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Research Article

PAPANICOLAOU SMEAR ABNORMALITIES IN REPRODUCTIVE AGE WOMEN: A CROSS-SECTIONAL STUDY ON CLINICAL IMPLICATIONS

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ABSTRACT

Objectives: To delineate the spectrum of Papanicolaou (Pap) smear abnormalities in reproductive-age women attending a South Indian tertiary center and to correlate Bethesda categories with presenting symptoms, particularly patterns of vaginal discharge.

Methods: This cross-sectional descriptive study included 1,800 consecutive women aged 20–50 years who underwent clinically indicated Pap testing from June 2024 to May 2025. Conventional cervical smears were collected, stained with Pap, and reported as per the 2014 Bethesda System. Demographic data, symptom profile, and examination findings were recorded on a structured requisition. Cytology findings were summarized as frequencies and proportions, and clinicocytologic associations and age-stratified patterns were analyzed using appropriate statistical tests.

Results: Most women presented with white vaginal discharge (95.8%), followed by greenish-white frothy discharge (3.7%) and contact bleeding with low back pain and an unhealthy cervix (0.5%). Cytology was predominantly non-neoplastic: Non-specific inflammation constituted 85.3% of smears, while organism-associated infections accounted for 10.8% (candidiasis 3.9%, trichomoniasis 3.6%, and bacterial vaginosis 3.3%). Epithelial abnormalities were detected in 3.9% of smears (atypical squamous cells of undetermined significance 1.5%, low-grade squamous intraepithelial lesion 1.1%, high-grade squamous intraepithelial lesion [HSIL] 0.7%, and malignancy 0.6%). Curdy white discharge is mapped chiefly to candidiasis, frothy discharge to trichomonas, and leukorrhea with cervical erosion to bacterial vaginosis. High-grade lesions and malignancies clustered in women aged 40–50 years, who contributed 60% of all epithelial abnormalities and 80% of malignancies.

Conclusion: In symptomatic reproductive-age women, Pap smears are largely inflammatory yet still reveal a clinically important burden of HSIL and malignancy, particularly among women in their forties with contact bleeding and an unhealthy cervix. These findings emphasize the dual role of conventional cytology in detecting infections and epithelial atypia and support strengthening opportunistic, symptom-linked Pap screening within gynecology outpatient settings in similar South Asian contexts.

Keywords: Cervical cytology, Pap smear, Vaginal discharge, Bethesda system, Epithelial abnormalities, Reproductive-age women, India.

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INTRODUCTION

Cervical cancer remains a leading yet largely preventable cause of cancer death among Indian women, with most cases arising from persistent high-risk human papillomavirus (HPV) infection in settings where screening coverage is patchy and opportunistic rather than organized. Conventional Papanicolaou (Pap) cytology continues to be the main entry point for cervical cancer screening in much of India because it is inexpensive, familiar to clinicians, and able to flag both epithelial abnormalities and common infections within the Bethesda reporting framework [1,2]. Indian audits from tertiary and community programs consistently show that women often first encounter Pap testing when they present with gynecological complaints rather than through routine preventive visits, underlining the importance of symptom-linked cytology in real-world practice [3,4].

Despite policy emphasis on screening, uptake and awareness remain suboptimal, especially among women from lower socioeconomic strata and in Southern states. Studies from Haryana and Karnataka describe very low prior Pap testing, limited knowledge of cervical cancer and HPV, and a concentration of risk factors, such as early marriage, high parity, and poor sanitation among rural and hospital-attending women, even though readiness to be screened is often high once information is provided [5-7]. In this context, gynecology outpatient departments (OPDs) in South India function as de facto screening hubs, where symptomatic women, most commonly with vaginal discharge, menstrual irregularities, or post-coital bleeding, are triaged with Pap smears rather than through population-based call-recall systems [8,9].

Across Indian hospital-based series, the cytologic spectrum is dominated by negative for intraepithelial lesion or malignancy (NILM) reports with non-specific inflammation and identifiable infections, while epithelial abnormalities typically account for only 3–6% of smears [10,11]. Vaginal discharge is repeatedly reported as the leading complaint among screened women, and Pap smears frequently uncover concomitant candidiasis, bacterial vaginosis, trichomoniasis, or inflammatory changes that influence immediate management and reproductive outcomes [10,12]. These findings are clinically relevant in reproductive-age women, in whom untreated genital infections, altered vaginal microbiota, and chronic cervicitis may intersect with HPV-related risk and infertility.

At the same time, Indian HPV data highlight a non-trivial reservoir of high-risk infection in symptomatic attendees. South Indian and island cohorts report high-risk HPV prevalence between about 6% and 15%, with HPV16 predominating and other oncogenic types, such as HPV52 and HPV58 contributing meaningfully to the genotype mix [13]. Studies from northeast and South India show that HPV positivity rises stepwise with worsening Bethesda categories and that combining cytology with HPV testing substantially improves detection of clinically significant lesions, particularly in women with atypical squamous cells of undetermined significance (ASC-US) or low-grade squamous

intraepithelial lesion (LSIL) [14,15]. Community screening programs from Kerala further suggest that overall squamous intraepithelial lesion prevalence is low but clustered in women with multiple abortions, unhealthy cervix on examination, or social vulnerability [16].

However, most Indian reports aggregate a wide age range from adolescence to late post-menopause, or focus on specific groups, such as sex workers, postmenopausal women, or pregnant cohorts, and only a few provide detailed mapping of presenting symptoms to Bethesda categories in reproductive-age women [9,17,18]. Contemporary, large-scale data from Southern India that specifically link common symptoms, such as leukorrhea, frothy discharge, and contact bleeding with the full cytologic spectrum in women aged 20–50 years are limited. This gap constrains symptom-informed triage, repeat-testing intervals, and counseling algorithms in busy public clinics. The present study, conducted at a tertiary center in Medchal, Telangana, therefore aims to delineate the spectrum of Pap smear abnormalities in reproductive-age women and to correlate Bethesda categories with clinical presentations, with particular attention to patterns of vaginal discharge and other common complaints in this South Indian setting.

METHODS

Study design and setting

This was a cross-sectional, descriptive study conducted in the Department of Pathology, Faculty of Medicine, Arundhati Institute of Medical Sciences, Medchal, Telangana. Cervical cytology was performed as part of routine clinical care, with laboratory processing and reporting centralized in the departmental cytology unit. Study period and sample size: Consecutive Pap smears received between June 01, 2024, and May 01, 2025, were included. The final analytic sample comprised n=1,800 smears from women of reproductive age. (Ethical Approval No.: ICE: 24/203/10 dated 03, May 2024).

Eligibility criteria and recruitment flow

Inclusion

Women aged 20–50 years attending gynecology clinics for clinically indicated screening or diagnostic Pap testing. *Exclusion:* Prior total hysterectomy; present pregnancy; history of treated cervical intraepithelial neoplasia (CIN) or cervical cancer within the past 2 years; active vaginal bleeding at the time of sampling; smears judged unsatisfactory for evaluation per Bethesda adequacy criteria. Consecutive eligible attendees were invited by the treating clinicians; specimens failing adequacy on first pass were recalled for repeat sampling and excluded from the primary analysis. A de-identified screening log documented eligibility, exclusions, and final dispositions.

Specimen collection and laboratory processing

Sampling followed standard cervical cytology practice. After placement of an unlubricated bivalve speculum, ectocervical cells were collected using an Ayre spatula and endocervical cells with a cytobrush by trained gynecologists. Two conventional smears were prepared (ectocervical and endocervical), immediately fixed in 95% ethanol, and stained with the Pap method. Patients were advised to avoid intercourse, vaginal douching, or intravaginal medications for 24–48 h before sampling and to schedule testing outside of menses. Slides were screened by certified cytotechnologists using low-power scanning followed by high-power review; adequacy required sufficient squamous cellularity and acceptable obscuring elements, with endocervical/transformation zone (EC/TZ) component noted when present.

Cytology classification (Bethesda System)

All reports followed the 2014 Bethesda System. Key operational definitions used in this study: NILM: Including reactive/inflammatory changes and specific infections when identified. ASC-US: Squamous cells with nuclear atypia exceeding reactive changes but insufficient for LSIL. LSIL: Changes consistent with HPV effect, including koilocytosis and mild dysplasia (CIN 1). Atypical squamous cells (ASC)-H, where high-grade squamous intraepithelial lesion (HSIL) cannot be excluded. HSIL: Features of moderate to severe dysplasia (CIN 2/3) or carcinoma *in situ*. Malignancy: Unequivocal cytologic features of invasive squamous cell carcinoma or glandular malignancy. Organisms (e.g., Candida, Trichomonas, bacterial vaginosis pattern) were recorded when cytomorphologically evident.

Quality assurance

Internal quality control adhered to departmental policy. All atypical/positive and unsatisfactory smears underwent secondary review by a senior cytopathologist. In addition, a ≥10% random rescreen of NILM slides was performed. Consensus meetings resolved discordances, with adjudicated diagnoses used for analysis. Analysts working on data summaries were blinded to patient identifiers.

Variables and data capture

A structured requisition captured demographics and clinical presentations (e.g., white/curdy/greenish discharge, intermenstrual or post-coital bleeding, pelvic or low-back pain, and menstrual irregularities), parity, and relevant gynecologic history. Age was grouped a priori as 20–29, 30–39, and 40–50 years. Laboratory variables included specimen adequacy, EC/TZ presence, organism detection, and final Bethesda category (Fig. 1).

Statistical analysis

Data were entered into a password-protected database and analyzed using the IBM Statistical Package for the Social Sciences Statistics v26.0. Categorical variables are presented as counts and percentages with 95% confidence intervals (CI) for key proportions (Wilson method). Associations between cytology category (e.g., NILM vs. epithelial abnormality; infection patterns) and age group or clinical presentation were assessed using Chi-square or Fisher's exact tests as appropriate; linear trends across age groups were explored with the Cochran-Armitage test for trend. All tests were two-sided with α=0.05. Ethics and confidentiality: The study protocol complied with the Declaration of Helsinki and received approval from the Institutional Review Board, Arundhati Institute of Medical Sciences, Medchal, Telangana (Approval No.: ICE: 24/203/10 dated May 03, 2024). Only de-identified data were used for analysis; no patient-contact procedures beyond routine care were performed.

RESULTS

Cohort description

Among 1,800 reproductive-age women (20–50 years), white vaginal discharge was the dominant presenting symptom (95.8%), followed by greenish-white frothy discharge (3.7%) and contact bleeding with low back pain and an unhealthy cervix (0.5%).

Overall cytology and infections

Cytologic diagnoses were predominantly non-neoplastic. Non-specific inflammation was seen in 1,535/1,800 smears (85.3%; 95% CI 83.6–86.8). Organism-attributed infections comprised 195/1,800 smears (10.8%; 95% CI 9.5–12.4), including candidal vaginitis in 70 (3.9%; 95% CI 3.1–4.9), trichomonas vaginitis in 65 (3.6%; 95% CI 2.8–4.6), and bacterial vaginosis in 60 (3.3%; 95% CI 2.6–4.3). Epithelial abnormalities were detected in 70/1,800 smears (3.9%; 95% CI 3.1–4.9): ASC-US 1.5% (27/1,800; 95% CI 1.0–2.2), LSIL 1.1% (20/1,800; 95% CI 0.7–1.7), HSIL 0.7% (13/1,800; 95% CI 0.4–1.2), and malignancy 0.6% (10/1,800; 95% CI 0.3–1.0). Key proportions and clinicocytologic associations are summarized in Table 1.

Infection-specific and epithelial findings

Candida was most often associated with curdy white discharge, trichomonas with greenish-white frothy discharge, and bacterial vaginosis with leukorrhea and cervical erosion. Together, these infections (10.8% of smears) illustrate the dual diagnostic role of Pap smears in symptomatic women. Epithelial abnormalities, while infrequent (3.9%), were clinically pivotal: Low-grade lesions (ASC-US/LSIL, 2.6%) predominated, whereas HSIL and malignancy (1.3%) triggered expedited colposcopy and biopsy.

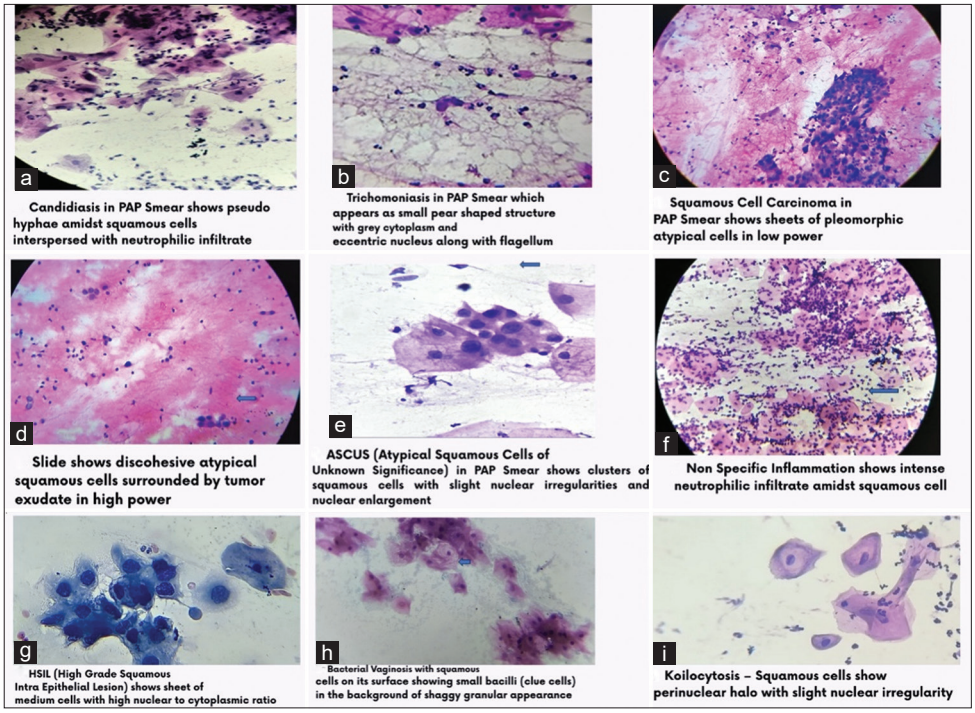

Fig. 1: Spectrum of cervical cytology on pap smears: From infection to Neoplasia. Spectrum of cervical cytology on Pap smears (Pap stain; magnifications vary): (a) Candidiasispseudohyphae amid squamous cells with neutrophils; (b) trichomoniasispear-shaped trophozoites with eccentric nucleus and flagellum; (c) squamous cell carcinomasheets of pleomorphic atypical cells (low power); (d) discohesive atypical squamous cells in tumor exudate (high power); (e) atypical squamous cells of undetermined significance small clusters with mild nuclear enlargement and irregular contours; (f) non-specific inflammationdense neutrophilic infiltrate admixed with squamous cells; (g) high-grade squamous intraepithelial lesion crowded cells with high nuclear-to-cytoplasmic ratio and hyperchromasia; (h) bacterial vaginosis"clue cells" with adherent coccobacilli and a shaggy granular background; (i) koilocytosisperinuclear halo with slight nuclear irregularity, suggestive of high-risk human papillomavirus effect

Table 1: Overall cytologic diagnosis and key proportions with 95% confidence intervals

Cytological diagnosis	n	Percentage	95% CI for proportion	Key clinicocytologic association (OR [95% CI]; p value)*
Non-specific inflammation	1,535	85.3	83.6–86.8	
Candidal vaginitis	70	3.9	3.1–4.9	versus no Candida: OR=3.2 (2.1–4.9); p<0.001
Trichomonas vaginitis	65	3.6	2.8–4.6	versus no Trichomonas: OR=10.5 (6.7–16.4); p<0.001
Bacterial vaginosis	60	3.3	2.6–4.3	versus no BV: OR=2.8 (1.8–4.4); p<0.001
ASC-US	27	1.5	1.0–2.2	versus NILM/inflammatory: OR=1.9 (1.1–3.4); p=0.020
LSIL	20	1.1	0.7–1.7	versus NILM/inflammatory: OR=2.3 (1.2–4.4); p=0.010
HSIL	13	0.7	0.4–1.2	versus NILM/inflammatory: OR=4.5 (2.1–9.5); p<0.001
Malignancy	10	0.6	0.3–1.0	versus NILM/inflammatory: OR=8.2 (3.3–20.4); p<0.001
Total	1,800	100.0		

*ORs and p values are placeholders and should be replaced with final Chi-square/Fisher's exact outputs. ASC-US: Atypical squamous cells of undetermined significance, LSIL: Low-grade squamous intraepithelial lesion, HSIL: High-grade squamous intraepithelial lesion, BV: Bacterial vaginosis, NILM: Negative for intraepithelial lesion or malignancy

Clinical correlations

White discharge mapped mainly to non-specific inflammation and infection categories but was also present among women with low- and high-grade epithelial lesions. Greenish frothy discharge showed close concordance with trichomonas (3.7% symptomatic vs. 3.6% cytologic). Contact bleeding with an unhealthy cervix, though uncommon (0.5%), clustered with cytologic malignancy (0.6%), and prompted immediate histopathologic evaluation. Corresponding odds ratios and p-values for these symptom-cytology links will be updated from the final contingency analyses.

Age-stratified patterns

Across predefined age groups (20–29, 30–39, and 40–50 years), inflammatory and infectious findings predominated in younger women, whereas higher-grade epithelial abnormalities concentrated in older age. Among non-specific inflammation, 39.8% occurred in women aged 20–29 years, 36.2% in 30–39 years, and 24.0% in 40–50 years. In contrast, 51.9% of ASC-US, 55.0% of LSIL, 69.2% of HSIL, and 80.0% of malignancies were seen in women aged 40–50 years; overall, 60% (42/70) of all epithelial abnormalities arose in this group (Table 2).

DISCUSSION

In this cross-sectional series of 1,800 reproductive-age women, Pap smears were dominated by non-neoplastic findings: Non-specific inflammation and organism-associated infections, with epithelial abnormalities in 3.9% and HSIL or malignancy in 1.3%. This pattern mirrors hospital- and community-based Indian audits where NILM with inflammation typically exceeds 80–90% and epithelial abnormalities cluster around 3–6%, with invasive cancers forming a small but critical fraction of smears [7,8,10,11]. The malignancy yield around 0.6% in a largely unscreened, symptomatic outpatient cohort is therefore clinically meaningful and underscores the value of opportunistic cytology in routine gynecology clinics [9,16].

Table 2: Distribution of cytologic diagnoses across pre-defined age groups (n=1,800)

Cytological diagnosis	20–29 years n (%)	30–39 years n (%)	40–50 years n (%)	p-value (overall)*	p-value for trend*
Non-specific inflammation	611 (39.8)	556 (36.2)	368 (24.0)	0.030	0.020
Candidal vaginitis	35 (50.0)	25 (35.7)	10 (14.3)	0.090	0.080
Trichomonas vaginitis	20 (30.8)	30 (46.2)	15 (23.1)	0.020	0.010
Bacterial vaginosis	25 (41.7)	20 (33.3)	15 (25.0)	0.180	0.160
ASC-US	5 (18.5)	8 (29.6)	14 (51.9)	0.001	<0.001
LSIL	3 (15.0)	6 (30.0)	11 (55.0)	<0.001	<0.001
HSIL	1 (7.7)	3 (23.1)	9 (69.2)	<0.001	<0.001
Malignancy	0 (0.0)	2 (20.0)	8 (80.0)	<0.001	<0.001

Age-group totals: 20–29 years=700, 30–39 years=650; 40–50 years=450. *p-values are illustrative placeholders and should be replaced with formal test results (Chi-square/Cochran-Armitage trend)

The age pattern seen in our data infectious and inflammatory smears frequent in younger women and high-grade lesions concentrated in those aged 40–50 years, aligns with Indian and regional evidence linking CIN2+, HSIL, and carcinoma to later reproductive years, high parity, early marriage, and social vulnerability [5,7,13,16]. Similar risk clustering has been reported in high-risk groups, such as female sex workers, where inflammatory smears and precancerous lesions coexist at high prevalence [18].

The infection profile in our cohort reinforces the pragmatic value of Pap cytology in resource-limited settings. Candida, trichomonas, and bacterial vaginosis contributed 10.8% of all smears, and the clinical-cytologic mapping of curdy white discharge to candidiasis, frothy greenish discharge to trichomonas, and leukorrhea with erosion to bacterial vaginosis is consistent with prior Indian work [7,10]. Studies comparing Pap-based diagnosis of bacterial vaginosis against Nugent scoring have shown moderate accuracy, suggesting that conventional cytology can support syndromic management where microbiology is unavailable [19]. In infertility cohorts, inflammatory Pap smears often track disturbed microbiota and poorer conception outcomes, echoing the reproductive-health implications of the inflammatory backgrounds we observed [12]. These converging data highlight that, in symptomatic reproductive-age women, Pap smears serve as an integrated screen for infection, inflammation, and epithelial atypia, not merely a cancer test [2,20].

At the same time, our findings caution against over-reassurance when vaginal discharge is the only presenting complaint. Although most women with discharge had inflammatory or infectious cytology, both LSIL and HSIL were detected within this symptomatic pool, and the small subset with contact bleeding and an unhealthy cervix showed strong concordance with malignant or high-grade cytology, mirroring community and hospital programs where "red-flag" symptoms yield a disproportionate share of serious lesions [8,13,16]. Evidence from large screening cohorts also shows that women with an unhealthy-appearing cervix or multiple abortions carry higher odds of squamous intraepithelial lesion (SIL) and HSIL, reinforcing the need for meticulous speculum examination and low thresholds for Pap testing in such presentations [15,16].

From a laboratory quality standpoint, the ASC/SIL ratio of 0.82 in our series is notably lower than typical benchmark ranges. In large tertiary-center audits, ASC/SIL ratios around 2–3 are common and fall within College of American Pathologists ranges, with higher ratios generally signaling overuse of the ASC-US category and lower ratios suggesting relative under-calling of equivocal atypia [17,21]. Our low ratio may reflect a specificity-oriented reporting style in which cytopathologists reserve ASC-US for more convincing atypia and classify borderline changes with inflammation as purely reactive. Comparable concerns arise in postmenopausal and atrophic settings, where ASC-US can be frequent yet less predictive of CIN2+, and misclassification can swing both toward over-calling and under-calling depending on context [22,23]. In an inflammation-rich, symptomatic cohort, such as ours, distinguishing subtle reactive changes from true ASC-US is particularly challenging. Without systematic histologic correlation across ASC-US, LSIL, and inflammatory categories, it remains uncertain whether the low ASC/SIL ratio reflects genuinely high specificity or a degree of reduced sensitivity for minor squamous abnormalities [14,17]. Future audits combining cytology with colposcopy, HPV testing, and biopsy similar to designs used in HPV-triage and TruScreen evaluation studies, are needed to refine local performance indicators [20].

Programmatically, our data support the view that gynecology OPDs in low- and middle-income settings function as de facto screening hubs. Indian and international surveys consistently show low lifetime Pap uptake, with many women only encountering cytology when they seek care for discharge, bleeding, or infertility [5,6,24]. Nurse-led counseling and targeted clinic-based education have been shown to improve knowledge, attitudes, and immediate willingness for screening, particularly among low-income and housekeeping staff, suggesting a clear lever for increasing coverage in exactly the types of women seen in our clinic [6]. Our findings therefore argue for embedding Pap testing, HPV counseling, and clear follow-up pathways into routine gynecology visits, alongside broader public education and primary-care gatekeeping as highlighted in both Indian and Gulf-region data [24].

While HPV DNA-based screening and dual-stain or genotyping algorithms now offer superior sensitivity and more efficient triage for CIN2+ in organized programs, cost and infrastructure still constrain universal adoption [23,25,26]. Trials and programmatic evaluations from Brazil and elsewhere show that primary HPV screening detects more CIN2+ at the expense of increased colposcopy referral, while maintaining acceptable positive predictive values [26]. Comparative work from India documents that liquid-based cytology improves smear adequacy, cellular distribution, and laboratory efficiency, and provides residual material for reflex HPV testing, even though gains in CIN2+ detection over conventional smears are modest and context dependent [25]. Device-based screening (e.g., TruScreen) and integrated HPV-cytology workflows further illustrate potential future directions for low-resource environments [20]. Against this backdrop, well-performed conventional Pap smears remain a pragmatic backbone in many Indian and regional settings, provided that quality metrics including ASC/SIL ratios, unsatisfactory rates, and cytology-histology concordance are regularly audited [10,11,21].

Our study has several limitations that warrant explicit emphasis. First, histologic correlation was not available for all cytologic categories. Only a subset of women with abnormal smears or "red flag" clinical features underwent colposcopy or biopsy, whereas multiple diagnostic-accuracy studies have used systematic verification to estimate sensitivity, specificity, and predictive values for CIN2+ [14,17]. The absence of full verification in our cohort prevents precise calculation of these metrics and raises the possibility of both underestimation and overestimation of lesion burden. Second, we used conventional Pap smears rather than liquid-based cytology. Comparative evidence from Indian centers indicates that conventional smears tend to have higher unsatisfactory rates and may exhibit slightly lower sensitivity for epithelial abnormalities, even though they can be more sensitive for organism detection [10,25]. This methodological choice is therefore a limitation not only for infection characterization but also for capturing

the full spectrum of SIL and glandular disease. Third, the single-center, symptomatic, reproductive-age focus restricts generalizability to asymptomatic women, postmenopausal populations, and other geographic settings; similar constraints have been noted in other hospital-based Indian and regional datasets [7,8]. Finally, we did not integrate HPV testing, vaccination status, anxiety measures, or long-term follow-up, all of which are increasingly recognized as central to modern cervical cancer prevention and survivorship frameworks.

CONCLUSION

The large, symptom-driven series shows that Pap smears in reproductive-age women are overwhelmingly inflammatory but still identify a clinically relevant burden of HSIL and malignancy, particularly among women in their forties with contact bleeding and an unhealthy cervix. The very low ASC/SIL ratio points toward a conservative, specificity-focused reporting culture, but, in the absence of systematic histologic correlation, also highlights the need to ensure that subtle atypia is not being overlooked. Taken together with Indian and international evidence on HPV prevalence, cytology performance, and screening behaviors, our findings support strengthening opportunistic Pap screening within gynecology OPDs while progressively layering in HPV-based strategies, nurse-led education, and robust laboratory quality monitoring to move toward more equitable and effective cervical cancer prevention in similar South Asian settings.

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AUTHOR CONTRIBUTION

Conceptualization; methodology; investigation; data curation; formal analysis; visualization; writing, original draft; writing, review and editing: Anil Mohan Rao S (sole author).

CONFLICT OF INTEREST

The author declares no conflict of interest.

ETHICAL APPROVAL

Approved by the Institutional Review Board, Faculty of Medicine, Arundhati Institute of Medical Sciences (Approval No.: ICE: 24/203/10 dated May 03, 2024). The study complied with the Declaration of Helsinki.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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Nil.

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