



The role of neutrophil/lymphocyte ratio, platelet/lymphocyte ratio and mean platelet volume in diagnosis of hydrosalpinx

Hidrosalpinks tanısında nötrofil/lenfosit oranı, trombosit/lenfosit oranı ve ortalama trombosit hacminin rolü

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ABSTRACT

Aim: Our study aimed to investigate the role of Neutrophil/Lymphocyte Ratio (NLR), Platelet/Lymphocyte Ratio (PLR), and Mean Platelet Volume (MPV) values in the diagnosis of patients who had Hydrosalpinx.

Materials and Methods: Between March 2018 and June 2023, 349 patients who underwent hysterosalpingography (HSG) due to the diagnosis of infertility in our hospital were included. Demographic and clinical data of 89 patients with hydrosalpinx detected on imaging were compared with 260 patients with normal Hsg findings.

Results: Neutrophil and Platelet levels were found to be significantly higher in the Hydrosalpinx-group than the control group ($p<0.001$). The presence of Hydrosalpinx was found to be significantly higher in patients who were diagnosed with secondary infertility ($p<0.001$). Neutrophil and Platelet levels were significantly higher in the bilateral-Hydrosalpinx-group than the unilateral-Hydrosalpinx-group ($p:0.036$, $p:0.012$, respectively). The NLR and PLR were found to be significantly higher in the bilateral-Hydrosalpinx-group than the unilateral-Hydrosalpinx-group ($p:0.038$, $p:0.009$, respectively). MPV were found to be significantly lower in the bilateral-Hydrosalpinx-group than the unilateral-Hydrosalpinx-group ($p:0.011$).

Conclusion: The findings of our study support the literature data on the relationship between NLR, PLR, MPV, and chronic inflammatory processes. These markers deserve to be evaluated again and again in prospective and controlled studies, in which they will be considered together with clinical findings, to investigate their ability to predict the diagnosis of Hydrosalpinx, its severity, and clinical outcomes in infertile patients.

Keywords: Hydrosalpinx, infertility, platelet/lymphocyte ratio, neutrophil/lymphocyte ratio, mean platelet volume.

Öz

Amaç: Bu çalışmanın amacı hidrosalpinksli hastaların tanısında Nötrofil/lenfosit oranı, Platelet/lenfosit oranı ve Mean Platelet volume değerinin rollerini ortaya koymaktır.

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Gereç ve Yöntem: Mart 2018 – Haziran 2023 tarihleri arasında hastanemizde infertilite tanısı nedeniyle histerosalpingografi (HSG) işlemi uygulanan 349 hasta dahil edilmiştir. Görüntülemeye hidrosalpinks saptanan 89 hastanın demografik ve klinik verileri, normal Hsg bulguları olan 260 hasta ile karşılaştırıldı.

Bulgular: Hidrosalpinks grubunda nötrofil düzeyi ve platelet düzeyi, kontrol grubuna kıyasla anlamlı yüksek tespit edilmiştir ($p<0.001$). Sekonder infertilite tanılı hastalarda hidrosalpinks varlığı anlamlı yüksek saptanmıştır ($p<0.001$). Bilateral hidrosalpinks grubunda nötrofil düzeyi ve platelet düzeyi unilateral hidrosalpinks grubu ile kıyasla anlamlı yüksek saptanmıştır ($p:0.036$, $p:0.012$ sırasıyla). Bilateral hidrosalpinks grubunda platelet/lenfosit oranı ve nötrofil/lenfosit oranı, unilateral hidrosalpinks grubu ile kıyasla anlamlı yüksek saptanmıştır ($p:0.038$, $p:0.009$ sırasıyla). Bilateral hidrosalpinks grubunda mean platelet volüme düzeyi, unilateral hidrosalpinks grubuna göre anlamlı düşük saptanmıştır ($p:0.011$).

Sonuç: Çalışmamızdaki bulgular Platelet/lenfosit oranı, Nötrofil/lenfosit oranı ve Mean Platelet volume ile kronik inflammatuar süreçler arasındaki ilişkiye dair önceki literatürü desteklemektedir. Bu belirteçlerin, infertil hastalarda, hidrosalpinks tanısını, hastalığın şiddetini ve klinik sonuçlarını tahmin etme yeteneklerini araştırmak için, klinik bulgularla birlikte ele alındıkları prospektif, kontrollü çalışmalarda yeniden değerlendirilmeyi hak etmektedir.

Anahtar Sözcükler: Hidrosalpinks, infertilite, platelet/lenfosit oranı, nötrofil/lenfosit oranı, mean platelet volume.

INTRODUCTION

It is considered that many different mechanisms are effective in the relationship between Hydrosalpinx and infertility. Hydrosalpinx, as its name suggests, occurs when the fallopian tubes become obstructed and filled with clear fluid (1). It can affect one or both fallopian tubes simultaneously, with infertility becoming inevitable if it occurs in both (1). Pregnancy can theoretically be achieved when Hydrosalpinx is unilateral, but its detrimental effects on fertility remain significant (2). Although the precise mechanism reducing pregnancy rates in the presence of Hydrosalpinx has not been fully elucidated, there is a possibility that the fluid within the tube may exert toxic effects on the embryo, and its spread to the endometrial tissue during ovulation may have a toxic impact on the embryo as well (3). Hysterosalpingography (HSG) is used as the gold standard diagnostic criterion for the investigation of tubal pathologies, particularly in infertility etiology (4). HSG is a diagnostic radiologic procedure that is widely used as a first-line investigation for assessing fallopian tube patency (5). Hydrosalpinx typically develops due to adhesions resulting from previous infections, endometriosis, and fallopian tube surgeries (5), which can cause narrowing or blockage of the fallopian tubes at their ends (6). The presence of infections and endometriosis sets the stage for chronic inflammatory processes (6). In recent years, there has been

increasing recognition of the role of inflammatory markers in various diagnoses (7). Blood tests monitoring the neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are employed to assess the body's inflammatory responses and infections (8). The average NLR is typically less than 2.5, while a high ratio might be a sign of an inflammatory illness. The typical PLR is less than 150, and a high ratio might point to an infection or inflammatory reaction within the body (9). PLR and NLR values are commonly used to identify illnesses and inflammatory reactions in the body. However, elevated PLR and NLR values might potentially be a sign of infections or other inflammatory diseases including cancer (9). The Mean Platelet Volume (MPV) is a statistic showing the average platelet volume that is assessed during blood tests (10). Blood clotting involves thrombocytes. MPV is utilized to assess the platelets' functioning and activation levels (10). An increased proportion of larger platelets is associated with the progression of an inflammatory state, often following procoagulation, intracellular production of pro-inflammatory cytokines, granule degranulation, and the release of splenic platelets into circulation (11). These cells rapidly migrate to the site of inflammation upon activation (12), which explains the decreased MPV values observed in patients with ongoing inflammation (13). A comprehensive analysis of hematological parameters can provide physicians with important knowledge in the diagnosis of Hydrosalpinx. It is

very important to uncover the relationship between Hydrosalpinx, which occurs as a result of chronic inflammatory processes, and inflammatory markers. The present study aimed to investigate the roles of NLR, PLR, and MPV in the diagnosis of individuals with Hydrosalpinx.

MATERIALS and METHODS

This study was designed as a retrospective observational case-control study and was designed in line with the Helsinki Declaration Principles. Informed consent forms were received from the individuals in this current research. This study was started after receiving Ethics Committee approval number 2024/229 from our hospital. The present study comprised 349 individuals who had sought treatment at our infertility clinic between March 2018 and June 2023. These individuals were diagnosed with either primary or secondary infertility and underwent Hysterosalpingography (HSG) to explore the causes of their infertility. HSG scans for all patients were conducted within the first 5 days following the conclusion of menstruation. Laboratory data and HSG results of the participants were retrospectively collected from patient records and hospital databases. Participants were divided into two groups based on whether Hydrosalpinx was detected in their HSG results. Among the patients included in the study, 89 participants with Hydrosalpinx and 260 patients without Hydrosalpinx were divided into two separate groups. Demographic data such as age, gravida, parity, Body Mass Index (BMI), etc., were retrospectively compared between the groups with and without Hydrosalpinx. The groups with and without Hydrosalpinx were compared retrospectively with regard to preoperative complete blood count (Platelet, Lymphocyte, Neutrophil, Leukocyte, PLR, NLR, and MPV). Conditions that might cause changes in blood parameters, such as the presence of endometriosis, presence of adenomyosis, hematological diseases, chronic systemic diseases, anticoagulant use, and oral contraceptive use, were considered as exclusion criteria. Neutrophil, Lymphocyte, and the Beckman Coulter Gen-S System instrument (Beckman-Coulter Inc.) were utilized in our laboratory to conduct a complete blood count, during which Mean Platelet Volume (MPV) characteristics were assessed. The PLR parameter was calculated by dividing the platelet

count by the absolute lymphocyte count, while the NLR parameter was obtained by dividing the absolute neutrophil count by the absolute lymphocyte count.

Statistical Analysis

For the analyses of the data, the SPSS 26.0 (IBM Inc., Chicago, IL, USA) was utilized. The Kolmogorov-Smirnov Test was employed to determine the normalcy of the analysis. In addition to the statistical methods (mean±standard deviation) for identification, the Independent t-test was employed to compare the pair groups in the study data evaluation, and the qualitative data were compared using the Chi-Square Test. There was a 95% Confidence Interval (CI) used in the analysis of the result values. For the p-value, less than 0.05 indicated statistical significance.

RESULTS

In the present research, the average age was 29.55 ± 4.01 in the group with Hydrosalpinx and 29.36 ± 4.53 in the control group, with no significant difference found between the groups ($p: 0.704$). Hemoglobin levels were found to be 9.94 ± 2.88 g/dL in the Hydrosalpinx group and 10.29 ± 2.79 g/dL in the control group, with no significant difference observed between the groups ($p: 0.327$). However, the neutrophil level was determined to be 6.60 ± 1.45 in the Hydrosalpinx group and 5.64 ± 1.11 in the control group, showing a significantly higher level in the Hydrosalpinx group ($p<0.001$). The platelet level was 291.60 ± 64.91 in the hydrosalpinx group and 256.82 ± 56.940 in the control group, with a significant difference observed between the two groups ($p<0.001$). The NLR was 2.68 ± 3.63 in the hydrosalpinx group and 2.10 ± 0.44 in the control group, with no significant difference observed between the groups in this regard ($p: 0.134$). The PLR was 123.22 ± 168.85 in the hydrosalpinx group and 94.21 ± 24.57 in the control group, with no significant difference observed between the groups ($p: 0.108$). The MPV was 8.02 ± 1.24 in the hydrosalpinx group and 8.28 ± 1.71 in the control group, with no significant difference observed among the groups ($p: 0.124$) (Table-1).

There were 264 patients in the primary infertility group, with 53 (20.1%) patients diagnosed with hydrosalpinx, and 211 (79.9%) patients without hydrosalpinx. In the secondary infertility group, there were 85 patients, with 36 (42.4%) patients diagnosed with hydrosalpinx, and 49 (57.6%)

patients without hydrosalpinx. When comparing patients in terms of primary and secondary infertility and the presence of hydrosalpinx,

hydrosalpinx was found to be significantly more prevalent in secondary infertile participants ($p < 0.001$) (Table-2).

Table-1. Comparison of clinical and demographic data based on the existence of Hydrosalpinx.

	Hydrosalpinx (+) n:89	Hydrosalpinx (-) n:260	p
Age(years)	29.55±4.01	29.36±4.53	*0.704
Body Mass Index (kg/m²)	22.74±1.71	22.49±1.45	*0.208
Hemoglobin (g/dL)	9.94±2.88	10.29±2.79	*0.327
Neutrophil (n/mL)	6.60±1.45	5.64±1.11	*<0.001
Platelet (n/mL)	291.60±64.91	256.82±56.940	*<0.001
Lymphocyte (n/mL)	3.16±0.49	3.00±0.80	*0.860
NLR	2.68±3.63	2.10±0.44	*0.134
PLR	123.22±168.85	94.21±24.57	*0.108
MPV (fl)	8.02±1.24	8.28±1.71	*0.124

*Independent sample t-test, BMI: Body mass index, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, MPV: Mean platelet volume

Table-2. The Relationship between infertility type and Hydrosalpinx.

	Primary Infertility 264-(%)	Secondary Infertility 85-(%)	Total 349-(%)	p
Hydrosalpinx (-)	211-(79.9%)	49-(%57.6)	260-(74.5%)	*<0.001
Hydrosalpinx (+)	53-(%20.1)	36-(%42.4)	89-(%25.5)	

* Chi Square test

Table-3. Comparison of clinical and demographic data according to the Hydrosalpinx type.

	Bilateral Hydrosalpinx n:53	Unilateral Hydrosalpinx n:36	p
	Mean ±SD		
Age (years)	29.66±5.1	28.92±3.76	*0.451
Body Mass Index (kg/m²)	22.44±1.37	22.56±1.57	*0.697
Hemoglobin (g/dL)	9.97±2.98	9.91±2.78	*0.936
Neutrophil (n/mL)	6.64±1.35	6.14±1.46	*0.036
Platelet (n/mL)	305.66±57.1	270.89±70.91	*0.012
Lymphocyte (n/mL)	3.12±0.48	3.22±0.51	*0.361
NLR	2.52±0.28	2.07±0.62	*0.038
PLR	99.76±23.40	86.03±24.25	*0.009
MPV (fl)	7.72±2.51	8.66±0.62	*0.011

*Independent sample t-test, BMI: Body mass index, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, MPV: Mean platelet volume

In our study, the average age was 29.66±5.1 in the group with bilateral hydrosalpinx and 28.92±3.76 in the unilateral hydrosalpinx group, and no significant difference between the groups ($p > 0.05$). The neutrophil level was 6.64±1.35 in

the bilateral hydrosalpinx group, 6.14±1.46 in the unilateral hydrosalpinx group, and was significantly higher in the bilateral hydrosalpinx group ($p < 0.036$). The platelet level was 305.66±57.1 in the bilateral hydrosalpinx group,

270.89±70.91 in the unilateral hydrosalpinx group, and was significantly higher in the bilateral hydrosalpinx group (p:0.012). NLR was 2.52±0.28 in the bilateral hydrosalpinx group, 2.07±0.62 in the unilateral hydrosalpinx group, and was significantly higher in the bilateral hydrosalpinx group (p:0.038). PLR was 99.76±23.40 in the bilateral hydrosalpinx group, 86.03±24.25 in the unilateral hydrosalpinx group, and was found to be significantly higher in the bilateral hydrosalpinx group (p:0.009). MPV was 7.72±2.51 in the bilateral hydrosalpinx group, 8.66±0.62 in the unilateral hydrosalpinx group, and was significantly lower in the bilateral hydrosalpinx group (p:0.011). There are 20 patients in the right unilateral hydrosalpinx group and 16 patients in the left unilateral hydrosalpinx group (Table-3).

DISCUSSION

As one of the causes of primary and secondary infertility, Hydrosalpinx can be seen bilaterally or unilaterally as the cause of a chronic inflammatory process or a previous surgery. Although the Hysterosalpingography Method is used commonly for the diagnosis of Hydrosalpinx, the widespread use of inflammatory markers in gynecological diseases in recent years has brought to mind its possible relationship with Hydrosalpinx. Many recent investigations have proven that NLR, PLR, and MPV might have the potential as markers of gynecological inflammatory disorders and obstetric problems and malignancies (e.g., endometriosis, adenomyosis, adnexal torsion, endometrial hyperplasia, and preeclampsia) (14-17). In our study, we found that there was no significant difference in NLR, PLR and MPV levels between the hydrosalpinx group and the non-hydrosalpinx group.

It is already known that Systemic inflammation brought on by infections and adhesions results in a reduction in lymphocytes and an increase in neutrophils. NLR is a straightforward indicator of the inflammatory response that shows how well the cellular immune system is able to counteract the degree of systemic inflammation brought on by infection and adhesions (18, 19). The first cells to reach the infection site are Neutrophils. The increase in the Neutrophils causes a decreased lymphocytes, causing increased NLR, which is the primary parameter investigated in this present research (18, 19).

In the research conducted by Duan et al., a significant relationship was found with the NLR level, which is considered an inflammation indicator in infertility patients (20). In another research in the literature, unexplained infertile patients were analyzed by employing a comparison with the control group, and no differences were reported in terms of NLR and Neutrophil parameters (21). It is considered that the contradiction between studies in the literature occurred depending on the cause of infertility. In this current research, no significant differences were detected between the Hydrosalpinx group and non-Hydrosalpinx group based on NLR. However, Neutrophil levels were observed to be significantly greater in the Hydrosalpinx group.

In the literature, in an investigation in which infertile patients were evaluated, a negative relationship was detected between PLR and implantation (21). In the study conducted by Duan et al., a significant relation was detected with the PLR level, which is considered an indicator of inflammation in infertility patients (20). It was proved in an investigation that was conducted by Yang et al. to be highly associated with inflammation in infertile patients who were diagnosed with endometriosis. A positive correlation was found with PLR value in infertile women (22). In the literature, a correlation was found with PLR value in unexplained infertile patients and in patients who had infertility detected as a cause of endometriosis. In this present research, contrary to the literature data, no significant differences were detected between the group with and without Hydrosalpinx based on PLR and Platelet counts. However, the relationship with Hydrosalpinx has not been analyzed directly in other studies in the literature.

A study conducted by Avcioglu et al. reported that in order to differentiate between the early and severe stages of endometriosis, which results in infertility, MPV and other Platelet indicators may be useful biomarkers (23). In an infertility-based research by Li et al., MPV was found to be significantly elevated in women with PCOS when made a comparison to women without PCOS (24). In our study, contrary to the literature data, no significant differences were reported between the group with and without Hydrosalpinx based on MPV. The relationship with Hydrosalpinx has not been directly evaluated in other studies in the literature.

Patients who had primary and secondary infertility were evaluated in a previous study conducted by Al Subhi T et al., and the Hydrosalpinx rate was found to be 19% in primary infertile patients and 29% in secondary infertile patients, and a significant difference was uncovered (25). In the study of Benksim et al., no significant differences were detected based on tubal factor prevalence in the etiology of primary and secondary infertility (26). The rate of Hydrosalpinx was observed to be significantly greater in individuals who were diagnosed with secondary infertility in our study. The reason for the contradiction in studies in the literature might be that tubal factor and the presence of Hydrosalpinx are considered as two separate criteria.

Bilateral tubal obstruction was shown to be the most typical reason of infertility in women, and the most typical reason of obstruction of the fallopian tubes was pelvic inflammatory disease in a study that was conducted by Abebe et al. (27). In the investigation conducted by Ambildhuke et al., tubal obstruction was shown to be the most typical reason of infertility in females (28). In the research of Elsharif et al., the relation between previous infections and pelvic inflammatory disease was reported to be the most typical reason of tubal obstruction in women (29). In the research conducted by Seçkin et al., the NLR was found to be significantly higher in individuals who were diagnosed with pelvic inflammatory disease (30). In this present research, the NLR was found to be significantly greater in individuals who had bilateral Hydrosalpinx than in patients who had unilateral Hydrosalpinx. Considering the relationship between previous infections and pelvic inflammatory disease in the etiology of bilateral Hydrosalpinx, our data were found to be compatible with the literature data. In the research conducted by Guo et al., the PLR was

found to be significantly greater in patients who had endometriosis and pelvic adhesion (31). The PLR in patients who had bilateral Hydrosalpinx was found to be significantly greater in our study than in individuals who had unilateral Hydrosalpinx. Considering the relationship between chronic inflammatory processes such as pelvic adhesions and endometriosis in the etiology of bilateral Hydrosalpinx, our data were found to be compatible with the literature data. In the study that was conducted by Hoccoğlu et al., MPV was found to be significantly lower in individuals who were diagnosed with pelvic inflammatory disease (32). MPV in patients who had bilateral Hydrosalpinx was observed to be significantly lower than in individuals who had unilateral Hydrosalpinx in our study. Considering the relationship between previous infections and pelvic inflammatory disease in the etiology of bilateral Hydrosalpinx, our data were found to be compatible with the literature data.

CONCLUSION

The current findings corroborate information from earlier studies about the connection between chronic inflammatory processes, NLR, PLR, and MPV. As far as the authors are aware, this is the first research to compare and contrast MPV, PLR, and NLR as inflammatory markers in patients who have Hydrosalpinx. NLR, PLR, and MPV seem to be useful markers that can be used for the diagnosis of bilateral Hydrosalpinx and merit a second assessment in prospective, controlled trials where they are taken into account with clinical results to look at their potential to predict the diagnosis of hydrosalpinx, the severity of the condition, and clinical outcomes in individuals who are sterile.

Conflict of interest: No conflict of interest was declared between the authors.

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