ORIGINAL RESEARCH

Nutritional status, hemoglobin, and albumin levels in predicting platinum resistance in ovarian cancer at Dr. Saiful Anwar Hospital, Malang, Indonesia

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ABSTRACT

Objective: This study aimed to determine whether nutritional status, hemoglobin, and albumin levels could serve as reliable predictors for predicting platinum resistance in patients with ovarian cancer.

Materials and Methods: Conducted as a cross-sectional analysis, this study included 80 ovarian cancer patients who had completed six cycles of platinum-based chemotherapy. Patients were divided into two categories: those with platinum-resistant cancer and those with platinum-sensitive cancer, based on recurrence status following chemotherapy. Nutritional status was assessed through body mass index (BMI), and both hemoglobin and albumin levels were measured pre- and post-chemotherapy to investigate potential differences between the groups.

Results: The analysis revealed no significant difference in BMI between the platinum-sensitive and platinum-resistant groups ($p = 0.743$), suggesting that nutritional status, as measured by BMI, did not correlate with platinum resistance. Hemoglobin levels were similarly non-significant before ($p = 0.072$) and after chemotherapy ($p = 0.055$), indicating no clear association between hemoglobin levels and platinum response. However, hemoglobin levels showed significant increases post-chemotherapy in both the platinum-sensitive ($p = 0.002$) and platinum-resistant ($p = 0.025$) groups, though without affecting resistance outcomes. Pre-chemotherapy albumin levels did not significantly differ between the two groups ($p = 0.218$); but a significant post-chemotherapy difference was observed ($p = 0.027$), with both groups experiencing substantial increases from pre- to post-chemotherapy ($p = 0.000$).

Conclusion: The findings suggest that BMI, hemoglobin, and albumin levels are not reliable predictors of platinum resistance in ovarian cancer patients. Although both hemoglobin and albumin increased significantly after chemotherapy, these changes did not correspond with platinum resistance status.

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Highlights:

1. Nutrition status, hemoglobin, and albumin levels are not predictors for platinum resistance.
2. Hemoglobin and albumin levels increased in both platinum-sensitive or platinum-resistant.

INTRODUCTION

Ovarian cancer is the third malignancy among all types of gynecological cancer after cervical and uterine cancer.[1] Despite its low prevalence, ovarian cancer has a poor prognosis and the second-highest mortality rate among cervical and uterine cancers.[2] Ovarian cancer is more prevalent among Caucasian women, with the median age of diagnosis being 63 years old in the United States.[3] At Saiful Anwar Hospital, Malang, Indonesia, in 2017-2019, ovarian cancer cases were 37.8% of all gynecological cancer.[4] Ovarian cancer has a lower survival rate than other cancers. It is because this cancer is usually detected at an advanced stage. However, this cancer can have a survival rate of up to 90% if found early and treated immediately.[5] Most types of ovarian cancer are epithelial types (90%) which originate from invagination of the ovarian surface epithelium.[6] Due to its complex varying degrees of heterogeneity, makes ovarian cancer difficult to detect and treat.[7]

The management of ovarian cancer involves performing surgery the first step and followed by systemic chemotherapy, particularly in advanced stages. Patients who exhibit platinum resistance at the beginning of treatment have a lower chance of survival. In addition, a patient's nutritional status can also affect the development of metastases and overall cancer prognosis.[5] However, a previous study found that advanced stage, lack of lymphadenectomy, positive lymph nodes and history of breast cancer was increased the risk of platinum-based drug resistance which leading to the poor prognosis.[8]

Body mass index (BMI) and serum albumin levels are used to evaluate the nutritional status of cancer patients. Hypoalbuminemia is caused by malnutrition and cachexia in cancer patients due to the body's response to the tumor and anti-tumor therapy.[9] Platinum chemotherapy binds to protein in plasma which influence their pharmacokinetics significantly.[10] Regarding its effect on resistance to platinum-based chemotherapy, albumin in serum is important to be examined. In addition to the adverse effects on quality of life, the presence of anemia itself is associated with shorter survival times for some types of cancer. Hypoxia may contribute to the malignant behavior of the disease by providing selection pressure for tumor cells with higher mutation rates, ultimately resulting in increased growth of cells, decreased cell response to apoptotic signals, and therapy resistance.[11] This study, therefore, aimed to assess whether nutritional status, hemoglobin levels, and albumin levels can be used as predictors of platinum resistance among ovarian cancer patients after 6 series of chemotherapy at Dr. Saiful Anwar Hospital, Malang, Indonesia.

MATERIALS AND METHODS

This was a cross-sectional study, conducted by collecting data from the medical record of the patients. This study was approved by the Ethics Committee of Dr. Saiful Anwar General Hospital with number 400/228/K.3/102.7/2022. The population in this study included all ovarian cancer patients who had undergone surgery in Dr. Saiful Anwar Hospital, Malang, from July - December 2022.

This study used consecutive sampling and with the inclusion and exclusion criteria. The inclusion criteria were: 1) patients with ovarian carcinoma diagnosed by a clinician at the Oncology Clinic of the Department of Obstetrics and Gynecology who have undergone platinum-based chemotherapy 6 series, 2) patients underwent laparotomy to confirm the results of the clinical examination, 3) patients who had albumin and hemoglobin examined before and after chemotherapy at the Clinical Pathology Laboratory of Dr. Saiful Anwar Hospital, Malang. The exclusion criteria were: 1) patients with adnexal masses which did not originate from the ovaries, 2) patients suffering from other malignancies, 3) patients with infected adnexal masses.

Patients' data were collected at the Oncology Clinic of the Department of Obstetrics and Gynecology, Dr. Saiful Anwar Hospital, Malang. The data collected included age, type of chemotherapy, BMI, albumin, and hemoglobin levels of patients before and after chemotherapy. The BMI data itself were later classified into underweight (BMI <17 kg/m^2), normal (BMI 17-23 kg/m^2), overweight (BMI 23-27 kg/m^2), and obesity (BMI >27 kg/m^2).[12] Platinum-resistant is defined as the recurrence of cancer under 6 months after the last chemotherapy session.[13] Recurrence in this study meant the reappearance of the tumor in the ovary with an increase in Ca125 values and/or the detection of new metastases. Then, the collected data were analyzed using SPSS Software 20 with the Mann-Whitney U test for numerical data and Chi-square for categorical data. Results were considered significant if $p < 0.05$.

RESULTS AND DISCUSSION

The participants were divided into two groups, each consisting of 40 participants which then characterized by the age, types of chemotherapy, and BMI (Table 1). Participants in the platinum-resistant group had the mean age of 52.55 ± 11.15 years while in platinum-sensitive had the mean age was 50.75 ± 11.14 years. There was no significant difference between groups regarding age (p = 0.785). Most of the participants were given Carboplatin Docetaxel which 55% in platinum-resistant and 60% in platinum-sensitive. There was no significant difference between groups regarding types of chemotherapy (p = 0.899). BMI showed that most of participants were in normoweight which 60% in platinum-resistant and 55% in platinum-sensitive. There was no significant difference between groups regarding BMI (p = 0.557).

Ovarian cancer typically manifests during the peri-menopausal or post-menopausal period, with 80-90% of cases occurring in individuals above the age of 40, peaking at 60 years old.[14] The disease's 5-year survival rate is low (48%) due to 70% of cases being diagnosed at stages III and IV. This worse prognosis is related to the metastatic process.[15] Beyond the worst prognosis, advanced stages also contribute to a higher recurrence rate within 5 years, with 70% of cases experiencing recurrence.[16] The nutritional status of cancer patients has a significant impact on their quality of life. Research shows that weight loss and decreased appetite are closely linked to decreased quality of life.[17] In addition, studies have found that being overweight or obese increases a person's risk of developing ovarian cancer and experiencing severe symptoms of the disease.[18]

In this study, platinum-resistant patients had mean of BMI of 21.63 ± 3.90 and 21.94 ± 3.83 in platinum-sensitive patients with p = 0.743. Based on the results obtained, there seems to be no significant difference between the BMI and the incidence of platinum resistant among ovarium cancer patients who underwent six rounds of chemotherapy. This finding contradicted previous research that indicated that that obesity can play a role in tumor progression and resistant. Obesity can negatively impact the survival rates of ovarian cancer patients. This effect may be due to changes in the M1/M2 tumor-associated macrophage ratio as well as increased fibrosis, which can reduce chemosensitivity.[19] It is possible that this study comprised a large population of individuals with a normal BMI rather than being overweight or obese, which could account for the contrasting results observed in other studies that suggested obesity could have an impact on pharmacokinetics, metabolic dysregulation, the induction of platinum resistance, or the decision to reduce therapeutic doses to minimize toxicity.

Hemoglobin is a commonly measured parameter in cancer patients, as it can be affected by the cancer itself, its treatment, and patient-related factors.[20] Among the platinum-resistants (Table 2), the measurement of hemoglobin levels before chemotherapy revealed 10.58 ± 1.72, then changed significantly (p = 0.025) to 11.01 ± 0.94. A significant increase (p =0.002) also occurred in platinum-sensitive patients, with initial hemoglobin from 9.92 ± 1.49 to 10.56 ± 1.16. When comparing hemoglobin levels before and after chemotherapy, there was no significant difference in hemoglobin in the two groups pre-chemotherapy (p = 0.072) and post-chemotherapy (p = 0.055).

Table 1. Characteristics of study population.

Characteristics	Platinum-resistant (n=40)	Platinum-sensitive (n=40)	p-values
Age (mean ± SD)	52.55 ± 11.15	50.75 ± 11.14	0.785
Types of chemotherapy			
• Carboplatin Brexel	17 (42.5%)	15 (37.5%)	
• Carboplatin Docetaxel	22 (55%)	24 (60%)	0.899
• Carboplatin Paclitaxel	1 (2.5%)	1 (2.5%)	
BMI (mean ± SD)	21.63 ± 3.90	21.94 ± 3.83	
• Underweight	9 (22.5%)	9 (22.5%)	
• Normoweight	24 (60%)	22 (55%)	0.557
• Overweight	6 (15%)	9 (22.5%)	
• Obesity	1 (2.5%)	0 (0%)	

BMI: body mass index

Table 2. Changes in hemoglobin levels

Hemoglobin	Pre-Chemotherapy	Post-Chemotherapy	p-values
Platinum-sensitive	9.92±1.49	10.56±1.16	0.002*
Platinum-resistant	10.58±1.72	11.01±0.94	0.025*
p-values	0.072	0.055	

*p<0.05

Table 3. Changes in albumin levels

Albumin	Pre-Chemotherapy	Post-Chemotherapy	p-values
Platinum-sensitive	3.22± 0.68	3.40± 0.60	0.000*
Platinum-resistant	3.41± 0.67	3.69± 0.54	0.000*
p-values	0.218	0.027	

*p<0.05

This study implies that platinum resistance does not influence hemoglobin levels, and similarly, changes in hemoglobin do not affect platinum resistance. Interestingly, the hemoglobin levels increased significantly in both groups after chemotherapy, which contradicted the conventional theory that states that hemoglobin levels tend to decrease after chemotherapy.[20] However, due to the lack of documentation of oral or transfusion therapy prior to chemotherapy, this could have biased the results. Additionally, low hemoglobin levels can reduce oxygen supply and cause hypoxia, which is linked to resistant to chemotherapy and radiation, increased tumor growth, tissue invasion, metastasis, and poor prognosis.[21]

Albumin plays multiple roles in the body, including functioning as an antioxidant and trapping free radicals.[22] It also serves as an indicator of nutritional status and can help in evaluating the body's response to inflammation. In cases where a tumor leads to hypoalbuminemia, it can reduce the effectiveness of therapy and increase the risk of mortality.[23] As it is known that albumin is a protein in plasma which then bind with platinum chemotherapy and significantly influence their pharmacokinetics, particularly in terms of factors like renal excretion rate. In general, when the leaving group of platinum complexes is not readily replaced by a ligand, their protein-binding ratio tends to be lower, leading to a longer half-life and a higher rate of renal excretion.[10]

In this study, albumin levels before chemotherapy in platinum-resistant patients (Table 3) increased significantly before chemotherapy 3.41 ± 0.67 to 3.69 ± 0.54 with p = 0.000. It was also the same in platinum-sensitive patients, which increased from 3.22 ± 0.68 to 3.40 ± 0.60 with p = 0.000. For albumin levels before chemotherapy, the p-value = 0.218, indicating no significant difference in albumin before chemotherapy. However, after chemotherapy, the p-value became 0.027 which showed a significant difference between the two groups, which was higher in platinum resistance.

Albumin serves as a regulator in acid-base physiology, facilitating the binding and transportation of crucial components in the bloodstream such as hormones, fatty acids, and bilirubin to organs. Additionally, it inhibits platelet function, controls vascular permeability, and helps maintain colloid-osmotic pressure in the body.[24] In chemotherapy, low albumin levels are associated with chemotherapy-induced toxicity.[25] Other study stated that albumin-bound paclitaxel (ABP) blends the hydrophobic paclitaxel with a carrier of human serum albumin. This combination enhances the efficient transportation of paclitaxel to tumor tissues through endocytosis. Additionally, utilizing albumin as the carrier for paclitaxel enables the attainment of higher drug concentrations, increasing the efficacy.[26] This study experienced the opposite, where there was a significant increase in albumin in the platinum-resistant and platinum-sensitive groups. However, it is necessary to pay attention to the history of albumin administration, diet, insulin levels, and history of use of drugs such as corticosteroids, which can influence albumin levels which could have biased the results. This result might be showed that the decrease of albumin was not correlated with the protein-binding but could be the result of the cancer itself.

Limitations of this study lie in its small sample size, caused by incomplete data. Furthermore, this study did not record a history of transfusions, blood-boosting drugs, administration of extra albumin, or other therapies that could potentially be biased. It was because there were several incomplete pieces of data and documentation in the patients' record. Additionally, this study did not reassess the patient's body mass index after undergoing chemotherapy overlooking potential clinical changes.

CONCLUSION

This study confirms that nutritional status is not a determining factor in platinum resistance. Similarly, hemoglobin and albumin levels do not directly influence platinum resistance. However, an increase in albumin levels has been observed in platinum-resistant cases. The findings suggest that nutritional status, hemoglobin, and albumin are not reliable predictors of platinum resistance. Nonetheless, patients with good nutritional status, as indicated by their BMI, may experience elevated hemoglobin and albumin levels. Further research is warranted to explore other potential factors contributing to platinum resistance.

DISCLOSURES

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Conflict of interest

The authors declare there is no conflict of interest.

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Author contribution

All authors have contributed to all processes in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

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