North Asian International Research Journal of Multidisciplinary

IRJIF IMPACT FACTOR:7.001

ISSN: 2454-2326 Vol.12, Issue, 1 January-2026

Index Copernicus Value: 58.12 Indian Citation Index

NAIRJC Approved Journal as per New UGC Guidelines

EVALUATION OF HUMAN PAPILLOMA VIRUS BY PCR IN CERVICAL SAMPLES OF WOMEN NEAR BHOPAL (MADHYA PRADESH), INDIA: MOLECULAR BIOLOGY, GENOTYPING, EPIDEMIOLOGY, AND CLINICAL IMPLICATIONS

[1]HEMRAJ SINGH & DR. ABHJEETA NANDA [2]

[1]*Research scholar, Kalinga University Naya Raipur, Chhattisgarh*
[2]*Assistant Professor, Department of Biotechnology, Kalinga University Naya Raipur Chhattisgarh*

Department: Science, *Kalinga University,*
Address: Village Kotni, Near Mantralaya, Naya Raipur, Chhattisgarh 492101,
**Corresponding Author E-mail: hemraj_in@hotmail.com*

ABSTRACT

Background:
Cervical cancer remains one of the most common malignancies affecting women in low- and middle-income countries, with India contributing a substantial proportion of the global disease burden. Persistent infection with oncogenic Human Papillomavirus (HPV) is recognized as the necessary etiological factor for cervical carcinogenesis. Molecular detection of HPV using polymerase chain reaction (PCR) has emerged as a highly sensitive and specific diagnostic approach, enabling early identification of infection and genotype-based risk stratification. Despite the increasing emphasis on HPV-based screening, region-specific molecular epidemiological data from central India remain limited.

Objective:
To evaluate the prevalence and genotype distribution of Human Papillomavirus using PCR-based molecular techniques in cervical samples of women residing near Bhopal, Madhya Pradesh, India, and to provide an extensive review of HPV biology, molecular pathogenesis, and public health implications.

Methods:
A cross-sectional molecular study was conducted on 50 cervical samples collected from women attending gynecology and diagnostic clinics in and around Bhopal. DNA was extracted and amplified using consensus PCR primers targeting the HPV L1 gene region. Genotype-specific PCR assays were employed for detection of high-risk HPV genotypes. Relevant epidemiological and molecular data were analysed descriptively.

Results:
HPV DNA was detected in 15 of 50 cervical samples, indicating an overall prevalence of 30%. High-risk

HPV genotypes predominated, with HPV-16 being the most frequently detected genotype, followed by HPV-18 and HPV-31. The PCR assay demonstrated high analytical sensitivity and specificity for HPV detection.

Conclusion:
The study reveals a substantial burden of high-risk HPV infection among women near Bhopal and highlights the critical role of PCR-based molecular screening in cervical cancer prevention. Region-specific HPV epidemiological data are essential for optimizing screening strategies and guiding vaccination policies in central India.
KEYWORDS: ***Human papillomavirus; HPV PCR; cervical samples; molecular diagnostics; HPV genotyping; cervical cancer; India***

1. INTRODUCTION

Cervical cancer represents a major global public health challenge and continues to rank among the leading causes of cancer-related morbidity and mortality in women worldwide. According to the World Health Organization, cervical cancer is the fourth most common cancer in women globally, with an estimated 604,000 new cases and over 340,000 deaths annually. The burden is disproportionately higher in low- and middle-income countries, where organized screening programs and preventive healthcare infrastructure remain inadequate.

India alone accounts for nearly one-fifth of the global cervical cancer burden, with cervical cancer ranking as the second most common cancer among Indian women. Data from the National Cancer Registry Programme and the National Family Health Survey (NFHS-5) indicate alarmingly low participation in cervical cancer screening, with fewer than 2% of eligible women having ever undergone screening. Sociocultural barriers, lack of awareness, limited access to healthcare services, and dependence on cytology-based screening methods contribute significantly to delayed diagnosis and poor outcomes.

Persistent infection with oncogenic Human Papillomavirus (HPV) has been conclusively established as the necessary cause of cervical cancer. HPV is a small, non-enveloped, double-stranded DNA virus belonging to the family *Papillomaviridae*. More than 200 HPV genotypes have been identified, of which approximately 14 are classified as high-risk due to their oncogenic potential. Among these, HPV-16 and HPV-18 together account for nearly 70% of cervical cancer cases worldwide.

The carcinogenic potential of HPV is mediated through the integration of viral DNA into the host genome and sustained expression of viral oncoproteins E6 and E7. These oncoproteins disrupt critical cell-cycle regulatory pathways by promoting degradation of tumor suppressor proteins p53 and retinoblastoma (Rb), leading to genomic instability and malignant transformation. Given this strong causal association, detection of HPV DNA has become central to cervical cancer screening, early diagnosis, and prevention strategies.

Conventional cytology-based screening methods, including the Papanicolaou (Pap) smear and Liquid-Based Cytology (LBC), have contributed significantly to reductions in cervical cancer incidence in high-income countries. However, these methods suffer from limited sensitivity, require repeated testing, and depend heavily on trained personnel and laboratory infrastructure. In contrast, molecular techniques such as polymerase chain

reaction (PCR) offer superior sensitivity and specificity, enabling early detection of HPV infection even before cytological abnormalities develop.

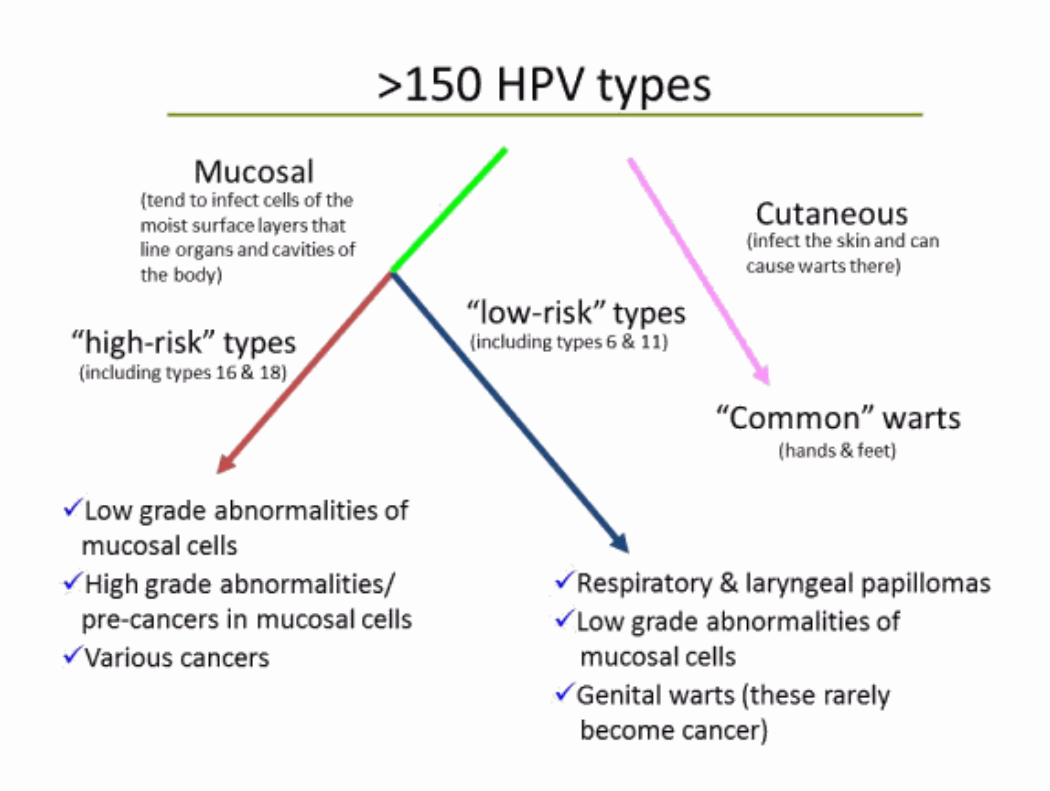
Despite increasing adoption of HPV DNA testing in screening programs, region-specific molecular epidemiological data from central India, particularly Madhya Pradesh, remain scarce. Bhopal and surrounding regions represent a diverse population with unique sociocultural and healthcare access challenges. Understanding HPV prevalence and genotype distribution in this region is essential for designing effective screening strategies, guiding vaccination programs, and reducing the burden of cervical cancer.

2. BIOLOGY OF HUMAN PAPILLOMAVIRUS (HPV)

2.1 Classification and Taxonomy of Papillomaviridae

Human Papillomaviruses belong to the family *Papillomaviridae*, a large and diverse group of epitheliotropic DNA viruses that infect a wide range of vertebrate hosts. Papillomaviruses are highly species-specific and have co-evolved with their hosts over millions of years. More than 200 genetically distinct HPV genotypes have been identified in humans, classified based on nucleotide sequence homology within the L1 gene.

HPV genotypes are broadly categorized into **low-risk** and **high-risk** groups based on their association with malignancy. Low-risk types, such as HPV-6 and HPV-11, are commonly associated with benign lesions like genital warts, whereas high-risk types, including HPV-16, HPV-18, HPV-31, HPV-33, HPV-45, HPV-52, and HPV-58, are implicated in cervical and other anogenital cancers.



Source: Doorbar J. Molecular biology of human papillomavirus infection and cervical cancer. Virology. 2013;445(1–2):1–21. doi:10.1016/j.virol.2013.06.017

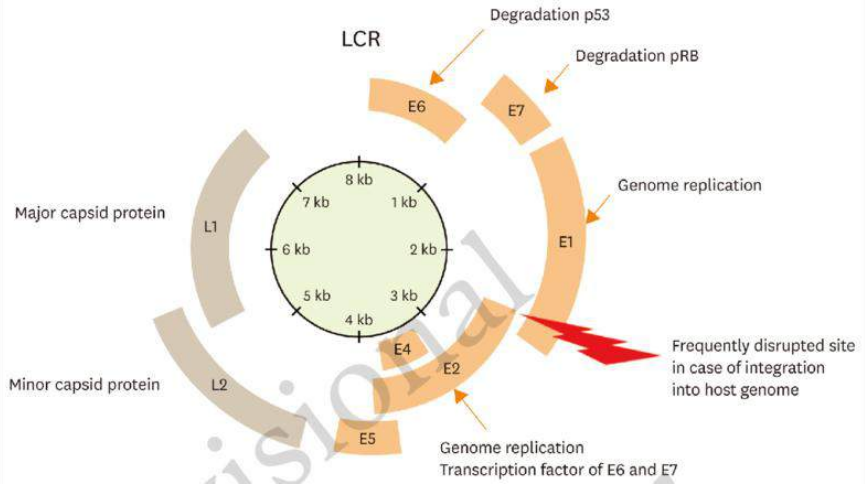
2.2 Structure and Genome Organization of HPV

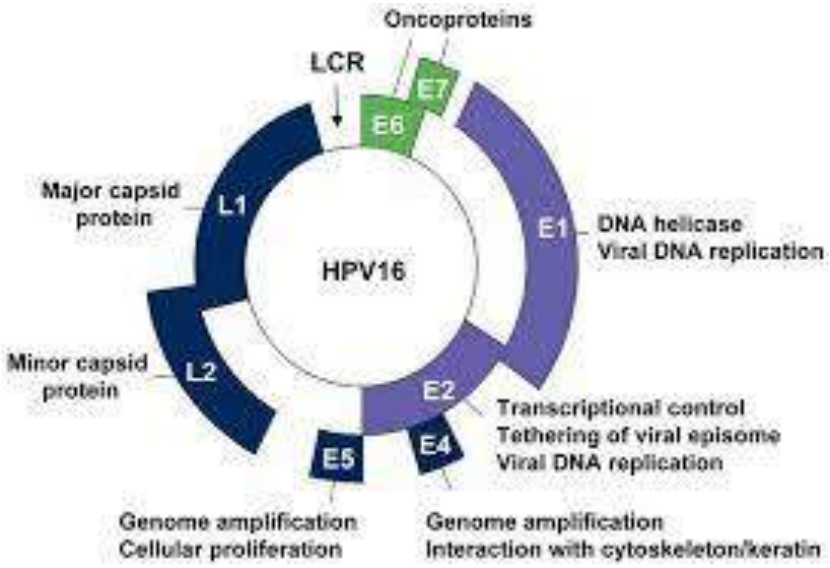
HPV is a small, non-enveloped virus approximately 55 nm in diameter, containing a circular double-stranded DNA genome of about 8 kilobases. The viral genome is organized into three functional regions:

Upstream Regulatory Region (URR):
Contains transcriptional control elements and the origin of replication.

Early Region (E):
Encodes proteins E1–E7 involved in viral replication, transcriptional regulation, and cellular transformation.

Late Region (L):
Encodes structural capsid proteins L1 and L2, which assemble to form the viral capsid.

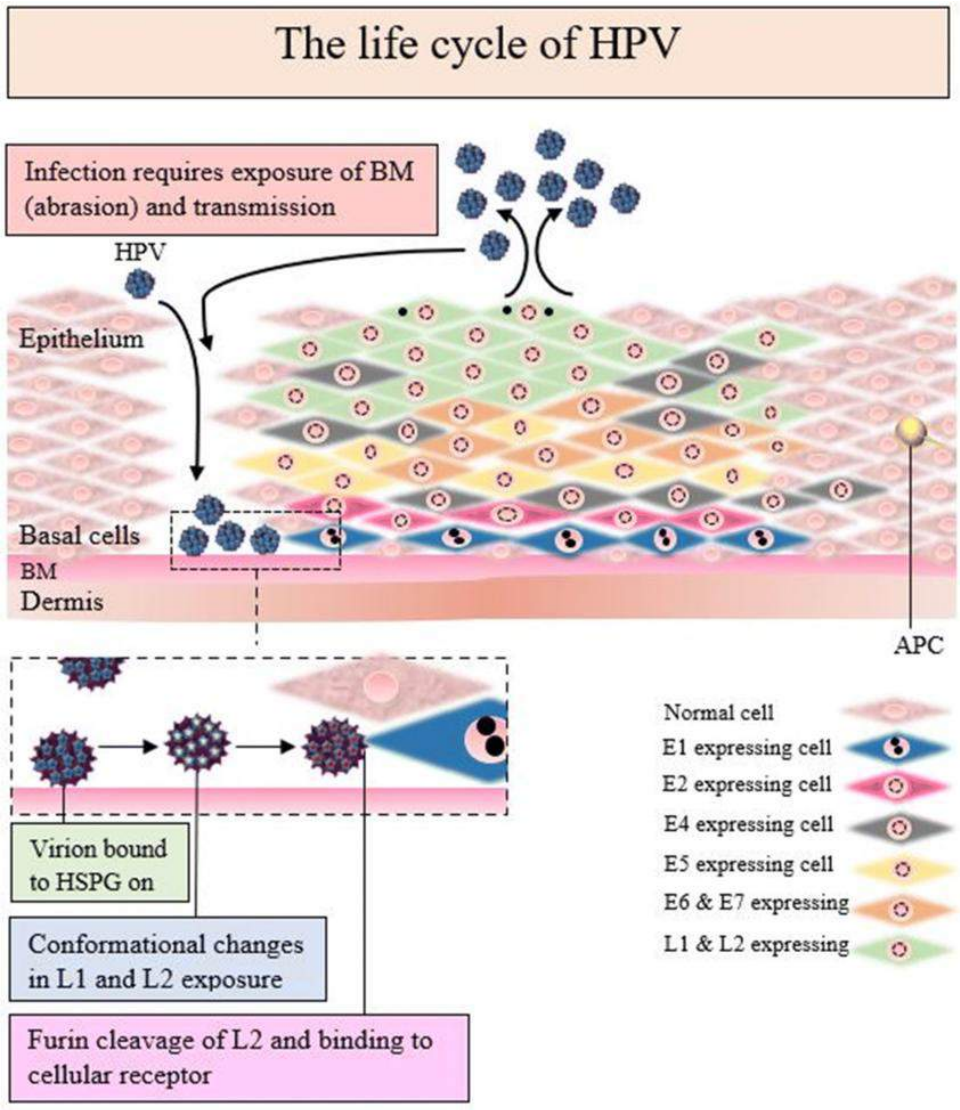




Source: Doorbar J, et al. The biology and life-cycle of human papillomaviruses. Nat Rev Microbiol. 2012;10:543–556. doi:10.1038/nrmicro2812

2.3 HPV Life Cycle

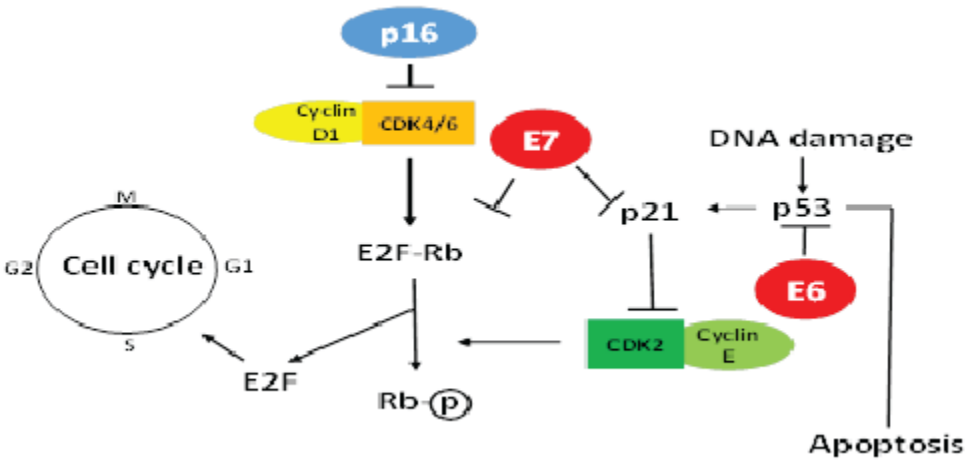
The HPV life cycle is intricately linked to the differentiation program of stratified squamous epithelial cells. Infection occurs through micro-abrasions in the epithelium, allowing the virus to access basal keratinocytes. Viral DNA is maintained as episomes in the nucleus and replicates synchronously with host cell DNA. As infected keratinocytes differentiate and migrate toward the epithelial surface, late gene expression is initiated, leading to viral genome amplification, capsid protein synthesis, and assembly of infectious virions.



Source: Van Keer S, et al. The human papillomavirus life cycle. Clin Chim Acta. 2017;466:54–61. doi:10.1016/j.cca.2017.01.006

2.4 Molecular Pathogenesis: Role of E6 and E7 Oncoproteins

High-risk HPV types express E6 and E7 oncoproteins that play a central role in malignant transformation. E7 binds to and promotes degradation of the retinoblastoma (Rb) protein, resulting in uncontrolled cell cycle progression. E6 targets the tumor suppressor protein p53 for ubiquitin-mediated degradation, inhibiting apoptosis and DNA damage response mechanisms. Persistent expression of these oncoproteins leads to genomic instability and accumulation of oncogenic mutations.



Source: zur Hausen H. Papillomaviruses and cancer. Nat Rev Cancer. 2002;2:342–350. doi:10.1038/nrc798

3. EPIDEMIOLOGY OF HUMAN PAPILLOMAVIRUS INFECTION

3.1 Global Epidemiology of HPV

Human Papillomavirus infection is one of the most common sexually transmitted viral infections worldwide. It is estimated that more than 80% of sexually active individuals will acquire at least one HPV infection during their lifetime. While most HPV infections are transient and cleared spontaneously by the host immune system within 1–2 years, persistent infection with high-risk HPV genotypes poses a significant risk for progression to malignancy.

Globally, HPV prevalence varies considerably across regions, influenced by factors such as sexual behavior, age at first intercourse, number of sexual partners, socioeconomic status, access to healthcare, and effectiveness of screening programs. High prevalence rates are reported in sub-Saharan Africa, Latin America, and South Asia, regions that also bear a disproportionate burden of cervical cancer. In contrast, countries with well-established HPV vaccination and organized screening programs have witnessed significant declines in HPV prevalence and cervical cancer incidence.

High-risk HPV genotypes, particularly HPV-16 and HPV-18, are consistently identified as the most prevalent oncogenic types worldwide. Meta-analyses of HPV genotype distribution indicate that HPV-16 alone accounts for approximately 50–60% of cervical cancer cases, followed by HPV-18 (10–15%), with other genotypes contributing variably depending on geographic region.

3.2 Epidemiology of HPV Infection in India

India represents a unique epidemiological setting for HPV infection and cervical cancer due to its vast population diversity, sociocultural heterogeneity, and uneven healthcare access. Multiple studies conducted across different regions of India have reported HPV prevalence ranging from 10% to over 40%, depending on study population, age group, screening method, and diagnostic technique used.

Northern and central Indian states, including Madhya Pradesh, Uttar Pradesh, and Rajasthan, have reported relatively high prevalence of high-risk HPV infection, particularly among women with limited access to routine gynecological care. Studies from hospital-based and community-based settings consistently demonstrate a predominance of HPV-16, followed by HPV-18 and other high-risk genotypes such as HPV-31, HPV-33, and HPV-45.

Data from the National Family Health Survey (NFHS-5) highlight alarmingly low cervical cancer screening coverage in India, with less than 2% of women aged 30–49 years reporting having undergone any form of cervical screening. This low uptake underscores the need for sensitive, scalable, and acceptable screening modalities such as PCR-based HPV testing.

3.3 HPV Epidemiology in Central India and Madhya Pradesh

Central India remains underrepresented in HPV epidemiological literature despite bearing a significant cervical cancer burden. Studies conducted in Madhya Pradesh, including regions such as Rewa, Gwalior, and Bhopal, have reported a high incidence of abnormal Pap smears and a substantial prevalence of high-risk HPV infection.

Research from Rewa district has demonstrated a high proportion of cytological abnormalities among screened women, coupled with low awareness regarding cervical cancer and HPV infection. Similarly, studies from Gwalior have highlighted limited knowledge and suboptimal attitudes toward HPV vaccination among adolescents, emphasizing gaps in preventive education.

The Bhopal region, characterized by a mix of urban, semi-urban, and rural populations, presents unique challenges related to healthcare access and screening participation. The paucity of molecular HPV prevalence data from this region necessitates targeted studies to inform region-specific screening strategies. The present study contributes valuable baseline data on HPV prevalence and genotype distribution among women near Bhopal.

4. HPV AND CERVICAL CARCINOGENESIS

4.1 Natural History of HPV Infection

HPV infection follows a well-defined natural history that determines clinical outcome. Following initial exposure, the virus infects basal epithelial cells through micro-abrasions. In the majority of cases, the host immune response successfully clears the infection within 6–24 months without clinical consequences.

However, persistence of high-risk HPV infection, particularly with oncogenic genotypes such as HPV-16 and HPV-18, can lead to progressive cellular abnormalities. Factors contributing to viral persistence include

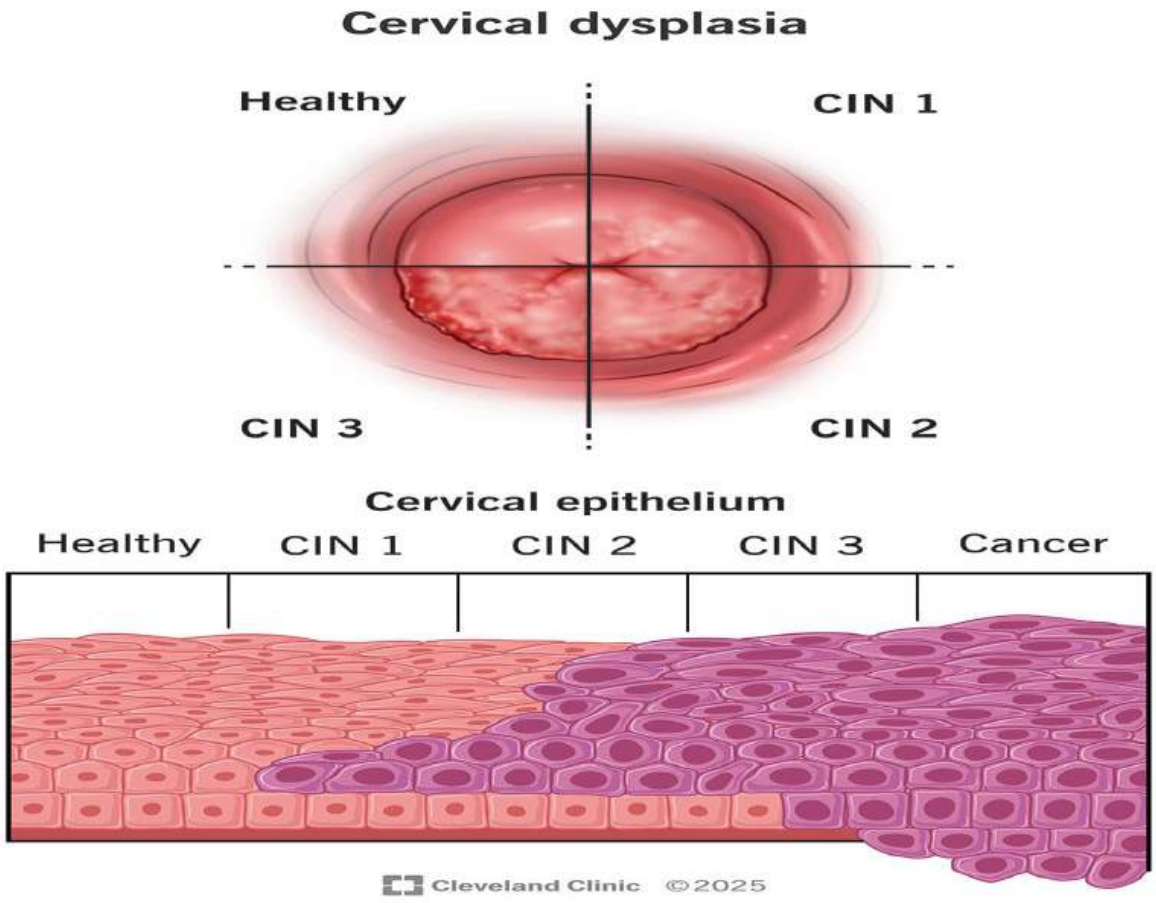
immunosuppression, smoking, long-term oral contraceptive use, co-infection with other sexually transmitted pathogens, and host genetic susceptibility.

4.2 Cervical Intraepithelial Neoplasia (CIN) Progression Model

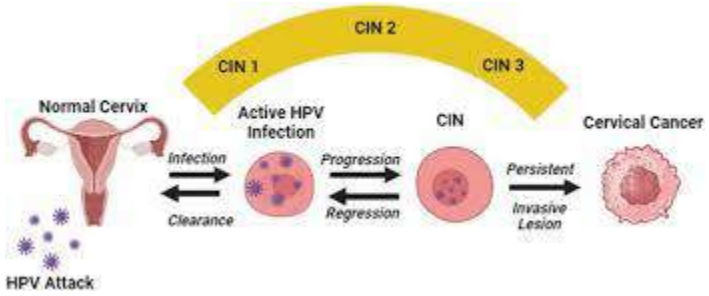
The progression from HPV infection to cervical cancer typically occurs through well-recognized precursor lesions collectively termed cervical intraepithelial neoplasia (CIN). CIN lesions are graded based on the extent of epithelial involvement:

- **CIN I:** Mild dysplasia, often associated with transient HPV infection and high rates of spontaneous regression.
- **CIN II:** Moderate dysplasia with increased likelihood of persistence.
- **CIN III:** Severe dysplasia or carcinoma in situ, representing a high-risk precursor to invasive cancer.

Persistent infection with high-risk HPV genotypes drives progression through these stages over several years, providing a critical window for early detection and intervention through screening.



Source: Schiffman M, et al. Human papillomavirus and cervical cancer. Lancet. 2007; 370:890–907. doi:10.1016/S0140-6736(07)61416-0



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doi:10.1016/S0140-6736(07)61416-0

4.3 Molecular Events in Cervical Carcinogenesis

The transition from productive HPV infection to malignant transformation is characterized by integration of viral DNA into the host genome. This event disrupts the viral E2 gene, resulting in deregulated expression of E6 and E7 oncoproteins. Sustained activity of these oncoproteins leads to chromosomal instability, accumulation of genetic mutations, and evasion of immune surveillance.

Molecular studies have demonstrated that detection of HPV DNA, particularly high-risk genotypes, precedes cytological abnormalities by several years. This observation forms the basis for HPV DNA testing as a primary screening tool capable of identifying women at risk before the development of overt disease.

5. DIAGNOSTIC APPROACHES FOR HPV DETECTION

5.1 Cytology-Based Screening Methods

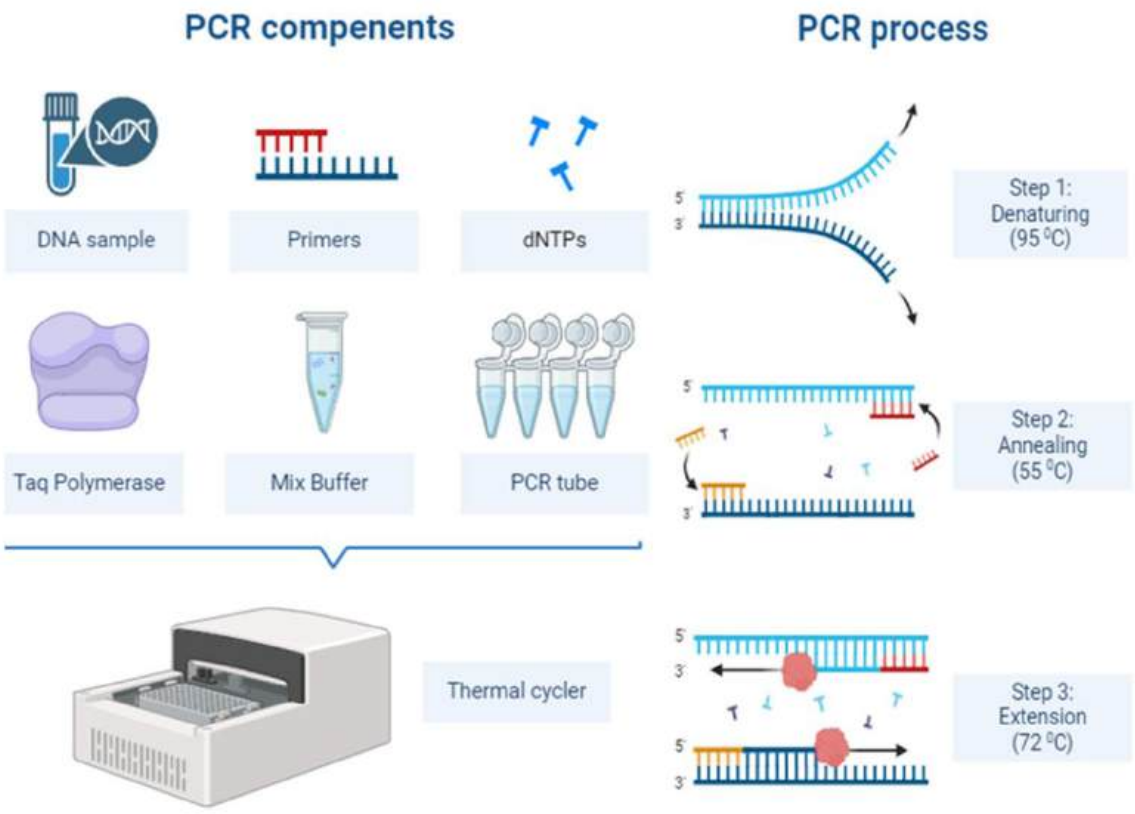
The Papanicolaou (Pap) smear has historically been the cornerstone of cervical cancer screening. While cytology has contributed significantly to reductions in cervical cancer incidence in high-income countries, it suffers from several limitations, including moderate sensitivity, inter-observer variability, and the need for repeated testing.

Liquid-Based Cytology (LBC) offers improvements in sample adequacy and slide quality; however, it remains dependent on trained cytotechnologists and laboratory infrastructure. Furthermore, cytology detects morphological changes rather than the underlying viral etiology, limiting its effectiveness for early detection.

5.2 Molecular Techniques for HPV Detection

Molecular detection of HPV DNA using PCR-based assays has revolutionized cervical cancer screening. PCR offers high analytical sensitivity, enabling detection of low viral loads and multiple HPV genotypes. Targeting conserved regions such as the L1 gene allows broad detection of diverse HPV types.

Genotype-specific PCR assays provide additional clinical value by identifying high-risk HPV types associated with increased risk of disease progression. Numerous studies have demonstrated superior sensitivity and negative predictive value of HPV DNA testing compared to cytology, supporting its use as a primary screening modality.



Source: Coutlée F, et al. Human papillomavirus DNA detection and genotyping. J Clin Virol. 2015; 69:104–109. doi:10.1016/j.jcv.2015.06.090

5.3 Role of PCR in Regional Screening Programs

PCR-based HPV testing is particularly suited for regions with limited cytology infrastructure. The ability to process large numbers of samples with high accuracy makes PCR an attractive option for population-based screening programs. Integration of molecular screening with existing public health initiatives could significantly improve early detection and reduce cervical cancer mortality in India.

6. MATERIALS AND METHODS

6.1 Study Design and Study Area

A cross-sectional, descriptive molecular study was conducted between 2024-2025 in and around **Bhopal, Madhya Pradesh**, including urban, peri-urban, and semi-rural populations. Cervical samples were collected from women attending gynecology outpatient departments and diagnostic centers for routine gynecological evaluation, cervical screening, or related complaints.

The study region represents a heterogeneous population with varying socioeconomic backgrounds, healthcare accessibility, and awareness regarding cervical cancer screening, making it suitable for regional HPV epidemiological assessment.

6.2 Study Population and Sample Size

A total of **50 women** aged **21–65 years** were enrolled after obtaining written informed consent. The sample size was selected based on feasibility and to generate preliminary regional molecular epidemiological data.

6.3 Inclusion and Exclusion Criteria

Inclusion criteria:

- Sexually active women aged 21–65 years
- Willingness to participate and provide informed consent

Exclusion criteria:

- Pregnant women
- Active vaginal bleeding at the time of sampling
- History of hysterectomy
- Women undergoing treatment for cervical malignancy

6.4 Cervical Sample Collection

Cervical samples were collected by trained healthcare professionals using a **sterile cervical cyto-brush**. The brush was rotated gently at the transformation zone to ensure adequate exfoliation of epithelia1 cells. Samples were immediately transferred into transport medium and stored under recommended conditions until laboratory processing.

6.5 DNA Extraction

Genomic DNA was extracted using **commercial silica-column-based DNA extraction kits** following the manufacturer's protocol. Extracted DNA was quantified and assessed for purity using spectrophotometric analysis (A260/A280 ratio). DNA samples were stored at −20 °C until PCR amplification.

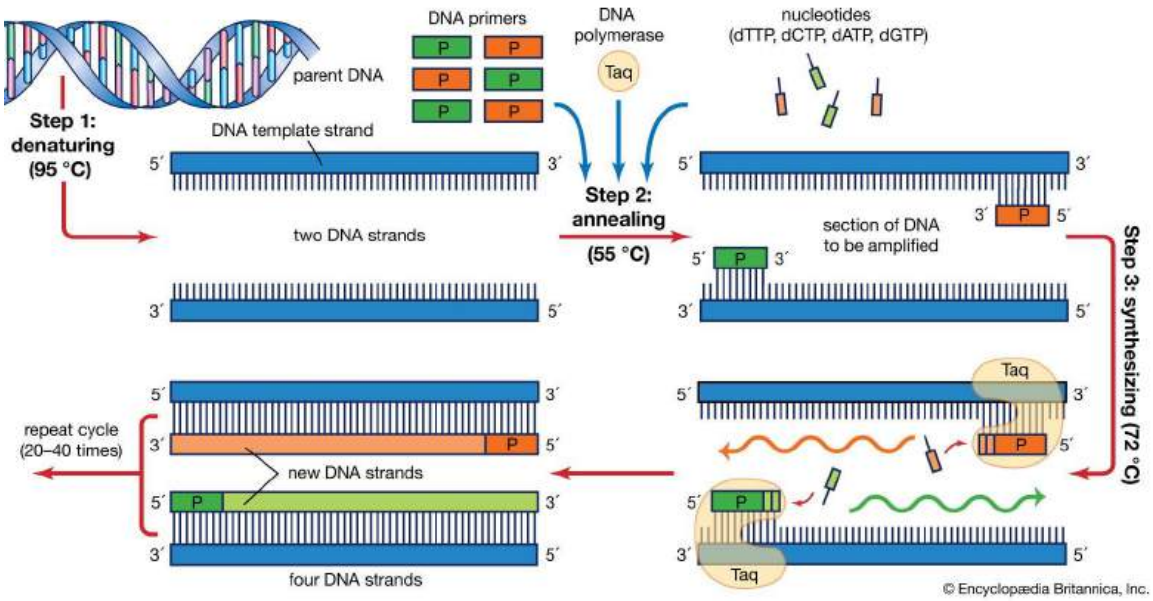
6.6 PCR Amplification and HPV Detection

HPV DNA detection was performed using **consensus PCR primers targeting the L1 gene region**, which is highly conserved among HPV genotypes. PCR reactions were carried out in a total volume of 25 µL containing extracted DNA, primers, nucleotides, buffer, $MgCl_2$, and Taq DNA polymerase.

Thermal cycling conditions included:

- Initial denaturation at 95 °C
- 35 cycles of denaturation, annealing, and extension
- Final extension at 72 °C

PCR products were analysed by **agarose gel electrophoresis**, visualized under UV illumination after ethidium bromide staining.



Source: Pattyn J, et al. Analytical performance of HPV PCR assays. Expert Rev Mol Diagn. 2019; 19:959–968. doi:10.1080/14737159.2019.1685933

6.7 HPV Genotyping

Samples positive for HPV DNA were subjected to **genotype-specific PCR assays** for detection of high-risk HPV genotypes, including **HPV-16, HPV-18, HPV-31, HPV-33, HPV-45, HPV-52, and HPV-58**. Appropriate positive and negative controls were included in each run to ensure assay validity.

6.8 Statistical Analysis

Data were entered into Microsoft Excel and analyzed descriptively. HPV overall prevalence and genotype distribution were expressed as frequencies and percentages.

7. RESULTS

7.1 HPV Prevalence

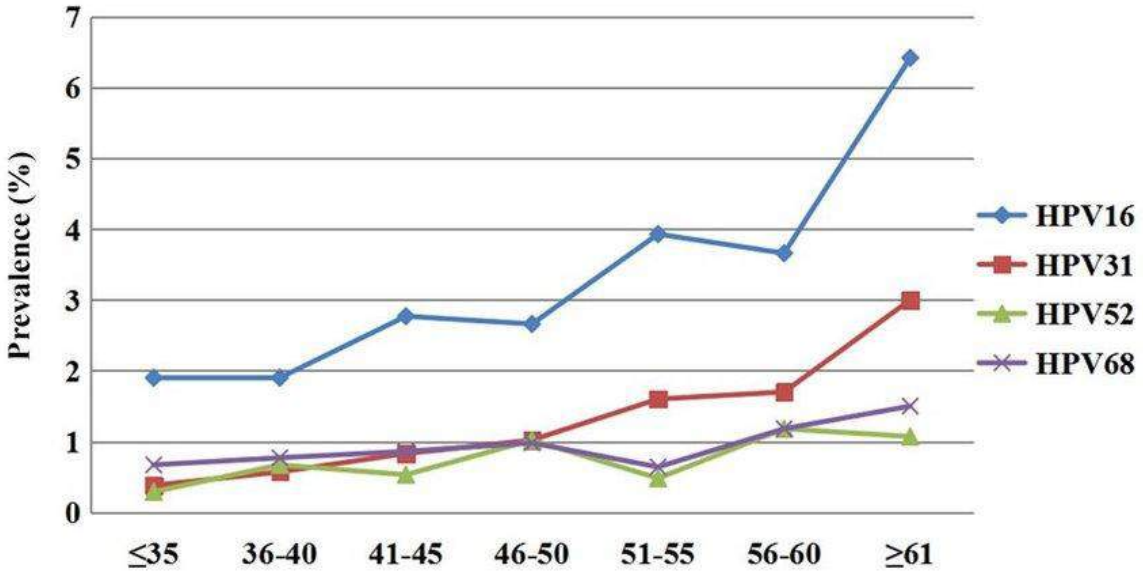
Out of **50 cervical samples**, **15 samples tested positive for HPV DNA**, yielding an overall HPV prevalence of **30%**. The remaining **35 samples (70%)** were negative for HPV DNA.

7.2 Distribution of High-Risk HPV Genotypes

Among the HPV-positive samples:

- **HPV-16** was the most prevalent genotype

- **HPV-18** was the second most common
- **HPV-31** was detected in a smaller proportion
- A few samples showed **co-infection with multiple high-risk genotypes**



Source:
Present study data generated by PCR-based HPV genotyping analysis conducted at Diagno Sphere Labs, Bhopal, Madhya Pradesh, India (2024–2025)

7.3 Summary of Key Findings

- Overall HPV prevalence: **30%**
- Predominance of **high-risk HPV genotypes**
- Strong representation of oncogenic HPV-16 and HPV-18
- PCR demonstrated **high analytical sensitivity and specificity**

8. DISCUSSION

The present study provides **important molecular epidemiological insights** into HPV infection among women residing near Bhopal, Madhya Pradesh. The observed HPV prevalence of **30%** is consistent with reports from other Indian regions, particularly central and northern India, where prevalence rates between **20–40%** have been documented.

The predominance of **HPV-16 and HPV-18** aligns with global and national data, reinforcing their central role in cervical carcinogenesis. These genotypes are responsible for the majority of cervical cancer cases worldwide and are primary targets of currently available HPV vaccines.

PCR-based detection proved to be a **highly sensitive and reliable method** for identifying HPV infection. It enables detection of viral DNA before cytological abnormalities become apparent, thereby offering a significant advantage over cytology-based screening methods.

Comparative analysis with studies from Rewa, Gwalior, and other parts of Madhya Pradesh reveals similar trends of **high-risk HPV dominance** and highlights persistent gaps in screening coverage and awareness. These findings underscore the urgent need for **molecular screening integration** in regional public health programs.

9. PUBLIC HEALTH AND CLINICAL IMPLICATIONS

- Early detection of high-risk HPV can significantly reduce cervical cancer incidence
- PCR-based screening is suitable for resource-limited settings
- Genotype distribution data support HPV vaccination strategies
- Region-specific data enable tailored screening policies

10. LIMITATIONS

The study has certain limitations, including a relatively small sample size and single-center design, which may limit generalizability. Lack of histopathological correlation and longitudinal follow-up restricts assessment of disease progression. Nevertheless, the study provides valuable baseline data from an underrepresented region.

11. CONCLUSION

The PCR-based evaluation of Human Papillomavirus in cervical samples of women near Bhopal revealed a **substantial burden of high-risk HPV infection**. The predominance of oncogenic genotypes such as HPV-16 and HPV-18 highlights the need for **strengthened molecular screening programs** in central India. PCR-based HPV testing represents a powerful tool for early detection and prevention of cervical cancer.

12. RECOMMENDATIONS

1. Integration of PCR-based HPV testing into routine screening programs
2. Expansion of molecular diagnostic facilities in central India
3. Community-based awareness and education initiatives
4. Large-scale population studies with follow-up
5. Utilization of genotype data for vaccine impact assessment

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