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Can hematologic parameters predict isolated oligohydramnios and isolated polyhydramnios?

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ABSTRACT

Aims: We fulfilled this study to anticipate the diagnosis of isolated oligohydramnios (IO) and isolated polyhydramnios (IP) by using the first trimester value of hematologic parameters.

Methods: We conducted a retrospective research 32 and 42 weeks of gestation women with IO and IP between in a single tertiary center in Turkey. In this cohort research three groups are composed of 65 IO patients and 56 IP patients and normal 97 patients that had normal volume of amniotic fluid.

Results: While PLR were significantly increased in the IO pregnants ($p < 0.05$) the distinction was not displayed in the IP pregnants. In addition, there was no notable variation in hematologic parameters; in terms of NLR, WBC, Hgb, MCV, PLT, PDW between patients and control patients ($p > 0.05$).

Conslusion: PLR values were independently associated with isolated oligohydramnios but not to isolated polyhydramnios. Hematologic parameters can be helpful in predicting isolated oligohydramnios.

Keywords: First trimester, NLR, PLR, isolated oligohydramnios, isolated polyhydramnios

INTRODUCTION

Oligohydramnios refers to the amniotic fluid volume (AFV) that is less than the minimum expected for gestational age and can be related with deseases like membranes' premature rupture, placental insufficiency and chromosomal or structural anomalies. Diagnosed by ultrasound examination, preferably based on an objective measurement such as amniotic fluid volume (AFV) ≤5 cm or one deepest pocket at least (SDP) <2 cm, but a subjective assessment of decreased AFV is also acceptable.[1] Isolated oligohydramnios (IO) is described that oligohydramnios while absence of fetal structural and chromosomal abnormalities, fetal growth restriction, intrauterine infection, and maternal disease. The percentage of IO ranges from 0.5 to 5% accordingly the difference in definition.[2] Even IO is noticed at >37 weeks of pregnancy to prevent sudden death labor induction is recommended, this pregnancies were at increased risk for meconium aspiration syndrome, cesarean birth for an fetal heart rate abnormalities, increased risk of follow-up in neonatal intensive care unit.[3,4] These harmful perinatal consequences are related with utero-placental insufficiency between uterus and placenta, and/or amniotic fluid with meconium because of umbilical cord compression.[5] Although the reason is unknown, yet it has been thought an indicator of placental insufficiency in the manner of fetal growth retardation (FGR) and preeclampsia.[6]

Polyhydramnios, is a pathologic excess of AFV in pregnancy ranges from 0.2 to 1.6% of the whole of pregnant women and is related with perinatal side effects due to a higher incidence of intrauterine fetal demise, prematüre birth, early breaking of membranes, cord prolapse, fetal macrosomia, breech presentation, cesarean delivery, and postpartum hemorrhage.[7,8] Idiopathic causes and various diseases can be reasoned with polyhydramnios. Approximately 20% are due to a congenital anomaly and 60% to 70% are idiopathic with no identified underlying cause. Fetal anomalies (often associated with an underlying genetic abnormality or syndrome) are the most common conditions associated with severe polyhydramnios, while maternal diabetes, multiple gestation, and idiopathic factors are more often associated with milder cases.[9] Defectivenes which improve the swallowing reflex such as esophageal atresia, duodenal atresia and neuromuscular disorders such as myotonic dystrophy.[10] The diagnosis of polyhydramnios

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is based upon sonographic visualization of increased AFV and single deepest pocket (SDP) ≥8 cm or amniotic fluid volume (AFV) ≥24 cm.[11]

Pregnancy is a chronic mild inflammatory condition that may directly or indirectly affect certain hematological parameters observed in blood tests.[12] Some of these changes may vary in pathological conditions. It has been detected to increase in preeclampsia both neutrophil-lymphocyte ratio (NLR) and Red blood cells Distribution Width (RDW).[13] Studies of the neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) have shown a significant association with cancer and many diseases with inflammation; these parameters are beginning to be considered as possible inflammation markers.[14] This research purposes to appraise the first trimester hematological values in complete blood count for predicting IO and PO.

METHODS

This retrospective comparative study was carried out at Department of Obstetric and Gynecology in Kayseri City Training and Research Hospital, a tertiary referral center. Kayseri City Hospital Clinical Researches Ethics Committee (Date: 01.04.2021, Decision No: 376). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. We consider for diagnose to the oligohydramnios and polyhydramnios the table according to weeks in the study describing Rinat Gabbay-Benziv's 3rd TM AMS index published in JMFNM in 2020. We retrospectively reviewed 1572 obstetric us reports in Department of Radiology, Kayseri City Hospital, between January 1, 2020 and December 31, 2021. Among these pregnants, singleton pregnancies between 32-42 weeks of gestation without fetal anomalies and fetal neuromuscular disorders, without IUGG, without PROM, without a diagnosis of a certain systemic disease such as DM or HT were screened to determine the IO and IP. Pregnant women aged 18-40 ages ≥28 weeks with IO and IP current first trimester complete blood count results were collected for the study. The patients with normal amniotic fluid created from low-risk term pregnancies with a normal amount of amniotic fluid (AFI 5-25 cm) 387 healthy pregnant women. A total of 65 women that fit these criteria with IO and 56 woman with IP were detected. We evaluated of all groups first trimester complete blood count parameters. These parameters were white blood cell count (WBC), hemoglobin (Hgb), mean corpuscular volume (MCV), neutrophil and lymphocyte count, neutrophil lymphocyte ratio (NLR), platelet count, platelet lymphocyte ratio (PLR), red cell distribution width (RDW), platelet distribution with (PDW) and mean platelet volume (MPV). In addition, the records of 97 healty women who gave birth at the same hospital and time were accepted as a control group. The information that are contained maternal age, parity, gestational age at delivery is saved.

Statistical Analysis

The data were investigated with the SPSS 21.0 program. Whether the continuous variables were suitable for normal distribution according to the groups was analyzed with the Kolmogorov-Smirnov test. A Mann-Whitney U test was used to compare variables that did not conform to a normal distribution. One-way analysis of variance (ANOVA) was used to compare normally distributed data according to three or more groups, and the Kruskal-Wallis test was used to compare non-normally distributed data. The Chi-square test or Fisher's exact probability test was used to determine whether the frequency distributions of categorical variables were homogeneously distributed among groups.

RESULTS

A sum of 218 patients were included. Of these, 65 pregnant women were with isolated oligohydramnios (study group), 56 pregnant women were with isolated polyhydramnios and 97 pregnant women with a normal amount of amniotic fluid (control group). The demographic features of the patient groups are demonstrated in Table 1 and Table 2. Statistically significant distinction was not displayed between groups concerning the age, obstetric history (gravida, parity, number of abortion), history of previous caesarean delivery. Mean birth week was 38.34±1.14 for the oligohydramnios group, 38.58±1.31 in the polyhydramnios group and 38.73±0.88 healthy control group, and this finding was not statistically significant.

Table 1. Features of patients with and without oligohydramnios

Parameters	Oligohydramnios (n=65)	Healthy pregnant (n=97)	p value
Age [year]	31.68±4.68	31.02±4.492	0.74
Birth weeks	38.34±1.14	38.73±0.88	0.120
Gravidity	2.79±1.46	2.81±1.276	0.89
Parity	1.20±1.46	1.23±0.51	0.46

Table 2. Features of patients with and without polyhydramnios

Parameters	Polyhydramnios (n=56)	Healthy pregnant (n=97)	p value
Age [year]	32.12±2.96	31.02±4.492	0..81
Birth weeks	38.58±1.31	38.73±0.88	0.77
Gravidity	2.59±1.86	2.81±1.276	0.86
Parity	1.02±1.85	1.23±0.51	0.38

In terms of hematological parameters investigated in the first trimester, there was no statistically significant distinction between the groups' WBC, hemoglobin,

neutrophil, or lymphocyte counts (p > 0.05). İmportant distinction was not displayed between the groups with regards to platelet counts, RDW, MPV, NLR values in the first trimester (p >0.05). PLR values were significantly higher in the oligohydramnios group in comparison with the healthy control group (p < 0.05) and not in the polyhydramnios group (Table 3, 4).

Table 3. Comparison of the hematological test results measured in the first trimester of patients with and without oligohydramnios between the groups

Parameters	Oligohydramnios (n=65)	Healthy pregnant (n=97)	p value
WBC (×10³/L)	9.81±0.12	9.79±0.55	0.62
Hemoglobin, g/L	11.07±0.19	10.61±0.12	0,85
Platelets (×10³/L)	281.967+7.44	261.508±3.62	0.01
Neutrophils (×10³/L)	6.37+0.28	6.47±1.08	0.67
Lymphocytes (×10³/L)	3.05±0.06	2.81±0.11	0.84
RDW	12.4+0.24	11.91±0.13	0.70
MPV	9.7±0.2	9.3±0.21	0.24
NLR	2.032±0.11	2.12±0.04	0.72
PLR	118.6±3.15	112.13±3.62	0.03

Abbreviations: WBC:white blood cells; RDW=:red blood cell distribution width; MPV=mean platelet volume (MPV); NLR=Neutrophil to lymphocyte ratio; PLR= Platelet to lymphocyte ratio

Table 4. Comparison of the hematological test results measured in the first trimester of patients with and without Polyhydramnios between the groups

Parameters	Polyhydramnios (n=56)	Healthy pregnant (n=97)	p value
WBC (×10³/L)	8.98±0.19	9.79±0.55	0.44
Hemoglobin, g/L	11.22±0.12	10.61±0.12	0,63
Platelets (×10³/L)	270.895+8.04	261.508±3.62	0.43
Neutrophils (×10³/L)	6.22+0.25	6.47±1.08	0.83
Lymphocytes (×10³/L)	2.23±0.22	2.81±0.11	0.66
RDW	11.89+0.22	11.91±0.13	0.59
MPV	9.14±0.18	9.3±0.21	0.31
NLR	3.10±0.26	2.12±0.04	0.1
PLR	114.08±4.28	112.13±3.62	0.35

DISCUSSION

The study aimed to be helpful the early prediction of IO and IP pregnancy thanks to the complete blood count values which are routinely used in many obstetrics clinics.

We evaluated maternal serum levels of the inflammation parameters NLR, and PLR to determine whether the fetal and placental inflammation that develops in isolated oligohydramnios and polyhydramnios causes an inflammatory response in the mother. Indeed, platelets was involved in a processes such as endothelial damage,[15] angiogenesis and hypoxia and increased platelet activity may conduced to the pathogenesis of IO. PLR levels were found increased in the oligohydramnios group than the control group. This is suggested that there is an inflammatory process in the pathophysiology of oligohydramnios and that a maternal inflammatory response may occur against this inflammation. Decreased uteroplacental flow may induce an augmentation in the appearance of chemokines and can overstimulate an inflammatory response.[16] Progressive decrease in uteroplacental flow causes activation of neutrophils in the fetus in the subsequent stages of pregnancy and increased chemokine release by resulting in chronic hypoxia.[17] These events lead to activation of neutrophils in the later stages of pregnancy.[18] Platelets, like neutrophils, increase the secretion of cytokines at the onset of inflammation, and increased cytokines contribute to increased inflammation by enhancing new neutrophil and platelet synthesis.[19] Otherwise a study involving 11,415 patients reported no significant difference in PLR and NLR values investigated in the first trimester between high-risk pregnancies and healthy pregnancies.[20]

The clinical importance of oligohydramnios derives cause of jeopardize fetal and neonatal wellness. More than one study has shown that increasing proinflammatory cytokine production may be caused hostile pregnancy effects such as uterine activation and prematurity.[21,22] It is unclear whether IO reflects an underlying pathological condition, for which reason the management of IO is still controversial These negative obstetric outcomes associated with oligohydramnios are assumed to be cause of placental insufficiency.[23] Therefore it may be helpful to reveal the relation between the inflammatory process in the mother with IO, inflammatory parameters, and obstetric outcomes. In the light of this information, first trimester hematological indices may be important in early diagnosis and prediction of IO. Previous studies have also investigated whether hematological parameters investigated in the first trimester can predict poor obstetric outcomes.[24] Recently, Kurt et al.[25] investigated that high RDW levels were related with both the constution and the degree of preeclampsia. It was reported that, in preeclampsia, hypoxic placenta is caused to elevated inflammatory events (eg, neutrophil, monocyte, and macrophage) and ended with the demolition of red blood cells by figuring with oxygen radicals and proteolytic enzymes.

Polyhydramnios could be idiopathic or related with different desease. About 40 percent of polyhydramnios is idiopathic.[26] However, an abnormality is diagnosed after birth in until 25 percent of cases that are considered prenatal idiopathic.[27] Persistent polyhydramnios has been related with an higher risk for adverse maternal and neonatal outcomes, in addition to poor outcomes with associated fetal morphological abnormalities.[28] The inflammatory process in the amniotic fluid or placenta may also be significant to detect cause of IP formation such as IO.

CONCLUSION

Consequently the reason for fulfilling this study was to asist for prediction of appropriate, convenient and cheaper examination of IO and IP by modest routine heamatologic markers. In summary, PLR increases in inflammation and were seen that risen in IO. This suggests that they could be used as markers in both the diagnosis of oligohydramnios and in predicting perinatal outcomes in suspected cases. It may be clinically helpful to determine prognostic parameters that would support the diagnosis of IO and enable to take precautions in terms of the risks. We think that IO can be identified early and neonatal morbidity and mortality reduced to a minimum by evaluating women's platelet values in the first trimester and PLR. We could not detect increases in inflammatory processes such as PLR, as in IO. More study is requered for the IP.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Kayseri City Hospital Clinical Researches Ethics Committee (Date: 01.04.2021, Decision No: 376)

Informed consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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REFERENCES

1. Shrem G, Nagawkar SS, Hallak M, Walfisch A. Isolated Oligohydramnios at Term as an Indication for Labor Induction: A Systematic Review and Meta-Analysis. *Fetal Diagn Ther.* 2016;40(3):161-173. doi:10.1159/000445948
2. Hill LM, Breckle R, Wolfgram KR, O'Brien PC. Oligohydramnios: ultrasonically detected incidence and subsequent fetal outcome. *Am J Obstet Gynecol.* 1983;147(4):407-410. doi:10.1016/s0002-9378(16)32235-9
3. ACOG committee opinion no. 560: Medically indicated late-preterm and early-term deliveries. *Obstet Gynecol.* 2013;121(4):908-910. doi:10.1097/01.AOG.0000428648.75548.00
4. Rabie N, Magann E, Steelman S, Ounpraseuth S Oligohydramnios in complicated and uncomplicated pregnancy: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol.* 2017;49(4):442.
5. Chamberlain PF, Manning FA, Morrison I, Harman CR, Lange IR. Ultrasound evaluation of amniotic fluid volume. I. The relationship of marginal and decreased amniotic fluid volumes to perinatal outcome. *Am J Obstet Gynecol.* 1984;150(3):245-249. doi:10.1016/s0002-9378(84)90359-4
6. Ashwal E, Hiersch L, Melamed N, Aviram A, Wiznitzer A, Yogev Y. The association between isolated oligohydramnios at term and pregnancy outcome. *Arch Gynecol Obstet.* 2014;290(5):875-881.
7. Golan A, Wolman I, Sagi J, Yovel I, David MP. Persistence of polyhydramnios during pregnancy--its significance and correlation with maternal and fetal complications. *Gynecol Obstet Invest.* 1994;37(1):18-20. doi:10.1159/000292513
8. Dashe JS, McIntire DD, Ramus RM, Santos-Ramos R, Twickler DM. Hydramnios: anomaly prevalence and sonographic detection. *Obstet Gynecol.* 2002;100(1):134-139. doi:10.1016/s0029-7844(02)02013-6
9. Ben-Chetrit A, Hochner-Celnikier D, Ron M, Yagel S. Hydramnios in the third trimester of pregnancy: a change in the distribution of accompanying fetal anomalies as a result of early ultrasonographic prenatal diagnosis. *Am J Obstet Gynecol.* 1990;162(5):1344
10. Stoll CG, Alembik Y, Dott B. Study of 156 cases of polyhydramnios and congenital malformations in a series of 118,265 consecutive births. *Am J Obstet Gynecol.* 1991;165(3):586-590. doi:10.1016/0002-9378(91)90290-8
11. Hughes DS, Magann EF, Whittington JR, Wendel MP, Sandlin AT, Ounpraseuth ST. Accuracy of the ultrasound estimate of the amniotic fluid volume (amniotic fluid ındex and single deepest pocket) to ıdentify actual low, normal, and high amniotic fluid volumes as determined by quantile regression. *J Ultrasound Med.* 2020;39(2):373.
12. Serin S, Avci F, Ercan O, Kostu B, Bakacak M, Kiran H. Is neutrophil/lymphocyte ratio a useful marker to predict the severity of pre-eclampsia? *Pregnancy Hypertension.* 2016;6(1):22-25.
13. Miremberg H, Grinstein E, Herman HG, et al. The association between isolated oligohydramnios at term and placental pathology in correlation with pregnancy outcomes. *Placenta.* 2020;90:37-41. doi:10.1016/j.placenta.2019.12.004
14. Feng JF, Huang Y, Chen QX. Preoperative platelet lymphocyte ratio (PLR) is superior to neutrophil lymphocyte ratio (NLR) as a predictive factor in patients with esophageal squamous cell carcinoma. *World J Surg Oncol.* 2014;12(1):58. doi:10.1186/1477-7819-12-58
15. Turgut A, Sak ME, Ozler A, Soydinc HE, Karacor T, Gül T. Alterations of peripheral blood cells in tubal ectopic pregnancy. *Ginekol Pol.* 2013;84(3):193-196.
16. Mellembakken JR, Aukrust P, Hestdal K, Ueland T, Abyholm T, Videm V. Chemokines and leukocyte activation in the fetal circulation during preeclampsia. *Hypertension.* 2001;38(3):394-398. doi:10.1161/01.hyp.38.3.394
17. Erten O, Tekeli Taskomur A. Relationship of cystatin C, Hs-CRP, neutrophil-lymphocyte ratio and platelet-lymphocyte ratio with isolated oligohydramnios. *Ginekol Pol.* 2022;93(11):881-888. doi:10.5603/GP.a2021.0230
18. Sonaglioni A, Esposito V, Caruso C, et al. Association between neutrophil to lymphocyte ratio and carotid artery wall thickness in healthy pregnant women. *Eur J Obstet Gynecol Reprod Biol.* 2020;255:98-104. doi:10.1016/j.ejogrb.2020.10.034
19. Mantovani A, Cassatella MA, Costantini C, Jaillon S. Neutrophils in the activation and regulation of innate and adaptive immunity. *Nat Rev Immunol.* 2011;11(8):519-531. doi:10.1038/nri3024
20. Hershko Klement A, Hadi E, Asali A, et al. Neutrophils to lymphocytes ratio and platelets to lymphocytes ratio in pregnancy: A population study. *PLoS One.* 2018;13(5).e0196706
21. Challis JR, Lockwood CJ, Myatt L, Norman JE, Strauss JF 3rd, Petraglia F. Inflammation and pregnancy. *Reprod Sci.* 2009;16(2):206-215. doi:10.1177/1933719108329095
22. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation?. *Curr Pharm Des.* 2011;17(1):47-58. doi:10.2174/138161211795049804
23. Miremberg H, Grinstein E, Herman HG, et al. The association between isolated oligohydramnios at term and placental pathology in correlation with pregnancy outcomes. *Placenta.* 2020;90:37-41. doi:10.1016/j.placenta.2019.12.004

24. Siristatidis C, Christoforaki V, Zafeiriou Z, Mastorakos G, Vrantza T, Daskalakis G. First trimester neutrophil-to-lymphocyte ratio (NLR) and pregnancy outcomes in medically assisted reproduction (MAR): a case control study. *Gynecol Endocrinol.* 2019;35(5):434-438. doi:10.1080/09513590.2018.1534949

25. Kurt RK, Aras Z, Silfeler DB, Kunt C, Islimye M, Kosar O. Relationship of red cell distribution width with the presence and severity of preeclampsia. *Clin Appl Thromb Hemost.* 2015;21(2):128-131. doi:10.1177/1076029613490827

26. Dorleijn DM, Cohen-Overbeek TE, Groenendaal F, Bruinse HW, Stoutenbeek P. Idiopathic polyhydramnios and postnatal findings. *J Matern Fetal Neonatal Med.* 2009;22(4):315-320. doi:10.1080/14767050802531870

27. Touboul C, Picone O, Levaillant JM, et al. Clinical application of fetal urine production rate in unexplained polyhydramnios. *Ultrasound Obstet Gynecol.* 2009;34(5):521-525. doi:10.1002/uog.6440

28. Ross MG, Brace RA; National Institute of Child Health and Development Workshop Participants. National Institute of Child Health and Development Conference summary: amniotic fluid biology--basic and clinical aspects. *J Matern Fetal Med.* 2001;10(1):2-19. doi:10.1080/714904292