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Research Article

Comparison of Urine and Cervical Samples for Genotyping Via HPV DNA Test

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Abstract

Background: Human papillomavirus (HPV) is a key factor in cervical cancer development. This study aimed to compare the efficacy of urine and cervical samples for HPV genotyping, evaluating their diagnostic performance in detecting high-risk HPV genotypes. *Methods*: This comparative cross-sectional study conducted over one year at the Department of Gynaecological Oncology, BSMMU, Dhaka, the study enrolled 74 women aged 30-60 years with positive visual inspection with acetic acid (VIA) results or abnormal Pap test findings. Urine samples (20 ml) and cervical samples were collected from each participant. The samples were analyzed using multiplex real-time PCR to amplify high-risk HPV types (16, 18, and others). DNA was extracted using the Qiagen viral DNA extraction kit. Sensitivity and specificity of HPV detection in urine samples were compared to cervical sampling, the gold standard. Data were analyzed with SPSS 22.0, and agreement was assessed using the Kappa index. *Result*: Cervical samples detected HPV in 17.56% of participants, while urine samples identified HPV in 5.40%. The agreement between urine and cervical samples was moderate, with a kappa value of 0.743. Among 74 cases, 5 cases were detected as HPV 16 and HR (co-injection) in both cervical and urine sample, 2 cases as HPV 16 in both cervical and urine samples, 2 cases as only HR type in both cervical and urine sample. The kendall's correlation of agreement was 0.361 and a significance of 0.002. *Conclusion*: Cervical samples are more reliable for HPV detection compared to urine samples, though urine testing shows high sensitivity.

Keywords

Human Papillomavirus (HPV), Genotype Distribution, Urine Samples, HPV Detection, Cervical Cancer Screening

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1. Introduction

Cervical cancer is a leading cause of morbidity and mortality among women worldwide, particularly in developing countries [1]. Despite significant advancements in the prevention and treatment of cervical cancer, the disease remains a pressing public health issue in regions such as Bangladesh, where the incidence and mortality rates are disproportionately high. Cervical cancer is primarily caused by persistent infection with high-risk types of human papillomavirus (HPV), a sexually transmitted virus [2]. The natural history of cervical cancer underscores the critical importance of early detection and timely intervention in reducing the disease's burden. Effective screening programs can identify precancerous lesions before they progress to invasive cancer, thus offering a powerful tool for cervical cancer prevention [3].

Traditional cervical cancer screening methods, including the Papanicolaou (Pap) smear and visual inspection with acetic acid (VIA), have been instrumental in reducing the incidence of cervical cancer in many parts of the world. [4] The Pap smear, introduced in the mid-20th century, revolutionized cervical cancer screening by enabling the early detection of abnormal cells that could progress to cancer if left untreated. [5] VIA, on the other hand, is a simpler, cost-effective technique that involves the application of acetic acid to the cervix, allowing healthcare providers to visually identify abnormal areas that may require further investigation. [6] Both methods have proven effective in various settings; however, they also have limitations, particularly in low-resource environments like Bangladesh.

One of the primary challenges associated with traditional screening methods is accessibility. Pap smears and VIA require a pelvic examination, which can be difficult to perform in resource-limited settings due to a lack of trained personnel, infrastructure, and equipment. [7] Additionally, cultural and socio-economic factors often deter women from seeking screening services. [8] Many women in Bangladesh and similar contexts are reluctant to undergo pelvic examinations due to fear, embarrassment, and the stigma associated with gynecological procedures. [9] These barriers contribute to low screening coverage and delayed diagnosis, ultimately resulting in higher rates of advanced cervical cancer and poorer outcomes.

Moreover, the sensitivity of traditional screening methods can vary, particularly in low-resource settings where the quality of screening may be compromised by inadequate training and lack of quality control. [10] Pap smears, while highly specific, can have variable sensitivity depending on factors such as sample collection, slide preparation, and interpretation. [11] VIA, although more accessible, is also less sensitive and specific than the Pap smear, leading to potential under- or over-diagnosis. [12] These challenges underscore the need for alternative screening methods that are not only effective but also more accessible and acceptable to women in these settings.

In recent years, there has been growing interest in non-invasive alternatives to traditional cervical cancer screening methods. One such alternative is urine-based HPV testing, which offers several advantages over Pap smears and VIA. [13] Urine sampling is non-invasive, does not require a pelvic examination, and can be self-collected by the patient in the privacy of her home. [14] These features make urine-based HPV testing a potentially attractive option for women who are hesitant to undergo traditional screening or who live in areas where access to healthcare services is limited.

2. Objectives

The objective of this study was to compare the diagnostic accuracy of urine-based HPV testing with cervical sampling in detecting high-risk HPV genotypes among women aged 30-60 years with abnormal cervical cytology or VIA-positive results in Bangladesh.

3. Methodology & Materials

This comparative cross-sectional study was conducted in the Department of Gynaecological Oncology at Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, over one year from June 2022 to May 2023. The study population included women aged 30-60 years who tested positive for visual inspection with acetic acid (VIA) or had abnormal cytology (Pap test) results. Based on sample size calculation using a 98% confidence interval, a prevalence of 42.1% for HPV positivity in urine samples, and an allowable error of 30%, the required sample size was 83. However, 74 participants were ultimately selected using purposive sampling method. Inclusion criteria were women aged 30-60 years with VIA-positive results or abnormal cytology tests (Pap test) who consented to participate in the study. Exclusion criteria included women previously vaccinated against HPV, those who had received prior treatment for cervical disease, pregnant women or those who had given birth within the last three months, and those who did not consent to participate. Participants were instructed not to urinate or wash their genitalia one hour before sample collection. Urine samples (20 ml) were collected before pelvic examination, and cervical samples were obtained using sterile polypropylene swabs under aseptic conditions. Samples were promptly transported in temperature-controlled conditions to the Department of Virology for analysis. Urine samples underwent modified aliquoting prior to DNA extraction using the Qiagen viral DNA extraction kit. Multiplex real-time PCR was performed to amplify the LCR/E6/E7 regions of high-risk HPV types (16, 18, and others). For viral nucleic acid purification, the QIAamp MinElute Virus Spin Kit was used, ensuring minimal elution

volumes for higher sensitivity. All procedures were conducted at room temperature with stringent safety protocols. Data were analyzed using SPSS 22.0. Demographic data and baseline characteristics were summarized using frequency and percentages. Continuous variables were represented by mean ± standard deviation or median with interquartile range, depending on normality. Sensitivity and specificity of HPV DNA detection in urine samples were calculated, using cervical sampling as the gold standard. The Kappa index was employed to determine the agreement between paired samples. Ethical approval was obtained from the BSMMU IRB, and informed consent was secured from all participants. Data confidentiality was maintained, with anonymized records stored securely. Each patient was assigned a unique ID number for all study procedures, ensuring privacy and traceability throughout the study.

4. Result

Table 1 shows total sample size (n) was 74. 20.3% (15 individuals) fell within the age range of 25-34. 54.1% (40 individuals) fell within the age range of 35-44. 25.7% (19 individuals) were aged 45 or older. The mean age was 40.07 years with a standard deviation (SD) of 7.58. The median age was 39 years, ranging from 25 to 62. 89.2% (66 individuals) of the participants were married. 4.1% (3 individuals) were divorced, 6.8% (5 individuals) were widow/widower. 24.3% (18 individuals) were primipara and 75.7% (56 individuals) were multipara. Regarding smoking habits, a quarter of the participants reported being smokers (25.7%), while the majority indicated that they do not smoke (74.3%).

Table 1. *Distribution of the participants according to socio demographic characteristics (n=74).*

Variables	Frequency (n=74)	Percentage (%)
Age		
30-39	43	58.1
40-49	17	23
≥50	14	18.9
Mean±SD	40.26±7.14	
Median (min-max)	39 (30-60)	
Marital status		
Married	66	89.2
Divorced	3	4.1
Widow/widower	5	6.8
Parity		
Primipara	18	24.3
Multipara	56	75.7
Smoking		
Yes	19	25.7
No	55	74.3

Data expressed as frequency (percentage)
Mean±SD, median (min-max)

Figure 1. *Distribution of the participants according to monthly family income.*

Figure 1 describes the distribution of the participants according to monthly family income. More than 70% participants were from lower middle class background, the rest of them were from upper middle class background.

Table 2. *Distribution of the participants according to obstetric and gynaecological history.*

Variables	Frequency (n=74)	Percentage (%)
Age of marriage		
<18 year	50	67.6
≥18 year	24	32.4
Age of 1st live birth		
<18 year	29	39.2
≥18 year	45	60.8
No. of sexual partner		
One	73	98.6
More than one	1	1.4
Mode of delivery		
NVD	65	87.8
C/S	9	12.2

Data expressed as frequency (percentage)
Mean±SD, median (min-max)

From the above table 2 we observe that 67.6% (50 individuals) participants got married before the age of 18 and 32.4% (24 individuals) participants got married at or after the age of 18. 29 individuals (39.2%) had their first live birth before the age of 18 and 45 individuals (60.8%) had their first live birth at or after the age of 18. About 98.6% (73 individuals) patients reported having only one sexual partner and 1.4% (1 individual) reported having more than one sexual partner. More than 80% (65 individuals) had a normal vaginal delivery (NVD) and 12.2% (9 individuals) had a cesarean section (C/S) delivery.

Transitioning to more health-related aspects, table 3 outlines BMI distribution, revealing that a significant majority of participants have a normal BMI (71.6%), while a smaller portion is categorized as overweight (28.4%).

Table 3. *Distribution of the participants according to information regarding disease.*

Variables	Frequency (n=74)	Percentage (%)
BMI		
Normal	53	71.6
Overweight	21	28.4

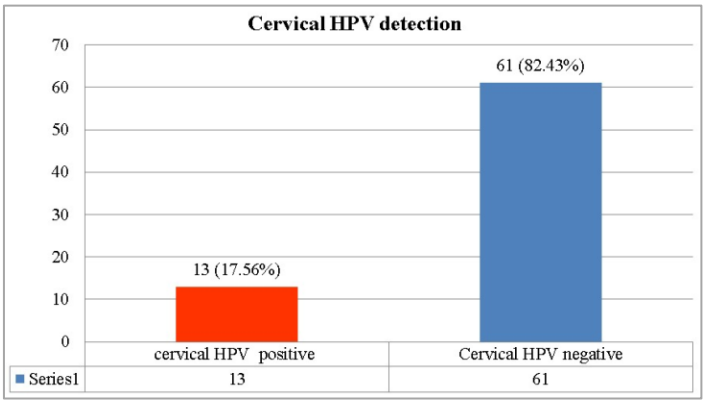
Data expressed as frequency (percentage)
Mean±SD, median (min-max)

Table 4. *Association of variables with Urine HPV test and cervical HPV test.*

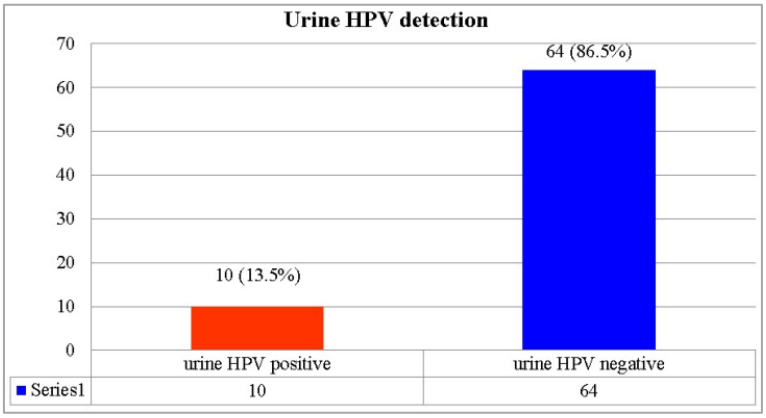
Variables	Urine HPV report		P value
	Positive	Negative	
Age of 1st live birth	Cervical HPV report		
<18 years	10 (34.5%)	19 (65.5%)	[a]0.002[s]
≥18 years	3 (6.7%)	42 (93.3%)	

Data expressed as frequency (percentage)
a= chi-square test
s= statistically significant at 0.05 levels

There was also a statistically significant association ($p<0.002$) between the age of 1st live birth and cervical sample HPV in Table 4.



a) Cervical HPV detection



b) Urine HPV detection

Figure 2. *Distribution of the participants according to Urine and Cervical sample HPV report.*

Cervical sample was able to detect 13 (17.56%) patients HPV positive. Urine sample was able to detect 4 (5.40%) patients HPV positive in Figure 2.

Table 5. *Accuracy of urine sample in comparison to cervical sample in detecting HPV detection.*

Urine sample HPV report	Cervical HPV report		Cohen's Kappa of agreement	P value
	Positive	Negative		
Positive	9 (90%)	1 (10%)	[k]0.743	0.002[s]
Negative	4 (6.2%)	60 (93.8%)		

Data expressed as frequency (percentage)
k= Cohen's kappa test for agreement
s= statistically significant at 0.05 levels

Table 5 describes the agreement between the urine and cervical sample HPV report. The kappa was 0.743 which indicated towards moderate agreement. The significance of cohen's Kappa was 0.002 which was highly significant.

Table 6. *Genotype detection by urine sample and cervical sample.*

Variables	Cervical HPV genotype				Kendall's tau correlation	P value
	No genotype detected	HPV 16	HPV 16 HR	HR		
Urine HPV genotype						
No genotype detected	61 (95.3%)	1 (1.6%)	3 (3.1%)	0		
HPV 16	1 (50%)	1 (50%)	0	0.		
HPV-16 HR	0	0	5 (100%)	0	0.361	[c]0.002[s]
HR	0	0	1 (33.3%)	2 (66.7%)		

Data expressed as frequency (percentage)
c= Kendall's tau correlation
s= statistically significant

Among 74 cases, 5 cases were detected as HPV 16 and HR (co-injection) in both cervical and urine sample, 2 cases as HPV 16 in both cervical and urine samples, 2 cases as only HR type in both cervical and urine sample. The kendall's correlation of agreement was 0.361 and a significance of 0.002 in Table 6.

5. Discussion

Our study aimed to compare the efficacy of urine and cervical samples for HPV genotyping, with a total sample size of 74 participants. This comparison is crucial given the potential for less invasive testing methods in HPV screening, particularly in resource-limited settings.

The study cohort's mean age was 40.07 years (SD = 7.58), with a majority (54.1%) falling into the 35-44 year age range. This demographic profile aligns with Ducancelle et al. and Franciscatto et al., which also reported similar age distributions in their studies. [15, 16] The marital status data showed that 89.2% of participants were married, and over 70% were from lower-middle-class backgrounds. These findings reflect socioeconomic patterns observed in similar research, reinforcing the relevance of our study population.

Early marriage and childbirth were notable in our cohort, with 67.6% of participants marrying before the age of 18 and 39.2% having their first live birth before 18. These statistics are consistent with Padhy et al., who reported comparable early marriage and childbirth patterns. [17] The predominance of multipara (75.7%) among participants reflects broader trends observed in other studies, where multiple childbirths are common in similar demographic groups. [18]

Our study found that 98.6% of participants had only one sexual partner, and 80.1% had a normal vaginal delivery. These findings align with Padhy et al., who observed similar rates of sexual partner exclusivity and delivery methods. [17] Smoking rates in our study (25.7%) are consistent with other regional studies from Singh et al., which report similar prevalence among women in comparable socioeconomic backgrounds. [19]

Our results indicate that cervical samples were more effective in detecting HPV (17.56%) compared to urine samples (5.40%). This finding is consistent with Cho et al. and Cómbita et al., who found cervical samples to be more reliable for HPV detection. [20, 21] This conclusion is supported by Yang et al., who reported that cervical samples generally offer higher detection rates and more reliable results compared to urine samples. [22]

The agreement analysis revealed a kappa value of 0.743, indicating moderate agreement, and a Kendall's tau value of 0.361, suggesting a tendency toward disagreement. This is in line with Sahasrabuddhe et al., who reported moderate agreement and high sensitivity for urine-based HPV tests [23].

HPV 16 and high-risk (HR) types were detected in both samples in 5 cases, HPV 16 alone in 2 cases, and HR types alone in 2 cases. The Kendall's tau correlation of 0.361 with a significance of 0.002 indicates moderate correlation, suggesting that while there is some agreement between urine and cervical samples, discrepancies do exist. Our findings align with Bernal et al., who reported higher HPV detection rates in urine samples compared to cervical samples, though these differences were not statistically significant. [24] Specifically, HPV-16 was detected more frequently in cervical samples, highlighting variability in genotype detection between sample types.

Bernal et al., found that HPV-16 was often detected in cervical samples but not always in urine samples, which is consistent with our findings [24]. This variability underscores the importance of considering sample type in HPV testing and suggests that while urine samples can be a useful adjunct, they may not replace cervical samples entirely. [25]

Recent studies have continued to explore the efficacy of urine-based HPV testing. For example, Tranberg et al., reported a sensitivity of 95% for urine-based HPV detection, which is similar to our study's findings but with a slightly lower agreement level [26]. Similarly, Yang et al., found moderate agreement and high sensitivity for urine-based HPV tests, reinforcing the notion that while urine testing is promising, it may not yet match the reliability of cervical samples. [22, 27]

Cho et al. and Cómbita et al., both observed significant associations between cervical HPV detection and the presence of HPV genotypes, further supporting our findings that cervical samples are generally more reliable. [20, 21] However, studies like those by Sahasrabuddhe et al. and Bernal et al., have highlighted that urine-based HPV testing can still provide valuable information, particularly when access to cervical sampling is limited. [23, 24]

6. Limitations of the Study

The study's relatively small sample size of 74 participants may restrict the generalizability of the findings. Increasing the sample size could enhance the robustness of the results and the statistical power of the analysis. Additionally, the use of purposive sampling might introduce selection bias, as participants were not randomly chosen. The focus on high-risk HPV types (16, 18, and others) may have missed other potentially significant HPV genotypes. Future research should include a wider range of HPV types for a more comprehensive evaluation.

7. Conclusion

In conclusion, while our study confirms that cervical samples remain more effective for HPV detection compared to urine samples, urine-based tests offer a less invasive alternative that could complement traditional methods. Future re-

search should continue to refine urine-based testing methodologies to improve their reliability and accuracy.

Abbreviations

BSMMU	Bangabandhu Sheikh Mujib Medical University

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Ethical Approval

The study was approved by the Institutional Ethics Committee.

Author Contributions

Fatema Nihar: Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

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Jannatul Ferdous: Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

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Md. Mostafizur Rahman: Data curation, Formal Analysis, Methodology, Software, Visualization, Writing – review & editing

Conflicts of Interest

The authors declare no conflicts of interest.

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