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Comparative Study Between HPV E6/E7 mRNA Test and HPV DNA Test in Detecting Cervical Pre-cancer

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ABSTRACT

Background: Cervical cancer remains a major health burden in low-resource countries, such as Bangladesh. Persistent high-risk HPV infections, particularly HPV 16 and 18, are the principal etiological factors. Although HPV DNA tests are widely used, they often lack specificity, leading to overtreatment. HPV E6/E7 mRNA testing offers improved specificity by identifying active oncogene expression, potentially serving as a better screening tool than HPV DNA testing. This study aimed to compare the diagnostic performances of the HPV E6/E7 mRNA and HPV DNA tests in detecting cervical pre-cancer in VIA-positive women.

Methods: This cross-sectional analytical study was conducted from November 2023 to January 2025 at BSMMU, Dhaka. A total of 264 VIA-positive women were purposively enrolled. Cervical samples were collected and tested for both HPV DNA and E6/E7 mRNA. Colposcopy followed by Histopathological analysis of the biopsy specimens was performed in every participant. The diagnostic performance metrics, including sensitivity, specificity, accuracy, PPV, NPV, +LR, -LR and Youden Index, were calculated using SPSS v25.

Results: The HPV DNA and mRNA positivity rates were 34.47% and 28.79%, respectively. E6/E7 mRNA showed higher specificity (96.9% vs. 82.2%), accuracy (up to 97%), and PPV for detecting CIN II+ lesions. mRNA positivity increased with lesion severity and was 100% in SCC cases. The Youden Index was consistently higher for mRNA testing. The kappa value between the tests was 0.555, indicating a moderate agreement.

Conclusion: E6/E7 mRNA testing exhibited superior diagnostic performance compared to HPV DNA testing in identifying clinically significant cervical lesions. Integrating mRNA testing into cervical screening programs could reduce unnecessary interventions.

Keywords: *HPV E6/E7 mRNA, HPV DNA, cervical pre-cancer, screening, specificity, sensitivity, VIA-positive women.*

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1. INTRODUCTION

Cervical cancer remains a critical public health concern, particularly in low- and middle-income countries such as Bangladesh, where routine screening uptake is suboptimal. In 2022, over 600,000 new cases of cervical cancer were diagnosed globally, with more than 340,000 deaths, disproportionately affecting developing regions [1]. Persistent infection with high-risk human papillomavirus (hrHPV), particularly types 16 and 18, is the fundamental cause of cervical carcinogenesis [2].

Traditional screening methods, such as the Papanicolaou (Pap) test and visual inspection with acetic acid (VIA), have low sensitivity and reproducibility [3,4]. This has led to an increased reliance on molecular assays, particularly HPV DNA testing, which is widely accepted for primary screening [5]. HPV DNA tests identify the presence of viral genetic material but cannot differentiate between transient and transforming infections, often resulting in high false-positive rates and unnecessary interventions and follow-up procedures [6].

To address this limitation, HPV E6/E7 mRNA testing has emerged as a promising alternative, capable of detecting oncogenic transcripts that are more closely associated with cervical transformation [7]. Unlike DNA tests, mRNA tests target the expression of viral oncogenes E6 and E7, which are essential for malignant progression and are rarely expressed during latent infections [2,8]. Consequently, mRNA testing may offer superior specificity in identifying clinically significant lesions, thereby reducing overtreatment [9].

Recent studies, including the ATHENA trial and others, have demonstrated that mRNA tests maintain comparable sensitivity to DNA tests while offering improved specificity [5,10]. Additionally, several meta-analyses and comparative effectiveness studies have shown that mRNA assays provide better predictive value for high-grade lesions, such as CIN II+ or CIN III+ [11,12]. The World Health Organization (WHO) has also acknowledged the potential of HPV mRNA testing in its guidelines, recommending its consideration in screening programs [4].

Despite these advances, limited data are available from South Asian populations, particularly Bangladesh, regarding the comparative effectiveness of HPV mRNA and DNA testing. Moreover, the unique epidemiological and sociodemographic contexts necessitate local validation before large-scale implementation. This study was designed to fill this knowledge gap by comparing the performance of HPV E6/E7 mRNA and HPV DNA tests in detecting histologically confirmed cervical precancerous lesions in VIA-positive Bangladeshi women.

This study aimed to determine whether the mRNA assay could serve as a more specific and equally sensitive tool compared to conventional DNA testing and resource utilization in low-resource settings including Bangladesh. These results may have important implications for national cervical cancer screening policies.

Methodology

This was a cross-sectional analytical study conducted at the National Center for Cervical and Breast Cancer Screening and Training (NCCBCST), under Bangabandhu Sheikh Mujib Medical University (BSMMU) in Dhaka, Bangladesh, from November 2023 to January 2025. A total of 264 women who tested positive on Visual Inspection with Acetic Acid (VIA) were purposively selected and included in this study.

Sample Selection

Inclusion Criteria:

- Women aged 25–60 years.
- VIA-positive cases referred for colposcopy.
- Willing to provide informed consent for participation.

Exclusion Criteria:

- Pregnant women at the time of screening.
- Women with a history of hysterectomy.
- Women with history of therapeutic procedure in cervix.
- Patients with visible cervical growths are suspicious of invasive carcinoma.

Data Collection Procedure: Data collection was initiated following VIA-based screening. Participants who were VIA positive at NCCBCST were included in this study. Cervical samples were obtained using a cytobrush and processed for HPV DNA and E6/E7 mRNA testing using standardized molecular techniques. HPV DNA testing was performed using a polymerase chain reaction (PCR)-based assay, which detects the presence of high-risk HPV genotypes, including HPV 16, 18, and other high-risk variants. These tests were done using Cobas 4800 platforms at the NCCBCST.

HPV E6/E7 mRNA test was performed at the Department of Virology of BSMMU. The E6/E7 mRNA expression was

detected from the 15 high-risk (hr) HPV by PCR test according to the manufacturer's (MACRO & MICRO-TEST) instructions. This test specifically identifies the expression of the hrHPV E6 and E7 oncogenes, which play a key role in HPV-mediated cervical carcinogenesis. This test included three steps: mRNA extraction, amplification & detection of amplified product. In the amplification curve, when the copy number was ≤38, the result was deemed as detected or overexpressed. Biopsies were performed under colposcopic guidance and histopathologically evaluated. The laboratory personnel and pathologists were blinded to each other's results. Data accuracy was ensured through double-entry and periodic validation.

Ethical Considerations: Ethical approval was obtained from the Institutional Review Board of BSMMU. All participants provided written informed consent before inclusion. The confidentiality of the participants' data was strictly maintained, and all research procedures adhered to the ethical guidelines of the Declaration of Helsinki.

Statistical Analysis: Data were analyzed using SPSS version 25.0. Descriptive statistics (frequency, percentage, and mean) were used to summarize participant characteristics. Inferential statistics, including the chi-square test, t-test, and calculation of sensitivity, specificity, accuracy, PPV, NPV, +LR, -LR and Youden Index were applied to evaluate the diagnostic performance of HPV tests. Kappa statistics were used to measure test agreement. A p-value ≤ 0.05 was considered statistically significant.

2. RESULTS

Table 1: Age distribution of the participants (n=264)

Age group (years)	Frequency (n)	Percentage (%)
25-30	30	11.36
31-40	134	50.76
41-50	67	25.38
51-60	33	12.50
Total	264	100.00

Table 1 summarizes the age distribution of the participants. The largest age group was 31–40 years (134 individuals, 50.76%). This was followed by 41–50 years (25.38%), 51–60 years (12.50%), and 25–30 years (11.36%). The majority of the participants were between 31 and 50 years of age.

Table 2: Distribution of HPV DNA genotypes and HPV E6/E7 mRNA among the participants (n=264)

Type of HPV	Positive		Negative	
	n	%	n	%
HPV-DNA-Total*	91	34.47	173	65.53
➢ HPV-16	55	20.83	209	79.17
➢ HPV-18	5	1.89	259	98.11
➢ HPV-others**	31	11.74	233	88.26
HPV-mRNA-Total	76	28.79	188	71.21

*HPV DNA Total: 14hr-HPV types in aggregate

**HPV-others: other 12hr-HPV types excluding HPV-16 and HPV-18

Table 2 presents the overall positivity rates for HPV DNA and E6/E7 mRNA testing. HPV DNA was detected in 91 participants (34.47%), with HPV-16 being the most frequently identified genotype (20.83%), followed by HPV-other types (11.74%) and HPV-18 (1.89%). HPV mRNA was positive in 76 participants, corresponding to 28.79% of the sample population.

Table 3: Correlation between HPV E6/E7 mRNA and DNA detection by HPV types (n=264)

HPV-DNA		n	HPV E6/E7 mRNA			P value
			Positive	Negative	Positive rate (%)	
HPV-DNA-Total*	Positive	91	58	33	63.74	0.00
	Negative	173	18	155	10.40	
HPV-16	Positive	55	42	13	76.36	0.00
	Negative	209	34	175	16.27	
HPV-18	Positive	5	2	3	40.00	0.58
	Negative	259	74	185	28.57	
HPV-others**	Positive	31	14	17	45.16	0.03
	Negative	233	62	171	26.61	

*HPV DNA Total: 14hr-HPV types in aggregate

**HPV-others: other 12hr-HPV types excluding HPV-16 and HPV-18

Table 3 shows the cross-tabulation between the HPV DNA and mRNA test results for each genotype. Among HPV DNA-positive individuals (n = 91), 58 were also positive for mRNA (63.74%). The strongest concordance was observed in HPV-16 cases, where 76.36% of DNA-positive participants were also mRNA-positive. The mRNA positivity rate was significantly higher in DNA-positive cases than in DNA-negative cases for all genotypes except HPV-18 (p = 0.58).

Table 4: Histopathological findings among the participants (n=264)

Histopathological diagnosis	Frequency (n)	Percentage (%)
Chronic cervicitis	163	61.74
CIN-I	22	8.33
CIN-II	15	5.68
CIN-III	46	17.42
AIS/CIS	12	4.55
SCC	6	2.27
Total	264	100

CIN=Cervical Intraepithelial Neoplasia, AIS=Adenocarcinoma in situ, CIS= Carcinoma in situ, SCC= Squamous Cell Carcinoma

Table 4 outlines the distribution of histological findings from the cervical biopsies. Chronic cervicitis was the most common diagnosis, observed in 163 participants (61.74%) which regarded as normal. Cervical intraepithelial neoplasia grade III accounted for 17.42% of the cases, followed by CIN-I (8.33%), CIN-II (5.68%), adenocarcinoma in situ/carcinoma in situ (AIS/CIS) (4.55 %), and squamous cell carcinoma (SCC) (2.27 %).

Table 5: Status of HPV DNA and HPV E6/E7 mRNA in chronic cervicitis (n=163)

Tests		Frequency (n)	Percent (%)
HPV-DNA	Positive	29	17.79
	Negative	134	82.21
HPV-mRNA	Positive	5	3.07
	Negative	158	96.93
Total		163	100.00

Table 5 presents the results of HPV testing in patients diagnosed with chronic cervicitis. Among them, twenty-nine patients (17.79%) tested positive for HPV DNA, while only five (3.07%) tested positive for E6/E7 mRNA.

Table 6: HPV positive rate by the severity of histopathological diagnosis (n=264)

Tests		Chronic cervicitis (n=163)		CIN-I (n=22)		CIN-II (n=15)		CIN-III (n=46)		AIS/CIS (n=12)		SCC (n=6)		P-value
		n	%	n	%	n	%	n	%	n	%	n	%	
HPV DNA Total*	Positive	29	17.8	9	40.9	13	86.7	26	56.5	9	75.0	5	83.3	0.00
	Negative	134	82.2	13	59.1	2	13.3	20	43.5	3	25.0	1	16.7	
HPV-16	Positive	8	4.9	8	36.4	10	66.7	20	43.5	6	50.0	3	50.0	0.00
	Negative	155	95.1	14	63.6	5	33.3	26	56.5	6	50.0	3	50.0	
HPV-18	Positive	4	2.5	0	0.0	0	0.0	0	0.0	1	8.3	0	0.0	0.46
	Negative	159	97.5	22	100.0	15	100.0	46	100.0	11	91.7	6	100.0	
HPV-others**	Positive	17	10.4	1	4.5	3	20.0	6	13.0	2	16.7	2	33.3	0.37
	Negative	146	89.6	21	95.5	12	80.0	40	87.0	11	83.3	6	66.7	
E6/E7 mRNA	Positive	5	3.1	6	27.3	14	93.3	34	73.9	10	91.7	6	100.0	0.00
	Negative	158	96.9	16	72.7	1	6.7	12	26.1	1	8.3	0	0.0	

*HPV DNA Total: 14hr-HPV types in aggregate

**HPV-others: other 12hr-HPV types excluding HPV-16 and HPV-18

Table 6 presents a distribution of HPV positivity among different grades of cervical disease. HPV DNA positivity increased with lesion severity, from 17.8% in chronic cervicitis to 83.3% in SCC. Similarly, E6/E7 mRNA positivity increased from 3.1% in chronic cervicitis to 100% in SCC cases. The highest mRNA detection rates were observed in CIN II (93.3%), AIS/CIS (91.7%), and SCC (100%).

Table 7: Diagnostic Test Results for HPV DNA and HPV E6/E7 mRNA Testing in CIN-I, CIN-II, CIN-III, CIS/AIS & SCC Biopsies (n=264)

Tests	Total	HPV-DNA total		E6/E7 mRNA		P-value
		Positive	Negative	Positive	Negative	
CIN-I	22	9 (40.9%)	13 (59.1%)	6 (27.3%)	16 (72.7%)	0.00
CIN-II	15	13 (86.7%)	2 (13.3%)	14 (93.3%)	1 (6.7%)	
CIN-III	46	26 (56.5%)	20 (43.5%)	34 (73.9%)	12 (26.1%)	
AIS/CIS	12	9 (75.0%)	3 (25.0%)	11 (91.7%)	1 (8.3%)	
SCC	6	5 (83.3%)	1 (16.7%)	6 (100.0%)	0 (0.0%)	

CIN=Cervical Intraepithelial Neoplasia, AIS=Adenocarcinoma in situ, CIS= Carcinoma in situ, SCC= Squamous Cell Carcinoma

Table 7 presents the number and percentage of HPV DNA- and mRNA-positive results among patients with CIN-I, CIN-II, CIN-III, AIS/CIS, and SCC. HPV mRNA had higher positivity rates than that of HPV DNA in CIN II (93.3% vs. 86.7% for DNA), CIN III (73.9% vs. 56.5%), AIS/CIS (91.7% vs. 75.0%), and SCC (100.0% vs. 83.3%). In CIN-I, HPV DNA showed higher positivity (40.9%) than mRNA (27.3%).

Table 8: Age-specific distribution of positive HPV DNA and E6/E7 mRNA tests (n=264)

Test		Age								Total
		25-30		31-40		41-50		51-60		
		n	%	n	%	n	%	n	%	
HPV-DNA total*	Positive	12	40.0	42	31.3	18	26.9	19	57.6	91
	Negative	18	60.0	92	68.7	49	73.1	14	42.4	173
HPV-16	Positive	7	23.3	29	21.6	8	11.9	11	33.3	55
	Negative	23	76.7	105	78.4	59	88.1	22	66.7	209
HPV-18	Positive	1	3.3	1	0.7	2	3.0	1	3.0	5
	Negative	29	96.7	133	99.3	65	97.0	32	97.0	259
HPV-others**	Positive	4	13.3	12	9.0	8	11.9	7	21.2	31
	Negative	26	86.7	122	91.0	59	88.1	26	78.8	233
E6/E7 mRNA	Positive	4	13.3	32	23.9	23	34.3	17	51.5	76
	Negative	26	86.7	102	76.1	44	65.7	16	48.5	188

*HPV DNA Total: 14hr-HPV types in aggregate

**HPV-others: other 12hr-HPV types excluding HPV-16 and HPV-18

Table 8 shows the distribution of positive HPV DNA and mRNA results by age group. The highest DNA positivity was in the 51–60 age group (57.6%), followed by 25–30 (40.0%), 31–40 (31.3%), and 41–50 (26.9%) age groups. HPV mRNA positivity also increased with age, peaking at 51.5% in the 51–60 group and being lowest in the 25–30 group (13.3%). HPV-16 was the most prevalent genotype across all age groups.

Table 9: Diagnostic performance of HPV DNA and HPV E6/E7 mRNA for the evaluation of CIN-I, CIN-II, CIN-III, CIS/AIS, and SCC (n=264)

Diagnostic performance	CIN-I		CIN-II		CIN-III		CIS/AIS		SCC	
	DNA	mRNA	DNA	mRNA	DNA	mRNA	DNA	mRNA	DNA	mRNA
Sensitivity (95% CI)	40.9 (20.7–63.6)	27.3 (10.7–50.2)	86.7 (59.5–98.3)	93.3 (68.1–99.8)	56.5 (41.1–71.1)	73.9 (58.9–85.7)	75.0 (42.8–94.5)	91.7 (61.5–99.8)	83.3 (35.9–99.6)	100.0 (54.1–100.0)
P-value	0.34		0.54		0.07		0.27		0.29	
Specificity (95% CI)	82.2 (75.5–87.7)	96.9 (93.0–99.0)	82.2 (75.5–87.7)	96.9 (93.0–99.0)	82.2 (75.5–87.7)	96.9 (93.0–99.0)	82.2 (75.5–87.7)	96.9 (93.0–99.0)	82.2 (75.5–87.7)	96.9 (93.0–99.0)
P-value	<0.001		<0.001		<0.001		<0.001		<0.001	
Accuracy (95% CI)	77.3 (70.6–83.1)	88.6 (83.2–92.8)	82.6 (76.2–87.8)	96.6 (92.8–98.8)	76.6 (70.2–82.1)	91.9 (87.3–95.2)	81.7 (75.2–87.1)	96.6 (92.7–98.7)	82.2 (75.6–87.7)	97.0 (93.2–99.0)
P-value	0.001		<0.001		<0.001		<0.001		<0.001	
PPV	23.7 (11.4–	54.5 (23.4–	31.0 (17.6–	73.7 (48.8–	47.3 (33.7–	87.2 (72.6–	23.7 (11.4–	68.8 (41.3–	14.7 (5.0–	54.5 (23.4–

(95% CI)	40.2)	83.3)	47.1)	90.9)	61.2)	95.7)	40.2)	89.0)	31.1)	83.3)
P-value	0.03		0.02		<0.001		0.02		0.14	
NPV (95% CI)	91.2 (85.4–95.2)	90.8% (85.5–94.7%)	98.5 (94.8–99.8)	99.4 (96.5–100.0)	87.0 (80.7–91.9)	92.9 (88.0–96.3)	97.8 (93.7–99.5)	99.4 (96.5–100.0)	99.3 (95.9–100.0)	100.0 (97.7–100.0)
P-value	0.88		0.32		0.04		0.12		0.17	
LR+	2.30	8.80	4.87	30.10	3.17	23.84	4.21	29.58	4.68	32.6
LR−	0.72	0.75	0.16	0.07	0.53	0.27	0.30	0.08	0.20	0.00

Table 9 presents the diagnostic performance parameters, including sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratios (LR+ and LR−) for HPV DNA and mRNA tests. HPV mRNA consistently demonstrated higher sensitivity, specificity, and overall accuracy across most histological categories.

Table 10: Youden Index (J) for HPV DNA and HPV E6/E7 mRNA by Histological Category

Histology	Youden Index – HPV DNA	Youden Index – HPV mRNA	Best Performing Test
CIN I	0.231	0.242	mRNA
CIN II	0.689	0.903	mRNA
CIN III	0.387	0.708	mRNA
AIS/CIS	0.572	0.886	mRNA
SCC	0.655	0.969	mRNA

Table 10 compares the Youden Index, a summary measure of test effectiveness, for HPV DNA and mRNA. The index was higher for mRNA testing in all disease categories, indicating its diagnostic utility.

Table 11: Agreement of HPV E6/E7 mRNA and HPV DNA total (n=264)

DNA		Kappa value	Observed agreement (%)
HPV-DNA total	Positive	0.555	80.68
	Negative		

Table 11 presents the overall agreement between the two tests. The observed agreement was 80.68%, and the kappa value was 0.555, indicating moderate agreement between HPV DNA and E6/E7 mRNA detection results.

3. DISCUSSION

This comparative study between HPV E6/E7 mRNA and HPV DNA testing among 264 VIA-positive women demonstrated that E6/E7 mRNA testing offers superior diagnostic performance in identifying high-grade cervical lesions. The study findings indicate that while HPV DNA testing had a higher positivity rate overall (34.47% vs. 28.79%), mRNA testing exhibited significantly better specificity (96.9% for HPV E6/E7 mRNA vs. 82.2% for HPV DNA), positive predictive value, and accuracy, particularly for detecting lesions of CIN II or higher.

The correlation between histological severity and mRNA positivity was more robust than that with DNA, underscoring the biological significance of E6/E7 oncogene expression in disease progression. Among participants with high-grade lesions (CIN II, CIN III, AIS/CIS, and SCC), the sensitivity of mRNA testing was consistently higher, reaching 93.3% in CIN II, 73.9% in CIN III, and 100% in SCC cases. These results are consistent with the findings of Munkhdelger et al., who reported the superior diagnostic value of E6/E7 mRNA testing for high-grade cervical intraepithelial neoplasia [13].

Although DNA testing remains a reliable tool, its lower specificity often leads to overtreatment. For instance, in this study, DNA-positive results were common even in low-grade lesions, such as chronic cervicitis and CIN I. Conversely, mRNA positivity was rare in these categories, reinforcing the idea that mRNA testing can better differentiate between transient infections and clinically significant diseases. This is supported by Rad et al., who demonstrated a reduced risk of overtreatment when mRNA testing was used for triage [14].

The discordant results between the two tests are particularly noteworthy. Among the 163 women diagnosed with chronic

cervicitis, 29 tested positive for HPV DNA, whereas only five were mRNA-positive. Similarly, in CIN I, DNA was positive in 40.9% of cases compared to 27.3% for mRNA. These discrepancies are significant, indicating that HPV DNA testing may result in a considerable number of false positives, particularly in low-grade or non-dysplastic lesions, potentially leading to psychological stress, unnecessary colposcopies, and health system strain. The ability of mRNA testing to exclude such cases makes it a valuable tool in low-resource settings. Ge et al. observed that mRNA testing significantly improved specificity and reduced the burden of unnecessary follow-ups [15].

The Youden Index, which combines sensitivity and specificity into a single metric, further emphasizes the superiority of mRNA. For CIN II, the Youden Index was 0.903 for mRNA compared to 0.689 for DNA; for SCC, it was 0.969 for mRNA versus 0.655 for DNA. Similar trends were reported by Zhang et al., who concluded that mRNA testing was more accurate in detecting high-grade lesions and minimizing overtreatment [8].

The likelihood ratios further underscore the diagnostic superiority of HPV E6/E7 mRNA testing. The positive likelihood ratio (+LR) for mRNA was markedly higher than that for DNA across all histological grades, indicating a stronger association between mRNA positivity and high-grade lesions. Conversely, the negative likelihood ratio (-LR) for mRNA was lower, reflecting its ability to more reliably rule out disease when negative. These findings align with those of Arbyn et al., whose meta-analysis demonstrated that mRNA assays consistently yielded higher +LRs and lower -LRs than DNA tests, reinforcing their utility in risk stratification and clinical decision-making [12].

Kappa statistics revealed moderate agreement (0.555) between the two tests, suggesting that they are not interchangeable but complementary. This reflects the fundamental biological difference: HPV DNA testing detects the presence of viral genetic material regardless of activity, whereas E6/E7 mRNA testing identifies active transcription of oncogenes, which is more closely linked to carcinogenesis. Wallace and Galloway highlighted this mechanistic distinction, asserting that E6 and E7 expressions drive cellular transformation [7].

Age-stratified data further demonstrated that mRNA positivity increased with age, peaking in the 51–60 age group (51.5%), similar to DNA positivity (57.6%). HPV DNA positivity was more (40%) in young age group (25-30 years) than mRNA positivity (13.3%). This is consistent with the global patterns of persistent HPV infection and delayed clearance in older women [16,17].

The implications of these findings are significant and far-reaching. The World Health Organization's 2021 guidelines acknowledged the role of mRNA testing and recommended its integration into screening algorithms, where feasible [4]. The results of this study support this direction, especially in resource-constrained environments, where the cost of unnecessary procedures is high.

Notably, HPV-18 detection was low in this cohort (1.89%), and mRNA positivity in HPV-18-positive cases did not differ significantly from that in HPV-18-negative cases. This aligns with the findings of Wei F et al., who observed considerable regional variation in genotype distribution, with HPV-16 being consistently dominant [18].

In summary, this study confirms that HPV E6/E7 mRNA testing is a more clinically meaningful diagnostic tool than HPV DNA testing for detecting cervical pre-cancer in VIA-positive women. It offers high sensitivity for high-grade lesions while minimizing false-positives in benign cases. Integrating mRNA testing into screening programs could lead to more accurate diagnosis, better allocation of healthcare resources, and improved patient outcomes.

4. LIMITATIONS AND RECOMMENDATIONS

The study was limited by its cross-sectional design and purposive sample from a single center (National Center of Cervical Cancer Screening), which limited its generalizability. HPV vaccination status was not considered in this study. Future studies should use multicenter longitudinal designs to assess ’s predictive value of HPV mRNA. Given its superior performance, it is recommended that E6/E7 mRNA testing be incorporated into national cervical screening programs, as a method of primary screening.

5. CONCLUSION

This study demonstrated that HPV E6/E7 mRNA testing outperformed HPV DNA testing in terms of specificity, accuracy, and predictive value for detecting high-grade cervical lesions in VIA-positive women. While DNA testing remains sensitive, mRNA testing better reflects disease severity, reducing unnecessary follow-ups. These findings support the integration of mRNA-based testing into cervical screening algorithms, particularly in resource-constrained settings.

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Conflicts of interest

There are no conflicts of interest.

Ethical approval

The study was approved by the Institutional Ethics Committee.

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