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Original Research Paper

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COMPARISON OF HIGH RISK HUMAN PAPILLOMA VIRUS DNA TESTING AND PAP SMEAR CYTOLOGY FOR SCREENING OF CERVICAL CANCER IN HIGH RISK GROUP OF PATIENTS

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ABSTRACT

Objective: To compare high risk HPV DNA testing and conventional pap smear cytology for screening of cervical cancer in high risk group of patients.

Methods: A hospital based prospective, comparative and observational study conducted in department of Obstetrics and Gynecology, Government medical college, Kota on 150 eligible cases who were sexually active between age group 30-65 years. All eligible women underwent Pap's smear testing and HPV DNA testing from ecto-cervix and endo-cervix for screening of carcinoma cervix.

Result: Out of all 150 cases, 11 cases were positive for HPV DNA testing. Pap's smear was positive in 29 cases. ASCUS were 14%, LSIL were 2.67%, HSIL were 2% and SCC 0.66%.all LSIL, HSIL cases were HPV positive and all 21 ASCUS positive cases were HPV DNA test negative. Colposcopy was done in 11 HPV DNA positive cases, we found that 3 were having grade 1 colposcopy and 4 were having grade 2 colposcopy and 4 were having grade 3 colposcopy and all 4 slides were cytological positive (HSIL).colposcopy was done for Pap's smear positive cases (ASCUS and higher).Out of 4 LSIL cases, 2 were grade 1 and 2 were grade 2 and all HSIL were showing grade 3 colposcopy. In HPV positive cases, colposcopy was significant in 72.72% cases and in Pap's smear positive cases colposcopy was significant in 28.57% cases, we found 3 HPV positive and cytology negative cases.

Conclusion: In comparison to conventional Pap's smear, HPV DNA test is more superior for detection of missed cervical abnormalities and women diagnosed as HR -HPV DNA positive needs close surveillance and treatment as required.

KEYWORDS : Pap's smear, HPV DNA testing, screening of carcinoma cervix

INTRODUCTION:

Cervical cancer accounts for 10% of all female cancers, making it fourth leading cause of cancer death in women, the disease is common enough to justify mass screening. Early detection and appropriate treatment are possible if robust screening is cervical cancer.

Early cervical epithelial changes can be identified by a Pap smear test, which is the primary screening test for detection of precancerous cervical changes. Overall sensitivity of pap's test in detecting high grade squamous intraepithelial lesion is 70-80%.

Infection of uterus and cervix with high risk HPV is associated with development of cervical cancer. and HPV DNA is detected virtually in all cervical cancer so new screening technique of detecting HPV DNA have raised hopes and expectation for better prevention of disease .

In 2014 food and drug administration approved HPV DNA test as primary cervical cancer screening test.

In august 2018, updated screening guidelines were released by the United States preventive services task force.

- Women ages 21 to 29 should be screened with a Pap test every 3 years.
- Women ages 30 to 65 should be screened with any of three tests:
- Every 5 years with high risk HPV testing alone.
- Every 3 years with Pap test alone

Women with certain risk factors may need to have more frequent screening or to continue screening beyond age 65.these risk factors include:

- Being infected with HIV.
- Being immunosuppressed.
- Having been exposed to diethylstilbestrol before birth.
- Having been treated for a precancerous cervical lesion or cervical cancer.

Screening for cervical cancer is not recommended for:

- Women younger than 21 years.
- Women older than 65 years who have had adequate prior screening, with normal results.
- Women who have had total hysterectomy for benign lesion and no history of high grade cervical lesion or cervical carcinoma.

There is a need to spread cervical cancer screening awareness programs, educate women regarding the symptoms of cancer, and motivate them to visit the hospital for a cancer screening .thus, we have to strengthen our health services and healthcare system to include screening at primary health centers.

OBJECTIVE:

To compare high risk HPV DNA testing and conventional pap smear cytology for screening of cervical cancer in high risk group of patients.

MATERIAL AND METHODS:

This study was hospital based comparative and observational, conducted in department of obstetrics and gynecology, Government Medical College, Kota on 150 eligible women.

Inclusion criteria:

All sexually active females between 30-65 years of age in high risk group.

Exclusion criteria:

1. Diagnosed case of cancer cervix
2. Females who had undergone total hysterectomy
3. females having acute bleeding, infective discharge or urinary tract infection

Samples of HR-HPV DNA and Pap's smear were taken in all eligible and consenting women in same sitting.

In HPV DNA test (done by hybrid capture 2 technique) a titre of >=1pg/ml was considered positive. Results of pap smear were analyzed using Bethesda classification. ASCUS and any greater abnormality was considered positive.

hybrid capture 2 is an assay that uses a pooled mixture of probes to detect 13 of the high risk HPV types(16,18,31,33, 35,39,45,51,52,56,58,59,68) but not type specific. This is FDA approved test for HPV detection.

Table1: Demographic profile of study population

Profile	Numbers	%
Age		
30 To 49 Yrs.	147	98.0
>49 Yrs.	3	2.0
Residence		
Rural	76	50.7
Urban	74	49.3
Literacy		
Literate	89	59.3
Illiterate	61	40.7
Socio Economic Status		
Upper	8	5.4
Middle	92	61.3
Lower	50	33.3
Parity		
Nullipara	1	0.7
Primipara	11	7.3
Multipara	138	92.0

Table2: Cases according to present complaints

Present Complaints	Present No.	%	Absent No.	%
Discharge P/V	120	80.0	30	20.0
Post Coital Bleeding	21	14.0	129	86.0
Painful Coitus	37	24.7	113	75.3

Table 3: Cases according to method of contraception

Method of Contraception	NO(n=86)	%
Barrier	29	33.7
OPC's	16	18.6
IUCD	10	11.6
Permanent	31	36.0
Total	86	100.0

Table 4: Cases according to high risk factors

High Risk Factors	Numbers	%
Age At Coitus<18 Yrs.	27	18
First Conception<20 Yrs.	38	25
Multiple Sexual Partners	0	0
Low Socio Economic Status	50	33
Smoking	10	6.7
Multiparty	100	67
OCPS	16	19

Table 5: Distribution of cases According to HPV- DNA tests Results

HPV-DNA test result	No. of cases	%
Positive	11	7.3
Negative	139	92.7
Total	150	100.0

Table 6: Correlation of Pap's smear Findings with Colposcopic Grading

Pap's Smear	Colposcopic Grading		
Grading	1st	2nd	3rd
ASCUS	21	0	0
LSIL	2	2	0
HSIL	0	0	4
total	23	2	4

Table 7: Correlation between HPV DNA Test and Colposcopic Grading:

HPV DNA	Colposcopic Grading		
Test	1st	2nd	3rd
Positive (11)	3	4	4
Negative (139)	0	0	0
Total (150)	**3**	**4**	**4**

Table 8: Comparison of HPV-DNA Test Result with Pap's smear Grading:

HPV – DNA Test Result	Pap'S Smear Garding (Bethesda System)					
	Normal	ASCUS	ASH-H	LGSIL	HSGIL	SCC
Positive (11)	3	0	0	4	3	1
Negative (139)	118	21	0	0	0	0
Total (150)	121	21	0	4	3	1

Table 9: Colposcopy Grading in HPV and Pap's Smear Positive Cases:

	Pap's Smear Garding				
Colposcopic Grading	HPV	ASC-US	LSIL	HSIL	SCC
1st	3	21	2	0	0
2nd	4	0	2	0	0
3rd	4	0	0	3	1
Total	11	21	4	3	1

RESULTS:

Out of all 150 cases, 11 cases were positive for HPV DNA testing. Pap's smear was positive in 29 cases. ASCUS were 14%, LSIL were 2.67%, HSIL were 2% and SCC 0.66%.all LSIL, HSIL cases were HPV positive and all 21 ASCUS positive cases were HPV DNA test negative. Colposcopy was done in 11 HPV DNA positive cases, we found that 3 were having grade 1 colposcopy and 4 were having grade 2 colposcopy and 4 were having grade 3 colposcopy and all 4 slides were cytological positive (HSIL).colposcopy was done for Pap's smear positive cases (ASCUS and higher).Out of 4 LSIL cases, 2 were grade 1 and 2 were grade 2 and all HSIL were showing grade 3 colposcopy. In HPV positive cases, colposcopy was significant in 72.72% cases and in Pap's smear positive cases colposcopy was significant in 28.57% cases, we found 3 HPV positive and cytology negative cases.

DISCUSSION:

In our study most of women were in age group 30-49 years,from rural area,from middle class society, literate and multipara.Most of women came with white discharge.Barrier method was most common used contraceptive method, Multiparity was high risk factor commonly seen.

HPV DNA was positive in 11 cases out of 150 and out of these 11 cases 3 were having normal Pap smear.and colposcopy was also significant in HPV DNA positive cases. so HPV DNA test is more sensitive than Pap smear according to our study.

Recent Canadian trial (Aug 2018) published in journal of American medical association also concluded that HPV testing is more sensitive in screening for risk of cervical cancer than pap smear.

HPV FOCAL (2008-2012, followed in 2016, published in 2018) was largest clinical trial in North America. Goal of this study was to determine if a screening test for HPV was better than the standard pap smear as primary screening for cervical cancer .conclusion of study was four year after receiving the first test, significantly fewer high grade pre-cancer cervical changes detected in women who had HPV testing than in women who had cytology testing and cervical pre-cancer changes was found earlier in women who had HPV testing, which provided opportunity for earlier treatment.

The study done by Mark Schiffman, national cancer institute, Bethesda, Maryland interpreted that HPV testing alone as a cervical cancer screening option would be nearly as effective as combination HPV cytology co-testing

Dr. Schiffman and colleagues 2017 examined screening

histories that preceded detection of both cervical cancer and pre-cancer to assess relative contributions of Pap's and HPV test and found that HPV testing appeared more sensitive for detecting localized cancer and marginally less sensitive for distant cancer vs cytology.

CONCLUSION:

It is proven that 80% cervical cancer can be prevented by well-organized high quality screening programs, on the other hand in several countries decrease in cervical cancer incidence of only 40-65% has been documented. There are still countries with very high morbidity and mortality rates from this disease. It suggests various shortcomings of cervical cytology like relatively low sensitivity of single Pap, as well as incomplete coverage of population in screening program and follow up failures.

In comparison to conventional Pap's smear, HPV DNA test is more sensitive for detection of missed cervical abnormalities, women diagnosed as HR -HPV DNA positive needs close surveillance and treatment as required. Only drawback is that HPV tests are less specific. In most cases HPV infections clears spontaneously and lead to more unnecessary referrals, however negative HPV test is more reassuring than negative cytology. Cytological test has greater chances of being false negative which lead to delay in receiving appropriate treatment.

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