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The Relationship Between Risk Factors and Cervical Cancer Stage at the Gynecologic Oncology Polyclinic of RSUDZA

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ABSTRACT

Introduction: Cervical cancer remains a major global health problem, particularly in developing countries such as Indonesia. Most deaths from cervical cancer are caused by delayed diagnosis, resulting in patients being detected at advanced stages. Although many studies examine risk factors for cervical cancer incidence, studies linking these same factors to the stage at diagnosis are limited representing a research gap this study addresses. This study aimed to determine the relationship between five cervical cancer risk factors and cancer stage at diagnosis at the Gynecologic Oncology Polyclinic of RSUDZA Banda Aceh.

Methods: Observational analytic cross-sectional study using secondary data (medical records). A non-probability total sampling technique was applied (N = 54; n = 52 after exclusion). Bivariate analysis used Fisher's Exact and Mann–Whitney tests (95% CI, α = 0.05). Ethical approval was obtained from the Health Research Ethics Committee FK USK RSUDZA (No. 221/EA/FK-RSUDZA/2021, 26 July 2021).

Results: No significant relationship was found between age at marriage (p = 1.000), parity (p = 0.595), education (p = 0.894), income (p = 0.102), or oral contraceptive use (p = 1.000) and cervical cancer stage.

Conclusion: Stage at diagnosis is more strongly determined by access to and uptake of early-detection services and health-seeking behavior than by these demographic or reproductive risk factors. Strengthening community-based screening (VIA, Pap smear) and HPV vaccination is essential to reduce the proportion of patients diagnosed at advanced stages.

Keywords: Cervical Cancer; Cervical Cancer Stage; Risk Factors; Indonesia.
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INTRODUCTION

Cancer is a disease that is highly feared by the community because it often leads to death.[1] According to the World Health Organization (WHO), cancer accounts for approximately 13% of all deaths globally, resulting in 6.2 million fatalities each year.[2] The most common cancers in women worldwide are breast cancer (38 per 100,000 women) and cervical cancer (16 per 100,000 women).[3]

Based on GLOBOCAN 2020, cervical cancer ranks second globally in cancer incidence among women with 604,127 cases out of 9,227,484 total cancer cases. Approximately 200,000 deaths were caused by cervical cancer, and 46,000 occurred in women aged 15–49 years in developing countries.[4] In Indonesia, new cervical cancer cases are estimated at 90–100 per 100,000 population annually, with approximately 40,000 cases per year.[5] Cervical cancer cases at RSUDZA Banda Aceh increased in 2015, 2016, and 2017 with 54, 67, and 80 cases, respectively.

Cervical cancer is influenced by many factors reproductive factors (parity, age at first pregnancy), sexual factors (age at first intercourse, number of partners, sexually transmitted infections), and socioeconomic factors (income, education), as well as smoking and lack of proper screening such as VIA (Visual Inspection with Acetic Acid).[6,7] Cervical cancer causes infertility, morbidity, and mortality in women and represents a serious public-health challenge.

Most published studies on the above risk factors evaluate their association with cervical cancer *incidence*. However, mortality from cervical cancer is overwhelmingly determined by the *stage at diagnosis*, because 5-year survival declines sharply from ~92% at stage I to approximately 16% at stage IV.[8,9] Whether the same risk factors that drive incidence also influence the stage at which disease is detected either by accelerating biological progression or by delaying early detection remains less well studied, particularly in the Indonesian setting.[10] This represents the research gap that the present study addresses. The objective was to examine the relationship between age at marriage, parity, education, income, and oral contraceptive use and the *stage* of cervical cancer at diagnosis in women treated at the Gynecologic Oncology Polyclinic of RSUDZA Banda Aceh.

METHODS

This was an observational analytic cross-sectional study conducted at the Gynecologic Oncology Polyclinic of dr. Zainoel Abidin Regional General Hospital, Banda Aceh (April–September 2021; data collection 6–20 August 2021).

Ethical approval was obtained prior to data collection from the Health Research Ethics Committee (Komite Etik Penelitian Kesehatan), Faculty of Medicine, Universitas Syiah Kuala–RSUD dr. Zainoel Abidin, Ethical Approval No. 221/EA/FK-RSUDZA/2021, dated 26 July 2021. The study used secondary data only and complied with the seven WHO 2011 ethical standards as referred to in CIOMS 2016 guidelines.

The population was all cervical cancer patients aged 35–65 years treated at the polyclinic from January 2019 to December 2020 (N = 54). Because the entire eligible population was used, a total sampling technique was applied a form of non-probability sampling in which all members meeting inclusion/exclusion criteria are enrolled as the sample. Inclusion criterion: complete medical records (cancer stage and all study variables documented). Exclusion criteria: concurrent primary cancer; current pregnancy. Two patients were excluded (incomplete records), yielding a final sample of n = 52.

Secondary data (cancer stage, age at marriage, parity, education, income, oral contraceptive use) were extracted from medical records via a structured worksheet. Cancer stage was categorized as early (FIGO 0–IIA) or advanced (FIGO IIB–IV) following the FIGO classification.[7] Univariate analysis described frequency distributions; bivariate analysis used Fisher's Exact test (2×2 tables) or the Mann–Whitney test (ordinal data) where Chi-square assumptions were not met, at 95% confidence (α = 0.05).

RESULTS

Fifty-two cervical cancer patients met inclusion/exclusion criteria and were included.

Univariate Analysis

Frequency distributions of the dependent variable (cervical cancer stage) and independent variables are presented in Tables 1 and 2.

Table 1 shows that advanced-stage cervical cancer accounted for 55.8% (n = 29) and early-stage for 44.2% (n = 23) of cases consistent with the pattern of late presentation in low-and-middle-income countries.[8,9]

Table 1. Frequency distribution of cervical cancer by stage at RSUD dr. Zainoel Abidin Banda Aceh

Cervical Cancer Stage	Frequency (n)	Percentage (%)
Early stage (FIGO 0–IIA)	23	44.2
Advanced stage (FIGO IIB–IV)	29	55.8
Total	**52**	**100**

Bivariate Analysis

Fisher's Exact test: p = 1.000 (>0.05); PR = 0.76. No significant relationship between age at marriage and cervical cancer stage.

DISCUSSION

More than half of patients (55.8%) were diagnosed at an advanced stage, a pattern consistent with findings from other LMICs where late presentation predominates because of limited screening uptake and delays in health-seeking behavior.[9,10,11] None of the five risk factors examined showed a statistically significant association with cervical cancer stage. The discussion below interprets each finding in relation to disease *stage* considering both biological-progression and delayed-detection pathways.

Age at marriage and cervical cancer stage

Marrying before age 20 exposes the immature cervical epithelium and the actively metaplastic squamocolumnar junction to early HPV contact, theoretically causing longer cumulative carcinogen exposure and potentially more advanced disease at presentation.[12,13] Additionally, women who marry young may have reduced autonomy in seeking healthcare, which could delay diagnosis and result in a later stage at detection.[10,14]

In our sample, however, the proportions of advanced-stage disease were nearly identical (early marriage 50.0%; not early marriage 56.8%), and the PR of 0.76 did not support early marriage as a risk factor for advanced stage. Several explanations are plausible. First, only 8 of 52 patients (15.4%) had a history of early marriage, limiting statistical power. Second, the implementation of Law No. 16 of 2019 raising the minimum marriage age to 19 has reduced early marriage in this region. Third, *stage at diagnosis is more strongly determined by the interval between symptom onset and care-seeking than by the duration of HPV exposure*; women who marry later but never undergo screening can present at equally advanced stages.[8,11]

Table 2. Frequency distribution by risk factor at RSUD dr. Zainoel Abidin Banda Aceh

Risk Factor	n	%
Age at marriage		
Early marriage (<20 years)	8	15.4
Not early marriage (≥20 years)	44	84.6
Parity		
Nulliparous	4	7.7
Primiparous	2	3.8
Multiparous	46	88.5
Education		
No formal education	0	0
Elementary school	5	9.6
Junior high school	12	23.1
Senior high school	29	55.8
College / University	6	11.5
Income		
< UMP	42	80.8
= UMP	4	7.7
> UMP	6	11.5
Oral contraceptive use		
Using	3	5.8
Not using	49	94.2

Prior studies linking early marriage to cervical cancer risk examined incidence rather than stage. A study at Dr. Wahidin Sudirohusodo Hospital, Makassar (2016), found that age ≤20 years at marriage increased cervical cancer risk 4.08-fold (p = 0.021).[15] Aziyah et al. (2017) reported OR = 4.56; p = 0.001,[16] and Ningsih et al. (2016) found OR = 2.41; p = 0.003.[17] The discrepancy with our results reflects the different outcomes evaluated (incidence vs. stage) and the small subgroup size.

Parity and cervical cancer stage

High parity drives cervical carcinogenesis through repeated cervical birth trauma and the HPV-promoting effects of high progesterone during pregnancy.[18,19,20] Translating to stage, multiparous women might present with more advanced disease

through cumulative cervical injury. However, in our study nulliparous patients had the highest proportion of advanced-stage disease (75.0%), compared with multiparous (54.3%) and primiparous patients (50.0%). A plausible stage-specific explanation is that *multiparous women have more frequent contact with maternal healthcare services (antenatal care, family planning), providing opportunistic access to gynecologic examination and earlier detection.*[21] Nulliparous women, outside this care pathway, may present only when symptoms become severe i.e., at a more advanced stage. The very small nulliparous (n = 4) and primiparous (n = 2) subgroups further limit precision.

Existing studies link multiparity to cervical cancer *incidence*: RSUD Abdul Moeloek Lampung 2014 (OR = 2.37),[19] RSUP Dr. M. Hoesin Palembang 2017 (~22.7-fold risk),[18] and RSUP Dr. Kariadi Semarang 2016 (p = 0.000).[16] None of these studies examined stage, supporting our interpretation that parity drives incidence more than stage.

Education level and cervical cancer stage

Lower education is associated with poorer health literacy, lower screening uptake, and unhealthier lifestyles pathways that could delay diagnosis and result in a later stage at detection.[22,14] In our sample, the proportion of advanced-stage disease was highest in patients with elementary-school education (80.0%), consistent with this mechanism. However, the overall test was non-significant (p = 0.894), most likely because of the small sample in the lowest education category (n = 5) and because in the current digital era health information reaches women across all education levels through television, social media, and community promotion.[22]

Our finding is consistent with Ningsih et al. at RSUP Dr. Sardjito (p = 0.991).[17] It contrasts with Swapnajaswanth et al. (OR = 3.9),[23] but that study examined incidence. A systematic review from Kenya found no formal education was independently associated with late-stage diagnosis (cOR = 7.2),[14] reinforcing that the education–stage link is mediated primarily by access to and uptake of screening rather than by formal schooling alone.

Table 3. Relationship between age at marriage and cervical cancer stage

Age at marriage	Advanced stage (FIGO IIB–IV)		Early stage (FIGO 0–IIA)		Total		p-value / PR
	n	%	n	%	n	%	
Early marriage (<20 y)	4	50.0	4	50.0	8	100	p = 1.000 PR = 0.76
Not early marriage (≥20 y)	25	56.8	19	43.2	44	100	

Table 4. Relationship between parity and cervical cancer stage

Parity	Advanced stage (FIGO IIB–IV)		Early stage (FIGO 0–IIA)		Total		p-value / PR
	n	%	n	%	n	%	
Nulliparous	3	75.0	1	25.0	4	100	p = 0.595 (Mann–Whitney)
Primiparous	1	50.0	1	50.0	2	100	
Multiparous	25	54.3	21	45.7	46	100	

Mann–Whitney test: p = 0.595 (>0.05). No significant relationship between parity and cervical cancer stage.

Table 6. Relationship between income and cervical cancer stage

Income	Advanced stage (FIGO IIB–IV)		Early stage (FIGO 0–IIA)		Total		p-value / PR
	n	%	n	%	n	%	
< UMP	26	61.9	16	38.1	42	100	p = 0.102 (Mann–Whitney)
= UMP	0	0.0	4	100.0	4	100	
> UMP	3	50.0	3	50.0	6	100	

Mann–Whitney test: p = 0.102 (>0.05). No significant relationship between income and cervical cancer stage.

Table 7. Relationship between oral contraceptive use and cervical cancer stage

OCP use	Advanced stage (FIGO IIB–IV)		Early stage (FIGO 0–IIA)		Total		p-value / PR
	n	%	n	%	n	%	
Using	2	66.7	1	33.3	3	100	p = 1.000 PR = 1.63
Not using	27	55.1	22	44.9	49	100	

Fisher's Exact test: p = 1.000 (>0.05); PR = 1.63. No significant relationship between oral contraceptive use and cervical cancer stage.

Income and cervical cancer stage

Low income limits access to nutrition, hygiene, and most importantly for stage healthcare services including screening.[25,26] In our sample, 61.9% of patients with income below the UMP were diagnosed at an advanced stage, compared with 50.0% of patients above the UMP. The non-significant result (p = 0.102) is partly attributable to the very small equal-to-UMP subgroup (n = 4, 0% advanced-stage), which distorted the overall pattern. The higher absolute proportion of advanced-stage disease in the <UMP group aligns with the mechanism of financial barriers to timely care.[24]

Mukharomah and Cahyati (RSUD Semarang, 2014) found low income predicted delayed diagnosis (p = 0.001; OR = 6.818).[24] Berraho et al. (Morocco, 2012: p = 0.09)[27] and Gyenwali et al. (Nepal, 2013: p = 0.574)[28] reported non-significant results. In Indonesia, the JKN national health insurance scheme launched in 2014 and covering 82.3% of the population by 2020 has progressively equalized access to cervical cancer diagnostics across income groups, potentially attenuating the income–stage relationship in contemporary data.[29,30]

Oral contraceptive use and cervical cancer stage

Long-term combined oral contraceptive (OCP) use has been linked to cervical carcinogenesis through estrogen-mediated effects on cervical epithelium and facilitation of HPV DNA transcription WHO reported a 1.19-fold relative-risk increase and IARC reported a fourfold increase among HPV-positive women using OCPs >5 years.[31,32] In our sample, OCP users had a higher proportion of advanced-stage disease (66.7% vs. 55.1%; PR = 1.63), consistent with a biological-progression effect. However, the result was non-significant (p = 1.000), almost certainly because of the very small OCP-user subgroup (n = 3). OCPs are not expected to delay *detection* women on OCPs typically have regular clinical contact so the higher proportion of advanced disease in users may reflect a true biological progression effect that this underpowered study could not confirm.[8,11] Studies at RSUD Abdul Moeloek Lampung (Jasa, 2015: p = 0.019)[33] and RSUP Dr. M. Hoesin Palembang (Trifitriana et al., 2017: p = 0.0005)[18] reported significant associations with cervical cancer incidence not stage consistent with the pattern observed across all variables in this study.

Limitations

The main limitations are: (1) small sample size (n = 52) and very small subgroups for some variables (OCP users n = 3; nulliparous n = 4; early-married n = 8), limiting statistical power; (2) cross-sectional design and secondary medical-record data, precluding assessment of confounders such as HPV status, smoking, age at first intercourse, number of sexual partners, screening history, and time from symptom onset to diagnosis; and (3) possible misclassification in variables recorded in the medical records rather than collected specifically for research.

CONCLUSION

In this cross-sectional study of 52 cervical cancer patients at the Gynecologic Oncology Polyclinic of RSUDZA Banda Aceh (2019–2020), more than half were diagnosed at an advanced stage. None of the five risk factors examined—age at marriage, parity, education, income, or oral contraceptive use—was significantly associated with cervical cancer stage at diagnosis. These findings suggest that the stage at diagnosis is more strongly determined by access to and uptake of early-detection services than by these demographic or reproductive risk factors, highlighting the importance of strengthening cervical cancer screening programs in this setting.[8,9,10]

SUGGESTIONS

Because none of the studied variables was significantly associated with cervical cancer stage, recommendations should focus on reducing cervical cancer *incidence* and improving early detection. Healthcare providers are encouraged to: (1) strengthen and expand routine cervical cancer screening (VIA and Pap smear) among women of reproductive age, including those without classical risk factors;[34,29] (2) scale up HPV vaccination programs for adolescent girls; (3) intensify community-based health education to shorten symptom-to-diagnosis intervals; and (4) support implementation of Indonesian Law No. 16 of 2019 on minimum marriage age. Future research should use larger multi-centre samples and include HPV status, screening history, and time-to-diagnosis to better characterise determinants of cervical cancer stage.

DISCLOSURES

FUNDING

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

All authors contributed to the conception, design, data collection, analysis, and writing of the manuscript, and have approved this final version for submission.

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