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A CALL TO ACTION: LOW CERVICAL CANCER SCREENING RATES IN SÉTIF

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Abstract

Cervical cancer is closely linked to infection by Human papillomavirus (HPV), non-enveloped DNA viruses, with types 16 and 18 most often associated with this tumour. HPV is a sexually transmitted virus usually cleared by the immune system within six months to two years, but persistent infection can lead to invasive cancer. A retrospective study of 4,747 cervico-vaginal smears (CVS) from Sétif, Ain El-Kebira, and Amoucha between January 1, 2022, and March 31, 2024, evaluated cervical cancer screening activities and demonstrated the value of cervico-vaginal smear (CVS), called cytologic "Pap Test" in detecting cervical lesions. Systematic HPV surveillance and early-stage screening via CVS, with follow-up for abnormal results, are crucial. Despite increasing smear percentages, initial screenings showed higher abnormal smear rates compared to regular check-ups. The study revealed low smear coverage rates in Ain El-Kebira (0.88%), Amoucha (0.81%), and Sétif (1.26%), highlighting the severe screening situation in these localities and in the Algeria overall, reflecting broader national challenges. Cervical cancer screening is essential for reducing incidence and mortality, necessitating measures like education and awareness campaigns, and distribution of accurate, accessible information to diverse socio-economic groups. These efforts are vital to improve screening and address critical local challenges, requiring a concerted national response.

Key words: Cervical cancer, Human papillomavirus, Cervico-vaginal smear, Screening.

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1. Introduction

Cervical cancer is one of the most concerning public health issues globally, ranking fourth worldwide in 2022 and fifth in Algeria in 2020. This cancer's occurrence is closely linked to infection by Human papillomavirus (HPV), non-enveloped DNA viruses belonging to the Papillomaviridae

family, with a viral particle diameter of approximately 55 nm [1]. Among the many types of human papillomaviruses (HPV), types 16 and 18are most often associated with cervical cancer. These viruses are sexually transmitted and are mostly cleared by the immune system within six months to two years; however, persistent infection can lead to cellular lesions and their transformation into invasive cancer [2]. HPV infection is often asymptomatic, and its progression depends on the interaction between the viral genotype and the immune escape mechanisms, the host (type of infected cells, immune response), and environmental factors, like smoking, oral contraceptive use, and other sexually transmitted infections [2]. Therefore, the risk of this sexually transmitted infection is not solely related to the presence of the virus after contamination but to its persistence, which can lead to cancer development depending on the HPV type involved [3]. The cervico-vaginal smear (CVS) and HPV test are currently the reference examinations for cervical cancer screening to reduce both the incidence and mortality of the disease. The widespread use of the CVS has significantly reduced the mortality associated with this type of cancer by enabling the early detection of cellular abnormalities before they progress to precancerous or cancerous lesions, thus facilitating early therapeutic intervention [4]. However, to be effective, CVS must be performed according to standards. A conventional CVS must contain a minimum of 8,000 to 12,000 well-visible cells on the microscope slide to be considered satisfactory [5]. The sensitivity of this technique depends also on several factors, including the sampler's experience, the cervix's anatomy, homogeneous cell spreading on the slide, and proper fixation and staining of the sample [6].

A study in Sétif, Algeria, investigated cervical cancer screening practices. The study took place between January 2022 and March 2024 in three districts: Sétif, Ain El-Kebira, and Amoucha. We analyzed 4,747 pap smears to assess how many women were getting screened. The goal was to determine the current screening coverage and identify ways to improve it.

2. Materials and Methods

2.1. **Study Populations:** This is a retrospective study based on the results of cervical smear samples collected from public health facilities (EPSP) located in the commune of Sétif, as well as the communes of Amoucha and Ain El-Kebira. The collection of smears was conducted over a period from January 1, 2022, to March 31, 2024, spanning 27 months. During this period, a total of 4,747 smears were performed and analyzed: 4,112 in Sétif, 384 in Ain El-Kebira, and 251 in Amoucha. The study included women aged between 20 and 65 years who reside in the communes of Sétif, Ain El-Kebira, and Amoucha and who sought services from the nearby EPSP.

2.2. The Cervico-vaginal Smear (Pap smear)

The Pap test has made cervical cancer one of the easiest cancers to prevent and detect at an early stage. The test involves collecting cells lining the transformation zone (where the squamous external cells of the cervix meet the glandular internal cells of the endocervix), preparing smears from the collected cells, staining them with Papanicolaou stain, and analyzing them under a microscope to detect any abnormalities [7]. The smear should be

performed away from sexual intercourse (48 hours), outside the menstrual period, without any local treatment or infection, and if necessary, after estrogen treatment in postmenopausal women [8]. For exocervical collection, the tip of the spatula is inserted into the orifice, and with light pressure and a hand change during rotation, the spatula performs a 360° rotation. The rounded end (Ayre) of the spatula is used in multiparous women, while the elongated end (Aylesbury) is intended for nulliparous women. The squamocolumnar junction must be fully scraped, and if significant ectropion is present, the exocervix must be scraped separately. The sample is then spread evenly on a slide and immediately fixed in a conservation spray for at least 2 hours. Endocervical sampling is performed using a cotton swab that allows access up to 1 cm in depth, and the sample is then spread on a slide by uniformly rolling out the cotton swab and immediately fixed. Spreading on a slide is a single gesture, regardless of the site and instrument used for sampling; it involves gently spreading the entire surface of the spatula or brush on a clean glass slide. Irregular spreading movements (convolutions, back and forth) are to be avoided, as they crush cells and create artifacts. Fixation must follow immediately after spreading to avoid desiccation, which deforms cells and alters their staining affinities. Without letting go of the slide, it is sprayed with a specific cytology fixative. After fixation, the slides must be placed in a cardboard or plastic envelope (transport plate) accompanied by their screening forms and then sent to the pathology service for staining with Papanicolaou stain [8].

Also known as the conventional technique, Papanicolaou staining remains the most widely used method to date. It involves several variants of cytoplasmic stains, with EA36 and EA50 being the most commonly used in combination with OG6. The nuclear stain is hematoxylin, which stains nuclei blue after mordanting with potassium alum. After staining, a mounting between a slide and cover slip is performed with synthetic balm to allow microscopic examination.

3. Results and discussion

3.1. Age-Based Cervical Cancer Screening

A distinct distribution based on age groups and the frequency of screenings (once, twice, or thrice) was observed. The majority of screenings are concentrated in the 30-44 age groups, with a peak between 35 and 39 years. Specifically, the total numbers of screenings for the 30-34, 35-39, and 40-44 age groups are 702, 843, and 765, respectively (Figure 1).

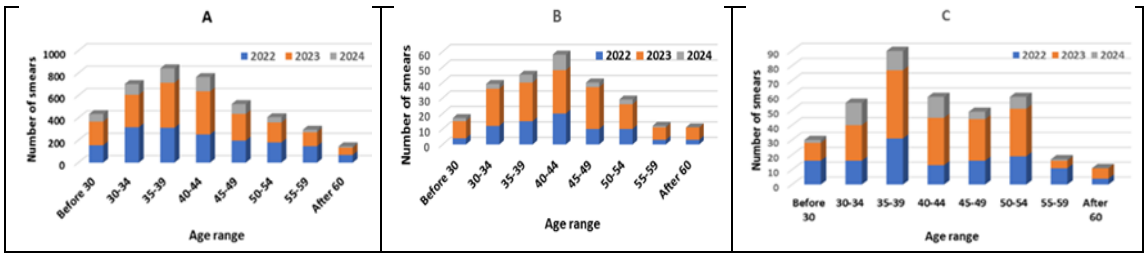


Figure 1 : Number of Pap smears conducted by age group and number of screenings per patient. (A : Sétif, B : Amoucha, C : Ain El Kebira).

In contrast, there is a progressive decrease in the number of screenings among older age groups, particularly from 45 to 59 years, with totals of 523, 406, and 294, respectively. This trend might be due to a decrease in the attention given to screening post-menopause or logistical and sociocultural barriers affecting older women. Women under 30 and those aged 60 and above have the lowest numbers of screenings, with totals of 434 and 145, respectively. This is consistent with the general trend, where approximately 6 million CVSs are performed annually, with 7-10% of them being performed on women over 65 years [9]. Considering the demographics of Sétif in 2010, with women aged 20-65 years, the observed screening coverage is very low (approximately 1%) compared to the coverage in countries with national programs for over 20 years, reaching up to 70%. French recommendations from the 1990 Lille conference advocate for a Pap smear every three years after two annual normal smears for all women aged 25-65 who have or have had sexual intercourse. Beyond 65 years, screening may cease if women have been regularly monitored and if at least two consecutive smears were normal [9].

In Amocha, participation is generally the lowest across all age groups compared to Sétif and Ain El-Kebira. This could be due to differences in available resources for screening or lower awareness among women in this region. In Ain El-Kebira, data also show relatively low participation, although some age groups (35-39 and 40-44 years) have higher screening numbers compared to Amoucha. For example, the 35-39 age group has 90 screenings, and the 40-44 age group has 59.

3.2. Distribution of Cervical Lesions

Cytological Results Distribution in Sétif

The results of the microscopic examination of smears performed in Sétif (Figure 2) show a majority of normal smears (n= 2443). A significant proportion of smears show atypical squamous cells of undetermined significance (ASC-US): 527 cases in 2022, 734 cases in 2023, and 177 cases in the first quarter of 2024. These results typically require further monitoring or additional tests, such as HPV testing or colposcopy, to determine the nature of these abnormalities (figure 2).

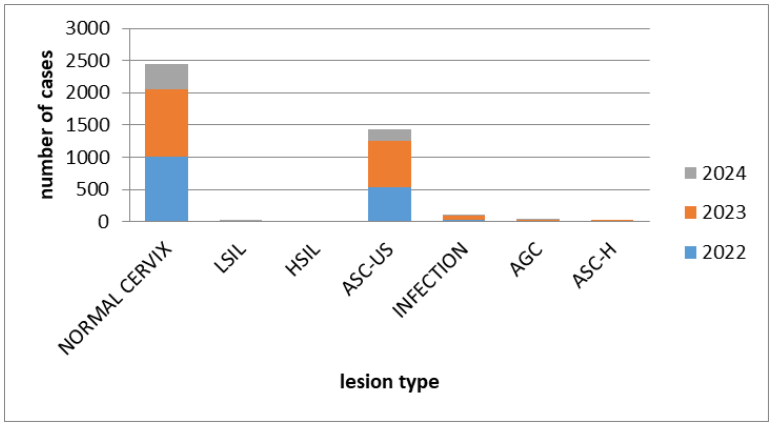


Figure 2: Distribution of smears by lesion type (Sétif)

There were only two cases of high-grade intraepithelial lesions (HSIL) during this period, but 14 cases of low-grade intraepithelial lesions (LSIL) were recorded, half of which (7 cases) were detected in the first quarter of this year. Additionally, 28 cases of atypical glandular cells (AGC) and 23 cases of atypical squamous cells (ASC-H) were detected, requiring particular attention as these cells may be associated with precancerous or cancerous conditions. Infections were detected in 97 cases, the majority (58 cases) of which were registered in 2023.

Distribution of Lesions in Amoucha

Out of a total of 238 cervical smears, the number of ASC-US smears (117 cases) is slightly higher than the number of normal smears (102 cases), with 11 cases of infection, 9 of which were recorded in 2023, and 8 cases of HSIL (Figure 3). These results reflect a degraded state of health in the commune.

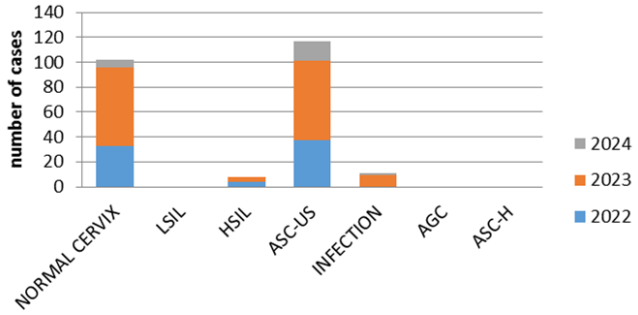


Figure 3 : Distribution of smears by lesion type (Amoucha).

Distribution of Lesions in Ain El-Kebira

Over the 27-month study period, out of a total of 357 smears, only 97 are normal (27%), while infections are presented by 51 cases. Inflammations account for twice as many smears as normal with 207 cases, indicating a poorer state of health compared to the other two communes (figure 4).

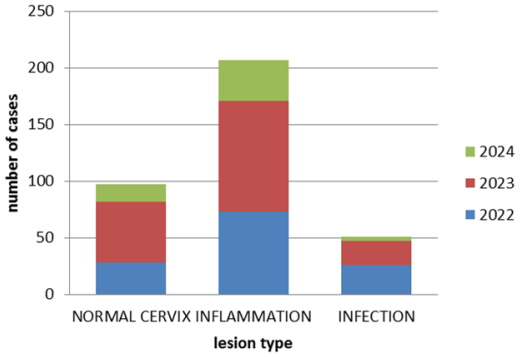


Figure 4 : Distribution of smears by lesion type (Ain El-Kebira)

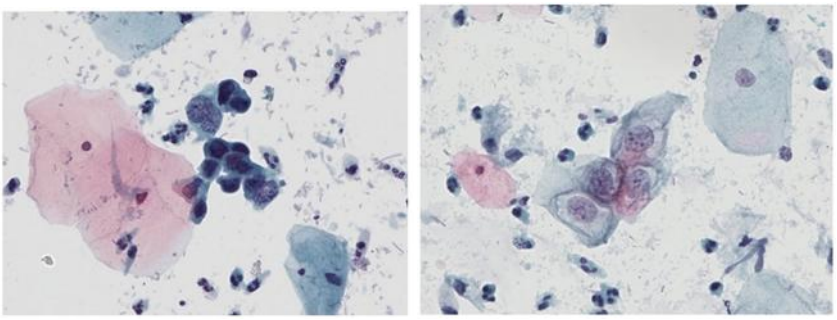
The absence of various classes of lesions may be due to poor interpretation of the smears, an inadequately equipped laboratory, or limited knowledge of health professionals. It has been reported that women with abnormal smears are referred to Sétif-town for further follow-up. Cytological examination classifies abnormalities according to Bethesda 2014 terminology [10], this relatively new version has changed little from the Bethesda 2001 version:

a) Atypical squamous cell abnormalities

This category is associated with 5-10% of high-grade squamous intraepithelial lesions on biopsies. The term "squamous cell atypia of undetermined origin" (ASC-US) is used for abnormalities suggestive of a low-grade squamous intraepithelial lesion (LSIL) without a true koilocyte. Atypia associated with inflammation should not be included in this group. World-wide, only 3% of cytological specimens merit this designation. In Sétif ASC-US account for approximately 25%. These "squamous cell atypia", does not exclude a high-grade squamous intraepithelial lesion (ASC-H), is proposed for basal cell abnormalities that are not characteristic of a high-grade squamous intraepithelial lesion (HSIL), but do raise suspicion [11].

b) Squamous intraepithelial lesions

Productive infection of human papillomavirus corresponds to the expression of late genes (L1 and L2) enabling virion construction. Productive infection is characterized by the presence of koilocytes in superficial and intermediate cells, and its cytological translation is the "low-grade squamous intraepithelial lesion" (LSIL) (figure 5); it is frequent in young women and usually regresses spontaneously within 12 months [11].



A **B**

Figure 5 : Low-grade squamous intraepithelial lesion (A) and High-grade squamous intraepithelial lesion (Bergeron, 2020).

Expression of the E6 and E7 genes leads to marked abnormalities of the basal cells of the squamous epithelium, defining "high-grade squamous intraepithelial lesion" (HSIL) according to the Bethesda system [11].

3.3. Cervical smear interpretability:

The results of smears Out of a total of 4112 smears, performed in Sétif during the years 2022-2024., 4037 (98%) were interpretable, while 75 (2%) were non-interpretable. In Amoucha, the results indicate that 238 smears (95%) were interpretable, and 5% need to be redone (Figure 6). In the commune of Ain El Kebira, out of 384 smears included in the study, 357 (93%) are interpretable, and 27 (7%) need to be redone.

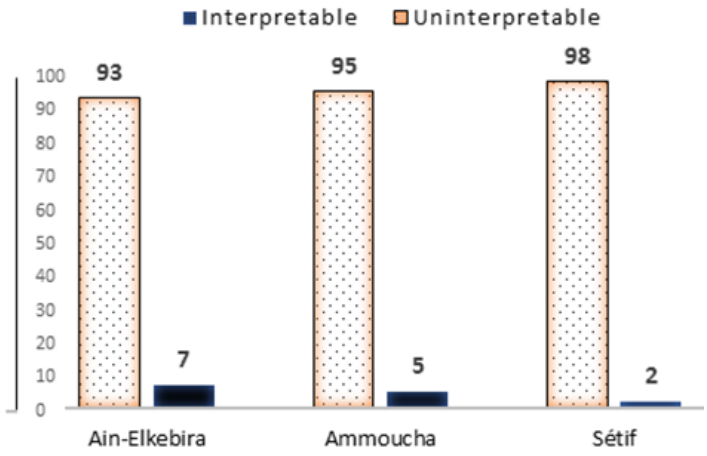


Figure 6: interpretable and non-interpretable smear results from the years 2022, 2023, and 2024 in Sétif.

Non-interpretable smears can be attributed to various factors. Sampling defects, such as when the sample is not taken from the transformation zone, can lead to non-interpretable results. Proper sampling is crucial for accurate interpretation. Reading errors, which involve the failure to recognize or the misinterpretation of atypical cells, mistakenly considering them normal, also contribute to non-interpretable smears [12]. Technically unacceptable slides, such as broken slides that cannot be repaired, fall into this category [13]. Insufficient cell collection, issues such as inadequate cell collection, cells remaining on the sampling tool, or cells being poorly fixed or obscured by inflammatory elements and blood, can cause non-interpretable results [14]. Additionally, an insufficient squamous epithelial component, where well-preserved and analyzable squamous epithelial cells cover less than 10% of the slide surface, makes the sample non-interpretable [13]. These factors highlight the importance of proper sampling techniques, accurate reading, and handling of slides to ensure high-quality and interpretable smear results. Proper training and adherence to guidelines can help reduce the percentage of non-interpretable smears, ultimately improving the accuracy of diagnostic procedures.

3.4. Screening follow-up

The cervical cancer screening results in the regions of Sétif, Ain El-Kebira, and Amoucha show notable differences in participation and follow-up of CVSs. These disparities may reflect variations in healthcare access, awareness of screening, and health behaviors in each region (figure 7).

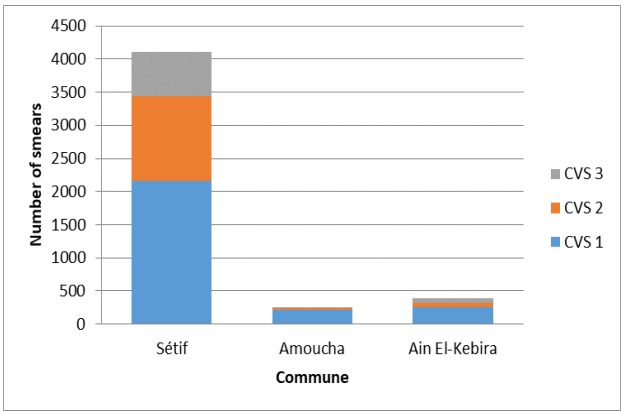


Figure 7: Screening follow up in each commune

In Sétif, the majority of women underwent FCU only once (CVS1), with a total of 2158. Those who screened twice (CVS2) numbered 1287, while those who screened three times (CVS3) were the least numerous, with a total of 667. This distribution suggests that while many women initiate screening, regular follow-up is less frequent. In Ain El-Kebira, the number of screenings performed once (CVS1) is significantly lower, with a total of 256. Screening performed twice (CVS2) and three times (CVS3) are even less frequent, with only 65 and 63 screenings respectively. This indicates a need to strengthen follow-up initiatives to improve early detection and management of cervical abnormalities.

In Amoucha, the data show a similar situation. The majority of screenings are concentrated on CVS1 (212 screenings), with a much lower number for CVS2 with 33 screenings and only 6 screenings for CVS3. This trend also reflects insufficient follow-up after the first screening. WHO recommends starting cervical cancer screening at age 25. For cytology, screening should occur every three years if results are normal. HPV testing should be done every five years if normal. Co-testing (HPV and cytology) is advised every five years. Screening can typically end at age 65, provided previous screenings have been consistently negative and there is no history of cervical disease [15]. These guidelines aim to ensure early detection and effective management of cervical cancer, adaptable to various healthcare settings to increase accessibility.

4. Conclusion

The study revealed very low smear coverage rates in Ain El-Kebira (0.88%) and Amoucha (0.81%), both rural areas, and in Sétif (1.26%), the capital of the Wilaya. These findings significantly underscore the gravity of the cervical cancer screening situation in these regions, reflecting broader

national challenges. The results highlight critical local challenges and emphasize the need for a concerted national response to address this issue effectively. Reducing the incidence and mortality of cervical cancer involves prevention, early detection, and treatment. Administering the HPV vaccine to girls aged 9-14 before they become sexually active is a key strategy recommended by the WHO, significantly reducing cervical cancer incidence.

Implementing regular screening programs is crucial for early detection. Screening methods such as cytology (Pap smear), HPV testing, and visual inspection with acetic acid (VIA) help identify precancerous lesions early. The WHO recommends starting screening at age 25, with cytology every three years, HPV testing every five years, and co-testing every five years. Screening can typically end at age 65 if previous results have been consistently negative. Promptly treating detected precancerous lesions is essential to prevent their progression to cervical cancer. Ensuring access to healthcare, especially in low-resource settings, is critical. This involves training healthcare providers, equipping facilities, and raising awareness about the importance of regular screening. Integrating cervical cancer prevention and treatment services with other health services, such as sexual and reproductive health programs, can help reach more women. Implementing national policies and allocating sufficient funding for vaccination programs, screening initiatives, and treatment facilities are also necessary to support cervical cancer prevention and control.

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