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Exploring Risk Factors for Cervical Cancer that lead to Biopsy Examination in the United States: A Logistic Regression Analysis

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Abstract:

Introduction:

Cervical cancer remains a significant global health concern with a substantial impact on women's lives, particularly in less-developed countries where resources are already limited. The disease is primarily caused by high-risk subtypes of human papillomavirus (HPV) but is largely preventable.

Objective:

The primary objective of this study was to examine the factors that contribute to the development of cervical cancer and explore whether these factors are linked to the choice of cervical biopsy.

Methods:

The dataset from the UCI Repository was analyzed. Bivariate analysis was conducted to identify risk factors significantly associated with the occurrence of biopsy. Multiple logistic regression modeling was used to identify key predictors of biopsy likelihood.

Results:

Bivariate analysis showed several risk factors that were significantly associated with biopsy occurrence, including the duration of hormonal contraceptive use, a history of sexually transmitted diseases (STDs), specific STD types, cervical screening methods, and the number of STDs among patients. Further analysis using multiple logistic regression modeling identified two key predictors: prolonged hormonal contraceptive use (for 5 to 9 years) and the use of the Schiller cervical screening method.

Conclusion:

The findings of this study indicate the importance of targeted screening and prevention strategies in cervical cancer management, which could play a crucial role in reducing the disease burden.

Keywords:

Cervical cancer, Risk factors, Logistic regression, HPV, Biopsy

Introduction:

Each year, more than half a million women are diagnosed with cervical cancer, resulting in over 300,000 deaths worldwide. Most cases occur in less-developed countries, where no effective screening systems are available (1). High-risk subtypes of the human papilloma virus (HPV) are the cause of the disease in most cases, accounting for approximately 99.7% of cases; however, the disease is largely preventable through effective vaccines and screening (2).The known risk factors for developing cervical cancer are HPV, low socioeconomic status, smoking, marrying before the age of 18 years, young age at first coitus, multiple sexual partners, multiple sexual partners of spouse, and multiple childbirths. Other suspected risk factors for cervical cancer include oral contraceptive usage and certain nutritional deficiencies; however, it is not clear whether these factors operate independently of HPV (3-4). A range of sexually transmitted organisms commonly coexist with abnormal growth of cells in the cervix. Although cervical cancer is considered an AIDS-defining cancer, the influence of HIV on the risk of cervical cancer and cancer appears to be marginal. In addition, infection with other STD agents, such as Chlamydia trachomatis, further complicates the picture. Therefore, the impact of various potential risk factors, which may have changed over recent times (such as HPV exposure, sexual behavior, and cigarette smoking), on disease rates remains uncertain (5-7).The primary objective of this study was to examine the factors that contribute to the development of cervical cancer and explore whether these factors are linked to the choice of cervical biopsy.

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Methodology Data Source:

The data source was an online dataset shared by Kaggle (8). This dataset was originally gathered from the UCI Repository and contains a comprehensive list of the risk factors associated with cervical cancer. It includes a range

of variables such as age, number of sexual partners, age at first sexual intercourse, number of pregnancies, smoking habits, duration of smoking (years), intensity of smoking (packs/year), usage of hormonal contraceptives, duration of hormonal contraceptive usage (years), usage of intrauterine devices (IUD), duration of IUD usage (years), history of various STDs, number of different types of STDs, and specific STDs including Condylomatosis, Vaginal Condylomatosis, Vulvo-Perineal Condylomatosis, Syphilis, Pelvic Inflammatory Disease, Genital Herpes, Molluscum Contagiosum, HIV, Hepatitis B, and HPV. The dataset also includes the count of STD diagnoses, outcomes from medical tests like Hinselmann, Schiller, and Cytology, as well as the necessity for cervical biopsy examinations, commonly referred to as "Biopsy."

Data Pre-processing:

During the data pre-processing phase, several essential tasks were performed to enhance the quality and usefulness of the raw dataset for analysis. Variable names were made consistent to ensure clarity, variable types were modified to match analytical requirements, and categorical variables were introduced to simplify the complex data structures. The dataset also underwent a thorough cleaning process in which inappropriate, missing, or unnecessary data points were eliminated to reduce noise and focus on relevant information. As a result, the total number of observations decreased from 858 to 668.

Statistical Analysis:

Data analysis was conducted using R Studio version R-4.2.1. To understand the dataset, descriptive analysis was performed, followed by the chi-squared test for independence to assess how cervical cancer risk factors influenced biopsy or cytology examinations. Statistical significance was set at $P < 0.05$. Multiple logistic regression analysis was conducted to identify the associations between risk factors and examination outcomes.

Results:

Descriptive statistics Table 1 provides an overview of the key characteristics of the participants. On average, participants were approximately 27.26 (±8.73) years old. They reported an average of 2.52 sexual partners (±1.64), and had their first sexual experience at around 17.14 years old (±2.85). The average number of pregnancies was 2.32 (±1.46). Smoking was reported by 14.4% of participants, with an average smoking duration of 1.23 years (±4.19) among smokers. Approximately 64.4% of participants reported using hormonal contraceptives, averaging 2.30 (±3.72) contraceptives per year among users, and 11% of participants reported using an IUD, with an average rate of 0.52 (±2.0). Approximately 9.7% of the participants were diagnosed with one or more STDs, 4.5% underwent Hinselmann, 9.4% underwent Schiller and Cytology, and 6.7% underwent a biopsy for cervical cancer.

Table 1. General characteristics of study participants

Variable	Description
Age in years (M±SD)	27.26±8.73
Number of sexual partners (M±SD)	2.52±1.64
First sexual intercourse (M±SD)	17.14±2.85
Number of pregnancies (M±SD)	2.32±1.46
Smoking (N, %):	
Yes	96 (14.4%)
No	572 (85.6%)
Smoking years (M±SD)	1.23±4.19
Hormonal contraceptives (N, %):	
Yes	430 (64.4%)
No	238 (35.6%)
Number of hormonal contraceptives per year (M±SD)	2.30±3.72
IUD (N, %):	
Yes	75 (11.2%)
No	593 (88.8%)
IUD per year (M±SD)	0.52±2
STDs (N, %):	
Yes	65 (9.7%)
No	603 (90.3%)
Hinselmann (N, %):	
Yes	30 (4.5%)
No	638 (95.5%)
Schiller (N, %):	
Yes	63 (9.4%)
No	605 (90.6%)
Cytology (N, %):	
Yes	63 (9.4%)
No	605 (90.6%)
Biopsy (N, %):	
Yes	45 (6.7%)
No	623 (93.3%)

Results of bivariate analysis:

Table 2 shows the distribution of various factors, among which the duration of hormonal contraception use among users (in years), a history of STDs, specific STD types such as condylomatosis and vulvo-perineal condylomatosis, and the status of various cervical screening methods (Hinselmann, Schiller, Cytology) were significantly correlated with undergoing a biopsy for cervical cancer at a significance level of 1% ($p < 0.01$),

whereas the number of STDs among patients was significant at the 5% level ($p < 0.05$). The findings indicated a significant relationship between the duration of hormonal contraception use among users (in years) and the likelihood of undergoing a biopsy ($p < 0.001$). Women who used hormonal contraception for more than 10 years had the highest percentage (22.22 %) of undergoing biopsy, while women who used hormonal contraception for 5 to 9 years had the lowest rate (3.00%) of undergoing biopsy. A significant association was observed between history of STDs and women undergoing biopsy ($p < 0.01$). Women with a prior history of STDs had a higher likelihood of undergoing biopsy (15.38%), in contrast to women without a history of STDs (5.80%). Specific types of STDS, such as condylomatosis and vulvo-perineal condylomatosis, were also significantly associated with the occurrence of biopsies ($p < 0.01$). Of the women who underwent biopsies, 18.92% had a history of STD-condylomatosis, whereas 6.02% did not. Similarly, 19.44% of patients had STD-vulvo-perineal condylomatosis, whereas 6.01% did not. The use of different cervical screening methods (Hinselmann, Schiller, and Cytology) was another significant factor associated with the likelihood of undergoing biopsies ($p < 0.001$). Among women who underwent biopsies, 66.66% had also undergone Hinselmann screening and 63.49% had undergone the Schiller and Cytology screening methods. The number of STDs among the patients was found to be statistically significant at the 5% level ($p < 0.05$). Among women, those with up to two STDs had the highest biopsy rate at 19.35%, whereas women with either one or three STDs had rates of 11.11% and 16.67%, respectively. In contrast, women without STDs had a lower biopsy rate (5.80 %).

Table 2. Distribution of risk factors for cervical cancer that lead to Biopsy examination

Variables	Levels	N	%	Biopsy (%) No	Biopsy (%) Yes	D.F	Chi-square	*p*-value
Age	<18	61	9.1	98.36	1.64	5	10.754	.056
	18-24	233	34.9	92.70	7.29			
	25-29	139	20.8	92.80	7.19			
	30-44	214	32	93.92	6.07			
	45-64	17	2.5	76.47	23.53			
	65+	4	0.6	100.0	0.00			
No. of Sexual Partners	1	163	24.4	93.25	6.75	2	0.283	.867
	2-3	390	58.4	93.59	6.41			
	4+	115	17.2	92.17	7.82			
First Sexual Intercourse	<16	213	31.9	95.30	4.69	2	5.679	.058
	16-19	363	54.3	91.18	8.81			
	20+	92	13.8	96.73	3.26			
No. of Pregnancies	0-1	228	34.1	94.74	5.26	2	3.755	.153
	2-3	317	47.4	93.69	6.31			
	4+	123	18.4	89.43	10.57			
Smoking	No	572	85.6	93.53	6.47	1	0.206	.649
	Yes	96	14.4	91.66	8.33			
Smoking (Years)	<5	607	90.8	93.41	6.59	2	1.593	.451
	5-9	26	3.9	96.15	3.84			
	10+	35	5.2	88.57	11.43			
Hormonal Contraception	No	238	35.6	93.69	6.30	1	0.029	.863
	Yes	430	64.3	93.03	6.97			
Hormonal Contraception (Years)	<5	532	79.6	93.61	6.39	2	16.064	< .001
	5-9	100	14.9	97.00	3.00			
	10+	36	5.4	77.77	22.22			
IUD	No	593	88.7	93.91	6.07	1	2.841	.091
	Yes	75	11.2	88.00	12.00			
IUD (Years)	<5	635	95.0	93.39	6.61	2	0.502	.778
	5-9	25	3.7	92.00	8.00			
	10+	8	1.1	87.50	12.50			
STDs	No	603	90.3	94.19	5.80	1	7.114	.007
	Yes	65	9.7	84.61	15.38			
No. of STDs	0	603	90.3	94.19	5.80	4	10.527	.032
	1	27	4.0	88.89	11.11			
	2	31	4.6	80.64	19.35			
	3	6	0.9	83.33	16.67			
	4	1	0.1	100.0	0.00			
Types of STDs	Condylomatosis					1	7.314	.006

	No Yes	631 37	94.4 5.5	93.97 81.08	6.02 18.92			
	Vaginal Condylomatosis No Yes	664 4	99.4 0.6	93.22 100.0	6.77 0.00	1	0.00	1.00
	Vulvo-Perineal Condylom No Yes	632 36	94.6 5.4	93.98 80.55	6.01 19.44	1	7.759	.005
	Syphilis No Yes	653 15	97.7 2.2	93.11 100.0	6.89 0.00	1	0.283	.595
	PID No Yes	667 1	99.8 0.1	93.25 100.0	6.75 0.00	1	0.00	1.00
	Genital Herpes No Yes	667 1	99.8 0.1	93.40 100.0	6.59 0.00	1	2.983	.084
	Molluscum Contagiosum No Yes	667 1	99.8 0.1	93.25 100.0	6.75 0.00	1	0.00	1.00
	HIV No Yes	655 13	98.05 1.95	93.59 76.92	6.41 23.08	1	3.294	.069
	Hepatitis B No Yes	667 1	99.8 0.1	93.25 100.0	6.75 0.00	1	0.00	1.00
	HPV No Yes	666 2	99.7 0.3	93.24 100.0	6.76 0.00	1	0.00	1.00
Cervical Screening	Hinselmann No Yes	638 30	95.5 4.5	96.08 33.33	3.92 66.66	1	169.72	< .001
	Schiller No Yes	605 63	90.6 9.4	99.17 36.51	0.82 63.49	1	346.74	< .001
	Citology No Yes	605 63	90.6 9.4	99.17 36.51	0.82 63.49	1	346.74	< .001

Results of logistic regression analysis:

Multiple logistic regression model was applied using the categorical predictor variables which were found to be significant in the bivariate analysis, using backward elimination method. The findings, presented in Table 3, indicate that only two of these predictor variables showed statistically significant associations with the likelihood of undergoing a biopsy for cervical cancer, i.e., the duration of hormonal contraception use (for 5 to 9 years) and the utilization of Schiller method of cervical screening.

Table 3. Logistic regression results of Biopsy examination

	B	**S.E.**	**z-value**	**Sig.**	**Exp(B)**	**95 % CI for Exp(B)**	
						Lower	**Upper**
Hormonal contraception (ref.cat=10+) **<5** **5-9**	-1.146 -2.109	0.746 1.009	-1.535 -2.092	0.125 0.036	0.318 0.121	0.072 0.015	1.339 0.816
STDs (ref.cat=No) **Yes**	0.879	0.628	1.399	0.162	2.407	0.707	8.416
Hinselmann (ref.cat=No) **Yes**	0.567	0.555	1.021	0.307	1.762	0.601	5.378
Schiller (ref.cat=No) **Yes**	5.027	0.579	8.680	< .001	152.54	52.527	525.43

Ref.cat= reference category

Interpretation of logistic regression coefficients:
The outcomes, as presented in Table 3, show that the likelihood of undergoing a biopsy was significantly associated with the duration of hormonal contraception use. Women using hormonal contraception for less than 5 years had odds of experiencing a biopsy that were not significantly different from those using it for over 10 years. However, the odds of experiencing a biopsy for those with 5 to 9 years of hormonal contraception use were 0.121 times higher than for those using it for more than 10 years.
According to the model, the log of the odds of a woman to experience biopsy was positively related to the use of Schiller cervical screening method ($p < 0.001$), showing that the women who underwent Schiller method of cervical screening were more likely to experience biopsy for cervical cancer than those who did not.
Experiencing biopsy was not significantly associated with the presence of STDs and utilization of Hinselmann method of cervical screening. However, women with STDs were 2.407 times more likely to undergo biopsies compared to those without STDs. Similarly, women who used the Hinselmann cervical screening method were more likely to experience biopsies than those who did not.

Evaluating model fit:
To ensure suitability and effectiveness of the applied logistic model, two categories of techniques were used: predictive power and goodness-of-fit. Regarding predictive assessment, three specific measures were utilized—McFadden's R-squared, the area under the ROC curve, and accuracy and confusion matrix. To assess the goodness-of-fit of the model, Hosmer-Lemeshow statistic was used. The results are summarized in Table 4.
The c-statistic, or AUC, scored 0.943 which shows a very high level of accuracy and discrimination for the model. The ROC curve displaying model accuracy can be seen in Figure 1.
The McFadden's R-squared value was found to be 0.594 with 6 degrees of freedom, suggesting that the model is moderately effective at capturing and explaining the observed patterns in the data, and approximately 60% of the variation in the data can be explained by the model.
The Hosmer and Lemeshow goodness-of-fit test yielded non-significant results ($\chi^2 = 0.10459$, df = 1, p-value = 0.746). Thus, we do not have evidence to reject the null hypothesis that the model fitted the data well.
The model's accuracy, determined from the confusion matrix, was 95.81%, meaning it accurately predicted outcomes for almost 96% of cases with few misclassifications.

Table 4. Logistic Model Evaluation: Predictive Power and Goodness-of-Fit Measures

Test	Result
ROC Curve	AUC: 0.9435
McFadden's R-squared	0.5947 (df=6)
Hosmer-Lemeshow	$\chi^2 = 0.1046$, p-value = 0.746
Accuracy	95.81%
Confusion Matrix	
True Positive	37
True Negatives	603
False Positives	20
False Negative	8

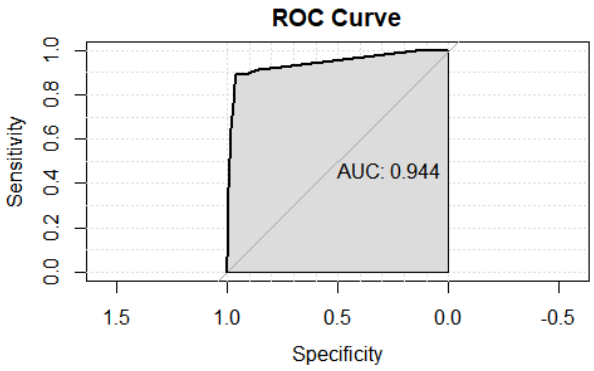

Figure 1. ROC Curve Displaying Model Accuracy in Predicting Biopsy Risk

Discussion:
This study analyzed factors influencing the likelihood of women in the U.S. undergoing a cervical cancer biopsy. Prolonged use of hormonal contraception was found to be a significant factor, consistent with other studies (9-12) linking long-term use to increased cervical cancer risk. Specifically, using hormonal contraceptives for over five years is associated with up to a 4.2 times higher risk (13-14).
Hormonal factors such as pregnancy, oral contraceptive use, and menopausal hormone therapy may impact the risk of cervical cancer and precancerous lesions by altering the immune response to HPV and influencing the progression from HPV infection to cervical intraepithelial neoplasia and cervical cancer (15-16).
A history of STDs emerged as another significant risk factor for undergoing a cervical biopsy during the bivariate analysis. Studies show STDs increase cervical cancer risk by disrupting host cell DNA and accelerating cancer development (17-18). HPV infection, key in early cervical cancer development, disrupts DNA repair and apoptosis. Genomic alterations linked to mutational

signatures, DNA repair deficiencies, and chromatin remodeling have also been observed (19-20).
The status of various cervical screening methods, particularly the Schiller method, was strongly associated with an increased risk of undergoing a biopsy during logistic modeling. This underscores the importance of further research and evaluation in clinical settings to identify the most effective and patient-friendly screening protocols for cervical cancer detection. Interestingly, one study found the Schiller test to be more sensitive than the Pap smear in detecting cervical dysplasia, suggesting its potential value in screening strategies (21).

Bivariate analysis also identified the number of STDs in patients as a key factor for undergoing biopsy, aligning with previous studies that demonstrate a strong correlation between STD prevalence and cervical cancer (22). Among specific infections, Chlamydia has been found to have a significant association with the development of cervical cancer (23). Meanwhile, the prevalence of Trichomoniasis in cervical cancer patients varies widely, ranging from 0.022% to 87.7%, and the relationship between the two remains inconsistent (24). Overall, patients with STDs are reported to be 2.5 times more likely to test positive for suspected cervical cancer compared to those without STDs (25).

Conclusion:

The aim of this study was to investigate the factors related to cervical cancer biopsy in the United States. Among 668 women, 45 had undergone biopsies, and chi-square test found significant associations between biopsy occurrence and several variables, including the duration of hormonal contraceptive use, a history and type of STDs, and the use of specific cervical screening methods like Schiller. Logistic regression analysis further identified prolonged hormonal contraceptive use (5–9 years) and the Schiller method as the most significant predictors of biopsy occurrence. These findings highlight the importance of tailored cervical cancer prevention strategies, including regular screenings and education on the risks associated with prolonged hormonal contraception use and STDs. Also, screening protocols should be updated to include these risk factors and a risk-based approach should be adopted to enhance clinical and public health practices, reducing the burden of cervical cancer.

Recommendations:

We recommend that targeted cervical cancer screening should prioritize high-risk groups, such as women with prolonged hormonal contraceptive use (5–9 years) or a history of STDs, using the Schiller method for improved detection accuracy. Longitudinal studies are needed to explore the role of hormones and immunity in cervical cancer progression, informing better prevention and treatment.

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Author's Contribution:
Muqadas Bhatti: Conception and Design of work, drafting and critical evaluation for intellectual context.