Are the Mean Platelet Volume and Neutrophil/Lymphocyte Ratio Predictive for Gestational Cholestasis?

Hasan EROGLU[1], Harun Egemen TOLUNAY[1], Kemal SARSMAZ[1], Gokcen ORGUL[1], Dilek SAHIN[1], Aykan YUCEL[1]

Ankara, Turkey

ABSTRACT

OBJECTIVES: We aimed to determine whether mean platelet volume value and/or neutrophil/lymphocyte ratio values are useful as a predictive marker for gestational cholestasis.

STUDY DESIGN: Retrospective analysis of the data of patients diagnosed with pregnancy cholestasis between 2018-2019 in a perinatology clinic. 352 pregnant women were enrolled in the study (122 pregnant women with Intrahepatic cholestasis as study group and 230 pregnant women with no morbidity as the control group)

RESULTS: Mean platelet volume was significantly higher in pregnant women with intrahepatic cholestasis compared to the healthy controls, 9.30 (7-18) and 8.6 (6.7-11.5), respectively. The neutrophil/lymphocyte ratio was significantly higher in pregnant women with intrahepatic cholestasis compared to the healthy controls, 3.93 (0.46-13.75) and 4.25 (0.87-17.1), respectively. There was a statistically significant difference between the two groups for mean platelet volume (p <0.001). In the roc analysis, 8.85 fL for mean platelet volume had a sensitivity of 65% and a specificity of 59%.

CONCLUSION: When compared with healthy pregnancies, mean platelet volume value in gestational cholestasis increases significantly. However, the predictive strength of mean platelet volume for cholestasis is not strong enough to recommend its usage as a single parameter in clinical practice.

Keywords: Intrahepatic cholestasis of pregnancy, Neutrophil to lymphocyte ratio, Mean platelet volume

Gynecol Obstet Reprod Med 2021;27(2):105-108

Introduction

Intrahepatic cholestasis of pregnancy (ICP) is the most common liver disease due to pregnancy. It is a pregnancy-specific liver disease whose incidence varies worldwide (ranging from <1% to 27.6%). The etiology is based on the association of genetic, hormonal, and environmental factors that elevate bile acids, although it has not been established. It is characterized by pruritus and elevated serum bile acid concentrations. Typically, it occurs during the third trimester of pregnancy, with itching that can affect any part of the human body. It is characterized as liver dysfunction with increased serum bile acids as biochemically. Spontaneous preterm delivery, fetal distress, meconium staining of amniotic fluid, and sudden fetal death are clinical characteristics of the disease (1-4).

Mean platelet volume (MPV), an indicator of platelet size, is an easily detectable marker measured during whole blood count. A factor as an indicator of platelet activation, larger platelets are responsible for increased platelet aggregation and increased thromboxane A2 release. After all; it may cause vasoconstriction and increased vascular complications. Besides, the usage as an inexpensive and widely available marker, neutrophil to lymphocyte ratio (NLR) has also been proposed in the different obstetrics and gynecology medical practices (5-7).

In this paper, we aimed to evaluate (complete blood count parameters) the third-trimester NLR and MPV values in pregnancies complicated by ICP.

Material and Method

The medical records of Etlik Zubeyde Hanim Maternity and Women's Health Teaching and Research Hospital,

[1] *Etlik Zubeyde Hanim Maternity and Women's Health Teaching and Research Hospital, Ankara, Turkey*

Address of Correspondence: *Hasan Eroglu*
Etlik Zubeyde Hanim Maternity and Women's Health Teaching and Research Hospital, 06050 Etlik, Ankara Turkey
e-mail: drhasaner@gmail.com

Submitted for Publication: 16.01.2020 Revised for Publication:04.06.2020
Accepted for Publication: 29.07.2020 Online Published: 02.08.2021

ORCID IDs of the authors: *HE:0000-0002-1180-5299*
HET: 0000-0002-8922-4400 *KS: 0000-0003-0028-3576*
GO: 0000-0003-0578-4230 *DS: 0000-0001-8567-9048*
AY: 0000-0002-5888-692X

Quick Response Code:	Access this article online
	Website: www.gorm.com.tr e- mail: info@gorm.com.tr
	DOI:10.21613/GORM.2020.1064

How to cite this article: Eroglu H. Tolunay HE. Sarsmaz K. Orgul G. Sahin D. Yucel A. Are the Mean Platelet Volume and Neutrophil/Lymphocyte Ratio Predictive for Gestational Cholestasis? Gynecol Obstet Reprod Med. 2021; 27(2):105-108

Perinatology Department were reviewed. One hundred and twenty-two pregnant women with ICP and 230 pregnant women with no morbidity were retrospectively evaluated in the study. The control group was randomly selected from age and BMI matched healthy pregnant women. Pregnant women in the control group were selected from patients without maternal hypertension, concomitant vascular diseases, kidney diseases, liver diseases, presence of diabetes mellitus, and autoimmune diseases. Ethical approval was obtained for the study (04/19-07). Informed consent was obtained for data usage. Our study was conducted in accordance with the Declaration of Helsinki.

Third-trimester complete blood count parameters of the pregnant were examined. Complete blood count parameters that we evaluated, are consisted of blood samples taken in the routine third-trimester examination when the pregnant women have come to the hospital for delivery, NLR and MPV are inexpensive and easily calculated. NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count and, MPV was determined by the complete blood count machine, automatically.

The statistical package for the social sciences (SPSS) version 20.0 for Windows was used for all statistical analyses. Non-parametric tests were preferred, according to the tests of normality results. We used the Mann-Whitney U test to compare continuous variables. P-value <0.05 was considered as statistically significant. A Roc analysis was performed to determine the sensitivity and specificity of MPV in the prediction of the disease.

Results

The median age of cases of ICP and control group was 29.5 and 28, respectively. The median gravida number of cases of ICP and control group was 2. The median parity number was 1 in both groups. The median gestational week of cases with ICP and control group was 37 and 39.3, respectively (Table I). NLR and MPV values of the pregnant women complicated by ICP, were 3.93 (0.46-13.75) and 9.30 (7-18), respectively. NLR and MPV values of the pregnant women in the control group were 4.25 (0.87-17.1) and 8.6 (6.7-11.5), respectively. There was a statistically significant difference between the two groups for MPV (p<0.001) (Table II). In the Roc analysis, 8.85 fL for MPV had a sensitivity of 65% and a specificity of 59% (Figure 1).

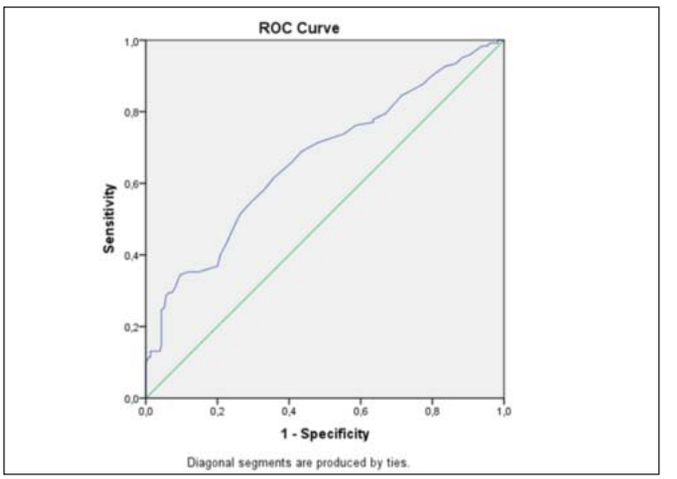

Figure 1: *Roc curve analysis of mean platelet volume results of patients diagnosed with cholestasis of pregnancy*

Table I: *Comparison of the control group and patients with gestational cholestasis according to some clinical and pregnancy characteristics*

	G. Cholestasis (n=122)		Control (n=230)		
ariables	Mean ±SD		Median Mean ±SD	Median	*p**
Age	29.11±6.21	29.5	28.64±5.18 ±5,18 ±5,18	28	0.0644
BMI	29.08±4.27	28.0	29.17±4.66	29	0.242
Gravida	2.13±1.36	2.0	2.69±1.32	2	0.383
Parity	0.88±1.14	1.0	1.32±1.09	1.0	0.761
Abortion	0.26±0.62	0.0	0.37±0.67	0.0	0.018
Birth week	36.97±1.61	37.0	39.25±1.056	39.3	<0.001
Day	3.10±1.79	3.0	2.87±3.42	2	0.042
Birth weight	3052±498.9	3090	3339±425	3345	0.597

p<0.05. SD: BMI:

Table II: *Comparison of the control group and patients with gestational cholestasis in terms of mean platelet volume and neutrophil to lymphocyte ratio*

	Gestational Cholestasis		Control		
Variables	Median	Minimum-Maximum	Median	Minimum-Maximum	*p**
Mean platelet volume	9.30	7-18	8.6	6.7-11.5	**<0.01**
Neutrophil lymphocyte ratio	3.93	046-13.75	4.25	0.87-17.1	**0.14**

*p<0.05 *Mann Whitney U test*

Discussion

We showed that third trimester NLR and MPV are higher in the ICP group compared to the control group. MPV values were statistically significantly higher in the ICP group. There are a few studies to examine NLR parameters in pregnant women complicated with ICP, to our knowledge. But no study evaluates MPV in pregnant with cholestasis.

Although the etiology of ICP is not established; genetic, hormonal, and environmental factors that increase bile acids are accused. Low selenium levels affect the antioxidant of liver capacity. Thus, hepatocyte damage leads to intrahepatic cholestasis due to the bile acid increase in the cell. Inflammation and oxidative processes are accused of in the pathogenesis of the disease (8,9).

Fetal and neonatal complications include prematurity, low birth weight, perinatal death, stillbirth, meconium aspiration syndrome, fetal in labor distress, and fetal-neonatal arrhythmia (10). In the pathophysiology of preterm labor due to ICP, a guiding study has shown that increased bile acids are effective in myometrium contraction (11). It is shown in an animal study that the accumulation of bile acid in fetal cardiomyocytes is responsible for the formation of arrhythmias (12). ICP scanning in general obstetric populations is based on a broad determination of risk factors and physically assessing fetal growth. After clinical suspicion, the fetus, placenta, and amniotic fluid are evaluated in detail. Early diagnosis is important for proper management in ICP.

NLR and MPV have been used as markers of inflammation in recent years. These parameters can be obtained quickly and cheaply from whole blood count. NLR and MPV are increasingly used as indicators of cancer and various systemic diseases as well as systemic inflammation. Although there are studies on whether these parameters may have predictive value in cases such as preeclampsia, endometriosis, and tuba ovarian abscess in gynecology and obstetrics practice, there is no study on the value of these parameters in ICP (13-15).

Some authors reported that maternal inflammation and organization of vascular beds, which are to be indicated by NLR, were associated with fetal development and preterm delivery. Consistent with our results, the literature data also showed that the increased maternal inflammatory response was accompanied by ICP (16).

High NLR and MPV values appear to reflect increased inflammation. Increased placental inflammation in the etiology of ICP may support this condition. Our study shows that increased NLR and MPV values may contribute to the diagnosis of ICP.

The absence of the determination of the severity of cholestasis, the low number of patients, and the absence of newborn outcomes are our study limitations.

Conclusion

The usage of NLR and MPV by complete blood count tests may facilitate the diagnostic process of ICP. One of the most important causes of obstetric follow-up is to identify patients at risk for perinatal problems (17). Early recognition of the disease and early treatment interventions are very important to reduce the rates of morbidity and mortality in ICP. MPV value in pregnancy cholestasis increases significantly. The usage of MPV may be useful in the diagnosis of ICP. However, the predictive strength of MPV for cholestasis is not strong enough to recommend its use as a single parameter in clinical practice. It should be kept in mind that the diagnosis of disease and appropriate management are extremely important for both fetal and maternal prognoses.

Acknowledgment: None
Funding Source: None
Author Contributions: HE, HET, KS: Concept, Writer, Design, Data processing, Analysis, and interpretation. HET, HE: Data processing, analysis, and interpretation, Design, Statistical analysis. GO, HET: Data collection, Processing, Analysis, and interpretation. HE: Data collection, Processing, Analysis, and interpretation. AY, DS: Supervision, Statistical analysis, Design. AY, DS: Supervision, Concept
Conflict of Interest: No conflict of interest

References

1. Ovadia C, Williamson C. Intrahepatic cholestasis of pregnancy: Recent advances. Clin Dermatol. 2016;34(3):327-34. doi: 10.1016/j.clindermatol.2016.02.004.
2. Oh CC, Oon H. Intrahepatic cholestasis of pregnancy. Cutis. 2018;102(3): E26-E27. PMID: 30372720.
3. Ozkan S, Ceylan Y, Ozkan OV, Yildirim S. Review of a challenging clinical issue: Intrahepatic cholestasis of pregnancy. World J Gastroenterol. 2015;21(23):7134-41. doi: 10.3748/wjg.v21.i23.7134.
4. Turkmen Gencosmanoglu G, Yilmaz ZV, Oguz Y, Yakut K, Sanhal CY, Uygur D. Intrahepatic cholestasis of pregnancy is associated with gestational diabetes mellitus. Gynecol Obstet Reprod Med. 2019;25(3):133-7 doi: 10.21613/GORM.2018.855.
5. Hershko Klement A, Hadi E, Asali A, Shavit T, Wiser A, Haikin E, et al. Neutrophils to lymphocytes ratio and platelets to lymphocytes ratio in pregnancy: A population study. PLoS One. 2018;13(5):e0196706. doi: 10.1371/journal.pone.0196706. eCollection 2018.
6. İlhan M, İlhan G, Gök AFK, Bademler S, Verit Atmaca F, Ertekin C. Evaluation of neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and red blood cell distribution width-platelet ratio as early predictor of acute pancreatitis in pregnancy. J Matern Fetal Neonatal Med. 2016; 29(9):1476-80. doi: 10.3109/14767058.2015.1051026.
7. Yıldız Ç, Karakuş S, Akkar Bozoklu Ö, Topbaş T, Çetin

M, Yanık A, et al. The significance of neutrophil-lymphocyte ratio and mean corpuscular volume in diagnosis of preeclampsia. Gynecol Obstet Reprod Med. 2016; 22(2):75-9.

8. Biberoglu E, Kirbas A, Daglar K, Kara O, Karabulut E, Yakut HI, et al. Role of inflammation in intrahepatic cholestasis of pregnancy. J Obstet Gynaecol Res. 2016; 42(3):252-7. doi: 10.1111/jog.12902. Epub 2016 Jan 19.
9. Kauppila A, Korpela H, Mäkilä UM, Yrjänheikki E. Low serum selenium concentration and glutathione peroxidase activity in intrahepatic cholestasis of pregnancy. Br Med J (Clin Res Ed). 1987;294(6565):150-2. doi: 10.1136/ bmj. 294.6565.150.
10. Alsulyman OM, Ouzounian JG, Ames-Castro M, Goodwin TM. Intrahepatic cholestasis of pregnancy: perinatal outcome associated with expectant management. Am J Obstet Gynecol. 1996;175(4 Pt 1):957-60. doi: 10. 1016/s0002-9378(96)80031-7.
11. Germain AM, Kato S, Carvajal JA, Valenzuela GJ, Valdes GL, Glasinovic JC. Bile acids increase response and expression of human myometrial oxytocin receptor. Am J Obstet Gynecol. 2003;189(2):577-82. Doi: 10.1016/s000 2-9378(96)80031-7.
12. Sheikh Abdul Kadir SH, Miragoli M, Abu-Hayyeh S, Moshkov AV, Xie Q, Keitel V, et al. Bile acid-induced arrhythmia is mediated by muscarinic M2 receptors in neonatal rat cardiomyocytes. PLoS One. 2010;5(3):e9689. doi: 10.1371/journal.pone.0009689.
13. Bozdag H, Bör Demirçivi E, Akdeniz E. The predictive value of total leukocyte count and leukocyte differential for severe preeclampsia. Perinat J. 2018;26(1):25-31. doi: 10.2399/prn.18.0261007
14. Toprak E, Bozkurt M, Dinçgez Çakmak B, Özçimen EE, Silahlı M, Ender Yumru A, et al. Platelet-to-lymphocyte ratio: A new inflammatory marker for the diagnosis of preterm premature rupture of membranes. J Turk Ger Gynecol Assoc. 2017;18(3):122-6. doi: 10.4274/jtgga. 2017.0028.
15. Kalem Z, Şimşir C, Bakırarar B, Namlı Kalem M. The additional diagnostic value of NLR and PLR for CA-125 in the differential diagnosis of endometrioma and benign ovarian cysts in women of reproductive age: a retrospective case-control study. The European Research Journal. 2020;6(2):111-9. doi: 10.18621/eurj.483442.
16. Rogers LK, Velten M. Maternal inflammation, growth retardation, and preterm birth: insights into adult cardiovascular disease. Life Sci. 2011;89(13-14):417-21. doi: 10. 1016/j.lfs.2011.07.017.
17. Marschall HU. Management of intrahepatic cholestasis of pregnancy. Expert Rev Gastroenterol Hepatol. 2015;9 (10):1273-9. doi: 10.1586/17474124.2015.1083857.