

CERVICAL CANCER SCREENING AND ASSOCIATED FACTORS AMONG WOMEN OF REPRODUCTIVE AGE IN LHOKSEUMAWE, ACEH

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ABSTRACT

Keywords:

Pap Smear,
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parity,
menstrual cycle

Cervical cancer is the second most prevalent cause of cancer-related mortality among women worldwide. Indonesia has the second-highest incidence of cervical cancer worldwide. The etiology of cervical cancer in women is multifactorial. This study aimed to investigate the Pap smear screening tests and analyze the risk factors associated with cervical cancer in women of reproductive age in Lhokseumawe, Aceh, Indonesia. This quantitative study used a cross-sectional design. The data source comprised secondary data collected between January and September 2023 at a clinical laboratory in Lhokseumawe, Aceh, Indonesia. The study sample consisted of 100 women who underwent the Pap smear test. The independent variables examined were age, age at first childbirth, age at menarche, parity, menstrual cycle, history of contraceptive use, and history of miscarriage, whereas the dependent variable was the Pap smear test results. Chi-square analysis demonstrated significant correlations between miscarriage history ($p=0.05$), parity ($p=0.001$), menstrual cycle duration ($p=0.049$), and Pap smear cytological results. Logistic regression revealed that women with a previous miscarriage, more than two children, and menstrual cycles exceeding 28 days were 3.46, 1.32, and 2.53 times more likely, respectively, to have abnormal Pap smear results. Therefore, high-risk women should undergo regular cervical cancer screening to detect the precancerous lesions.

ABSTRAK

Kata Kunci:

Pap Smear,
kanker serviks,
wanita,
paritas,
siklus menstruasi

Kanker serviks merupakan penyebab kematian kedua akibat kanker pada wanita di seluruh dunia. Indonesia memiliki jumlah kasus kanker serviks tertinggi kedua di dunia dengan perkiraan 32.469 kasus per tahun. Penyebab timbulnya kanker serviks pada wanita bersifat multifaktorial. Penelitian ini bertujuan untuk menilai prevalensi dan faktor-faktor yang berhubungan dengan deteksi skrining kanker serviks pada wanita usia subur di Lhokseumawe, Aceh. Penelitian kuantitatif ini menggunakan pendekatan cross-sectional. Data penelitian merupakan data sekunder dari Laboratorium klinik bulan Januari-September 2023 di Lhokseumawe, Aceh, Indonesia. Besar sampel penelitian adalah 100 wanita yang telah melakukan pemeriksaan Pap Smear. Variabel bebas yang diteliti adalah usia, usia pertama kali melahirkan, usia menarche, paritas, siklus menstruasi, riwayat alat kontrasepsi dan riwayat keguguran, sedangkan variabel terikatnya adalah hasil pemeriksaan Pap Smear. Hasil uji chi-square menunjukkan terdapat hubungan antara riwayat keguguran, paritas, siklus menstruasi, dan pemeriksaan sitologi Pap Smear. Hasil uji regresi logistik menunjukkan pasien dengan riwayat keguguran (3,46 kali), paritas lebih dari dua (1,32 kali) dan siklus menstruasi lebih dari 28 hari (2,53 kali) lebih tinggi memiliki sitologi abnormal pada tes Pap Smear. Wanita dewasa yang berisiko tinggi harus menjalani skrining kanker serviks secara berkala untuk mendeteksi lesi pra kanker pada serviks.

INTRODUCTION

Reproductive health encompasses more than just the absence of disease. It includes a complete state of physical, psychological, and social well-being in relation to the reproductive

system, and its associated functions and processes. Cervical cancer is the second most common cause of cancer-related mortality among women worldwide and represents a significant reproductive health concern (1).

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Cervical cancer is the second most common cancer among women in Indonesia. The Global Cancer Observatory reported that by 2022, there were 36,633 new cases of cervical cancer (9.3%) out of 396,914 new cancer cases in the country. This cancer caused 234,511 deaths, and the number is expected to rise without preventive measures (2). Data from a hospital in Surabaya revealed 8–10 new cervical cancer admissions daily, with 70% in advanced stages, severely reducing the chance of recovery. East Java Province ranks second in Indonesia for cancer prevalence, following Yogyakarta, with 1.1% (21,313 cases) (3).

Cervical cancer is the second most prevalent malignancy-affecting women, following breast cancer, in Indonesia. Cervical cancer, caused by Human Papilloma Virus (HPV) infection, results in malignant tumors in the cervix. Early stages often show no symptoms until the cancer enlarges and invades nearby tissue. Common symptoms then include abnormal vaginal bleeding (post-sex, post-menopause, between periods, or unusually long/heavy periods) and pelvic pain (4).

Contributing factors include delayed early detection due to inadequate disease awareness. Proper hygiene in the female genital area is especially vital (5). The number of cervical cancer cases is increasing because of several factors. Human Papillomavirus (HPV) infection is the primary cause of infection in 90% of the cases. The remaining 10% are linked to risk factors, such as tobacco use, early sexual activity, multiple partners, prolonged oral contraceptive use, high parity (more than five births), immunocompromised status, and lack of regular screening via visual inspection with acetic acid (VIA) or Pap smear tests (6).

Parity is a significant risk factor for cervical cancer. Physiological stress during childbirth can weaken the immune system and increase the risk of HPV infection. Women with three children are at a higher risk. The correlation between parity and cervical cancer is linked to hormonal changes, especially an increase in progesterone levels during pregnancy, which may stimulate HPV. Additionally, tolerance of the immune system to semi-allogeneic fetal tissue suppresses the immune response, facilitating HPV transmission. Dilation of the postpartum birth canal also increases risk by creating a favorable environment for HPV infection (7).

The epidemiological landscape of cervical cancer in Indonesia is characterized by late-stage diagnoses, with approximately 80% of cases presenting at an advanced stage (8). This is compounded by socioeconomic factors, including limited access to healthcare services and low awareness of the importance of early detection and screening (9,10). The substantial mortality rate associated with cervical cancer in Indonesia is further compounded by insufficient screening initiatives that reach only a limited segment of the female population; nationwide screening coverage is reportedly as low as 12% (11,12). The implementation of comprehensive public health initiatives, encompassing widespread HPV immunization programs and enhanced screening accessibility, is essential to reduce the impact of cervical cancer, both in Indonesia and globally (11,12).

Papanicolaou (Pap) smear is a cost-effective, minimally invasive test for evaluating cervical cells and detecting cervical cancer. The low participation rate of reproductive-aged women in Pap smear screening is due to factors such as a lack of symptoms including vaginal discharge, abnormal bleeding, fear of diagnosis, embarrassment about the procedure, and insufficient awareness of its importance. This limited awareness is partly due to inadequate information dissemination regarding the significance of Pap smear examinations in married women of reproductive age (13,14).

Since 2014, the Indonesian National Health Insurance has provided full coverage for Pap smear screening for married women aged ≥ 30 years. Despite this, a significant majority (81%) of the study participants had never undergone a Pap smear test. Furthermore, 28% of the participants were unaware of cervical cancer and 33% had no knowledge of the Pap smear test (13). There were 85% coverage rate among this demographic group is required to significantly lower cervical cancer morbidity and mortality. Despite the low screening rates, over 3,700 health centers nationwide are trained to offer early detection services (15).

This study aimed to identify the causes of abnormal Pap smear results and to recommend periodic cervical cancer screening for at-risk adult women. Therefore, this study aimed to assess the prevalence and associated factors for the detection of cervical cancer screening among women of reproductive age in Lhokseumawe, Aceh.

METHODS

This quantitative study used a cross-sectional design. Secondary data from January to September 2023 were used in this study. This study was conducted in a clinical laboratory in Lhokseumawe, Aceh. This study was funded by the Universitas Malikussaleh Non-Tax State Revenue Grant or *Penerimaan Negara Bukan Pajak* (PNBP) research grant 2023.

The study sample comprised of 100 women who underwent Pap smear tests. Pap smear results are categorized as normal and abnormal based on histopathological analysis of the presence or absence of precancerous stage lesions, namely cervical intraepithelial neoplasia (CIN). The dependent variable was the Pap smear test, whereas the independent variables were age, age at first childbirth, age at menarche, parity, menstrual cycle, contraceptive history, and miscarriage history.

Women's ages were categorized as 20-45 years and over 45 years. Age at first childbirth was grouped into ≤ 21 and > 21 years. Age at menarche was classified as ≤ 12 or > 12 years. Contraceptive history was divided into "Yes" and "No." Miscarriage history was also divided into "Yes" and "No." Parity and menstrual cycle data were recorded numerically as the number of children and interval between menarches. This study used a ratio scales for the variables of parity and menstrual cycle, because the ratio scale allows proportional comparison. Ratio scales data can be directly calculated and interpreted, allowing for precise comparisons of values.

Bivariate and multivariate analyses were conducted using Statistical Package for

the Social Sciences (SPSS) 16.0 (Chicago, SPSS Inc.). The chi-square test assessed relationships between categorical variables, while the t-test examined numerical data relationships. Multivariate analysis employed multiple logistic regression to identify key independent factors influencing the dependent variable with a 95% confidence level ($\alpha = 5\%$).

RESULTS

In the present study involving data from 100 female participants, 69% had normal Pap smear results, whereas 31% showed abnormalities (Table 1). The majority of the patients (53%) were 20-45 years old. Additionally, 58% had their first childbirth at or before age 21, 85% experienced menarche at or before age 12, 57% used contraceptives, and 79% had no history of miscarriages. The study population showed a mean age of 2.7 ± 1.46 years, with an average menstrual cycle length of 28.02 ± 11.58 days observed among the participants.

Bivariate Analysis

Table 2 outlines the correlations between various sociodemographic and clinical factors and Pap smear test outcomes. Chi-square test analysis indicated significant associations with parity ($p = 0.001$), menstrual cycle ($p = 0.049$), and miscarriage history ($p = 0.05$). However, age ($p = 0.976$), age at first childbirth ($p = 0.654$), age at menarche ($p = 0.263$), and a history of contraceptive use ($p = 0.343$) were not significantly associated.

Table 1. Characteristics of the study participants (n = 100)

Characteristics	Frequency (n)	Percentage (%)
Pap smear test		
Normal	69	69.0
Abnormal	31	31.0
Age		
20-45 years	53	53.0
>45 years	47	47.0
Age of first childbirth		
≤ 21 years	58	58.0
> 21 years	42	42.0
Age at menarche		
≤ 12 years	85	85.0
>12 years	15	15.0

Characteristics	Frequency (n)	Percentage (%)
History of contraceptive		
Yes	57	57.0
No	43	43.0
History of miscarriage.		
Yes	21	21.0
No	79	79.0
Parity; mean (SD)	27 (1.46)	
Menstrual cycle; mean (SD)	28.02 (11.58)	

Table 2. Characteristics Respondents of women had undergone Pap smear test

Variable	Pap smear Result						p value
	Normal		Abnormal		Total		
	n	%	n	%	n	%	
Age							
20-45 years	36	67.9	17	32.1	53	100	0.976
>45 years	33	70.2	14	29.8	47	100	
Age of first childbirth							
≤ 21 years	39	67.2	19	32.8	58	100	0.654
> 21 years	30	71.4	12	28.6	42	100	
Age at menarche							
≤ 12 years	61	71.8	24	28.2	85	100	0.263
>12 years	8	53.3	7	46.7	15	100	
History of contraceptives							
Yes	42	73.7	15	26.3	57	100	0.343
No	27	62.8	16	37.2	43	100	
History of miscarriage							
Yes	18	85.7	3	14.3	79	100	0.05*
No	51	64.6	28	35.4	21	100	
Parity; mean (SD)	2.48 ± 1.18		3.19 ± 1.86		100		0.001*
Menstrual cycle; mean (SD)	27.96 ± 0.46		28.16 ± 0.63		100		0.049*

Analyzed by chi-square test; *p<0.05 was significant

Multivariate Analysis

Multiple logistic regression was used for the multivariate analysis. Variables such as age, age at first childbirth, age at menarche, and a history of contraceptive use were excluded from the final model. The analysis revealed that the significant risk factors for abnormal Pap smear results included parity, menstrual cycle,

and a history of miscarriage (p<0.05). Notably, a history of miscarriage posed the highest risk, increasing the likelihood of abnormal results by 3.466 times. Table 3 presents the logistic regression test results for risk factors associated with Pap smear outcomes in women of reproductive age.

Table 3. Logistic Regression Analysis Risk Factors of Pap Smear Test Results in Women of Reproductive Age

Variables	B	p wald	OR	95% CI	p value	R ²
History of miscarriage	1.243	3.197	3.466	0.88-13.53	0.074	0.107
Parity	0.278	3.247	1.320	0.97-1.78	0.072	
Menstrual cycle	0.932	2.282	2.539	0.75-8.50	0.132	

DISCUSSION

The objective of this study was to determine the factors associated with abnormal Pap smear results in adult women who are considered high-risk for cervical cancer. The majority of patients who underwent a Pap smear were aged between 20 and 45 years (53%). For women aged 25 to 65 years with cervical cancer, the American Cancer Society (ACS) advocates 5-yearly screening using exclusively an HPV test. In circumstances where this preferred method is unavailable, alternative screening approaches may be performed. These include either a combination HPV/Pap test performed every five years or a Pap test conducted every three years (16,17). Advocates recommend early screening for young sexually active women, citing that HPV is the most common sexually transmitted infection, typically contracted within three months of the first sexual intercourse. Thus, these women are at risk of HPV infection and subsequent Cervical Intraepithelial Neoplasia (18).

The present study also revealed that the majority of participants who underwent Pap smear examinations initiated childbearing before 21 years of age. A marriage below 20 years of age is considered premature for engaging in sexual intercourse. Ideally, sexual activity should commence after a woman reaches physiological maturity. Assessment of maturity extends beyond the onset of menstruation. Maturity is also contingent upon the development of mucosal cells present in the epithelial lining of body cavities. Cervical mucosal cells typically achieve full maturation only after a woman has surpassed 20 years of age. Prior to this developmental milestone, these cells remain in an immature state, exhibiting heightened sensitivity to external stimuli, including chemical constituents present in spermatozoa. This increased susceptibility makes the cells more prone to alterations that may lead to neoplastic transformation. Cancerous cells are characterized by their dynamic nature and undergo continuous cell death and regeneration cycles. When subjected to stimulation, the rate of cellular proliferation may exceed that of apoptosis, thereby disrupting the equilibrium of the normal cellular turnover. This imbalance, which results in the accumulation of excess cells, can ultimately lead to the development of malignant neoplasms (19,20).

Bivariate analysis revealed that age, age at first childbirth, and history of contraceptive use were not significantly associated with the Pap smear results. This result is consistent with a previous study that found no association between the use of oral contraceptives (OCs) and the occurrence of cervical dysplasia or cancer (21). The lack of correlation between contraceptive use duration and cervical cancer can be explained by the primary cause of HPV infection, along with other risk factors such as age, high parity, poor feminine hygiene, and inadequate diet, which increase the risk of cervical cancer. The effects of combined oral contraceptives and other contraceptive methods can vary among individuals irrespective of the duration of use. This variability is due to differing hormone levels in each combined oral contraceptive formulation, resulting in diverse physiological responses when administered (22).

Furthermore, individual and social factors, including education and awareness, may have a more pronounced effect on screening behaviors than demographic factors, such as age or contraceptive history. This suggests that although certain demographic factors may influence the likelihood of undergoing screening, they do not necessarily predict the results of the Pap smear itself. The lack of significant associations in our study underscores the need for a multifaceted approach to understand cervical cancer screening outcomes, which should consider a broader range of psychosocial and health system factors beyond demographic characteristics (23,24).

The present study found a statistically significant correlation between miscarriage history and Pap smear outcomes ($p < 0.05$). This supports a U.S. cohort study showing that 58.9% of individuals who underwent Pap smear tests for cancer had a prior miscarriage. The results of our study corroborated the findings of a study conducted in the Obstetrics and Gynecology Division of the Regional General Hospital or *Rumah Sakit Umum Daerah* (RSUD), Dr. Saiful Anwar Malang. This prior study established a statistically significant association between a history of abortion and cervical cancer occurrence (OR = 3.265). From an epidemiological perspective, this risk factor is substantial. Data analysis indicated that women with a history of abortion exhibited a 3.2-fold increased susceptibility to cervical

cancer development compared to those who had never undergone the procedure (25). Abortion can occur either spontaneously or through induction. Induced abortion is associated with an increased risk of cervical cancer due to potential uterine injury during removal of the residual conceptus. However, cervical injuries may also occur, and consequently, a higher frequency of induced abortions may elevate the risk of cervical cancer compared with women without a history of abortion (26).

The present study revealed a significant correlation between parity and the Pap smear results (OR = 1.32). This finding is consistent with a previous study, which indicated an elevated risk of cervical cancer development associated with increased childbirth frequency. High parity has been associated with an increased risk of cervical neoplasia, because multiple pregnancies may lead to repeated trauma and inflammation of the cervix, potentially facilitating the persistence of HPV infection, a known precursor of cervical cancer (27). This finding is consistent with a previous study that noted that various factors, including parity, can influence the cytological outcomes of Pap smears (28). A research conducted in 2020 identified a correlation between high parity (defined as more than three childbirths) and cervical cancer incidence, which is potentially linked to physiological changes during parturition. Notably, women who experience childbirth at a young age face risks comparable to those of women with multiple pregnancies (29,30).

A potential explanation is that the concentrations of estrogen and progesterone in the blood increase during pregnancy and reach peak levels in the final weeks of gestation. These hormonal changes are hypothesized to be responsible for the alterations in the junction between the squamous and columnar epithelia (transformation zone) that occur during pregnancy. The increased risk of cervical cancer among women with high parity is postulated to be associated with a high rate of cervical abnormalities during pregnancy, a high HPV detection rate among pregnant women, and physical changes in cervical cells due to trauma during vaginal delivery (31).

The present study revealed a significant association between menstrual cycle and Pap smear results (OR = 2.539). These findings align with a U.S. study, which also observed that patients diagnosed with irregular

menstruation had considerably higher odds (OR = 1.582) of being diagnosed with cervical cancer (32).

The correlation between menstrual cycle length and Pap smear results is consistent with existing studies, indicating that hormonal changes affect cervical cytology. Longer menstrual cycles are associated with decreased ovarian steroid production, potentially altering cervical cell features and affecting Pap smear findings (33). Studies have indicated that the phase of the menstrual cycle during which Pap smear collection occurs can impact sample quality. Specifically, specimens obtained during menstruation frequently yield unsatisfactory results because the presence of red blood cells interferes with proper analysis (34,35). The timing of the Pap smear during the menstrual cycle may have significantly influenced the interpretation of the results. Hormonal fluctuations throughout the cell cycle can alter the appearance of cells and potentially increase the risk of false-negative results (34).

Menstrual cycle irregularities or extended amenorrhea may contribute to an increased cancer risk in hyperestrogenic conditions. Studies have indicated that women with irregular menstrual patterns exhibit a higher overall incidence of cancer than those with regular menstrual cycles. Protracted and erratic menstrual cycles can result in the accumulation of blood cells within the uterine cavity, forming a reservoir of stagnant blood that can potentially promote the development of cancerous cells. Given these implications, it is imperative to conduct regular medical assessments to address potential health concerns (32,35).

CONCLUSIONS AND SUGGESTIONS

Conclusion

This study demonstrated a statistically significant association between abnormal Pap smear test results and three key factors: parity, menstrual cycle characteristics, and prior miscarriage experiences. Notably, history of miscarriage was the most significant risk factor for abnormal Pap smear outcomes.

Suggestion

This study can disseminate information regarding cervical cancer prevention, risk factors, and early detection methods. High-risk

adult women should undergo regular cervical cancer screening to identify precancerous lesions early in life.

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