio, NLR=neutrophil to lymphocyte ratio, PLR=platelet to lymphocyte ratio

Table 2. Platelet indices in teenagers compared to adult pregnant patients

Platelet indices (units)	<20 years (37)	≥20 years (130)	P
PLT (*10 ³ /μL)	270.00 (94)	251.5 (91)	.216
MPV (fL)	7.99 (.78)	7.86 (1.04)	.104
PDW (%)	17.23 (2.59)	17.64 (3.81)	.131
PCT (%)	.22 (.08)	.20 (.06)	.043
P-LCR (%)	23.03 (5.88)	21.9 (8.11)	.200
NLR	3.60 (2.3)	2.61 (1.35)	.013
PLR	111.33 (51.78)	102.62 (41.64)	.073

Median values and interquartile range for platelet indices for teenagers compared to adult healthy pregnant patients just before vaginal delivery. PLT= platelet count, MPV=mean platelet volume, PDW=platelet derived width, PCT=plateletcrit, P-LCR=platelet large cell ratio, NLR=neutrophil to lymphocyte ratio, PLR=platelet to lymphocyte ratio

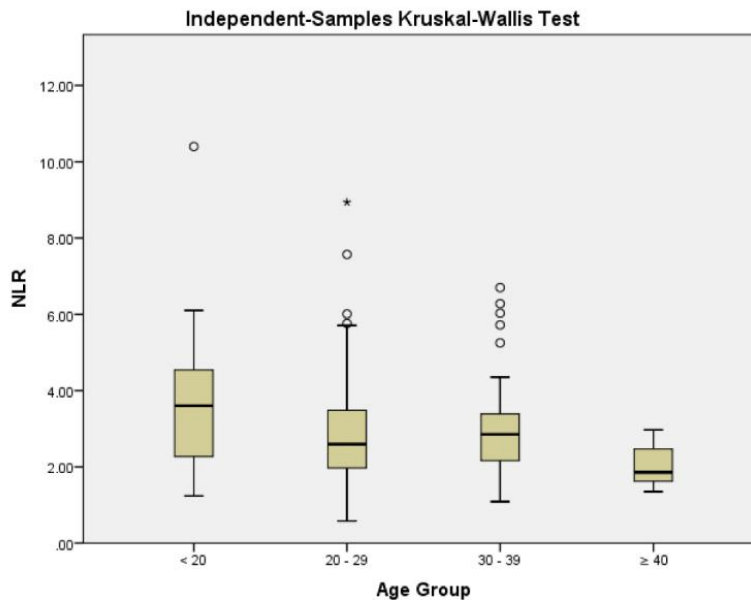


Fig. 1. The NLR values in different age groups of healthy pregnant patients

Table 3. The statistical significance of comparison of neutrophil to lymphocyte ratio values between different age groups of healthy pregnant patients

Age groups compared	NLR	P
≥ 40 / 20 – 29 years	1.86/2.595	.364
≥ 40 / 30 – 39 years	1.86/2.85	.246
≥ 40 / < 20 years	1.86/3.6	.024
20 – 29 / 30 – 39 years	2.595/2.85	1.000
20 – 29 / < 20 years	2.595/3.6	.127
30 – 39 / < 20 years	2.85/3.6	.878

P ≤ .05 was considered significant

4. DISCUSSION

We studied 167 patients, aged between 14-46 years old. To the best of our knowledge, no reports in the medical literature have been published regarding the difference between platelet count or platelet indices between different age groups of healthy pregnant patients just before vaginal delivery, although there are reports regarding the mean value for platelet count or platelet indices in healthy patients with uncomplicated pregnancies.

In a systematic review, Reese et al. [18] reports mean platelet count decreasing from 251,000/ μL in first-trimester pregnant patients, to 238,000/ μL in the second trimester, to 224,000/ μL in the third trimester up to 237,000/ μL at delivery, then increasing, to 247,000/ μL at 4-8 weeks postpartum. Li et al. [19] also reported platelet count decreasing during pregnancy, with a median platelet count value regardless of the trimester of $202 \times 10^9/\text{L}$. Alemu et al. [20] described a mean platelet count of 196.07 ± 48.88 among pregnant women regardless of trimester. Bakrim et al. [21] also reported significant variations of hematological parameters between the first, second, and third trimester of pregnancy. No one has reported platelet count during different age groups.

There was no difference ($P=0.18$) between platelet counts in the age groups, and the median values were normal. Platelet count was not significantly different ($P=0.216$) in teenagers versus adults. Reese et al. [18] reported 9.9% of women with uncomplicated pregnancies having a platelet count below 150,000 per cubic millimeter. We only had 2 patients (1.19%) with platelet count below 150,000 per cubic millimeter. Reese also reports 1% of patients with uncomplicated pregnancies and deliveries having the mean platelet count under 100,000 per cubic millimeter. We found no patient with such a low platelet count. Reese reports no

patient with platelet count over 450,000 per cubic millimeter. We report 2 patients (1.19% of patients) with elevated platelet counts. In a previous article, the same author, Reese et al [22], reported the mean platelet counts in patients with normal pregnancies increasing from 224,000/ μL in the third trimester to 237,000/ μL at delivery. We found no such low values in any of our 4 age groups of patients.

According to the American College of Obstetricians and Gynecologists' Committee of Practice Bulletins – Obstetrics [23], from September 2016, thrombocytopenia occurs in 7-12% of pregnancies. In all births in our study of healthy patients who delivered vaginally, we only found 1.19% of healthy pregnant patients with thrombocytopenia.

Al-Sheeha et al. [24] reported a platelet count cutoff of $248.0 \times 10^3/\mu\text{L}$ for the diagnosis of preeclampsia. We report 70 patients (41.91% of patients) with platelet counts under $248.0 \times 10^3/\mu\text{L}$ able to deliver vaginally. In our study group, no preeclampsia pregnant patient delivered vaginally at term.

There was no difference ($P=0.133$) between mean platelet volumes in the 4 age groups. No teenage patient had an abnormal MPV value. There was no difference ($P=0.104$) between the mean platelet values of teenagers versus adults. Mayer-Pickel et al. [25] reported a cutoff value of 10.85fL for MPV for the prediction of preeclampsia. We report 3 pregnant patients (1.79%), who had MPV over 10.85 (range, 11.24-12.99) and were able to deliver vaginally. Tesfay et al. [26] reported a cutoff MPV value of 9.45fL for the prediction of preeclampsia. We report 8 patients (4.79%) with MPV over 9.45fL (range, 9.51-12.99) who were able to deliver vaginally at term. Hassan et al. [27] reported a significant decrease in platelet count and a significant increase in MPV as biomarkers for preeclampsia. We report 2 patients (1.19%) with decreased

platelet count and 3 patients (1.79%) with increased MPV who gave birth vaginally at term. We report no patient with simultaneous decreased platelet count and increased MPV.

There was no difference ($P=0.364$) between platelet derived width numbers in the 4 age groups; nonetheless, the >40-year-old group had the median value over normal values (PDW=18.3%). No teenage pregnant patient had a decreased PDW value, whereas of the 130 adult pregnant patients, 4 (3.07%) had decreased PDW values. There was no difference ($P=0.131$) between the PDW values of teenagers versus adults.

Artunc Ulkumen et al. [28] reported increased PDW values in ectopic pregnancy, especially in ruptured ectopic pregnancy. We report 40.71% of healthy patients, with increased PDW values, who were still able to give birth vaginally. Karateke et al. [29] reported PDW and MPV significantly higher in preeclampsia patients compared with normal pregnant patients. We report increased values of PDW in 40.71% of healthy patients who gave birth vaginally. Artunc Ulkumen et al. [30], in another study, reported lower MPV and increased PDW in threatened preterm labor patients, with a cutoff value of 16.15 for the PDW values. We report increased PDW values in 40.71% of healthy patients who gave birth vaginally at term. We also report 123 patients (73.65%) with PDW values over 16.15 who delivered vaginally at term.

There was no difference ($P=0.119$) between plateletcrit percents in the 4 age groups. No pregnant patient, either teenager or adult, had abnormal plateletcrit values. The plateletcrit value was significantly increased ($P=0.043$) in adolescents as compared to adults, but they were in normal ranges.

Yücel et al. [31] and Karateke et al. [29] reported significantly decreased plateletcrit values in preeclamptic pregnant women versus healthy pregnant women. We report no abnormal plateletcrit values in healthy pregnant women just before at-term vaginal birth.

No significant difference ($P=0.258$) occurred between P-LCR values in the 4 different age groups. No teenage pregnant patient had abnormal P-LCR values, whereas of the 130 adult pregnant patients, 7 (5.38%) had abnormal, elevated, or decreased P-LCR values. There was no difference ($P=0.2$) between the P-LCR values of adolescents versus adults.

Sitotaw et al [32] reported that P-LCR significantly increased in preeclampsia patients versus healthy patients. We report 1.19% of patients healthy enough to give birth vaginally having increased P-LCR values. In our study group, no preeclampsia pregnant patient delivered vaginally at term.

The values of neutrophil-to-lymphocyte ratio were significantly higher ($P=0.024$) in teenage pregnant patients compared to adult pregnant patients; moreover, the median values were slightly over the normal limits. Gogoi et al. [33] reported higher NLR values in preeclampsia diagnosed at term women versus healthy pregnant women (6.8 ± 7.6 vs 3.0 ± 0.98), whereas Yücel et al. [31] reported no significant difference in NLR values in mild or severe preeclampsia patients compared with normotensive pregnant patients. We report no preeclampsia pregnant patient who delivered vaginally at term. Siristatidis et al. [34] reported NLR at the time of oocyte retrieval positively correlated with maternal age, and medically assisted reproduction failure associated with lower NLR values. We also reported significantly higher NLR values in healthy adolescents versus healthy adults, immediately before vaginal birth.

No significant difference ($P=0.287$) was found between the platelet-to-lymphocyte ratio values of the 4 pregnant patients' age groups, but value was slightly higher in teenage patients compared with the other age groups. PLR values were not significantly different in the teenagers versus adults ($P=0.073$). Hershko Klement et al. [35] detected no difference between high-risk and normal pregnant patients, for PLR and NLR, in each trimester; nevertheless, a weak, statistically significant correlation was detected between patients' age and either PLR or NLR. We also reported a significant difference in NLR values, and no significant difference in PLR values in teenagers versus adults, just before vaginal birth.

This work has some weaknesses: all the patients studied were Caucasian, because most of the population in Romania is Caucasian, with very few people of other races, and therefore the results of this study may not be applicable to other populations. Second, the number of pregnant patients over 40 years old was small ($n=7$); therefore, the mean values could not be calculated for this group, so we considered the median values to be more appropriate. The total number of patients ($n=167$) was also small, so a future cohort study including a much larger group

of healthy patients, will also be required to confirm or not these results.

5. CONCLUSION

Even if plateletcrit values or neutrophil-to-lymphocyte ratio values in teenage pregnant patients may be slightly higher than in adults, this was normal to happen in healthy patients, and required no therapeutic measures. Although there was no indication of differences between adolescents and adults, and also no increase in morbidity and mortality during childbirth due to the number of platelets and their variants, there is an increase in number in teenage mothers in Romania, compared to previous years, which raises the important demand of exploring as much as possible the current values before any emergency occurs. This study is important because whenever the need for therapeutic interventions, as well as consequences or complications during or after delivery, occur, the practitioners will be aware of the normal values in teenage pregnant patients, and will be able to proceed to informed decisions.

CONSENT

Informed consent was obtained from all the patients upon hospital admission.

ETHICAL APPROVAL

This study received the Elena Doamna Obstetrics and Gynecology University Hospital Research Ethics Committee Approval number 2 from February 5th, 2020. This study was approved by the Ethics Committee of the hospital.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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