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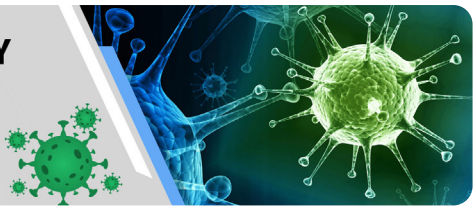
Research Article

ARCHIVES OF MICROBIOLOGY & IMMUNOLOGY

ISSN: 2572-9365



Comparative Analysis of Cytological and Histopathological Findings in Cervical Lesions among VIA-positive Patients and Their Correlation with High-Risk Human Papillomavirus Infection Regarding Cervical Carcinoma

Mahmuda Naznin*[,1], Zahid Hossain[2], Farzana Ashrafi Neela[3]

Abstract

Background: The accuracy of VIA (Visual Inspection with Acetic Acid) in detecting cervical abnormalities varies, necessitating cytology and histopathology. High-risk human papillomavirus (HPV) types are strongly linked to cervical cancer, enhancing diagnostic accuracy and risk assessment when correlated with cytological and histopathological findings. The study aimed to compare cytological and histopathological findings in cervical lesions among VIA-positive patients and to correlate these findings with high-risk human papillomavirus infection status.

Methods: This cross-sectional descriptive study took place at the Department of Pathology, Rajshahi Medical College, and the Department of Gynaecology and Obstetrics, Rajshahi Medical College Hospital, Rajshahi, Bangladesh, spanning from July 2019 to June 2022. A total of 1000 VIA test-positive cases of cervical lesions, were purposively enrolled as study subjects. Cytological, histopathological, and HPV DNA test results were collected and analyzed by using the SPSS version 23.0 program.

Results: According to histopathological findings, out of 1000 participants, 31.0% had either cervical carcinoma (5.3%), Cervical Intraepithelial Neoplasia-I (CIN-1), CIN-II, or CIN-III. According to cytological findings, 25.3% had either cervical carcinoma (4.6%), Low-grade Squamous Intraepithelial Lesion (LSIL), or High-grade Squamous Intraepithelial Lesion (HSIL). The frequency of HPV-positive cases was 24%. The correlation of cervical carcinoma detection between histopathological and HPV-DNA tests and between cytological and HPV-DNA tests was found statistically significant.

Conclusion: There are significant relationships between HPV DNA test results and histopathological and cytological diagnoses. However, none of the testing methods alone are suitable. Therefore, a combination of cytology, histopathology, and HPV DNA typing would ultimately be more useful in assessing cervical lesions or carcinoma.

Keywords: Cytological, Histopathological findings, Cervical lesions, VIA-positive, Correlation, Carcinoma

Introduction

Cervical cancer is the third most common cancer among women globally, after breast and colorectal cancer. [1] It contributes to more than 2.7 million years of life lost among women aged 25 to 64 globally [2]. In 2018, Bangladesh reported 8,068 new cases of cervical cancer, representing

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Received: March 29, 2024
Accepted: April 12, 2024
Published: May 17, 2024

Naznin M, et al., Arch Microbiol Immunology 2024
DOI:10.26502/ami.936500166

a rate of 10.6 per 100,000 women, along with 5,214 deaths, indicating a rate of 7.1 per 100,000 women [3]. Indeed, histopathology and cytopathology serve as the fundamental scientific and clinical components in the prevention and treatment of cervical cancer. In a study [4] it was reported that histopathology plays a crucial role in diagnosing cancer and precancerous conditions by examining the microscopic organization of cells in tissue sections obtained from biopsies or surgical specimens. They also mentioned that cervical cytopathology involves the analysis of exfoliated cells collected from the cervix surface and is the primary method used in successful cervical cancer screening programs. These diagnostic techniques are essential for effective management and prevention strategies in cervical cancer care. In another study [5], it was noted that countries that have effectively implemented cytological screening programs have witnessed a remarkable reduction in the incidence and mortality rates of cervical cancer by 70% or more. On the other hand, Histopathology remains pivotal in guiding crucial treatment decisions for both precancerous and invasive cervical cancer cases. [4] Consequently, it has been instrumental in establishing clinical endpoints for research endeavors focused on cervical screening, human papillomavirus (HPV) vaccines, and biomarkers. While visual inspection with acetic acid (VIA) is a cost-effective, straightforward, and widely employed method for screening the early stages of cervical cancer, the overall evidence regarding its impact on reducing cervical cancer mortality and incidence remains inconclusive [6]. Visual inspection with acetic acid (VIA) serves as an alternative to the methods mentioned above. It involves applying 5% acetic acid directly onto the cervix, after which precancerous lesions appear as aceto-white areas, visible to the naked eye [7]. Visual inspection with acetic acid (VIA) is deemed operationally more feasible due to its simplicity, ease of use, and minimal training requirements. However, its effectiveness in reducing invasive cancer and mortality remains uncertain, as highlighted by the World Health Organization (WHO, 2012) and Sullivan et al. (2015) [8]. Studies such as the one conducted by Poli et al. (2015) in rural areas of South India have demonstrated that VIA is both safe and effective in resource-limited settings [9]. Nevertheless, conflicting results have emerged from previous randomized controlled trials regarding the impact of VIA screening on cervical cancer mortality and incidence, as evidenced by studies conducted by Sankaranarayanan et al. (2009) [10], Shatri et al. (2014) [11], and Thomsen et al. (2020) [12]. In this study, we included only VIA-positive cases as the study subjects. The objective of this study was to compare cytological and histopathological findings in cervical lesions among VIA-positive patients and to correlate these findings with high-risk human papillomavirus infection status.

Methodology

This cross-sectional descriptive study took place at the Department of Pathology, Rajshahi Medical College, and the Department of Gynecology and Obstetrics, Rajshahi Medical College Hospital, Rajshahi, Bangladesh, spanning from July 2019 to June 2022. The study involved the enrollment of 1000 cases of cervical lesions that tested positive on visual inspection with acetic acid (VIA), selected through purposive sampling. Patients who tested negative on the VIA test and those who had already been histopathologically diagnosed with cervical carcinoma were excluded from the study. After inspecting the cervix with Cusco's speculum, the cervical condition was recorded, and samples were collected using a cervical cyto-brush for Pap smear analysis. Furthermore, guided biopsies were obtained using colposcopy for histopathological evaluation. Hematoxylin and eosin (H&E) staining was utilized for both Pap smear examination and histopathological assessment. Additionally, all cytological observations were meticulously documented. Upon confirmation of histopathologically diagnosed cases of cervical carcinoma and various grades of CIN (n=310), genotyping of HPV DNA was performed using real-time PCR with the QIAscreen HPV PCR test kit (QIAGEN, Germany). This kit targets a conserved region within the E7 gene and can separately detect HPV-16, HPV-18, and 13 other high-risk types as a pool. Subsequently, DNA samples underwent analysis using MS Office tools. In addition to the aforementioned details, socio-demographic data, and reproductive health characteristics were gathered and documented in the data collection form. Following the acquisition of written consent, patient data were obtained via face-to-face interviews using a structured questionnaire. The collected information was subsequently analyzed using the SPSS version 23.0 program. Chi-square tests were conducted, with a significance level of $p<0.05$ considered for statistical analysis.

Result

Nearly half of our participants, 47.3%, belonged to the 35-44 years age group, followed by 31.9% from the 25-34 years age range. (Table 1). According to histopathological findings, out of the total 1000 participants, 310 individuals (31.0%) were diagnosed with cervical carcinoma or one of the lesions, including cervical intraepithelial neoplasia-I (CIN-1), CIN-II, and CIN-III. Among the total participants, the histopathological assessment found 53 (5.3%) cases of cervical carcinoma (Fig 1). According to cytological findings, out of the total 1000 participants, 253 individuals (25.3%) were diagnosed with cervical carcinoma or one of the lesions, including Low-grade Squamous Intraepithelial Lesion (LSIL), and High-grade Squamous Intraepithelial Lesion (HSIL). Among the total participants, the cytological assessment

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found 46 (4.6%) cases of cervical carcinoma. (Fig 2) In this study, HPV PCR tests were conducted on 310 participants who tested positive through histopathological assessment. Among the total 1000 participants, the frequency of HPV-positive cases was found to be 24% (Fig 3). The correlation of cervical carcinoma detection between histopathological and HPV-PCR assessment was examined in a study involving 1000 participants. (Table 3) Of these, 53 were diagnosed with cervical carcinoma via histopathological assessment, while 240 tested positive for HPV-PCR. The odds ratio was calculated at 0.177, with a 95% confidence interval of 0.1297 to 0.2422. The z statistic was 10.856, with a corresponding p-value of less than 0.001, indicating a significant association between histopathological diagnosis and HPV-PCR positivity in detecting cervical carcinoma. In the evaluation of cervical carcinoma, comparing cytological assessment to HPV-PCR, out of 1000 cases examined, 46 were identified through cytological assessment, while 240 tested positive using HPV-PCR. The odds ratio was calculated at 0.153, with a 95% confidence interval of 0.1098 to 0.2123. The z statistic yielded 11.177, and the p-value was found to be less than 0.001. This indicates a significant association, highlighting the competitive advantage of HPV-PCR over cytological assessment in detecting cervical carcinoma.

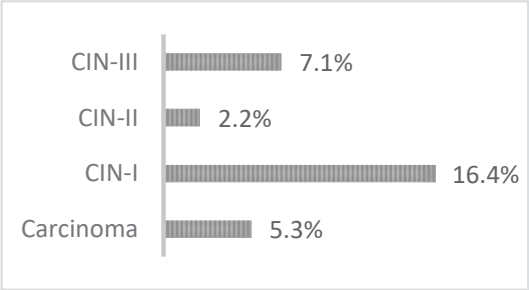

Figure 1: Histopathological findings (N=1000)

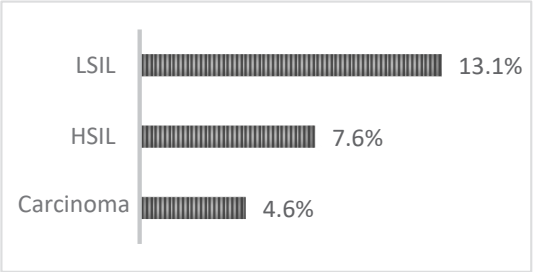

Figure 2: Cytological findings (N=1000)

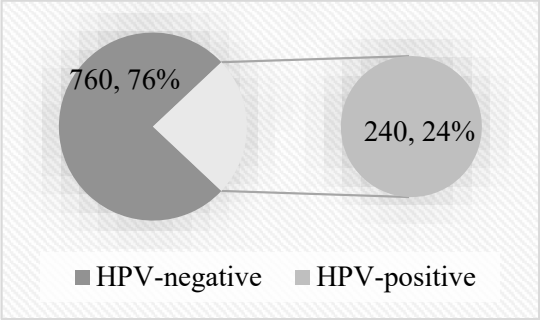

Figure 3: Frequency of HPV-positive cases

Table 1: Age distribution of participants

Age (Year)	n	%
15-24	76	7.60%
25-34	319	31.90%
35-44	473	47.30%
45-64	132	13.20%
Total	1000	100%

Table 2: Correlation of cervical carcinoma detection between histopathological and HPV-PCR assessment

Cervical carcinoma	Assessment (N=1000)		Odds ratio	95 % CI	z statistic	p-value
	Histopathological	HPV-PCR				
Yes	53	240	0.177	0.1297 to 0.2422	10.856	<0.001
No	947	760				

Table 3: Correlation of cervical carcinoma detection between cytological and HPV-PCR assessment

Cervical carcinoma	Assessment (N=1000)		Odds ratio	95 % CI	z statistic	p-value
	Cytological	HPV-PCR				
Yes	46	240	0.153	0.1098 to 0.2123	11.177	<0.001
No	954	760				

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Discussion

Approximately half (47.3%) of our participants fell within the 35-44 years age bracket, with a subsequent 31.9% representing the 25-34 years age group. However, many similar studies [13,14] included subjects from a broader age range. Our histopathological findings showed that among 1000 participants, 310 (31.0%) were diagnosed with cervical carcinoma or related lesions (CIN-I, CIN-II, and CIN-III). Additionally, 53 cases (5.3%) were confirmed as cervical carcinoma. On the other hand, as per cytological assessment, out of 1000 participants, 253 (25.3%) were diagnosed with cervical carcinoma or related lesions (LSIL and HSIL). Among all participants, cytological assessment revealed 46 cases (4.6%) of cervical carcinoma. So, in detecting cervical carcinoma both histopathological as well as cytological assessment showed similar effectiveness. In a study conducted in Bangladesh [15], a similar trend was observed, although the detection ratios of both procedures were higher compared to ours. It's possible that the differences in detection ratios between our study and that study were influenced by factors such as sample size. Their study had a smaller sample size, which could have impacted the observed detection rates. The findings from the recent study [16] align closely with our own, indicating a strong correlation between cervical cytology and cervical biopsy results. This suggests that Pap smear remains a valuable screening tool for identifying both precancerous and cancerous lesions of the cervix. This study analyzed the correlation of cervical carcinoma detection between histopathological and HPV-DNA assessment in a cohort of 1000 participants. This stark contrast underscores the competitive effectiveness of HPV-DNA tests over histopathological assessment in detecting cervical carcinoma, supported by an odds ratio of 0.177 (95% CI: 0.1297 to 0.2422) and a significant p-value of less than 0.001, suggesting its superior diagnostic utility. Indeed, the false-positive rate of HPV DNA testing is a notable concern in cervical cancer screening. Coste et al. (2003) highlighted this issue, reporting a false-positive rate of 6.2% for HPV DNA testing when employed in cervical cancer screening protocols [17]. Our findings also underscored the competitive advantage of HPV-PCR over cytological assessment in detecting cervical carcinoma, supported by an odds ratio of 0.153 (95% CI: 0.1098 to 0.2123) and a significant p-value of less than 0.001, suggesting its superior diagnostic utility. Research indicates that HPV DNA testing, particularly with the Hybrid Capture II assay (HCII) by Digene, has demonstrated superior performance compared to repeated cytology in triaging patients with ASC (atypical squamous cells) [18]. Furthermore, reflex high-risk HPV DNA testing has been shown to provide comparable life expectancy outcomes while also being more cost-effective than alternative management strategies [19].

Conclusion

In this prospective single center observational study, we found that critically ill COVID-19 patients exhibited a lower rate of oxygen extraction by peripheral tissues than non-COVID-19 patients, which may represent an adaptive mechanism to hypoxemia. This hypothesis needs to be further investigated.

Limitation of the study

Being single-centered and conducted over a short duration, this study's findings may not accurately represent the broader scenario across the entire country. Therefore, caution should be exercised when generalizing the results to the wider population. Further research across diverse settings and longer durations is warranted for comprehensive insights.

Conclusion

Significant relationships exist between HPV DNA test results and histopathological as well as cytological diagnoses in the assessment of cervical lesions or carcinoma. However, relying solely on any single testing method may not be sufficient for accurate diagnosis. Instead, a comprehensive approach combining cytology, histopathology, and HPV DNA typing offers greater utility in evaluating cervical lesions or carcinoma. This integrated approach allows for a more thorough assessment, leveraging the strengths of each method to enhance diagnostic accuracy and guide appropriate management decisions. By incorporating multiple testing modalities, healthcare providers can improve the detection and characterization of cervical abnormalities, ultimately leading to better patient outcomes through timely intervention and treatment.

Recommendation

Conducting similar further research with larger sample sizes and over an extended period is imperative. Expanding the scope of investigation in terms of sample size and duration allows for more robust data collection and analysis, increasing the reliability and generalizability of study findings.

Funding Information: NA

Conflict of Interest: None declare.

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