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Original Research Article

# Diagnostic Yield of Colposcopy in Women with ASC-US on Liquid-Based Cytology

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**Abstract:**

**Background:** Atypical squamous cells of undetermined significance (ASC-US) represent a common abnormal cervical cytological finding and encompass a heterogeneous spectrum ranging from benign reactive changes to clinically significant cervical intraepithelial neoplasia. Colposcopy with directed cervical biopsy provides histopathological confirmation in women requiring further evaluation of abnormal cervical cytology.

**Aim:** To evaluate the diagnostic yield of colposcopy-guided cervical biopsy in women with ASC-US detected on liquid-based cytology (LBC).

**Methods:** A cross-sectional analytical study was conducted in the Department of Obstetrics and Gynaecology, Maulana Azad Medical College and Lok Nayak Hospital, New Delhi, from September 2022 to February 2024. A total of 271 women aged 21–65 years underwent cervical cancer screening. Among them, 16 women with ASC-US on LBC constituted the study population for the present analysis. Colposcopy was performed following application of 5% acetic acid and Lugol's iodine, and suspicious lesions were subjected to directed cervical biopsy. Histopathological examination was considered the reference standard. The histopathological yield was assessed for CIN1+ and CIN2+ lesions.

**Results:** ASC-US was identified in 16 of 271 women (5.9%). Histopathological examination demonstrated normal cervical histology in 7 women (43.8%), chronic cervicitis in 1 (6.3%), CIN1 in 4 (25.0%), and CIN2 in 4 (25.0%). Thus, CIN1+ was identified in 8 of 16 women (50.0%), while CIN2+ was identified in 4 of 16 women (25.0%). No case of CIN3 or invasive cervical carcinoma was identified among women with ASC-US.

**Conclusion:** Colposcopy-guided biopsy demonstrated a substantial diagnostic yield among women with ASC-US on liquid-based cytology. Half of the women had CIN1+ and one-fourth had CIN2+, highlighting the heterogeneous nature of ASC-US and the importance of appropriate risk-based evaluation and histopathological confirmation.

**Keywords:** ASC-US; Liquid-Based Cytology; Colposcopy; Cervical Biopsy; Cervical Intraepithelial Neoplasia; CIN1; CIN2; Cervical Cancer Screening.

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## Introduction

Cervical cancer remains an important preventable malignancy worldwide. Persistent infection with oncogenic human papillomavirus (HPV) is the principal etiological factor in cervical carcinogenesis, and progression from HPV infection to invasive cancer generally occurs through recognizable precancerous epithelial abnormalities. This prolonged precancerous phase provides an important opportunity for screening, early detection, and treatment before invasive disease develops. [1]

Cervical cytology has traditionally played an important role in cervical cancer screening. Liquid-based cytology (LBC) was developed to improve specimen preparation by providing a more uniform cellular preparation and reducing obscuring material. It has become an established method for cervical cytological evaluation in many screening settings. [2]

The Bethesda System provides standardized terminology for reporting cervical cytological abnormalities. [3] Among epithelial abnormalities, atypical squamous cells of undetermined significance (ASC-US) represent a heterogeneous category. ASC-US is used when squamous cells demonstrate abnormalities greater than those attributable to benign reactive changes but

insufficient to classify the lesion definitively as a squamous intraepithelial lesion. [3]

The clinical significance of ASC-US lies in the variability of its underlying histopathology. Although many women with ASC-US have benign or inflammatory findings, a proportion may harbor cervical intraepithelial neoplasia, including clinically significant high-grade disease. Therefore, cytology alone may not adequately identify the underlying histological status in every woman with ASC-US.

High-risk HPV testing provides an important method of risk stratification in women with equivocal cytological abnormalities. Evidence from systematic reviews has demonstrated that HPV-based approaches have greater sensitivity for detection of clinically significant cervical precancer than cytology alone. [4]

Colposcopy is an important diagnostic procedure for women requiring further evaluation following abnormal cervical screening. It permits magnified examination of the cervix following application of acetic acid and Lugol's iodine and enables identification of suspicious epithelial abnormalities for directed biopsy. [5-7] The ASCCP Colposcopy Standards emphasize systematic examination, appropriate documentation, and adequate biopsy practice to improve detection of cervical precancers. [5-7]

The management of abnormal cervical screening results has increasingly shifted toward risk-based approaches. Current guidelines incorporate current cytology, HPV status, and previous screening history to estimate the risk of CIN3+ and determine appropriate clinical management. [8] This approach is particularly relevant for ASC-US, where the underlying risk of significant disease varies according to HPV status and previous screening history.

Histopathological examination of a colposcopy-guided biopsy remains an important method for establishing the definitive diagnosis of cervical intraepithelial neoplasia. Identification of CIN2 or higher is clinically important because these lesions represent significant cervical precancer requiring individualized management according to patient characteristics and risk. [8]

In the present study population, 271 women underwent cervical cancer screening, of whom 16 (5.9%) had ASC-US on liquid-based cytology. The histopathological findings among these women demonstrated a spectrum ranging from normal histology and chronic cervicitis to CIN1 and CIN2. The present study therefore evaluated the diagnostic yield of colposcopy-guided biopsy specifically among women with ASC-US on LBC.

**Aim:** To evaluate the diagnostic yield of colposcopy-guided cervical biopsy in women with ASC-US on liquid-based cytology.

**Objectives**

1. To determine the proportion of women with ASC-US on LBC who have histologically confirmed cervical intraepithelial neoplasia.
2. To determine the diagnostic yield of colposcopy-guided biopsy for CIN1+ lesions.
3. To determine the diagnostic yield of colposcopy-guided biopsy for CIN2+ lesions.
4. To describe the histopathological spectrum among women with ASC-US on LBC.

**Materials and Methods**

**Study Design and Setting:** This was a cross-sectional analytical study conducted in the Department of Obstetrics and Gynaecology, Maulana Azad Medical College and Lok Nayak Hospital, New Delhi.

The study was conducted from September 2022 to February 2024. A total of 271 women attending the Gynaecology Out-Patient Department were included in the study.

**Study Population:** Women aged 21–65 years attending the Gynaecology Out-Patient Department were eligible for participation.

For the present analysis, women with ASC-US on liquid-based cytology were evaluated.

Among the 271 women screened, 16 (5.9%) had ASC-US on LBC.

**Inclusion Criteria:** Women aged 21–65 years attending the Gynaecology Out-Patient Department during the study period were included.

**Exclusion Criteria**

Women with:

- Previously diagnosed carcinoma cervix;
- Previously diagnosed cervical intraepithelial neoplasia;
- Previous treatment for cervical cancer; or
- Previous total hysterectomy

were excluded.

**Sample Size:** The study included 271 women overall. Of these, 16 women had ASC-US on LBC and constituted the population analyzed in the present study.

Thus, the final study population for the present analysis was 16 women.

**Liquid-Based Cytology:** Cervical specimens were collected for liquid-based cytological examination and categorized according to standard cytological terminology.

Among the 271 women, 233 (86.0%) had NILM, 16 (5.9%) had ASC-US, 3 (1.1%) had LSIL, 2 (0.7%) had HSIL, and 2 (0.7%) had carcinoma cervix. No unsatisfactory LBC specimens were reported.

**Colposcopic Examination:** All women who were screen-positive by any of the screening modalities underwent colposcopy-guided cervical biopsy. Colposcopy was performed after clearing cervical mucus, followed by application of freshly prepared 5% acetic acid. The entire cervix was examined under magnification after one minute. Examination was subsequently repeated following application of Lugol's iodine.

Colposcopic findings were recorded using the Swede score. Any suspicious lesion identified during colposcopy was biopsied and submitted for histopathological examination.

**Histopathological Examination:** Cervical biopsy specimens were evaluated histopathologically.

Histopathological findings were categorized as:

- No atypia/no malignant cells
- Chronic cervicitis
- CIN1
- CIN2
- CIN3
- Squamous cell carcinoma of the cervix

Histopathological examination was considered the reference standard for determining the presence and grade of cervical intraepithelial neoplasia.

**Definition of Histopathological Outcomes**

**CIN1+** was defined as CIN1, CIN2, CIN3, or invasive carcinoma.

**CIN2+** was defined as CIN2, CIN3, or invasive carcinoma.

**Outcome Measures**

**Primary Outcome:** The primary outcome was the histopathological diagnostic yield of colposcopy-guided biopsy among women with ASC-US on LBC.

Secondary Outcomes

Secondary outcomes included:

- Proportion of women with CIN1+;
- Proportion of women with CIN2+; and
- Distribution of histopathological diagnoses.

**Statistical Analysis:** Categorical variables were expressed as frequencies and percentages.

Diagnostic yield was calculated as the proportion of women with the specified histopathological outcome among the 16 women with ASC-US.

Because of the small number of ASC-US cases, analysis was primarily descriptive.

**Results**

**Study Population:** A total of 271 women underwent cervical cancer screening. ASC-US was identified on liquid-based cytology (LBC) in 16 women (5.9%).

**Histopathological Findings:** Among the 16 women with ASC-US, histopathological examination following colposcopy-guided biopsy showed normal histology in 7 women (43.8%), chronic cervicitis in 1 woman (6.3%), CIN1 in 4 women (25.0%), and CIN2 in 4 women (25.0%). No CIN3 or invasive carcinoma was identified among women with ASC-US. The complete histopathological distribution is presented in Table 1 and illustrated graphically in Figure 1.

**Table 1: Histopathological Findings Among Women with ASC-US on LBC**

| Histopathological diagnosis | Number (n=16) | Percentage |
|---|---|---|
| Normal/no atypia | 7 | 43.8 |
| Chronic cervicitis | 1 | 6.3 |
| CIN1 | 4 | 25.0 |
| CIN2 | 4 | 25.0 |
| CIN3 | 0 | 0.0 |
| Invasive carcinoma | 0 | 0.0 |
| **Total** | **16** | **100.0** |

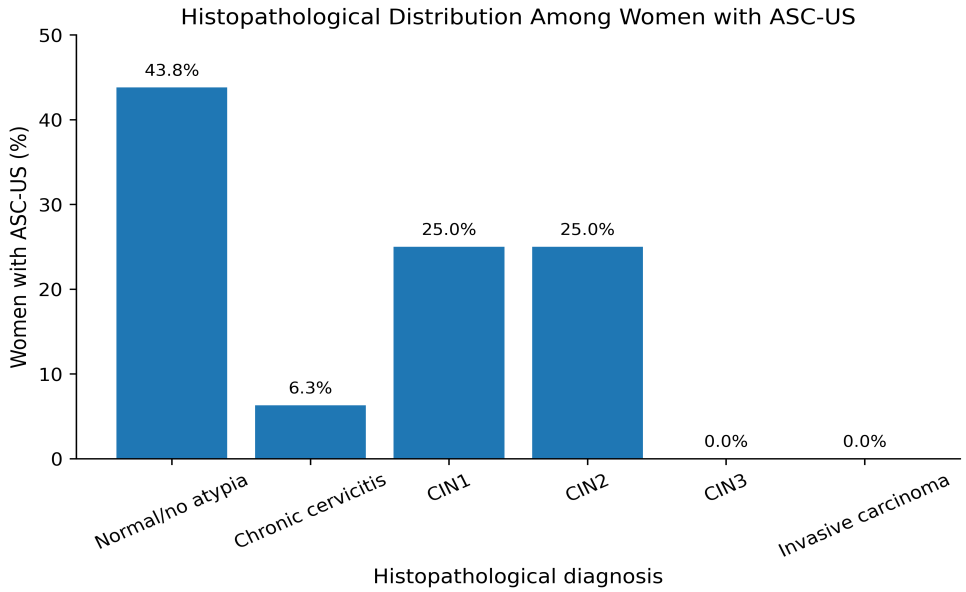



**Figure 1: Histopathological distribution among women with ASC-US on liquid-based cytology.**

Figure 1 illustrates the percentage distribution of histopathological findings among the 16 women with ASC-US, demonstrating that normal/no atypia was the most frequent finding (43.8%), followed by CIN1 (25.0%) and CIN2 (25.0%).

**Diagnostic Yield of Colposcopy-Guided Biopsy:** CIN1+ was identified in 8 of 16 women, consisting of 4 cases of CIN1 and 4 cases of CIN2. Therefore, the diagnostic yield of colposcopy-guided biopsy for CIN1+ was 50.0%.

CIN2+ was identified in 4 of 16 women, corresponding to a diagnostic yield of 25.0%. No CIN3+ lesion or invasive carcinoma was identified. The diagnostic yields according to histopathological endpoint are summarized in Table 2 and graphically presented in Figure 2.

**Table 2: Diagnostic Yield of Colposcopy-Guided Biopsy**

| Histopathological endpoint | Number | Diagnostic yield |
|---|---|---|
| CIN1+ | 8/16 | **50.0%** |
| CIN2+ | 4/16 | **25.0%** |
| CIN3+ | 0/16 | **0.0%** |
| Invasive carcinoma | 0/16 | **0.0%** |

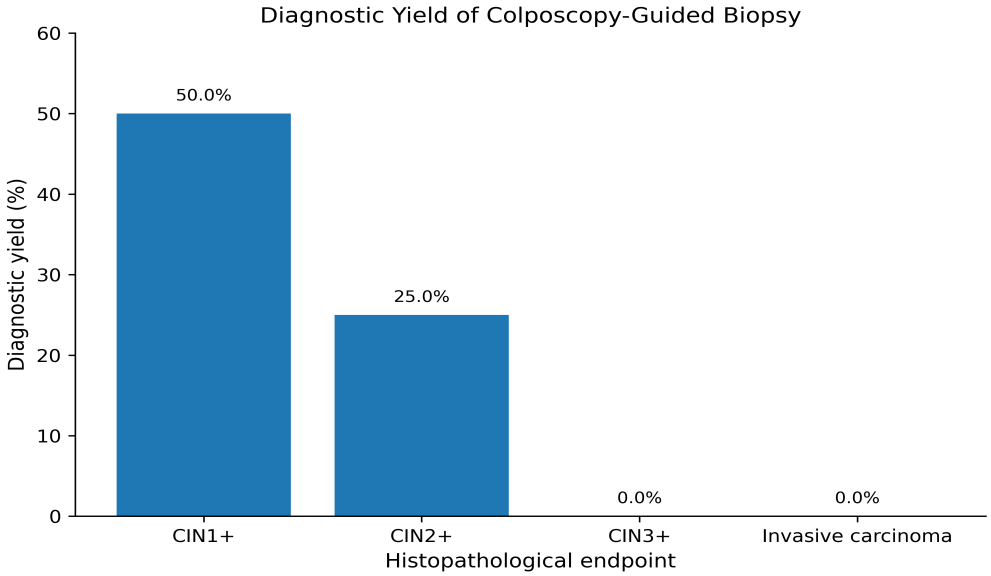



**Figure 2: Diagnostic yield of colposcopy-guided biopsy according to histopathological endpoint.**

Figure 2 demonstrates a diagnostic yield of 50.0% for CIN1+ and 25.0% for CIN2+, with no CIN3+ or invasive carcinoma identified among women with ASC-US.

**High-Grade Lesions:** Among the seven CIN2 lesions identified in the overall screened cohort, four occurred in women with ASC-US on LBC, while the remaining three occurred among women with other cytological categories. The distribution of CIN2 lesions according to cytological category is shown in Figure 3.

Thus, 57.1% (4/7) of all CIN2 lesions identified in the overall cohort occurred among women with ASC-US, whereas 42.9% (3/7) occurred among women with other cytological categories. This finding demonstrates that clinically significant cervical precancer may be present despite an ASC-US cytological interpretation.

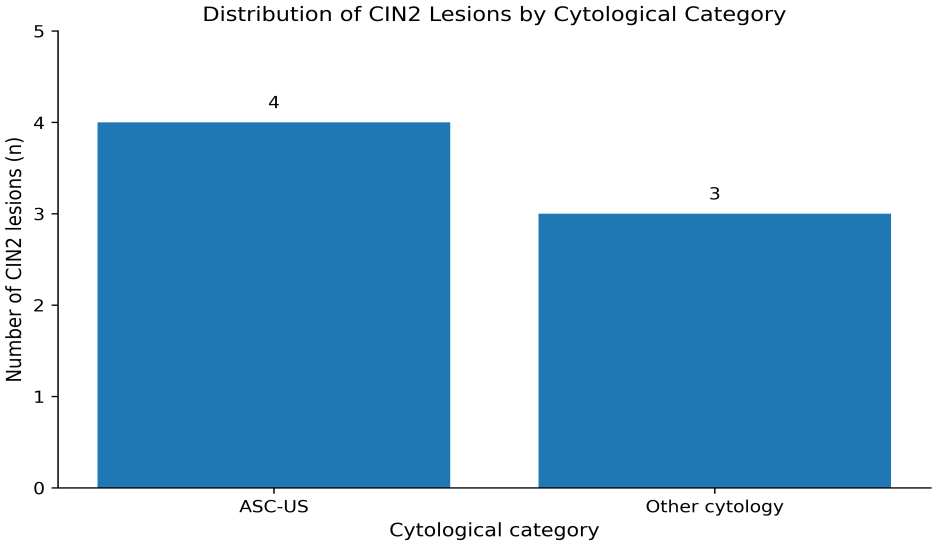



**Figure 3: Distribution of CIN2 lesions according to cytological category.**

Figure 3 shows that four of the seven CIN2 lesions occurred among women with ASC-US, while three occurred among women with other cytological categories.

**Discussion**

The present study evaluated the diagnostic yield of colposcopy-guided biopsy among women with ASC-US on liquid-based cytology. Among the 16 women with ASC-US, 50.0% had CIN1+ and 25.0% had CIN2+. These findings demonstrate the heterogeneous nature of ASC-US and indicate that clinically significant cervical precancer may be present even when cytological abnormalities are classified as indeterminate.

ASC-US is intentionally defined as a cytological category in which abnormalities are greater than those attributable to benign reactive changes but insufficient for definitive classification as a squamous intraepithelial lesion. [3] Therefore, the histological spectrum associated with ASC-US is expected to include both benign and neoplastic conditions.

The present study demonstrated that 7 of 16 women (43.8%) had normal histology, while 1 woman (6.3%) had chronic cervicitis. Thus, nearly half of the women did not have cervical intraepithelial neoplasia. Conversely, 8 women (50.0%) had CIN1 or higher, emphasizing that ASC-US cannot be assumed to represent benign disease.

The most clinically relevant finding was the presence of CIN2 in 4 of 16 women (25.0%). The source data also demonstrate that four of the seven CIN2 lesions in the overall cohort occurred in women with ASC-US. CIN2 represents a clinically significant cervical precancer and requires individualized management based on age, reproductive considerations, HPV status, screening history, and estimated future risk. [8]

The heterogeneous histopathological spectrum observed in the present study is consistent with the established role of HPV testing in risk stratification of women with equivocal cytology. HPV-based strategies generally provide greater sensitivity for detecting CIN2+ than cytology alone. [4] Current risk-based management approaches therefore integrate HPV results with cytology and previous screening history rather than relying on cytological category alone. [8]

Colposcopy provides a means of direct visualization of cervical epithelial abnormalities and allows targeted tissue sampling. The procedure in the present study involved application of 5% acetic acid followed by Lugol's iodine, examination under magnification, documentation using the Swede

score, and biopsy of suspicious lesions. These components are consistent with established principles of standardized colposcopic practice. [5-7]

ASCCP Colposcopy Standards emphasize systematic examination, documentation, and appropriate biopsy protocols to improve detection of prevalent cervical precancers. [5] The risk associated with referral to colposcopy varies considerably according to the preceding screening result, HPV status, and other clinical information. [6] Consequently, colposcopy should be integrated within an appropriate risk-based diagnostic pathway rather than being considered an isolated test.

The 50.0% CIN1+ diagnostic yield observed in this study is noteworthy. However, this value should not be interpreted as the prevalence of CIN1+ among all women with ASC-US in the general population. The study population consisted of women attending a tertiary-care setting, and the ASC-US subgroup contained only 16 participants. Referral patterns and underlying disease prevalence may therefore influence the observed diagnostic yield.

The 25.0% CIN2+ yield is particularly important from a clinical perspective. Although ASC-US represents an equivocal cytological category, one-fourth of the women in this cohort had CIN2. This finding illustrates the limitations of relying on cytology alone for exclusion of significant cervical disease.

At the same time, the finding that 43.8% of women had normal histology demonstrates the potential for unnecessary invasive evaluation if all ASC-US cases are managed identically without risk stratification. This supports the importance of HPV-based triage and contemporary risk-based management strategies. [4,8]

The role of HPV testing is especially important because the risk of significant cervical disease among women with ASC-US varies substantially according to HPV status. Risk-based guidelines therefore incorporate HPV testing, current cytology, and previous screening history to guide decisions regarding colposcopy and surveillance. [8]

The present study also provides evidence that high-grade disease can occur with relatively minor cytological abnormalities. Among the seven CIN2 cases identified in the overall cohort, four had ASC-US on LBC. This finding emphasizes that an ASC-US report does not completely exclude underlying high-grade cervical disease.

The absence of CIN3 or invasive carcinoma among the 16 ASC-US cases should be interpreted cautiously because of the small sample size. The study was not powered to estimate the frequency of uncommon outcomes such as CIN3 or invasive cervical cancer with precision.

The present findings have practical relevance in tertiary-care cervical screening programs. Colposcopy-guided biopsy can provide definitive histopathological information in women requiring further diagnostic assessment. However, because colposcopy may be associated with discomfort, anxiety, and other potential harms, appropriate risk-based selection remains important. [9]

Overall, the findings indicate that ASC-US represents a heterogeneous cytological category with a clinically meaningful proportion of underlying cervical intraepithelial neoplasia. The identification of CIN2 in one-fourth of the women studied supports careful triage, appropriate colposcopic evaluation when indicated, and histopathological confirmation of suspicious lesions.

**Clinical Implications**

The findings of the study have several clinical implications:

1. ASC-US represents a heterogeneous cytological category and should not automatically be considered benign.
2. In the present cohort, 50.0% of women had CIN1+, demonstrating a substantial histopathological yield.
3. CIN2+ was identified in 25.0% of women with ASC-US.
4. HPV testing can provide additional risk stratification in women with ASC-US. [4,8]
5. Colposcopy-guided biopsy provides histopathological confirmation when further evaluation is clinically indicated. [5-7]
6. Risk-based management is preferable to management based solely on the cytological category. [8]

**Limitations**

The present study has several limitations.

First, the ASC-US subgroup consisted of only 16 women, resulting in limited statistical precision.

Second, the study was conducted in a tertiary-care setting, which may limit generalizability to the general screening population.

Third, the analysis was based on a subgroup of the overall screening population and was not specifically powered to evaluate uncommon outcomes such as CIN3 or invasive carcinoma.

Fourth, no separate sample-size calculation was performed specifically for the ASC-US subgroup.

Fifth, the analysis primarily evaluated histopathological yield and did not assess long-term

persistence, regression, or progression of cervical lesions.

Finally, detailed individual-level colposcopic parameters and HPV-risk stratification were not available for all ASC-US cases in the summarized dataset. Therefore, the study focuses specifically on the histopathological diagnostic yield of colposcopy-guided biopsy.

## Conclusion

Colposcopy-guided cervical biopsy demonstrated a substantial diagnostic yield among women with ASC-US on liquid-based cytology. Among the 16 women studied, 50.0% had CIN1+ and 25.0% had CIN2+, while 43.8% had normal histology.

The presence of CIN2 in one-fourth of women with ASC-US demonstrates the heterogeneous nature of this cytological category and highlights that clinically significant cervical precancer may occur despite relatively minor cytological abnormalities.

Appropriate risk-based triage, consideration of HPV status, colposcopic evaluation when indicated, and histopathological confirmation remain important components of the diagnostic pathway for women with ASC-US.

## Declarations

**Ethics Approval:** Ethical approval was obtained from the institutional ethics committee before commencement of the study.

**Consent to Participate:** Written informed consent was obtained from all participants.

**Funding:** No external funding was received for the study.

**Conflict of Interest:** The authors declare no conflict of interest.

**Author Contributions:** All authors contributed to the study conception, data collection, analysis, interpretation of findings, manuscript preparation, and critical revision of the final manuscript according to their respective contributions.

**Data Availability:** The data supporting the findings of this study are available from the corresponding author on reasonable request, subject to institutional and ethical restrictions.

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