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Cervical cytology diagnostic screening findings in pap smears: Insights from a Saudi tertiary center

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Abstract

Cervical cancer is one of the most preventable malignancies, yet it remains a significant public health concern in countries with limited screening uptake, including Saudi Arabia. Cytology remains the primary screening method in such settings, identifying both neoplastic and non-neoplastic conditions. This retrospective cross-sectional audit evaluated Pap smears processed at a tertiary hospital, focusing on adequacy, prevalence of abnormal diagnoses, age distribution, and ancillary findings. A total of 551 smears were reviewed, of which 535 (97.1%) were satisfactory; the unsatisfactory rate was 3.9%, within the recommended <5% benchmark. Among satisfactory smears, most were negative for intraepithelial lesion or malignancy (NILM, 86.91%; 95% CI 83.6–89.6), while abnormal cytology constituted 9.16% (95% CI 7–11.9). High-grade squamous intraepithelial lesions, squamous cell carcinoma, or adenocarcinoma were identified in 0.75%, and invasive carcinoma in 0.2%. The ASC/SIL ratio was 2.5, consistent with international quality assurance standards. Non-neoplastic findings were frequent, including inflammatory/reactive changes (43.4%), atrophy (7.3%), and organisms such as *Candida spp.* (3.9%) and *Actinomyces spp.* (1.3%). Age data were available for 535 women, with no significant association between age and abnormal cytology ($\chi^2 = 6.12$, $p = 0.295$). Logistic regression showed higher odds of abnormal findings in women aged ≥65 years (OR 2.83, 95% CI 0.84–9.58), although this was not statistically significant ($p = 0.09$). These findings demonstrate a higher prevalence of abnormal cytology than recent Saudi reports but within regional variability. They underscore the value of Pap smears in cancer prevention and women's health, while supporting integration of HPV-based screening.

Keywords: Cervical cytology; Pap smear; Bethesda system; Cervical cancer screening; Non-neoplastic findings; Saudi Arabia; Human papillomavirus (HPV)

1. Introduction

Cervical cancer is one of the most preventable malignancies, yet it continues to represent a major global health burden [1], [2]. It is the fourth most common cancer among women, with an estimated 604,127 new cases and 341,831 deaths reported in 2020 [3]. In 2020, Saudi Arabia recorded 358 cervical cancer cases, with a crude incidence of 2.4 per 100,000 women and a mortality-to-incidence ratio of 0.5 [4]. By 2030, the global burden is projected to reach 700,000 new cases and 400,000 deaths without additional interventions [5]. Unlike the global decline, Saudi Arabia has witnessed a 453.6% rise in incidence since 1990, with an annual mortality of 179 [6]. This rising burden is driven by persistent infection with oncogenic types of human papillomavirus (HPV), the necessary cause of cervical carcinogenesis. Notably, the introduction of HPV vaccination and molecular screening has markedly reduced incidence in countries with organized prevention programs [7], [8], [9]. Building on this evidence, the World Health Organization

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(WHO) has launched its "90-70-90" strategy, aiming for 90% HPV vaccination coverage in girls, 70% screening coverage in women, and 90% access to treatment for precancerous lesions and invasive cancer, with the ultimate goal of eliminating cervical cancer as a public health problem [10], [11].

Despite these advances, wide disparities persist between countries. In regions where HPV vaccination uptake is low and HPV testing is not widely accessible, conventional cytology remains the primary tool for cervical cancer prevention [12], [13]. The Papanicolaou (Pap) smear, classified under the Bethesda System, continues to be one of the most widely applied, cost-effective screening modalities [14], [15]. Beyond identifying precursor lesions and malignancy, cytology also reports non-neoplastic findings such as reactive and inflammatory changes, atrophy, and the presence of organisms [16], [17]. These observations, although not malignant, provide important insight into gynecological and reproductive health and can guide clinical management.

In Saudi Arabia, cervical cancer is relatively rare compared with global averages, accounting for less than 2% of female cancers according to national registry data [18]. Nevertheless, its clinical impact is significant, as cases are often diagnosed at advanced stages, reflecting low awareness, potential sociocultural barriers to preventive gynecologic care, and the absence of a national screening program. Although the HPV vaccine is licensed and available in the national immunization schedule, its uptake remains very low, due to lack of awareness of HPV infection [19]. Thus, cytology remains the most feasible and widely implemented screening method in routine practice. Cost-effectiveness studies from the region have suggested that HPV-based testing and vaccination would ultimately provide substantial benefits [20], but these strategies are still in the early phases of integration.

Several cytology-based audits have been conducted across Saudi Arabia, reporting variable abnormal cytology rates ranging from 3% to 14%, with atypical squamous cells (ASC) being the most frequent abnormal category. A recent audit from Jeddah documented an abnormal prevalence of 3.05% and highlighted the ASC/SIL ratio as a key quality assurance metric [21]. The ASC/SIL ratio is widely recognized as a laboratory performance indicator, with international guidelines recommending a ratio of less than 3:1 to ensure that ASC diagnoses are not overused. Recent national data highlight that a substantial proportion of cancers present in stages III–IV [22], [23] emphasizing the need to strengthen prevention and early detection pathways. PubMed Central Screening uptake itself remains low: a 2024 national study reported low awareness and low Pap testing, particularly among younger women [24], while a 2024 meta-analysis across Arab countries estimated overall screening uptake at ~18%, pointing to shared barriers across the region [25]. While valuable, many of these studies were limited in scope and largely focused on abnormal or neoplastic outcomes.

From a regional perspective, cervical cancer incidence in Saudi Arabia remains low, however, an organized screening is uncommon, opportunistic Pap smears predominate, and HPV epidemiology remains incompletely characterized [26], [27]. In such contexts, audits of cytology practice not only provide prevalence estimates but also serve as quality assurance tools that can inform local policy and contribute to international datasets.

A further limitation of prior reports is the underrepresentation of non-neoplastic findings. Inflammation, atrophy, and the presence of organisms such as *Candida*, *Trichomonas*, and *Actinomyces* are frequently observed in Pap smears and carry direct clinical relevance [28], [29], [30]. Their documentation provides a more holistic picture of women's health and highlights the broader utility of cytology beyond cancer prevention. Yet, few published audits in Saudi Arabia have systematically quantified these findings.

Against this backdrop, the present study was designed to comprehensively evaluate the spectrum of cervical cytology in Pap smears at a Saudi tertiary center. Specifically, the study aimed to determine the prevalence of abnormal cytology, assess specimen adequacy, examine age-related patterns, and document the distribution of non-neoplastic findings. By integrating both neoplastic and non-neoplastic categories, this analysis contributes to the limited regional literature, strengthens local evidence for cervical cancer prevention, and supports ongoing quality assurance in cytology practice.

2. Methods

This retrospective cross-sectional audit was conducted in the King Faisal Medical Complex, a tertiary care center in Taif, Saudi Arabia. All cervical cytology smears (Pap smears) received during the study period January 2024 to December 2024 were included. Scientific Research Ethics Committee at King Faisal Medical Complex in Taif on 05/02/2025 (Approval no: 2025-E-12), and informed consent was waived because anonymized records were used.

A total of 551 liquid based cervical cytology Pap smears were retrieved from the electronic medical record and laboratory information system. Data were drawn from three complementary sources: a smear-level dataset containing age and diagnostic details, a supplementary file with Bethesda categories for a subset of cases, and a laboratory-

generated summary table consolidating Bethesda categories and non-neoplastic findings. The raw dataset was used for patient-level analyses, whereas the summary dataset provided the final prevalence values.

Age was available for 535 women and analyzed both as a continuous variable and in categories (≤24, 25–34, 35–44, 45–54, 55–64, ≥65 years).

Statistical analysis was performed using SPSS/Python. Frequencies and percentages were calculated, with 95% confidence intervals (CIs) estimated by the Wilson method. Associations between age and abnormal cytology were assessed using chi-square tests, and odds ratios with 95% CIs were calculated with 25–34 years as the reference group. The unsatisfactory rate was compared with the benchmark of <5%, and the ASC/SIL ratio was calculated as a laboratory quality indicator, with ratios between 2:1 and 3:1 considered acceptable.

3. Results

3.1. Adequacy of smears

A total of 551 Pap smears were examined during the study period. Of these, 535 (97.1%) were satisfactory for evaluation, while 21 (3.93%) were reported as unsatisfactory according to Bethesda 2014 criteria. The unsatisfactory rate was within the internationally recommended benchmark of less than 5%, reflecting good sample quality and laboratory performance [31], [32].

3.2. Total Distribution of Cervical Pap smear for diagnostic screening

Among the 535 satisfactory smears, the majority were negative for intraepithelial lesion or malignancy (NILM, 465 cases; 86.9%, 95% CI 83.6–89.6). Abnormal cytology was reported in 21 cases (3.9%, 95% CI 2.5–5.8). Within abnormal categories, atypical squamous cells of undetermined significance (ASC-US) accounted for 33 cases (6.2%, 95% CI 4.4–8.7), atypical squamous cells—cannot exclude HSIL (ASC-H) for 2 cases (0.37%, 95% CI 0.1–1.4), low-grade squamous intraepithelial lesion (LSIL) for 6 cases (1.1%, 95% CI 0.5–2.4), high-grade squamous intraepithelial lesion (HSIL) for 1 case (0.19%, 95% CI 0.03–1.1), and atypical glandular cells (AGC) for 6 cases (1.1%, 95% CI 0.5–2.4). A single case of invasive carcinoma was reported (0.19%, 95% CI 0.03–1.1). The prevalence of high-grade lesions (HSIL, AGC, carcinoma) was 0.75%, while invasive carcinoma alone accounted for 0.19%. The ASC/SIL ratio was 2.5, falling within the internationally accepted quality assurance benchmark (2–3:1). The detailed distribution is shown in **Table 1**, and the overall proportions are illustrated in **Figure 1.**

Table 1 Distribution of Pap smear results including unsatisfactory

Category	Number (n)	Percentage (%)
NILM	465	86.91
ASC-US	33	6.20
ASC-H	2	0.37
LSIL	6	1.12
HSIL	1	0.19
AGC	6	1.12
Invasive carcinoma	1	0.18
Total abnormal (ASC-US+)	49	9.16
Unsatisfactory	21	3.9
Total	551	100

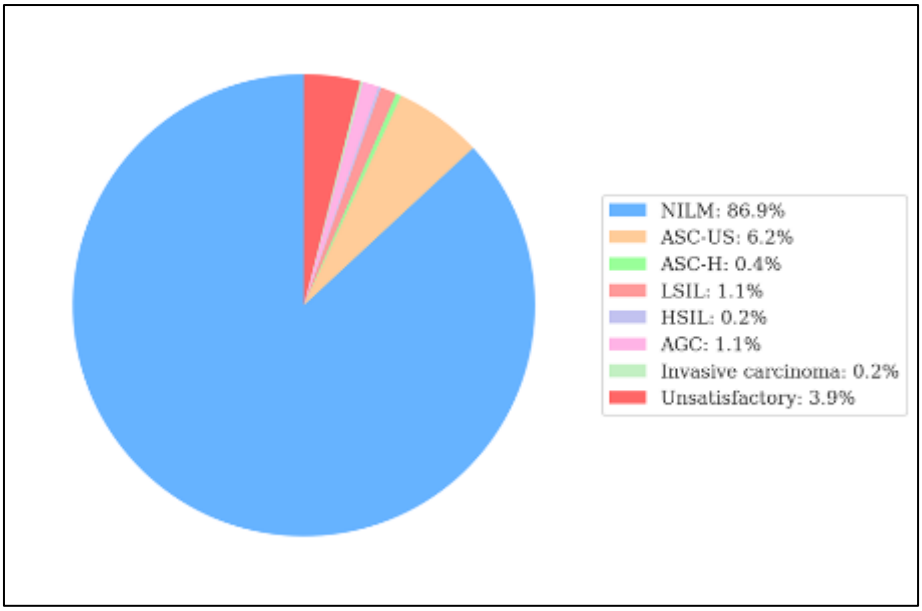

Figure 1 Total Distribution of cervical cytology diagnostic screening

Pie chart showing NILM (86.9%), abnormal categories (9.16% distributed as ASC-US, ASC-H, LSIL, HSIL, AGC, invasive carcinoma), and unsatisfactory smears (3.9%).

3.3. Non-neoplastic findings and organisms

Non-neoplastic cellular variations and reactive changes were frequently encountered in Pap smear interpretations. Overall, 259 of 535 satisfactory smears (48.4%) demonstrated some form of non-neoplastic change. The most common was inflammatory/reactive cellular changes, seen in 232 cases (43.4%), followed by atrophic changes in 39 cases (7.3%).

Among organisms identified, Candida spp. were detected in 21 cases (3.9%), while Actinomyces spp. were reported in 7 cases (1.3%). Trichomonas vaginalis was not identified in this cohort. These findings underscore the added diagnostic value of cervical cytology in detecting infections and hormonal changes in addition to screening for precancerous lesions. The distribution is shown in Table 2 and illustrated in Figure 2.

Table 2 Non-neoplastic findings and organisms detected in Pap smears

Category	
Non-neoplastic findings	**Organisms**
Inflammatory/reactive changes 43.4 % (*n*= 232)	Candida spp. 3.9% (*n*=21)
Atrophic changes 7.3% (*n*=39)	Actinomyces spp. 1.3% (*n*=7)

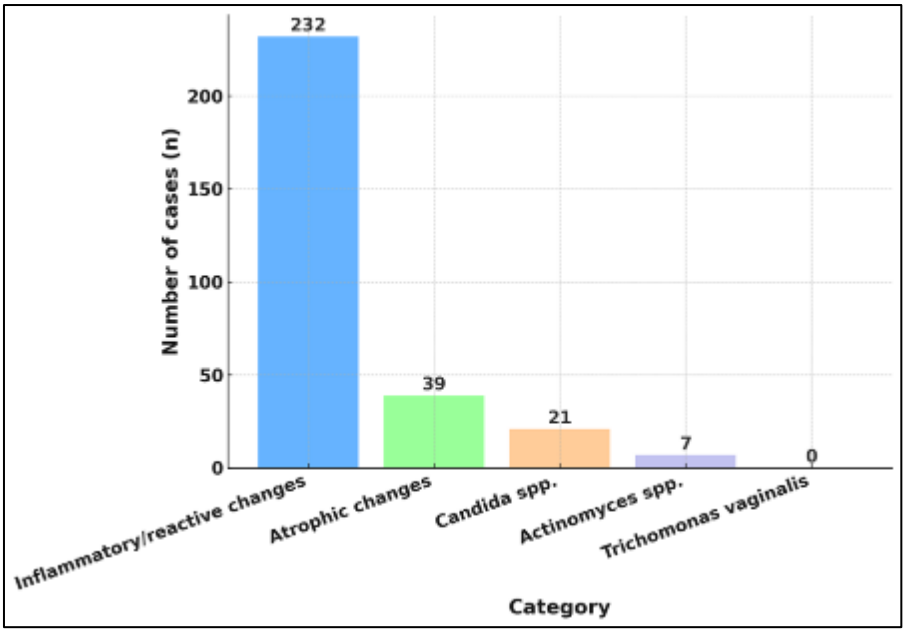

Figure 2 Non-neoplastic findings and organisms in Pap smears

A bar chart showing inflammatory/reactive changes, atrophy, and organisms (Candida, Actinomyces,).

3.4. Abnormal cytology prevalence and quality indicators

Abnormal cytology (ASC-US and above) was identified in 49 of 551 smears, corresponding to a prevalence of 9.16% (95% CI 7–11.9). Low-grade abnormalities (ASC-US, ASC-H, and LSIL) accounted for 41 cases (7.7%), while high-grade abnormalities (HSIL, AGC, and carcinoma) comprised 7 cases (1.3%). Invasive carcinoma was diagnosed in one case (0.2%). The ratio of atypical squamous cells (ASC-US + ASC-H) to squamous intraepithelial lesions (LSIL + HSIL) was 2.5, which falls within the internationally accepted quality assurance benchmark of 2–3:1. These findings are summarized in **Table 3** and illustrated in **Figure 3**.

Table 3 Abnormal cytology prevalence and quality indicators

Category	Number (n)	Percentage (%)	95% CI
Low-grade (ASC-US + ASC-H + LSIL)	41	7.7	5.7–10.2
High-grade (HSIL + AGC + carcinoma)	7	1.3	0.6–2.7
Invasive carcinoma	1	0.2	0.0–1.1
Total abnormal	49	9.16	7.0-11.9
ASC/SIL ratio	–	2.5	Benchmark: 2–3

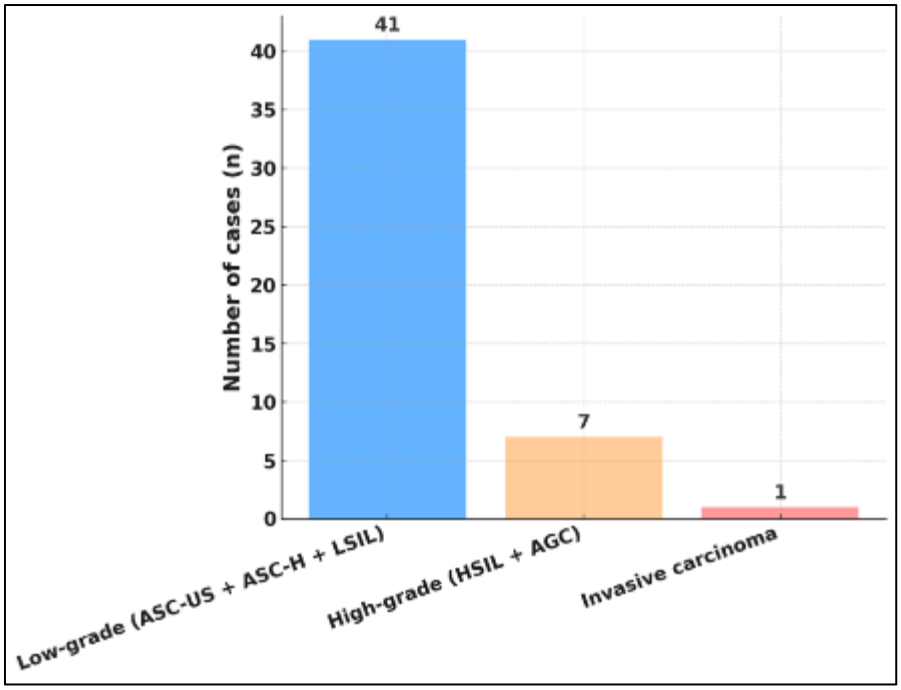

Figure 3 Distribution of abnormal cytology (low-grade, high-grade, invasive carcinoma)

Bar chart showing mutually exclusive categories: low-grade (41 cases), high-grade excluding carcinoma (7 cases), and invasive carcinoma (1 case). The total equals 58 abnormal smears.

3.5. Age distribution and association with abnormal cytology

Age was available for all 535 satisfactory smears. The mean age of women screened was 39.8 ± 10.7 years, and the largest group of participants were between 20 and 44 years. No abnormalities were detected among women younger than 25 years (0.0%, 95% CI: 0.0–43.4). In the 25–34 years group, 7 of 74 cases were abnormal, corresponding to a prevalence of 9.5% (95% CI: 4.7–18.3). A slightly higher prevalence was observed in the 35–44 years group, where 17 of 159 women (10.7%, 95% CI: 6.8–16.5) exhibited abnormalities. Interestingly, the prevalence declined in the 45–54 years group to 7.6% (15/198; 95% CI: 4.6–12.1), before showing a marginal increase in the 55–64 years group at 8.9% (5/56; 95% CI: 3.9–19.3). The highest prevalence was recorded among women aged ≥65 years, with 22.7% (5/22; 95% CI: 10.1–43.4) of cases being abnormal. Overall, out of 514 women examined, 49 presented with abnormalities, yielding a total prevalence of 9.5% (95% CI: 7.3–12.4). While the highest proportion of abnormalities was observed among women aged ≥65 years, chi-square analysis did not demonstrate a statistically significant association between age group and abnormal cytology ($\chi^2 = 6.12$, $p = 0.295$). Logistic regression analysis likewise indicated increased odds of abnormal cytology among women ≥65 years compared to those aged 25–34 years (OR 2.83, 95% CI 0.84–9.58), but this did not reach statistical significance ($p = 0.09$). These findings are summarized in Table 4 and illustrated in Figure 4.

Table 3 Age distribution of women with normal vs abnormal cytology

Age group (years)	Total cases (n)	Abnormal cases (n)	Abnormal (%)	95% CI (Wilson)
<25	5	0	0.0	0.0–43.4
25–34	74	7	9.5	4.7–18.3
35–44	159	17	10.7	6.8–16.5
45–54	198	15	7.6	4.6–12.1
55–64	56	5	8.9	3.9–19.3
≥65	22	5	22.7	10.1–43.4
Total	514	49	9.5	7.3–12.4

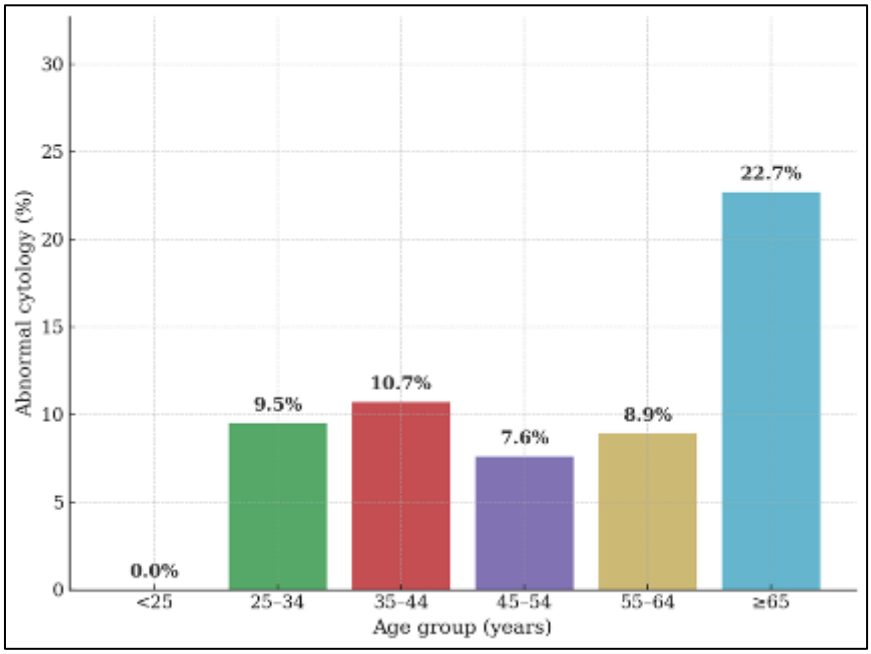

Figure 4 Age-specific prevalence of abnormal cytology

A bar chart showing proportions of abnormal smears across age groups, with the highest prevalence in women aged ≥65 years.

4. Discussion

This study provides one of the most recent cytology audits from a tertiary center in Taif city of Saudi Arabia, contributing valuable prevalence data and quality assurance indicators. By assessing specimen adequacy, distribution of different findings of cervical cytology for diagnostic screening, age-specific prevalence, and non-neoplastic findings, our analysis offers insights into both the performance of cytology as a screening tool and the broader implications for national screening programs.

Our unsatisfactory rate of 3.9% lies below the ≤5% benchmark recommended by the Bethesda System, underscoring strong specimen adequacy and technical quality. Similarly, the ASC/SIL ratio of 2.5 is within the internationally accepted range (2–3:1), reflecting interpretive consistency and avoiding over-calling atypical squamous cells [33], [34]. These quality metrics reinforce the robustness of cytology in our setting and strengthen confidence in the reliability of prevalence estimates.

The overall prevalence of epithelial cell abnormalities (9.16%) in our cohort is higher than that reported in many Saudi series, where abnormal rates have ranged from ~2.9–5% with ASC/SIL ratios close to international benchmarks. For example, a large retrospective review at Prince Sultan Military Medical City (Riyadh) from 2012–2021 reported 2.97% abnormal cytology with an ASC/SIL of 1.72, while a Western-region audit reported similar low rates with ASC/SIL ~2.6 [35], [36]. The higher prevalence in our study likely reflects referral bias at a tertiary center but may also signal a true higher burden in under-screened populations. Indeed, national estimates suggest Pap smear uptake remains below 20%, and more than 40% of cervical cancers in Saudi Arabia are still diagnosed at advanced stages [37].

Inflammatory/reactive changes were frequent in our cohort, and their prominence in peri- and postmenopausal ages likely reflects a mix of atrophy-related cytologic change and microbiome-driven inflammation. Contemporary work shows that the vaginal microbiome and inflammatory milieu are tightly linked to HPV acquisition/persistence, with dysbiosis and elevated cytokines associated with impaired viral clearance—mechanisms that help explain the high burden of inflammatory cytology in real-world screening programs [38], [39], [40]. While an "inflammatory smear" is not itself a cancer diagnosis, it highlights infections and hormonal atrophy that warrant clinical attention and, in HPV-limited settings, underscores cytology's added value beyond neoplasia detection.

Age-specific analysis revealed the highest abnormal cytology rate in women aged ≥65 years (22.7%). Although the association between age and abnormal findings did not reach statistical significance, this trend echoes reports from India and Iran where older age groups still contribute meaningfully to the burden of abnormalities [41], [42]. These findings suggest caution against prematurely discontinuing screening at age 65 in under-screened populations, particularly where HPV testing is not universal.

Non-neoplastic findings were also frequent, with nearly half of satisfactory smears showing inflammatory or reactive changes and Candida (3.9%) and Actinomyces (1.3%) as the most common organisms. These observations align with regional studies [43], [44] and emphasize the ancillary diagnostic value of cytology: beyond detecting intraepithelial lesions, it can reveal infections, atrophy, and hormonal influences features that HPV testing alone cannot provide.

An important observation in our cohort was the detection of glandular abnormalities, including atypical glandular cells (AGC, 1.1%) and a single case of adenocarcinoma (0.19%). Although less frequent than squamous lesions, these findings are clinically significant, as glandular lesions are more challenging to diagnose cytologically and often associated with higher-grade disease or endometrial pathology. The detection of such cases reinforces the diagnostic utility of liquid-based cytology in capturing the full spectrum of cervical and endocervical abnormalities.

Taken together, our findings highlight two complementary messages. Cytology in our setting demonstrates strong quality indicators and yields a higher-than-expected abnormal rate, indicating its continued relevance as a frontline tool. Beyond diagnostic yield, these findings also highlight the urgent need for public health interventions in Taif and similar regions. Increasing community awareness, education, and access to screening services remains essential for improving early detection and reducing the burden of cervical cancer.

5. Conclusion

This retrospective cytological review provides updated insight into cervical cancer screening in a tertiary care center in Saudi Arabia. Although the association between age and abnormal cytology did not reach statistical significance, the higher proportion of abnormalities in women aged ≥65 years underscores the importance of maintaining surveillance in older age groups, particularly in settings with low HPV vaccination and screening coverage. The frequent identification of non-neoplastic findings and organisms highlights cytology's ancillary diagnostic value beyond detecting intraepithelial lesions. The study is limited by its retrospective single-center design, absence of HPV DNA testing, and lack of histological confirmation for all abnormal cases. Overall, cytology, particularly in the form of liquid-based cytology, continues to serve as a reliable and informative screening tool in Saudi Arabia, not only for detecting precancerous squamous lesions but also for identifying glandular abnormalities such as AGC and adenocarcinoma, along with infections and hormonal changes.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of informed consent

Informed consent was waived because anonymized records were used.

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