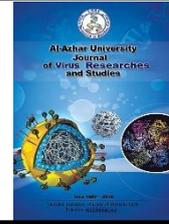




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The Study of Platelet-to-Lymphocyte Ratio and Neutrophil-to-Lymphocyte Ratio Change in Pregnant Women with Preterm Premature Rupture of Membranes and Threatened Preterm Labour

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Abstract

Preterm premature rupture of membranes (PPROM) is closely related with maternal and fetal complications. Therefore, early diagnosis is extremely important to provide maternal and fetal well-being. Many inflammatory markers have been evaluated for their ability to diagnose membrane rupture at early stages. The aim of this paper is to investigate peripheral blood platelets, neutrophils and lymphocytes counts in women with preterm premature rupture of membranes (PPROM) and threatened preterm labour (TPL) compared with gestation-matched controls in order to learn how they change. This is case – control study, was conducted at Obstetrics and Gynecology department in Al-Zahraa university hospital, Cairo, Egypt, on 80 pregnant women was divided into 3 groups; (group1); included 30 controls, (group 2a); included 25 preterm premature rupture of membranes, (group 2b); included 25 threatened preterm labor. There was statistically significant difference between the three studied groups regarding NLR. There was no statistically significant difference between the three studied groups regarding platelets and PLR. Based on our finding, NLR in preterm premature rupture of membranes group was significantly higher than in those had threatened preterm labor and control group. The leukocytes, neutrophils, lymphocytes, NLR and CRP statistically significant predictors of the preterm premature rupture of membranes, to be able to extrapolate these findings into clinical daily practice, further studies are needed.

Keywords: Preterm labour perinatal outcome, platelet-to-lymphocyte ratio.

1. Introduction

Preterm premature rupture of the membranes (PPROM) was defined as the rupture of membranes between 24 and 37 weeks of gestation diagnosed and confirmed with the presence of gross pooling of amniotic fluid in the vagina by sterile speculum examination. Threaten preterm labour (TPL) was defined as the presence of at least four regular and painful

uterine contractions in 20 min, which continued at least 30 s, as measured by an electronic cardiotocography device [1]. Preterm labour is an obstetric condition that complicates 5–9% of pregnancies. Spontaneous preterm labour with intact membranes and preterm premature rupture of the membranes (PPROM) are the main obstetric precursors leading to preterm

birth [2]. Spontaneous preterm labour with intact membranes and PPROM causes to adverse maternal morbidity and mortality including chorioamnionitis, endomyometritis, postpartum haemorrhage and increase in birth rates with caesarean delivery [3]. Both spontaneous preterm labour and PPROM are important risk factors for prematurity and infectious conditions such as sepsis that cause morbidity and mortality in the neonatal period. Early diagnosis and appropriate management are very important for preventing poor outcomes because of these serious problems. Regardless of causes, inflammation is the only pathologic process for a strong causal relation with preterm labour and PPROM has been defined [4]. Complete blood count is a simple, inexpensive and easily available laboratory test in clinical practice. Previous studies showed that increased platelet counts were associated with infection, inflammation and malignancy [5]. Recently, the platelet-to-lymphocyte ratio (PLR) and the neutrophil-to-lymphocyte ratio (NLR) were emerged as the novel potential inflammatory markers which have been linked to adverse outcomes in various pathologic conditions [6].

2. Patients and Methods

This study was case control study conducted at Obstetrics and Gynecology department in Al-Zahraa university hospital, Cairo, Egypt. This study was conducted on 80 pregnant women (24w-37w) who attending Al Zahraa University Hospital. These women subdivided into 2 groups: Group I (30) normal pregnant. Group II (50) subdivided into 2 groups: (25) PPROM and (25) TPL.

2.1 Inclusion Criteria

Pregnant female with a singleton pregnancy, Primigravida or Multiparas. 20 – 40 years old. Gestational ages were at (24- 37) weeks calculated to the date of last

menstrual cycle. Complaining of PPROM or TPL or normal pregnant

2.2 Exclusion Criteria

The patients with gestational diabetes mellitus and preeclampsia, systemic diseases and acute or chronic inflammatory diseases, such as multiple gestations, haematopoietic system disorders, malignancies.

2.3 Ethical Consideration

Study protocol had been submitted for approval by Institutional Review Board, Al-Azhar University. Informed verbal consent had been obtained from each participant sharing in the study. Confidentiality and personal privacy had been respected in all levels of the study.

2.4 Method

All The eligible subjects included in this study were subjected to the following: Informed consent was obtained from each participant. A detailed medical history, which include: The maternal age, gravidity, parity and the gestational age at admission, birth week, birth weight, neonatal intensive care unit (NICU) admission rate and the presence of neonatal sepsis were recorded from medical records. Examination: General physical examination including Vital sings especially temperature and obstetric examination. Investigations: Laboratory investigation: routine lab investigation including complete blood count. Blood sample: Samples of peripheral venous blood were obtained from the antecubital vein on admission (before administration of betamethasone and antibiotic prophylaxis) and were studied at the laboratory. Laboratory parameters (including complete blood count) of all the participants were recorded. Blood samples were taken into standardized tubes containing dipotassium ethylene dinitro tetraacetic acid (EDTA)

for complete blood count (CBC). The PLR was calculated as the number of platelets divided by the lymphocyte count, and NLR was calculated by dividing the neutrophil count by the lymphocyte count, both of which will be obtained from the same blood samples.

2.5 Statistical methods

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean \pm SD, the following tests were used to test differences for significance, correlation by Pearson's correlation or Spearman's.

3. Results

Our study regarding the basic characteristics of the three studied groups showed that, the mean age among group 1 was 28.5 ± 7.4 , it was 29.2 ± 8.1 among group 2a, and 27.8 ± 7.9 among group 2b. There was no statistically significant difference between the three studied groups regarding age. Regarding residency, there were 70% from rural area and 30% from urban areas among group 1, there were 64% from rural areas and 36% from urban areas among group 2a and 60% from rural areas and 40% from rural areas among group 2b. There was no statistically significant difference between the three studied groups regarding residency. The mean BMI was 24.9 ± 2.2 among group 1, 25.4 ± 2.3 among group 2a, 26.1 ± 2.6 among group 2b. There was no statistically significant difference between the three studied groups regarding BMI. In a similar recent study by *Ozel et al.*, [7] A total

number of 157 pregnant women, 60 with PPRM, 50 gestation-matched controls with TPL and 47 gestation matched healthy controls were included in this cross-sectional case control study, the mean age among Control group was 28.1 ± 2.2 , it was 30.5 ± 5.9 among PPRM group, and 27.8 ± 4.2 among TPL group. The mean maternal age was higher in the PPRM group ($p < 0.005$). Our results also showed that, the mean gravidity was 3.3 ± 1.5 among group 1, 3.6 ± 1.8 among group 2a, 2.9 ± 1.9 among group 2b. There was no statistically significant difference between the three studied groups regarding gravidity. The mean parity was 1.7 ± 1.4 among group 1, 1.8 ± 1.6 among group 2a, 1.6 ± 1.1 among group 2b. There was no statistically significant difference between the three studied groups regarding parity. There were 33.3% had previous CS and 76.7 didn't among group 1, 44% had previous CS and 66% hadn't among group 2a, and 40% had previous CS and 60% hadn't among group 2b. There was no statistically significant difference between the three studied groups regarding previous history of CS. *Ozel et al.*, [7] reported that, there was no statistically significant difference between the three studied groups regarding gravidity and parity. The mean gravidity among Control group was 2.4 ± 2.0 , it was 2.4 ± 1.9 among PPRM group, and 2.1 ± 1.4 among TPL group, the mean parity among Control group was 0.89 ± 1.2 , it was 0.93 ± 1.3 among PPRM group, and 0.74 ± 1.0 among TPL group.

Also, there was no statistically significant difference between the three studied groups regarding Hb, HCT and RBCs. The mean Hb was 12.1 ± 0.3 among group 1, 12.7 ± 0.2 among group 2a, 11.5 ± 0.4 among group 2b; The mean HCT was 36.1 ± 3.7 among group 1, 34.5 ± 2.6 among group 2a, 37.5 ± 2.8 among group 2b; The mean RBCs was 4.1 ± 0.7 among group 1, 4.3 ± 0.6 among group 2a, 4.5 ± 0.5 among group 2b p-values were 0.215, 0.501 and 0.211 respectively. *Daglar et al.*, [8] showed in Comparison of serum levels of blood

parameters among the Control (Group 1), Threatened PTL (Group 2) and Preterm Delivery (Group 3) groups that there was no statistically significant difference between the three studied groups regarding hemoglobin and WBC the mean hemoglobin was 12.1 ± 0.2 g/d among group 1, 11.7 ± 0.3 g/d among group 2, 12.4 ± 0.6 g/d among group 3; the mean WBC count was 8.7 ± 4.5 among group 1, 10.1 ± 3.4 among group 2, 10.8 ± 3.9 among group 3. Upon comparison between the three studied groups regarding Leukocytes, Neutrophils and lymphocytes, there was a statistically significant difference between the three studied groups. The mean leukocytes were 9.1 ± 1.3 among group 1, 10.8 ± 2.4 among group 2a, 10.7 ± 2.6 among group 2b, the mean Neutrophils was 7.8 ± 1.6 among group 1, 9.3 ± 2.5 among group 2a, 9.9 ± 1.9 among group 2b, the mean lymphocytes was 1.8 ± 0.4 among group 1, 1.6 ± 0.2 among group 2a, 1.4 ± 0.2 among group 2b, p-values were <0.001 , 0.003 and 0.011 respectively. **Ozel et al., [7]** showed that, there was a significant difference observed in neutrophil count between PPROM group and healthy controls, and in lymphocyte count between PPROM and TPL groups. The mean Neutrophils among Control group was 7228.3 ± 2143.0 , it was 8947.4 ± 2834.6 among PPROM group, and 8089.9 ± 2308.7 among TPL group, the mean lymphocytes among Control group was 1802.7 ± 552.3 , it was 1705.7 ± 605.9 among PPROM group, and 1998.7 ± 608.4 among TPL group. Another study by **Kim et al., [9]** showed that the mean counts of neutrophil (9175.3 ± 4027.9 vs. 7411.8 ± 2304.3 $P < 0.001$) in preterm delivery group were significantly higher than those in term delivery group, and lymphocyte count (1560.5 ± 655.3 vs. 1785.5 ± 585.9 $P = 0.02$) in preterm delivery group was significantly lower than that in term delivery group. Regarding NLR there was statistically significant difference between the three studied groups (p-value <0.001). While, there was no statistically significant

difference between the three studied groups regarding platelets (p-value = 0.129) and PLR (p-value = 0.051). ROC for predicting preterm premature rupture of membranes showed that, Lymphocytes (AUC = 0.811 ; Sensitivity= 0.900 ; Specificity= 0.278 and p-value= 0.001), Neutrophils (AUC = 0.769 ; Sensitivity= 0.800 ; Specificity= 0.333 and p-value= 0.005), Leukocytes (AUC = 0.756 ; Sensitivity= 0.800 ; Specificity= 0.444 and p-value= 0.007). The neutrophil-to-lymphocyte ratio (NLR) values were significantly higher in PPROM group than TPL group and healthy control group (6.1 ± 3.9 , 4.4 ± 1.7 , 4.4 ± 2.2 , $p=0.007$, $p=0.018$, respectively). While no significant difference was observed for platelet count and PLR values between the groups, the mean PLR among Control group was 131.3 ± 56.2 , it was 149.5 ± 74.9 among PPROM group, and 130.2 ± 56.8 among TPL group. [7]

Toprak et al., [10] in a prospective case-control study, in which 121 pregnant women were with PPROM and 96 ages matched pregnant women with spontaneous preterm labour, found higher NLR levels in the PPROM group.

In another study **Daglar et al., [8]** demonstrated that the NLR values were significantly higher in the women with spontaneous preterm labour than healthy controls. The mean NLR among Control group was 4.77 ± 3.18 , it was 5.21 ± 2.77 among Threatened PTL group, and 5.29 ± 2.98 among Preterm Delivery group (p-value < 0.01). **Kim et al., [9]** reported that, because the neutrophil and lymphocyte counts in preterm delivery group were significantly different from those of term delivery group, we calculated NLR and evaluated the diagnostic and prognostic significance of NLR. The NLR was significantly higher in preterm delivery group than term delivery group and was able to discriminate between preterm delivery group and term delivery group (7.1 ± 5.7 vs. 4.5 ± 1.7 $P < 0.001$). Our results showed that, there was not statistically

significant difference between the three studied groups regarding monocytes, eosinophils, and basophils p-values were 0.219, 0.501 and 0.711 respectively. ROC for NLR as predictor for preterm premature rupture of membranes showed that, NLR (AUC =0.836; Sensitivity=0.950; Specificity=0.278 and p-value were <0.001). **Kim et al., [9]** demonstrated that the mean counts of basophil (28.0 ± 22.0 vs. 22.3 ± 12.2 $P = 0.03$) in preterm delivery group were significantly higher than those in term delivery group. While there was no statistically significant difference between the two studied groups regarding monocytes (434.7 ± 180.0 vs. 416.4 ± 170.7) and eosinophils (102.7 ± 100.6 vs. 94.2 ± 72.2). In analysis of ROC curve for NLR, the AUC was 0.665 (95% CI: 0.586–0.744) and a cut-off value was 5.47 with 52.0% sensitivity and 78.1% specificity. **Ozel et al., [7]** reported that at a cut-off level of 5.14, NLR accurately predicted occurrence of neonatal sepsis AUC = 0.717 (95% confidence interval 0.610–0.824), $p = 0.001$ with sensitivity and specificity rates of 69.7% and 72.0%, respectively. Therefore, the main results are There was no statistically significant difference between the three studied groups regarding age. There was no statistically significant difference between the three studied groups regarding residency. There was no statistically significant difference between

the three studied groups regarding BMI. **Table (1)**. There was no statistically significant difference between the three studied groups regarding previous history of CS. **Table (2)**. There were 33.3% had previous CS and 76.7 didn't among group 1, 44% had previous CS and 66% hadn't among group 2a, and 40% had previous CS and 60% hadn't among group 2b. **Figure 3**. There was no statistically significant difference between the three studied groups regarding past history of abortion. **Table (3)**. There was no statistically significant difference between the three studied groups regarding Hb, HCT and RBCs. **Table (4)** Upon comparison between the three studied groups regarding Leukocytes, Neutrophils and lymphocytes, there was statistically significant difference between the three studied groups. **Table (5)**. There was statistically significant difference between the three studied groups regarding NLR. There was no statistically significant difference between the three studied groups regarding platelets and PLR. **Table (6)**. There was no statistically significant difference between the three studied groups regarding monocytes, eosinophils, and basophils. **Table (7)**. The leukocytes, neutrophils, lymphocytes, NLR and CRP statistically significant predictors of the preterm premature rupture of membranes **Table (8)**.

Table (1): Basic characteristics of the three studied groups.

Variables	Group 1 n= 30	Group 2a n= 25	Group 2b n= 25	P value
Age (years)				
Mean± SD	28.5± 7.4	29.2± 8.1	27.8± 7.9	0.115
Residency				
Rural n (%)	21 (70)	16 (64)	15 (60)	0.220
Urban n (%)	9 (30)	9 (36)	10 (40)	
BMI				
Mean± SD	24.9± 2.2	25.4± 2.3	26.1± 2.6	0.711

ANOVA; Chi square test; *p is significant at <0.05.

Table (2): Obstetric history among the three studied groups.

Variables	Group 1	Group 2a	Group 2b	P value
Gravidity Mean± SD	3.3± 1.5	3.6± 1.8	2.9± 1.9	0.442
Parity Mean± SD	1.7± 1.4	1.8± 1.6	1.6± 1.1	0.863
Previous CS Yes n (%) No n (%)	10 (33.3) 20 (76.7)	11 (44) 14 (66)	10 (40) 15 (60)	0.159

ANOVA; Chi square test; *p is significant at <0.05.

Table (3): Obstetric characteristics among the three studied groups.

Variables	Group 1 n= 30	Group 2a n= 25	Group 2b n= 25	P value
Gestational age (weeks) Mean± SD	35.1± 1.6	36.2± 0.9	33.5± 2.1	0.413
Past preeclampsia Yes n (%) No n (%)	8 (26.7) 22 (73.3)	6 (24) 19 (76)	5 (20) 20 (80)	0.192
Previous abortion Yes n (%) No n (%)	5 (16.7) 25 (83.3)	3 (12) 22 (88)	2 (8) 23 (92)	0.701

ANOVA; Chi square test; *p is significant at <0.05.

Table (4): Comparison between the three studied groups regarding RBCs metrics.

Variables	Group 1 n= 30	Group 2a n= 25	Group 2b n= 25	P value
Hb (mg/dl) Mean± SD	12.1± 0.3	12.7± 0.2	11.5± 0.4	0.215
HCT (%) Mean± SD	36.1± 3.7	34.5± 2.6	37.5± 2.8	0.501
RBCs (x 10¹²) Mean± SD	4.1± 0.7	4.3± 0.6	4.5± 0.5	0.211

ANOVA; Chi square test; *p is significant at <0.05.

Table (5): Comparison between the three groups regarding white blood cells.

Variables	Group 1 n= 30	Group 2a n= 25	Group 2b n= 25	P value
Leukocytes (X10⁹) Mean± SD	9.1± 1.3	10.8± 2.4	10.7± 2.6	<0.001*
Neutrophils (X10⁹) Mean± SD	7.8± 1.6	9.3± 2.5	9.9± 1.9	0.003*
Lymphocytes (X10⁹) Mean± SD	1.8± 0.4	1.6± 0.2	1.4± 0.2	0.011*

ANOVA; Chi square test; *p is significant at <0.05.

Table (6): Platelet, NLR and PLR among the three studied groups.

Variables	Group 1 n= 30	Group 2a n= 25	Group 2b n= 25	P value
Platelets (X10⁹/L) Mean± SD	235.1± 63.4	240.5± 67.3	238.6± 60.5	0.129
NLR Mean± SD	3.7± 2.1	6.3± 3.4	5.9± 4.1	<0.001*
PLR Mean± SD	140.3± 60.5	153.7± 63.1	152.4± 61.6	0.051

ANOVA; Chi square test; *p is significant at <0.05.

Table (7): Monocytes, Eosinophils and Basophils among the three studied groups.

Variables	Group 1 n= 30	Group 2a n= 25	Group 2b n= 25	P value
Monocyte (X10 ⁹ /L) Mean± SD	0.61± 0.2	0.59± 0.3	0.62± 0.3	0.219
Eosinophil (X10 ⁹ /L) Mean± SD	0.13± 0.03	0.15± 0.04	0.14± 0.02	0.501
Basophils (X10 ⁹ /L) Mean± SD	0.03± 0.01	0.04± 0.02	0.03± 0.02	0.711

ANOVA: *p is significant at <0.05.

Table (8): Multivariate analysis to predict preterm premature rupture of membranes.

Predictors	B	Wald	P value
Leukocytes	0.080	0.006	0.020*
Neutrophils	0.712	3.012	0.002*
Lymphocytes	0.129	2.071	0.012*
NLR	2.420	6.034	0.014*
CRP	-4.528	4.470	0.035*

Multiple logistic regression: *p is significant at <0.05.

4. Discussion

The main findings of our study are as follows: (1) NLR values were significantly higher in the PPRM group as compared with TPL group and healthy controls. (2) The leukocytes, neutrophils, lymphocytes, NLR and CRP statistically significant predictors of the preterm premature rupture of membranes (3). There was no significant difference in platelet count and PLR values between the groups. Although various factors are suspected in the pathogenesis of preterm labour and PPRM, infection or inflammation plays an important role in the initiation of preterm labour, and the best method is amniocentesis for the detection source of the intrauterine infection. However, amniocentesis is related to a risk of fetal loss of approximately 0.5%. Therefore, there is a much more need to use a non-invasive method rather than invasive methods. CRP, the erythrocyte sedimentation rate and the white blood cell count have been used in to determine the cases which associated inflammatory conditions in clinical practice. Several studies showed that also NLR and PLR, obtained from complete blood count in peripheral blood, have prognostic and predictive values in various benign and malignant diseases including inflammatory

diseases, coronary artery disease, preeclampsia and gynecologic or gastrointestinal malignancies (Kumtepe et al., 2011; Ying et al. 2014; Sarı et al. 2015; Sec,kin et al. 2016a, 2016b). (12) (13)

In a recent study, Lattanzi et al. (2018) demonstrated that higher neutrophils, lower lymphocytes and higher NLR upon admission were independently associated with poor outcome at 30 days after the intra-cerebral hemorrhage. We aimed to demonstrate in this study that the cytokines released from the inflammatory region in the choriondecidua during the early phase of inflammation can cause some changes in the number of leucocyte subsets in the women with PPRM and TPL. Our results were partially compatible with the recent reported literature.

5. Conclusion

Based on our finding, NLR in preterm premature rupture of membranes group was significantly higher than in those had threatened preterm labor and control group. The leukocytes, neutrophils, lymphocytes, NLR and CRP statistically significant predictors of the preterm premature rupture of membranes, to be able to extrapolate these findings into clinical daily practice, further studies are needed.

References

- 1- Song Q, Li Y, Wang Y, Wei C, Liu J, Liu M. Increase dneutrophil-to-lymphocyte ratios are associated with greater risk of hemorrhagic transformation in patients with acute ischemic stroke. *Current Neurovascular Research*. 2018; 15:326–335.
- 2- Lattanzi S, Brigo F, Trinka E, Cagnetti C, Di Napoli M, Silvestrini M. Neutrophil-to-lymphocyte ratio in acute cerebral hemorrhage: a system review. *Translational Stroke Research*. 2018; 10(2):137–145.
- 3- Jung EY, Park KH, Lee SY, Ryu A, Joo JK, Park JW. Predicting outcomes of emergency cerclage in women with cervical insufficiency using inflammatory markers in maternal blood and amniotic fluid. *International Journal of Gynecology and Obstetrics*. 2016; 132:165–169.
- 4- Kurtoglu E, Kokcu A, Celýk H, Tosun M, Malatyalyoglu E. May ratio of neutrophil to lymphocyte be useful in predicting the risk of developing preeclampsia? Apilotstudy. *The Journal of Maternal-Fetal and Neonatal Medicine*. 2015; 28:97–99.
- 5- Ekýn A, Gezer C, Kulhan G, Avcý ME, Taner CE. Can platelet count and mean platelet volume during the first trimester of pregnancy predict preterm premature rupture of membranes? *Journal of Obstetrics and Gynaecology Research*. 2015; 41:23–28.
- 6- Akboga MK, Canpolat U, Yuksel M, Yayla C, Yılmaz S, Turak O, et al. Platelet to lymphocyte ratio as a novel indicator of inflammation is correlated with the severity of metabolic syndrome: a single center large-scale study. *Platelets*. 2016; 27:178–183.
- 7- Ozel A, Davutoglu EA, Yurtkal A, Madazli R. How do platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio change in women with preterm premature rupture of membranes, and threaten preterm labour? *Journal of Obstetrics and Gynaecology*. 2019; DOI: 10.1080/01443615.2019.1621807.
- 8- Daglar H, Kýrbas A, Kaya B, Kýlýncoglu F. The value of complete blood count parameters in predicting preterm delivery. *European Review for Medical and Pharmacological Sciences*. 2016; 20:801–805.
- 9- Kim M, Lee BS, Park Y, Seo K. Serum markers for prediction of spontaneous preterm delivery in preterm labour. *Eur J Clin Invest*. 2011; 41 (7): 773–780. DOI: 10.1111/j.1365-2362.2011.02469. x.
- 10- Toprak E, Bozkurt M, Cakmak BD, Ozcýmen EE, Sýlahlý M, Yumru AE, et al. Platelet-to-lymphocyte ratio: a new in flammatory marker for the diagnosis of preterm premature rupture of membranes. *Journal of the Turkish German Gynecological Association*. 2017; 8:122.
- 11- Kumtepe Y, Dundar O, Cetinkaya K, Ingeç, M. 2011. Preeclampsia and eclampsia incidence in the eastern anatolia region of Turkey: the effects of high altitude. *Journal of the Turkish German Gynecological Association* 12:26.
- 12- Sarı I, Sunbul M, Mammadov C, Durmus E, Bozbay M, Kivrak T, Gerin F. 2015. Relation of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio with coronary artery disease severity in patients undergoing coronary angiography. *Kardiologia Polska (Polish Heart Journal)*, 73: 1310–1316.

- 13- Sec,kin KD, Karlı MF, Yücel B, Bestel M, Yıldırım D, Canaz E, Akbayır O. 2016a. The utility of tumor markers and neutrophil lymphocyte ratio in patients with an intraoperative diagnosis of mucinous borderline ovarian tumor. *European Journal of Obstetrics and Gynecology and Reproductive Biology* 196:60–63.