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Pap smear versus histopathology: A comparative study in identifying cervical cancer

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Abstract

Background/Objective: Cervical cancer remains a major public health problem, particularly in developing countries. The aim of this study was to compare the diagnostic accuracy of traditional Pap smears with histopathology in detecting cervical cancer in a population of Iraqi women.

Methods: This cross-sectional study included 75 women who underwent both a Pap smear and a biopsy in 2024. Pap smear results were classified according to the Bethesda 2001 system and histopathological findings were used as the gold standard. To assess the diagnostic accuracy of both methods, sensitivity, specificity, positive predictive value and negative predictive value were calculated.

Results: Pap smear showed moderate sensitivity (79.2%) and specificity (86.4%) compared to histopathology. False negative and false positive results were observed. Histopathology demonstrated superior accuracy with higher sensitivity (98.0%) and specificity (99.0%). Co-testing with both methods achieved a combined sensitivity and specificity of 99.6% and 85.5%, respectively, improving overall diagnostic accuracy.

Conclusions: This study highlighted the continued relevance of the Pap smear as an accessible tool for cervical cancer screening while emphasizing the superior diagnostic accuracy of histopathology. Efforts to optimize screening programs should prioritize reducing false negatives to improve early detection and outcomes. Integrating HPV DNA testing with Pap smears could improve screening accuracy.

Keywords: Cervical Cancer; Diagnostic Accuracy; Histopathology; Pap Smear; Screening

1. Introduction

Cervical cancer is the fourth most common cancer in women worldwide, with approximately 660,000 new cases and 350,000 deaths in 2022. The burden is disproportionately high in low- and middle-income countries (LMICs), where 94% of cervical cancer deaths occur. This highlights inequalities in access to HPV vaccinations, cervical cancer screenings and treatment services, which are compounded by social and economic determinants such as poverty and gender bias. Persistent infection with human papillomavirus (HPV), a sexually transmitted infection, is the leading cause of cervical cancer. Women with HIV are at six times increased risk compared to the general population and represent an estimated 5% of cervical cancer cases. The highest incidence and mortality rates are observed in sub-Saharan Africa, Central America and Southeast Asia, regions characterized by health care disparities and prevalent risk factors. Despite these challenges, cervical cancer is preventable and curable if detected early and treated promptly. Prophylactic HPV vaccination and screening for precancerous lesions have been shown to be cost-effective strategies that significantly reduce incidence and mortality. Recognizing this potential, countries around the world have committed to the World

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Health Organization (WHO) strategy to eliminate cervical cancer by achieving vaccination, screening and treatment targets by 2030, and emphasize the need to address health care disparities, particularly in LMICs, address to ensure equitable outcomes [1–3].

Cervical cancer develops in the cervix, the lower part of the uterus that connects to the vagina and occurs when persistent HPV infections cause cellular changes. Although the immune system often clears HPV, persistent infections can lead to DNA changes, uncontrolled cell growth, and tumor formation. Common symptoms include abnormal vaginal bleeding, pelvic pain, and unusual discharge. Risk factors include smoking, early sexual activity, multiple sexual partners, other sexually transmitted infections, and immune system suppression. Screening tests such as Pap smears and HPV DNA tests, along with HPV vaccination, are critical for prevention. Treatments vary depending on the stage of cancer and may include surgery, radiation, chemotherapy, targeted therapy, or immunotherapy. Early detection and preventive measures, including safe sexual practices and smoking cessation, significantly reduce the incidence and mortality of cervical cancer [4-9].

The American Cancer Society (ACS) updated its cervical cancer screening guidelines in 2020, introducing important changes to improve the accuracy of screening and reduce unnecessary procedures. The revised guidelines recommend started screening at age 25 instead of 21, reflecting the impact of HPV vaccination in reducing infections in younger populations. They also prioritize HPV testing every five years as the preferred method because of its higher sensitivity and reliability compared to Pap testing or HPV/Pap co-testing. Despite the Pap test's success in reducing cervical cancer rates, HPV testing is more efficient at identifying high-risk cases while minimizing overtreatment. Screening remains essential for vaccinated people as current recommendations aim to balance the benefits and risks of testing and avoid false positives and unnecessary procedures. These updates underscore the momentum of cervical cancer prevention, driven by advances in HPV vaccination, testing technologies, and evidence from large-scale trials [10].

Cervical cancer continues to represent a significant global health burden, particularly in developing countries such as India, where its advanced premalignant stage, cervical intraepithelial neoplasia (CIN), can be effectively detected by cervical cytology. The one from Dr. Conventional Pap smear introduced by George Papanicolaou has historically reduced the incidence of cervical cancer in developed countries, but has limitations such as unsatisfactory samples, false negative results and low sensitivity. To address these drawbacks, liquid-based cytology (LBC) was introduced in 1996, leading to numerous studies comparing its effectiveness to traditional Pap smears. While many studies favor LBC due to its improved sample quality and diagnostic accuracy, others advocate for traditional Pap smears in resource-poor areas such as India due to their cost-effectiveness [11].

Persistent high-risk human papillomavirus (HPV) infection is the leading cause of cervical lesions and represents a significant health problem, particularly in developing countries. In this study, cervical swabs from 50 symptomatic Iraqi women and 30 healthy controls were analyzed to identify oncogenes using endpoint multiplex PCR Identify HPV genotypes. Cytologic findings included ASCUS (30%), LSIL (24%), HSIL (20%), and other lesions, with high-risk HPV DNA detected in 19% of symptomatic cases. The most common genotypes were HPV-16, -18 and -58. The association of high-risk HPV with early lesions highlights its potential role as a prognostic factor for cervical cancer progression[12]. The main objective of this study is to compare the sensitivity and specificity of traditional Pap smears with the standard histopathological test for detecting cervical cancer.

2. Methodology

In this cross-sectional study, a total of 75 out of 150 women were selected based on inclusion and exclusion criteria and admitted to a local hospital in the city of Duhok in the Kurdistan Region of Iraq in 2024. All patients underwent a Pap smear and biopsy by the same gynecological team. All Pap smear examinations were performed according to standard protocol and samples were sent to the same laboratory for analysis and reporting. The inclusion criteria include female patients aged 21–65 years who underwent a Pap smear followed by confirmatory biopsy, as well as patients with complete medical records, including Pap smear results, histopathology reports, and clinical results. Exclusion criteria include patients without appropriate biopsy/histopathology results, patients with incomplete records or inadequate Pap smear samples, and patients with a previous diagnosis of cervical cancer.

Data are extracted from patients' medical records, focusing on Pap smear results classified using the Bethesda 2001, [13] system, histopathological findings from biopsy specimens, final clinical diagnosis including follow-up procedures, and demographic and clinical data such as Age, risk factors and history of cervical abnormalities. Statistical software is used to measure sensitivity (the proportion of true positive Pap smear results confirmed by histopathology), specificity (the proportion of true negative Pap smear results confirmed by histopathology), and calculate the positive predictive value (PPV), the probability that a positive Pap smear has been confirmed) (the result indicates cervical cancer or a

precancerous condition) and a negative predictive value (NPV, the Likelihood that a negative Pap smear result will rule out cervical abnormalities). A chi-square test was used to assess the significance of discrepancies between Pap smear and histopathological results.

3. Results

Table one provides an overview of the demographic characteristics, cervical cancer screening history, risk factors, Pap smear results, and histopathological findings of the study participants. The age of the participants was divided into three groups: 17.33% were under 30 years old, 54.67% were between 30 and 50 years old, and 28% were over 50 years old, with an average age of 40.32 ± 9.949 years, which suggests a predominantly middle-aged population. Regarding cervical screening history, 44% of participants underwent screening while 51% did not, suggesting that the majority do not adhere to recommended screening practices. As for risk factors, smoking and obesity are the most prevalent with 36% of participants, followed by smoking alone (26.7%), obesity (12%), poor diet (10.7%), alcohol consumption (5, 3%). no reported risk factors (9.3%). Pap smear results show that 25.6% of participants had negative results, 20.9% had ASCUS (Atypical Squamous Carcinoma of Undetermined Significance), 20.9% had LSIL (Low-Grade Squamous Intraepithelial Lesion), and 19.8 % had HSIL (High-Grade Squamous Cells of Undetermined Significance). Intraepithelial lesion), reflecting a diverse spectrum of cervical abnormalities. The histopathological findings were consistent with the Pap smear results: 25.6% of participants showed negative findings, 20.9% were diagnosed with CIN 1, 20.9% with CIN 2, and 19.8% with CIN 3. These results highlight the significant presence of risk factors and cervical cancer abnormalities within the study population, highlighting the need for improved cervical screening and treatment of modifiable risk factors to reduce the risk of progression to cervical cancer.

Table 1 Demographic and Clinical Characteristics of Participants, Risk Factors, Pap Smear Results, and Histopathology Findings

Variables	**N (%) Mean +/- 2SD**
Age	40.32+/- 9.949
< 30	31 (17.33%)
30-50	41 (54.67%)
>	21 (28.00%)
History of Cervical Screening	
Yes	44 (36%)
No	31 (51%)
Risk factors	
Smoking	20 (26.7%)
Obesity	9 (12.0%)
Poor nutrition	8 (10.7%)
Alcohol Consumption	4 (5.3%)
Smoking and Obesity	7 (9.3%)
None	27 (36.0%)
Pap Smear	
Negative	22 (25.6%)
ASCUS	18 (20.9%)
LSIL	18 (20.9%)
HSIL	17 (19.8%)
Golde Histopathology	

Negative	22 (25.6%)
CIN 1	18 (20.9%)
CIN 2	18 (20.9%)
CIN 3	17 (19.8%)

In table two, interpretation of the results shows the accuracy of the Pap smear test in identifying cervical abnormalities compared to histopathology. Forty-two patients were correctly identified as having cervical anomalies by both Pap smear and histopathology and classified as true positives (TP), demonstrating accurate detection of anomalies. Three patients tested positive on Pap smear, but no cervical abnormalities were detected on histopathological examination, representing false positives (FP). This suggests a misclassification where the Pap smear suggested abnormalities that were not confirmed by histopathology. Eleven patients tested negative on Pap smear but were later diagnosed with cervical abnormalities by histopathological analysis, which were classified as false negatives (FN). These cases indicate missed detections where the Pap smear failed to detect abnormalities that were later confirmed by histopathology. Finally, nineteen patients were correctly determined to have no cervical abnormalities by both Pap smear and histopathology and were classified as True Negatives (TN), reflecting accurate negative results for both tests. Overall, this interpretation highlights the diagnostic accuracy of the Pap smear, but also highlights opportunities for improvement, particularly in reducing the incidence of false negative and false positive results.

Table 2 Comparison of Pap Smear Results and Histopathology Findings in the Study Population

Test Result	**Histopathology Positive**	**Histopathology Negative**	**Total**
Pap Smear Positive	42	3	45
Pap Smear Negative	11	19	30
Total	53	22	75

Table 3 illustrates the superior diagnostic accuracy of histopathology compared to Pap smear. Histopathology shows higher sensitivity (98.0% vs. 79.2%) and specificity (99.0% vs. 86.4%), ensuring more accurate identification of true positive and true negative cases. It also outperforms the Pap smear in negative predictive value (97.0% vs. 63.3%) and slightly in positive predictive value (99.5% vs. 93.3%). Co-testing with both methods achieves a combined sensitivity and specificity of 99.6% and 85.5%, respectively, increasing overall diagnostic accuracy. While histopathology remains the gold standard for diagnosis due to its high diagnostic performance, its invasive nature and higher cost limit its practicality as a screening tool for large populations. In contrast, the Pap smear retains its important role as a practical, accessible and non-invasive screening method.

Table 3 Diagnostic Performance Metrics of Pap Smear Compared to Histopathology as the Gold Standard

Metrics	**Pap Smear**	**Histopathology**
Sensitivity	79.2%	98.0%
Specificity	86.4%	99.0%
Positive Predictive Value (PPV)	93.3%	99.5%
Negative Predictive Value (NPV)	63.3%	97.0%
Combined Sensitivity and Specificity (Co-Testing)	85.5%	99.6%

Table 4 shows that the chi-square test was performed to assess the association between Pap smear and histopathological results. Both the chi-square and Pearson likelihood ratio tests showed statistically significant results ($p < 0.05$), indicating a strong association between the Pap smear and the results of the histopathological test. The results highlight the diagnostic limitations of the Pap smear compared to gold standard histopathology, particularly regarding false negative and false positive results. These results highlight the importance of combining screening and confirmatory tests to improve the accuracy of cervical abnormality detection.

Table 4 The Relationship Between Pap Smear and Histopathology Results Using a Chi-square test

Pap Smear Result	Histopathology Result	Observed Frequency	Expected Frequency	χ^2 Contribution
Positive (1)	Positive (1)	42	38.5	0.32
Negative (0)	Positive (1)	11	14.0	0.64
Positive (1)	Negative (0)	3	7.5	2.70
Negative (0)	Negative (0)	19	15.0	1.07

Test	Value	Degrees of Freedom (DF)	P Value
Pearson Chi-Square	4.73	1	<0.05

Figure one shows the Global Cancer Observatory bar chart highlighting the projected global increase in cervical cancer cases from 2022 to 2045 in various regions. Asia is expected to see the largest increase, with cases increasing from 397,082 to 543,783 (36.9%), followed by Africa with an increase of 5.7% (125,059 to 132,179). Latin America and the Caribbean and Europe recorded modest increases of 2.5% and 4.4%, respectively. North America is forecast to see a slight decline of 1.6%, while Oceania is forecast to see a slight increase of 0.7%. These disparities highlight the disproportionate burden in Asia and Africa and underscore the need for targeted prevention efforts.

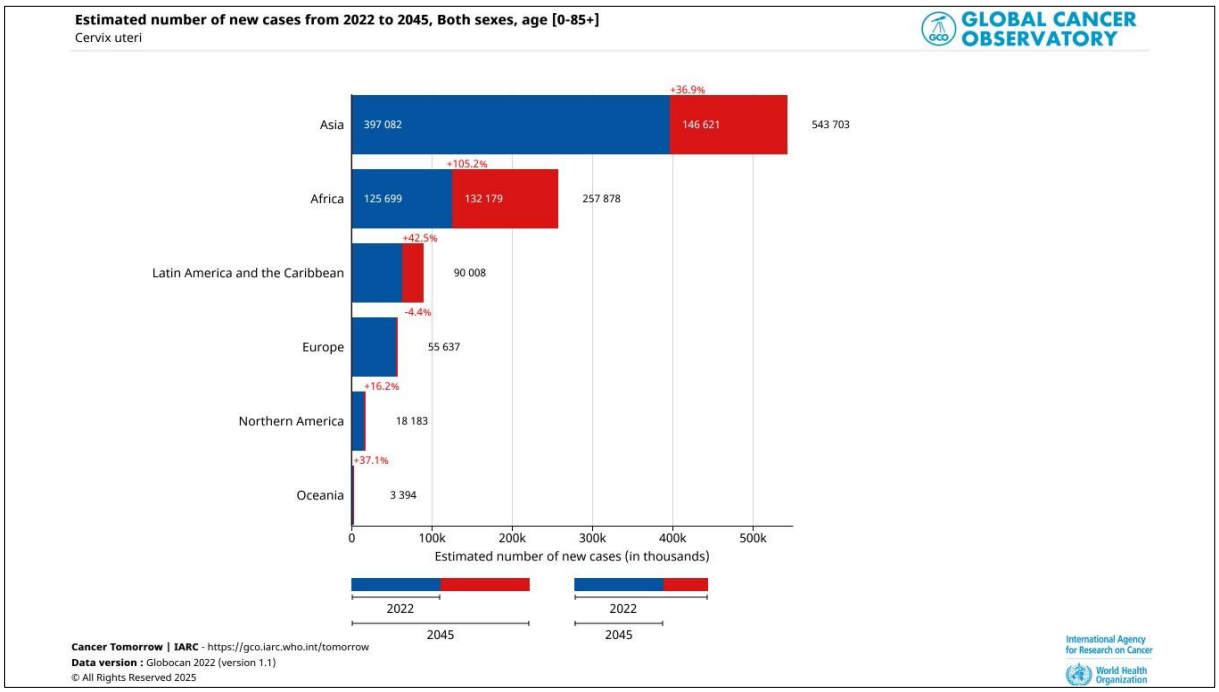

Figure 1 Projected Regional Trends in Cervical Cancer Incidence from 2022 to 2045: A Global Perspective

4. Discussion

This study evaluated the diagnostic accuracy of Pap smear tests compared to histopathology for detecting cervical abnormalities in a sample of 75 women in Duhok, Iraq, highlighting the global burden of cervical cancer, particularly in low- and middle-income countries [12]. Persistent high-risk HPV infection has been identified as the primary cause of cervical lesions, with HPV genotypes 16, 18, and 58 being the most common [12]. The results showed various cervical abnormalities: 25.6% of Pap smear results were negative, while 20.9% showed ASCUS or LSIL and 19.8% showed HSIL, closely consistent with the histopathological findings. The sensitivity and specificity of Pap smear were 79.2% and 86.4%, respectively, while histopathology achieved higher rates of 98% sensitivity and 99% specificity, supporting its role as a diagnostic gold standard despite its invasiveness and cost. Co-testing improved diagnostic accuracy with a combined sensitivity and specificity of 99.6% and 85.5%, respectively. The study highlights the practical value of the Pap smear as a non-invasive, accessible screening tool, despite limitations such as false-positive and false-negative

results and emphasizes the need for improved screening practices to address the significant risks of cervical cancer in the region to counteract [14].

The diagnostic parameters of Pap smear in our study are closely consistent with those described in previous literature. For example, the sensitivity (79.2%) and specificity (86.4%) of our study were consistent with studies by Simridhi, which reported similar diagnostic accuracy [14]. These results highlight the practical utility of the Pap smear as a first-line screening tool, particularly in resource-limited settings. Furthermore, the distribution of abnormal cytologic findings, including ASCUS, LSIL, and HSIL, showed parallels to studies by Banale and Makwana, supporting the global patterns of cytologic abnormalities. The high-risk HPV genotypes discovered in our study (HPV-16, -18 and -58) also reflect the genotype prevalence reported in international studies and highlight the universal role of HPV in the development of cervical cancer [15,16].

Despite these similarities, our study found a slightly higher prevalence of high-risk HPV DNA (19%) compared to previous studies. This discrepancy may be due to regional differences in HPV prevalence or differences in population demographics, including higher risk factors such as smoking and poor diet in our cohort. Furthermore, the sensitivity and specificity of our Pap smear easily exceeded the results of the studies by Banale and Joshi [15,17]. The variance could be due to differences in sample size, screening techniques, or laboratory protocols. Lower NILM percentages in our study compared to Alakananda et al. The study suggested that routine screening and advanced stage presentation were underutilized in our population [18].

The results of this study highlight the importance of removing barriers to cervical cancer screening and improving Pap smear accuracy to improve early detection in resource-poor settings. High diagnostic parameters of combined Pap smear and histopathological testing (sensitivity 99.6%, specificity 85.5%) highlight the potential of co-testing to reduce false-negative results, a critical problem in understudied populations. Our findings also shed light on the significant burden of cervical cancer in low- and middle-income countries and highlight the urgent need for comprehensive strategies that integrate HPV vaccination and public health education. These efforts could close gaps in screening adherence and reduce cervical cancer mortality worldwide.

5. Conclusion

This study showed that Pap smears are a practical and accessible screening tool for cervical cancer, but their accuracy is limited. Histopathology is the gold standard for diagnosis due to its high accuracy, but it is invasive and expensive. Combining Pap smears with HPV DNA testing could improve the sensitivity and accuracy of cervical cancer screening. Invasive histopathology may be reserved for confirmation of positive or inconclusive Pap smears or HPV DNA testing. This approach could improve the effectiveness of cervical cancer screening programs, particularly in developing countries.

Recommendations

While this study did not include HPV DNA testing, based on the results of this study, the integration of HPV DNA testing alongside traditional Pap smear screening is recommended to improve the sensitivity and overall diagnostic accuracy of cervical cancer screening. Future research should focus on integrating HPV DNA testing with traditional methods to improve early detection of high-risk cases, particularly in regions with limited healthcare infrastructure

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflicts of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Stelzle D, Tanaka LF, Lee KK, Khalil AI, Baussano I, Shah ASV, et al. (2020). Estimates of the global burden of cervical cancer associated with HIV. The Lancet Global Health. https://doi.org/10.1016/S2214-109X(20)30459-9

[2] Guida F, Kidman R, Ferlay J, Schüz J, Soerjomataram I, Kithaka B, et al. (2022). Global and regional estimates of orphans attributed maternal cancer mortality in 2020. Nature Medicine, 28:2563–72. https://doi.org/10.1038/s41591-022-02109-2

[3] Cancer.Net. Cervical cancer. https://www.cancer.net/cancer-types/cervical-cancer/view-all. Accessed 1/1/2025.

[4] David M. Gershenson, Gretchen M Lentz, Rogerio A. Lobo. (2021). Malignant diseases of the cervix. In: Comprehensive Gynecology. 8th ed. Elsevier. https://www.clinicalkey.com. Accessed 1/1/2025.

[5] Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE. (2019). Cancers of the cervix, vulva, and vagina. In: Abeloff's Clinical Oncology. 6th ed. Elsevier. https://www.clinicalkey.com. 1/1/2025.

[6] National Comprehensive Cancer Network. Cervical cancer. https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1426. Accessed 1/1/2025.

[7] AskMayoExpert. Cervical cancer screening (adult). Mayo Clinic; 2022.

[8] National Comprehensive Cancer Network. Palliative care. https://www.nccn.org/guidelines/guidelines-detail?category=3&id=1454. Accessed 1/1/2025.

[9] National Cancer Institute. What is cervical cancer? https://www.cancer.gov/types/cervical. Accessed 1/1/2025.

[10] National Cancer Institute. ACS's updated cervical cancer screening guidelines explained. [Internet]. Available from: https://www.cancer.gov/news-events/cancer-currents-blog/2020/cervical-cancer-screening-guidelines-acs. Accessed 1/1/2025.

[11] Dasgupta S. (2023). The efficiency of cervical Pap and comparison of conventional Pap smear and liquid-based cytology: a review. Cureus, 15(11): e48343. https://doi.org/10.7759/cureus.48343

[12] Jihad NA, Naif HM, Sabri EH. (2020). Prevalence of high-risk human papilloma virus among Iraqi women with abnormal cervical cytology. Gene Rep, 21:100871. doi: 10.1016/j.genrep.2020.100871.https://www.sciencedirect.com/science/article/pii/S2452014420302855

[13] Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. (2002). The 2001 Bethesda System: Terminology for reporting results of cervical cytology. JAMA, 287(16):2114–9. doi:10.1001/jama.287.16.2114.

[14] Bindroo S, Garg M, Gitika. (2019). Correlation of cervical Pap smear with histopathological diagnosis in cervical lesions: a 2-year retrospective study. Int J Contemp Med Res, 6(7): G17–G20.

[15] Banale M, Bansal C. (2017). Correlation of cervical Pap smear with histopathological diagnosis in patients with intraepithelial lesions. Int J Clin Obstet Gynaecol, 1(1):36–39. doi: 10.33545/gynae.2017.v1.i1a.1437

[16] Makwana A, Sorathya M, Desai NJ. (2023). A correlation study of cervical cytology on Pap smear with cervical biopsy in a tertiary care hospital: a 1-year study. Int J Clin Diagn Pathol, 6(2):5–7.

[17] Joshi C, Desai D, Nandeshwar S. (2015). Correlation of Pap smear and colposcopy in relation to histopathological findings in detection of pre-malignant and malignant lesions of cervix. Int J Sci Study, 3(7):137–141. doi:10.17354/ijss/2015/508

[18] Alakananda, Sarma U, Biswas I. (2016). Histopathological correlation with cervical cytology. IOSR J Dent Med Sci, 15(11):53–58. doi:10.9790/0853-1511085358.