RESEARCH ARTICLE

INDONESIAN JOURNAL OF CANCER

The Profile of Cervical Cancer Patients at Soedarso Hospital

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ARTICLE INFO

Received : 07 April 2021
Reviewed : 19 July 2021
Accepted : 13 August 2021

Keywords:
cervical cancer, epidemiology, histopathology, patients' haracteristics

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ABSTRACT

Background: The prevalence and mortality rates of cervical cancer differ by region with the highest rates found in Latin America, Southeast Asia, and Africa. In Indonesia, cervical cancer is the second-largest contributor to the latest cases in 2020. In West Kalimantan, over 20,000 women were diagnosed with cervical cancer in 2014. This study aims to describe the characteristics of cervical cancer patients in West Kalimantan.

Methods: A descriptive observational study was conducted on patients from 2017 to 2019 according to the Soedarso Hospital database. All medical records were reviewed and analyzed to obtain the variable data; they were age, ethnics, origin, stage of cervical cancer, histopathology types, and hemoglobin (Hb) level.

Results: Cervical cancer patients for the 2017–2019 period totaled 147 people with 30 deaths. In this study, 97 patients from 2017 to 2019 met the inclusion criteria. Cervical cancer was found from the age of 27 years with a peak at the age of 41–60 years. Most patients came from Pontianak and Kubu Raya cities (45.4% and 14.4%, respectively) with the most ethnic groups being Malays (41.2%). A total of 43.3% of patients had a parity amount of more than five times. Most patients came at stage IIIb (45.4%). The patients present with moderate to severe anemia with the lowest Hb level of around 2.3 g/dL. Based on histopathology, the type of squamous cell carcinoma ranks the highest (70.1%).

Conclusions: Cervical cancer incidence reaches the peak at adults to elderly. The amount of parity seems to contribute to the incidence of cervical cancer in West Kalimantan. Most patients came at an advanced stage and the type of squamous cell carcinoma with moderate to severe anemia.

INTRODUCTION

Cervical cancer is still the leading cause of cancer death in women, ranking ninth in the globe, based on the data from International Agency for Research on Cancer (IARC) in 2020. Meanwhile, in Indonesia, cervical cancer is the second-largest contributor to the latest cases in 2020 after breast cancer and the third leading cause of cancer death after lung and breast cancers [1]. The rates of prevalence and mortality differ by region with the highest rates found in Latin America, Southeast Asia, and Africa [2]. In West Kalimantan, over 20,000 women were diagnosed with cervical cancer in 2014 [3].

The microscopic arrangement of cells in tissue samples from biopsy or surgical specimens was identified as a classification by histopathology which defined the treatment for cancer and precancer [4]. In cervical cancer, the histological characteristic was revealed to be a significant independent prognostic factor. Squamous cell carcinoma (SCC) is the most common histological form of cervical cancer, accounting for three-quarters of all cases. Meanwhile, adenocarcinoma and adenosquamous cell carcinoma account for 10–15% of the total cases with the remaining 10–15% reflecting others or undefined histology [2,5]. Adenocarcinoma is commonly found in western countries, which accounts for up to 25% of cases. This is most likely a result of cytological screening since adenocarcinomas often occur inside the cervical canal [6].

The age of the first sexual intercourse, smoking, immune suppression, oral contraceptive use, high parity (multiple pregnancies), and human papillomavirus (HPV) infection have all been linked to cervical cancer development [6–8]. Research on risk factors and cervical cancer epidemiology in Indonesia, especially in West

Kalimantan, is limited. Therefore, this study aims to describe the characteristics of cervical cancer patients in West Kalimantan.

METHODS

A descriptive observational study was conducted on patients from 2017 to 2019 according to the Soedarso Hospital database. The patients who had a biopsy for cervical cancer SCC or adenocarcinoma or another type of cervix were eligible for inclusion in the study. All medical records were reviewed and analyzed to obtain the variable data; they were age, ethnics, origin, stage of cervical cancer, histopathology types, and Hb level. The medical record that was lack of complementary data needed was excluded. The gynecologist constructed the clinical diagnosis and staging. At the same time, the histopathology type was determined by the pathologist.

RESULTS

The prevalence of cervical cancer at Soedarso Hospital Pontianak for the period of 2017–2019 was obtained through data collection from the Hospital Health Promotion Section taken through the annual Patient Morbidity Data file. Based on the studies that have been conducted, cervical cancer patients for the 2017–2019 period totaled 147 people. The highest incidence of cervical cancer occurred in 2017, and 61 cases were recorded out of 147 patients during that period. The lowest incidence of cervical cancer occurred in 2019, and 41 cases were recorded out of 147 patients. Meanwhile, the number of incidents in 2018 was 45 cases. However, there were only 124 out of 147 patients who have complete information about the outcome.

The incidence of cervical cancer has decreased from 2017 to 2019, but the patient mortality rate has increased. There were 30 deaths recorded during the three years of the study. The highest death rate due to cervical cancer was found in 2019, namely 11 deaths from 38 patients (29%). Meanwhile, the lowest cervical cancer mortality rate occurred in 2017, namely 8 cases out of a total of 45 cervical cancer patients (17.8%). The patient mortality rate in 2018 was 11 cases (26.8%).

In this study, 97 patients from 2017 to 2019 met the inclusion criteria. Cervical cancer was found starting from the age of 27 years with a peak seen at the age of 41-60 years. The mean age was 48.7 years. The oldest age found for cervical cancer was 78 years. Most of the patients visiting Soedarso Hospital came from Pontianak and Kubu Raya cities, with the most ethnic groups being Malays, Dayaks, and Madura.

The number of marriages did not appear to be a significant risk factor for cervical cancer incidence in this study. In contrast, the amount of parity seems to contribute to the incidence of cervical cancer. A total of 43.3% of

Table 1. Characteristics of patients

Characteristics	n	Percentage (%)
Age (years)		
Over 60	13	13.4
51–60	26	26.8
41–50	39	40.2
31–40	14	14.4
21–30	5	5.1
Origin		
Pontianak	44	45.4
Kubu Raya	14	14.4
Mempawah	11	11.3
Bengkayang	1	1.0
Singkawang	2	2.1
Sambas	7	7.2
Landak	5	5.2
Sekadau	3	3.1
Sanggau	4	4.1
Melawi	2	2.1
Kapuas Hulu	2	2.1
Ketapang	2	2.1
Ethnics		
Malays	40	41.2
Dayaks	18	18.6
Chinese	7	7.2
Javanese	10	10.3
Madura	16	16.5
Batak	3	3.1
Sundanese	3	3.1
Number of marriages		
1x	68	70.1
2X	21	21.7
3X	5	5.2
≥4x	3	3.1
Parities		
P0	4	4.1
P1	6	6.2
P2	14	14.4
P3	20	20.6
P4	11	11.3
≥P5	42	43.3
Hb levels (g/dL)		
≥11	19	19.6
9 s/d 10	13	13.4
7 s/d 8	29	29.9
< 7	36	37.1
Histopathology types		
Adenocarcinoma	22	22.7
Squamous Cell Carcinoma	68	70.1
Adenosquamous Carcinoma	7	7.2
Stage		
IB	5	5.2
IIA	5	5.2
IIB	22	22.7
IIIA	10	10.3
IIIB	44	45.4
IV	11	11.3

patients had a parity amount of more than five times. It was noted that two patients had a history of 11 births, five had nine births, five patients had eight births, and 30 had a parity of 5–7 times. Although four patients had never given birth, 50% of them have been married twice.

Most of the patients came at an advanced stage, namely stage IIIB (45.4%), followed by stages IIB and IIIA. This is in line with the Hb levels of patients diagnosed with cervical cancer. Most of the patients present with moderate to severe anemia with the lowest Hb levels around 2.3 g/dL. Based on histopathology, the type of squamous cell carcinoma ranks the highest (70.1%). The dominant subtype was invasive non-keratinizing squamous cell carcinoma large cell type (55.7%). The detailed characteristics of the patients can be seen in **Table 1**.

DISCUSSION

Cancer is a non-communicable disease, which is quite unsettling. In Indonesia, almost 1.8 per-mile population (all ages) suffer from cancer with a peak prevalence at the age of 45–65. Meanwhile, in West Kalimantan, 1.5 per mill of the population has cancer [9]. Cervical cancer was expected to cause 13,240 cases and 4,170 deaths in the United States in 2019. In China, 98,900 new cases of cervical cancer were registered in 2015 with 30,500 deaths. Cervical cancer has reduced in developed countries due to increased screening and higher uptake of HPV vaccination. However, it remains one of the leading causes of cancer morbidity among females in developing countries. Cervical cancer patients with advanced stages have a poor survival rate [7].

In European populations, cervical cancer incidence starts growing at the age of 20–29 years and progressively rises to a peak around the age of 45–49 years. In the United States, the probability of having invasive cervix cancer is also higher in women aged 40 to 59 [2,10]. In India, the peak age for cervical cancer is 40 to 49 years old [11]. In Indonesia, a study conducted in Surabaya from March to August 2016 revealed cancer patients dominated by the age of 41–60, the mode was 51 years, and the mean was 48 [8].

The ectocervix, which is lined by squamous epithelium, and the endocervix, which is lined by simple glandular epithelium, are two main epithelial zones of the normal cervix. The endocervical epithelium is replaced by immature squamous epithelium during puberty and early adulthood, which eventually matures. This is known as the transformation zone, which is the most common site for cervical cancer progression [4]. The zone is located on the ectocervix in 94% of women younger than 25 years old. As the age increases, the proportion decreases to less than 2% after 64 years old. Women with a transformation zone on the ectocervix had a 1.8 times higher age-adjusted probability of finding a histologically confirmed dysplastic lesion than women with a transformation zone in the endocervical canal [8].

Many factors have been related to cervical cancer development, including the age of the first sexual intercourse, smoking, immune suppression, oral contraceptive use, high parity (multiple pregnancies), and HPV infection [6–8]. This study found that more than 40% of patients had given birth more than five times. There were even two patients who have a history of 11 deliveries. Research conducted by Putri et al. [8] in 2016 states that giving birth more than twice has a greater risk of developing cervical cancer than nulliparous, especially the type of SCC. The odds ratio for cervical cancer in women who give birth to 3 to 6 children is 2.6–2.8. Meanwhile, women who have given birth more than seven times have a risk of 3.8 times for cervical cancer.

Chronic cervical infection with approximately 15 carcinogenic HPV forms causes almost all cervical cancers [6,12,13]. Subtype HPV-16 was closely associated with SCC incidence while HPV-18 was more related to cervical adenocarcinoma [6,14]. Several theories explain the relationship between parity and cervical cancer incidence. The first theory is related to an increased likelihood of HPV infection during pregnancy due to hormonal changes. Another theory states that there is a decrease in the immune system during pregnancy so that it is easy to become infected with HPV. Local tissue damage during vaginal delivery is also strongly suspected as a cancer development mechanism related to the amount of parity [8].

In this study, 4 out of 97 patients were nulliparous (never giving birth). 50% of these nulliparas have adenocarcinoma while some are SCC. A Brazilian study mentioned a positive correlation between parity and SCC and a negative correlation between parity and adenocarcinoma. These results suggest that multiparous women are at an increased risk of SCC while nulliparous women are at risk of adenocarcinoma. Owing to the lack of pregnancy and lactation, nulliparous women have a higher number of ovulatory menstrual cycles with higher cumulative estrogen hormone exposure and/or lower cumulative progesterone hormone exposure. Progesterone has a direct effect on cancer cells, inhibiting their development and invasion [15].

The factors that affect the prognosis of patients with cervical cancer are multiple and complex. The histopathological type was a significant prognostic factor [2,16]. One of the conditions related to this is seen in advanced-stage cervical cancer treated by radiation therapy. A study conducted by Hossain et al. [16] showed that disease-free survival was longer in squamous cell carcinoma cases than adenocarcinoma. Small cell carcinoma, multiple subtypes of

P-ISSN: 1978-3744 E-ISSN: 2355-6811

adenocarcinoma-mucinous, clear cell, the typical form of adenocarcinoma, and adenosquamous carcinoma were the histological types to the worst prognosis [2].

This research discovered three types of tissue histopathology, squamous cell carcinoma, adenocarcinoma, and adenosquamous carcinoma. Squamous cell carcinoma is a histopathological form of epithelial cell tumor that is a flat cell that covers the cervix, which is the most common type of malignancy [17]. Rozario et al. [15] in 2019 in Brazil also showed that this type of SCC was more common than other types. The average age at which the cervical cancer type SCC was found was 49.5 years while the adenocarcinoma-type patients had an average age of 48.9. This is in line with a study by Balaya et al. [10] in France, where SCC dominates the histopathological type of cervical cancer (67.5%). The prognosis of cervical cancer, including that with squamous histology, is due to tumor factors such as nodal metastasis, parametrial involvement, tumor intensity, deep stromal invasion, and lymphovascular space invasion (LVSI). The degree of tumor differentiation may be another prognostic factor [18].

International Federation of Gynecology and Obstetrics (FIGO) determines staging in cervical cancer into FIGO stages I to IIA that are considered early stages of cervical cancer and stages IIB to IVB deemed to be advanced stages. In developing countries where advanced imaging modalities are not commonly available, the FIGO staging system is a widely accepted staging approach for cervical cancer. This FIGO stage showed significant effects on the prognosis of patients [16,19].

In this study, about 70% of cervical cancer cases in West Kalimantan were SCC, and most of them came at stage III. This study also has a similar result to the Cipto Mangunkusumo hospital research in 2005–2006 [20]. SCC can be classified into two groups based on the keratin patterns, keratin-high and keratin-low. Though PI3K/AKT signaling is associated with keratin-high tumors, keratin-low tumors are distinguished by a more aggressive tumor with epithelial-mesenchymal transformation. Women with tumors and epithelial-mesenchymal transformation did worse than those with PI3K/AKT abnormalities in terms of survival [18].

Adenocarcinoma is the second-most common histopathological type of cervical epithelial tumor after squamous cell carcinoma, which occurs in the cervical glands; it usually starts in the endo-cervical canal and spreads upwards and laterally. Adenocarcinoma seems to be more aggressive and has a lower survival rate than SCC with a distinct distribution pattern, more distant metastases, and a higher mortality rate. The three types of adenocarcinoma histopathology are divided into three grades, poorly differentiated type of adenocarcinoma (Grade 3), moderately differentiated of adenocarcinoma (Grade 2), and well-differentiated of adenocarcinoma (Grade 1) [17,21]. This study found 4.5% (one case) of poorly differentiated type of adenocarcinoma and 27.3% (6 patients) of moderately differentiated type, and most were included in the well-differentiated type of adenocarcinoma (15 of 22 cases). Research by Glaze et al. [21] also showed that the majority of adenocarcinoma patients were found in low-grade.

Due to the mixture of squamous cell carcinoma and adenocarcinoma types, adenosquamous carcinoma belongs to the epithelial tumor type, also known as a mixed tumor. Endocervical glands and ectocervical epithelial cell proliferation, an enlarged cell nucleus, and crude chromatin are adenosquamous cells carcinoma features. Adenocarcinoma includes the endocervical gland. Meanwhile, squamous cell carcinoma is characterized by the proliferation of ectocervical epithelial cells [17].

Cancer prevalence (per mile) based on Doctor's Diagnosis of All Age Population-based on Riskesdas 2018 shows that the urban population suffers from more cancer than the rural population [9]. This is in line with the research results, which showed that cervical cancer patients at Soedarso Hospital mostly came from the city of Pontianak. However, another study has shown that patients from rural areas are more at risk of developing cervical cancer than those from urban areas. This condition is due to poverty, low socioeconomic status, and the unavailability of health services in rural areas in the early stages of the disease [22,23].

Since invasive cervix cancer is associated with a long pre-invasive stage cervical intraepithelial neoplasia (CIN), it is susceptible to screening and treatment and deemed preventable cancer [11]. In developing countries, cytology screening with and without high-risk HPV DNA testing has significantly reduced the disease burden [13,14]. Women who had sufficient negative screening at the age of 50–64 years (at least three tests were negative, and one test was negative at age of 60–64 years) without high-grade cytology had an 84% lower chance of being diagnosed with cervical cancer at the age of 65 years or older than unscreened women [13].

Patients' understanding of the importance of self-checking is still lacking. The fact that most of the patients were diagnosed at stage III, even though none were observed at stage IA, demonstrates this. Most of the patients in this study came at an advanced stage, namely stage IIIB (45.36%), followed by stages IIB and IIIA. This result is in line with the research conducted in Surabaya from March to August 2016, where stage IIIB was found at most (60%) followed by stage IIB (31%) [8].

Some ethnic groups showed lower cervical screening coverage, which might be contributed by culture, socioeconomic status, language barriers in some ethnic minorities, and emotional barriers, namely fear, embarrassment, and anticipated shame [23–25]. Furthermore, cervical cancer screening access has been

investigated as a major factor in ethnic disparities. Women at high risk for cervical cancer do not have enough access to primary care services or choose not to use them. Cultural differences, such as distrust of the healthcare system, maybe a factor. Lack of awareness about cervical cancer screening was another risk factor. Many women were unaware of the significance of an irregular cervical smear or the importance of cervical cancer early detection. Community-based approaches may benefit these high-risk populations [22,26].

Anemia can be caused by a variety of factors prior to treatment for cervical cancer, including acute or chronic bleeding, malnutrition, and iron deficiency. The level of Hb in patients with cervical cancer is a well-known prognostic marker [27]. Two hypotheses link anemia and poor patient outcomes. First, anemia causes the tumor cells to become hypoxic and makes these cells resistant to radiotherapy. The second hypothesis states that hypoxia stimulates genomic changes in tumor cells and promotes malignant transformation [28]. This study shows that nearly 70% of patients present with moderate to severe anemia. Most of the anemia patients fall into the category of advanced stage. Only 3% came at stage IIA. It is necessary to do further research on the relationship between anemia and this clinical stage.

CONCLUSIONS

The incidence of cervical cancer in Soedarso Hospital has decreased from 2017 to 2019, but the patient mortality rate has increased. Cervical cancer was found starting from the age of 27 years with a peak seen at the age of 41–60 years. Most of the patients came from Pontianak city with the most ethnic groups being Malays. The amount of parity seems to contribute to the incidence of cervical cancer in West Kalimantan. Most of the patients came at an advanced stage and presented with moderate to severe anemia.

DECLARATIONS

Ethics Approval

This research has passed the ethical review stage with letter number 4959 /UN22.9/TA/2020 issued by the Ethical Clearance Committee of the Faculty of Medicine University of Tanjungpura.

Competing of Interest

The authors declare no competing interest in this study.

Acknowledgment

The author would like to thank the Faculty of Medicine, the University of Tanjungpura, who funded this research, and Soedarso Hospital for their cooperation in providing the opportunity for research using patient medical records.

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