Original Research Article

Prevalence and determinants of high risk human papilloma virus in Hyderabad, India

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ABSTRACT

Background: Cervical cancer is the most common cancer among india women and age standardized mortality rate are the highest in south central Asia. In the past decade an among aetiologic association between infection with high risk human papilloma virus and development of cervical cancer has been increased. The study was aimed at studying the prevalence and determinants of high risk human papilloma virus in these patients.
Methods: This study was conducted for a period of one year to know the prevalence and determinants of high risk human papilloma virus in the patients attending gynaec out patient department. A total of 266 married women between 15-75 were randomly selected for the study.
Results: There is high prevalence of HPV in low (43.3%)/mid (37.4%) socio economic class (17.6%). But the result was not statistically significant (p=0.149). higher prevalence of HPV was found in multiparas (39.4%) compared to multiparas (33.3%) which was not statistically significant (p=0.233). Husbands of 252 women were circumcised out of which 96 wives were positive for HPV DNA (38.1%). Among 14 women with no history of circumcision in their husband HPV DNA positive (28.6%). Correlation of cytology with HPV DNA among different age groups showed increasing prevalence with age but the result was not statistically significant (p=0.115). the result showed that age at marriage, higher the prevalence of HPV DNA. The result was statistically significant (p=0.017). with increasing state of education, the prevalence of HPV infection decreased, but the result was not statically significant (p=0.142).51.3% of women of who were not education were positive for HPV as against only 25% of graduates were HPV positive.
Conclusions: Genital hygiene, genetic polymorphisms and other environmental cofactors among HPV DNA positive women, which prevent oncogenesis.

Keywords: Bethesda system, Cervical cancer, Human papilloma virus

INTRODUCTION

Cervical cancer is the second most common cause of cancer in women worldwide. The estimated number of new cases per yr 4,93,100 and leading to approximately 2,73,000 deaths, of which 70% occur in developing countries.

Cervical cancer is the most common cancer among india women. Approximately 20,000 new cases were detected in the yr 2000. India's cervical cancer age standardized incidence rate (30.7 per 100,000) and age standardized mortality rate (17.4 per 100,000) are the highest in south central Asia. In the past decade a among aetiologic association between infection with high risk human papilloma virus and development of cervical cancer has been established.[1,2]

The prevalence of high risk HPV in specimen of invasive cervical cancer is greater than 90% in world wide samples tested by PCR (IARC) publications or equivalent technology. When corrections are made for non-

representative tissue and inadequate DNA it was shown that 99% percent of all carcinomas harbor high risk HPV risk HPV is present in 50% of ASCUS specimens, 80% of lsril, 90% to 95% of HSIL.

HPV is widely prevalent sexually transmitted virus. although the majority of infections are benign and transient, persistent infection is associated with the development of carcinoma cervix.

Owing to the strong association, it has been suggested that high risk HPV detection might be used as a tool to identify women at risk for the subsequent development of carcinoma cervix. Middle eastern and predominantly Muslim and Buddhist countries tended to have the lowest rates, while Latin American and predominantly Christian and Hindu countries generally had the highest rates.

Muslim women and jewish women are in general marked to have low prevalence carcinoma cervix and thus HPV infection (WHO data bank cervix uteri reports 1977-1997).[3] There is ample data on prevalence of HPV in women cervical cancer, however data on HPV prevalence in general population of various geographical regions and communities from India is scarce.

The present study addresses this issue. Studies examining risk factors for HPV infection not been entirely consistent, probably due to difference in the studied population and the detection methods. The point prevalence observed are country dependent and are strongly related to the dominant sexual behaviour patterns. Some of the identified determinants of HPV infection are age of woman at sexual initiation, the life time number of partners of woman and male sexual partners, and frequency of sexual contacts between men and prostitutes.

Possible determinants of HPV Prevalence include age of men at sexual initiation, the age difference within couples at first marriage and prevalence of male circumcision. Present study is to determine the prevalence and determinants of high risk-human papilloma virus infection in woman attending gynaecological outpatient department at Muslim maternity hospital.

METHODS

The present study was conducted at Muslim hospital. Muslim maternity hospital is a 200 bedded tertiary hospital with about 40-50 woman attending gynecology OPD for various complaints. These patients are predominantly Muslim woman details like socio economic status with specific social, cultural and sexual behaviour like early age at marriage, high parity, male circumcision was noted.

A total of 266 woman were enrolled for the study. A structured questionnaire designed especially for this study was administered by the gynecologist. The questionnaire included information on sociodemographic characteristics (age, educational level, marital status, occupation, country of birth), sexual practices (age of first sexual intercourse, number of lifetime sexual partners), reproductive health (number and dates of pregnancies, children, TOPs (voluntary termination of pregnancy), use of contraceptives methods), general health (smoking habits, weight and height, history of major illness), gynaecological history (previous cervical smears and results, past history of STI).

Smokers were classified according to having ever smoked or not and whether they had smoked in the last year. HIV, hepatitis B virus (HBV), hepatitis C virus (HCV) and syphilis serology were also recorded. The outcome variables were HR-HPV infection and SIL. All women had a cervical specimen taken for Papanicolaou cytology and HPV testing.

Smears were read blinded to all study variables in the reference Pathology service. HR-HPV infection was determined through the HPV DNA test Hybrid Capture II using the oncogenic or probe B cocktail (HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68), in accordance with the manufacturer's instructions.

The samples with a relative light unit/cut-off ratio >1·0 were considered positive for one or more HPV genotypes included in the probe B cocktail and the specimens with a relative light unit/cut-off ratio of between 1·0 and 2·5 were retested to confirm positive results.

Cervical smears were performed with an Ayre's wooden spatula and an endocervical brush. Samples were fixed with Labofix and classified according to Bethesda 2001.

The statistical analysis was done using SPSS version.

RESULTS

Overall the oncogenic HPV (16,18,31,35,51,52b,45) was found in 90 (37.6%) of the study subjects. The age group of the woman ranged from 17 to 75 yr, the man age was 35.77. The age distribution of the study population is given in the following table majority of the subjects belong to age group 30-40 yr.

Most common effected group is 30-40 years married women of middle socio economic class with primary or secondary level of education. Most of the woman were married below the age of 20 yr and were multiparas.

All most all the woman -252 were Muslim with history of circumcision in their partner. Only 14 patients were Hindus with no history of circumcision.

None of the study subjects had given the history of exposure or smoking husbands of 51 woman were smokers and hence these women exposed to passive smoking.

Table 1: Demographic distribution of the subjects.

	Frequency (n=266)	Percent
Age group (in years)		
<30	84	31.6
30-40	113	42.5
40-50	44	16.5
>50	25	9.4
Marital status		
Married	250	94.0
Widowed	5	1.9
Divorce	11	4.1
Socio economic status		
Low	67	25.2
Middle	182	68.4
High	17	6.4
Education		
None	39	14.7
Primary	66	24.8
Secondary	112	42.1
Graduate	36	13.5
Post graduate	13	4.9
Age at marriage or first intercourse		
<16	42	15.8
16-20	160	60.2
20-24	51	19.2
>25	13	4.9
Total	266	100
Parity		
Nullipara	16	6.0
Primipara	24	9.0
Multipara	226	85.0
Total	266	100

Most of the subjects never used contraception. 35 woman used oral contraceptive pills at sometime, 20 women used IUCD, 15 women gave history of usage of condom by their husbands.

The chief complaints with which the study population attended were white discharge (32.95%), menstrual disturbances (15.64%), and pain abdomen (18.35%).

Genital warts were not documented on clinical examination in any subject. Of the 267 pap smears taken, reporting done by the Bethesda system. Showed 253 smears negative for intraepithelial lesion (17-normal 236-specific or no specific inflammation) 1-ASUS, 7 reported as low grade squamous intra epithelial lesion, 2 as high grade squamous intra epithelial lesion, and 3 as squamous cell carcinoma.

The high reporting of inflammatory smears was because 32.95% of woman had chief complaint of white discharge.

Prevalence of HPV DNA among different age group showed increasing prevalence with age but the result was not statistically significant (p=0.115) Married, divorced or widowed had no difference in the HPV prevalence (p=0.99) education status of women-HPV. With increasing state, the prevalence of HPV infection decreased, but the result was not statistically significant (P=0.142).

Table 2: Prevalence of variables among the study subjects.

Circumcision	Frequency	Percent
Yes	252	94.7
No	14	5.3
Passive smoking		
Yes	51	19.2
No	215	80.8
Contraception		
None	196	73.7
OCP	35	13.2
IUCD	20	7.5
Condom	15	5.6
STD		
Yes	75	28.2
No	191	71.8
HPV DNA		
Positive	100	37.6
Negative	166	62.4
Total	266	100.0
Papmear		
Normal	17	6.4
Inflammatory	236	88.7
ASCUS	1	0.4
LSIL	7	2.6
HSIL	2	0.8
Cacervix	3	1.1
Total	266	100.0

51.3% of women who were not educated were positive for HPV as against only 25% of graduates or post graduates were HPV positive.

Results showed high prevalence of HPV in low (43.3%) mid (37.4%) socio economic class compared to high class (17.6%). But the result was not statistically significant (p=0.149).

The result showed at the younger the age at marriage, higher the prevalence of HPV DNA. Woman who had intercourse before 20yr of age had high prevalence of HPV infection. 50% prevalence observed in >28 yr age at marriage group was because only two women were in that group. The result was statistically significant (p=0.017).

Correlation of cytology with HPV DNA showed that 100% positivity in HSIL and squamous cell carcinoma. Only one case of ASCUS was reported which was HPV DNA positive reported as normal had 11.8% HIV DNA positive. 37.3% are smears with inflammation and 57.1% of lsil were HPV DNA was positive.

Table 3: Prevalence of HPV DNA among the papsmears in demographic variables.

Variable			HPV DNA		Total
Marital status	Married	Count	94	156	250
		%within marital status	37.6	62.4%	100
	Divorced	Count	2	3	5
		%within marital status	40	60.0%	100
	widowed	Count	4	7	11
		%within marital status	36.4%	63.6%	100
Education	None	Count	20	19	39
		%within education	51.3%	48.7%	100
	Primary	Count	24	42	66
		%within education	36.4%	63.6%	100
	Secondary	Count	44	68	112
		% within education	39.3%	60.7%	100
	Graduate	Count	9	27	36
		% within education	25.0%	75.0%	100
	Post graduate	Count	3	10	13
		%within education	23.1%	76.9%	100
Socioeconomic Status	Low	Count	29	38	67
		% within class	43.3%	56.7%	100
	Middle	Count	68	114	182
		% within class	37.4%	62.6	100
	High	Count	3	14	17
		%within class	17.6%	82.4%	100
Age at marriages	<16	Count	21	21	42
		%within age m-gr	50	50	100
	16-20	Count	65	95	160
		Within age m-gr	40.6	59.4	100
	20-24	Count	11	40	51
		Within age m-gr	21.6	78.4	100
	>25	Count	3	10	13
		%within age m-gr	23.6	76.9	100

There is higher prevalence of HPV was found of HPV was found on multiparas 39.4% compared to nulliparas (18.8%) and primiparas (33.3%). The result was not statistically significant (p=0.233) few women used condom and HPV prevalence was less in them compared to OCP/IUCD user's. the result was not statistically significant. Passive smoking had no effect on HPV prevalence. Husbands of 252 women were circumcised out of which 96 wives were positive for HPV DNA (38.1%) among 14 women with no history of circumcision in their husbands four were HPV DNA positive (28.6%) chi-square tests: p=0.474.

DISCUSSION

Incidence of cervical cancer varies by region of the world, ranging from 4.8 per 100,000 in western aia (i.e., 3.27/100,000 in Israel) to 44.3 in eastern Africa (i.e., 61.08/100,000 in Iraq and 5.76/100,000 in Swaziland). Middle eastern and predominantly Muslim and Buddhist country tended to have the lowest rates, while latin American and predominantly Christiana and Hindu countries generally had the highest rates.[4,5]

Muslim women and Jewish women are in general marked to have low prevalence carcinoma cervix and thus HPV infection.[6] There is ample data on prevalence of HPV prevalence in general population of various geographical regions and communities from india is scarce. The present study addresses this issue.

The prevalence of oncogenic HPV 16,18,31,32,51,52b,45 among the women in the index study was 37.6%. the study group had 94.7% of Muslim population with circumcision in male partners. The prevalence of HPV in these women was 38.1%. The high prevalence could be due to the selection of subjects who were symptomatic (32.95% came with complaint of white discharge) being a hospital-based study and the HPV types included were 16,18,31,33,51,52b and 45 while in most of the studies only HPV 16 and 18 were studied.

In spite of the prevalence of high risk HPV there were only 1.9% of cases with moderate to severe dysplasia and carcinoma cervix. Similar results were reported from study in Muslim population by Al-muammer et al in Riyadh Arabia, where in spite of high prevalence of HPV

16/18 (31.6%) follow up had shown low rate of progression to CIN.[7] Male circumcision has been given credibility for providing protective shelter to the female partners by getting lesser HPV infection and thus reducing the risk for Ca cx. This hypothesis however has been counter argued by others.

Table 4: Prevalence of HPV DNA among the papmears.

Variable			HPV DNA		Total
			Positive	Negative	17
Papsmear	Normal	Count	Positive	Negative	17
		% withih papasmear	2	15	100%
	Inflammatory	Count	11.8%	88.2%	236
		% within papsmear	88	148	100
	Ascus	Count	37.3%	62.7%	1
		% within papsmear	1	0	100
	LSIL	Count	100	0	7
		%within papsear	4	3	100
	HSIL	Count	57.1	42.9	2
		%within papsmear	2	0	100
	Ca cervix	Total	100	0	3
		%within papsmear	3	0	100
Parity	nulllipara	Count	3	13	16
		% within parity	18.8	81.3	100
	Primaipora	Count	8	16	24
		% within parity	33.3	66.7	100
	multipara	Count	89	137	226
		% within parity	39.4	60.6%	100
Smoking	Yes	Count	19	32	51
		% with smoking	37.3%	62.7%	100
	No	Count	81	134	215
		% within smoking	37.7	62.3	100
STD	Yes	Count	27	48	75
		% within std h/o	36	64	100
	No	Count	73	118	191
		% within std h/o	38.2	61.8	100
Contraception	None	Count	74	122	196
		% within contraception	37.8%	62.2%	100
	OCP	Count	14	21	35
		% within contraception	40.0%	60.0%	100
	ICDU	Count	7	13	20
		% within contraception	35.0%	65.0%	100
	Condom	Count	5	10	15
		%within contraception	33.3%	66.7%	100
Circumcision	yes	count	96	156	252
		% within circumcision	38.1%	61.9%	100%
	no	Count	4	10	14
		% within circumcision	28.6%	71.4%	100%

Whether circumcision has any protective role in preventing the carcinogenesis remains to be proven. According to Das et al both prevalence of ca cx and HPV infection among Muslim women from Jammu and Kashmir are the lowest in india. statements are also made that the rate of ca cx and HPV among India Muslim women is strikingly low as revealed from the India cancer registries.[8-10] Of interest in studies conducted in India and Pakistan, premarital sex is uncommon in the various religious groups in these and surrounding countries, where in general Muslims are circumcised and Hindus are not. In a study of 5000 cervical and 300 penile cancer cases in madras between 1982 and 1990 the incidence was low amongst Muslim women. When compared with and Christian and was not seen at all in Muslims men. In a case control study of 1107 Indian woman with cervical cancer, sex with uncircumcised men or those circumcised after the age of 1 yr was reported in

1993 to be associated with a 4-flod higher risk of cervical cancer. This figure was, moreover, obtained after controlling for factors such as age of intercourse, and education. Another study published various types of cancer in the valley of Kashmir concluded that universal male circumcision in the majority community was responsible for the low rate of cervical cancer compared with the rest of India.[11]

Promiscuity is a significant factor that has been known to be associated with HPV infection. Worldwide studies have reported higher number of lifetime sexual partners as a risk factor for HPV infection. In our study none of the women admitted promiscuity, very few reported promiscuities in their husbands. The sociocultural stigma of our society plays a role in the under reporting of this sensitive parameter.

In present study prevalence of HPV was less in nulliparas (18.8%) and primiparas (33.3%) but the difference was not statistically significant. Dattagupta et al, Arora et al, Locanzo et al too did not observe any significant association of HPV 16/18 with parity.[12-14] A history of STD has been identified as a risk factor for HPV infection. In this group of low-risk women, we did not detect any association between self-reported STD history and incidence of HPV.

The present report is few of its kind in the Indian context, where detection of HPV on Muslim women has been done. This kind of data not only reflects on the effect of socio-cultural behaviour between the religious groups on the prevalence and natural history of HPV, it can also be utilized in the prevention/control of ca cx in India. The study results reflect the need for further studies in understanding what lies between the causal exposure and the disease and point, and to focus on the exploration of additional associations with putative environmental cofactors, religions practices, sexual behaviour, makers of viral and host interactions among HPV-DNA positive women leading to progression to precancer.

CONCLUSION

Study generates epidemiological data prevalence of high risk HPV in the Muslim women visiSting the study has shown that in spite of the high prevalence of the oncogenic HPV in the study group, constituted chiefly of muslim population, the incidence of CIN2, CIN3 AS detected by colposcopy and guided biopsies where ever needed was less, reflecting the presence of factors preventing the oncogenesis in this set of population. The prevalence increased with early marriages, high parity, low socio-economic status of education.

Although good success has obtained in phase 3 clinical trials with vaccines against HPV 16 and 18 phases 2 trials on two other high-risk are in progress, it should be noted that there are 200 types of HPV, 50 of which have been described in the ano-genital region. Ideally vaccination

against the most common types (HPV 16-18) could prevent two-thirds of cervical cancers. Elimination of these from the population might take 20-30 yr. This falls short of 100% protection. However, and the fear is that at the population level HPV types that are currently rarer will take over and replace the types vaccinated against.

Study emphasizes the aspect of primary prevention by good education, modification of sexual behaviour, practice of good genital hygiene. The study results reflect the need for further studies in understanding what lies between the causal exposure and the disease end point, and to focus on the aspects of circumcision. Genital hygiene, genetic polymorphisms and other environmental cofactors among HPV DNA positive women, which prevent oncogenesis.

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