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# Epidemiological Patterns and Prevalence of HPV Genotypes in Iran: Implications for Prevention, Treatment, and Public Health Strategies

Nazanin Shabansalmani[a], Hesamoddin Ahmadi Afzadi[b], Seyed Ehsan Alavian[c,d], Zahra Ziafati Kafi[b], Fatemeh Shalchi[d], Kimia Ghadimi[e], Fatemeh Gheidar[e], Bahram Zarmehri[f], Behzad Purhossein[g*], Maryam Fazeli[h**]

a. Virology Department, Pasteur Institute of Iran, Tehran, Iran
b. Microbiology and Imminology Department, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran
c. Department of Biology, Parand Branch, Islamic Azad University, Tehran, Iran
d. Middle East Liver Diseases (MELD) Virology Laboratory, MELD Center, Tehran, Iran
e. Department of Biology, Science and Research Branch, Islamic Azad University, Tehran Iran
f. Department of Emergency Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
g. Pharmaceutical Sciences Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
h. Advanced Therapy Medicinal Product (ATMP) Department, Breast Cancer Research Center (BCRC), Motamed Cancer Institute, Academic Center for Education, Culture and Research (ACECR), Tehran, Iran.

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***Co-corresponding Authors:**
Behzad Pourhossein
Email: pourhosseinb@sbmu.ac.ir
AND
Maryam Fazeli
Email: fazeli@acecr.ac.ir

**ABSTRACT:**

Human Papillomavirus (HPV), underlying cervical cancer, emerges as a critical risk factor and plays a significant role in the disease burden. In several countries across the Middle East, the absence of structured HPV screening programs and limited public awareness have made HPV a growing concern for public health due to its potential impact on women's health. Thus, this study aims to investigate the genotype-specific prevalence of HPV infections and analyze their distribution across different age groups to inform tailored preventive strategies. A cross-sectional study examining the distribution of HPV genotypes was conducted on persons who accessed laboratory facilities in Tehran from 2022 to 2024. PCR-based testing was performed on 4,167 samples submitted for HPV detection and genotyping. Information concerning the age and gender of the patients and the distribution of HPV based on the different genotypes was collected and sorted for statistical analysis. Among the 4,167 individuals referred for HPV testing, the overall positivity rate was 39.9% (1,662/4,167). The highest positivity rates were observed in the 26–30 (18.4%) and 31–35 (23.4%) age groups, with a declining trend in older age groups. Women represented 93.5% of the tested individuals, with a positivity rate of 38.1%, while the rate in men was 65.2%. The most frequent high-risk genotypes detected were HPV-31 (22.4%), HPV-51 (16.7%), and HPV-16 (15.8%). A weak negative correlation was observed between age and HPV positivity ($r = -0.135$, $p < 0.001$). The distribution of HPV genotypes observed in this referred population showed a predominance of high-risk types among those tested. These findings are not generalizable to the broader population due to the inherent selection bias, as participants sought HPV testing for clinical reasons. Nonetheless, the results highlight the importance of implementing structured screening and surveillance systems to understand better and manage the HPV burden in the country. As this study was based on individuals referred for HPV testing in selected areas of Tehran, the results reflect referral-based patterns and should not be interpreted as representative of nationwide HPV prevalence across Iran.

**Keywords:** HPV; Cervical cancer; Genotype prevalence; Iran; Vaccination.

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## 1. Introduction

Human Papillomavirus (HPV) is the most common sexually transmitted infection worldwide, affecting people of all genders. However, its impact is particularly pronounced in women due to its strong link to cervical cancer, the fourth most common cancer among women globally. Persistent infections with high-risk HPV strains—especially HPV 16 and 18—are responsible for more than 99% of cervical cancer cases, contributing to about 70% of all occurrences. In addition to cervical cancer, HPV is associated with other malignancies, such as anal, vulvar, and oropharyngeal cancers, making it a substantial public health issue globally [1, 2].

HPV infects epithelial cells and has a tiny double-stranded DNA genome. Its lifecycle is tightly related to epithelial cell development in the host, and it may cause asymptomatic infections and aggressive malignancies. Despite the availability of effective vaccinations and screening methods, cervical cancer remains a leading cause of cancer-related death in low- and middle-income countries, accounting for 83% of cases globally. Other key causes include restricted healthcare access, poor vaccine coverage rates, and insufficient public education on prevention and early detection [3].

In Iran, cervical cancer is one of the leading causes of cancer-related deaths among women, following breast, stomach, and colorectal cancers. Despite its public health importance, research on the actual prevalence and genotype diversity of HPV and its associated cancers in Iran remains limited. Available studies suggest a cervical cancer prevalence of 3.1% in the general population, rising to 6.15% among women under 25 years of age [4, 5]. Furthermore, socio-cultural factors, such as early marriage, low screening uptake, and limited public awareness, contribute to the underestimation of the actual disease burden [6].

A study conducted in Tehran analyzed 571 cytological specimens from healthy women and 113 cervical cancer tissue samples using HPV genotype-specific primers. Results revealed HPV DNA in 24% of the healthy women, with 3.3% testing positive for high-risk genotypes and 11.6% for low-risk genotypes. Among cervical cancer cases, HPV DNA was detected in 78.8% of samples, with HPV 16 and 18 accounting for 43.4% and 8%, respectively. The absence of low-risk genotypes in these cases highlights the critical role of high-risk types in cervical carcinogenesis. Despite these findings, there is a notable gap in large-scale, representative studies on HPV genotype distribution in Iran [7].

Vaccination against high-risk HPV genotypes represents a cornerstone of primary prevention. The World Health Organization (WHO) recommends vaccination for males and females aged 9–26 years, with optimal efficacy observed when administered at 11–12. Evidence from global vaccination programs has demonstrated significant reductions in HPV-related conditions, including cervical intraepithelial neoplasia and anogenital warts. However, vaccination coverage remains suboptimal, particularly in developing regions, impeding the establishment of herd immunity. In Iran, cost, cultural barriers, and limited public awareness have slowed vaccine adoption, emphasizing the need for neutral, population-specific health education and capacity-building initiatives [8].

The present study aims to address the knowledge gaps in HPV epidemiology in Iran by providing a detailed analysis of HPV genotype distribution among different demographic groups. Utilizing recent data from individuals referred for HPV testing, this study investigates the prevalence of high-risk and low-risk HPV genotypes, patterns of infection by age and gender, and regional variations. Due to the referral-based nature of the sample, the results do not reflect population-level prevalence but offer essential insights into circulating genotypes among those tested. By bridging these gaps, the study will inform public health policies and contribute to the development of more effective prevention, treatment, and control strategies, ultimately reducing the burden of HPV-associated diseases in Iran.

## 2. Materials & Methods

### 2.1. Study Design and Population

This study was conducted as a cross-sectional analysis to determine the epidemiological patterns and distribution of HPV genotypes among individuals referred for molecular HPV testing in Iran, focusing on the implications for prevention and treatment strategies. Data were collected from patients who visited several laboratories in central, western, and northern Tehran, the capital of Iran, for HPV molecular testing between 2022 and 2024. Four thousand one hundred sixty-seven samples from individuals of varying demographics, including gender and age, were analyzed. The study population included male and female patients across diverse age groups, with samples reflecting referrals from different geographic regions of Iran.

### 2.2. Sample Collection

Standard collection kits were used to obtain swab samples from the participants' cervices, anus, oropharynx, and penis. Well-trained health professionals collected all samples under aseptic conditions. No additional clinical intervention was

performed for research purposes, and all procedures adhered to routine diagnostic protocols. The dataset received from the laboratories was fully anonymized, with no identifiable personal information. Therefore, according to local ethical regulations for anonymized retrospective data, formal IRB approval was not required. Nevertheless, the study strictly maintained data confidentiality to ensure participant privacy.

### 2.3. DNA Extraction and HPV Genotyping

According to the manufacturer's specifications, DNA was extracted from the collected samples using the QIAamp DNA Mini Kit (Qiagen, Germany). The extracted DNA was then subjected to purity and concentration determination using a NanoDrop spectrophotometer (Thermo Fisher Scientific, USA). HPV genotyping was conducted using the AmpliSens® HPV genotype-titre-FRT PCR kit, which can identify low-risk and high-risk HPV genotypes with high precision. Specifically, this kit detects low-risk genotypes HPV 6 and 11, as well as high-risk genotypes, including HPV 16, 18, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68, providing comprehensive coverage of clinically significant HPV strains. These genotyping methods are critical for the development of targeted preventive measures and therapies.

### 2.4. Data Collection and Analysis

Patient demographics at the time of submission included age, gender, and geographic location. For each patient, the HPV genotype present was recorded. Summary statistics were used to describe the prevalence of different genotypes by age, gender, and geographic distribution. Associations across categorical variables were analyzed using the chi-square test, among other association tests. Data analysis was performed using SPSS 25.0 software from IBM Corp, Armonk, NY, USA.

### 2.5. Ethical Considerations

This research has been performed in compliance with the Declaration of Helsinki. No direct intervention was performed; only anonymized laboratory data were used without personal identifiers. Therefore, no informed consent was required, nor was any approval by the Institutional Ethics Committee. However, confidentiality is ensured through the protection of privacy among participants.

### 2.6. Limitations

This study provides important insights into HPV genotype prevalence and distribution among individuals referred for testing in Tehran, contributing to the broader understanding of HPV epidemiology in Iran. However, several limitations should be acknowledged to contextualize the findings and guide future research, particularly prevention and treatment.
First, the data were collected from laboratory-based centers in central, western, and northern regions of Tehran, which, while reflecting diverse urban populations, do not capture the full demographic, geographic, and socio-cultural variability of the Iranian population. Therefore, the findings cannot be generalized to the entire country.
Second, the study employed a cross-sectional design, limiting its ability to assess longitudinal outcomes such as HPV infection persistence, progression to cervical lesions, or viral clearance. Follow-up cohort studies are necessary to address these aspects and provide a more comprehensive understanding of the natural history of HPV infection in this context, which will be crucial for informing clinical and public health strategies.
Third, although anonymized data ensured participant privacy, it precluded access to detailed demographic, behavioral, and clinical information, such as sexual behavior, vaccination history, and comorbidities, that could have provided more profound insights into HPV risk factors and disease progression.
Despite these limitations, this study establishes a robust foundation for understanding the circulating HPV genotypes among tested individuals. It underscores the need for more nationally representative and longitudinal studies integrating detailed clinical and behavioral data to support targeted prevention, early detection, and therapeutic interventions.
This study was conducted under the ethical principles of the Declaration of Helsinki. As the data were fully anonymized and retrospectively collected from routine laboratory records without direct involvement or intervention with human participants, formal ethical approval and individual informed consent were not required under local research governance policies. However, the study strictly adhered to data confidentiality and privacy standards to protect participant identity.
As only anonymized, retrospective data were used and no direct contact with patients occurred, individual informed consent was not required.

## 3. Results & Discussion

### 3.1. Prevalence and Demographic Distribution of HPV Infections

A total of 4,167 samples referred for HPV molecular testing were analyzed, revealing that 39.9% (1,662 samples) tested positive for HPV, while the remaining

**Table 1. Distribution of HPV Cases by Gender and Age Group.** The table illustrates the distribution of HPV-positive and HPV-negative cases across various age groups for both genders. Among the total 4167 samples, 3897 were from females, with 1486 (38.1%) testing positive and 2411 (61.9%) negative. In contrast, males contributed 270 samples, of which 176 (65.2%) were positive and 94 (34.8%) were negative. The 31–35 age group recorded the highest number of cases overall (956), while positivity rates were concentrated in the 26–35 age range for both genders. These findings underscore the critical importance of targeted prevention strategies, particularly for younger age groups. These results highlight patterns observed in individuals tested for HPV, rather than reflecting population-wide prevalence.

| Age Group (year) / Gender | 21-25 | 26-30 | 31-35 | 36-40 | 41-45 | 46-50 | 51-55 | 56-60 | <20 | >60 | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Female** | **579** | **695** | **888** | **784** | **547** | **194** | **94** | **36** | **59** | **21** | **3897** |
| Undetected | 304 | 389 | 549 | 506 | 386 | 132 | 73 | 26 | 27 | 19 | 2411 |
| Positive | 275 | 306 | 339 | 278 | 161 | 62 | 21 | 10 | 32 | 2 | 1486 |
| **Male** | **32** | **59** | **68** | **51** | **34** | **6** | **6** | **4** | **5** | **5** | **270** |
| Undetected | 12 | 19 | 22 | 18 | 13 | 2 | 1 | 3 | 1 | 3 | 94 |
| Positive | 20 | 40 | 46 | 33 | 21 | 4 | 5 | 1 | 4 | 2 | 176 |
| **Total** | **611** | **754** | **956** | **835** | **581** | **200** | **100** | **40** | **64** | **26** | **4167** |

60.1% (2,505 samples) were negative. A significant variation in positivity rates was observed between genders. Females constituted the majority of samples, with 3,897 cases, including 1,486 positive cases (38.1%) and 2,411 negative cases (61.9%). In contrast, males accounted for only 270 total cases, with 176 positive cases (65.2%) and 94 negative cases (34.8%).

The analysis of positive cases by age group revealed that the 26–30 age group had the highest proportion of positive cases among those tested, contributing to 18.4% of total positive cases (346 cases), followed by the 31–35 age group, which contributed 23.4% of positive cases (385 cases). The 21–25 age group also represented a substantial proportion of positive cases, with 295 cases (17.7%). Positivity rates declined steadily in older age groups, with the lowest proportions observed in individuals aged >60 and <20 years, collectively contributing fewer than 3% of positive cases (Table 1).

The mean age of individuals with positive results was 34.4 years, with the age of infected individuals ranging from 16 to 67 years. Females showed a consistent pattern of higher positive rates across all age groups, particularly in the 26–30 and 31–35 age groups, while males had fewer positive cases overall, but their positivity rates peaked in the same age ranges.

These findings reflect the concentration of HPV-positive results among individuals referred for testing, particularly females and those in their late twenties to mid-thirties, underscoring the importance of targeted prevention strategies, including age-informed screening approaches. Given the referral-based nature of the sample, caution should be exercised in generalizing these findings to the broader population. Furthermore, this highlights the need for early treatment interventions for those diagnosed with high-risk genotypes.

The mean age of individuals with positive results was 34.4 years, with the age of infected individuals ranging from 16 to 67 years. Females showed a consistent pattern of higher positive rates across all age groups, particularly in the 26–30 and 31–35 age groups, while males had fewer positive cases overall, but their positivity rates peaked in the same age ranges.

These findings emphasize the concentration of HPV infections among females and individuals in their late twenties to mid-thirties, underscoring the importance of targeted prevention strategies, including vaccination and early screening, particularly in these high-risk demographic groups. Furthermore, this highlights the need for early treatment interventions for those diagnosed with high-risk genotypes.

### 3.2. Genotype Distribution

The analysis identified 16 distinct HPV genotypes, categorized into high-risk and low-risk groups. Among the high-risk genotypes, HPV-31 was the most prevalent, accounting for 22.37% of positive cases, followed by HPV-51 (16.73%) and HPV-16 (15.82%). Other high-risk genotypes, including HPV-18, HPV-33, and HPV-45, comprised 16.33% of total positives. In the low-risk category, HPV-6/11 was the only detectable genotype, accounting for 14.13% of cases, while other low-risk genotypes were not identifiable (Figure 1).

High-risk genotypes were predominantly found in females, with HPV-31 and HPV-51 representing 23.1% and 17.2% of positive cases, respectively. In males, low-risk genotypes (6/11) were more prevalent, constituting 38.8% of male-positive cases. Statistical analysis revealed a significant association between gender and genotype distribution ($\chi^2 = 56.09$, $p < 0.001$).

**Table 2.** Mean age and range of positive cases by genotype.

| Genotype | 16 | 18 | 31 | 33 | 35 | 39 | 45 | 51 | 52 | 56 | 58 | 59 | 66 | 68 | 6/11 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mean Age** | 32.2 | 32.5 | 32.6 | 32.9 | 35.8 | 33.03 | 32.6 | 32.7 | 32.7 | 30.2 | 32.4 | 30.03 | 33.5 | 32.65 | 33.5 |
| **Age Range** | 31-35 | 21-35 | 26-35 | 26-35 | 31-35 | 31-40 | 21-35 | 26-40 | 26-35 | 21-35 | 26-35 | 21-35 | 26-35 | 26-40 | 21-40 |
| **Positive Cases** | 365 | 145 | 516 | 130 | 5 | 32 | 102 | 386 | 89 | 44 | 46 | 30 | 42 | 20 | 326 |
| **Total** | 1662 | | | | | | | | | | | | | | |

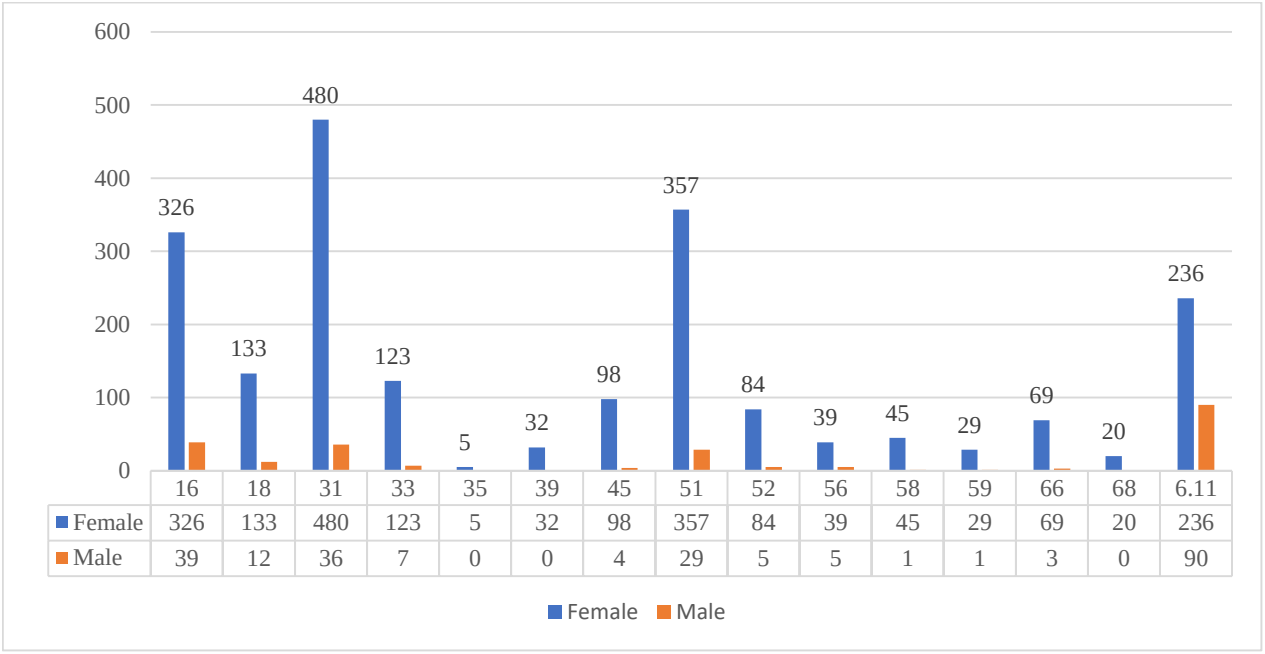


**Figure 1. Distribution of HPV genotypes by gender within the tested population.** This bar chart illustrates the frequency of various HPV genotypes in male and female participants. High-risk genotypes such as HPV-31 and HPV-51 are predominantly observed in females, with HPV-31 being the most prevalent (480 cases). HPV-16, another high-risk genotype, is also significantly more common in females (326 cases) than males. Conversely, low-risk genotypes, including HPV-6/11, show a relatively balanced distribution between genders, though still more frequent in females (236 cases). The data highlight significant gender disparities in the prevalence of both high-risk and low-risk HPV genotypes, emphasizing the need for targeted prevention and screening strategies.

### 3.3. Age Distribution

The age analysis showed distinct patterns for different genotypes. HPV-31, the most prevalent high-risk genotype, had a mean age of 32.6 years, while HPV-16 exhibited a similar mean age of 32.2 years. In contrast, HPV-6/11, a low-risk genotype, was associated with a slightly higher mean age of 33.5 years. HPV-35, another high-risk genotype, was more frequently detected in older individuals, with a mean age of 35.8 years. No statistically significant difference was found between the mean ages of high-risk and low-risk genotypes (P=0.28), suggesting similar age distributions across risk groups (Table 2).

### 3.4. Correlation Analysis

A weak negative correlation ($r=-0.135$, $t=-8.79$, $df=4165$, $p<0.001$) was observed between age and HPV positivity, indicating a slightly higher likelihood of infection in younger individuals. This statistically significant association aligns with global epidemiological trends, where HPV prevalence is highest among sexually active younger populations.
High-risk genotypes such as HPV-31 and HPV-16 were concentrated in individuals in their late twenties and early thirties, whereas HPV-35 and HPV-39 were more commonly observed in older age groups.

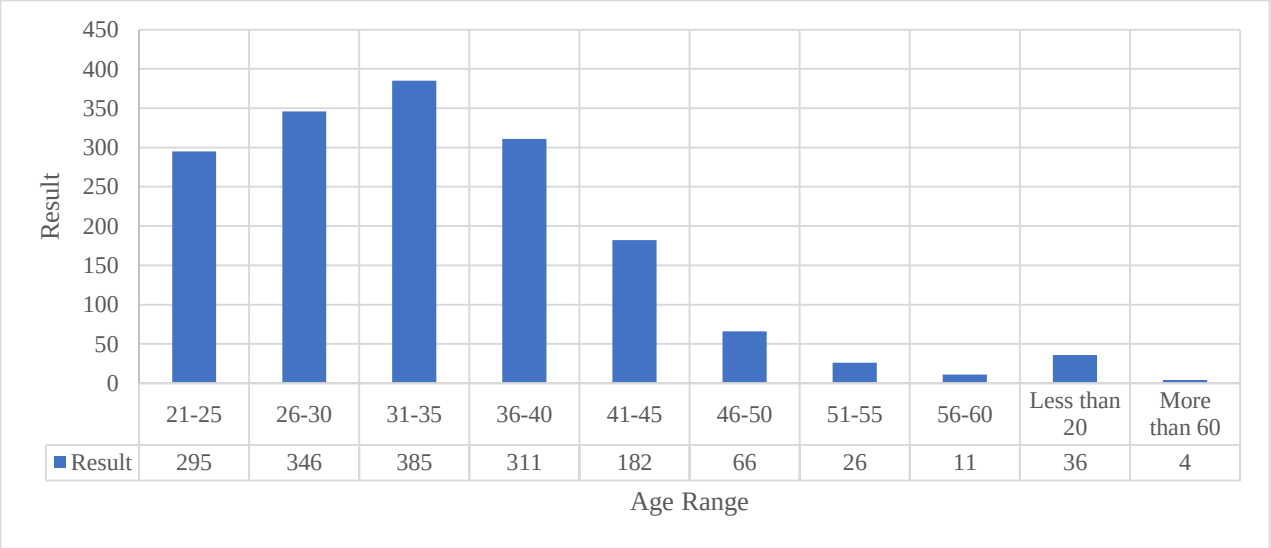


**Figure 2.** Distribution of HPV positive cases by age group.

The significant association between gender and HPV positivity ($\chi^2$=76.82, p<0.001) further underscored the higher burden of infections in females (Figure 2).

The findings of this study provide valuable insights into the distribution of HPV genotypes, gender differences, and age-related patterns among individuals referred for molecular testing in Tehran. Identifying HPV-31, HPV-16, and HPV-6/11 as the most frequently detected genotypes is consistent with international studies, where these types are known for their clinical relevance. HPV-16, in particular, is closely associated with cervical cancer, underscoring the importance of early detection and appropriate clinical management, especially in female populations.

The observed weak negative correlation between age and HPV positivity (r = –0.135, p < 0.001) suggests that younger individuals in the tested cohort were more likely to be infected, reflecting broader global epidemiological trends. A notably higher proportion of positive cases was observed in the 26–30 and 31–35 age groups, accounting for nearly 42% of all positives. This supports the well-established concept that individuals in their late twenties to early thirties are at increased risk of acquiring HPV. Additionally, the significant gender disparity, where women comprised the majority of cases and showed elevated positivity rates, indicates the need for gender-sensitive prevention strategies, including age-appropriate screening and follow-up care.

In terms of genotype distribution, the dominance of high-risk genotypes such as HPV-31 and HPV-16 in females underscores their pivotal role in cervical carcinogenesis [9]. In contrast, the relatively higher frequency of low-risk genotypes (e.g., HPV-6/11) in males suggests differing transmission dynamics and clinical implications between genders, which warrant further investigation. These findings may support the development of context-specific preventive programs, emphasizing early diagnosis and individualized care, particularly in at-risk populations.

Furthermore, the prevalence of multiple HPV infections among individuals referred for testing is a significant concern. Studies have indicated that co-infections with various HPV genotypes can increase the risk of developing high-grade cervical lesions and cervical cancer. For instance, research conducted in Mashhad, Iran, reported that 52% of HPV-positive individuals had infections with multiple genotypes, highlighting the necessity for comprehensive screening programs that can detect and manage such co-infections effectively [10, 11]. In addition, the distribution of HPV genotypes varies across different regions of Iran, underscoring the importance of region-specific data in informing public health strategies. A study from Urmia, Iran, found that high-risk genotypes such as HPV-16 and HPV-18 were predominant, while in Sari, HPV-56 and HPV-39 were more prevalent. These regional differences in genotype distribution suggest that vaccination and screening programs should be tailored to the specific epidemiological patterns of each area to maximize their effectiveness [12].

From a public health standpoint, this study highlights essential challenges in HPV control. Despite international recommendations, barriers such as limited awareness, cultural sensitivities, and cost-related issues continue to hinder the effectiveness of preventive efforts in many low- and middle-income settings. While our data are not generalizable to the national level due to the referral-based nature of sampling, they may contribute

to informing local strategies that address the most affected demographic groups through awareness, screening, and clinical follow-up. Studies from other countries have shown that integrating these measures with educational initiatives can reduce the incidence of HPV-associated conditions, including cervical intraepithelial neoplasia and anogenital warts [13, 14].

The significant association between genotype distribution and gender ($\chi^2 = 56.09$, $p < 0.001$) further supports the development of tailored public health messaging. Moreover, the detection of genotypes such as HPV-35 and HPV-39 more frequently in older age groups may indicate age-related shifts in HPV epidemiology that should be explored in future studies and potentially inform age-adjusted screening policies.

This study also draws attention to the geographic and demographic limitations of current HPV research in Iran. As our sample was limited to central, western, and northern districts of Tehran, it does not reflect the full diversity of the country. Broader, multiregional studies incorporating behavioral, clinical, and follow-up outcome data are essential for a comprehensive understanding of HPV epidemiology at the national level.

Despite the inherent limitations of a cross-sectional and referral-based study design, including the inability to evaluate infection persistence, clearance, or progression, this research establishes a strong basis for HPV surveillance in Iran. It emphasizes expanding diagnostic infrastructure, raising community awareness, and improving access to appropriate clinical care. Integrating HPV education into public health frameworks and promoting early clinical intervention for high-risk individuals can contribute meaningfully to reducing HPV-related morbidity.

Although this study provides critical insights into HPV genotype distribution in a tested cohort, the data originate from referral centers in Tehran. Therefore, these findings should be interpreted within the context of a laboratory-referred population and not as nationally representative data.

## 4. Conclusion

This study highlights the critical role of high-risk HPV genotypes in cervical carcinogenesis and the significant burden of HPV infections in Tehran. By addressing gaps in vaccination, screening, and treatment programs and implementing culturally appropriate public health interventions, the burden of HPV-related diseases in Iran can be substantially reduced.

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## Conflict of interest

There is no conflict of interest.

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## ORCIDs

Nazanin Shabansalmani:
https://orcid.org/ 0000-0002-1371-5190
Hesamoddin Ahmadi Afzadi:
https://orcid.org/ 0009-0005-7504-3296
Seyed Ehsan Alavian:
https://orcid.org/ 0009-0001-5481-7804
Bahram Zarmehri:
https://orcid.org/0000-0002-8687-1821
Behzad Purhossein:
https://orcid.org/0000-0002-4263-0612
Maryam Fazeli:
https://orcid.org/0000-0003-4048-4778

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