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Relationship Between Interleukin 8 Levels And Body Mass Index In Patients With Endometrial Cancer

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ABSTRACT

Introduction: Increased body mass index (BMI) is one of the risk factors for endometriosis cancer associated with chronic inflammatory processes that can be confirmed by increased inflammatory markers in obese patients such as interleukin 8 (IL-8). This study aims to evaluate the relationship between IL-8 levels to body mass index and clinicopathological characteristics of patients with endometrial carcinoma.

Methods: This was cross-sectional study that conducted from November 2022 to February 2023 in Endometrial Cancer. Demographic and clinicopathological data were collected. BMI and IL-8 serum were measured. Data were analyzed with SPSS 27.0, using the Mann-Whitney test, Kruskal Wallis test and Spearman correlation test.

Results: Lymphovascular Space Invasion (LVSI) and stage were not significantly associated with IL-8 levels ($p>0.05$). IL-8 levels were higher in obese patients than in non-obese patients but not statistically significant ($p>0.05$). Endometrial carcinoma type was significantly associated with IL-8 levels ($p<0.05$). Higher age was significantly associated with higher IL-8 levels ($p<0.05$).

Conclusion: Obesity was not correlated to IL-8 levels in endometrial carcinoma patients, but IL-8 levels are influenced by age and type of endometrial carcinoma.

Keywords: *body mass index, endometrial carcinoma, interleukin-8, obesity*

1. INTRODUCTION

Endometrial cancer is the second most common type of gynecological malignancy with an incidence of around 4.4% of all cancer cases in women in the world and mortality reaching 1.8 per 100,000 women in 2018. Indonesia ranks first with a prediction of 6745 cases. The death rate from this cancer in Indonesia reaches 1.9 per 100,000 women.[1]

Elevated body mass index (BMI) is an established risk factor for endometrial cancer and is thought to have a greater effect on the risk of this malignancy than other cancer types. Excess adiposity accounts for 34% of global endometrial cancer cases.[2] Recent studies have shown that visceral adipose tissue releases more circulating IL-8 than subcutaneous adipose tissue and that circulating IL-8 is increased in obesity.[3] In addition, interleukin-8 (IL-8) is expressed by many tumor cells, including breast, ovarian, cervical, and endometrial cancers. IL-8 expressed from tumor cells binds to CXCR1 and CXCR2 on tumor cells forming an autocrine loop. IL-8 secretes growth factors and further promotes tumor proliferation and growth, initiating a paracrine loop.[4]

Previous studies have reported a statistically significant correlation between endometrial cancer stage and IL-8 expression which can be assessed from lymphovascular space invasion (LVSI) as an early marker of metastasis, and tumor size.[5] Bălăşoiu et al.'s study reported in colorectal tumors that increased IL-8 values correlated with tumor growth and tumor, node, metastasis (TNM) stage.[6] In endometrial cancer, increased BMI, as a risk factor, is associated with chronic inflammatory processes, confirmed by increased inflammatory markers in obese patients. Public health interventions that reduce the overall prevalence of obesity may have the greatest impact on reducing endometrial cancer rates in the population. However, research

data on IL-8 levels in obese patients with endometrial cancer are still limited. This study aims to analyze the relationship between Interleukin 8 levels and obese patients diagnosed with Endometrial Carcinoma through assessment of various aspects including histopathological features, LVSI, tumor size, stage, and BMI.

2. METHODS

This study is an analytical observational study with a Cross-Sectional design conducted from November 2022 to February 2023, with a population of patients diagnosed with Endometrial Cancer at Ibnu Sina Hospital, Hasanuddin University Teaching Hospital, and Wahidin Sudirohusodo Hospital Makassar. Samples were taken using consecutive sampling techniques. Inclusion criteria included patients diagnosed with Endometrial Cancer and were willing to sign informed consent, while exclusion criteria were patients who were on a diet or had lysed blood samples.

BMI was measured through physical examination and blood was drawn to measure the levels of the pro-inflammatory cytokine IL-8 by the ELISA method using the RD-D800C kit. Data analysis was performed using SPSS version 27, including the Mann-Whitney test, Spearman correlation test, and Kruskal-Wallis test, according to the type of data and number of groups. The study was conducted after obtaining approval from the ethics committee of the Faculty of Medicine, Hasanuddin University based on ethical approval No. XXX.

3. RESULTS

A total of 39 patients diagnosed with cancer were collected with an average age of patients in this study of 52.18 years with an average BMI of 25.76. The majority of patients (53.8%) were included in the obese category (Table 1). The results of the analysis showed that IL-8 levels had a fairly strong correlation with age (rho = 0.72) and tumor size (rho = 0.32), compared to other variables. In addition, the type of endometrial carcinoma also affected IL-8 levels, where type 1 showed higher IL-8 levels than type 2, with a statistically significant difference (p = 0.04). These findings indicate a relationship between IL-8 levels and several clinical characteristics of patients, although not all relationships showed significance.

Table 1. Description of Research Patients

Variable	Mean (SD)	n (%)
Age (years)	52.18 (9.75)	
BMI	25.76 (5.29)	
Obesity		
Yes		21 (53.80)
No		18 (46.20)
IL-8 levels (pg/ml)	58.89 (88.42)	
Type carcinoma		
Tipe 1		29 (74.40)
Tipe 2		10 (25.60)
TNM Stage		
I		18 (46.20)
II		12 (30.80)
III		9 (23.00)
LVSI		
Positive		7 (17.90)
Negative		32 (82.10)

Table 2. IL-8 levels based on endometrial carcinoma clinicopathology

Clinicopathological parameters	IL-8 levels (pg/ml)	p-value
Cancer type[a]		
Type 1	72.28 (100.50)	0.04*
Type 2	20.07 (14.32)	
LVSI[a]		
Positive	39.19 (44.08)	0.63
Negative	59.49 (84.04)	
Clinical Stage[b]		
I	27.02 (18.26)	0.23
II	96.85 (105.98)	
III	58.81 (92.61)	
BMI		
Obesity	74.63 (99.79)	0.41
Non-obesity	33.93 (32.33)	

[a]Mann-Whittney test, [b]Kruskal-Wallis test

IL-8 levels were higher in patients with type 1 endometrial carcinoma compared to type 2 but did not show statistical significance. IL-8 levels were lower in patients with positive LVSI status compared to those with negative LVSI, but the difference did not show statistical significance. IL-8 levels were higher in patients with stage II endometrial carcinoma compared to stages I and III but were not significantly different. IL-8 levels tended to be higher in obese patients compared to non-obese patients but were not significantly different (Table 2).

Table 3. Correlation of Variables with IL-8 in Endometrial Carcinoma

	rho	p-value
BMI	0.15	0.36
Age	0.72	0.06

Spearman corrrelation test

The results of the correlation test also did not find a significant correlation between BMI and IL-8 levels. However, age was significantly associated with IL-8 levels (Tabel 3).

4. DISCUSSION

In this study, IL-8 levels were significantly higher in type 1 endometrial carcinoma compared to type 2. Previous studies have shown that more aggressive types of endometrial carcinoma, such as type 2 (serous carcinoma), tend to show higher IL-8 levels than type 1 (endometrioid carcinoma), because IL-8 supports a more inflammatory and pro-invasive tumor microenvironment.[7] However, not all studies found a significant association between IL-8 levels and tumor type, possibly due to differences in patient inflammatory responses and tumor microenvironment composition.[8] Studies have shown that IL-8 is more dominant in tumor types that have high neutrophil infiltration, which is often associated with further tumor progression.[9]

IL-8 levels were not associated with LVSI in this study. Similar results were reported that no significant association was found between IL-8 and LVSI, possibly due to the variability of inflammatory responses between individuals and the types of tissues involved in LVSI.[7] IL-8 levels that do not increase in certain cases may occur due to other factors, such as variations in IL-8 distribution within tissues or the dominant role of other inflammatory mediators.[10]

These results suggest that IL-8 levels are not related to cancer stage. This is due to differences in inflammatory responses between patients or variations in IL-8 expression in the tumor microenvironment.[11] In addition, IL-8 is known to increase

suppressive immune cells into the tumor microenvironment, which worsens the prognosis in more advanced cancers.[12]

In this study, obesity was not associated with IL-8 levels. Obesity increases the risk of endometrial carcinoma, where high BMI is associated with chronic inflammation that causes increased levels of IL-8, a pro-inflammatory cytokine.[13] IL-8 has a role in the tumor microenvironment by recruiting inflammatory cells that can support tumor growth.[8] However, in some studies, no significant relationship was found between BMI and IL-8 levels, possibly due to individual variability in the inflammatory response to obesity and the dominant type of fat tissue.[14] Pathophysiological mechanisms suggest that visceral adipose tissue is more pro-inflammatory than subcutaneous tissue, but the distribution of fat in an individual may influence the levels of cytokines produced.[15] Different fat distribution may explain why IL-8 levels are not always elevated in all obese patients with endometrial carcinoma.[16]

In this study, there was a positive relationship between IL-8 levels and age. In endometrial carcinoma patients, IL-8 levels tended to increase with age, which is associated with chronic inflammation and decreased immune response that occurs in the aging process.[9] IL-8 functions as a pro-inflammatory chemokine that recruits neutrophils and other immune cells to the tumor area, accelerating cancer progression in inflamed endometrial tissue.[7] IL-8 also plays a role in activating signals through the CXCR1/2 receptors, which increase cancer cell proliferation and invasive ability, especially in older patients with compromised immunity.[8] Variability in IL-8 levels may also be influenced by genetic differences or other health conditions that influence inflammation in older age.[17]

This study is limited to a small sample size. The study also did not limit age, which could be a confounding factor in the relationship between IL-8 levels and cancer clinicopathology.

5. CONCLUSION

IL-8 levels increase with increasing age and IL-8 levels are not related to cancer type, stage, LVSI and obesity in endometrial carcinoma cancer. IL-8 levels tend to be higher in obese patients can be a potential indicator of endometrial carcinoma incidence but the results are not significant so further research is needed to confirm the results.

REFERENCES

[1] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018; 68: 394–424.

[2] Hazelwood E, Sanderson E, Tan VY, et al. Identifying molecular mediators of the relationship between body mass index and endometrial cancer risk: a Mendelian randomization analysis. *BMC Med* 2022; 20: 1–24.

[3] Ciortea R, Mihu D, Mihu CM. Association between visceral fat, IL-8 and endometrial cancer. *Anticancer Res* 2014; 34: 379–383.

[4] Ewington L, Taylor A, Sriraksa R, et al. The expression of interleukin-8 and interleukin-8 receptors in endometrial carcinoma. *Cytokine* 2012; 59: 417–422.

[5] Ray I, Meira LB, Michael A, et al. *Adipocytokines and disease progression in endometrial cancer: a systematic review*. Springer US. Epub ahead of print 2022. DOI: 10.1007/s10555-021-10002-6.

[6] Bălăşoiu M, Bălăşoiu AT, Mogoantă SŞ, et al. Serum and tumor microenvironment IL-8 values in different stages of colorectal cancer. *Rom J Morphol Embryol* 2014; 55: 575–578.

[7] Roškar L, Pušić M, Roškar I, et al. Models including preoperative plasma levels of angiogenic factors, leptin and IL-8 as potential biomarkers of endometrial cancer. *Front Oncol* 2022; 12: 1–15.

[8] Ellis PE, Barron GA, Bermano G. Adipocytokines and their relationship to endometrial cancer risk: A systematic review and meta-analysis. *Gynecol Oncol* 2020; 158: 507–516.

[9] Mochizuki K, Oishi N, Kawai M, et al. Expressions of il-8 and cxcl5 in uterine endometrioid carcinomas which have frequent neutrophil infiltration and comparison to colorectal adenocarcinoma. *Histol Histopathol* 2020; 35: 1503–1510.

[10] Deng Y, Ning Z, Hu Z, et al. High interleukin-8 and/or extracellular signal-regulated kinase 2 expression predicts poor prognosis in patients with hepatocellular carcinoma. *Oncol Lett* 2019; 18: 5215–5224.

[11] Fousek K, Horn LA, Palena C. Interleukin-8: A chemokine at the intersection of cancer plasticity, angiogenesis, and immune suppression. *Pharmacol Ther* 2021; 219: 107692.

[12] Moku P, Shepherd L, Ali SM, et al. Higher serum PD-L1 level predicts increased overall survival with lapatinib versus trastuzumab in the CCTG MA.31 phase 3 trial. *Cancer* 2020; 126: 4859–4866.

[13] Kliemann N, Viallon V, Murphy N, et al. Metabolic signatures of greater body size and their associations with risk of colorectal and endometrial cancers in the European Prospective Investigation into Cancer and Nutrition. *BMC Med* 2021; 19: 1–14.

[14] Ostrowska L, Gornowicz A, Pietraszewska B, et al. Which salivary components can differentiate metabolic obesity? *PLoS One* 2020; 15: 1–10.

[15] van den Bosch AAS, Pijnenborg JMA, Romano A, et al. The role of fat distribution and inflammation in the origin of endometrial cancer, study protocol of the ENDOCRINE study. *PLoS One* 2022; 17: 1–9.

[16] Grandi G, Perrone AM, Chiossi G, et al. Increasing BMI is associated with both endometrioid and serous histotypes among endometrial rather than ovarian cancers: a case-to-case study. *Gynecol Oncol* 2019; 154: 163–168.

[17] Tiainen L, Hämäläinen M, Luukkaala T, et al. Low Plasma IL-8 Levels During Chemotherapy Are Predictive of Excellent Long-Term Survival in Metastatic Breast Cancer. *Clin Breast Cancer* 2019; 19: e522–e533.