

PREVALENCE OF HUMAN PAPILLOMAVIRUS INFECTION IN PATIENTS WITH UNHEALTHY CERVIX: A HOSPITAL BASED STUDY**Sabha Malik¹, Shahida Mir², Sabhiya Majid³, Shahnaz Taing⁴, Fida Mohammad⁵ and Mohammad Sarwar Mir^{*6}**

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Article Received on 04/10/2017

Article Revised on 25/10/2017

Article Accepted on 15/11/2017

ABSTRACT

Cancer of uterine cervix is the second most common malignancy in the world, but it is number one cause in Indian women, posing a major public health problem. One and a half year prospective study was carried out in Departments of Obstetrics and Gynaecology, Lalla Ded Hospital, GMC Srinagar to find prevalence of HPV infection in patients with unhealthy cervix. A total of hundred patients were studied during the research period. Majority of the patients (82%) belonged to the age group of 35-44 years. 44 % of the patients were > Para 3. Cervical erosion was the most common per speculum examination finding. Oral contraceptive pills was the most common form of contraception used. Prevalence of HPV infection was found to be 9%. Most of the positive cases belonged to the age group of 45 to 54 years and were para 4 or more. Maximum (15.4%) HPV positive cases had their first sexual exposure before 18 years. Maximum correlation of HPV infection was seen with cervix that bled on touch.

INTRODUCTION

Cancer of uterine cervix is the second most commonest malignancy in the world, but it is number one cause in Indian women, posing a major public health problem. According to World health organization every year cervical cancer is diagnosed in about 500000 women globally and is responsible for more than 280000 deaths annually. In India, 130000 new cases of cervical cancer with 70000 deaths occur annually. The growing risk of cervical cancer in women in India is 2.4% compared to 1.3% for the world. Eighty percent of the new cervical cancer cases occur in the developing countries like India.^[1]

Unhealthy cervix is a collective term for group of mostly chronic cervical lesions. It includes chronic cervicitis, erosions, ulcerations, eversion, polyp as well as leucoplakia of cervix. Symptoms of unhealthy cervix include offensive vaginal discharge, contact bleeding, irregular bleeding, dyspareunia and cervical pain.^[2]

Cancer cervix is different from most of the cancers by its invariable association with asymptomatic and precancerous lesions, which may have their onset 5-15 years before any clinical manifestations get noticed. Another very characteristic feature of this malignancy is that unlike other cancers, its etiology has been well established. Substantial pathological, virological and epidemiological evidences have established a major role of human papillomavirus in the etiology.^[3]

Epidemiological studies demonstrate the association of several risk factors for the development of cervical cancer. These risk factors include HPV infection, sexual promiscuity, multiplicity of sexual partners and exposure to sexual intercourse at an early age, use of oral contraceptives and number of pregnancies, cigarette smoking and malnutrition etc.^[4]

The association between HPV infection and invasive cervical cancer is very strong, specific and consistent and is independent from other known risk factors. The strength of relationship is even greater than the

association between smoking and lung cancer and other well established casual relationships in cancer.^[5]

HPV is a small non enveloped virus with a circular double stranded DNA. More than 85 well characterized. More than 85 well characterized genotypes are recognized. About 30 to 40 HPV types are typically transmitted through sexual contact and infect anogenital region. Mucosal and vaginal HPV's consisting of about 30 types are divided into low risk and high risk according to their presence in malignant lesions of cervix. The oncogenic potential of the virus has been attributed to E6 and E7 gene. These oncogenes interact with and inhibit the activities of critical components of the cell cycle regulatory system, in particular E6 with P53 and E7 and Rb.^[6]

Several molecular methods such as southern blotting, dot/slot blotting fluorescence in situ hybridization (FISH), tissue in situ hybridization (TISH) are being employed for detecting HPV. PCR is highly sensitive and specific method compared to all other techniques and can detect a single molecule of HPV DNA out of million cells. HPV detection by PCR in exfoliated cells from the cervix gives the prevalence of HPV infection in the studied population.^[7]

Objectives

1. To find out prevalence of HPV infection in patients with unhealthy cervix.
2. To evaluate association of HPV infection with unhealthy cervix.

Method

A prospective study was conducted over a period of one and half years in Department of Obstetrics and Gynecology, Lalla Ded Hospital, GMC Srinagar. Patients presenting with the chief complaints of offensive vaginal discharge, post menopausal bleeding, intermenstrual bleeding, contact bleeding and dyspareunia were included in the study. The socio-demographic features of the patients were recorded using a predesigned and pretested proforma. Informed consent was taken from each patient before enrollment. Confidentiality was maintained. The patients were selected after evaluating them for inclusion and exclusion criteria. In addition to routine investigations, every included subject underwent HPV testing using Bio pap kit. Bio Pap kit has been designed for detection of HPV in clinical samples and differentiation between

oncogenic and non-oncogenic genotypes, on a single reaction.

Inclusion Criteria

1. Women between the ages of 35-65 years with symptoms of increased or foul smelling vaginal discharge.
2. Women with history of contact bleeding
3. Women with history of postmenopausal bleeding.
4. Women with history of intermenstrual bleeding.
5. Women with history of chronic backache/pain lower abdomen.

Exclusion Criteria

1. Women between the ages of 35-65 years with healthy cervix.
2. Hysterectomized patients whose cervix has been removed.
3. Women < 35 years of age and > 65 years of age.

OBSERVATIONS

A total of 100 patients were studied during the study period.

Table 1: Age wise (years) distribution of the patients.

| Age | Frequency | Percentage (%) |
|--------|-----------|----------------|
| 35-44 | 82 | 82.0 |
| 45 -54 | 10 | 10.0 |
| 55-65 | 8 | 8.0 |

Table 2: Distribution of patients according to parity.

| Parity | Frequency | Percentage |
|-----------|-----------|------------|
| Para 1 | 13.91 | 11.0 |
| Para 2 | 12.07 | 18.0 |
| Para 3 | 27 | 27.0 |
| >Para 3 | 44 | 44.0 |
| Range-1,6 | | |

Table 3: Distribution of patients according to age at marriage/consummation.

| Age at Marriage (Years) | Frequency | Percentage |
|-------------------------|-----------|------------|
| <18 | 13 | 13.0 |
| 18 to 25 | 66 | 66.0 |
| >25 | 21 | 21.00 |

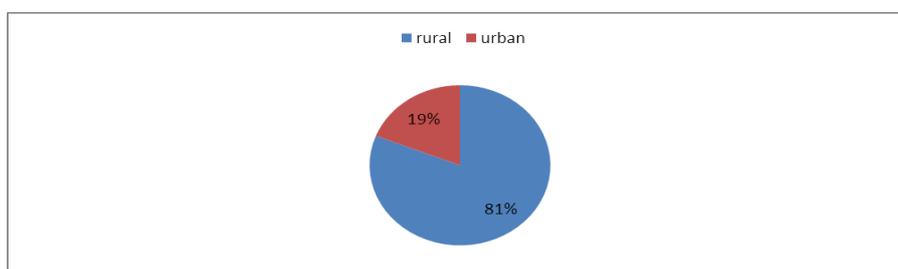


Figure 1: Distribution of patients according to domicile status.

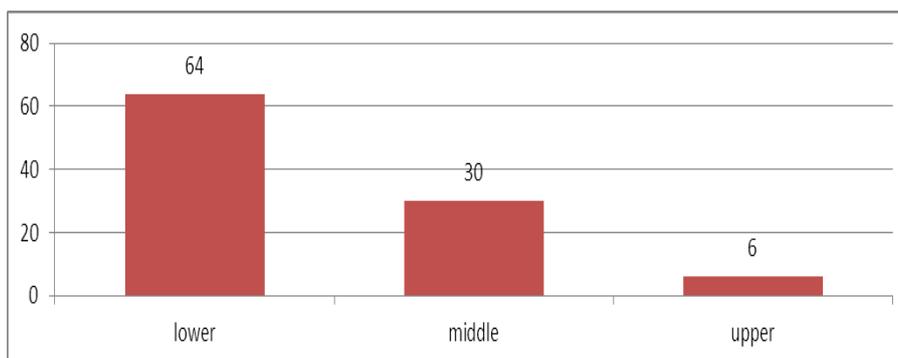


Figure 2: Distribution of patients according to socioeconomic status.

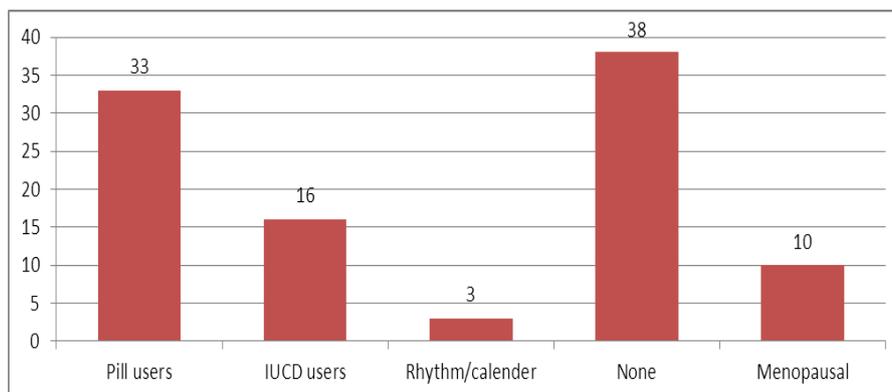


Figure 3: Distribution of patients with relation to contraception usage.

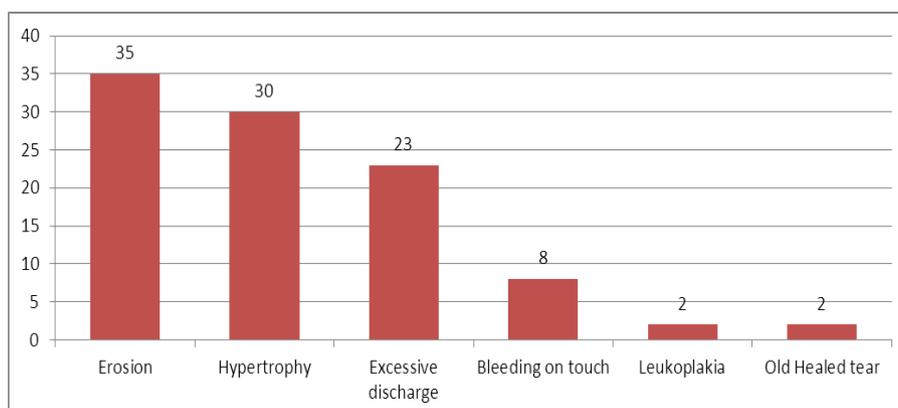


Figure 4: Findings of per speculum examination.

Table 4: Prevalence of HPV DNA positive cases in the Study Population.

| HPV DNA | Frequency | Percentage |
|---------|-----------|------------|
| Yes | 9 | 9.0 |
| No | 91 | 91.0 |

Table 4 shows that out of 100 cases studied, 9 Cases(9%) were positive for HPV DNA while as 91(91%) were negative.

Table 5: Prevalence of HPV infection in different age groups.

| Age (years) | Frequency | Percentage |
|-------------|-----------|------------|
| 35 to 44 | 5 | 6.1 |
| 45 to 54 | 3 | 30.0 |
| 55 to 65 | 1 | 12.5 |

Table 6: Correlation of HPV positive cases with parity.

| Parity | Frequency | Percentage |
|---------|-----------|------------|
| Para 1 | 1 | 3.6 |
| Para 2 | 1 | 5.6 |
| Para 3 | 1 | 10.0 |
| >Para 3 | 6 | 13.6 |

Table 7: Correlation of HPV infection in relation to domicile status.

| Demography | Frequency | Percentage |
|------------|-----------|------------|
| Rural | 9 | 11.0 |
| Urban | 0 | 0.0 |

Table 8: Correlation of HPV infection in relation to socioeconomic status.

| Socioeconomic Status | Frequency | Percentage |
|----------------------|-----------|------------|
| Lower | 6 | 9.4 |
| Middle | 2 | 6.7 |
| Upper | 1 | 16.7 |

Table 9: Correlation of HPV positive cases with age at marriage.

| Age at marriage in years | Frequency | Percentage |
|--------------------------|-----------|------------|
| <18 | 2 | 15.4 |
| 18 to 25 | 6 | 9.1 |
| >25 | 1 | 4.8 |

Table 10: Correlation of HPV infection with unhealthy cervix.

| Per speculum finding | Frequency | Percentage |
|----------------------|-----------|------------|
| Bleeding on touch | 5 | 62.5 |
| hypertrophy | 2 | 6.7 |
| Excessive Discharge | 1 | 4.3 |
| Erosion | 1 | 2.9 |
| Leukoplakia | 0 | 0.0 |
| Old healed Tear | 0 | 0.0 |

Table 10: Correlation of HPV infection with unhealthy cervix.

| Type of contraception | Frequency | Percentage |
|-----------------------|-----------|------------|
| Pill users | 1 | 3.0 |
| IUCD users | 3 | 18.8 |
| Excessive Discharge | 0 | 0.0 |
| Erosion | 4 | 10.5 |
| Leukoplakia | 1 | 10.0 |

DISCUSSION

Cervical cancer, one of the commonest neoplasia afflicting females, carries a high mortality and mortality. Attempts have been made from time to time to find out means and ways of detecting the disease in the preinvasive stage. The world wide incidence of death rate due to cervical cancer is about 27%. It is paradoxical that so many deaths occurring inspite of the fact that cervical cancer is a curable disease.^[8]

A prospective study was conducted in Lalla Ded hospital, the only tertiary care maternity hospital in Kashmir valley for a period of one and a half years. 100 women were enrolled with symptoms pertaining to unhealthy cervix according to inclusion and exclusion criteria.

The mean age of studied patients was 41.2 ± 7.1 years with range of 35-65. Maximum (82%) of the women were between 35-44 years of age. The findings are consistent with studies of Alexander Luyton *et al* (2009)^[8], Maria Adamopoulou *et al* (2003)^[9] and Rengaswamy Sankaranarayan *et al* (2009).^[10]

In our study it was found that as parity increased, the risk of intraepithelial abnormalities of the cervix also

increased. This was evident from the fact that 44% of the patients were from the higher parity and only 11% were para 1. Rengaswamy Sankaranarayan *et al* (2009)^[12], S.Sardana and N.S. Murthy (1999)^[13] also had similar findings.

Maximum number of patients (66%) were in age group of 18 to 25 years at the time of marriage whereas 13 % of the women got married at age less than 18 years. Mean age at marriage at first intercourse was found to be 21.2 ± 4 years. Our results are consistent with Denny *et al* (2000)^[14] who also found that mean age at first sexual intercourse was 17 years.

In our study we found that maximum patients (81%) were from rural areas and most of the patients belonged to lower socioeconomic status (64%). The findings go well with the studies of Jan Ponten *et al* (1995)^[15] and Francheschi *et al* (2003)^[16] that low socioeconomic status was an important risk factor for the development of cervical cancer.

In our study we found that 38% of the women were not using any contraception and in remaining 62% percent, maximum were using oral contraceptives pills (33%). The similar results were obtained by Patricia de Cremoux *et al* (2003)^[17] and Sreejata Ray Choudhary *et al* (2012).^[18]

100 selected patients with symptoms of unhealthy cervix underwent HPV testing where it was found that prevalence of HPV infection was 9%. The results are similar to findings of Duttagupta *et al* (2004).^[19]

Further in this study assessment of genital HPV infection prevalence revealed that women between age of 45 to 54 years had the highest prevalence (30%). The findings are consistent with findings of Lazcano E *et al* (2001).^[20]

It was also observed that the prevalence of HPV increased with parity. Our results are compatible with findings of S.Sardana and N.S Murthy *et al* (1999).^[13] Lynete Denny *et al* (2000)^[14] also reported mean parity of to be three.

Our Study showed that maximum number of HPV DNA positive cases (18.8%) used IUCD as method of contraception as against only 3% of the HPV DNA positive cases used OCPs. However our findings were inconsistent with the study conducted by Kotkoff *et al* (1998).^[21]

In significant our study significant correlation was observed between HPV infection and symptoms of unhealthy cervix. HPV infection correlated majorly with the cervix that bled on touch (62.5%). Our correlation was similar with the study conducted by Singh V *et al* (1995).^[22]

SUMMARY AND CONCLUSION

A total of hundred patients were studied in prospective research design. The age of the study group varied from 35-65 years with maximum number of patients falling in the age group of 35-44 years. Percentage of multiparous women i.e. para 4 or more was 44%. Most of the cases in the study group came from the rural areas and belonged lower socioeconomic status. Age at first coitus was generally between 18-25 years. Cervical erosion was the most common finding on per speculum examination. Prevalence of HPV infection was found to be 9%. Most of the positive cases belonged to the age group of 45 to 54 years and were para 4 or more. Maximum (15.4%) HPV positive cases had their first sexual exposure before 18 years. Maximum correlation of HPV infection was seen with cervix that bled on touch.

BIBLIOGRAPHY

- Misra JS, Srivasta S, Singh U, Srivasta AN. Risk factors and strategies for control of carcinoma cervix in India: hospital based study cytological screening experience of 35 years. *Indian J Cancer*, 2009; 46(2): 155-9.
- Charles D. Read. The treatment of non malignant unhealthy cervix. *BJOG An international Journal of Obstetrics and Gynaecology*, Oct, 1955; 62(5): 796-808.
- Boon M.E Fox C.H. Simultaneous Condyloma accumulatum and dysplasia of the uterine cervix. *Acta Cytol*, 1981; 25: 393.
- Shi JF, Belinson JL, Smith JS et al. Human papilloma virus testing for cervical cancer screening: Results from a six year prospective study in rural China. *Am J Epidemiol*, 2009; 170: 708-716.
- Ferenczy A, Franco E. Persistent human papillomavirus infection and cervical neoplasia. *Lancet Oncol*, 2002; 3: 116.
- Philips AC, Voudsen KH. Human papillomavirus and cancer: the viral transforming genes. *Cancer surv*, 1999; 33: 55-74.
- Melchers W, Vanden Brule A, Walboomers J et al. Increased detection of the polymerase chain as compared to modified FISH and southern-blot analysis. *J med Virol*, 1989; 27: 329-335.
- WHO/ICO information centre on HPV and cervical cancer (HPV information centre). Summary report on HPV and cervical cancer statistics in India (2007). www.who.int/hpvcentre/en.
- Partha Basu, Debjani Chowdhury. Cervical cancer screening and HPV vaccination: a comprehensive approach to cervical cancer control. *Indian J Med Res.*, Sept. 2009; 130: 241-246
- Alexander Luyton, Sarah Scherbring, Axel Reinecke-luthge et al. Risk adapted primary HPV cervical cancer screening project in Wolfsburg, Germany –Experience over 3 years. *Journal of clinical virology*, 2009; 46: S5-S10.
- Maria Adamopolou, Eleni Kalkani, Ekatherina Charvalos et al. Comparison of cytology, colposcopy, HPV typing and biomarker analysis in detecting cervical neoplasia. *anti cancer research*, 2009; 29: 13401-3410.
- Rengaswamy Sankaranarayan, Bhagwan M. Nene, Surendra S, Shastri et al. HPV screening for cervical cancer in rural India, 2009; 360: 1385-1394.
- S Sardana, Murthy NS, Sehgal A, Satyanarayan Das DK et al. Risk factors related to biological behaviour of precancerous lesion of the uterine cervix. *Br. J Cancer*, 1999; 732-6.
- Denny L, Kuhn L, Pollack A, Wainwright H et al. Evaluation of alternative methods of cervical cancer screening for resource poor setting. *Cancer*, Aug 15, 200; 89(4): 826-33.
- Jan Ponten, Hans-Oiov Adami, Reinhold. Strategies for global control of cervical cancer. *Int. J. Cancer*, 1995; 60: 1-26.
- Franceschi S, Raj Kumar T, Varella S et al. Human papillomavirus and risk factors for cervical cancer in Chennai, India: A case control study. *International Journal of cancer*, 2003; 107(1): 127-133.
- Patricia de Cremoux, Joel Coste, Xavier Sastre-Garau et al. Efficiency of hybrid capture 2 HPV DNA test in cervical cancer screening. *Am J Clin Patho*, 1, 2003; 120: 492-499.
- Sreejata Ray Chaudari, Sukanta Mandal. Socio-demographic and behavioral risk factors for cervical cancer and knowledge, attitude and practice in rural and urban area of North Bengal, India. *Asian Pacific Journal of Cancer prevention*, 2012; 13: 1093-1096.
- Dattagupta C, Sen Gupta S, Roy M, Sengupta D et al. Are muslim women less susceptible to oncogenic human papillovirus infection? A study from eastern India. *International Journal of Gynecological cancer*, 2004; 14(2): 293-303.
- Lazcano Ponce E et al. Epidemiology of HPV infection among Mexican women with normal cervical cytology. *International Journal of Cancer*, 2001; 91(3): 412-420.
- Kotloff KL, Wasserman SS, Russ K, Sharipo S, Daniel R, Brown W et al. Detection of genital human papillomavirus and associated cytological abnormalities among college women. *Sexually transmitted diseases*, 2008; 25(5): 243.
- Singh V, Sehgal A, Satyanarayan L et al. Clinical presentation of gynecological infections among Indian women, 1995; 85(2): 215-219.