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Differential effect of obesity on cervical neoplastic progression and human papillomavirus persistence: A retrospective cohort study

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Abstract

The role of obesity in human papillomavirus (HPV) persistence and the development of cervical neoplasia remains incompletely understood. This study evaluates the independent effects of obesity, smoking, and age on high-risk HPV persistence and the development of high-grade cervical lesions (cervical intraepithelial neoplasia [CIN]2+), and assesses whether obesity improves prediction of CIN2+. This retrospective cohort study included 445 women who underwent high-risk HPV testing between December 2023 and December 2025. HPV persistence was defined as detection of the same HPV genotype in at least two consecutive tests performed ≥ 12 months apart. Body mass index was categorized as non-obese (<30 kg/m^2) or obese (≥30 kg/m^2). Multivariable logistic regression analyses were performed to identify independent determinants of HPV persistence and CIN2+. Receiver operating characteristic curve analysis was used to compare a baseline model including age and smoking with an extended model additionally including obesity. Persistent HPV infection was identified in 59 women (13.3%). Smoking was a strong independent predictor of HPV persistence (adjusted odds ratio [aOR]: 13.07; 95% confidence interval [CI]: 6.54–26.09; $p < 0.001$), and increasing age was also independently associated with persistence (aOR: 1.04 per year; 95% CI: 1.01–1.07; $p = 0.023$). Obesity was not independently associated with HPV persistence. CIN2+ was detected in 95 women (21.3%). Obesity was independently associated with CIN2+ (aOR: 1.96; 95% CI: 1.14–3.38; $p = 0.015$), whereas smoking and age were not significant predictors. The addition of obesity modestly improved discrimination for CIN2+ prediction (area under the curve [AUC] 0.545 vs. 0.587). Smoking and age are key determinants of HPV persistence, whereas obesity appears to be associated primarily with cervical neoplastic progression rather than viral persistence. The modest increase in AUC suggests limited but measurable predictive contribution of obesity to CIN2+ risk.

Keywords: Human papillomavirus; Human papillomavirus persistence; Obesity; Smoking; Age

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1. Introduction

Cervical cancer remains a major global health concern, ranking as the fourth most common cancer among women worldwide, with approximately 661,000 new cases and 348,000 deaths reported in 2022.[1] Persistent infection with high-risk human papillomavirus (HPV) is responsible for nearly all cervical cancer cases and represents the central initiating event in cervical carcinogenesis.[2] Although most HPV infections are transient and spontaneously cleared by host immune responses within 6–24 months, a subset of women fail to eliminate the virus, resulting in persistent infection and possible progression to high-grade cervical intraepithelial lesions or invasive cancer.[3,4] Importantly, HPV persistence and cervical neoplastic progression are biologically related but distinct processes. Viral persistence primarily reflects the host immune system's ability to eliminate infected epithelial cells, whereas progression to cervical intraepithelial neoplasia (CIN)2+ involves additional mechanisms, including chronic inflammation, altered cytokine signaling, angiogenesis, oxidative stress, cellular proliferation, and genomic instability.[5] Despite this distinction, many previous studies have investigated host-related risk factors for HPV infection without clearly differentiating their effects on viral persistence from their effects on neoplastic progression.

Obesity is increasingly recognized as a chronic low-grade inflammatory condition associated with dysregulated adipokine secretion and altered immune signaling pathways. Elevated levels of inflammatory mediators such as interleukin-6 and tumor necrosis factor-α may impair cytotoxic lymphocyte activity, suppress immune surveillance, and promote epithelial proliferation and neoplastic transformation.[6–9] Consequently, obesity has been proposed as a potential host-related determinant of HPV persistence and cervical dysplasia, although the available evidence remains inconsistent.[10–13] Some studies have suggested impaired viral clearance among women with obesity, whereas others demonstrated stronger associations with cervical neoplastic progression rather than HPV persistence itself. The rationale for specifically examining obesity stems from its dual potential to influence both immune-mediated viral clearance and the inflammatory microenvironment that promotes neoplastic transformation. This makes obesity particularly relevant for distinguishing factors associated with HPV persistence from those associated with progression to CIN2+.

Smoking is another well-established cofactor in HPV-related disease. Tobacco exposure contributes to oxidative DNA damage, impaired local immunity, altered antigen presentation, and suppression of mucosal defense mechanisms, thereby facilitating viral persistence and carcinogenesis.[14–18] Increasing age has similarly been associated with delayed viral clearance, possibly reflecting immune senescence, cumulative HPV exposure, and hormonal changes affecting cervical immunity.[3,4] While obesity and smoking both influence immune and inflammatory pathways, it remains unclear whether their effects extend equally to HPV persistence and cervical neoplastic progression. Most previous studies have focused on individual host-related factors in isolation, and relatively few investigations have simultaneously evaluated obesity, smoking, and age within the same cohort while distinguishing their differential effects on HPV persistence and CIN2+. Clarifying these distinct associations may improve biologically informed risk stratification and provide insight into the heterogeneous natural history of HPV-associated disease.[19–21] Beyond identifying independent associations, evaluating obesity's discriminatory contribution to CIN2+ prediction may help determine whether metabolic factors provide clinically meaningful incremental value beyond conventional host-related variables such as age and smoking. Understanding the predictive utility of obesity may therefore contribute to improved risk stratification strategies in HPV-associated cervical disease.

Although obesity, smoking, and age have individually been investigated as host-related factors in HPV-associated disease, their differential effects on viral persistence and cervical neoplastic progression have not been clearly delineated within the same clinical cohort. The present study was designed to address this gap by simultaneously evaluating these factors in relation to two biologically distinct outcomes, high-risk HPV persistence and CIN2+, and by examining whether obesity provides incremental discriminatory information for CIN2+ beyond age and smoking. By separating viral persistence from neoplastic progression, this approach may provide a more biologically informed interpretation of host-related risk factors and may help refine risk stratification among women with high-risk HPV infection. The principal contribution of this study is the demonstration that host-related factors may differentially influence distinct stages of HPV-associated disease, with smoking and age being associated with viral persistence, whereas obesity appears to be more closely related to neoplastic progression. The general objective of this study was to determine whether obesity, smoking, and age are differentially associated with high-risk HPV persistence and cervical neoplastic progression. The specific objectives were to (i) identify independent determinants of HPV persistence, (ii) evaluate independent associations with CIN2+, and (iii) determine whether including obesity provides incremental discriminatory information for CIN2+ beyond age and smoking.

2. Materials and methods

2.1. Study design and setting

This single-center retrospective study was conducted at the Department of Gynecology, Afyonkarahisar State Hospital, Afyonkarahisar, Türkiye. Women who underwent high-risk HPV testing between December 1, 2023, and December 1, 2025, were identified through institutional and regional screening databases. The date of the first positive HPV test was defined as the index test for each participant.

2.2. Participants

Women aged 25–70 years with at least two available HPV test results and a minimum follow-up period of 12 months were considered eligible for inclusion. Although women up to 70 years of age were eligible according to the study protocol, no participants older than 62 years were identified during the study period. Therefore, the final analysis included women aged 25–62 years. Exclusion criteria were defined a priori and included a single HPV test without follow-up, a history of immunosuppressive disease or immunosuppressive therapy, pregnancy during the study period, prior treatment for CIN or cervical cancer, and incomplete clinical or laboratory data. After applying these criteria, 445 women were included in the final analysis.

2.3. Data collection and variables

Demographic and clinical data were extracted from electronic medical records using a standardized data collection form. The standardized form was used to ensure uniform extraction of predefined variables across all participants and to minimize variability and omission during retrospective data abstraction. Recorded variables included the age at index HPV test, smoking status, body mass index (BMI), HPV genotype, and histopathological findings. Age was treated as a continuous variable in all multivariable analyses. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2) and categorized as non-obese (<30 kg/m^2) or obese (≥30 kg/m^2) according to World Health Organization criteria[15]. Smoking status was classified as smoker or non-smoker based on self-reported data at the time of HPV testing. HPV genotypes were grouped as HPV 16, HPV 18, combined HPV 16 and 18 infection, and other high-risk HPV types. HPV persistence was defined as detection of the same HPV genotype in at least two consecutive tests performed at least 12 months apart. CIN2+ was defined as histopathologic detection of CIN2, CIN3, or invasive cervical carcinoma.

2.4. Statistical analysis

All statistical analyses were performed using IBM Statistical Package for Social Sciences software version 22.0. The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Continuous variables are presented as mean ± standard deviation or median with range, as appropriate, and categorical variables as frequencies and percentages. Unadjusted associations between host-related factors and HPV persistence or CIN2+ were evaluated using the chi-square test or Fisher's exact test for categorical variables and the Student's *t*-test or Mann–Whitney *U* test for continuous variables, as appropriate. Separate multivariable logistic regression models were constructed to identify independent determinants of HPV persistence and CIN2+. Age was included as a continuous variable in all multivariable models, whereas smoking status and obesity were included as binary variables. These variables were selected a priori based on biological plausibility and prior evidence suggesting their potential roles as confounders in HPV persistence and cervical neoplastic progression. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were calculated. To evaluate the incremental predictive contribution of obesity for CIN2+ discrimination, receiver operating characteristic (ROC) curve analysis was additionally performed. A baseline model including age and smoking status was compared with an extended model additionally including obesity. Areas under the curve (AUCs) were calculated to assess model discrimination. This analytical strategy was designed to distinguish independent host-related determinants of viral persistence from those associated with cervical neoplastic progression and to quantify the incremental discriminatory contribution of obesity to CIN2+ prediction. To explore whether the association between smoking and HPV persistence or CIN2+ differed according to obesity status, an interaction term between smoking and obesity was included in the multivariable logistic regression models as an exploratory analysis. A two-sided *p*-value of less than 0.05 was considered statistically significant.

3. Results

A total of 445 women met the inclusion criteria and were included in the final analysis. The median age of the study population was 34 years (range: 25–62 years), and the median body mass index was 32.3 kg/m^2 (range: 16.0–42.0 kg/m^2). Based on BMI classification, 150 women (33.7%) were classified as non-obese and 295 (66.3%) as obese. Smoking was reported by 111 participants (24.9%). High-risk HPV genotyping revealed HPV 16 in 128 women

(28.8%), HPV 18 in 45 (10.1%), combined HPV 16 and 18 infections in 11 (2.5%), and other high-risk HPV types in 261 women (58.7%). Persistent HPV infection, defined as detection of the same genotype in consecutive tests performed at least 12 months apart, was identified in 59 women (13.3%). High-grade cervical lesions (CIN2+) were diagnosed in 95 women (21.3%). The clinicopathologic characteristics of the study population are summarized in Table 1.

Table 1. Clinicopathologic characteristics of the study population (n = 445)

Variable	n (%) or median (range)
Age (years)	34 (25–62)
Body mass index category	
<30 kg/m² (non-obese)	150 (33.7%)
≥30 kg/m² (obese)	295 (66.3%)
Smoking status	
Smoker	111 (24.9%)
Non-smoker	334 (75.1%)
Human papillomavirus (HPV) genotype	
HPV 16	128 (28.8%)
HPV 18	45 (10.1%)
HPV 16 + 18	11 (2.5%)
Other high-risk types	261 (58.7%)
HPV persistence	
Yes	59 (13.3%)
No	386 (86.7%)
Histopathology	
Normal histology	74 (16.6%)
Chronic cervicitis	89 (20.0%)
CIN1	187 (42.0%)
CIN2	57 (12.8%)
CIN3	35 (7.9%)
Invasive cancer	3 (0.7%)

In unadjusted analyses, HPV persistence differed significantly according to smoking status and BMI category. Persistent infection was observed in 38.7% of smokers compared with 4.8% of non-smokers ($p < 0.001$). Persistence rates were also higher among non-obese women than obese women (21.3% vs. 9.2%, $p < 0.001$) (Table 2). Women with persistent HPV infection were older than those who cleared the infection, and age was significantly associated with persistence in univariate analysis (p = 0.023). To identify independent host-related determinants of HPV persistence, a multivariable logistic regression model was constructed including age, smoking status, and obesity. In the adjusted model, smoking emerged as a strong independent predictor of HPV persistence (aOR: 13.07; 95% CI: 6.54–26.09; $p < 0.001$). Increasing age was also independently associated with persistence (aOR: 1.04 per year; 95% CI: 1.01–1.07; p = 0.023). In contrast, obesity was not independently associated with HPV persistence after adjustment (aOR: 0.81; 95% CI: 0.42–1.57; p = 0.54) (Table 3). The inverse association between obesity and HPV persistence observed in unadjusted analyses was attenuated after multivariable adjustment, suggesting confounding by smoking, which was substantially more prevalent among non-obese participants. Among the entire cohort, 95 women (21.3%) were diagnosed with CIN2+ lesions. In unadjusted analyses, the prevalence of CIN2+ was significantly higher among obese women compared with non-obese women (24.4% vs. 15.3%; p = 0.028). Smoking status and age were not significantly associated with CIN2+ in univariate analyses ($p > 0.05$).

Table 2. Unadjusted associations between host factors and human papillomavirus persistence

Parameters	Persistent (n)	Cleared (n)	p-value
Body mass index group			
<30 kg/m² (non-obese)	32 (21.3%)	118 (78.7%)	<0.001*
≥30 kg/m² (obese)	27 (9.2%)	268 (90.8%)	
Smoking status			
Smoker	43 (38.7%)	68 (61.3%)	<0.001*
Non-smoker	16 (4.8%)	318 (95.2%)	

Note: *$p < 0.05$ was considered statistically significant.

In multivariable logistic regression analysis adjusting for age and smoking status, obesity remained an independent predictor of CIN2+ (aOR: 1.96; 95% CI: 1.14–3.38; p = 0.015). Neither smoking (aOR: 1.33; 95% CI: 0.77–2.31; p = 0.308) nor age (aOR: 0.99; 95% CI: 0.97–1.02; p = 0.400) showed a significant independent association with CIN2+ (Table 4). To assess whether the association between smoking and CIN2+ differed according to obesity status, an interaction term between smoking and obesity was included in the multivariable model as an exploratory analysis. No significant interaction was observed (interaction term $p >$ 0.05), and the interaction term was therefore not retained in the final model, indicating independent effects of these variables on CIN2+.

Receiver operating characteristic (ROC) curve analysis was additionally performed to evaluate the discriminatory contribution of obesity for CIN2+ prediction. A baseline model including age and smoking demonstrated limited

Table 3. Multivariate logistic regression analysis for predictors of human papillomavirus persistence

Parameters	Odds ratio	95% confidence interval	*p*-value
Obesity (body mass index ≥30 kg/m²)	0.81	0.42–1.57	0.54
Smoking	13.07	6.54–26.09	<0.001*
Age (per year)	1.04	1.01–1.07	0.023*

*$p < 0.05$ was considered statistically significant.

Table 4. Association between host factors and CIN2+

Variable	CIN2+ (*n*, %)	Non-CIN2+ (*n*, %)	Unadjusted *p*-value	aOR (95% CI)
Obesity (BMI ≥ 30 kg/m²)	72 (24.4%)	223 (75.6%)	0.028*	1.96 (1.14–3.38)
Smoking	25 (22.5%)	86 (77.5%)	0.789	1.33 (0.77–2.31)
Age (per year)	–	–	0.286	0.99 (0.97 to 1.02)

Note: *$p < 0.05$ was considered statistically significant. *p*-values refer to unadjusted analyses; aORs and 95% CIs were derived from the multivariable model including age as a continuous variable, smoking status, and obesity.
Abbreviations: aOR: Adjusted odds ratio; BMI: Body mass index; CI: Confidence interval; CIN: Cervical intraepithelial neoplasia.

discrimination (AUC = 0.545). The addition of obesity to the model modestly improved discrimination for CIN2+ prediction (AUC = 0.587), although overall predictive performance remained low. ROC curves comparing both models are presented in Figure 1. The differential associations of smoking, age, and obesity with HPV persistence and CIN2+ derived from multivariable logistic regression analyses are summarized in Figure 2.

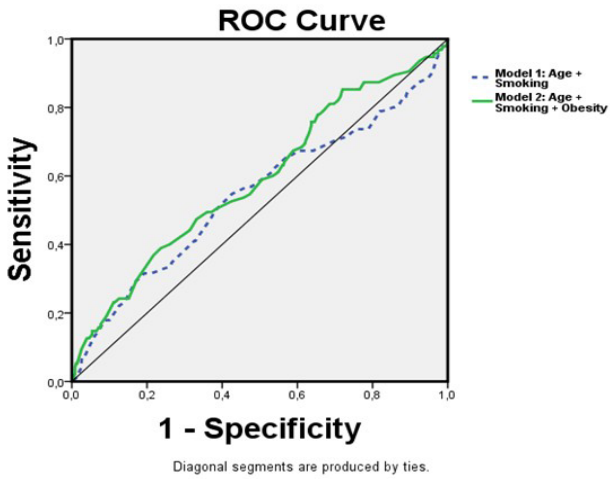


Figure 1. ROC curves comparing predictive models for CIN2+. The baseline model included age and smoking status (AUC = 0.545), whereas the extended model additionally included obesity (AUC = 0.587). The addition of obesity resulted in a modest improvement in model discrimination.
Abbreviations: AUC: Area under the curve; ROC: Receiver operating characteristic.

4. Discussion

In our study, we evaluated the independent effects of obesity, smoking, and age on high-risk HPV persistence and the development of high-grade cervical lesions. Our findings demonstrate that smoking and increasing age are strong independent predictors of HPV persistence, whereas obesity does not independently influence viral persistence after adjustment for confounding factors. In contrast, obesity was independently associated with CIN2+, suggesting that distinct biological pathways may underlie HPV persistence and cervical neoplastic progression. Persistent infection with oncogenic HPV types is a prerequisite for cervical carcinogenesis, yet most infections are transient and cleared by effective host immune responses within months to a few years.[2–4] Factors impairing cell-mediated immunity may delay viral clearance and facilitate persistent infection. Cigarette smoking is a well-established cofactor in HPV-related disease and exerts both local and systemic immunosuppressive effects through oxidative stress, impaired antigen presentation, altered cytokine signaling, and suppression of mucosal defense mechanisms.[14,16–18]. In our cohort, smoking emerged as the strongest independent determinant of HPV persistence, with smokers demonstrating markedly increased odds of persistence compared with non-smokers. This finding is consistent with previous epidemiologic and mechanistic studies linking smoking to persistent HPV infection and HPV-associated malignancies.[16–18] This observation is also supported by a recent prospective follow-up study by Ma *et al.*[22], in which current smokers had a significantly lower probability of HPV clearance than non-smokers, with a dose-dependent relationship between smoking exposure and reduced viral clearance. Although differences in

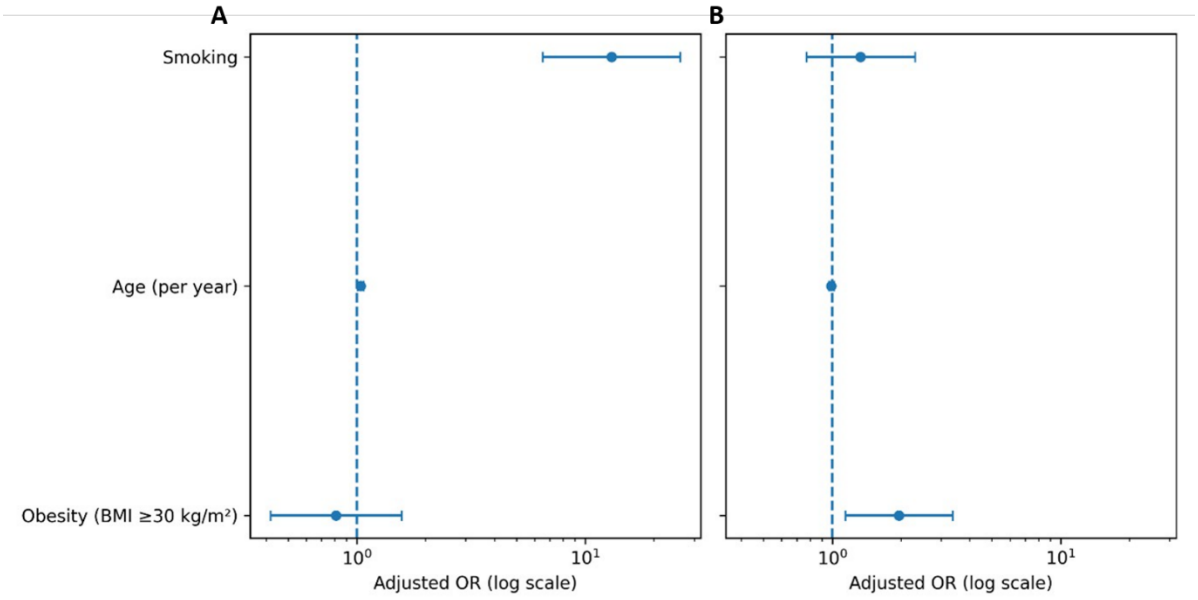


Figure 2. Forest plots of adjusted ORs derived from multivariable logistic regression analyses. Panel A demonstrates associations between host-related factors and high-risk human papillomavirus persistence, whereas Panel B demonstrates associations with CIN2+. Models were adjusted for age, smoking status, and obesity. Error bars represent 95% CIs.
Abbreviations: CI: Confidence interval; CIN: Cervical intraepithelial neoplasia; OR: Odds ratio.

study population and analytical approach preclude direct comparison of effect sizes, both studies support an adverse effect of smoking on the natural clearance of HPV infection.

Increasing age was also independently associated with HPV persistence in our analysis. Age-related immune senescence, cumulative HPV exposure, and hormonal changes affecting cervical immunity may contribute to delayed viral clearance among older women.[3,4] Although the effect size of age was modest, its independent association highlights the importance of host immune competence in determining HPV outcomes. Our finding is consistent with a recent systematic review and meta-analysis of 129 studies including more than 650,000 women, which reported a higher prevalence of persistent HPV infection among women older than 50 years compared with younger age groups. The authors suggested that age-related alterations in immune function may contribute to reduced viral clearance. Although our cohort was younger overall and age was analyzed as a continuous variable, the direction of the association was similar.[23]

Interestingly, obesity was not independently associated with HPV persistence after multivariable adjustment. The apparent inverse association observed in unadjusted analyses was attenuated after controlling for smoking status, likely reflecting confounding by the substantially higher prevalence of smoking among non-obese participants. These findings underscore the importance of adjusting for behavioral confounders when evaluating metabolic factors in HPV natural history and suggest that BMI alone may not adequately reflect the immunologic mechanisms involved in viral clearance. In contrast, obesity emerged as an independent predictor of CIN2+. This suggests that obesity may influence cervical neoplastic progression more than viral persistence. Obesity is characterized by chronic low-grade inflammation and dysregulated adipokine secretion, including elevated levels of interleukin-6 and tumor necrosis factor-α, which may promote epithelial proliferation, angiogenesis, oxidative stress, and genomic instability.[6–13] These mechanisms may create a microenvironment favorable for neoplastic transformation once persistent HPV infection has been established. Our findings are therefore consistent with previous studies linking obesity and metabolic dysfunction to increased risk of cervical dysplasia and gynecologic malignancies.[11–13,19–21] Recent evidence further illustrates the complexity of this relationship. A 2024 review evaluating metabolic syndrome and cervical carcinogenesis concluded that metabolic abnormalities may contribute to cervical cancer development and progression through chronic inflammation, oxidative stress, hormonal alterations, and immune dysfunction.[13] However, studies examining HPV persistence itself have yielded inconsistent

results. For example, previous population-based data have shown no independent association between obesity and high-risk HPV persistence after adjustment for behavioral factors, whereas metabolic syndrome as a composite condition has been associated with persistent infection in other cohorts. These discrepancies may reflect differences in how metabolic exposure is defined, study populations, HPV persistence criteria, and adjustment for behavioral confounders. Our findings suggest that BMI-defined obesity alone may be more relevant to neoplastic progression than to viral persistence.

To further explore the potential clinical relevance of obesity, ROC curve analysis was performed to evaluate whether obesity improved discrimination for CIN2+ prediction beyond conventional host-related variables. The addition of obesity to the baseline model, including age and smoking, resulted in a modest increase in AUC from 0.545 to 0.587. Although overall discriminatory performance remained limited, this finding suggests that obesity contributes incremental predictive information for CIN2+ risk. At the same time, the relatively low AUC values indicate that host-related factors alone are insufficient to accurately predict cervical neoplastic progression and that additional viral, immunologic, and clinical determinants likely play substantial roles. No significant interaction between smoking and obesity was observed in multivariable analyses. This suggests that smoking and obesity may contribute independently to HPV-related disease through distinct biological mechanisms rather than synergistic pathways. The differential associations identified in our study support the concept that HPV persistence and cervical neoplastic progression represent overlapping but biologically distinct stages of HPV-associated disease. While smoking and aging appear to primarily influence viral persistence through immune-related mechanisms, obesity may predominantly contribute to lesion progression through chronic inflammatory and metabolic pathways. This distinction may have important implications for individualized risk stratification and preventive strategies in HPV-associated cervical disease.

From a clinical perspective, these findings suggest that host-related factors may have different relevance at different stages of HPV-associated cervical disease. Smoking and increasing age may help identify women at greater risk of persistent high-risk HPV infection, whereas obesity may provide additional information regarding the risk of progression to CIN2+. However, the relatively low discriminatory performance of the predictive models indicates that these factors should not be used as stand-alone clinical predictors. Rather, they may complement established virological, cytological, and histopathological parameters when considering individualized risk assessment and follow-up strategies.

Several limitations should be acknowledged. First, the retrospective design may have introduced selection bias and limits causal interpretation. Second, potentially relevant confounding variables, including HPV vaccination status, sexual behavior, hormonal contraceptive use, metabolic comorbidities, and socioeconomic factors, were unavailable and could not be incorporated into the analyses. Third, HPV persistence was evaluated using a fixed-time binary definition rather than a time-to-event approach, which may have limited assessment of dynamic viral clearance patterns. Finally, the relatively low AUC values indicate limited predictive performance of the evaluated host-related variables alone. Despite these limitations, the study has several strengths, including the relatively large cohort size, standardized HPV genotyping, simultaneous evaluation of multiple host-related factors, and incorporation of ROC-based discrimination analysis. Together, these findings provide further evidence that obesity may influence cervical neoplastic progression through mechanisms distinct from those underlying HPV persistence.

5. Conclusion

Smoking and increasing age were independently associated with high-risk HPV persistence, whereas obesity was independently associated with CIN2+. These findings support the concept that HPV persistence and cervical neoplastic progression may involve partially distinct host-related biological mechanisms. Clinically, smoking and age may contribute to identifying women at increased risk of persistent infection, while obesity may provide additional information regarding the risk of cervical neoplastic progression. However, because the overall discriminatory performance of the evaluated models remained limited, these factors should be considered complementary rather than stand-alone predictors and should be interpreted together with established virological, cytological, and histopathological findings.

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Conflict of interest

The authors declare no conflict of interest.

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Conceptualization: Cem Yagmur Ozdemir
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Investigation: Cevdet Doğu
Methodology: Cem Yagmur Ozdemir
Supervision: Dagistan Tolga Arioz
Writing–original draft: Cem Yagmur Ozdemir
Writing–review & editing: Cem Yagmur Ozdemir, Cevdet Doğu, Dagistan Tolga Arioz
All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Afyonkarahisar Health Sciences University Hospital (approval number: 2025/15). Institutional permissions were obtained from the Ministry of Health and the Afyonkarahisar Provincial Health Directorate. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data

The datasets analyzed during the current study are available from the corresponding author upon reasonable request, subject to institutional approval and applicable patient confidentiality requirements.

AI tools statement

This manuscript was prepared with the assistance of ChatGPT (GPT-4o, OpenAI) for language refinement and structural editing. All outputs generated by the AI tool were reviewed, verified, and revised by the authors to ensure accuracy and compliance with ethical standards.

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