Original Article

Distribution of Genital HPV Infection in Women of Reproductive Age Group in a North Indian City Screened for Cervical Cancer by Pap Smears

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ABSTRACT

Introduction: Carcinoma cervix is one of the leading causes of morbidity and mortality worldwide but has a benefit of being identified at a precancerous stage before the invasion starts and hence is amenable to early detection and treatment. HPV infection as the etiological agent of carcinoma cervix and its precursor lesions is well established. High risk HPV (16,18) is most commonly associated with invasive cervical carcinomas worldwide. The aim of this study is to find the prevalence of genital HPV infection in women of reproductive age group in a north Indian city that were screened for cervical cancer by Pap smears.

Methods: The was a prospective study conducted from Jan 2014 to June 2016 on women in reproductive age group (< 49 years) who were screened for cervical cancer by Pap smears and HPV testing was done by PCR (sample was sent to higher center for testing). HPV was classified into high risk HPV DNA and low risk HPV DNA. Proper informed consent was taking from the participating women.

Results: A total of 1549 tests were received during the above period.1068 (69%) were CPS and 481 (31%) were LBC. HPV testing was carried out in 169 cases of which 20 cases were found to be positive for HPV DNA (11.8%). High risk DNA was found in 17 cases (85%) and low risk DNA in 03 cases (15%). The annual rate of HPV detection showed a gradual slight increase from 10.3% in 2014 to 12.8% in 2016. Abnormal cytological findings were detected only in 5/20 cases (25%), which were subjected to HPV DNA testing pressing home the advantage of HPV testing in the reproductive age group.

Conclusion: The study still establishes the important role of HPV as an etiological agent in carcinoma cervix and the need to get HPV testing included in the cervical cancer-screening program so as to diagnose the precursor lesions at an early stage leading to early treatment and reduction in morbidity and mortality from a world wide prevalent and preventable cancer.

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Introduction

Carcinoma cervix is one of the leading causes of morbidity and mortality worldwide, more so in the developing countries. However one major advantage for clinicians is that this is one cancer that can be identified at a precancerous stage before the invasion starts and hence is amenable to early detection and treatment. Papanicolaou (Pap) smear was introduced way back in 1940 and has successfully led to a reduction in cervical carcinoma load.[1,2]

Initially introduced as Conventional pap smear (CPS), it is gradually being replaced by Liquid based cytology (LBC) with the latter offering substantial advantages over CPS most important one being the ability to use the same sample for Human Papilloma Virus (HPV) DNA testing. This negates the need for reexamination and resampling for HPV testing in case it needs to be done.[1,3]

HPV infection as the etiological agent of carcinoma cervix and its precursor lesions is well established and is one of the commonest sexually transmitted infections. Although there are huge variations in the genotypes of HPV, high risk HPV (16,18) are most commonly associated with invasive cervical carcinomas worldwide. Other factors i.e. use of oral contraceptives, high parity, smoking also play their role. HPV infection occurs in most of the sexually active people at some stage of life but usually this is a transient infection and subsides gradually. However in a few women, this persists possibly due to impaired immunity, which slowly but surely affects the cervical epithelium and can lead to cervical intraepithelial lesions and in later stages invasive cervical carcinoma in case it is not detected and treated at an early stage.[1,2,3]

According to updated guidelines, women aged 21-29 years should be screened with a Pap test every 3 years. Women between 30-65 years can then be screened every 5 years with Pap and HPV co-testing or every 3 years with Pap test alone. For women younger than 30 years, HPV screening does not seem to confer any additional benefit. There also seems to be no benefit in reducing cancer incidence and mortality by screening women < 21 years of age. Same applies to women > 65 years or those who underwent hysterectomy provided they were not diagnosed with a high-grade precancerous lesion. Thus, no screening needs to be done in such women. [4]

The aim of this study is to find the prevalence of genital HPV infection in women that were screened for cervical cancer by Pap smears.

Materials and Methods

The was a prospective study conducted from Jan 2014 to June 2016 done in a private medical laboratory on women in reproductive age group (<49 years) who were screened for cervical cancer by Pap smears and HPV testing was done by Polymerase chain reaction (PCR) (sample was sent to higher center for testing). The pap smears were collected either as CPS or by LBC. HPV DNA co-testing was done as and when asked by the clinician and if the patient agreed to be a part of the study. Informed consent was taken from the patients. The detection rates of HPV by PCR were expressed as percentages. HPV was classified into high risk HPV DNA and low risk HPV DNA. Proper informed consent was taking from the participating women.

Pregnant women, women that had undergone hysterectomy and those >49 years were excluded from the study.

Results

A total of 1549 tests were received during the above period.1068 (69%) were CPS and 481 (31%) were LBC. The age of the patients ranged from 23 to 49 years. HPV testing was carried out in 169 cases of which 20 cases were found to be positive for HPV DNA (11.8%).High risk DNA was found in 17 cases (85%) and low risk DNA in 03 cases (15%) (Table 1). High risk DNA were type 16 (11 cases), type 18 (3 cases), type 35 (1 case), type 45 (1 case) and type 39 (1 case) (Table 2). Low risk DNA were type 6 (2 cases), and type 11 (1 case) (Table 3). Age wise distribution of genital HPV detection was 1 case (<25 years) (5%), 12 cases (25-34 years) (60%) and 7 cases (35-49 years) (35%) (Table 4).

The annual rate of HPV detection showed a gradual slight increase from 10.3% in 2014 to 12.8% in 2016 (Table 1). Abnormal cytological findings were detected only in 5/20 cases (25%) (Table 1), which were subjected to HPV DNA testing pressing home the advantage of HPV testing in the reproductive age group. Out of these, 4 were detected on LBC and only 1 on CPS. This further proves the superiority of LBC over CPS in diagnosing intraepithelial lesions of cervix.

Table 1: Year wise rates of HPV detection.

Period	Cases for HPV screening	Abnormal findings in Cytology	HPV detected in
Jan 2014-Dec 2014 (1 year)	58	1 (CPS)	6 (10.3%)
Jan 2015-Dec 2015 (1 year)	72	2 (LBC)	9 (12.5%)
Jan 2016-June 2016 (6 months)	39	2 (LBC)	5 (12.8%)
Total	**169**	**5**	**20 (11.8%)**

Table 2: High risk HPV types.

TYPES	CASES DETECTED
16	11
18	03
35	1
45	1
39	1
Total	**17**

Table 3: Low risk HPV types.

TYPES	CASES DETECTED
6	2
11	1
Total	**3**

Table 4: Age distribution of 20 HPV positive cases.

Age	CASES DETECTED
<25 years	1 (5%)
25-34 years	12 (60%)
34-49 years	7 (35%)

Discussion

Cervical carcinoma is distributed through out the world and is one of the leading causes of death in females. Pap smear was developed in order to identify the women at risk while still in the precancerous stage and thus reduces the cancer mortality. HPV is a proven etiological agent for cervical carcinoma and hence its detection at an early stage of infection can be beneficial for the patient due to the early treatment given to her.[1,2,4]

In this study, HPV testing was carried out by PCR in 169 cases of which 20 cases were found to be positive for HPV DNA (prevalence rate of 11.8%). This finding correlates well with various other studies done. [1,2,3]High risk DNA detected were type 16 (11 cases), type 18 (3 cases), type 35 (1 case), type 45 (1 case) and type 39 (1 case). Low risk DNA were type 6 (2 cases), and type 11 (1 case). Most of HPV positive cases were in the age group of 25-34 years comprising 60% of the cases. This was slightly different from other studies that established the peak age of HPV infection in the younger age group.[1,2,3,5,6] This could be probably due to small sample size in our study and hence the findings need to be corroborated with study on a larger population.

The annual rate of HPV detection showed a gradual slight increase from 10.3% in 2014 to 12.8% in 2016 in this study. This could be due to more awareness among general public and increase initiative on the part of the clinicians to convince the women to undergo HPV testing.

HPV can be divided into high risk and low risk types. Major high-risk HPV types include type 16, 18, 31, 33, 35, 39, 45, 51, 52, 56,58, 68 and 69. Of these types 16 and 18 account for a majority of the infections. Similar results were obtained in our study in which both of these accounted for 14/17 (82.3%) high risk HPV detected. Low risk HPV types include type 6, 11, 40, 42, 43, 44, 53, 54, 61, 72, 73 and 81. Among these, types 6 & 11 are the commonest to cause infection, which was also seen in our study where all the low risk HPV DNA detected were either type 6 or 11.[1,2,8,9,10,11,12]

On comparing HPV results with cytology, it was found that abnormal cytological results were obtained in only 5/169 cases (2.95%) that underwent HPV detection. Of these, 1 was diagnosed on CPS and 4 on LBC. Other studies done showed comparable results to our study [2,3,11,12]This further underlines the importance of HPV testing to be incorporated in to the cervical cancer screening program and also highlights the superiority of LBC over CPS in diagnosing pre invasive cervical lesions.

There are numerous known strains of HPV and the association of high risk HPV 16,18 with invasive cervical carcinoma is well known. Most of the HPV types lead to rather innocuous lesions on the skin commonly known as warts. The high-risk strains also require other environmental, genetic and other molecular factors to aid in the transformation of normal cervical epithelium to dysplastic and ultimately invasive carcinoma. The appropriate diagnostic method can arrest the transformation at a precursor level and prevent the occurrence of full-blown invasive carcinoma cervix in susceptible women. [13] These lesions can be recognized at an early stage by various methods that include CPS, LBC and MPV testing. Among these, HPV testing is the most sensitive method as it can detect HPV strains even when recognizable morphological changes have not yet been produced to be recognized by CPS or LBC. In addition, if the technique is faulty and the squamocolumnar junction has not been adequately sampled, the precursor lesions are very likely to be missed even if they are present.[12,13] Same findings were noted in our study in which the sensitivity of HPV detection by PCR was much more as compared to LBC and CPS. This gains more importance, as now the vaccination against HPV is available which is a major advancement in the prevention against cervical carcinoma. Thus the screening methods can provide us with more conclusive data on the effectiveness of HPV vaccination for prevention against cervical carcinoma And HPV detection should be a part of it due to its effectiveness in detection of low risk and

high risk HPV strains as against CPS and LBC.[13,14,15] The higher cost of HPV detection however can be a deterrent in this especially in cost sensitive developing countries like India.

Conclusion

Although our study is limited by a small sample size and limited age group included in the inclusion criteria, the study still establishes the important role of HPV as an etiological agent in carcinoma cervix and the need to get HPV testing included in the cervical cancer screening program so as to diagnose the precursor lesions at an early stage leading to early treatment and reduction in morbidity and mortality from a world wide prevalent and preventable cancer.

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None

Competing Interests

None Declared

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