Research Article

High-risk Human Papillomavirus Detection in Self-Sampling compared to Clinician Sampling : A Cross-Sectional Study

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Abstract

Objective: To evaluate the diagnostic accuracy of high-risk human papillomavirus (HPV) DNA detection using the Hybrid Capture II assay in self-collected samples compared with clinician-collected samples.

Methods: This cross-sectional diagnostic accuracy study enrolled women with abnormal cervical cytology or positive visual inspection with acetic acid (VIA) results at Dr. Cipto Mangunkusumo General Hospital, Jakarta. Participants performed self-sampling followed by clinician-collected sampling. High-risk HPV DNA was detected using the Hybrid Capture II assay. Clinician-collected samples served as the reference standard.

Results: High-risk HPV prevalence was 44.9%. Self-sampling showed substantial agreement with clinician-collected sampling ($\kappa = 0.76$), with 88.41% accuracy, 80.65% sensitivity, 94.74% specificity, 92.59% PPV, and 85.71% NPV.

Conclusion: Self-sampling demonstrated comparable diagnostic performance to clinician-collected sampling and may be a reliable alternative for improving cervical cancer screening coverage in Indonesia.

Keywords: cervical cancer screening; clinician-collected sampling; high-risk human papillomavirus; Hybrid Capture II; self-sampling.

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INTRODUCTION

Cervical cancer is the fourth most common cancer among women worldwide, following breast, colorectal, and lung cancers. According to the World Health Organization (WHO), cervical cancer remains a major public health concern, particularly in low- and middle-income countries [1]. Based on GLOBOCAN 2022 estimates from the International Agency for Research on Cancer (IARC), cervical cancer accounted for approximately 662,000 new cases and 348,000 deaths globally, representing one of the leading causes of cancer-related mortality among women [2]. In Indonesia, cervical cancer is the second most common cancer among women, with a substantial disease burden despite the availability of preventive strategies [3]. Previous studies in Indonesia have also evaluated HPV DNA self-sampling using Hybrid Capture II assays[4,5].

Persistent infection with high-risk human papillomavirus (hr-HPV), particularly HPV types 16 and 18, is the primary cause of cervical cancer. Therefore, the WHO recommends primary prevention through HPV vaccination before sexual debut and secondary prevention through cervical cancer screening using visual inspection with acetic acid (VIA), cytology, or hr-HPV DNA testing[1].

The Hybrid Capture II assay is a United States Food and Drug Administration (FDA)-approved method for detecting hr-HPV DNA and has been widely used in cervical cancer screening programs. Compared with cytology alone, hr-HPV DNA testing provides higher sensitivity for detecting high-grade cervical intraepithelial neoplasia (CIN2+) and offers a high negative predictive value, allowing longer screening intervals for women with negative test results[1].

A meta-analysis including 37 studies involving

18,516 women from 24 countries demonstrated high acceptability of self-sampling and a preference for self-sampling over clinician-collected sampling. Self-sampling also reduces financial and logistical barriers while improving privacy and autonomy, thereby increasing participation in cervical cancer screening programs [6]. Furthermore, HPV testing using self-collected samples has been shown to effectively increase screening uptake among underscreened women and is recommended as an alternative screening strategy in appropriate populations[7,8].

These challenges are also encountered in Indonesia, where cervical cancer screening coverage remains low. According to the Indonesian Ministry of Health, the national cervical cancer screening coverage was only approximately 7.5%, indicating that a large proportion of eligible women have never undergone screening [3]. Considering Indonesia's diverse geographical, cultural, and socioeconomic conditions, self-sampling may provide a practical approach to improve screening accessibility and participation. Therefore, this study aimed to evaluate the diagnostic accuracy of hr-HPV DNA detection using the Hybrid Capture II assay in self-collected samples compared with clinician-collected samples [4,5]. The findings are expected to provide evidence supporting the implementation of HPV self-sampling as an alternative strategy in Indonesia's national cervical cancer screening program.

METHODS

This was a crossover diagnostic clinical study in Ciptomangunkusumo Hospital's Colposcopy Oncology Policlinic. The study was conducted between January and May 2018. The total sample consisted of 70 subjects who were consecutively selected and participated in vaginal swab self-sampling and cervical Clinician sampling. This study was approved by the Medicine Faculty University of Indonesia Ethics Committee (registration number 783/UN.2F1/ETIK/2017). The inclusion criteria were all patients who were referred to Ciptomangunkusumo Hospital with Visual Inspection with Acetic acid (VIA) - positive or abnormal pap smear results. Sampling was performed using a cytobrush from Digene® and high-risk HPV DNA examination using Hybrid Capture II methods from Qiagen Labs. Clinician sampling results were used as the reference standards.

Cross-tabulation was analyzed using SPSS statistical program version 22. The variables of self-sampling and Clinician sampling were analyzed using the chi-square formula and Fisher's test if all prerequisites were met. The significance limit (α) was set to 5%. The agreement of the results in percentages of discordant pairs between self-sampling and Clinician-sampling was calculated. The strength of the agreement was categorized into six levels according to the κ statistics, where $\kappa < 0$ was poor, 0 to 0.20 was slight, 0.21 to 0.40 was fair, 0.41 to 0.60 was moderate, 0.61 to 0.80 was substantial, and 0.81 to 1.00 was almost perfect. The sensitivity and specificity of self-sampling were estimated and calculated based on the hr-HPV DNA results from Clinician sampling. Thus, we made a stratified analysis with adjusted data from all abnormality Pap smears only and calculated sensitivity and specificity based on an abnormal pap smear.

RESULTS

Characteristics of Study Subject.

The mean age of the subjects was 41.9 years (SD 10.6), with the largest age group being 40–49 years (37.7%). The median age at menarche was 13 years (range 10–18), and the mean age at first sexual intercourse was 23 years (SD 3.9). Most subjects (89.9%) were married once, 56.5% were multiparous, and 43.5% did not use contraception (Table 1).

Table 1. Characteristics of Study Subject

Characteristic	Total (N=69)
Age (year, mean (SD)	41,89 (10,57)
Age group, n (%)	
20-29 year	10 (14,5)
30-39 year	19 (27,5)
40-49 year	26 (37,7)
50-59 year	10 (14,5)
≥60 year	4 (5,8)
Menarche age (year), median (min-max)	13 (10-18)
First sexual intercourse (year), mean (SD)	23 (3,9)
Marital status	
Single	2 (2,9)
1 time	62 (89,9)
2 times	5 (7,2)
Parity History	
Nulliparous	13 (18,85)
Primiparous	13 (18,85)
Multiparous	39 (56,5)
Grandemultiparous	4 (5,8)

Sexual partner	
0	1 (1,4)
1	63 (91,4)
2	2 (2,9)
3	3 (4,3)
Sexual intercourse frequency, median (min-max)	4 (0-12)
Contraception methods	
Not using	30 (43,5)
Condom	1 (1,4)
IUD	19 (27,5)
Pill	4 (5,8)
Implant	1 (1,4)
1-month injection	2 (2,9)
3 months injection	11 (15,9)
Tubectomy	1 (1,4)

Subject Symptoms Most subjects did not report symptoms during sexual intercourse; only 14.5% experienced post-coital bleeding. Vaginal discharge was reported by 27.5%, and 21.7% had discharge accompanied by foul odor. One subject (1.4%) had uterine prolapse, while 49.3% reported no genital symptoms.

HPV Infection Risk Factors Risk factors included multiple partners (8.7%), smoking (4.3%), alcohol use (1.4%), and drug use (1.4%). The majority (92.8%) reported no additional risk factors.

Age Group-specific HPV DNA Results The highest prevalence of hr-HPV DNA positivity was found in the 40–49 year age group, with 11 subjects (40.7%) positive in self-sampling and 12 subjects (38.7%) positive in clinician sampling. Other age groups showed lower positivity rates: 20–29 years (18.5% vs 16.1%), 30–39 years (18.5% vs 22.6%), 50–59 years (14.8% vs 16.1%), and ≥60 years (7.5% vs 6.5%).

Hybrid Capture HPV DNA II Results High-risk HPV DNA was detected in 44.9% (31/69) of subjects in clinician sampling and 39% (27/69) in self-sampling. Twenty-five subjects (36.2%) were positive in both methods, while 36 (52%) were negative in both. The agreement between methods was substantial, with $\kappa = 0.76$ (Table 5).

Table 2. Crosstabulation Hybrid Capture HPV DNA II self-sampling and Clinician sampling

		Clinician sampling Hybrid Capture DNA II		Total	Agreement test (Kappa)
		+	-		
Self-sampling	+	25 (92,6%)	2 (7,4%)	27	0,763
Hybrid Capture DNA II	-	6 (14,3%)	36 (85,7%)	42	p<0,01
		31	38	69	

Self-sampling showed sensitivity of 80.7% (95% CI: 63.7–90.8) and specificity of 94.7% (95% CI: 82.7–98.5) compared to clinician sampling. The positive predictive value was 92.6% (95% CI: 76.6–97.9) and the negative predictive value 85.7% (95% CI: 72.2–93.3).

Stratified Analysis (Pap Smear Abnormalities) Among 55 subjects with abnormal Pap smears, self-sampling had sensitivity of 81.5% (95% CI: 63.3–91.8) and specificity of 96.4% (95% CI: 82.3–99.4). The PPV was 95.7% (95% CI: 79.0–99.2) and NPV 84.4% (95% CI: 78.2–94.9).

Diagnostic Performance Overall accuracy of self-sampling was 88.4%, with $\kappa = 76.3\%$. In the stratified analysis, accuracy was 89.1% and $\kappa = 78.1\%$ (Table 7).

Table 3. Diagnostic test of hr-HPV DNA with self-sampling compared to Clinician sampling

Diagnostic value	Self sampling (CI 95%)	Adjusted self sampling (CI 95%)
Sensitivity	80,65% (63,72-90,81)	81,48% (63,3-91,82)
Spesificity	94,74% (82,71-98,54)	96,43% (82,29-99,37)
Positive Predictive Value	92,59% (76,63-97,94)	95,65% (79,01-99,23)
Negative Predictive Value	85,71% (72,16-93,28)	84,38% (78,17-94,9)
Accuracy	88,41%	89,09%
Kappa	76,3%	78,12%

Factors Influencing Agreement Age, education, and parity were analyzed for their influence on agreement between self-sampling and clinician sampling. No significant correlation was found ($p > 0.05$). Agreement was high across all subgroups: age <40 years (87.5%) vs >40 years (89.2%), basic education (92.3%) vs higher education (83.3%), and multiparous (93.0%) vs nulli/primiparous (80.8%).

DISCUSSION

The mean age of the 69 subjects in this study was 41.65 years. This is consistent with a similar study in China (2020), where the average age of a patient with hr-HPV DNA positive was 39.29 years old [9]. It also fits the pathophysiology of cervical cancer that progresses slowly, and WHO recommends that women aged 30–49 years undergo cervical cancer screening at least once in their lifetime[1].

Overall, the highest prevalence of positive hr-HPV DNA was found in the age groups 30–39 years and 40–49 years (18.5% and 40.7% in self-sampling, and 22.6% and 38.7% in clinician sampling, respectively). According to previous studies, age was one of the dependent factors affecting HPV infection[5,7]. A population-based RCT conducted in Amsterdam on ~45,000 women aged 29–56 years concluded that early screening with HPV DNA testing should start at age 29[10]. Similarly, results in Chinese women revealed that the age group of 30–49 years had the highest prevalence of hr-HPV DNA at 36.4%[9].

Most participants were multiparous women (56.5%). This indicates that the risk of cervical cancer increases with parity. A study in Guatemala found that the average cervical cancer patient had parity ≥3[11]. Other risk factors such as promiscuity, smoking, alcohol consumption, and drug use were not predominant in our study. In contrast, the average age at first sexual intercourse was 23 years. WHO data show that sexual intercourse at an age younger than 20 years carries a 2.3 relative risk of cervical cancer[1].

Most subjects did not experience complaints, consistent with the fact that precancerous lesions are asymptomatic and only present clinical symptoms in later stages, making early detection difficult without proper screening[1].

This study showed strong agreement between self-sampling and clinician sampling in Hybrid Capture HPV DNA II results, with $\kappa = 0.76$ and accuracy of 88.41%. A study reported that although women liked the self-sampling HPV DNA test, they questioned its accuracy. Patient education is therefore essential to reassure and maintain interest in self-sampling[12].

Other studies found comparable prevalence and diagnostic values between self-samples and clinician samples. For HPV16/18, sensitivity and specificity in self-samples were 82.4% and 96.9%, respectively, with good concordance ($\kappa = 0.64$)[13]. In Tanzania, hr-HPV prevalence was 19.0% in provider samples and 13.8% in self-samples, with overall agreement of 90.5% ($\kappa = 0.66$)[14]. In 2019, another study showed no significant difference in diagnostic value between self-sampling and clinician sampling, with hr-HPV detected in 47% vs 46.7% of women, respectively[15]. In Thailand, HPV DNA testing with self-sampling had diagnostic value equivalent to 74.5% of clinician sampling ($\kappa = 0.46$)[16]. Similar results were reported in Finland[17].

Our study results were consistent with these findings, showing sensitivity of 80.65% and specificity of 94.74% for self-sampling compared to clinician sampling, with PPV 92.59% and NPV 85.71%. Accuracy was 88.41%. Stratified analysis in abnormal Pap smear cases showed sensitivity 81.48%, specificity 96.43%, PPV 95.65%, and NPV 84.38%, with accuracy 89%. No significant factors (age, education, parity) influenced agreement between methods. Education level and age are benchmarks for knowledge, which in turn affect attitudes toward screening. A study in India showed that attitudes toward screening depended on age, income, marital status, and knowledge, which are also influenced by government participation in community-based programs[7].

Another advantage of this study was the high prevalence of HPV DNA (44.9%), much higher than the prevalence in the United States (~20.4%) [18]. This suggests our population is high-risk, highlighting the importance of HPV vaccination and distribution in Indonesia.

CONCLUSION

This study demonstrated that HPV DNA detection using Hybrid Capture II with self-sampling showed substantial agreement with clinician sampling ($\kappa = 0.76$) and high diagnostic accuracy (88.41%). The sensitivity and specificity of self-sampling were above 80%, with positive and negative predictive values exceeding 85%, indicating that self-sampling is a reliable

alternative method for cervical cancer screening.

Stratified analysis in women with abnormal Pap smears confirmed comparable diagnostic performance, further supporting the feasibility of self-sampling in high-risk populations. No significant sociodemographic factors (age, education, parity) influenced agreement between methods, suggesting that self-sampling can be applied broadly across different groups.

Given the low coverage of cervical cancer screening in Indonesia[3], self-sampling offers a practical solution to overcome barriers related to time, cost, privacy, and cultural constraints. These findings align with international evidence[7–15] and highlight the potential of HPV DNA self-sampling to improve screening coverage and early detection of precancerous lesions.

Therefore, HPV DNA self-sampling should be considered as an alternative strategy in national cervical cancer screening programs, complementing clinician-based approaches to achieve wider population coverage and reduce cervical cancer burden.

CONFLICT OF INTEREST

There is no conflict of interest in this research

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