
RESEARCH ARTICLE**Correlation of Leukopenia with Vitamin D Levels in Ovarian Cancer Patients Undergoing Platinum-Taxane-Based Chemotherapy**

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Abstract

Introduction: Ovarian cancer is a significant cause of death in women. One of the management of advanced ovarian cancer patients is chemotherapy. The effects of administering Platinum-Taxane-Based chemotherapy to ovarian cancer patients show side effects of myelosuppression, one of which is leukopenia.

Methods: This type of study is a correlation analytical study with a cross-sectional design from October 2023 to May 2024 at Dr. M. Djamil Central General Hospital Padang. The patients included were ovarian cancer patients who underwent Platinum-Taxane-Based chemotherapy with laboratory results of leukopenia.

Results: From 70 patients, it was found that 37 patients (52.9%) had grade I leukopenia, 27 patients (38.6%) had grade II, and 6 patients (8.6%) had grade III. Based on the results obtained, in grade I leukopenia, the average vitamin D value is 13.162 ng/mL, grade II has an average vitamin D value of 11.851 ng/mL, grade III has an average vitamin D value of 14.333 ng/mL. The study results showed a relationship between leukopenia and vitamin D levels $p = 0.034$ ($p < 0.05$).

Conclusion: There was a relationship between leukopenia and vitamin D levels in ovarian cancer patients undergoing Platinum-Taxane-Based Chemotherapy at Dr. M. Djamil Central General Hospital Padang.

Keywords: Ovarian Cancer, Chemotherapy, Platinum-Taxane, Leukopenia, Vitamin D

INTRODUCTION

Ovarian cancer is the leading cause of death in women diagnosed with gynecologic cancer. Most cases are diagnosed at an advanced stage, which leads to poor outcomes of the disease.¹ Ovarian cancer ranks fifth in cancer deaths among women, accounting for more deaths than any other cancer of the female reproductive system.²

Treatment of advanced ovarian cancer patients consists of a combination of surgical staging or cytoreduction with chemotherapy. Due to difficulties in early detection, diagnosis, and treatment, the overall survival of patients with ovarian cancer is poor.³

Chemotherapy works on the cytotoxic principle, namely damaging the mitotic process of cancer cells so they cannot divide, especially cancer cells that can divide rapidly. The effects of paclitaxel and carboplatin in ovarian cancer patients showed myelosuppressive side effects, namely leukopenia (98%).⁴ Afandi et al.'s study showed an increase in leukopenia after chemotherapy (57.6%).⁵

Vitamin D is a steroid-like hormone that works by binding to the vitamin D receptor (VDR). It plays a significant role in calcium homeostasis and metabolism. In addition, vitamin D exerts other significant effects called "non-classical actions." Vitamin D regulates immune cell function and hematopoietic cell differentiation and proliferation.⁶

Emerging evidence suggests that vitamin D deficiency may be linked to increased risk and severity of chemotherapy-induced complications, including leukopenia. Vitamin D may play a protective role in hematopoiesis by modulating immune and inflammatory responses, thus influencing white blood cell production. However, studies investigating the relationship between vitamin D levels and leukopenia in ovarian cancer patients, particularly those undergoing platinum-taxane-based chemotherapy, remain limited.

Therefore, this study aims to analyze the correlation between leukopenia and vitamin D levels in ovarian cancer patients undergoing platinum-taxane-based chemotherapy, in order to explore whether vitamin D status may contribute to the incidence or severity of chemotherapy-induced leukopenia.

METHOD

This study is a correlational analytical study with a cross-sectional design to assess the relationship between the incidence of leukopenia and vitamin D levels in ovarian cancer patients undergoing Platinum-Taxane-Based chemotherapy at Dr. M. Djamil Padang General Hospital. The study was conducted from October 2023 to May 2024.

The inclusion criteria are ovarian cancer patients who have been diagnosed based on anamnesis, physical examination, and supporting examinations, ovarian cancer patients undergoing chemotherapy with the Platinum-Taxane regimen, and ovarian cancer patients with one or all laboratory results showing leukopenia. The exclusion criteria are ovarian cancer patients with blood

disorders/blood malignancies.

Leukopenia is grouped into 3 grades :

Grade 1: 2001- 3500/ mm³

Grade 2: 1001- 2000/ mm³

Grade 3: 0- 1000/ mm³

In this study, univariate analysis was used to explain the distribution of ovarian cancer patients based on age, parity, history of hormonal contraception, histopathology results, determine the frequency of leukopenia in ovarian cancer patients, and determine their average vitamin D levels.

Bivariate analysis determined the relationship between one independent variable (free variable) and one dependent variable (bound variable). The normality test will be used to determine whether the study data has a normal distribution or not. The normality test used in this study is the Kosmolgorov-Smirnov normality test. This is because the amount of data in each variable is >50. If the p-value <0.05, the data has an abnormal distribution; if the p-value ≥0.05, the data has a normal distribution.

The bivariate analysis used in determining the relationship is the ANOVA Test, which determines if the data is normally distributed, and analyzed using Kruskal-Wallis if the data is not normally distributed. A significant relationship between independent and dependent variables is determined by p-value < 0.05. If the p-value ≥ 0.05 indicates no relationship between the independent and dependent variables.

RESULTS

Based on Table 1, the average age of patients is 46.928, with a standard deviation value of 13.803. The patients with nulliparous criteria were 18 patients (25.7%), primiparous were 4 patients (5.7%), multiparous were 46 patients (65.7%), and grand multiparous were 2 patients (2.9%). The patients who had a history of contraception were 1 patient (1.4%), and those who did not have a history of contraception were 69 patients (98.6%). Regarding histopathology results, the epithelial type was 58 patients (82.9%), while the non-epithelial type was 12 patients (17.1%).

Table 1. Characteristics of Ovarian Cancer Patients

Variable	Amount (n)
Age (Mean±SD)	46.928 ± 13.803
Parity	
Nulliparous	18 (25.7%)
Primiparous	4 (5.7%)
Multiparous	46 (65.7%)
Grand Multiparous	2 (2.9%)
Contraceptive History	
Yes	1 (1.4%)
No	69 (98.6%)
Histopathology Results	
Epitel	58 (82.9%)
Non Epitel	12 (17.1%)

According to Table 2, 37 patients (52.9%) have grade I leukopenia, 27 patients (38.6%) have grade II leukopenia, and 6 patients (8.6%) have grade III leukopenia.

Table 2. Frequency of Leukopenia in Ovarian Cancer Patients

Leukopenia	Frequency	%
Grade I	37	52.9
Grade II	27	38.6
Grade III	6	8.6

Based on Table 3, the minimum value of vitamin D is 7 ng/mL, with a maximum value of 22 ng/mL. The average vitamin D level obtained is 12.7571 ng/mL, with a standard deviation of 3.424 and a median of 13 ng/mL.

Table 3. Average Levels of Vitamin D in Ovarian Cancer Patients

Vitamin D	
Mean ± SD	12.7571 ± 3.424
Median	13 ng/mL
Min	7 ng/mL
Max	22 ng/mL

Based on the Table 4, it was obtained that out of 70 patients, 28 patients (40%) experienced vitamin D <20 ng/mL (deficiency), 40 patients (57.1%) experienced vitamin D 12 – 20 ng/mL

(insufficiency), and only 2 patients (2.9%) had >20 ng/mL (sufficiency) vitamin D levels.

Table 4. Frequency of Vitamin D Levels in Ovarian Cancer Patients

Vit D Levels	Frequency	%
<20 ng/mL (Deficiency)	28	40
12 – 20 ng/mL (Insufficiency)	40	57.1
>20 ng/mL (Sufficiency)	2	2.9

Based on Table 5, in grade I leukopenia, the average vitamin D value is 13.162 ng/mL, grade II has an average vitamin D value of 11.851 ng/mL, and grade III has an average vitamin D value of 14.333 ng/mL. In addition, a p-value of 0.034 is obtained; the value is <0.05, so it can be concluded that with a 95% confidence level, the results of H0 are accepted, and H1 is rejected, which means there is a relationship between leukopenia and vitamin D levels.

Table 5. The Relationship between Leukopenia and Vitamin D Levels

Leukopenia	Mean $\pm$ SD	P-value
Grade I	13.162 $\pm$ 3.745	0.034
Grade II	11.851 $\pm$ 2.783	
Grade III	14.333 $\pm$ 2.065	

DISCUSSIONS

The incidence of ovarian cancer is higher in women over 65 years old. According to previous studies, the average age at diagnosis is 50-79 years. However, the average age in this study was 46 years old, which is lower than the previously mentioned studies. This may be because, in this study, the age range was wide, namely 12-79 years old, and the sample age <50 years was 55% of the total sample.⁷

In parity, patients with nulliparous criteria were 18 patients (25.7%), primiparous were 4 patients (5.7%), multiparous were 46 patients (65.7%), and grand multiparous were 2 patients (2.9%). The risk of ovarian cancer was 24% higher in nulliparous women compared to women who had one child. In addition, the risk increased more than 12-fold [OR = 12.5 (95% CI: 2.4–63.80)], when nulliparous women were compared to multiparous women.⁸

In this study, patients who had a history of contraception were 1 patient (1.4%), and those who did not have a history of contraception were 69 patients (98.6%). In a study of women of reproductive age (<50 years) living in Denmark, it was found that the use of any hormonal contraception was associated with a decreased risk of ovarian cancer.⁹

In this study, the histology results showed that the epithelial type was present in 58 patients (82.9%), while the non-epithelial type was present in 12 patients (17.1%). This is in line with other

studies, which have shown that about 90% of ovarian cancers develop from ovarian surface epithelial cells. The majority of ovarian cancers arise from ovarian epithelial cells.^{8,10}

Based on Table 2, 37 patients (52.9%) have grade I leukopenia, 27 patients (38.6%) have grade II leukopenia, and 6 patients (8.6%) have grade III leukopenia. This study is in line with previous studies, namely that the effects of administering paclitaxel and carboplatin to ovarian cancer patients showed side effects of myelosuppression, namely leukopenia (98%). In the study by Akin et al., it was also stated that there were side effects of myelosuppression in the administration of the Paclitaxel and Carboplatin regimen in ovarian cancer patients, namely leukopenia (all grades) 87 - 98%, (grade 3 or 4) 17 - 51%.¹¹

Based on Table 5, in grade I leukopenia, the average vitamin D value is 13.162 ng/mL, grade II has an average vitamin D value of 11.851 ng/mL, and grade III has an average vitamin D value of 14.333 ng/mL. In addition, a p-value of 0.034 was obtained, the value is <0.05, so it can be concluded that with a 95% confidence level, the results of H0 are accepted, and H1 is rejected, which means there is a relationship between leukopenia and vitamin D levels.

Based on information taken from other studies, it can be said that vitamin D can increase the number of leukocytes by increasing the dose. Other studies have shown that vitamin D can regulate systemic cytokines and increase the number of leukocytes. Vitamin D plays a vital role in the immunomodulation of the immune system. This suggests that vitamin D may be a valuable treatment for many inflammatory diseases and prevent disease progression.¹²

In another study, vitamin D was directly related to the number of white blood cells (leukocytes) and differences in leukocyte formula components, neutrophil to lymphocyte ratio, monocyte to lymphocyte ratio, and C-reactive protein.¹³ Epidemiological evidence suggests that lower circulating vitamin D levels are associated with a higher risk of ovarian cancer. Furthermore, a recent meta-analysis showed that vitamin D supplementation was associated with a 13% reduction in cancer mortality.¹⁴

CONCLUSIONS

There was a relationship between leukopenia and vitamin D levels in ovarian cancer patients undergoing Platinum-Taxane-Based Chemotherapy at Dr. M. Djamil Central General Hospital Padang. Further study is required to test vitamin D levels in leukopenia over an extended period and with more samples to add clinical evidence of the relationship between leukopenia and vitamin D levels.

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