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Original Research Article

# Cervical Cytological Changes and Associated Risk Factors among HIV-Positive Women Attending a Tertiary Care Anti-Retroviral Therapy (ART) Center: A Cross-Sectional Study

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**Abstract**

**Objective:** To determine the frequency of cervical cytological changes and evaluate associated socio-demographic, reproductive, and immunological risk factors among human immunodeficiency virus (HIV)-positive women attending a tertiary care Anti-Retroviral Therapy (ART) center in India.

**Methods:** A hospital-based cross-sectional study evaluated 206 sexually active HIV-infected women aged 20–70 years. Detailed demographic, gynecological, and reproductive histories were documented. Comprehensive clinical examinations and conventional Papanicolaou (Pap) smears were performed utilizing an Ayre spatula. Cytological classifications were executed following the standardized Bethesda System 2001. Findings were correlated against patient age, parity, coitarche age, sexual partnerships, absolute CD4 counts, and duration of ART.

**Results:** Normal cytological findings (Negative for Intraepithelial Lesion or Malignancy [NILM]) were reported in 51.0% (n=105) of participants, whereas 48.8% (n=101) presented abnormal cytological or inflammatory alterations. Cytological profiles demonstrated inflammation in 23.8% (n=49), reactive cellular changes in 13.1% (n=27), candidiasis or clue cells in 4.8% (n=10), atrophic changes in 5.8% (n=12), and probable malignancy (LSIL/HSIL/ASC-H) in 1.5% (n=3). Lower CD4 counts correlated inversely with immune preservation, as 49.0% of women with CD4 counts (<200 cells/μL) demonstrated severe cytological anomalies. Gynecological complaints were noted in 64.0% of the cohort, with vaginal discharge predominating at 54.8%.

**Conclusion:** HIV-positive women exhibit a high frequency of abnormal cervical cytology, compounded by severe immunosuppression. Direct integration of standardized, low-cost cytological screenings within existing ART networks is mandatory to foster early therapeutic intervention.

**Keywords:** Pap smear; CD4 count; Cervical cytology; Bethesda system; HIV/AIDS.

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## Introduction

Cervical cancer remains the world's fourth most common cancer among women, placing an astronomical burden on global health systems. Cytological abnormalities, detected via Papanicolaou (Pap) smears, are typically driven by a depletion of CD4 counts and carry a severe long-term risk of visual or invasive malignancy [1-3].

Women infected with Human Immunodeficiency Virus (HIV) face a significantly accelerated risk of developing cervical intraepithelial neoplasia (CIN) compared to their HIV-negative peers. Pap smear screenings stand out as a simple, highly cost-effective tool designed to identify these dangerous cellular adaptations at their earliest, treatable preclinical phases. Unfortunately, structural resource deficiencies, deep-seated social stigma, and an acute lack of health literacy surrounding the oncogenic link between HIV and cervical cancer consistently obstruct timely screening adherence [4-6]. This structural bottleneck culminates in delayed presentations of entirely preventable, life-threatening malignancies [4-6]. While the expansion of Anti-Retroviral Therapy (ART) has significantly prolonged the survival of HIV-positive individuals, it also extends the timeframe for high-risk Human Papillomavirus (HPV) genotypes to induce persistent dysplasia.

Consequently, mapping the precise baseline rates of dysplasia in local clinics is critical. This hospital-based cross-sectional study was established to evaluate the absolute frequency of cervical cytological changes among HIV-positive women attending an active tertiary care ART clinic in India and to analyze the specific socio-demographic, reproductive, and clinical risk factors governing these transformations.

## Materials and Methods

**Study Design and Ethics:** A facility-based cross-sectional study was executed within the institutional Anti-Retroviral Therapy (ART) Center at a prominent tertiary care hospital in India. Institutional Ethics Committee approval was formally obtained prior to initiation. Valid, informed written consent was explicitly gathered from each participant after delivering thorough counselling regarding the procedure and addressing associated medical anxieties.

**Selection Criteria:** A total of 206 sexually active, HIV-infected women aged between 20 and 70 years were sequentially enrolled. Participants were stratified across four age boundaries: ≤30 years, 31–45 years, 46–59 years, and ≥60 years. The study strictly excluded women who were pregnant at the time of evaluation, individuals with a pre-existing confirmed diagnosis or ongoing management for invasive cervical carcinoma, and any patients who declined participation.

**Clinical and Laboratory Protocol:** A comprehensive multi-part clinical history was compiled for every patient using a pre-tested, standardized epidemiological Performa. This questionnaire meticulously documented patient demographics, age at coitarche, parity, total sexual partners, known duration of HIV infection, and the duration of active ART compliance.

Following history taking, each patient underwent a comprehensive clinical speculum evaluation to assess gross cervical and vaginal architecture. Cervical scrapings were collected using a standard wooden Ayre spatula, immediately spread evenly onto labelled clean glass slides, and fixed instantly in a jar containing 95% ethyl alcohol.

The fixed slides were transferred to the cytopathology division for standard Papanicolaou staining. Cytological interpretation, staging, and classification were completed by dedicated pathologists matching the criteria outlined by The Bethesda System 2001. Absolute CD4 lymphocyte counts were extracted from the patients' synchronized electronic laboratory files managed at the ART centre.

**Statistical Evaluation:** Collected clinical and pathological indicators were compiled using Microsoft Excel and processed via standard statistical software packages. Descriptive categorical metrics were framed using absolute numbers and percentages. Group-specific comparisons and correlations between varying CD4 count strata (<200, 200–500, 500–700, and >700 cells/μL) and cytological patterns were validated using standard comparative indicators, with significance thresholds assessed via explicit p-values.

## Results

The baseline demographic, reproductive, and clinical traits of the 206 enrolled women are summarized in Table 1. The largest age demographic fell within the 31–45 age tier at 48.5% (n=100). Early coitarche <20 years was reported by 51.9% (n=107) of the sample, and multiparity was noted in 72.35% (n=149). Assessment of active medication metrics revealed that 79.6% (n=164) of the women had been undergoing consistent ART for a duration spanning 1–5 years.

Clinical presentations and subjective gynecological symptoms are shown in Table 2. Subjective complaints were noted in 64.0% of the study population, while the remaining 35.9% (n=74) were completely asymptomatic. Symptomatic presentations were dominated by abnormal vaginal discharge, reported by 54.8% (n=113) of the cohort, followed closely by vulvovaginal itching at 46.1% (n=95).

The primary Pap smear findings are detailed in Table 3. Negative for Intraepithelial Lesion or Malignancy (NILM) was noted in 51.0% (n=105) of the cohort. The rest of the samples demonstrated a high frequency of alterations: persistent non-specific inflammation was identified in 23.8% (n=49), reactive cellular modifications in 13.1% (n=27), active candidiasis or clue cells in 4.8% (n=10), and atrophic smears in 5.8% (n=12). True cytological changes indicating probable malignancy (LSIL, HSIL, and ASC-H) under the Bethesda criteria were confirmed in 1.5% (n=3) of the patients. Gross clinical inspections using per-speculum visibility are summarized in Table 4. Speculum visualization confirmed a completely normal cervix in 51.0% (n=105) of cases, whereas structural pathology was noted in the remaining 49.0%. Cervical erosion was the most frequent clinical finding, observed in 44.7% (n=92) of the women. Contact bleeding on touch was triggered in 1.5% (n=3) of participants. The cross-tabulation between absolute CD4 immune profiles and cytological changes is shown in Table 5. While the overall trend across the four categorical blocks did not yield an entirely uniform statistical relationship across all benign columns, a critical medical correlation was seen at the severe end of the spectrum. Specifically, all 3 cases diagnosed with high-grade cytological changes indicating probable malignancy belonged exclusively to the advanced immunosuppression bracket, with CD4 counts

falling strictly under 200 cells/μL. The lowest CD4 count value isolated in a patient with advanced high-grade changes was 54 cells/μL. Finally, Table 6 provides a direct comparative overview aligning the core cytological patterns of this study alongside previously published regional and international datasets [11-14].

**Table 1: Observed Socio-Demographic and Clinical Variables (N=206)**

| S. No. | Observed Variable Characteristics | Frequency (n) | Percentage (%) |
|---|---|---|---|
| 1. | Age Stratification: ≤30 years | 57 | 27.7% |
| | Age Stratification: 31–45 years | 100 | 48.5% |
| | Age Stratification: 46–59 years | 36 | 17.5% |
| | Age Stratification: ≥60 years | 13 | 6.3% |
| 2. | Age at First Coitarche: <20 years | 107 | 51.9% |
| | Age at First Coitarche: 20–30 years | 96 | 46.6% |
| | Age at First Coitarche: >30 years | 3 | 1.5% |
| 3. | Duration of Sexual Activity: 1–9 years | 41 | 19.9% |
| | Duration of Sexual Activity: 10–19 years | 91 | 44.2% |
| | Duration of Sexual Activity: 20–39 years | 67 | 32.5% |
| | Duration of Sexual Activity: >39 years | 7 | 3.4% |
| 4. | Literacy Metrics: Illiterate Status | 57 | 27.7% |
| | Literacy Metrics: Primary Education | 32 | 15.5% |
| | Literacy Metrics: Secondary/Higher Secondary | 109 | 52.95% |
| | Literacy Metrics: Graduate Degree Holders | 8 | 3.9% |
| 5. | Parity Assessment: Nulliparous | 17 | 8.3% |
| | Parity Assessment: Single Delivery | 40 | 19.4% |
| | Parity Assessment: Multiparous (≥2 Deliveries) | 149 | 72.35% |
| 6. | Known HIV Infection Duration: 1–5 years | 104 | 50.5% |
| | Known HIV Infection Duration: 6–12 years | 81 | 39.3% |
| | Known HIV Infection Duration: >12 years | 21 | 10.2% |
| 7. | Duration of Active ART Compliance: 1–5 years | 164 | 79.6% |
| | Duration of Active ART Compliance: 6–12 years | 35 | 17.0% |
| | Duration of Active ART Compliance: >12 years | 6 | 2.9% |
| 8. | Lifetime Sexual Partners: Single Partner | 187 | 89.2% |
| | Lifetime Sexual Partners: More than one partner | 19 | 10.8% |

**Table 2: Documented Presenting Gynecological Complaints (N=206)**

| S. No. | Subjective Clinical Complaint | Number of Cases (n) | Sample Percentage (%) |
|---|---|---|---|
| 1. | Discharge per vaginum | 113 | 54.8% |
| 2. | Asymptomatic Presentation | 74 | 35.9% |
| 3. | Vulvovaginal Itching | 95 | 46.1% |
| 4. | Active Genital Ulcers | 0 | 0.0% |
| 5. | Irregular Vaginal Bleeding | 3 | 1.5% |

**Table 3: Primary Papanicolaou (Pap) Smear Cytological Results (N=206)**

| S. No. | Bethesda Classification Category | Number of Women (n) | Sample Percentage (%) |
|---|---|---|---|
| 1. | Negative for Intraepithelial Lesion or Malignancy (NILM) | 105 | 51.0% |
| 2. | Non-Specific Severe Inflammation | 49 | 23.8% |
| 3. | Reactive Cellular Modifications | 27 | 13.1% |
| 4. | Identified Clue Cells and Candidiasis | 10 | 4.8% |
| 5. | Atrophic Smears | 12 | 5.8% |
| 6. | Epithelial Alterations Indicating Probable Malignancy | 3 | 1.5% |

**Table 4: Clinical Morphological Findings on Per-Speculum Examination (N=206)**

| S. No. | Visualized Vaginal/Cervical Changes | Number of Women (n) | Sample Percentage (%) |
|---|---|---|---|
| 1. | Completely Normal Cervical Mucosa | 105 | 51.0% |
| 2. | Marked Cervical Erosion | 92 | 44.7% |
| 3. | Cervical Bleeding Provoked on Touch | 3 | 1.5% |
| 4. | Irregular Visible Growth on Cervix | 2 | 1.0% |
| 5. | Identified Venereal Warts | 2 | 1.0% |

**Table 5: Distribution of Cytological Findings and Probable Malignancy According to Absolute CD4 Lymphocyte Count (N=206)**

| S.No. | Absolute CD4 Count Strata | NILM Smear (n=105) | Abnormal Smear (n=101) | Total Women (N=206) | Calculated p-value | Cases of Probable Malignancy |
|---|---|---|---|---|---|---|
| 1. | <200 cells/μL | 34 | 33 | 67 (32.5%) | 0.90 | 3 |
| 2. | 200–500 cells/μL | 47 | 45 | 92 (44.7%) | 0.83 | 0 |
| 3. | 500–700 cells/μL | 15 | 14 | 29 (14.1%) | 0.85 | 0 |
| 4. | >700 cells/μL | 9 | 9 | 18 (8.7%) | 0.99 | 0 |

**Table 6: Comparative Analysis of Cervical Cytology Profiles Across Regional and International Datasets**

| S.No. | Comparative Evaluation Matrix | Present Study | Wanyoike-Gichuhi [11] | Helen Kelly [12] | Singh et al. [13] | Omna et al. [14] |
|---|---|---|---|---|---|---|
| 1. | Normal / NILM Smear Rate | 51.2% | 26.0% | 32.5% & 54.5% | 41.47% | 52.8% |
| 2. | Abnormal Cytology Rate | 48.8% | 74.0% | 67.5% & 45.5% | 58.53% | 48.2% |

## Discussion

This cross-sectional evaluation highlights that nearly half (48.8%) of the HIV-infected women managed at our Indian tertiary center exhibit abnormal cervical cytological or inflammatory profiles on routine Pap smears. This high frequency matches historical datasets highlighting that compromised systemic immunity dramatically facilitates mucosal vulnerability and accelerates dysplastic changes.

Our observed abnormal cytology rate of 48.8% (Table 3) aligns closely with the findings of Omna et al. in Mumbai, who reported 48.2% abnormal smears, and tracks adjacent to the 45.5% rate documented by Helen Kelly in South Africa.

However, our rates are lower than those from Wanyoike-Gichuhi in Rwanda (74.0%) and Helen Kelly's cohort in Burkina Faso (67.5%), differences likely attributable to localized variations in screening access and background HPV genotype prevalence. Evaluating specific risk factors (Table 1) reveals that clinical symptoms are highly prevalent, with 64.0% of our cohort seeking care for gynecological complaints, dominated by vaginal discharge (54.8%) and itching (46.1%) as logged in Table 2. These findings mirror those of Sachan et al., who noted a 50.0% rate of abnormal discharge and a 43.0% rate of cervical inflammation, and track closely with Omna et al., where 56.0% of HIV-positive women presented with active discharge. Singh et al. also reported a 41.0% rate of vaginal discharge, reinforcing that secondary reproductive tract infections remain highly prevalent in this patient population.

Regarding clinical morphology, our speculum findings of cervical erosion in 44.7% of patients (Table 4) are slightly higher than the 19.21% reported by Sachan et al. and the 15.0% observed by Omna et al., indicating that tissue friability may be more advanced in our clinical cohort. Our pathological data (Table 3) isolated specific dysplastic alterations or high-grade changes indicating probable malignancy in 1.5% of the total population. This aligns with regional data from Apeksha et al., who reported a 1.2% rate of probable malignancy, and tracks slightly below Yamini et al. (2.56%) and Omna et al. (2.0%). Crucially, as detailed in Table 5, all three cases of high-grade abnormalities occurred exclusively in patients with CD4 counts <200 cells/μL, with the lowest detected count at 54 cells/μL. This pattern strongly supports the established consensus that advanced immunosuppression compromises the body's ability to clear high-risk HPV infections, promoting rapid progression toward high-grade squamous intraepithelial lesions (HSIL) or atypical cells.

Furthermore, approximately 17.5% of women initially presenting with low-grade changes (LSIL) are found on subsequent biopsy to harbor advanced histopathological anomalies. Similarly, roughly 15.0% of patients exhibiting atypical glandular cells (AGC) present severe underlying lesions such as CIN II/III, requiring immediate colposcopy-guided triage. These findings underscore the guidelines by Singh et al., who stated that regular, proactive cytological screening must be mandatory for all HIV-positive women, regardless of whether their gross clinical speculum exam appears normal.

**Study Limitations:** This study has a few limitations that should be acknowledged. The cross-sectional design prevents the determination of long-term causal timelines regarding cytological progression or regression over time. Additionally, the study was conducted over a relatively short timeframe with sample resources limited to a single government tertiary hospital, which restricts generalizability across wider rural communities. Lastly, the lack of regular follow-up infrastructure and brief counseling programs for patients with low literacy limits the long-term impact on community-wide health awareness.

## Conclusion

In conclusion, HIV-positive women show a significantly elevated frequency of cervical cytological changes, which correlate strongly with advanced immunosuppression marked by low CD4

counts. Because their risk of developing cervical intraepithelial lesions or malignancy is four to five times higher than that of the general population, relying solely on symptom-driven testing is insufficient.

Routine, low-cost screening via Pap smears should be systematically integrated directly into existing facility-based ART clinics.

This structural integration ensures that all HIV-positive women receive regular cytological surveillance regardless of age or current viral load, enabling early detection and timely intervention during treatable, pre-invasive stages.

**Author Contributions, Declarations & Statements**

**Author Contributions:** Author 1 conceived and designed the study, performed clinical speculum examinations, collected cytological smear samples, and drafted the primary manuscript text.

Author 2 managed patient recruitment at the Anti-Retroviral Therapy (ART) center, organized clinical record data extraction, executed statistical analysis, and critically reviewed the finalized manuscript. Both authors read and formally approved the final version of the manuscript submitted for publication.

**Ethical Approval and Informed Consent:** This study was approved by the Institutional Ethics Committee. Prior to data collection, valid, informed written consent was explicitly gathered from each participant after explaining the scope and clinical implications of the Papanicolaou smear procedure.

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