

Research Article

NEOADJUVANT CHEMOTHERAPY RESPONSE OF CERVICAL CANCER PATIENT STAGE IIB IN SANGLAH GENERAL HOSPITAL DENPASAR

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ABSTRACT

Cervical cancer is a malignancy of the cervix caused by the human papillomavirus. The therapy administered on stage IIB cervical cancer is neoadjuvant chemotherapy. The purpose of this study was to determine the characteristics based on age, histopathological type, family history, parity, contraceptive history, chemotherapy response, and operability status in cases of cervical cancer stage IIB after neoadjuvant chemotherapy at Sanglah Hospital Denpasar. This study is a retrospective descriptive study sourced from the patient's medical record with a total sampling technique. The population and sample of this study were stage IIB cervical cancer patients post-neoadjuvant chemotherapy at Sanglah Hospital Denpasar for the 2020-2021 period according to the inclusion criteria. The results showed that there were 40 stage IIB cervical cancer patients with the highest number of cases aged 40-49 years (45%). The most common histopathological type was squamous cell carcinoma (85%). Patients without a family history of cervical cancer were 92.5%. Patients with parity > 2 were 52.5%. Patients with a history of contraceptive use were 65%. Good chemotherapy response was found in more than 70% of the patients. Patients with operable status were 57.5%.

Keywords: characteristics, cervical cancer stage IIB, neoadjuvant chemotherapy.

INTRODUCTION

Cervical cancer is a malignant tumor that attacks the cervix where this condition may cause abnormal structural changes and uncontrolled growth of cervical cells.¹ Oncogenic Human Papillomavirus (HPV) infection is still the most common cause of cervical cancer. HPV types 16, 18, 31, 33, 52, and 58 are often associated with cervical cancer.² Cervical cancer is listed as the fourth most common cancer among women worldwide (576,600 estimated new cases) and the fourth most common cancer cause of death (265,700 deaths).³ Referring to the data presented by the Indonesian Ministry of Health, as of January 31, 2019, there were 23.4 per 100,000 population cervical cancer with an average death rate of 13.9 per 100,000 population. Based on the study conducted at Sanglah Hospital, Denpasar, 206 cases of gynecologic malignancy during the period of July 2012-June 2013 were found, on which the highest cases were cervical cancer with as many as 89 cases (43.2%).⁴ According to the International Federation of Gynecology and Obstetrics (FIGO), cervical cancer is divided into stage 0, stage I (IA1, IA2, IB, IB1, IB2), stage II (IIA, IIB), stage III (IIIA, IIIB), and stage IV (IVA, IVB). Treatment options for cervical cancer at each stage are different: at stage IA1, a simple hysterectomy is performed; at stage IA2 a modified radical hysterectomy and pelvic lymphadenectomy are performed; for both stage IB1 and IIA, a radical hysterectomy and pelvic lymphadenectomy are performed; and for stage IB2 and IIB-IV, radiation therapy with cisplatin is performed.²

In stage IIB-IVA cervical cancer, FIGO recommends standard therapy, namely external radiation and brachytherapy, concomitant with chemotherapy known as chemoradiation. However, at stage IIB cervical cancer, there is currently no standard therapy. Special

treatment is given to patients with stage IIB cervical cancer patients which is different from the FIGO's recommendation, which includes the administration of platinum-based neoadjuvant chemotherapy. The purpose of administering neoadjuvant chemotherapy to patients with stage IIB cervical cancer is to reduce tumor size and obtain a wider reaction area so that surgery is possible. There are several factors that influence the success of this therapy, including the general condition of the patient, tumor diameter, histopathological type, degree of cell differentiation, and applied chemotherapy regimen.⁴ This study will discuss the characteristics of patients with cervical cancer stage IIB after being treated with neoadjuvant chemotherapy. This paper aimed as a prior study in order to predict neoadjuvant chemotherapy success on cervical cancer stage IIB patients.

METHOD AND MATERIAL

This research is a cross-sectional descriptive retrospective study conducted in Sanglah Hospital, Denpasar, within the period of January 2020 to August 2021. The samples included in this research were based on the inclusion and exclusion criteria, namely cervical cancer patients stage IIB post-neoadjuvant chemotherapy registered in Sanglah Hospital with complete data. This study involved 40 patients as the sample. The sample collection used a non-randomized total sampling method. The source of data in this study is secondary data obtained from the registration at the Obstetrics and Gynecology Polyclinic and the Medical Record Installation at Sanglah Hospital Denpasar in the form of medical records. The patient data included age, histopathological type, family history of cervical cancer, parity, history of contraception, chemotherapy response, and operability status. Histopathological types were divided into squamous cell carcinoma, adenocarcinoma, and adenosquamous carcinoma. The chemotherapy response was categorized as good if there was 'complete response, partial response' and poor if there was 'progressive disease, stable disease'. Operable status is divided into

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operable and non-operable. The patient data obtained were then processed by a univariate method using Microsoft Excel.

RESULTS

The subjects in this study were 40 people based on the inclusion criteria, namely, stage IIB cervical cancer patients after neoadjuvant chemotherapy who were recorded in the Medical Record Section of Sanglah Hospital Denpasar and had complete data.

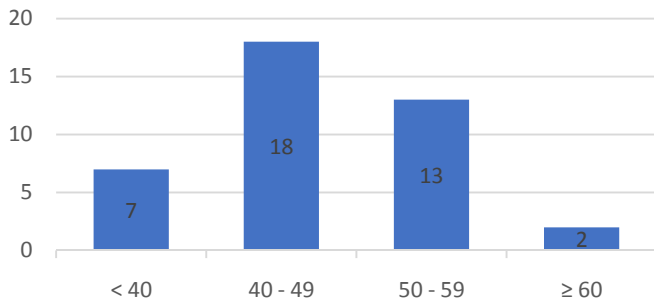


Figure 1. Patients distribution based on age

Figure 1 shows the characteristics of the sample based on age, from 40 samples, the highest cases were in the 40-49 year age group as many as 18 people (45%), followed by the 50-59 year age group (32.5%), the <40 year age group. (17.5%), and at least 2 people (5%).

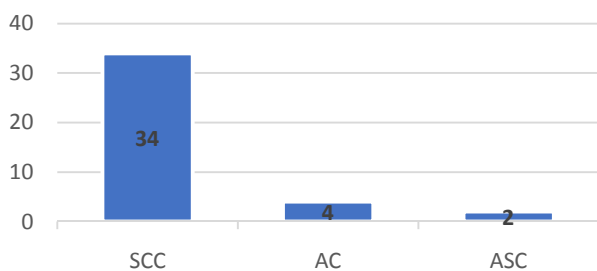


Figure 2. Patients distribution based on histopathology type

Figure 2 showed the characteristic based on the type of histopathological findings, squamous cell carcinoma is the most commonly found histopathological characteristic with 34 people (85%), followed by adenocarcinoma with 4 people (10%), and adenosquamous carcinoma with 2 people (5%).

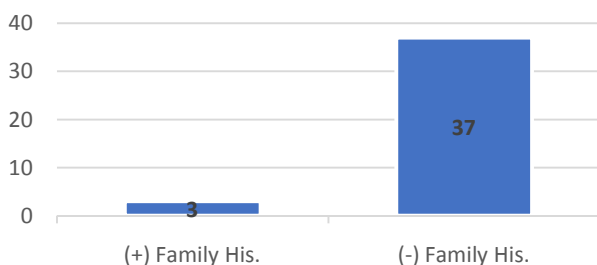


Figure 3. Patients distribution based on family history with cervical cancer

Figure 3 showed the distribution of family history among 40 post neoadjuvant chemotherapy stage IIB cervical cancer patients in Sanglah Hospital from 2020-2021. Results show that there are 37 cases without a family history of cervical cancer (92.5%) and 3 cases with a family history of cervical cancer (7.5%).

Figure 4 showed the parity of post-neoadjuvant chemotherapy stage IIB cervical cancer patients in Sanglah Hospital from 2020-2021. From 40 cases there are 21 patients with >2 parity (52.5%) and 19 patients with ≤2 parity (47.5%). According to figure 5 from a total of 40 cases diagnosed with stage IIB cervical cancer, there are 26 people (65%) with a history of using contraception and 14 people (35%) who did not have a history of using contraception.

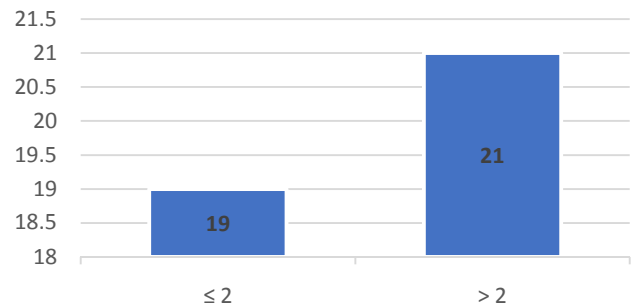


Figure 4. Patients distribution based on parity

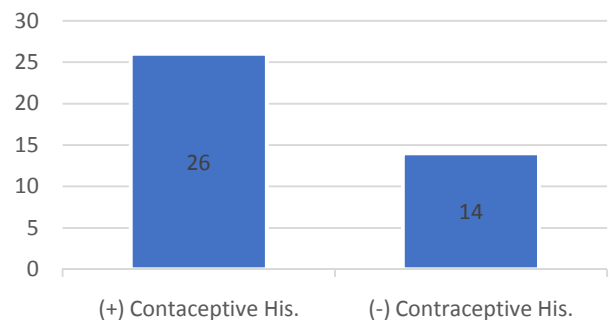


Figure 5. Patients distribution based on contraceptive history

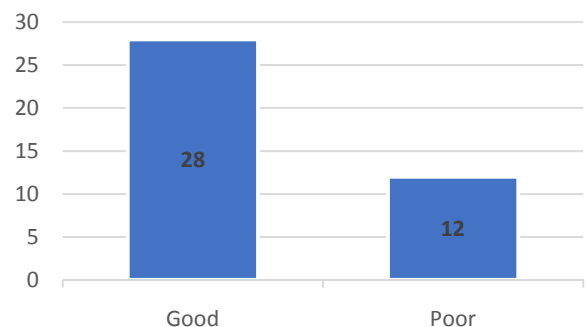


Figure 6. Patients distribution based on chemotherapy respon

Figure 6 showed that from a total of 40 samples of post neoadjuvant chemotherapy stage IIB cervical cancer patients 28 cases (70%) responded well to chemotherapy while 12 cases (30%) responded badly to chemotherapy. Table 1 showed the evaluation of response to chemotherapy on stage IIB cervical cancer patients after neoadjuvant chemotherapy. Up to 24 patients (70.6%) of patients with squamous cell carcinoma showed a good response to chemotherapy while 10 other patients of the same type (29.4%) responded badly. Patients with adenocarcinoma type histopathological findings overall have a good response to chemotherapy (100%). Up to 2 patients (50%) with adenosquamous carcinoma showed a good response to chemotherapy while 2 other patients of the same type (50%) showed a bad response.

Table 1. Chemotherapy response assessment based on patients' histopathology

Histopathology type	Chemotherapy Response		Total
	Good	Poor	
Squamous Cell Ca.	24 (70,6%)	10 (29,4%)	34 (100%)
Adenocarcinoma	2 (100%)	0 (0%)	2 (100%)
Adeno Squamous Ca.	2 (50%)	2 (50%)	4 (100%)

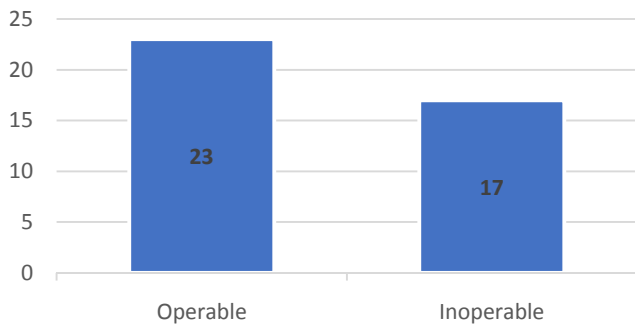


Figure 7. Patients distribution based on operability status

Figure 7 showed the distribution of operability status on stage IIB cervical cancer patients after neoadjuvant chemotherapy. From 40 patients that fit the inclusion criteria, the number of patients with an operable status is as many as 23 people (57.5%) and patients with inoperable status reached up to 17 people (42.5%).

DISCUSSION

AGE

The 40-49 year age group was found the most in this study, which was 45%. These results are consistent with the 2016 study by Manoppo regarding the relationship between parity and maternal age with cervical cancer in 45 cases of cervical cancer diagnosed. This study showcased that the peak number of stage II cervical cancer patients was in the age range of 46-55 years.⁵ This finding is also in accordance with research conducted by Herlana *et al.*, 2017 regarding the characteristics of cervical cancer patients based on age in 82 diagnosed cases. The study showed that the majority of cervical cancer patients were more than 35 years old.⁶ Immunity begins to decline as a person ages. This is related to the amount and increasing time of exposure to carcinogens as well as the decreased affinity of the immune system in dealing with cancer cells by slowing down their expansion and progression. When this decrease in immunity occurs, the Human Papilloma Virus easily attacks the body so that as you age, the risk of cervical cancer increases.⁷

HISTOPATHOLOGICAL TYPE

In this study, the most common type of histological finding is the squamous cell carcinoma with a percentage of 85%. This finding is in accordance with a study by Herlana *et al* in 2017 related to the characteristics of cervical cancer patients based on histopathological findings in 82 cervical cancer cases which showed that squamous cell carcinoma was more commonly found than adenocarcinoma with a total of 52 cases (63.4%). Another study by Khatimah and Muhammad in 2019 regarding the relationship between histopathological types and the response to neoadjuvant chemotherapy in cervical cancer patients in 35 cases found that the number of cases with Squamous Cell Carcinoma type was 71.4%.⁸

FAMILY HISTORY OF CERVICAL CANCER

A total of 37 patients diagnosed with stage IIB cervical cancer were found in this study. These results are in accordance with the research conducted by Surbakti *et al.*, 2020 regarding the relationship between the characteristics, family history, and knowledge of mothers suffering from cervical cancer that found that there are more samples that did not have a family history of cervical cancer 60.9%.⁹ Patients who have a family history of cancer have an increased chance of developing cancer 2 to 3 times higher in their offspring. In the case of cervical cancer, if there is a family history of cervical cancer, there is a 74-80% greater chance of women who have mothers or siblings who have a history of cervical cancer than women in general. This is related to the similarities between the condition of the host's immune system and genetic factors that also play a role in the occurrence of cancer.^{10, 11}

HISTORY OF CONTRACEPTION USE

In this study, there were more patients with a history of contraception than patients without a history of using contraception, as many as 26 people. This is in accordance with a study conducted by Nindrea in 2017 on the factors that influence cervical pre-cancerous lesions, that showed that patients with a history of using contraceptives are as many as 17 people (94.4%) and patients without a history of using contraceptives are as many as 1 person (5.6%).¹³ However, research by Wulandari in 2016 regarding the relationship of risk factors for the use of oral contraceptives and sexual activity with the incidence of cervical cancer in 37 cervical cancer patients at Dr. Hospital. Saiful Anwar Malang found that a history of oral contraceptives has no relationship with the risk of cervical cancer.¹⁴

CHEMOTHERAPY RESPONSE

Patients with complete response and partial response were the most frequently found in this study, as many as 70%. This finding is consistent with the study by Salihi *et al* in 2017 regarding the response to paclitaxel-carboplatin chemotherapy in stage 1-2 cervical cancer in 15 patients diagnosed with stage IIB cervical cancer, getting good chemotherapy response results as much as 93.3% and poor chemotherapy response as many as 6.7%.¹⁵ Research by Da Costa *et al* in 2019 also found the same results regarding the comparison of cisplatin-gemcitabine neoadjuvant chemotherapy followed by chemoradiation with single chemoradiation, in 55 cases diagnosed with cervical cancer who received neoadjuvant chemotherapy treatment obtained 80% results resulting in good chemotherapy response outcomes and as many as 20% showed a poor response to chemotherapy.¹⁶ Neoadjuvant chemotherapy response is known to be better in squamous cell carcinoma than non-squamous cell carcinoma and patients with cervical cancer type squamous cell carcinoma are said to have a significant 5-year survival rate.¹⁷ Tumor diameter affects chemotherapy response in cervical cancer, the larger the tumor size, the worse the response to chemotherapy is given and tumors with a diameter of more than 4 cm are at risk of not responding to chemotherapy.¹⁸ Hemoglobin levels are said to play an important role in this, such as hypoxia in tumors, causing resistance to chemotherapy, and increasing tumor angiogenesis as a result of anemia in children. patient. Hypoxic conditions in the tumor result in the unresponsiveness of the lesion to radiotherapy given, besides that it has a tendency to increase in progression and distant metastases.⁸

OPERABILITY STATUS

As many 23 patients are deemed as operable and 17 others are inoperable in this study. This is in accordance with a study conducted by Salihi et al. from 2017 regarding the response to paclitaxel carboplatin chemotherapy in stage 1-2 cervical cancer among 15 patients who were diagnosed with stage IIB cervical cancer, where it was found that there are 10 operable cases and 5 inoperable cases.¹⁵ This result is in accordance with the findings of this study where it was found that 57.5% of patients are operable. Meanwhile, a study conducted by Arsyad in 2020 regarding the operability in 40 cases of post neoadjuvant chemotherapy stage IIB cervical cancer patients showcased that 47.5% of patients are operable and 52.5% of patients are inoperable after receiving neoadjuvant chemotherapy. According to said study, the probability of reaching an operable status was influenced by multiple factors such as tumor gene expression.¹⁹

CONCLUSION

The characteristics of stadium IIB cervical cancer patients post neoadjuvant chemotherapy from 2020-2021 in Sanglah General Hospital Denpasar are an age group majority of 40-49 years old, squamous cell carcinoma type histopathological findings, without any family history of cervical cancer, >2 parity, with history of contraception usage, good response to chemotherapy, and operable status. While conducting the study there were problems regarding the incomplete medical records which has become the main limitation of this study. This had the potential to impact the accuracy and quality of the study results significantly.

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