Body weight, hemoglobin, and absolute neutrophil count in patients with advanced-stage epithelial ovarian cancer who received chemotherapy: A single-center study

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Abstract. The side effects of chemotherapy, a treatment modality of ovarian cancer, can disrupt overall treatment. To date, the clinical and laboratory profiles of ovarian cancer patients during chemotherapy have not been investigated. This study aimed to elucidate the clinical and laboratory profiles of patients with advanced-stage epithelial ovarian cancer who received chemotherapy in Dr. Cipto Mangunkusumo Hospital, including body mass index (BMI), hemoglobin (Hb), and absolute neutrophil count (ANC). To generate these clinical and laboratory profiles, we collected secondary data from the medical records of advanced-stage epithelial ovarian cancer patients who received six cycles of carboplatin and paclitaxel chemotherapy. We enrolled 23 patients with advanced-stage epithelial ovarian cancer patients who received six cycles of chemotherapy. Mean patient BMI before and after chemotherapy was 22.86 kg/m² and 21.78 kg/m², respectively. Hb levels before chemotherapy were 8–13 g/dl, with Hb < 10 g/dl in one patient (4.35%) and Hb ≥ 10 g/dl in 22 patients (95.65%). Mean ANC was 5845.6 ± 3325.0. An average of 24.65% of patients experienced anemia after each cycle of chemotherapy. Mean ANC before chemotherapy was 3.5582 ± 3.3250. An average of 26.81% of patients had ANC <1500 after each cycle of chemotherapy; no patients had ANC <1500 before chemotherapy initiation. After six cycles of chemotherapy, three patients (13.04%) had mild neutropenia, four patients (17.39%) had moderate neutropenia, and one patient (4.35%) had severe neutropenia. Of the 22 patients with Hb ≥ 10 g/dl before chemotherapy, 16 (72.72%) experienced a decrease in ANC during chemotherapy. Of the 20 patients (60.87%) with normal BMI or higher, 14 experienced a decrease in ANC during chemotherapy. The mean patient body weight decreased after six cycles of chemotherapy. Hb and ANC were persistently decreased in approximately a quarter of the 23 subjects. The decrease in ANC was not influenced by initial Hb and BMI.

1. Introduction
Chemotherapy is one of the modalities for treating advanced-stage ovarian cancer [1-5]. The active ingredients in chemotherapy are cytotoxic, killing rapidly dividing cells, including healthy non-cancerous cells such as those found in bone marrow, the gastrointestinal tract, and hair follicles [6,7]. This results in alopecia, inflammation of the digestive tract mucosa (mucositis), and suppression of the formation of blood cells (myelosuppression) and immune system cells (immunosuppression) [6-8].

Chemotherapy administration can disrupt the normal physiological processes, resulting in life-threatening conditions. In addition, because chemotherapy can decrease the body’s ability to fight
infection, the monitoring of chemotherapy administration is critically important [9]. Laboratory tests such as complete blood count and absolute neutrophil count (ANC) count should be performed between each cycle of chemotherapy, before the next cycle is initiated. The ANC is critical because neutrophil granulocytes in the blood play an important role in the functioning of the immune system [8]. Clinical and laboratory profiles vary for each patient and no data are available about these profiles. Therefore, in this study, we monitored and evaluated the medical records of advanced-stage epithelial ovarian cancer patients who received carboplatin and paclitaxel chemotherapy.

2. Materials and Methods
This retrospective study was based on secondary data of advanced-stage epithelial ovarian cancer patients who received six cycles of carboplatin and paclitaxel chemotherapy from June 2015 until December 2015. We recruited all patients who met the inclusion and exclusion criteria. Inclusion criteria were advanced-stage epithelial ovarian cancer treated with chemotherapy in Building A of Dr. Cipto Mangunkusumo Hospital from June 2015 until December 2015. Exclusion criteria were the presence of another malignancy, immunosuppressive disease, hematological disorder, or renal, bone marrow, and metabolic disease. Body Mass Index (BMI), Hemoglobin (Hb) level, and ANC data were analyzed using Statistical Program for Social Sciences (SPSS) 20.0 version in order to generate clinical and laboratory profiles.

3. Results and Discussion
3.1 Results
A total of 23 patients with advanced-stage epithelial ovarian cancer received six cycles of carboplatin and paclitaxel chemotherapy. Of these, 56.52% of patients were older than 55 years, 65.21% graduated from senior high school, 65.21% were housewives, 65.22% were multiparous, and 60.87% were post-menopausal (Table 1).

| Characteristic                  | N  | %    |
|--------------------------------|----|------|
| **Age (years)**                |    |      |
| <50                            | 7  | 30.43|
| 50–54                          | 3  | 13.04|
| >55                            | 13 | 56.52|
| **Hometown**                   |    |      |
| Jakarta                        | 11 | 47.82|
| Outside Jakarta (Java Island)  | 11 | 47.82|
| Outside Java Island            | 1  | 4.34 |
| **Education**                  |    |      |
| Primary school                 | 3  | 13.04|
| Junior high school             | 1  | 4.34 |
| Senior high school             | 15 | 65.21|
| University/ diploma            | 3  | 13.04|
| Others                         | 1  | 4.34 |
| **Occupation**                 |    |      |
| Housewife                      | 15 | 65.21|
| Entrepreneur                   | 4  | 17.39|
| Government employee            | 2  | 8.69 |
| Private employee               | 1  | 4.34 |
| Student                        | 1  | 4.34 |
| **Parity**                     |    |      |
| P0                             | 3  | 13.04|
| P1                             | 5  | 21.74|
| Multi                          | 15 | 65.22|
| **Menopause status**           |    |      |
| Post                           | 14 | 60.87|
| Pre                            | 9  | 39.13|
| **Family history of cancer**   |    |      |
| Yes                            | 2  | 8.69 |
| No                             | 19 | 82.61|
| N/A                            | 2  | 8.69 |
Mean patient body weight decreased from 54.73 kg ± 8.46 before chemotherapy to 51.58 kg ± 8.11 before chemotherapy. The mean BMI of the 23 patients decreased from 22.86 kg/m² before chemotherapy to 21.78 kg/m² after chemotherapy. Based on WHO guidelines for BMI-based classification, two patients (8.69%) were underweight, 18 patients (78.26%) were normal weight, and three patients (13.04%) were overweight.10 The blood Hb level before chemotherapy was 8–13 g/dl, with Hb < 10 g/dl in one patient (3.57%) and Hb ≥ 10 g/dl in 22 patients (95.65%). Anemia was observed in an average of 24.65% of patients after every cycle. Of these 16 patients, 11 (68.75%) experienced recurrent anemia 2–4 times over the six cycles, and the remaining five patients (31.25%) experienced anemia only once. Four patients (17.39%) experienced anemia after the first cycle of chemotherapy; five patients (21.74%) after the second, third, and sixth cycle; seven patients (30.43%) after the fourth cycle; and eight patients (34.78%) after the fifth cycle. Mean Hb level before and after chemotherapy was 11.30 g/dl and 10.68 g/dl, respectively. During early chemotherapy, none of the patients developed neutropenia. After six cycles of chemotherapy, three patients (13.04%) developed mild neutropenia, four patients (17.39%) developed moderate neutropenia, and one patient (4.35%) developed severe neutropenia. The mean ANC decreased by 44.72% after six cycles of chemotherapy (Figure 1, Table 2).

**Table 2.** Clinical profiles of advanced-stage epithelial ovarian cancer patients who underwent six cycles of chemotherapy (n = 23)

| Laboratory Profiles | Pre-chemo | After 1st Cycle | After 2nd Cycle | After 3rd Cycle | After 4th Cycle | After 5th Cycle | After 6th Cycle |
|---------------------|-----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                     | Mean SD   | Mean SD         | Mean SD         | Mean SD         | Mean SD         | Mean SD         | Mean SD         |
| Hb                  | 11.30     | 10.79           | 10.69           | 10.39           | 10.67           | 10.96           | 10.68           |
| ANC                 | 3558.18   | 3294.78         | 2361.79         | 2854.63         | 2138.88         | 1801.35         | 1966.85         |

ANC=Absolute Neutrophil Count; Hb=hemoglobin; SD=Standard Deviation

**Figure 1.** Mean absolute neutrophil count during chemotherapy

Patients were classified into three groups on the basis of hemoglobin level before chemotherapy: Hb < 8 g/dl, Hb 8–10 g/dl, and Hb > 10 g/dl. The ANC decreased in 16 patients (69.57%), although their initial Hb level was >10 g/dl. In contrast, ANC was stable or increased in six patients (26.09%; Table 3).
Table 3. Change in absolute neutrophil count during chemotherapy according to hemoglobin level before chemotherapy

| Hemoglobin (g/dl) | Number of patients with decreasing ANC | Number of patients with stable or increasing ANC |
|------------------|----------------------------------------|-----------------------------------------------|
| <8               | 0                                      | 0                                             |
| 8–10             | 0                                      | 1                                             |
| >10              | 16                                     | 6                                             |

ANC, absolute neutrophil count.

Patient BMI before chemotherapy is shown in Table 2. The ANC decreased in 14 patients (77.77%) and increased in four patients (17.39%) who were normal weight (Table 4). Body weight and BMI are not predictive of neutropenia and bone marrow disorder.

Table 4. Change in absolute neutrophil count during chemotherapy according to body mass index before chemotherapy.

| Body Mass Index | Absolute neutrophil count | Decrease | Stable/Increase |
|-----------------|---------------------------|----------|----------------|
| Underweight     |                           | 1        | 1              |
| Normal weight   |                           | 14       | 4              |
| Overweight      |                           | 2        | 1              |

Underweight: BMI <18.5; Normal weight: BMI 18.5–24.9; Overweight: BMI 25–30; and Obese: BMI > 30

3.2 Discussion

Of the 23 patients in this study, 13 (56.52%) were older than 55 years. This was consistent with the findings of a previous study, which indicated that most epithelial ovarian cancer cases occur in the 60–64-year-old population [10,11]. Patients’ financial condition, knowledge, socioeconomic status, and culture influence their willingness to seek medical help. However, most patients in this study 15 patients (65.21%) had graduated from senior high school. Improving patient education can increase their understanding of their condition and therapy. Ovulation, multiparity, and breastfeeding history are protective factors against ovarian cancer. Pregnancy can decrease the risk of ovarian cancer by as much as 13–19% [12–15]. A 40% decrease in ovarian cancer risk occurs after delivering the first baby, and every additional pregnancy can decrease the risk by 14% [16]. Purdie et al., found that a regular ovulation cycle over a period of a year decreases the ovarian cancer risk by 6% [17–21]. In the present study, 15 patients (65.22%) were multiparous, indicating that the etiology of ovarian malignancy remains unclear, with many predisposing factors [12].

In the present study, two subjects (8.69%) had a first-degree relative with ovarian cancer and endometrial cancer, and these two cases potentially involved BRCA 1 and BRCA 2 mutation. In approximately 20% of cases, epithelial ovarian cancer is inherited genetically. Thus, information about a family history of cancer is very important. Early examination should be performed in individuals with a family history of malignancy. Thus, proactive steps can be taken for early detection, timely treatment, and improved prognosis in patients with ovarian cancer [22]. Decreases in body weight and BMI were observed in patients in the present study. Patients with malignancy who receive chemotherapy can lose their appetite, which decreases their quality of life. This finding is inconsistent with the results of a study by Hess et al., who found that a carboplatin and paclitaxel combination can increase body weight in ovarian cancer patients [5].

A meta-analysis by Olsen et al. revealed a relationship between ovarian cancer and being overweight (BMI: 25–29.9) or obese (BMI > 30).15 Obese patients have higher risk of ovarian cancer than overweight patients do. Out of 23 patients in the present study, most had normal weight: two patients (8.69%) were underweight, 18 patients (78.26%) had normal body weight, and three patients (13.04%) were overweight. Thus, these findings do not support the conclusion of the meta-analysis by
Olsen et al. [15] Chemotherapy can decrease Hb levels. In the present study, the Hb level before chemotherapy was 8–13 g/dl. Of the 23 patients, one (3.57%) had Hb of 8 g/dl, and 22 patients (95.65%) had Hb in the normal range. Mean Hb level before and after chemotherapy was 11.30 ± 1.28 g/dl and 10.68 ± 1.04 g/dl, respectively. Thus, the decrease in Hb levels after chemotherapy in the present study was not as pronounced as the 50–60% decrease reported in previous studies [16-19].

Chemotherapy can result in a decrease in leukocyte count, and the consequent leukopenia could increase the risk of infection. Leukopenia with a markedly decreased neutrophil count could result in febrile neutropenia. Neutrophils are an important component of the immune system, and therefore, infection can occur if the ANC drops to ≤1500. ANC can be calculated by multiplying the total leukocyte count by the neutrophil percentage obtained from a leukocyte differential count [20]. Before chemotherapy, none of the patients had neutropenia. After six cycles of chemotherapy, three patients (13.04%) developed mild neutropenia, four patients (17.39%) developed moderate neutropenia, and one patient (4.34%) developed severe neutropenia. The mean neutrophil count decreased by as much as 42.9% after chemotherapy. Infection in a neutropenic state could result in worsening of the patients’ condition or even death.

According to ASCO guidelines, granulocyte colony stimulating factor (G-CSF) can be administered for early neutropenia prevention. However, Lackey et al. concluded that G-CSF should not be given to advanced-stage epithelial cancer patients who had undergone intravenous chemotherapy because the prevalence of febrile neutropenia was low in their study [8]. In the present study, no relationship was found between Hb level before chemotherapy and ANC decrement after each cycle. Chemotherapy could suppress the maturation of bone marrow blast cells resulting in a simultaneous decrease in the counts of both erythrocytes and leukocytes such as neutrophils. In the present study, no relationship was found between ANC changes and BMI before chemotherapy. This result is inconsistent with the findings of Dignam et al., who found that the prevalence of neutropenia was low in obese patients [21].

4. Conclusion
In this study, mean BMI and body weight decreased after six cycles of chemotherapy. ANC and mean Hb level decreased after each cycle of chemotherapy. Approximately a quarter of the patients experienced neutropenia after each cycle of chemotherapy. ANC was not influenced by Hb level or by initial body weight or BMI.

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