RESEARCH PAPER | Medical Science | Volume : 5 | Issue : 2 | Feb 2015 | ISSN - 2249-555X

Human Papillomavirus Testing in Midlife, just once !

KEYWORDS: AyuGen, HPV, Cancer cervix, Dysplasia, Cervical Intraepithelial Neoplasia

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ABSTRACT *OBJECTIVES - Study to compare & correlate PAP smear & Colposcopy with digene Human Papilloma Virus (HPV) test (Hybrid Capture-II).*

METHODS- Study conducted from 1st Jan 2012 to 30 July 2012 at Department of obstetrics & Gynaecology Shrimati Kashibai Navale Medical College & General Hospital Narhe Pune.

Present study is a prospective & ongoing. A total of 183 women, who were ready to pay for the HPV test formed the material. All the study subjects underwent PAP smear, colposcopy & HPV testing by digene HPV test (Hybrid Capture-II). HPV testing has been presumed to be the most sensitive and specific test for detection of cancer cervix. The sensitivity and specificity of PAP smear and colposcopy were compared to that of HPV testing.

Results: The sensitivity and specificity of PAP has been found to be 30% and 79.7% respectively. And that of Colposcopy has been found to be 90% and 91.3% respectively as compared to those of HPV testing.

CONCLUSION- Colposcopy correlated better with HPV as compared to PAP.

INTRODUCTION

Three most common cancers among Indian women are Cervical (17.1%), stomach (14.1%) & then breast (10.2%)[1]

Prevention of cervical cancer by early detection using once-only screening test (HPV test) is now possible. The sensitivity of Digene HPV test is about 94% [2,3]. Now a days this is the only test recommended after 30yrs of age.

The purpose of present study is to compare sensitivity & specificity of PAP smear & Colposcopy to that of HPV testing. It happens so often in our practice that a cervix which bleeds on touch or a woman with Post coital bleeding we are unable to get proper slide for PAP. Thus HPV testing with its very high negative predictive value comes handy.

MATERIAL & METHODS

183 women attending the Gynaec OPD, who consented for the study, formed the material.

INCLUSION CRITERIA

Any lady who walks in to Gynaecological OPD and willing to pay for test and are above 30yrs of age.

EXCLUSION CRITERIA-

- Women who are under 30yrs of age.

- Women who do not consent for the test

Sample collection center:
Shrimati Kashibai Navale Medical College (SKNMC), Pune

Patients with gynaecological problems underwent the following :

- Colposcopic examination of the cervix
- Pap test
- Histopathology
- Patient follow-up

Testing centre:
AyuGen Biosciences Private Limited, Pune

- The cervical sample collected using DNA Pap C ervical was processed for *digene* hc2 HPV test.
- Results were interpreted and generated.
- Patient's data was processed and analyzed using statistical methods.

STUDY DESIGN

All the women who consented for the study were subjected to HPV testing after explaining to them that this is a screening test for cancer cervix. When the women came for HPV testing, they were also subjected to PAP smear examination and colposcopy.

The women who were PAP negative and HPV negative were advised to follow up every 5 years. The women who were PAP positive and/or HPV positive underwent colposcopically directed biopsy. All the findings were correlated. All the women who were either PAP positive or HPV positive were advised to follow up every year.

RESULTS

A total of 10 cases (5.5%) were positive for *digene* HPV test out of 183 women studied.

Table 1 shows histopathologic findings and PAP result of HPV positive women. Five out of 7 women who tested positive on HPV test had cervical neoplasia. PAP was less sensitive and less specific in diagnosing cervical neoplasia.

Table 2 shows PAP results in those who were positive and negative on HPV testing. This reveals that PAP is less sensitive and less specific.

Table 3 shows Colposcopy findings in those women who tested positive and negative on HPV testing. The sensitivity and specificity of colposcopy in diagnosing cervical neoplasia is 90% and 91.3% respectively.

Volume : 5 | Issue : 2 | Feb 2015 | ISSN - 2249-555X

DISCUSSION

The HPV positivity in the present study is 5.5%.

As we find in our daily practice PAP has failed us many times. When cervix looked suspicious, reports came as inflammatory smear. Women having problem of postcoital bleeding had bloody smears so reporting of "bloody slide" and "slide not well made" is quite common. Endocervical brush, again gives us bloody smears. Thus sensitivity of cervical cytology for diagnosis of cervical neoplasia by PAP appears less. This is supported by many studies like Mexican study [5] showing only 40% sensitivity of cervical cytology as against ours which stood at 30%, for detecting histologically confirmed CIN2/3 cases. A study conducted by Dr. Basu [6], showed cytological sensitivity of 29.5%. Thus Availability of HPV testing with hybrid capture-II technology giving a very high negative predictive value of 99.4% [6] has definitely placed us at confident decision making process.

The incidence of Positivity for HPV is 5.5% in our study. Shankarnarayanan et al, in their screening for cervical cancer in rural India by HPV testing had incidence of 10.3%.[7] The detection rates were similar for both Cytology and HPV testing as against our study where PAP smear testing showed less sensitivity and specificity. The study by Gravitt PE *et al*, which was done in a peri-urban community in Andhra Pradesh, India, showed HPV DNA testing was both more sensitive and specific than PAP cytology and VIA[8].

Our impression is as follows,

PAP smear has several problems such as,

- Ambiguity(ASCUS- Atypical Squamous Cells of Unknown Significance)
- Low sensitivity.
- High subjective variation.
- Difficult in bleeding patients, and
- It does not tell the cause.

Colposcopy, although very good diagnostic tool, has few problems such as,

- Difficult when patient is bleeding.
- Subjective variation.
- Takes time and requires expertise with relevant experience.
- Not feasible as primary screening test.

Merits of digene HPV test are,

- Currently Gold Standard with over 94% median sensitivity.
- It has high negative predictive value (99.7%)
- It is an objective test.
- It has been tested in Indian population successfully.
- If positive, predicts risk of cervical cancer for more than 15 years. If negative, warrants repeat test after every 5 years as against every year in case of PAP smear test.

Conclusion

- PAP cytology was less sensitive and specific than HPV testing.
- HPV testing correlated well with colposcopy findings.
- The HPV test helped in better patient management who had cervical abnormalities and doubtful/abnormal cytology or colposcopy findings (due to its high NPV).
- The HPV test was also useful in cases where it was difficult to do PAP & colposcopy.

Table 1: showing histopathology finding and PAP results of women who were HPV positive

Histopathology result	No of women	PAP Result
Cancer Cervix IIB	2	Inadequate
Carcinoma in situ	2	HSIL
Cervical intraepithelial Neoplasia III	1	LSIL
Normal	2	LSIL
Dropouts for Biopsy	3	LSIL, HSIL & Negative

Table No 2 – Showing PAP findings of HPV negative and HPV positive women

HPV	PAP Results						
HPV result	HSIL	Inadequate	LSIL	Negative	Total	Sensitivity	Specificity
Negative	9	9	17	137	172	30%	79.7%
Positive	3	2	4	1	10		
Total	12	11	21	138	182		

Table No 3: showing Colposcopy findings in HPV positive and HPV negative women.

HPV results	Abnormal	Doubtful	Normal	Unsatisfactory	Total	Sensitivity	Specificity
Negative	11	3	158	1	173	90%	91.3%
Positive	7	2	1	-	10		
Total	18	5	159	1	183		

Volume : 5 | Issue : 2 | Feb 2015 | ISSN - 2249-555X

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