ORIGINAL RESEARCH

Clinical profile of geriatric cervical cancer patients in a tertiary hospital in Surabaya, Indonesia

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ABSTRACT

Objective: To identify the distribution of age, histopathology type, clinical stage, treatment type, parity, first complaint, and referral origin of geriatric cervical cancer patients at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. **Materials and Methods**: This study was a retrospective study observing data from medical records and presented the data descriptively. The medical records were taken from Oncology Outpatient Clinic in Dr. Soetomo Hospital, from 2020-2021, covering geriatric patients aged more than 55 years old. The data were screened and processed.

Results: At Dr. Soetomo Hospital, in 2020-2021 there were 228 cervical cancer patients. From 176 patient data that met the inclusion criteria, the average age was 65.38 ± 4.86 years, with 4 types of histopathology dominated by squamous cell carcinoma (82.39%), adenocarcinoma (11.93%), adenoquamous (3.41%) and others (4%), divided into 8 clinical stages and dominated by stages IIIB (77.27%), IIB (15.9%), IVB (2.84%), IIIA and IB had same number (1.14%), 1A (0.57%) and no cases of IIA were found. The treatments were dominated by chemotherapy (86.36%), radiation therapy (7.38%), no treatment (3.41%), hysterectomy (1.7%), while for conization and palliative therapy each in 1 case (0.57%). Most experienced 3 parity (29.5%), followed by 4 parity (17.61%), >5 (13.07%), 5 (10.23%), 1 (6.82%) and no parity (2.27%). The three first complaints were vaginal bleeding (82.38%), vaginal discharge (46.02%), and pain (82.38%), and the patients were dominated by referrals from Java Island other than Surabaya City (78.40%), outside Surabaya in Java Island as many as 36 referrals (20.45%) and outside Java Island 2 referrals (1.14%).

Conclusion: There were 176 geriatric patients with cervical cancer at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, in the 2020-2021 period, dominated by age 56-65 years, the histopathology type of squamous cell carcinoma, stage IIIB patients, most received therapy was chemotherapy, most were multiparous with 3 parities, the majority experienced complaints of vaginal bleeding when diagnosed with cervical cancer, and were dominated by referrals from Java Island outside Surabaya.

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Highlights:

- 1. Squamous cell carcinoma majorly covered in histopathologic of the records, while adenosquamous followed second
- 2. Most of the subjects were referral patients to Dr. Soetomo General Academic Hospital. They were mostly originated from Java outside Surabaya.



INTRODUCTION

Cervical cancer (CC) is known as gynecologist malignant, occurs often in women, caused mainly by human papillomavirus (HPV) type 16 and 18. The infection will trigger the transformation of c epithelial cells in the cervix, leading to pre-cancer lesions and gradually developing to cancer.¹

According to World Health Organization (WHO) in 2022, cervical cancer has become the second leading cancer for women living in developing countries. There are approximately 540,000 new cases in 2018 alone and about 311,000 women died of cervical cancer during that year.² Aligned with the stated data from WHO, according to United Nations Programme on HIV and AIDS (UNAIDS), about 500,000 women suffer from cervical cancer each year, and half of the number passed away.²

Based on data served by *Himpunan Obstetri Ginekologi Indonesia* (HOGI) in 2017, 70-80% of the patients with cervical cancer in Indonesia were mostly geriatric. Therefore, early detection to see the possibilities of manifestation in the cervix is needed. The widely used screening method is a pap smear to retrieve the abnormality of the cervix, covering normal smear data, inflammation process, LSIL, HSIL, in situ, or invasive carcinoma. When the test result shows an abnormality, it could be concluded that there are changes in cells around the cervix.³

Despite efforts to combat cervical cancer, it remains a significant global health problem with high mortality rates. In light of the data mentioned above, it is imperative to study the current trends and clinical profiles of cervical cancer patients, particularly geriatric patients, in one of Indonesia's largest General Academic Hospitals, the Dr. Soetomo General Academic Hospital, in Surabaya, Indonesia. This study aimed to describe the distribution of the clinical profile of geriatric patients with cervical cancer in Dr. Soetomo General Academic Hospital during 2020-2021.

MATERIALS AND METHODS

This study used medical records as the main source of data. Here we extracted patients' age, histopathology, clinical staging, management, parity information, clinical manifestations, and patient's referral origin. Excluded medical records contained patients with incomplete variables needed. The research was conducted at Integrated Oncology Outpatient Clinic at Dr. Soetomo General Academic Hospital from 2020-2021. Data were processed using Microsoft Excel, went

through editing, and coding, and were processed by SPSS software, cleaning. The results of this study will be presented in the form of distribution tables. This study has been approved by the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital Surabaya with the document number 1011/108/4/X/2021.

RESULTS AND DISCUSSION

Sample as many as 228 medical records were obtained. From 228 medical records, 52 were excluded due to incomplete data. Patients' ages were more than 55 when they were first diagnosed. The patients were divided into two categories of age, 56-65 years old and older than 65 years old.

Table 1. Age distribution of cervical cancer in geriatric patients at Dr. Soetomo General Academic Hospital, Surabaya in 2020-2021.

Age Categories	Frequencies	Percentage
56-65	108	61.36%
>65	68	38.64%
Total	176	

Patients aged 56-65 years were the majority of the subjects with a total of 108 cases (61.36%) (Table 1). The research subjects in this study were elderly, persons aged more than or equal to 55 years. In this study, the majority aged 56-65 years (61.36%) with an average age of cervical cancer patients at Dr. Soetomo General Academic Hospital, Surabaya was 65.38 ± 4.86 years old (SD 4.86356). The age range of the subjects was 56-65 years, so all subjects had experienced menopause. Menopause itself does not affect the risk of cervical cancer.4 However, it has been recognized that the older the age, the less capable the immune system, resulting in an increase of infection. In addition, the CDC (2012) also reported that oncogenic HPV is related to cervical cancer and the incidence rate of this cancer increases after the age of 50 years.

Cervical cancer can develop in women of all ages, but generally develops in women aged 35-55 years with a varied peak age of incidence in each population. The results of this study showed that the highest incidence of cervical cancer was found in the age group of 56-65 years, comprising 108 patients (61.36%). This was different from several other studies, as reported by Putri et al. (2019) and Pratiwi et al. (2022), that the majority of cervical cancer patients aged 41-50 years. Whereas, a research in Jambi was dominated by ages 46-55 years, and 41-50 years in Bali. However, the results of this study were in line with a study in India that the



Maj Obs Gin, Vol. 31 No. 1 April 2023 p-ISSN: 0854-0381; e-ISSN: 2598-1013

majority of cervical cancer patients were found at the age of more than 60 years (38.4%), followed by ages 50-59 years (31.2%). The difference in the age of cervical cancer may be caused by several factors. One of which is the time when the patient is screened for cervical cancer. The earlier the patient is screened for cervical cancer after marriage, the earlier the cervical cancer can be detected. Another factor is due to the country's economic progress, and the age of having sexual activity for the first time. 10

Table 2. Histopathology distribution of cervical cancer in geriatric patients in Dr. Soetomo General Academic Hospital, Surabaya in 2020-2021.

Etiology	Frequency	Percentage
Adenocarcinoma	21	11.93%
Squamous cell carcinoma	145	82.39%
Adenosquamous	6	3.41%
Others	4	2.27%
Total	176	

Table 2 shows that the histopathology distribution of geriatric patients with cervical cancer in Dr. Soetomo General Academic Hospital, Surabaya in 2020-2021 is dominated by squamous cell carcinoma (82.39%), followed by adenocarcinoma cases in 21 patients (11.93%), adenosquamous in six patients (3.41%) and others in four patients (2.27%).

Histopathological examination can be defined as a microscopic examination of a tissue to determine the course or level of disease. 11,12 In the context of cervical cancer, histopathological examination is the reference standard used by many clinicians and health institutions to diagnose cervical neoplasms. In addition, the determination of treatment for cervical cancer patients (inpatient or outpatient) can also depend on the results of histopathological examination. 12

Among cervical cancer patients at Dr. Soetomo General Academic Hospital, Surabaya in 2020-2021, from various histopathological types, invasive, non-keratinizing squamous cell carcinoma was found as the most common histopathological type. Squamous cell carcinoma, or is a cancer that develops from squamous epithelial cells. This type of epithelial cells is found in various parts of the body, including the surface of the skin, the surface of hollow organs, the surface of the respiratory organs, digestion, and also the genital organs. Therefore, squamous cell carcinoma may show different manifestations according to where it occurs.

Based on its morphology, squamous cell carcinoma can be divided into keratinizing, non-keratinizing, and nonkeratinizing types with maturation. Microscopically, the keratinizing type of squamous cell carcinoma appears as infiltrative nests with desmoplastic formations in the dominant stroma, while the non-keratinizing type usually appears as large nests with lots of mitotic formation, necrosis, and little reaction in the stroma. Clinically, the non-keratinizing type of squamous cell carcinoma is more likely to be associated with human papilloma virus (HPV) infection than the keratinizing type. In some cases, a tumor structure with both keratinizing and non-keratinizing characteristics is found. Such tumor cases are usually referred to as the hybrid type or non-keratinizing type with maturation. This type is also usually associated with HPV infection, but is less frequently detected than purely nonkeratinizing tumors. 13

The results of this study were consistent with the results of a previous study by Rasjidi (2009) which stated that the most common histopathological type of cervical cancer was squamous cell carcinoma (85%), followed by adenocarcinoma (10%), and the remaining 5% were other types. Let us a adenosquamous, clear cell, small cell, verucous, etc. Another study by Kaseka et al (2022) showed that squamous cell carcinoma is the most dominant malignant histopathological type in the cervical cancer patient population. Let

The clinical stage classification distribution of geriatric cervical cancer patients in Dr. Soetomo General Academic Hospital, Surabaya in 2020-2021, showed that the majority was IIIB stage as many as 136 cases (77.27%), followed by stage IIB of 28 cases (15.9%) (Table 3).

Cervical cancer stage indicates the severity of cervical cancer based on its size and distribution at the time of diagnosis according to the results of clinical examination. The stages of cervical cancer according to the Federation of Gynecology and Obstetrics (FIGO) consist stage I (1A, 1A1, 1A2, 1B, 1B1, 1B2), stage II (IIA and II B), stage III (IIIA and IIIB), and stage IV (IV A and IVB). In stage I, the carcinoma is still confined to the uterus, stage II has involved the vagina but does not involve the lower 1/3 of the vagina, stage III has extension to the pelvic wall and has involved the lower 1/3 of the vagina, and stage IV has extended beyond the reproductive organs. Meanwhile, the preinvasive or in situ cancer stage is referred to as stage 0.16

In this study, it was found that the majority of cervical cancer patients at Dr. Soetomo Hospital for the 2020-2021 period was at stage IIIB (77.27%). This result was in line with many other studies where stage IIIB was the most commonly found type of cervical cancer



Maj Obs Gin, Vol. 31 No. 1 April 2023 p-ISSN: 0854-0381; e-ISSN: 2598-1013

stage. 8,17,18 However, in contrast to the results of Sharma's study, the results showed that most cervical cancer patients were in stage IIB (32.5%), followed by stage IIIB. 6

Table 3. Clinical stage distribution of cervical cancer in geriatric patients in Dr. Soetomo General Academic Hospital, Surabaya in 2020-2021.

Clinical stages	Frequency	Percentage (%)
IA	1	0.57%
IB	2	1.14%
IIA	0	0
IIB	28	15.9
IIIA	2	1.14
IIIB	136	77.27
IVA	2	1.14
IVB	5	2.84

This study showed that the majority of cervical cancer patients at Dr. Soetomo General Academic Hospital was in an advanced stage of IIIB. This is because cervical cancer at an early stage does not yet cause specific clinical symptoms or complaints and in general the patients come for treatment after the symptoms or complaints arose. Symptoms that occur in the early stages are generally vaginal discharge which is often ignored by the the patients, whereas in later stages there is pain in the lower abdomen and vaginal bleeding which disturbs the patients. In addition, the level of knowledge is also a risk for cervical cancer. Research on cervical cancer at Dr. Soetomo General Academic Hospital, Surabaya in 2014 showed that 85% did not receive cervical cancer education. 19 It has been reported that there is a significant relationship between the level of knowledge and the stage of cervical cancer. 20,21 Thus, the low level of knowledge about cervical cancer can be a cause of delay in diagnosis in patients which can then affect the prognosis. In addition, low socioeconomic status can also be a risk factor.21

Table 4. Management distribution of cervical cancer in geriatric patients in Dr. Soetomo General Academic Hospital, Surabaya in 2020-2021

Etiology Classification	Frequency	Percentage (%)
Histerectomy	3	1.7
Chemotherapy	152	86.26
Conization	1	0.57
Palliative	1	0.57
Radiation	13	7.38
Receive no therapy	6	3.41
Total	176	

Majority of treatment received by the patient was chemotherapy which covered 86.25% of the total cases or 152 out of 176 cases, followed by radiation in 13 cases (7.38%), no therapy cases were found as many as 6 cases (3.41%), while histerectomy history was found in 3 medical records (1,7%). Palliative and conization were recorded each in 1 case (0.57%).

The treatment modalities for cervical cancer vary depending on the clinical stage of the patient. Based on the results of this study which showed that the majority of cervical cancer patients were in stage IIIB, the management was in the form of chemoradiation or radiation. In addition, if a patient with stage IIIB is accompanied by CKD, the form of treatment is nephrostomy/hemodialysis if needed, and chemoradiation with a non-cisplatin regimen or radiation.²²

There are various types of cervical cancer therapy options, both surgical and non-surgical. In this study, there were 5 types of therapy received by cervical cancer patients at Dr. Soetomo General Academic Hospital, Surabaya in 2020-2021, ie. hysterectomy, chemotherapy, conization, radiation, and palliative therapy.

Conization, also known as cold knife conization, is a surgical method of treating cervical cancer. Conization uses a scalpel to remove malignant tissue from the cervix and cervical canal of the uterus. In some cases, all cancerous tissue can be removed using this conization method. This procedure is performed under general anaesthesia.²²

Hysterectomy is a surgical procedure to remove the entire uterus. When performed on cervical cancer patients, hysterectomy usually also removes other structures around the uterus. There are several types of hysterectomy, including total hysterectomy, the removal of the uterus and cervix; radical hysterectomy, removal of the uterus, cervix, part of the vagina, and the ligaments and surrounding tissue; and modified radical hysterectomy, removal of the uterus, cervix, upper part of the vagina, ligaments, and other tissues around it.²²

Radiation therapy for cervical cancer patients usually uses high-energy x-ray waves to stop the growth of cancer cells. This therapy damages the DNA of malignant cells to prevent them from spreading to other locations. There are several types of radiation therapy, including external radiation, which is the use of machines outside the body to shoot radiation to areas of the body affected by cancer, and internal radiation, which is the use of facilities such as needles, seeds, wires, or catheters to give radiation right near location of the cancer lesion.²²



Chemotherapy is a pharmacological therapy that aims to stop the growth of cancer cells, either by killing cancer cells directly or stopping their proliferation. Some of the drugs used in cervical cancer chemotherapy are cisplatin, carboplatin, gemcitabine, phosphamide, irinotecan, paclitaxel, topotecan, and vinorelbine. These drugs can also be used as combination therapy.²²

Palliative therapy is a type of therapy that focuses on improving the quality of life of patients and their families. This therapy is a common therapy given to patients with terminal conditions. This therapy does not focus on healing the patient's illness, but focuses on the identification and management of pain, as well as physical, psychosocial and spiritual management aimed at alleviating the burden on patients and their families. The basic concept of palliative therapy is to provide humane dignity to patients in the final phases of their lives.

Although radiotherapy is one of the main therapies used to treat patients with advanced cervical cancer, based on the data, it was found that there were limitations in the use of radiotherapy for the treatment of advanced cervical cancer at Dr. Soetomo Hospital, Surabaya.

Table 5. Parity status distribution of cervical cancer in geriatric patients in Dr. Soetomo General Academic Hospital, Surabaya in 2020-2021.

Parity	Frequency	Percentage (%)
0	4	2.27
1	12	6.82
2	36	20.45
3	52	29.55
4	31	17.61
5	18	10.23
>5	23	13.07

Data on the distribution of parity status shows that majority of the patients with 3 partus history were in 52 cases (29.55%), followed by 2 partus history in 36 cases, and 4 partus history in 31 cases.

Parity is a term used to describe the number of times a woman successfully gives birth at term, whether born alive or not. This term must be distinguished from gravidity, which means the number of pregnancies a woman has gone through, whether the birth was successful or not.²³ Parity and gravidity are usually asked when clinicians perform obstetric history on pregnant women.²⁴ Women who have never had a pregnancy before 20 weeks are called nulliparas or para 0, women with a parity score of 1 are called primiparas, while women with a parity score of more than 1 are called multiparas.²⁵

In this study, 97.7% of cervical cancer patients in Dr. Soetomo General Academic Hospital, Surabaya in 2021-2022 had parity score of 1 or more, which means that most of the research subjects had given birth to term before. This was in line with research by Tekalegn et al (2022) which stated that high parity is related to the incidence of cervical cancer. The study found that women with high parity are twice as likely to experience cervical cancer. ²⁶ A study at Dr. Moewardi Hospital, Surakarta, Indonesia, also found a relationship between parity numbers (especially above 3) and the incidence of cervical cancer. ²⁷

From a number of previous studies, there are several explanations about the relationship between parity and cervical cancer. Parity can be seen as a reflection of a woman's sexual activity. The higher the parity number, the more often a woman gives birth, and this can be seen as an illustration of higher sexual activity. In addition, there are also hormonal influences on the incidence of cervical cancer. Blood concentrations of the hormones progesterone and estrogen are known to increase during pregnancy and reach a peak in the last weeks of pregnancy. Increased level of this hormone is believed to be related to changes in the transformation zone or the boundary between the squamous and columnar epithelium in the cervix. Squamous cell metaplasia is also known to increase in the third trimester of pregnancy.²⁶

Table 6. Clinical manifestations of cervical cancer in geriatric patients in Dr. Soetomo General Academic Hospital, Surabaya in 2020-2021.

Variables	Frequency	Percentage (%)
Bleeding per vaginam		
Yes	145	82.38
No	31	17.62
Discharge		
Yes	81	46.02
No	95	53.98
Pain		
Yes	81	46.02
No	95	53.98

The clinical manifestation of geriatric patients with cervical cancer in Dr. Soetomo General Academic Hospital from 2020-2021 showed that most of the patients came with bleeding per vagina (82.38%). The distribution of patients with and without discharge was almost even, with more patients without discharge (52.98%). Patients with pain and without pain were also almost even (46.02% vs 52.98%) (Table 6).

Patients with cervical cancer are often asymptomatic in the early stages, and only have symptoms when the



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stage has increased. Some of the symptoms that often occur in patients with cervical cancer are vaginal bleeding, especially after sexual intercourse, the presence of discharge from the vagina or vaginal discharge with characteristics of liquid, mucoid, purulent or foul-smelling. In a more severe course of cancer, symptoms can include pain that radiates from the back and pelvis towards the lower extremities. 28

In cervical cancer patients at Dr. Soetomo General Academic Hospital, Surabaya for the 2020-2021 period, the majority of patients (82.38%) experienced complaints of vaginal bleeding. The same results were obtained from a study in Mangalore City, India, which found vaginal bleeding as the most frequent complaint or clinical manifestation in cervical cancer patients. In contrast to the results of research by Kumar in 2020, the results showed vaginal bleeding experienced by patients as much as 28.40% of the total number of cases. Similar findings were also found in a study in Jambi in 2022 majority of the patients' complaints were vaginal bleeding, as much as 58.9%.

Vaginal bleeding is bleeding that occurs outside of normal menstrual periods. The incidence rate of vaginal bleeding in cervical cancer varies from 0.7% to 100%. ³⁰ In addition, vaginal bleeding is also one of the causes of death in cervical cancer, as much as 6%. Vaginal bleeding can occur acutely or chronically. Acute vaginal bleeding is a secondary symptom due to tumor growth which causes angiogenesis, local tumor invasion to systemic effects of the body due to side effects of cancer treatment itself. Treatment for vaginal bleeding can be done through anticoagulants and nonsteroidal anti-inflammatory drugs (NSAIDs). ³⁰

In geriatric cervical cancer patients at Dr. Soetomo General Academic Hospital for the 2020-2021 period, it was found that 46.02% of the patients experienced vaginal discharge. The majority of the medical record data obtained was that there was no vaginal discharge in 95 cases (53.98%). For patients with complaints of vaginal discharge, there were 81 cases (46.02%). The results in the Mangalore city study showed statistics of 33.5% of patients experiencing vaginal discharge. Quite different results were obtained in Naufaldi's study that the vaginal discharge was reraly found as a symptom that was present only in 3.6% of the total cases. ⁹

Leucorrhoea is one of the abnormal symptoms of cervical cancer because cervical cancer usually does not have clinical symptoms that are complained of at an early stage. When several symptoms appear, it indicates that it has already been in a more advanced stage.

Data found that 53.98% of patients without pain complaints in cervical cancer patients at Dr. Soetomo General Academic Hospital, Surabaya for the 2020-2021 period and 46.02% had complaints of pain. In a study in Mangalore City, India, data found that 33% of the total cases experienced pain. Similar results were also found in Naufaldi's study, with a percentage of 37.5% of patients experiencing pain.

According to Schmidt, pain in cancer is caused by the interaction between cancer cells and the surrounding sensory nerves, different from inflammation or neuropathy mechanisms. Chronic pain is found more in female patients who are taking medication. In addition, chronic pain is found in women in the abdomen and pelvis, twelve months after undergoing radiotherapy. 22

Out of all patients recorded in this study, majority of the cases, as many as 138 (78.40%) patients were referred to Surabaya to be treated, followed by 36 patients originated from Surabaya, and 2 (1.14%) patients originated from outside the island of Java.

Dr. Soetomo General Academic Hospital is the main and largest referral hospital in Eastern Indonesia. Dr. Soetomo Hospital has an Integrated Oncology Clinic (POSA) which consists of an oncology outpatient unit and a traditional medicine outpatient unit. The subjects of this study were cervical cancer patients who underwent outpatient care at the Obstetric Oncology Outpatient Clinic at the POSA.

Table 7. Origin distribution of cervical cancer in geriatric patients in Dr. Soetomo General Academic Hospital, Surabaya in 2020-2021.

Origin	Frequency	Percentage (%)
Surabaya	36	20.45
Java outside	138	78.40
Surabaya		
Outside Java	2	1.14
Total	176	

Based on Minister of Health Regulation No. 1 of 2012 concerning Referral System for Individual Health Services Article 3, the health service referral system is the implementation of health services that regulates the delegation of tasks and responsibilities for health services reciprocally both vertically and horizontally.³³ This referral system is mandatory for patients, whether they are participants in health insurance or social health insurance and health service providers or not. Referral patients have been given a previous referral letter that has been approved by the patient and/the patient's family, to the referral hospital so that communication is created between the referrer and the referral recipient.



Maj Obs Gin, Vol. 31 No. 1 April 2023 p-ISSN: 0854-0381; e-ISSN: 2598-1013

This referral is only given if the patient requires specialist health services and the primary health facility appointed to serve the participant is unable to provide health services according to the participant's needs due to limited facilities, services, and/or staff.

Most of the reasons why patients are referred to Dr. Soetomo General Academic Hospital, Surabaya is due to limited facilities at the primary service level. With such limited facilities and infrastructure, a screening or early detection program can be carried out with the VIA test. However, patients will require higher-level diagnostic measures, such as biopsy and anatomical histopathological examination to determine the stage. In addition, cervical cancer patients are generally treated in the form of chemotherapy, radiation, and in some cases surgery is required. Therefore, most cervical cancer patients need to be referred to higher health facilities, such as Dr. Soetomo General Academic Hospital, Surabaya, to obtain the health services needed by patients with adequate facilities.

CONCLUSION

There were 176 cervical cancer patients in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, in 2020-2021 period. The patients were dominated by patients aged 56-65 years. The most common type of histopathological anatomy found in the cervical cancer patients was invasive, non-keratinizing squamous cell carcinoma. The majority of cervical cancer patients at Dr. Soetomo General Academic Hospital was at stage IIIB cancer patient. Chemotherapy was the most widely used type of treatment for cervical cancer patients. Most of the cervical cancer patients at Dr. Soetomo General Academic Hospital were multipara, with the highest number of parities being three parities. The majority of the patients experienced complaints of vaginal bleeding when diagnosed with cervical cancer, but did not experience complaints of pain or vaginal discharge. The cervical cancer patients in the hospital were dominated by patients who came from Java outside Surabaya.

DISCLOSURES

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Conflict of interest

The author declared that there is no conflict of interest.

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Author Contribution

The authors contribution are as followed: ND drafting and revising the manuscript, acquisition of data, analysis of the data. BA: revising the manuscript, study concept or design, interpreting the data responsibility for conduct of research. BU: revising the manuscript, analysis of the data. NK: revising the manuscript, analysis of the data.

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