

How to Cite:

Javed, M., Nadeem, S., Arif, S., Ishaque, A., Javaid, F., & Ali, A. (2023). The relationship between HPV positivity and abnormal cervical cytology changes with age in perimenopausal women. *International Journal of Health Sciences*, 7(S1), 776–782. <https://doi.org/10.53730/ijhs.v7nS1.14272>

The relationship between HPV positivity and abnormal cervical cytology changes with age in perimenopausal women

Dr Mahvish Javed

Assistant Professor, Department of Anatomy, Khyber Girls Medical College, Peshawar

Dr Saima Nadeem

Assistant Professor, Department of Pathology, Khyber Girls Medical College, Peshawar

Corresponding author email: samnadeem1979@gmail.com

Dr Sunia Arif

Demonstrator, Department of Pathology, Khyber Medical College. Peshawar

Dr Anjum Ishaque

Lecturer, Department of Pathology, Khyber Girls Medical College, Peshawar

Dr Faryal Javaid

Post Graduate Resident, Rehman Medical Institute, Peshawar

Dr Amjad Ali

Senior Lecturer, Department of Pathology, Muhammad College of Medicine, Peshawar

Abstract---Background: In this research, premenopausal women with HR-HPV infections and atypical cervical smears were compared by age. Materials and method: 200 regularly screened women between the ages of 36 and 60 had a cervical smear and HPV detection. Demographic, behavioral, and medical data were gathered by telephone surveys. Descriptive analysis was used to look at the connection between HR-HPV infections and cervical aberrations by age. Results: Age significantly decreased the number of cases of cervical abnormalities, HR-HPV, and human papillomavirus, as well as the correlation among these disorders. In younger females with abnormalities, HR-HPV detection was 60%; however, it steadily decreased to 30% in "50-54-year-old" women, without abnormalities found in 55-60 years old females. Different relationships between HR-HPV infection and anomalies remained found in females over 45, a

pattern not observed in females who were young by age. Conclusion: Age had no effect on several kinds of low-grade and severe anomalies, but we saw a decline in the agreement among cytological results and HR-HPV tests.

Keywords--HPV, abnormal cervical cytology, menopause, perimenopausal women, human papilloma virus.

Introduction

Annual cervical Pap smear screening has significantly decreased cervical cancer-related morbidity and mortality in the US Throughout the past forty years. The “American Society for Colposcopy and Cervical Pathology (ASCCP)” advises HR-HPV testing along with cytogenetic screenings performed regularly on females over the age of Thirty (1-3). Females under the age of 30 have an extremely low likelihood of aggressive cancer of the cervical cavity but have a significant likelihood of acquiring the prevalent but temporary human papillomavirus infection; recent regulations stratify their suggestions at the age of thirty. On the contrary, older women have a lower prevalence of HPV than younger women; it has greatly improved the human Pap Virus DNA test's specificity when assessing older women (4-6).

Although classification according to age at 30 years is definitely warranted when employing HPV DNA testing in screening, it is unclear if the suggestions for females above thirties are similarly true during the life span of a woman of screening. “Because the rate of pre-neoplastic disease is low (8), few studies of women over age 30 have the power to further stratify by age in order to better inform guidelines” (7-11)

Women with all grades of "pathology-confirmed cervical intraepithelial neoplastic (CIN)" showed a reduction in HR-HPV identification with age, with the most pronounced decline seen for HPV 16 infection, according to a recent study from the ATHENA trial, that contained data on more than thirty five thousand women aged thirty and older. “In the HPV in Perimenopause (HIP) cohort of routinely screened women age 35–60 years, we observed a similar trend of decreasing correlation between HR-HPV detection and cervical abnormalities with increasing age” Our goal was to learn more about the relationship between age-related aberrant cytology and either HPV and HR-HPV detection (12-14).

Methodology

Women from 2021 March to August 2021 at Hayatabad Medical Complex, Peshawar (Pakistan) were invited to participate in a potential study examining the normal development of Human Papillomavirus (HPV) throughout the nearing menopause phase. The inclusion criteria include women of the 39-60 age range, who had an intact cervix. the exclusion criteria were if they were pregnant and either HIV-positive or had previous experiences of receiving an organ transplant. Baseline questionnaire and gynecological examination after expressing informed permission. Data on socioeconomic background, menstruation, reproductive

history, use of hormone replacement therapy, lifelong sexual history, and present sexual activity. Additionally, information on female cervical examinations and therapeutic histories was acquired, considering the possibility that they had undergone a colposcopy or other cervical therapies, had a past Pap abnormality, or had done Pap or HPV testing. A standard transportation solution was used to keep the cervical brush at 4 °C for a maximum of twenty-four hours prior to its vortexes and kept at 80 °C.

The handling of smear test results followed standard clinical procedure. In the following three months following taking the examination and the HPV DNA test, 12% of women weren't given a Pap test since some providers do not do annual cytology screens. "Pap results were categorized as negative for intraepithelial lesion or malignancy (NILM), atypical squamous cells of unknown significance (ASCUS), low-grade squamous intraepithelial lesion (LSIL), atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion (ASC-H), high-grade squamous intraepithelial lesion (HSIL), or cancer. ASCUS or more was deemed abnormal cytology for research purposes" All women's cervical tissues have been genotyped and HPV DNA was found in the baseline samples. The LA test includes the identification of DNA by beta-globin-specific PCR, which was used to confirm the suitability of the material.

Statistical analysis

The link between possible risk variables for HPV positive and cervical abnormalities was estimated using exact logistic regression with 95% confidence intervals.

Result

Among the 200 women that participated in this research, Initial HPV recognition rate was 20% (n = 150), 10% (n = 15), and 6% (n = 10), with 5 "ASCUS", 4 "LSIL", and 1 ASC-H case detections. Age-related reductions in the number of cases of any-HPV (p=0.0045), HR-HPV (p=0.0023), and irregular cytology of the cervical cavity (p=0.0023). The frequency of high-risk HPV decreased from those who were youngest to the elderly by nearly a factor of five from 20% (25/140) through 5% (5/60). No anomalies were discovered in the most elderly group of women, and an equivalent decrease in abnormal cytology was observed. With age, the percentage of females who tested -ive with both screenings spiked whereas the percentage of women who tested +ive with either test fell in line with the declining rate.

In both age categories, unmarried females showed a greater likelihood of being identified with HR-HPV than married females. Regardless of their age, females who said that they had a new sex during the previous six months exhibited a greater likelihood of having HR-HPV identified than those who did not. Compared to women in the highest income bracket, younger women (45 years aged) had a higher likelihood of being diagnosed with HRHPV and having cervical abnormalities.

Women aged 45 and older with relatively small risk HPV infections had a six-fold higher prevalence of cytological abnormalities than those who tested HPV-

negative. When it came to youthful ladies, this association was not seen. After adjusting for HR-HPV, the risks of cytologic abnormalities rose among current smokers under 45 (OR: 3.3 (2.0, 17.9)).

Table 1 the prevalence of HPV and cervical abnormalities

Age range	HPV DNA +	HR HPV DNA +	LR HPV DNA +	Cervix cell study
39-40	40	38	35	40
40-45	70	67	65	67
45-55	80	91	90	90
55-60	10	34	10	3
P value	0.0045	0.0023	0.0023	0.0025

Table 2 Association of age between HPV and cytology

Age range	Hpv negative pap-	Hpv positive pap-	Hpv negative pap+	Hpv positive pap+
39-40	20	18	10	11
40-45	21	17	8	5
45-55	100	11	12	4
55-60	49	10	4	2
P value	0.0023	0.0045	0.0027	0.0034

Discussion

All women over 30 should be screened for cervical cancer according to recent recommendations. The reliability with which the results of Pap and HPV tests are taken into account in this age group is seriously questioned by these findings. Despite the number of mild & high-grade irregularities remaining unchanged with aging (15, 16), that our study discovered that as age grew, there was less of a link between the detection of "HR-HPV" and cytological issues.

According to our results, the research of almost a million women between the ages of 30-64 also discovered that the number of cases of HPV declined with ageing across every level of atypical cytology. Multiple research investigations have demonstrated that older females with poor-quality cytological irregularities may benefit from HPV testing to help differentiate between cervical pre-cancers that are really infections and those that are not and to help identify genuine illnesses that may proceed into cervical pre-cancers. In contrast, a US randomized controlled experiment found that low-grade lesions were not significantly affected by HR-HPV triage. (17, 18)

Despite the fact that the prevalence of HR-HPV dropped linearly with age in females with cytological defects, the HPV-HPV was shaped like "U" and was most prevalent in older females. This trend would indicate that "LR-HPV and HR-HPV" infection may both have a role in the detection of cervical abnormalities in older women. In fact, only low-risk HPV strains were associated with cervical abnormalities in women over 40 (OR: 5.3 (2.6, 15.9), whereas younger women

(OR: 2.8 (1.3, 7.6)) did not show this connection. This is consistent with two well-established facts, such as the receding of the cervical conversion zone towards the operating environment in older women (19).

Our study has the advantage of allowing us to compare the associations of Human papilloma virus septicity according toward the age to the associates of irregular cell structure. The Human papilloma virus connections remained generally alike in both older & younger females. The correlation between older women's reported lifetime sex partner counts and HPV detection was a startling exception, showing that grown-up females are extra probable to have long-standing determined contagion. "In younger women aged 30-44 years, HPV associations were equivalent to cervical dysplasia correlations." The traits we anticipated to be linked using equally Human papilloma virus & irregularities, however, were only seen in older women (20), despite the significant causal connection that exists between HPV with cervical irregularities.

The occurrence of cervical irregularities remained generally modest, and none of the 120 women between the ages of 55 and 60 had any abnormalities. Nevertheless, the bulk of abnormalities (ASCUS and LSIL) were low-grade, which is most probably owing to the group's low-risk features and extensive prior screening.

Human papillomavirus testing in females elder than thirty is growing as a result of the ASCCP's consensus guidelines advocating the screening of Pap smears with supplementary HPV testing in females of age more than thirty, as well as an increase in the number of women who are asking for the test. Our results suggest that a third classification by age at 45 years and above should be included in the ongoing assessment of HPV and histology outcomes for cervical cancer surveillance programmers. According to research, women between the ages of 45 and 50 with low-grade anomalies may be triaged using an age-based approach for HPV testing (21).

Conclusion

Age had no effect on a number of low- and high-grade abnormalities, but we did see a decline in the agreement between cytological results and HR-HPV tests.

References

1. Aker SŞ, Ađar E, Tinelli A, Hatirnaz S, Ortađ F. The Impact of HPV Diagnosis and Abnormal Cervical Cytology Results on Sexual Dysfunction and Anxiety. *International journal of environmental research and public health*. 2023;20(4):3630.
2. Al Niyazee AAQ, Abedalrahman SK, Abdulrahman ZN, Zadawy IA. Prevalence of human papilloma virus positivity and cervical cytology. Is there a new HPV gene? *Middle East Journal of Family Medicine*. 2019;7(10):10.
3. Alay I, Kaya C, Karaca I, Yildiz S, Baghaki S, Cengiz H, et al. The effect of being diagnosed with human papillomavirus infection on women's sexual lives. *Journal of Medical Virology*. 2020;92(8):1290-7.

4. Aydogan Kirmizi D, Baser E, Demir Caltekin M, Onat T, Sahin S, Yalvac ES. Concordance of HPV, conventional smear, colposcopy, and conization results in cervical dysplasia. *Diagnostic Cytopathology*. 2021;49(1):132-9.
5. Chang C-L, Ho S-C, Su Y-F, Juan Y-C, Huang C-Y, Chao A-S, et al. DNA methylation marker for the triage of hrHPV positive women in cervical cancer screening: Real-world evidence in Taiwan. *Gynecologic Oncology*. 2021;161(2):429-35.
6. Choi MS, Lee YJ, Lee EH, Ji YI, Park MJ. Factors Associated with Cyto-Histological Misinterpretation of Cervical Smear according to Menopausal Status. *Journal of Menopausal Medicine*. 2022;28(2):78-84.
7. Donkoh ET, Asmah RH, Agyemang-Yeboah F, Dabo EO, Wiredu EK. Prevalence and distribution of vaccine-preventable genital human Papillomavirus (Hpv) genotypes in Ghanaian women presenting for screening. *Cancer Control*. 2022;29:10732748221094721.
8. Elasy AN, Aziza A-K, Hamed BM. The relation between human papilloma virus serotype infection and colposcopic, cytological and histopathological abnormalities among the Egyptian women: retrospective study Short title: Colposcopy, cytology, and histopathology of Egyptian women with HPV.
9. Kaiser LA, Kupec T, Najjari L, Stickeler E, Wittenborn J. Predictors of CIN2+ in Patients with PAP III-P (ASC-H): A Cross-Sectional Study. *Diagnostics*. 2023;13(6):1066.
10. Koc S, Yuksel D, Kayikcioglu F. Colposcopic histopathology results of patients over 50: Is HPV genotyping useful? *Current Problems in Cancer*. 2022;46(1):100764.
11. Landy R, Hollingworth T, Waller J, Marlow LA, Rigney J, Round T, et al. Non-speculum clinician-taken samples for human papillomavirus testing: a cross-sectional study in older women. *British Journal of General Practice*. 2022;72(721):e538-e45.
12. Li Y, Luo H, Zhang X, Chang J, Zhao Y, Li J, et al. Development and validation of a clinical prediction model for endocervical curettage decision-making in cervical lesions. *BMC cancer*. 2021;21:1-11.
13. Liu Q, Zhang T, Chen L, Zhou X, Zhang X, Zheng W, et al. Correlation of immediate prevalence of cervical precancers and cancers with HPV genotype and age in women with ASC-US/hrHPV+: a retrospective analysis of 2292 cases. *Journal of Clinical Pathology*. 2023.
14. Long T, Zhang C, He G, Hu Y, Lin Z, Long L. Bacterial vaginosis decreases the risk of cervical cytological abnormalities. *Cancer Prevention Research*. 2023;16(2):109-17.
15. Salibay C, Chen Z, Ma B, Pan H, Hijazi M, Elatre W, et al. High-risk HPV testing improves accuracy in detection of CIN2+ lesions in ASC-H postmenopausal women? An academic hospital experiences. *Journal of the American Society of Cytopathology*. 2023;12(1):58-65.
16. Shashidhar SC, Sonkusare S, Ramesh PS, Shetty AK, Shetty V, Devegowda D. Prevalence of high-risk human papillomavirus in women with normal and abnormal pap smear: a cross sectional study from a tertiary hospital in South India. *Indian Journal of Gynecologic Oncology*. 2021;19:1-8.
17. Sugisawa A, Toyoda Z, Tanabe Y, Uehara K, Oshiro A, Yamazato R, et al. Cytological characteristics of premalignant cervical epithelial lesions in postmenopausal women based on endocrine indices and parakeratosis. *Menopause*. 10.1097.

18. Williams MP, Kukkar V, Stemmer MN, Khurana KK. Cytomorphologic findings of cervical Pap smears from female-to-male transgender patients on testosterone therapy. *Cancer Cytopathology*. 2020;128(7):491-8.
19. YALCINKAYA C. Prevalence of cervical high-risk human papillomavirus and cytological abnormalities in elderly Turkish women. *Marmara Medical Journal*. 2022;35(3):288-92.
20. Yu H, Ma L, Bian M, Li Q, Liang H. Association of abnormal vaginal microflora and HPV infection in cervical precancerous lesions: a retrospective study. *The Journal of Infection in Developing Countries*. 2022;16(06):1089-95.
21. ZERGEROĞLU S, Özkan ZS, AYDIN AH. Are the correlation results of HPV positive cases with cervical smear always consistent? *Journal of Medicine and Palliative Care*. 2023;4(2):158-62.