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Original Article

# Prevalence of precancerous and cancerous cervical lesions in women from Batna, Algeria

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### Abstract

**Background and aims:** Cervical cancer is the fourth most frequently diagnosed cancer among Algerian women and the seventh in Batna. This study sought to evaluate the prevalence of precancerous and cancerous cervical lesions and identify the target age groups for focused screening efforts to facilitate the early detection of uterine cervical neoplasms.

**Methods:** A cross-sectional study was conducted for seven years, from January 2017 to December 2023. A total of 12623 Algerian women, aged 25 to 65, were screened cytologically using the Papanicolaou test as part of a national screening program for early detection of cancerous lesions and precursor lesions of cervical cancer.

**Results:** The predominant age group was 30-39 years, accounting for 39.42%. In 98.19% of adequate smears, results were negative for intraepithelial lesions or malignancy (NILM). Of these, 3617 (29.66%) were standard, and 8301 (68.07%) exhibited non-specific inflammation. Epithelial cell abnormalities (ECAs) were observed in 225 (1.81%) of the smears. No cases of squamous cell carcinoma (SCC), adenocarcinoma, or adenocarcinoma in situ were reported. No significant association was detected (P<0.05) between age groups and the presence of precancerous cervical lesions. However, most abnormal Pap smears were found in women over 60 years old with 24 cases (4.10%) and 56 cases (3.13%) in the 50-59 age group.

**Conclusion:** The study found that 1.81% of cervical smears exhibited ECAs, with atypical glandular cells (AGCs) being the most prevalent (46.67%). The highest prevalence of abnormalities was observed in women over 50 years of age.

**Keywords:** Uterine cervical neoplasms, Screening, Papanicolaou test, Precancerous conditions, Algeria

### Introduction

Cervical cancer is a significant global health concern that primarily affects women in less developed regions.<sup>1</sup> Persistent infection with high-risk strains of human papillomavirus (HPV) is the leading factor in the development of cervical cancer, which can lead to the development of abnormal cells that, if left undetected and untreated, may progress to cancer.<sup>2</sup> Women with cytological abnormalities in the cervix are at an increased risk of developing cervical cancer.<sup>3</sup> The asymptomatic nature of precancerous lesions generally leads to gradual progression and, with multiple curable lesions present before developing into invasive cancer.<sup>2</sup> Routine screenings such as the Papanicolaou smear (Pap) are crucial in detecting abnormal cervical cells before they evolve into invasive cancer.1 HPV vaccination, early detection, and timely treatment are key preventive measures significantly reducing morbidity and mortality rates.4 A biopsy and histological confirmation are required

to validate abnormal cytologic results.<sup>5</sup>

Globally, cervical cancer is the fourth most prevalent cancer among women, accounting for 660 000 new diagnoses and 350 000 fatalities in 2022.<sup>1</sup> According to the American Cancer Society, cervical cancer was the leading cause of cancer-related deaths among women in 2022 in 37 countries, 29 of which are located in sub-Saharan Africa (with rates ranging from 28.4 to 95.9 per 100 000). In recent statistics, Eswatini reported the highest incidence rate globally, with 96 cases per 100 000 women. The United States is among the countries with the lowest incidence rates, with 6 cases per 100 000 women. Other countries with low incidence rates include New Zealand, Australia, and countries in the eastern Mediterranean, with rates ranging from 2.1 to 6.4 per 100 000.<sup>6</sup>

In Algeria, cervical cancer is the fourth most prevalent cancer among women, following breast, colorectal, and thyroid cancers, and it ranks as the seventh most common cancer among women aged 15 to 44, with an incidence rate

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of 7.66. Current estimates indicate that 1663 women are diagnosed with cervical cancer annually, and 930 women die from the disease. Approximately 2.1% of women in the general population are infected with HPV types 16/18 at any given time, with these two types accounting for 76.8% of invasive cervical cancers.<sup>7</sup> According to the 2011 Batna cancer registry, cervical cancer was the seventh most frequent cancer in the female population of Batna, with a standardized incidence rate of 2.60 per 100 000.<sup>8</sup>

In response to this, the Ministry of Health and Population in Algeria initiated a national cervical cancer screening program in 2001 to reduce the incidence of cervical cancer. Effective cervical cancer prevention programs, which have significantly reduced mortality rates, share key strategic elements such as targeting a specific age group and reaching a substantial proportion of women within that group.<sup>9</sup>

However, no information is available regarding the prevalence and peak age distributions of epithelial cell abnormalities (ECAs) in the uterine cervix in Batna, located in northeastern Algeria. Thus, this study aimed to evaluate the prevalence of precancerous and cancerous cervical lesions in this region and to identify the age groups that require prioritized screening for early detection of cervical cancer.

## Materials and Methods

## Selection and Description of Participants

This cross-sectional study used data collected over seven years, from January 2017 to December 2023. It involved the cytological screening of 12.623 Algerian women as part of a national program aimed at early detection of both cancerous and precancerous cervical lesions. This study was approved by the Ethics Committee of Mustapha Ben Boulaid, Batna 2 University (Reference number: 18/ CED4B2/2024). Cervicovaginal smears were carried out in compliance with ethical considerations at the specialized hospital for mothers and children, Meriem Bouatoura, and at Maternal and Child Protection Services within local public health establishments in Batna city and El'Madher located in Batna province in Algeria's eastern region.

The study included women aged 21 to 65 years, following the World Health Organization's (WHO's) recommendations for cervical cancer screening. Eligible participants were those who had not undergone a conventional cervical smear in the previous three years and those with a family history of cervical cancer, which was considered an additional risk factor. The targeted population primarily consisted of asymptomatic women with no previous history of cervical cancer; however, women presenting mild symptoms such as abnormal bleeding were also evaluated. Additionally, women with a history of HPV infections or other recognized risk factors were included.

Recruitment efforts focused on ensuring proper follow-up care for women in the targeted regions. However, accessibility remains a limitation, especially in remote areas. This could potentially lead to the underrepresentation of women without healthcare access or those reluctant to participate in screenings, which may introduce bias in the data collection process.

The study excluded women who had undergone a total hysterectomy, as they no longer had a cervix, as well as those with a history of cervical cancer treatment, unless for follow-up or extended examinations. Pregnant women or those with medical conditions that could pose health risks to either the mother or fetus during screening were also excluded.<sup>9</sup>

#### **Technical Information**

Conventional cervicovaginal smears were obtained using Ayre's spatula and cytobrush from the exocervix and endocervix. The collected cells were evenly spread thinly on a glass slide and fixed with a cytological fixative spray. Two samples were collected from each patient, and the smears were stained using the Papanicolaou method. The cytological slides were then forwarded to regional hospital laboratories for examination. Optical microscope readings were decentralized in screening units installed as part of this national program.<sup>9</sup> Smear interpretation followed the guidelines outlined in the 2014 New Bethesda System for Reporting Cervical Cytology.<sup>10</sup>

This study utilized data from annual reports evaluating Algeria's national cervical cancer screening efforts. The data, collected through a standardized form, systematically recorded comprehensive patient information and cytological findings, ensuring consistency and accuracy in monitoring screening outcomes. Women were categorized into five age brackets: 25–29, 30–39, 40–49, 50–59, and  $\geq$  60 years. The adequacy of each smear was noted and categorized as satisfactory or unsatisfactory for interpretation, with reasons for unsatisfactory smears such as insufficient cellular material also recorded.

Cytological findings were classified based on the presence or absence of intraepithelial lesions or malignancy. Negative results were further subdivided into standard smears or those showing non-specific inflammation or infections (e.g., Trichomonas, Mycotic, Bacterial, Herpes, Chlamydia). Cases with epithelial abnormalities were categorized as atypical squamous cells (ASC-US or ASC-H), low-grade squamous intraepithelial lesions (LSILs), high-grade squamous intraepithelial lesions (HSILs), atypical glandular cells (AGCs), adenocarcinoma in situ (AIS), or squamous cell carcinoma (SCC).

Based on cytological outcomes, recommendations for follow-up actions were recorded, including repeat smears, treatment, colposcopy, biopsy, or further diagnostic tests such as HPV testing.

#### **Statistical Analysis**

Statistical analysis and graph creation were performed using SPSS version 25 and GraphPad Prism. Categorical variables were presented in terms of frequencies and percentages and analyzed using chi-square tests, with a significance threshold set at P < 0.05.

#### Results

During the study period, 12.623 cervical smears were cytologically screened. Of these, 90.48% were first smears, 7.84% were second-time smears, and 1.68% were third-time smears. A total of 12.419 smears (98.38%) were found satisfactory for evaluation, while 204 smears (1.62%) were unsatisfactory.

The findings revealed that the 30-39 age group had the largest number of participants, accounting for 39.42%, followed by the 40-49 age group with 28.52%. The percentage is relatively low at 14.39% for women aged 50-59 and 12.96% for those under 30 years old. The over-60 age group presented the smallest percentage at 4.72% (Figure 1).

In 98.19% of all adequate smears, the result was negative for intraepithelial lesions or malignancy (NILM). Out of 12194 NILM cases, 3617 (29.66%) were standard, while 8301 (68.07%) were non-specific inflammation, followed by Candidiasis (147 cases, 1.21%), bacterial vaginosis (92 cases, 0.76%), Trichomonas infection (11 cases, 0.09%), chemotherapy effects (10 cases, 0.08%), X-ray therapy effects (9 cases, 0.07%), Chlamydia infection (6 cases,



Figure 1. Age-wise Distribution of the Total Number of Patients

Table 1. Distribution of Cervical Smears According to Cytopathological Diagnosis

0.05%), and Herpes simplex virus infection (1 case, 0.01%). The cytologically observed results are presented in Table 1.

ECAs were observed in 225 smears, accounting for 1.81% of all satisfactory smears. AGCs were the most common abnormality, with 105 cases (46.67%), followed by atypical squamous cells of undetermined significance (ASC-US) in 59 cases (26.22%). Other abnormalities included atypical squamous cells-cannot exclude HSIL (ASC-H) in 45 cases (20%), LSIL in 8 cases (3.56%), HSIL in 5 cases (2.22%), and AGC lesions in 3 cases (1.33%). No instances of SCC, endocervical adenocarcinoma, endometrial adenocarcinoma, AIS, or other rare tumors were observed. Premalignant and malignant lesions are summarized in Table 1.

The age-wise distribution of smears with ECA is summarized in Table 2. No significant relationship was found (P=0.22) between age groups and the presence of precancerous cervical lesions. Nevertheless, the majority of abnormal Pap smears were found in women over 60 years and in the 50-59 age group, with 24 cases (4.10%) and 56 cases (3.13%), respectively. In this age group, AGC was the most frequent abnormality, followed by ASC-US and ASC-H.

Most recommendations indicated that cervical smears should be repeated within one year (78.67%), with the second most frequent recommendation being a cervical screening (CPS) after six months (9.14%). In contrast, recommendations to conduct a repeat smear as soon as possible (0.22%), perform an HPV test (0.1%), or undertake a colposcopy (0.36%) were less common. Furthermore, the recommendation for biopsy (0.51%) was the least frequently suggested.

## Discussion

This study revealed that the 30-39-year-old age group was the most prevalent in our cohort, comprising 39.42%.

| Absence of Intraepithelial Lesion or Sign of Malignancy (n=12194) |               |         |                   |                        |                                |            |       |                     |                 |                           |  |  |
|---|---------------|---------|-------------------|------------------------|--------------------------------|------------|-------|---------------------|-----------------|---------------------------|--|--|
| Normal  | Inflammation  |         | Trichomonas       | Mycosi                 | Herpes                         | Bacteria   |       | Chlamydia           | Chemotherapy    | X-ray Therapy             |  |  |
| 3617  | 8301          |         | 11                | 147                    | 1                              | 92         | 6     |                     | 10              | 9                         |  |  |
| 29,66%  | 68.07         | 68.07 % |                   | 1.21%                  | 0.01%                          | 0.76%      | 0.05% |                     | 0.08%           | 0.07%                     |  |  |
| Epithelial Cell Abnormality (n=225)                               |               |         |                   |                        |                                |            |       |                     |                 |                           |  |  |
| ASC-US  | ASC-H         | LSIL    | HSIL              | SCC                    | AGC                            | AGC Lesion | AIS   | Endocervical<br>ADC | Endometrial ADC | Other                     |  |  |
| 59  | 45            | 8       | 5                 | 0                      | 105                            | 3          | 0     | 0                   | 0               | 0                         |  |  |
| 26.22%  | 20%           | 3.56%   | 2.22%             | 0                      | 46.67%                         | 1.33%      | 0     | 0                   | 0               | 0                         |  |  |
|   |               |         |                   |                        | Recommendation                 | (n=12631)  |       |                     |                 |                           |  |  |
| CST in 6<br>Months  | CST in 1 Year |         | CST in 3<br>Years | CST post-<br>treatment | To Redo as<br>Soon as Possible | HPV Test   |       | Colposcopy          | Biopsy          | Endocervical<br>Curettage |  |  |
| 1154  | 993           | 9937    |                   | 1079                   | 28                             | 12         |       | 45                  | 65              | 94                        |  |  |
| 9.14%   | 78.6          | 78.67%  |                   | 8.54%                  | 0.22%                          | 0.1%       |       | 0.36%               | 0.51%           | 0.74%                     |  |  |
|   |               |         |                   |                        |                                |            |       |                     |                 |                           |  |  |

Note. ASC-US: Atypical squamous cells of undetermined significance; ASC-H: Atypical squamous cells-high-grade squamous intraepithelial lesion cannot be excluded; AGC: Atypical glandular cells (favor neoplastic); LSIL: Low-grade squamous intraepithelial lesion; HSIL: High-grade squamous intraepithelial lesion; SCC: Squamous cell carcinoma; ADC: Adenocarcinoma; AIS: Adenocarcinoma in situ; CST: Cervical smear test.

## Table 2. Distribution of Epithelial Cell Abnormalities by Age Group

|       | Total Number of Cases (%) | ASC- US | ASC-H | LSIL | HSIL | SCC | AGC | AGC Lesion | Total (%) |
|-------|---------------------------|---------|-------|------|------|-----|-----|------------|-----------|
| <30   | 1609 (12.96)              | 4       | 1     | 0    | 0    | 0   | 2   | 0          | 7 (0.44)  |
| 30-39 | 4895 (39.42)              | 6       | 3     | 2    | 0    | 0   | 25  | 0          | 36 (0.74) |
| 40-49 | 3542 (28.52)              | 12      | 7     | 3    | 0    | 0   | 26  | 1          | 49 (1.38) |
| 50-59 | 1787 (14.39)              | 15      | 13    | 3    | 4    | 0   | 20  | 1          | 56 (3.13) |
| >60   | 586 (4.72)                | 6       | 7     | 1    | 0    | 0   | 10  | 0          | 24 (4.10) |

Note. ASC-US: Atypical squamous cells of undetermined significance; ASC-H: Atypical squamous cells-high-grade squamous intraepithelial lesion cannot be excluded; LSIL: Low-grade squamous intraepithelial lesion; HSIL: High-grade squamous intraepithelial lesion; SCC: Squamous cell carcinoma; AGC: Atypical glandular cells (favor neoplastic).

Sapkota et al and Melhag et al supported this result, with 32.68% and 50% of patients falling within the same age range.<sup>11,12</sup> Moreover, these results align with those reported by Nahet et al,<sup>13</sup> who found that the 36-40 and 41-45 age groups were the most represented. An additional analysis indicated that women aged 30–39 years (73.3%) were more likely to have been screened for cervical cancer among Korean women.<sup>14</sup> However, these results differ from previous research, which found a higher mean age than what was obtained in the present study.<sup>15-17</sup>

In a previous study in Algeria, 40-50-year-olds represented the largest age group.<sup>18</sup> Many authors suggest that this age similarity is due to increased exposure to sexually transmitted diseases among these patients, allowing for earlier Pap smear collection.<sup>3,19</sup>

Out of 12194 (98.19%) NILM smears, non-specific inflammation was the predominant form, with a rate of 68.07%, while normal smears accounted for 29.66%. Our results are slightly similar to those found in Algeria (65.20%) but lower than those reported in previous studies.<sup>19-21</sup> These findings are consistent with studies conducted in Algeria's Northwestern and Southern regions, where non-specific inflammatory findings were also the most common.<sup>13,22</sup>

The current study identified a high prevalence of non-specific inflammation, which can complicate cervical cancer screening by leading to false positives or reducing the accuracy of diagnostic methods. Non-specific inflammation, often seen in conditions like HPV infections and benign lesions, can overlap with early neoplastic changes, necessitating more precise diagnostic methods.<sup>23</sup> Advancements in molecular biomarkers could improve the accuracy of screening and reduce false positives.<sup>24</sup> Additionally, inflammation may influence treatment decisions, potentially leading to overdiagnosis or underdiagnosis, particularly in resource-limited settings. Elevated inflammation levels in specific cohorts may also require more frequent follow-up to ensure early detection.<sup>25</sup>

Likewise, our findings demonstrated that among the 12194 NILM cases, 257 (2.11%) women had infections, including candidiasis (1.21%), bacterial vaginosis (0.76%), Trichomonas (0.09%), chlamydia (0.05%), and herpes simplex virus (0.01%). Previous research indicates that 65.20% of women had different levels of cervicitis, with 63.50% of these cases being non-specific.<sup>19</sup> In addition,

7.41% of women in eastern Algeria had a history of recurrent genital infection.<sup>26</sup> However, in Boukabene and colleagues' study, intra-epithelial lesions associated with Chlamydia, Trichomonas, Herpes, and mycosis were not detected.<sup>22</sup>

Recurrent genital infections such as chlamydia, herpes, and trichomonas can increase the risk of developing cervical cancer.<sup>27</sup> Consequently, the high prevalence of inflammation (68.07%) in the smears of our study population raises significant concerns.

The ECA rate in our study was 1.81%, with AGC being the predominant form, followed by ASC-US, ASC-H, and other types. When AGC is associated with highrisk HPV types, the risk of developing advanced cervical intraepithelial neoplasia or invasive adenocarcinoma in situ is significantly elevated.<sup>28</sup> This result aligns with that of Chikhaoui et al (1.54%), where AGC had the highest prevalence rate, but lower than the findings of Boublenza and Nahet (5.1%).<sup>13,18,19</sup> In contrast, LSIL was the most common form in Meziani and colleagues' study, while ASC-US had the highest prevalence in Laissaoui and colleagues' investigation.<sup>29,30</sup> Another study conducted in rural Uganda reported that 7.6% of women participating in cervical cancer screening had precancerous lesions.<sup>31</sup> Similarly, a study in Saudi Arabia found that 3.05% of women had abnormal Pap smears, with ASC-US being the most frequent abnormality.32

In our study, no cases of cervical cancer were reported. These results are consistent with those of Yasmin and Mukherjee, where no cancerous lesions were detected.<sup>33</sup> In contrast, malignant lesions were reported in a study conducted in the western region of Algeria, where 1.5% of cases were SCC and 1.9% were adenocarcinoma, respectively.<sup>18</sup>

No significant association was observed between patients' age and the presence of precancerous lesions in our study. However, most abnormal Pap smears were found in women over 60 years and in the 50-59 age groups. The highest incidence of HSIL and LSIL occurred in the fifth decade, while AGC, ASC-US, and ASC-H were most commonly observed in individuals aged over 60 years. These findings align with the study by Das et al but differ from Chikhaoui and colleagues' report, where the 41–50 age group represented the peak age for precancerous lesions of the cervix. These discrepancies may be attributed to variations in the characteristics of the populations studied.19,20

Previous research indicates that the risk of developing cytological abnormalities increases significantly with age.<sup>34,35</sup> Nevertheless, some studies have contradicted this observation. Makuza et al identified age as a protective factor, whereas Moumouni et al did not find a significant relationship between women's age and the occurrence of cellular changes.<sup>21,36</sup>

Our study reveals a lower-than-expected rate of LSIL in women under 40, despite the expected higher HPV prevalence in this sexually active population. HPV infections are typically transient, especially among women under 30, and are often linked to the resolution of cytological and histological abnormalities.<sup>37</sup> Additionally, HPV infection occurs in 25% to 40% of women aged 15-25, often without the presence of underlying lesions.<sup>36,38</sup>

Only 1202 (9.52%) patients had previously undergone a Pap smear, which falls below the target set by Algeria's national program launched in 2001. The program aims for a coverage rate greater than 70%, as recommended by a good screening campaign.<sup>39</sup>

These data are lower than those reported in previous studies conducted in Medea and Tiaret, Algeria, where 16% and 38.37% of participants had undergone screening, respectively.<sup>13, 19</sup> Research in Saudi Arabia revealed that 17.2% of women in Al Hassa and 33.4% of women in Jeddah had received a cervical smear at some point in their lifetime.<sup>40, 41</sup> Furthermore, only 22.37% of women in Liaoning, China, reported having been screened for cervical cancer in the past three years.<sup>42</sup> Nevertheless, our Pap test results exceed those reported by Koç et al and Sandjong et al, which were only 1.1% and 106 (8.5%), respectively.<sup>15,43</sup>

According to the cytological findings, the predominant recommendations included repeating cervical smears within one year, followed by suggesting CPS after six months. This differs from the study by Boukabene et al, which found that the most common recommendation was to repeat the CPS after six months. After one year, a second test is necessary for individuals undergoing their initial smear, while women already under surveillance are required to undergo a test every three years.<sup>22</sup>

#### Conclusion

The results of the study revealed a relatively high prevalence of precancerous lesions in postmenopausal women. The most common findings included atypical glandular lesions and ASC-US, with no invasive cancer detected. Most women had non-specific inflammation or other benign infections such as Candidiasis and bacterial vaginosis. No significant association was observed between age groups and the presence of precancerous cervical lesions. Accordingly, active surveillance across all age groups is recommended. These findings align with Algeria's national guidelines, which recommend CPS every five years for women aged 30 and older, following two consecutive negative results. Future research should include longitudinal studies to track the progression of precancerous lesions, especially in postmenopausal women. Additionally, further studies are needed to evaluate the barriers to CPS among postmenopausal women and explore the integration of HPV testing as a complementary method to cytology. Understanding the progression of precancerous lesions in women can help refine screening intervals and treatment protocols, potentially reducing cervical cancer incidence and mortality in this vulnerable population.

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#### **Authors' Contribution**

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## **Competing Interests**

The authors declare no conflict of interests.

#### **Ethical Approval**

Ethical considerations in this study included obtaining permission from the Ethics Committee of Mustapha Ben Boulaid, Batna 2 University (Reference number: 18/CED4B2/2024).

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