



Original Research Article

A prospective study of incidence of cervical HPV infection & its association with aetiological factors & cervical cancer in adult women of Jamnagar

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ABSTRACT

Introduction: Etiological link between cervical cancer & HPV is independent of other risk factors but their geographic variations need to be explored. Cervical cancer with profile of Sexually Transmitted Disease has consistent causal connection with persistent cervical HPV infection, so such carrier women are at High risk. Thus, study evaluate risk of HPV infection in women of Jamnagar region by exploring aetiological determinants related to their sexual life.

Aim: To explore incidence of cervical HPV infection along with its association with cervical cancer as well with commonly proposed aetiological factors in adult women of Jamnagar

Materials and Methods: The study was conducted in 2004 on random 110 women attending Gynecology out patient department of GG Hospital at MSPGMC Jamnagar by taking their cervical smear and administering them questionnaires about their sexual life. HPV infection was diagnosed based on cytopathic effects of HPV, by Microbiological staining techniques. Association of cervical HPV positive status of women in relation to common aetiological factors and carcinoma cervix were analyzed.

Results: 10.9% of women exhibited cervical HPV infection out of them 20% belonged to higher age group (50-59 years) followed by 16.6% of young age group (20-29). 15.3% of women with HPV infection were having 6 -10 years of active married life. Accordingly 18.18% HPV infected women were multipara - bearing 3 - 4 children whereas nullipara had no HPV infection. 75% of women with carcinoma cervix were positive for cervical HPV which endorse strong causal connections.

Conclusions: Study concludes that cervical HPV is prevalent in 10.9% adult women of Jamnagar region and is significantly attributable to cervical cancer. HPV positive woman have profile of sexually active life of initial years, early age at first coitus or had longer but active married life, so sexual transmission happens to be the predominant mode of HPV acquisition. Similarly, multiparity has aetiological association with positive cervical HPV. Study reflects women's HPV status at single point in time, so longitudinal observations are recommended. However, certain recommendations are made considering associated aetiological factors as guiding principle to derive HPV prevention strategy.

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1. Introduction

There were about 500 000 incident cases of and 275 000 deaths due to cervical cancer worldwide in 2002, equivalent to about a tenth of all deaths in women due to cancer.¹ The burden of cervical cancer is disproportionately high (>80%) in the developing world with its remarkable prevalence especially in the south-east-Asian regions^{2,3} Many long

clinical & epidemiological studies have supported beyond reasonable doubt the universally consistent aetiology of cervical cancer and causal connection of persistent cervical human papilloma virus infection having prominent profile of sexual transmission.^{4,5}

Human papilloma virus (HPV) are group of more than 200 closely related viruses which are non-enveloped viruses that are 55nm in diameter and have an icosahedral capsid composed of 72 capsomers enclosing a double stranded,

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circular DNA genome. Virion particles contain at least two capsid proteins. The major capsid protein constitutes 80 percent of the virion by weight and has a molecular weight of about 56000.³ Out of their two different types, Low-risk HPV types cause genital warts – bumps on the penis or vagina whereas at least 13 are cancer-causing (also known as high risk type) and amongst them two HPV types (16 and 18) cause 70% of cervical cancers and precancerous cervical lesions.⁶

Although little is known about the first stage of HPV infection, it is assumed that the virus replicative cycle begins with the entry of particles into stratum germinatum, because viral DNA has been detected in the nuclei of the basal cells. As the basal cells differentiate and progress to the surface of the epithelium, HPV DNA replicates and transcribes and viral particles are assembled in the nucleus. Ultimately, complete virions are released when dead keratinocytes are shed. Viral replication is associated with excessive proliferation of all epidermal layers except the basal layer. This process produces acanthosis, parakeratosis, and hyperkeratosis. Some infected cells undergo characteristic transformation of koilocytosis.³

Cervical HPV infections do not cause any symptoms or disease & usually clear up spontaneously without any intervention within a few months after acquisition. (About 90% clear within 2 years)⁷ although, a small proportion of infections with certain types of HPV can persist and progress to cancer in span of about 10-30 years. Thus, in practical terms, persistent presence of HPV has been identified as the “necessary cause” of a cervical cancer which is theoretically considered a preventable disease.

Developing countries where prospects for treatment of cervical cancer may be poor, resulting in a higher rate of death should resort to cervical cancer screening among women who have no symptoms and may feel perfectly healthy. Such screening is recommended for every woman from aged 30 to 49 at least once in a lifetime and ideally more frequently to detect pre-cancerous lesions, which can be easily treated to prevent or cure potential cancer.

Study was done as random single point cervical smear screening to know the incidence of cervical HPV positive status of adult women of Jamnagar while revealing incidence of associated cervical cancer as well. Moreover, in past decades many research has focused on risk factors for HPV persistence and development of cervical cancer with reporting of observations that early first sexual intercourse, multiple sexual partners, Tobacco use, and immune suppression are at higher risk of HPV infection. Most of these factors are now viewed either as surrogates of HPV exposure or as relevant cofactors given the presence of HPV. Therefore present study is also an attempt to explore the profile of associations of such etiological factors or non viral cofactors or surrogates of HPV exposure in cervical HPV positive women of Jamnagar.

2. Materials and Methods

2.1. Study type

Prospective -Observational - Cross sectional

2.2. Study site

M. P. Shah Government Medical College Jamnagar, Gujarat (With tertiary care G.G. General Hospital Jamnagar, Gujarat),

2.3. Study population

110 Adult women – (Random selection amongst patients)

2.4. Study criteria

2.5. Inclusion criteria

Adult woman aged above 20 years, able to communicate & giving consent to allow pelvic examination when explained the purpose of study.

2.6. Exclusion criteria

Virgin adult women, history of Hysterectomy

2.7. Data collection

Present study was conducted at M. P. Shah Government Medical College & G.G. General Hospital, Jamnagar in 2004 after due permission of Dean of college & Head of Microbiology & Gynecology department as per the prevalent procedure. Study subjects were randomly selected adult woman attending Gynecology -Outpatient department of hospital & fulfilling inclusion criteria. Prospective study subjects were explained the purpose and procedure of study to obtain informed consent. Such consenting women were subjected to detailed clinical history inclusive of history about common aetiological factors associated with HPV. All such history comprise of personal, social, marital data etc about that woman.

Total 110 cervical smear samples collected under implied consent after completion of history taking were stained by Giemsa staining for microscopic examination. HPV infected cervical cells were identified based on specific cytopathic effects. Cytological finding of 'Koilocytes' is considered hall mark of HPV infection.² Additionally, dyskeratosis, hyperchromatic nucleus, binucleation or multinucleation, clear cytoplasm, keratohyaline granules, perinuclear halos and spindle cells can also be attributed to HPV load in smear.⁴ In present study cellular alteration like koilocytosis, dyskeratosis and clear cytoplasm were considered as consequences of viral cytopathic effects & such smears were considered as HPV positive. Thus, final inferences were drawn based on reexamination of history of clinical & aetiological factors

of HPV positive women.

3. Results

A total of 110 randomly selected adult women attending Gynecology OPD of G. G. General Hospital Jamnagar were subjected to detail clinical history & examination for presence of cervical HPV infection by cytological examination of their cervical smear. Out of those 12 (10.9%) women having cytological changes like koilocytosis, dyskeratosis and clear cytoplasm in cervical cells were considered as cervical HPV positive. Such HPV positive women's history of clinical & aetiological factors was reexamined to tabulate & analyze their associations.

Table 1: Age wise distribution of incidence of cervical HPV infection

Age (years)	Number of samples	Cervical smear positive for HPV	Percentage (%)
20-29	24	4	16.6%
30-39	39	3	7.6%
40-49	31	3	9.6%
50-59	10	2	20%
60-69	2	0	0%
>70	4	0	0%

It is evident that cervical HPV infection is in highest proportion (20%) among age group of 50-59 years (20%) followed by 16.6% in younger age of 20-29 years

Table 2: Association of cervical HPV infection in relation to age at first coitus

Age at first coitus (years)	Number of samples	Cervical smear positive for HPV	Percentage (%)
< 20	48	9	18.75%
20-25	62	3	4.8%

It is observable that incidence of cervical HPV infection has significant peak (18.75%) if woman is having low age at first coitus (< 20 years)

Table 3: Association of cervical HPV infection with duration of active married life

Period of active married life (years)	Number of samples	Cervical smear positive for HPV	Percentage (%)
1-5	21	2	9.5%
6-10	13	2	15.3%
11-20	37	3	8.1%
>20	39	5	12.8%

Results are revealing that incidence of cervical HPV infection remains higher with active married life of 6-10 years (15.3%) & 1-5 years (9.5%). So for initial 10 years of active span it become 24.8% as compared to later span of 11-20 years where HPV positive cervical smear is in 8.1% only.

Table 4: Relation of parity with cervical Human papilloma virus infection

Parity	Number of samples	Cervical smear positive for HPV	Percentage (%)
0	8	0	0%
1	14	0	0%
2	26	1	3.8%
3	22	4	18.18%
4	22	4	18.18%
>4	18	3	16.6%

It is clear that high parity (3 or 4) has significantly high & constant association 18.18% with cervical HPV infection.

Table 5: Association cervical of HPV infection with carcinoma cervix

Diagnosis	Number of samples	Cervical smear positive for HPV	Percentage (%)
Carcinoma cervix	04	03	75%
Other diagnosis	106	09	8.49%

Cervical HPV infection was found in 75% women having Carcinoma cervix.

4. Discussion

Our study shows incidence of cervical HPV infection by cervical smear cytology in adult women of Jamnagar is 10.9%. As we have used single measurement to characterize a woman's HPV status we could not be certain if it is a transient or persistent HPV infection. However Infection may present in various ways. Latent HPV may be asymptomatic and identifiable only by molecular biology techniques or subclinically seen on colposcopy.⁸ Our study is limited by the fact that we have relied on cytological changes in cervical smear to designate HPV positive status which is less sensitive for detection of HPV than molecular testing.⁹ Only about a third of women with HPV infections detectable by DNA testing have recognized cytopathology.⁹

We have randomly included all adult women soon after they become sexually active so as to establish their cervical HPV infection status at any age. Infection by cervical HPV has reached to epidemic proportion in certain age groups.¹⁰ It has been calculated that - there is a lifetime risk of becoming HPV infected as approximately 80%¹¹ The prevalence of HPV infection has been reported to

be age dependent, peaking in the 20 to 24 year-old-age-range and then declining with increasing age¹² Such decline with high age is due to reduced risk behavior through established monogamous relationships and due to increased acquired immunity at the systemic and mucosal level over time.⁵ However, present study has contrast of high cervical HPV infection in age group of 50-59 (20%) followed by age group of 20-29 (16.6%). This could be because cytological abnormalities in early adulthood are transient, more probably go undetected. Stuart Collins¹³ have shown higher incidence of cervical HPV infection in mean age of 17.5 (37.8%).

Cross-sectional surveys reveal a high prevalence of cytological abnormality in sexually active teenagers.¹⁴ In present study also It is observable that incidence of cervical HPV infection has significant peak (18.75%) if woman is having low age at first coitus (<20 years) As the peak time for acquiring infection for both women and men is shortly after becoming sexually active.⁷ Though the probability of infection per sexual act is not known but is clearly high.¹⁵ Moreover, Anogenital HPV infections are transmitted mainly by skin-to-skin or mucosa-to-mucosa contact.¹⁶ but penetrative sex is not required for transmission.⁷ This is consistent with our results that cervical HPV infection remains higher in initial 10 years of active married life span (24.8%) as compared to later span of 11-20 years where HPV positive cervical smear is in 8.1% only. Thus, cervical HPV infection has significant association with some key risk factors that reflect sexual behavior such as the number of sexual partners (merely reflect probability of HPV exposure⁷), an early age at first intercourse, or any previous STD.¹⁷

Similarly, multiparity¹⁸ is yet an other non viral cofactor of cervical HPV infection which can double or triple the risk of pre cancer and cancer among infected women.⁹ In our study parity was defined as number of live & still births & it exhibited that multi parity (3 or 4) had significantly high & constant association of 18.18% with cervical HPV infection. High parity increases the risk of squamous cell carcinoma of the cervix among HPV-positive women.¹⁹ Previous studies have ascribed such association with sexual behaviour.²⁰ However, two recent investigations have demonstrated an independent effect of parity with cancer of cervix (Brinton et al., 1989; Parazzini et al., 1989)

HPVs are widespread throughout the population, produce epithelial tumors of the skin and mucous membranes, and have been closely associated with genital tract malignancies.³ Pappiomaviruses manifest a pronounced tropism for epithelial tissues, unlike other tumour viruses.²¹ An association of HPV infection with the development of cervical carcinoma is now well accepted²² and the same was observed in present study also as 75% women having Carcinoma cervix were positive for cervical HPV infection. In study carried out by Limpaboon T. (2000)²³

incidence of cervical human papilloma virus infection was 100% in women's with cervical carcinoma. Bosch et al²⁴ reported incidence of 93% in women's with cervical carcinoma. In the study carried out at New Delhi, India incidence of cervical Human Papilloma Virus infection was 72% in women's with cervical carcinoma as revealed by Gopalkrishna V²⁵ Therefore, it is reasonable to assume that eradication of HPV infection should decrease the incidence of cervical neoplasia in women.²⁶

5. Conclusion

Our study observed 10.9% incidence of cervical HPV infection in adult woman of Jamnagar. Such cervical HPV positive status show stronger association with early age at first coitus, initial active married life and multi parity as like other studies, whereas contrasting finding of high cervical HPV positive older women could be due to undetected transient infections in young adults. Study reveals strongest correlation of carcinoma cervix with positive cervical HPV status so it's reasonable to assume that prevention of cervical HPV can reduce number of cases of cervical cancer.

Nevertheless, study is hospital based & confined to random adult women sampling, therefore, only limited inferences can be drawn from the characterization of a woman's HPV status at a single point in time. Only longitudinal observations will ascertain how often this pattern of cervical HPV infection is seen with profile of associated aetiological factors & Carcinoma cervix.

However, considering varying needs and values of this region (Jamnagar-Gujarat) primary prevention has to begin with education about safe sexual practices, delayed start of sexual activity and promotion and provision of condoms for those engaged in sexual activity along with extensive adoption of HPV testing screening protocol. Secondary choice would be to include vaccination & treatment options for the prevention and management of cervical neoplasia. Hence, problem of cervical cancer can be solved with aligned focus on education, existing or soon-to-be available technology, modest resources and sufficient will.

6. Conflict of Interest

None.

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