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A Study On Prevalence &Determinants Of HPV In High-Risk Women In The Age Group (30-59yrs) Attending Gynecology OPD Of A Tertiary Care Hospital Of Jharkhand.

Dr. Ela Jha.[1], Dr Manju Merina Bara[2], Dr. Silbina Murmu[3], Dr. Lata Singh[4*], Dr. Arun Kumar Jha[5], Dr. Budhan Baitha[6], Dr. Rajan Kumar Barnwal[7], Kumar Vimal[8]

[1]Professor of Obs. &Gynecology, MGM Medical College & Hospital, Jamshedpur.
[2]Professor, Obs. &Gynecology, MGM Medical College & Hospital, Jamshedpur.
[3]Associate Professor Pathology, SBMCH, Hazaribagh, Jharkhand,
[4*]Assistant Professor Obs. &Gynecology,ESIC Medical College and Hospital, Bihta, Patna, Bihar.
[5]Professor of Pathology, MGM Medical College & Hospital, Jamshedpur.
[6]Associate Professor of Pathology, PJMC, Dumka, Jharkhand.
[7]Associate Professor of Community Medicine, Medinirai Medical College, Palamu, Jharkhand.
[8]Research Scientist I, MRU, MGM Medical College, Jamshedpur.

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Abstract:

Background: Human papillomavirus is an STD that generates malignancies of the genital tract, including cervical cancer. Persistent HPV infection is linked to the development of cervical carcinoma. In order to lessen the impact of cervical cancer and encourage cancer registration, epidemiological data on the prevalence, distribution, and conditions of HPV are essential. The study aimed to estimate the prevalence and determinants of HPV infection in women aged 30-59 in the Kolhan region of Jharkhand.

Material & Methods: A cross-sectional study was conducted over a period of two years from January 2022 to December 2023 at a tertiary care teaching hospital in Jharkhand. We enrolled a total of 321 women (30-59 years) for the study. We screened all participants for HPV molecular testing and collected demographic data through a standard questionnaire. The study used a chi-square test to correlate qualitative variables, and a P-value <0.05 was considered statistically significant.

Results: The study found that the overall prevalence of HPV infections was 23/321 (7.2%). There is a high prevalence of HPV in (32-34 years) at 34.8% and in (45-49 years) at 26.1%. The prevalence of HPV was 13% in tribal women. The results showed no statistical significance. In this study, the most prevalent genotypes were multiple groups of HR HPV genotypes (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68), followed by HPV 16 and HPV 18.

Conclusion: The Kolhan division of Jharkhand has a high prevalence of high-risk HPV, particularly among women aged 30-34 and 45-49, recommending rural-based cervical screening and vaccination programs.

Key words:HPV, High Risk HPV, Cervical Cancer, HPV genotype distribution and DNA PCR.

Introduction

HPV is a small, non-enveloped, icosahedral DNA virus having a diameter of 52 to 55 nanometres. A single double-stranded DNA molecule of approximately 8000 base pairs, bound to cellular histones, makes up the viral particles, which also contain a protein capsid. HPV is a sexually transmitted infection that plays a major role in the development of

cervical cancer. [1]
Cervical cancer is India's second most common cancer, accounting for one-fifth of the global burden. In 2020, it caused 123,907 incident cases and 77,348 deaths, with an incidence rate of 18 per 100,000 women.[2] Jharkhand showed significant reductions in incidence and mortality from 1990 to 2019.[3] To reduce the impact of cervical cancer and promote cancer registration, it is crucial to collect epidemiological data on the prevalence, determinants, and distribution of HPV.
In 2022, there were approximately 660,000 new cases of cervical cancer, ranking it as the fourth most common cancer among women globally. In that particular year, countries with low or medium income levels accounted for more than 94% of the 350,000 cervical cancer deaths. In terms of both incidence and mortality rates, cervical cancer is most common in Southeast Asia, Central America, and Sub-Saharan Africa. [4]
Oncogenic strains of HPV link to a staggering 98% of cervical cancer cases, making them a major risk factor in the disease. [5] Sexual contact can spread more than 200 different forms of HPV. The most oncogenic genotypes of HPV are 16 and 18; others are 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. Two of the oncogenic HPV strains that cause cervical cancer are HPV 16 and HPV 18. [6-7] The continuous production and activity of viral proteins E6 and E7 by HPV causes cancer. [8]. These proteins interact with other proteins in cells to alter cellular function and promote tumor formation. To determine the complete impact of HPV infections, it is essential to estimate incidence and prevalence. While the majority of HPV infections resolve on their own, every woman runs the risk of developing aggressive cervical cancer if the infection persists. [9-10]
India's cervical cancer survival rate is 46%, with advanced-stage disease having a lower survival rate of 7.4% compared to localised cancer's 73.2%. [11] Cervical cancer makes up 6-29% of all cancers in women in India. [12] Cervical cancer was the second most prevalent cancer among women in India in 2020, accounting for 18.3% of cases and 18.7% of cancer-related deaths, with a 5-year prevalence of 18.8%. [13] The study found a 2% prevalence of high-risk HPV, with HPV 16 and HPV 33 genotypes being significantly higher in Kerala compared to other detected HPV types. [14]In 2015, the prevalence of HPV in Jharkhand was 13.4%.[15] From 1990 to 2019, Jharkhand exhibited the most significant percentage reductions in cervical cancer incidence (-50.22%) and mortality (-56.16%), followed by Himachal Pradesh, which achieved incidence and mortality reductions of -48.34% and -53.37%, respectively. [3]
There has been a lack of research on HPV infection in Jharkhand, especially in the Kolhan Division. The absence of HR-HPV detection in screening programs has slowed down improvements, treatments, and preventative efforts for cervical cancer. It is essential to have epidemiological data on the prevalence, distribution, and conditions of HPV in order to lessen the burden of cervical cancer, guide the introduction of vaccines, boost screening programs, encourage cancer registration, and start national policy discussions.
Therefore, the main aim of this study was to estimate the prevalence and determinants of HPV in high-risk women in the age group of 30–59 years who have attended gynaecology OPD at MGM Medical College Hospital Jamshedpur.

Material & Methods

After institutional ethical committee approval, a cross-sectional study was conducted in the department of Obs. &Gynecology at MGM Medical College, Jamshedpur, from January 2022 to December 2023. In which 321 women were enrolled. The study included consenting married women aged 30-59 years, sexually active women with abnormal vaginal discharge, post-coital bleeding, bleeding on straining, and symptoms of cervical malignancy. The study excludes non-consenting unmarried women, pregnant women, those who underwent total hysterectomy, and those who tested positive for HIV.
After obtaining consent, we collected data using a standardised questionnaire, which participants received before clinical examinations and sample collection. The questionnaire included information on sociodemographic characteristics (age, educational level, marital status, occupation, country of birth), sexual practices (age of first sexual intercourse and number of sexual partners), reproductive health (parity, number and frequency of pregnancies, MTP, use of contraceptive methods), general health (smoking habits, weight and height, history of major illness), and gynaecological history (previous cervical smears and results, past history of STI).
According to the study protocol, each participant was checked for cervical, perineal, vulvar, and vaginal areas for any lesions, ulcers, discharge, or signs of inflammation before collecting clinical samples and conducting clinical examinations.
After applying 5% glacial acetic acid and taking all standard precautions, we performed a visual inspection of the cervix,

followed by a single-visitcolposcopic examination. After VIA and colposcopy, cervical samples were collected using liquid-based cytology (Regenix Drug Limited Ltd. *mur&mur Division, Chennai,* Tamil Nadu, India). The samples were sent to the Multi-Disciplinary Research Unit, MGM Medical College, Jamshedpur, for cytological and molecular testing. The cytology results were classified using the Bethesda system. HR-HPV infections were detected through an HPV DNA test. We used a fully automated DNA extractor (Magnapure LC 2.0, Roche Machine) to extract DNA from a positive case sample. We used Roche RT-PCR on the confirmed case to identify different HPV strains (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68). We used a tool named GENOSENS to test fourteen types of HR-HPV, including those associated with cervical cancer (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68).
Epi-Info software was used to analyse the data. We presented categorical variables in numbers and percentages. We used the chi-square test to correlate the qualitative variables (HPV DNA-positive and HPV DNA-negative women). A P-value <0.05 was considered statistically significant.

Results:

Socio-demographic characteristics of Study population

The study enrolled a total of 321 women. All subjects produced sufficient specimens for HR-HPV testing. The majority of the respondents, comprising 78 individuals (24%), were in the age group of 30–34 years. The mean (± standard deviation) age for enrolled women was 41.24±8.062 years. 267 [83.2%] are Hindus, and 48 [15%] are from the Muslim community. 292 [91%] live in urban areas. 86 [26.8%] are tribal populations. (Table 1).

Socio-demographic characteristics of Study population (Table:1)

Variables	**Frequency**	**Percentage**
Age of participants		
Mean ± SD (range)	**41.24±8.062**	
30-34	78	24.3
35-39	60	18.7
40-44	68	21.2
45-49	62	19.3
50-54	26	8.1
55-59	27	8.4
Religion		
Hindu	267	83.2
Muslim	48	15.0
Christian	4	1.2
Other	2	.6
Residence		
Urban	292	91.0
Rural	29	9.0
Household		
Non Slum area	313	97.5
Slum area	8	2.5
Community		
Tribal	86	26.8
Non Tribal	235	73.2
Education		
Illiterate	162	50.5
Primary	31	9.7
Middle	83	25.9
Secondary	24	7.5
Graduation	14	4.4

Post Graduation	7	2.2
Occupation		
Govt Service	7	2.2
Private Service	9	2.8
House work	291	90.7
Unskilled Labour	6	1.9
Others	8	2.5

Behavioural and reproductive characteristics of the Study participant

The participants' ages ranged from 13.24 to 1.384 years at menarche, 19.52 to 9.54 years at first intercourse, and 29.02 to 55.87 years at first pregnancy. 22 (6.9%) had a history of contraceptive use, 83 (24.9%) had attended middle school, 291 (90.7%) were house workers, and 303 (94.4%) of the participants were married. 26 [8.1%] women had spontaneous abortion, while 27 [8.4%] had voluntary abortion. The percentages were 25.9% and 25.5% in Parity 3 and 4-9, respectively. (Table 2).

Behavioural and reproductive characteristics of the Study participant (Table:2)		
Variables (Table:2)	**Frequency**	**Percentage**
Age of menstruating: Mean age (SD)	13.24±1.384	
Age at first intercourse: Mean age (SD)	19.52± 9.54	
Age at First pregnancy	29.02±55.87	
Use of Hormonal contraceptive		
Current Pills use	22	6.9
Pills used in past	7	2.2
Never used pills	279	86.9
Not aware	13	4.0
Parity		
0	20	6.2
1	35	10.9
2	101	31.5
3	83	25.9
4-9	82	25.5
History of spontaneous abortion		
Yes	26	8.1
No	295	91.9
History of voluntary abortion		
Yes	27	8.4
No	294	91.6

Cervical Cytology (PAP) and HPV DNA PCR Findings.

Table 3 indicates that the normal smear had a thickness of 15.0%. ASCUS was the most common, accounting for about 45.2%, followed by LSIL (7.8%), HSIL (1.9%), and acute inflammation (29.3%).

Out of the 23 (7.2%) Hr HPV positive cases, 5 (1.6%) tested positive for HPV 16, and 1 (.3%) tested positive for the high-risk HPV type, HPV 18. The remaining samples showed multiple combinations of HPV types, with the most common genotypes being 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 [5.0%]. Other combinations observed were 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68, along with genotype 16. The most common high-risk genotype of HPV was a multiple-group HPV infection, followed by HPV 16 (1.6%).

Cytology (PAP) and HPV DNA PCR Findings (Table:3)

Variables	Frequency	Percentage
Cytology(PAP) Findings		
Acute inflammatory	94	29.3
ASCUS	145	45.2
Atypical Glandular Cells	3	.9
HSIL	6	1.9
LSIL	25	7.8
Normal smear	48	15.0
HPV DNA Positive & Negative		
HPV Positive	23	7.2
HPV Negative	298	92.8
HPV Genotype distribution		
HPV16	5	1.6
HPV18	1	.3
HPV 31,33,35,39,45 ,51,52,56,58,59,66,68 (Multiple group HR HPV Infection)	16	5.0
HPV 31,33,35,39,45,51,52,56,58, 59,66,68 along with 16 (Multiple group HR HPV Infection)	1	.3
HPV Negative	298	92.8

Prevalence of High riskHuman Papillomavirus (HPV)

The HRHPV test prevalence using PCR based methods was 23 (7.2%). The most HPV-positive group was age 30-34 8 [34.8%] and age 45-49 6 [26.1%]. The prevalence of HPV among women with illiterate education status was found in 15 [65.2%] and 3 [13.0%] tribal groups. Furthermore, women who are married (22 [95.7%], 21 [91.3%]) and whose husbands never use condoms had a high prevalence of HPV (Table 3& 4, Figure Number 1 & 2).

Figure: 1: Age wise Prevalence of HR HPV

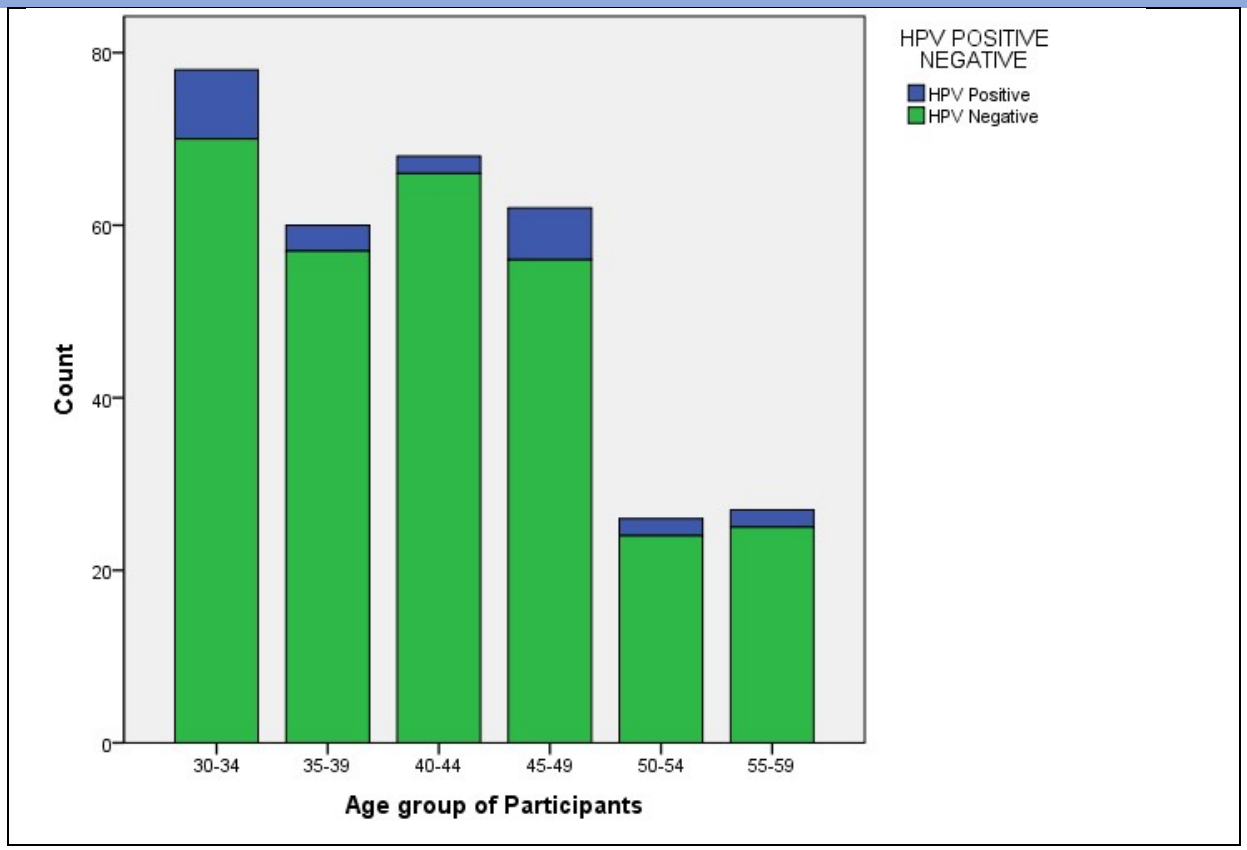
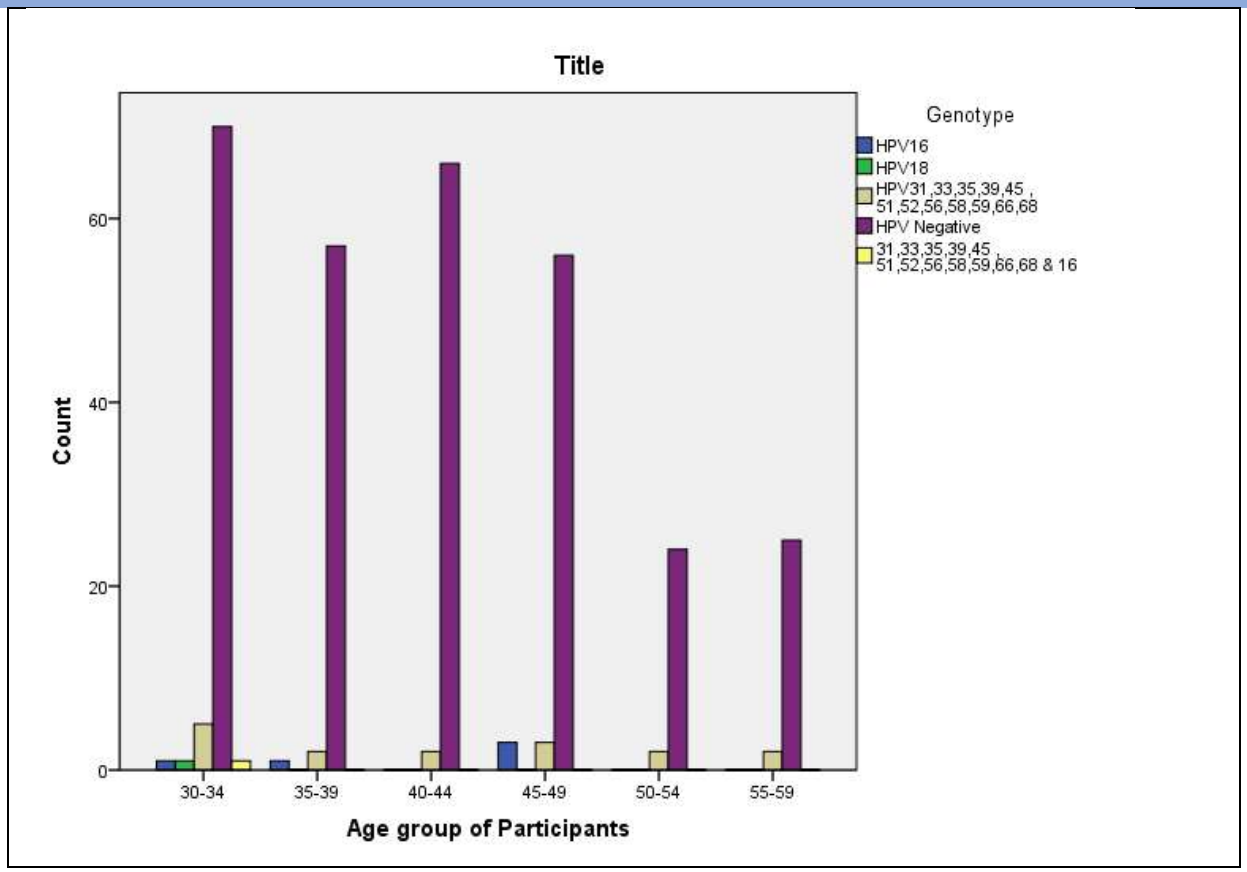


Figure: 02: Age wise Genotype distribution of HR HPV



Risk Factors associated with Hr HPV infections.

We found HPV positive in 8 [34.8%] of the 30-34-year-old women and 6 [26.1%] of the 45-49-year-old women. 19 [82.6%] of menstruating women in the age group of 13–15 years were HPV positive. Among the early-stage marriage patients, 10 [43.5%] of women in the age group of 16–20 were HPV positive. 10 [43.5%] of HPV-positive women had their first intercourse at the age of 17–21 years. 12 [52.2%] of HPV-positive women gave birth to their first child between the ages of 20 and 25 years, while 10 [48.5%] of women in the age group of 15 to 19 years were HPV-positive. Among the HPV-positive women, 10 [43.5%] had given birth twice, 6 [26.1%] thrice, and 5 [21.7%] had delivered birth to 4-6 children. 3 [13.0%] of the HPV-positive women had spontaneous abortions, while 2 [8.7%] had voluntary abortions. 20 [87.0%] of the HPV women never took the pill, while 21 [91.3%] of their husbands did not use condoms during sexual intercourse. 22 [95.7%] of the HPV-positive women experienced abnormal vaginal discharge, while 9 [39.1%] experienced swelling in both lower extremities. The HPV-positive women did not smoke, tobacco, or consume alcohol. [Table no:4]

Risk Factors associated with Hr HPV Infection. (Table 04)				
Variables	**HPV**			
	Positive	**Negative**	**χ2**	***P***
Age of Participants				
30-34	8[34.8%]	70[23.5%]	3.969	.554
35-39	3[13.0%]	57[19.1%]		
40-44	2[8.7%]	66[22.1%]		
45-49	6[26.1%]	56[18.8%]		
50-54	2[8.7%]	24[8.1%]		
55-59	2[8.7%]	25[8.4%]		

Community				
Tribal	3[13.0%]	83[27.9%]	2.387	.122
Non Tribal	20[87.0%]	215[72.1%]		
Age of menstruating			5.765	.217
10-12	2[8.7%]	69[23.2%]		
13-15	19[82.6%]	219[73.5%]		
16-18	1[4.3%]	7[2.3%]		
19-21	1[4.3%]	2[0.7%]		
22-24	0[0.0%]	1[0.3%]		
Age at marriage				
11-15	7[30.4%]	56[18.8%]	4.507	.342
16-20	10[43.5%]	184[61.7%]		
21-25	6[26.1%]	49[16.4%]		
26-30	0[0.0%]	7[2.3%]		
31-35	0[0.0%]	2[0.7%]		
Age at First Intercourse				
11-16	8[34.8%]	79[26.5%]	2.633	.621
17-21	10[43.5%]	170[57.0%]		
22-26	5[21.7%]	42[14.1%]		
27-31	0[0.0%]	5[1.7%]		
32-35	0[0.0%]	2[0.7%]		
Age at First birth				
9-14	1[4.3%]	4[1.3%]	5.203	.392
15-19	10[43.5%]	129[43.3%]		
20-25	12[52.2%]	122[40.9%]		
26-31	0[0.0%]	19[6.4%]		
32-36	0[0.0%]	2[0.7%]		
37-40	0[0.0%]	22[7.4%]		
Parity				
0	0[0.0%]	20[6.7%]	2.932	.569
1	2[8.7%]	33[11.1%]		
2	10[43.5%]	91[30.5%]		
3	6[26.1%]	77[25.8%]		
4-9	5[21.7%]	77[25.8%]		
Spontaneous abortion				
Yes	3[13.0%]	23[7.7%]	.813	.367
No	20[87.0%]	275[92.3%]		
Voluntary abortion				
Yes	2[8.7%]	25[8.4%]	.003	.959
No	21[91.3%]	273[91.6%]		
Use of hormonal contraceptives				
Current Pills use	2[8.7%]	20[6.7%]	.668	.881
Pills used in past	0[0.0%]	7[2.3%]		
Never used pills	20[87.0%]	259[86.9%]		
Not aware	1[4.3%]	12[4.0%]		
Husband use of condom				
Current use	2[8.7%]	13[4.4%]	1.407	.495
Used only in the past	0[0.0%]	7[2.3%]		
Never used condom	21[91.3%]	278 [93.3%]		

Clinical Symptoms				
Abnormal Veginal discharge	22[95.7%]	281[94.3%]	.123	.940
Genital sore or Ulcer	1[4.3%]	16[5.4%]		
Genital Wart	0[0.0%]	1[0.3%]		
Pain				
Persistent Back Pain	14[60.9%]	184[61.7%]	1.250	.535
Leg Pain	4[17.4%]	31[10.4%]		
Pelvic Pain	5[21.7%]	83[27.9%]		
Swelling of a leg or both lower extremities				
Present	9[39.1%]	82[27.5%]	1.418	.234
Absent	14[60.9%]	216[72.5%]		
Smoking Habit				
Yes currently	0[0.0%]	2[0.7%]	1.405	.495
Yes but only in the past	1[4.3%]	4[1.3%]		
No	22[95.7%]	292 [98.0%]		
chewed tobacco Habit				
Yes currently	0[0.0%]	8[2.7%]	.715	.700
Yes but only in the past	0[0.0%]	1[0.3%]		
No	23[100.0%]	289[97.0%]		
Alcohol consumption				
Yes currently	0[0.0%]	1[0.3%]	.392	.822
Yes but only in the past	0[0.0%]	4[1.3%]		
No	23[100.0%]	293[98.3%]		

Discussion:

Worldwide, the cervical cancer incidence rate is 13.1 per 100,000 women and the mortality rate is 6.9 per 100,000 women; however, in India, these rates are much higher at 14.7 per 100,000 and 9.2 per 100,000, respectively. [17] States like Arunachal Pradesh and Assam have lower rates due to geographical factors. While 2.5% of cervical cancer cases are found in Northern America, 58.2% are found in Asia. The disease affects 27,85 million women annually and is diagnosed with 56,984,7 new cases worldwide. Researchers Singh M. et al. found that cervical cancer rates in India had dropped significantly over the last 30 years. [16] Serious cellular cancers and cervical cancer can develop from persistent high-risk HPV infections. [18] Sub-Saharan Africa has the highest cervical HPV prevalence among women at 24%, followed by Latin America and the Caribbean at 16%, Eastern Europe at 14%, and Southeast Asia at 14%. [19] HPV prevalence estimates in India ranged from 2.3% to 36.9%, according to studies. [20]

However, only a handful of studies have focused on cervical cancer, and no research has explored HR HPV genotyping infections among patients in the Kolhan division of Jharkhand. In this study, we investigated the prevalence and determinants of HR-HPV in 321 women who underwent screening and HPV DNA typing.

The study found a 7.2% HPV infection prevalence rate, consistent with previous studies in India by Parvez R. et al. [20] and Sabeena S. et al. [21]. P. Sangeeta et al. reported a high prevalence of HPV infection in 37.3% of the study [22]. A study by Shakya S et al. [23] found that 14.4% of women had HPV, 7.9% had high-risk types, and 6.5% had low-risk types. The high-risk type prevalence was 8.3% in women with abnormal cytology and 7.7% in women without abnormal cytology. The tribal community had a prevalence of HPV infection of 3.0%. Sharma K et al found in their study that extremely high prevalence of HPV infection is found in adolescent and young adult tribal girls, possibly due to different socio-sexual behaviour, indicating a serious health concern for Indian tribal women. [40].

Abnormal cytology revealed that ASCUS and LSIL had the highest prevalence of Hr HPV infection, with malignant cytology being more common. Women showed HPV-positivity in these histologically confirmed cases of cervical cancer. [22]

In this study, the most common genotypes were the multiple group high-risk HPV genotypes (31, 33, 51, 52, 56, 58, 59, 66, 68), followed by HPV 16 and HPV 18. Many individuals who tested positive for HR-HPV had multiple genotypes. These findings align with studies that utilized similar molecular techniques for hr-HPV DNA detection, such as those conducted by Nang, D.W., et al. [24] and Mishra, R., et al. [25]. Over time, one of 21 HPV strains infected more than one-third of women, with HPV 16 being the most common, followed by HPV 31, 58, and 56, according to Muwonge R. et al. [26]

The study reveals high rates of HPV infection in women with abnormal vaginal discharge, a finding consistent with Nang, D.W. et. al. [24]. The loss of protective microorganisms and other changes from vaginal infections may make it easier to acquire and persist sexually transmitted infections, suggesting clinicians should consider HPV screening.

In this study, we found that 34.8% of people aged 30 to 35 and 26.1% of people aged 45 to 49 were susceptible to HPV infection. Before this study, Ginindza TG et al., Saldana-Rodriguez P et al., and Zheng L-l et al. found similar rates. [27-29]

Studies show that starting sexual intercourse earlier with HPV infection, between 11-16 (34%) and 17-21 (43.5%), increases the risk of HPV and cervical cancer and also leads to women giving birth before 18 years old. [30] The ages of first sexual intercourse and marriage significantly impact cervical cancer risk, with women under 16 having a 2.4-fold higher risk compared to those over 21. [31] Spontaneous and voluntary abortion history significantly increases the likelihood of HPV infection in women compared to those without a history of miscarriage. [32] The study revealed that women who smoked tobacco had no HPV positive results, while non-smokers had the highest incidence of HPV infection, despite previous studies suggesting smoking increases the risk of cervical cancer. [33] In this study, the highest number of HPV positive cases was 19 [82.6%] in the menarche age group of 13–15 years. According to Sharma, P. et al., a significant risk factor for cervical cancer is the age at menarche of 13–14 years. [34]

The study revealed that HPV infection rates were higher in women aged 18 or younger, and pre-malignant or malignant cervical lesions were more prevalent among those starting early in sex. We also observed this link in developing countries, where abnormal Pap test results were on the rise. [35]

A systematic review and meta-analysis showed that multiple pregnancies may increase cervical abnormality detection due to endocervix migration and vaginal delivery traumas. However, high vaginal parity isn't sufficient unless HPV infection is present. Women with HPV infection and multiple pregnancies have a higher risk of cervical cancer. [36]

We found no consistent evidence linking the use of oral contraceptives to an elevated risk of cervical cancer after accounting for HPV infection. [37]

The study found that husbands not using condoms during intercourse caused 21 [91.3%] cases of HPV infection. Pierce Campbell CM et. al. suggested that consistent condom use can protect against HPV in men, reducing the risk of new infections and decreasing the duration of infections. Nonmonogamous and non-stable partners benefit more from consistent condom use. Promoting correct condom use is crucial for STI risk reduction, and HPV prevention should focus on both condom use promotion and vaccination. [38]

We also assessed the risks of chewing tobacco, smoking, and alcohol in women and found that they were not statistically significant. Studies indicate smoking is a significant risk factor for carcinoma in situ stage 3 and invasive cervical cancer, with a direct association between tobacco and HPV prevalence in 98% cases. A large cohort study found that quitting smoking for 10 years reduced cancer risk by half compared to those who continued to smoke. The duration of smoking also correlates with increased cervical cancer risk. [39]

Conclusion:

The present study provides information about the genotype distribution among high-risk women of Kolhan region of Jharkhand, which will help in planning an appropriate strategy for disease monitoring. Thus an effective vaccination program based on regional HPV epidemiological profiles, along with cervical cancer screening, can be developed to reduce the burden of cervical cancer in Jharkhand. The HPV surveillance and screening program will benefit the rural population. Also this study will offer the baseline data for future research.

Strength and Limitation of the study

Our findings enhance epidemiological understanding of the burden, genotype distribution, and factors linked to hr-HPV infection. Our research was conducted in a hospital setting; therefore, to acquire more accurate data on distribution and prevalence rates in this geographical area, we must extend the study to encompass the community level, incorporating both rural and urban sectors. The HPV DNA test identifies HPV types 16, 18, and 12 additional high-risk variants in a collective analysis. Consequently, we could not independently ascertain the prevalence of the remaining 12 kinds of hr-HPV.

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All authors conceptualised and designed the study. Dr. M.M. Bara, Dr. Lata Singh, Dr.Silbina Murmu, Dr. A.K. Jha, Dr. Budhan Baitha, and Kuber Chandra Setua helped draft the laboratory protocols and analyse the cervical specimens for the HR-HPV DNA molecular test. Manish Kumar performed the data entry. Dr. Rajan Kumar Barnwal& Kumar Vimal performed the statistical analysis. All the authors made contributions toward reviewing, revising, and finalising the manuscript. The research team expresses gratitude to all study participants and the Department of Obs. & Gynaecology for their cooperation.

Conflict of Interest: The author declare no conflict of Interest

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