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# Association of Interleukin-8 (Il-8) Level on Benign and Malignant Type of Ovarian Neoplasm

**Surya Setiawan[1], Sharvianty Arifuddin[2], Masita Fujiko[3], St. Nur Asni[4], Eddy R. Moeljono[5], Irma Savitri Ch. Rasjad[6]**

[1,2,3,4,5,6]Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Hasanuddin, Makassar, South Sulawesi, Indonesia

**ABSTRACT**

**Objective :** Ovarian cancer is a global problem and is the eighth most common type of cancer in women. The proinflammatory IL-8 cytokine has been established as an immunoregulatory cytokine. Ovarian cancer cells continuously secrete this cytokine which increases its tumorigenicity.

**Methods :** Observational study with cross-sectional design. The sample of this study were ovarian neoplasm patients who underwent surgery at Dr. Wahidin Sudirohusodo hospital and the networking hospitals. The sampling was done by consecutive random sampling. Measurement of serum IL-8 was conducted using the ELISA method. Data were analyzed by chi-square test.

**Result:** Serum IL-8 levels were found to be associated with staging and histopathological results in ovarian neoplasms with a significant elevation of IL-8 levels at a mean value of 146.10 pg/mL ($p < 0.05$) in advanced stage ovarian neoplasm and at a mean value of 152.43 pg/mL ($p < 0.05$) in ovarian neoplasm with epithelial histopathology results. Although an increase in serum IL-8 levels was also observed in the ovarian neoplasm group with an abnormal CA-125 result with a mean value of 124.16 pg/mL ($p > 0.05$), malignant RMI with a mean value of 148.91 pg/mL ($p > 0.05$), and cytology containing malignant cells with a mean value of 167.68 pg/mL ($p > 0.05$), these findings were not statistically significant.

**Conclusion:** In this study, it was concluded that IL-8 levels were significantly increased in ovarian neoplasms with advanced stage and histopathological results of epithelial type.

**KEYWORDS**: interleukin-8, malignancy, ovarian neoplasm

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## INTRODUCTION

Ovarian neoplasms are estimated to reach 250,000 cases and cause 152,000 deaths each year (Ferlay et al., 2015). The highest prevalence of this cancer is in Eastern Europe (11.4 per 100,000) and Central Europe (6 per 100,000). Statistical data from the American Cancer Society states that the incidence of death from ovarian neoplasms in the world is around 5% of all malignancies in women and is ranked fifth as the cause of death from cancer, after lung, mammary, colorectal and pancreatic cancer.[1]

Interleukin-8 was originally described as a chemokine whose primary function is to attract polymorphonuclear inflammatory leukocytes that act on CXCR1/2. It has recently been found that tumors very frequently duplicate the production of these chemokines, which in a malignant context confer distinct pro-tumor functions. Reportedly, this includes angiogenesis, signaling cancer stem cell survival and myeloid cell attraction.[2] It was found that interleukin-8 levels were increased in ovarian cyst fluid, ascites and tumor tissue from ovarian cancer. Increased interleukin-8 expression correlates with a poor prognosis of survival. Further studies have shown that cell proliferation stimulated by Interleukin-8 is associated with cell cycle distribution which increases Cylin D1 and Cylin B1 proteins which activate Pl3K/Akt and Raf/MEK/ERK, whereas IL-8 increases invasiveness of ovarian neoplasm cells associated with increased activity and expression of MMP-2 and MMP-9. Secretion of IL-8 by ovarian neoplasms promotes malignant cell behavior through induction of intracellular molecular signaling.[3]

Several studies have shown an increase in IL-8 in patients with ovarian cancer, as well as an increase in patients with metastases. IL-8 is expected to be one of the determinants of prognosis in NOK which becomes malignant. In Indonesia, research on IL-8 in patients with ovarian neoplasms and even ovarian carcinoma has not been studied much, so research on this matter is needed.

## METHOD

This research is a cross-sectional study conducted at several teaching hospitals in the Obstetrics and Gynecology department of the Faculty of Medicine Universitas Hasanuddin (UNHAS), namely Central General Hospital Dr. Wahidin Sudirohusodo and other educational network hospitals, namely: UNHAS Hospital, Ibnu Sina Hospital. The study population was all patients with newly diagnosed ovarian neoplasms based on anamnesis, physical examination, supporting examination and histopathology. Sampling was carried out using consecutive sampling, namely population subjects at the research site who met the inclusion requirements were taken as research samples. Patients who meet the criteria are then examined for Inteleukin-8 levels which will then be operated on and then examined histopathologically. The data contained in the study was then analyzed using SPSS software version 25.0.

## RESULT

The research subjects were taken by consecutive sampling of 44 samples of patients diagnosed with malignant type ovarian cystic neoplasms, this sample exceeded the estimated target sample where the estimated target was 34 samples of ovarian neoplasms. Furthermore, all subjects were examined for IL-8 levels using the ELISA method. The diagnosis of ovarian neoplasms was established based on anamnesis, physical examination and supporting examinations that met the study inclusion criteria, then an analysis based on characteristics was carried out, then a statistical analysis was carried out to look for a relationship between levels of interleukin-8 and ovarian neoplasms of benign and malignant types. The characteristics of the research sample can be seen in Table 1.

**Table 1. Characteristucs research sample**

| Characteristic | Ovarian Neoplasm Malignancy Type | | Ovarian Neoplasm Bening Type | | Total | p* |
|---|---|---|---|---|---|---|
| | n | % | n | % | | |
| **Age** | | | | | | |
| < 35 years | 20 | 45,5% | 10 | 22,7% | 30 (34,1%) | 0,115 |
| > 35 years | 24 | 54,5% | 34 | 77,3% | 58 (65,9%) | |
| **BMI** | | | | | | |
| Underweight | 1 | 2,3% | 4 | 9,1% | 5 (5,7%) | 0,009 |
| Normal | 24 | 54,5% | 9 | 20,5% | 33 (37,5% | |
| Overweight | 18 | 40,9% | 29 | 65,9% | 47 (53,4%) | |
| Obesity | 1 | 2,3% | 2 | 4,5% | 3 (3,4) | |
| **Menarrche** | | | | | | |
| <12 year | 2 | 50,0% | 2 | 50,0% | 4 (100 %) | 1,000 |
| ≥12 year | 42 | 50,0% | 42 | 50,0% | 84 (100 %) | |
| **Marital Status** | | | | | | |
| Married | 36 | 81,8% | 34 | 77,3% | 70 (79,5%) | 0,792 |
| Single | 8 | 18,2% | 10 | 22,7% | 18 (20,5%) | |
| **Contraception** | | | | | | |
| Hormonal | 23 | 48,9% | 24 | 51,1% | 47 (100,0%) | 1,000 |
| Non hormonal | 21 | 51,2% | 20 | 48,8% | 41 (100,0%) | |
| **Family History of Cancer** | | | | | | |
| Yes | 6 | 13,6% | 5 | 11,4% | 11 (12,5%) | 1,000 |
| No | 38 | 86,4% | 39 | 88,6% | 77 (87,5%) | |

| Characteristic | Ovarian Neoplasm Malignancy Type | | Ovarian Neoplasm Bening Type | | Total | p* |
|---|---|---|---|---|---|---|
| **Parity** | | | | | | |
| Nulli | 14 | 31,8% | 14 | 31,8% | 28 (31,8%) | 0,383 |
| Primi | 7 | 15,9% | 3 | 6,8% | 10 (11,4%) | |
| Multi | 23 | 52,3% | 27 | 61,4% | 50 56,8%) | |
| **Haemoglobin** | | | | | | |
| Anemia | 6 | 13,6% | 1 | 2,3% | 7 (8,0%) | 0,110 |
| Not Anemia | 38 | 86,4% | 43 | 97,7% | 81 92,0%) | |
| **White Blood Cells** | | | | | | |
| Normal | 36 | 81,8% | 39 | 88,6% | 75 (85,2%) | 0,548 |
| Abnormal | 8 | 18,2% | 5 | 11,4% | 13 (14,8) | |
| **Thrombocytes** | | | | | | |
| Normal | 20 | 45,5% | 31 | 70,5% | 51 (58,0%) | 0,031 |
| Abnormal | 24 | 54,5% | 13 | 29,5% | 37 (42,0%) | |
| **CA-125** | | | | | | |
| Normal | 1 | 2,3% | 6 | 13,6% | 7 (8,0%) | 0,110 |
| Abnormal | 43 | 97,7% | 38 | 86,4% | 81 (92,0%) | |
| **MRI** | | | | | | |
| <200 | 11 | 25,0% | 40 | 90,9% | 51 (58,0%) | 0,001 |
| ≥200 | 33 | 75,0% | 4 | 9,1% | 37 (42,0%) | |
| **Cell Cytology** | | | | | | |
| Contain of Malignant Cells | 17 | 38,6% | 2 | 4,5% | 19 (21,6) | 0,001 |
| Not Contain of Malignant Cells | 27 | 61,4% | 42 | 95,5% | 69 (78,4) | |
| **Stadium** | | | | | | |
| Early stage | 16 | 84,2 % | 3 | 15,8 % | 19 (100,0%) | 0,001 |
| End stage | 21 | 84,0% | 4 | 16,0% | 25 (100,0%) | |

* Chi Square (p <0,05)

**Table 2. Correlation between markers of ovarian neoplasm malignancy and IL-8 levels**

| Variable | Interleukin - 8 | | | Nilai p |
|---|---|---|---|---|
| | n | Mean | SD | |
| **CA-125** | | | | |
| Normal | 7 | 102,37 | 59,06 | 0.734* |
| Abnormal | 81 | 124,16 | 124,16 | |
| **RMI Score** | | | | |
| Malignant | 37 | 103,2 | 42,4 | 0.970* |
| Benign | 51 | 148,9 | 183,7 | |
| **Cytology** | | | | |
| Contain of Malignant Cells | 19 | 167,28 | 228,90 | 0.369* |
| Not Contain of Malignant Cells | 69 | 110,08 | 72,6 | |
| **Stage** | | | | |
| Early stage | 19 | 80,70 | 16,50 | 0.010** |
| End stage | 25 | 146,10 | 203,16 | |

| | | | | |
|---|---|---|---|---|
| NOK | 44 | 127,00 | 84,47 | |
| **Cytopathology Cells** | | | | |
| Malignant | 44 | 152,43 | 167,88 | 0.035* |
| Benign | 44 | 92,43 | 37,09 | |

*Mann Whitney ($p < 0,05$)
**Kruskal Wallis ($p < 0,05$)

Table 2 describes the relationship between the variable markers of malignancy and IL-8 levels. Based on the CA-125 value, it was found that the group with normal CA-125 (< 35 u/ml) had an average IL-8 level of 102.37 pg/ml. Meanwhile, the abnormal CA-125 group (> 35 u/ml) had IL-8 levels of 124.16 pg/ml. Although descriptively the IL-8 level in the group with abnormal CA-125 was observed to be higher, this finding was not statistically significant (p value 0.734; > 0.05).

In this study we used RMI values to divide cystic ovarian neoplasms into malignant and benign types. In the RMI <200 group, the average IL-8 level was 103.21pg/ml, while in the RMI > 200 group, the average IL-8 level was 148.9 pg/ml. Although an increase in IL-8 levels was observed in the group with malignant RMI scores, statistical tests did not find any significance between RMI and IL-8 scores (p 0.970; p > 0.05).

The results of cytological examination showed that there was a difference in the average IL-8 level in the group with cytology results containing malignant cells and those that did not contain malignant cells, where the average IL-8 level in the group with cytology results that did not contain malignant cells was 110 .08 and cytology results with malignant cells worth 167.28. Even so, this finding was also not statistically significant.

In this study, the stages were divided into early stages, advanced stages and NOK. The average level of IL-8 in the group with advanced stages was found to be at a value of 146.1 pg/mL, followed by the group with NOK with a value of 127 pg/mL and the group with an early stage value of 80.7 pg/mL. Subsequent statistical tests found a significant relationship between IL-8 levels and stage as evidenced by a p value of 0.01 (p <0.05).

Furthermore, based on the cytopathology results, the average value of IL-8 in non-epithelial type ovarian neoplasms was 92.43 pg/ml, whereas in epithelial type ovarian neoplasms a higher average value was observed, namely 152.43 pg/ml. After statistical analysis, it was found that there was a significant relationship between increased IL-8 levels in the group with the cytopathology results of epithelial type cystic ovarian neoplasm with a p value of 0.035% (p <0.05). The relationship between IL-8 levels and ovarian cancer histology is shown in Table 3

**Table 3. Correlation between IL-8 levels in histological subtypes of ovarian cancer**

| Variable | Interleukin - 8 | | | P value |
|---|---|---|---|---|
| | n | Mean | SD | |
| **Histopathology** | | | | |
| HGSC | 20 | 184,13 | 227,98 | 0,090 |
| Benign | 44 | 92,43 | 37,09 | |
| LGSC | 3 | 242,06 | 232,43 | 0,082 |
| Benign | 44 | 92,43 | 37,09 | |
| mucinous | 16 | 115,45 | 45,02 | 0,091 |
| Benign | 44 | 92,43 | 37,09 | |
| Endometrioid | 2 | 78,03 | 5,82 | 0,518 |
| Benign | 44 | 92,43 | 37,09 | |
| Germ cell | 3 | 98,26 | 2,44 | 0,761 |
| Benign | 44 | 92,43 | 37,09 | |

*Mann Whitney ($p < 0,05$)

**Table 4. Correlation between IL-8 levels in histological subtypes of ovarian cancer**

| Variable | Interleukin - 8 | | | P Value |
|---|---|---|---|---|
| | n | Mean | SD | |
| **Histopathology** | | | | |
| HGSC | 20 | 184,13 | 227,98 | 0.147 |
| LGSC | 3 | 242,06 | 232,43 | |

| | | | |
|---|---|---|---|
| mucinous | 16 | 115,45 | 45,02 |
| Endometrioid | 2 | 78,03 | 5,82 |
| Germ cell | 3 | 98,26 | 2,44 |
| Benign | 44 | 92,43 | 37,09 |

*Kruskal Wallis ($p < 0,05$)

## DISCUSSION

A total of 44 patients diagnosed with malignant ovarian neoplasms and 44 patients diagnosed with benign ovarian neoplasms. All subjects were examined for IL-8 levels using the ELISA method. The diagnosis of this cystic ovarian neoplasm was established based on anamnesis, physical examination, histopathology/laboratory and radiology which met the study inclusion criteria. The mean age of respondents in the malignant type of ovarian neoplasm group at diagnosis was 65.9 years, which was 31.8 years higher than the average age of the benign type of ovarian neoplasm group which was 34.1 years. Similar studies suggest that malignant ovarian neoplasms are generally diagnosed at an average age of ≥ 55 years with the incidence of this cancer increasing in women over 65 years of age, with an average age at diagnosis of 50-79 years. An increase in age at diagnosis is associated with more severe disease and lower survival rates.[4] In line with the different course of the disease between the two types of neoplasms, this difference is also influenced by the level of public awareness to carry out early detection when ovarian malignancy is still at an early stage. On the other hand, the factor of delay in diagnosis has a new obstacle in the last 3 years where the pandemic condition has become one of the reasons patients do not immediately seek medical help. The results of a similar study conducted by Tortorella where malignant type ovarian neoplasms are more common in old age because there is a longer exposure to estrogen which can damage DNA, the function of immunity which provides a level of protection against cancer decreases with age, and takes a long time to develop. the process of changing normal cells into cancer cells approximately 20 -30 years.[5]

Based on the characteristics of the nutritional status in this study, most of the subjects in this study were found with normal and overweight Body Mass Index (BMI). BMI >30 kg/m2 increases the risk of ovarian cancer by 30-83% (Tsilidis et al. 2011). High BMI increases the risk of ovarian cancer through hormonal mechanisms. Aromatization of androgens in fat tissue is the main source of estrogen in postmenopausal women Research shows that the risk of ovarian cancer increases in overweight women (BMI 25-29.9 kg/m2) and obese women (BMI ≥30 kg/m2) compared to normal women (BMI 18.5-24.9 kg/m2) The increased risk of ovarian cancer is almost 10% for every 5 kg/m2 increase in BMI for the high grade serous subtype.[6]

Based on the age of menarche, the majority of patients with ovarian neoplasms have a menarche age of more than or equal to 12 years. The results of the comparison test showed that there was no significant difference in the menarcheal age of the study subjects between malignant and benign neoplasms wherein most of the patients with malignant and benign ovarian neoplasms had a menarcheal age of more than or equal to 12 years. In line with this study, previous studies reported that the mean age at menarche in ovarian neoplasm patients was 13.59 ± 2.706 years.[7] Epidemiological studies have reported inconsistently the relationship between menarche age and ovarian cancer risk. One meta-analysis concluded that there is an inverse relationship between menarche age and ovarian cancer risk.[8] The slower age of menarche will result in a decrease in the incidence of ovarian cancer by reducing the number of ovulations in women.[7]

Obesity may also affect ovarian cancer survival through its effects on inflammatory cytokines, markers of insulin resistance and obesity-related hormones such as estrogen, via the conversion of androgens to estrogens in adipose tissue. In-vitro studies show that estrogen has a pro-proliferative action on ovarian cancer cells.[9] Estrogen receptors are expressed in up to 80% of epithelial ovarian cancers with the highest expression in serous and endometrioid tumors.[10,11] estrogens may also play a role in motility and invasion of cancer cells to the ovary.[12] Marital status has been shown to be correlated with patient survival in various types of cancer, especially in the female population of epithelial type ovarian cancer. The relationship between marital status and prognosis varies according to different conditions. Widowed patients have a worse prognosis than other groups in most conditions, whereas the group who have never been married show the same risk of death as those who are married.[13]

Based on the characteristics of a family history of malignancy, 11 (12.5%) samples had a family history of malignancy. These results are similar to the results of a study conducted by Girolimetty et al, 2014, namely a family history of ovarian cancer with or without known hereditary gene mutations, correlates with an increased risk of cancer by 2.9-3.6 times. BRCA 1/2 mutations are present in 65-75% of cases of hereditary ovarian cancer. In ovarian cancer that correlates with BRCA 1/2 mutations, mutations in the tumor protein gene (TP5) occur early in the development of the high-grade serous cancer (HGSC) subtype.[14] In this study, more samples of malignant cystic ovarian neoplasms were found in the multiparity group. The causes of ovarian cysts can range from normal physiological processes to genetic mutations involving tumor suppression and growth. Risk factors for ovarian cysts and ovarian cancer include nulliparity and low parity. Several studies have shown that women with parity are estimated to have a 30-60% lower

risk of developing ovarian cancer.[15] However other studies report that infertility and low parity increase the risk of ovarian cancer and multiparity and use of oral contraceptives reduce the risk of ovarian cancer.[7]

Based on hemoglobin levels, the majority of ovarian neoplasm patients had normal hemoglobin levels (92.0%). In this study, anemia was defined as a hemoglobin concentration of less than 12 g/dl according to WHO standards for non-pregnant women. In previous studies with ovarian cancer, it was found that 20.5% of patients with anemia were at stage 3 and only 34.1% of patients with anemia were included in stage 3.[16] The results of the comparative test in this study showed that there was no significant difference in hemoglobin levels between malignant and benign neoplasms, in which both malignant and benign ovarian neoplasms had abnormal preoperative hemoglobin levels. Similar results were reported in a study in Turkey that hemoglobin levels did not differ significantly between benign and malignant ovarian neoplasms.[17]

Based on leukocyte levels, the majority of ovarian neoplasm patients had normal leukocyte levels and only 14.8% of patients had leukocytosis. Leukocytosis is defined as an increase in the number of white blood cells> 10 x 103 /µL.[18] In previous studies with ovarian cancer, 33.3% of patients with leukocytosis were at stage 2 and 52.4% of patients with leukocytosis had grade 3 tumors.[16]

Leukocytes are immune cells involved in protecting the body from disease and pathogens. White blood cells are distributed throughout the body, including the blood and lymphatic systems. White blood cells make up about 1% of the total blood volume of a healthy adult. There are five main subtypes of leukocytes: lymphocytes, monocytes, neutrophils, eosinophils, and basophils. When an immune response occurs, such as in the case of cancer, the number of leukocytes will increase.[19]

The results of the comparison test showed that there was no significant difference in leukocyte levels between epithelial and benign types of malignant neoplasms where both malignant and benign types of ovarian neoplasms had mostly normal leukocyte levels. This result is in line with Yildirim et al. in Turkey that there was no significant difference in leukocyte levels between patients with benign and malignant ovarian neoplasms.[20] Similar results were also reported in a study in Turkey that leukocyte and hemoglobin levels did not differ significantly between benign and malignant ovarian neoplasms.[17]

In this study, the majority of ovarian neoplasm patients had abnormal platelet levels (42.0%). In previous studies with ovarian cancer, it was found that 61.1% of patients with thrombocytosis were at stage 3 and 61.1% of patients with thrombocytosis had grade 3 tumors.[16] The results of the comparison test showed that there was no significant difference in platelet levels between the malignant and benign types of ovarian neoplasms where the majority of malignant ovarian neoplasms had thrombocytosis. whereas in patients with ovarian neoplasms of the benign type, most of them have normal preoperative platelet levels. Previous studies reported that thrombocytosis results from cancer cell-mediated release of IL-8, which stimulates production of liver-derived thromboproietin and/or cancer cells to promote platelet overproduction. In human samples, ovarian tumor and plasma IL-8 expression were also significantly associated with plasma thrombopoietin levels and thrombocytosis. There is some evidence that in cancers with PIK3CA mutations, such as endometrioid and clear cell ovarian cancer, upregulation of the nuclear factor-kappa B (NF-κB) pathway may promote IL-8 expression, possibly related to the known association between increased NF-κB expression and prognosis. poor in ovarian cancer on the mechanism underlying the association with thrombocytosis.[21]

CA-125 levels were found to be increased in the malignant type of ovarian neoplasm sample group where the abnormal CA-125 average value was 124.16 (10.00 - 209.82), although there was no statistically significant relationship. Likewise the interaction between IL-8 and CA-125 levels where an increase in IL-8 was found in samples that had an increased CA-125 value. Increased levels of CA-125 is the main marker of cancer progression. Although the CA-125 test is not specific for diagnosing ovarian cancer, it has the potential to be used to assess, monitor, and evaluate response to therapy in ovarian cancer. Serous type epithelial ovarian cancer expresses CA-125 significantly higher than other types of epithelial ovarian cancer.[6] There is a strong relationship between disease progression and regression with fluctuations in CA-125 levels.[22] -125 levels are increased in 90% of cases of stage II, III, and IV ovarian cancer, but only 50% of stage I ovarian cancer have elevated CA-125 levels.[23]

CA-125 increase was present in 80% of the subjects in this study. CA-125 levels also correlate with histological grade in primary ovarian neoplasms, especially high-grade malignant tumors.[24] Previous studies have also reported increased IL-8 levels in ovarian cancer patients. As reported by Kampan et al, the use of CA-125 in combination with IL-8 achieved a higher predictive value than CA-125 alone. Another theory also suggests that the pro-inflammatory properties of IL-8 play an important role in the pathogenesis of ovarian cancer.[25]

The interaction between RMI scores and IL-8 levels in this study explained that the malignant type of ovarian neoplasm group had an average IL-8 score higher than the benign type ovarian neoplasm group, where the average malignant RMI value was 148.91 (42.85 - 1019.91). RMI is a scoring system of a combination of various clinical features. RMI has been developed to improve diagnostic accuracy for ovarian malignancy.[26] RMI is stated to be more accurate than other individual criteria in differentiating malignant and benign masses.[27] Using a cut-off level of 200 to indicate

malignancy, RMI provides a sensitivity of 70.6% and a specificity of 83.9%.[26]

IL-8 levels in ovarian neoplasms with malignant histopathological results with an average value of 152.43 pg/uL (66.80 – 1019.91) and advanced stage results with an average value of 146.10 were found to be more elevated than in early-stage ovarian neoplasms and those of the benign type. IL-8 in the benign and malignant groups were both higher than the healthy control group ($p < 0.001$), serum expression levels of IL-8 and IL-10 in cancer patients Ovarian stage III and IV were higher than stages I and II ($p < 0.001$) and also serum IL-8 and IL expression levels in patients with malignant ovarian tumors before chemotherapy were higher than after chemotherapy ($p < 0.001$). IL-8 can accelerate tumor angiogenesis and promote the advancement of ovarian cancer. It is widely accepted that IL-8 plays an important role in tumor angiogenesis.[28]

Several signaling pathways are known to induce IL-8 receptor downstream highlighting the importance of this chemokine in promoting cancer progression. Many studies have demonstrated overexpression of IL-8 by tumor cells, often induced in response to chemotherapeutic interventions or environmental stress such as hypoxia. Increased synthesis and secretion of IL-8 from tumor cells has a broad impact on the tumor microenvironment due to the specific features of CXCR1 and CXCR2 receptor expression on cancer cells, endothelial cells, and neutrophil/tumor macrophages.

## CONCLUSION

Based on the results of the study and discussion, it can be concluded that increased IL-8 levels are associated with an advanced stage and histopathological outcome of malignant ovarian neoplasms. Although unrelated, IL-8 was observed to be increased in cases with CA-125 results, RMI scores, and cytology suggestive of an epithelial type cystic ovarian neoplasm. Further research is needed with a larger number of samples and more varied characteristics regarding the comparison between IL-8 levels and benign and malignant ovarian neoplasms. It is hoped that in the future, research can be conducted to assess IL-8 levels in ascitic fluid samples with the hope that the results of the research can better describe the condition of malignancy locally.

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