

## Evaluation of cervical cytological abnormalities in the Albanian population

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### Abstract

**Aim:** Cervical cancer is one of the most common female malignancies with high mortality rates in developing countries. Our purpose was to determine the prevalence of cervical cytological abnormalities in the population and the detection rate of epithelial abnormalities by cervical cytology (CC).

**Methods:** A total of 5416 conventional pap-smear tests collected between January 2009 and January 2012 from Tirana University Hospital Obstetrics-Gynecology “Queen Geraldine” were retrospectively analyzed.

**Results:** A total of 258 (4.8%) cases had epithelial abnormalities. The numbers and rates of epithelial abnormalities were as follows: Atypical squamous cell of undetermined significance (ASCUS;  $n=150$  [2.76%]); atypical glandular cell of undetermined significance (AGUS;  $n=8$  [0.14%]); low-grade squamous intraepithelial lesion (LSIL;  $n=87$  [1.6%]); high-grade squamous intraepithelial lesion (HSIL;  $n=10$  [0.18%]); and squamous cell carcinoma (SCC;  $n=3$  [0.05%]).

**Conclusion:** The prevalence of cervical cytological abnormality in our study was 4.8%. A larger community-based study may establish the exact prevalence of malignant and premalignant lesions, in order to plan for future screening.

**Keywords:** Cervical cancer, Cytology, PAP-smear.

## Introduction

Cervical cancer is one of the most common female malignancies with high mortality rates in developing countries. All over the world, the estimated new cases of cervical (uterine cervix) cancer were 493,000 and deaths were estimated at 274,000 in 2002 (1). According to the 2011 Census in Albania, the population was estimated at 2.8 million, while in 2009, Albania had a population of 3,639,453 citizens with 1,409,931 females (49.8%) (2).

The burden of communicable diseases is decreasing in general terms, but some infections (e.g. HIV/AIDS) are increasing. As of the end of 2008, however, Albania was still considered a low HIV prevalence country. Yet, there is an upward trend in the number of the newly diagnosed cases, and current estimates indicate higher numbers of undiagnosed cases. About 90% of HIV infections occur as a result of sexual contact. Most cases of HIV in Albania have been diagnosed among women and men aged 25-44 years (3). The epidemiological profile is changing though: levels of cardiovascular diseases, cancer and external causes of death are increasing.

In Albania, cervical and breast cancer are the most frequent cancers among women of all ages and the leading cause of cancer death among women (1). Currently, cancer accounts for 16% of all deaths in Albania and breast cancer is the second leading cause of death in women aged 35-54 years after the stomach cancer (4). Because no national cancer registry has been established in Albania to date, the data on the incidence and mortality rates for cervical cancer more likely represent estimates than a reliable reflection of the current situation. According to GLOBOCAN 2008, among the female population of 1.6 million with an estimated 124 cases of cervical cancer, the crude incidence rate was 7.8/100,000 (world age-standardized incidence rate: 7.1/100,000); and with an estimated 49 deaths from cervical cancer the crude mortality rate was 3.1/100,000 (world age-standardized mortality rate: 2.1/100,000) (1).

In addition, despite the fact that cervical cancer represents the second most common cancer among

women aged 15-44 years, and most cancers are diagnosed at stage III to IV, only 8% of women that have ever had a routine gynecological exam also had a Pap-smear (5).

There is no organized cervical cancer screening program in Albania. The Pap-smear is offered in some gynecological-obstetrical centers and private clinics in Tirana, the capital city (5).

In this framework, our purpose was to determine the prevalence of cervical cytological abnormalities in the Albanian population and the detection rate of epithelial abnormalities by CC.

## Methods

A total number of 5416 conventional pap-smear tests were collected between January 2009 and January 2012 at the University Hospital Obstetrics-Gynecology "Queen Geraldine", located in Tirana. Local ethical committee approval was obtained for the current study. Conventional samples (CC) were collected and smeared into the slide and immediately fixed with polyethylene glycol. The samples were evaluated on the Laboratory of Pathology, part of the maternity. The results were assessed as satisfactory and unsatisfactory. Satisfactory results were based on the 2001 Bethesda system and subdivided as "negative" (including "atypia, favors reactive"), "squamous cell atypia" (atypical squamous cells of undetermined significance [ASCUS] and atypical squamous cells, cannot exclude high-grade lesions [ASCH]), "atypical glandular cells" (AGUS), "low-grade squamous intraepithelial lesion" (LSIL), "high-grade squamous intraepithelial lesion" (HSIL), "squamous cell carcinoma" (SCC), and "adenocarcinoma".

The statistical analysis was performed by the SPSS software, version 20.0.

## Results

A total number of 5416 samples were retrospectively analyzed. The mean age of the participants was 42.8 years (range: 13-83 years). The mean age of the patients was 42.8 years (standard deviation: 10.9 years). Cytological findings of the smear results are listed in Table 1.

**Table 1. Cytological findings of 5416 conventional smear samples**

Cytological findings	CC number (percentage)
<b>Total</b>	<b>5416 (100)</b>
Satisfactory	5366 (99.07)
Unsatisfactory	50 (0.9)
Normal results	5156 (94.31)
ASCUS	150 (2.76)
AGUS	8 (0.14)
LSIL	87 (1.6)
HSIL	10 (0.18)
SCC	3 (0.05)

abnormalities were as follows: ASCUS ( $n=150/ 2.76\%$ ); AGUS ( $n=8/ 0.14\%$ ); LSIL ( $n=87/ 1.6\%$ ); HSIL ( $n=10/ 0.18\%$ ); and SCC ( $n=3/ 0.05\%$ ).

These data show that the unsatisfactory rate for the CC technique was 0.9% ( $n=50$ ). The main causes for CC inadequacy were samples obscured by red blood cells and inflammation. Normal cytology results were seen in 5156 (94.31%) of the samples. The most common reported benign result was chronic cervicitis with 2441 cases (45.1% of all samples).

A total number of 258 (4.8%) cases had epithelial abnormalities. The numbers and rates of epithelial

**Table 2. Cytology diagnosis correlation with age-group**

Cytology Diagnosis	Age- group (years)				Total
	<25	26-35	35-45	>46	
Positive CYTOLOGY	3.80%	5.50%	6.30%	3.30%	4.80%
Normal	449	1033	1686	1940	5108
AGUS	0	0	0	8	8
ASCUS	9	38	69	34	150
LSIL	9	22	40	16	87
HSIL	0	0	5	5	10
SCC	0	0	0	3	3
Total*	467	1093	1800	2006	5366

\*Total without unsatisfactory cases.

The patients (Table 2) were divided into four age-groups, 1 (<25 years), 2 (26-35 years), 3 (36-45 years), 4 (>45 years). The positively diagnosed cases increased by 5.5% at the age-group of 26-35 years, up to 6.3% at the age-group of 35-45 years, with most of LSIL stage. The precancerous lesions can evolve in cervical cancer, with the persistent cofactors such as smoking, partners, oral contraception, and the missing of cervical cancer screening, and if precancerous lesions are not treated, they can progress to cancer often in ages >46 years or less. The increasing age and abnormal cytology were significantly associated in our study ( $P=0.001$ ). The precancerous lesions were more frequent in persons less than 45 years old and cervical cancer was discovered often later than 45 years old. In our data, three cases with SCC were diagnosed (mean age: 59.3 years). From 2006-2010, the median age at diagnosis for the cancer of the cervix uteri was 49 years (13).

## Discussion

The screening coverage among women of reproductive age in Albania is extremely low, probably the lowest in the region: only 3.2% of women 15 to 44 years old reported having ever been screened with a Pap-smear, with additional differences observed among women in urban (4.9%) and rural areas (1.8%) (5).

In our study, altogether, 2.7% of women 15 to 44 years old reported having had a Pap-smear performed regularly every three years (4.3% of women in urban areas compared to 1.5% of women in rural areas) (5). Cost of health care, consults by the doctors, lack of perceived need (i.e., no symptoms), were the dominant concerns among these women (6). These issues kept women far away from routinely cervical screening. All these factors may be the reason of diagnosed SCC in advanced stage in Albania.

According to the IARC data, the incidence for

Albania is as low as 3.2/ 100,000 and ASR is 7.1/ 100,000 (7-9).

The overall prevalence of genital HPV infection in the Albanian population was found to be 15.1% and it ranged from 25.2% in women aged <30 years to 13.6% in women aged  $\geq$ 30 years (10,11).

As cervical smears are not routinely performed in Albania, it is difficult to obtain figures for the prevalence of preclinical disease. According to IARC data researches, the highest incidence rates of cervical cancer are observed in sub-Saharan Africa, Melanesia, Latin America, the Caribbean, South Central Asia, and Southeast Asia (12,13). Currently, the incidence rates in developed countries are generally low, with age-standardized rates less than 14.5/ 100,000. The incidence was 38.0/ 100,000 in the Second National Cancer Survey of the United States (14). Also, very low rates are observed in China (6.8/100,000) and Western Asia (5.8/100,000); the lowest recorded rate is 0.4/ 100 000 in Ardabil, northwest Iran (15).

In the present study, the detection rates for ASCUS and over lesions were found to be 4.8% ( $n=258$ ). Our results were also significantly lower than those of the multi-centered studies reported from Europe and U.S.A (7.0%-3.6%) (16).

The low prevalence of abnormal smears in Albania, compared with data from Western populations, could be due to the inherent bias of health awareness in the women who attended our hospital.

Beerman *et al.* (17) (0.87%) and Abdullah (20) (0.45%) found lower detection rates of ASCUS. Of all, 150 cases (2.76%) were classified as ASCUS in this study. Recently, Davey *et al.* (18) reviewed 56 studies and found higher detection rates (3.8%) of ASCUS with the CC examination. Moreover, Lawson *et al.* (19) found the ASCUS rate among low-income women as 5.2%.

The major cause of cervical cancer is Human papilloma virus (HPV), a large family of small double-stranded DNA viruses that infect squamous epithelia.

Genital HPV infections are very common sexually transmitted, and have the peak prevalence between ages 18 and 30 years. The figures reported in our study are very similar to those observed in many other countries and, hence, patterns of transmission in Albania are also likely to show little correlation

with promiscuity. In addition, because HPV can be transmitted by any skin-to-skin contact, condoms are not as effective in preventing HPV infection as they are in preventing other STIs that are transmitted in body fluids (21,22).

Exposure to tobacco smoking which is a co-risk factor for cervical cancer has become a great concern in Albania. Results from the Albanian Tobacco adult survey indicated a smoking prevalence of 64% among Albanian men and a continuously increasing smoking prevalence among women (5).

This difference may be due to a lower prevalence of risk factors reported by females, such as multiple sexual partners 1.1, smoking 3.9 % and the use of oral contraceptives 6.2% in the Albanian population (23). About 0.5% of women had sexual intercourse before the age of 15 years, and 15.4% of women had sexual intercourse before the age of 18 years (23). These factors are known to contribute to the disease in younger women.

Circumcision as a strategy to reduce the transmission of STIs and HIV has received a great deal of international attention, and there is increasing evidence that circumcision helps to reduce the risk of STIs and HIV in men.

The data shows that almost half of all men (48%) in Albania have been circumcised (23), and Albania is categorized as having an intermediate (20%-80%) male circumcision prevalence according to the WHO (24). Overall, 11% of women and 5% of men reported having an STI, an abnormal discharge, or a genital sore in the 12 months preceding the survey, and 12% of men reported having an STI or one of the other symptoms associated with STIs (23).

One of the most important risk factors for cervical cancer is the absence of screening with the pap-smear test which was first introduced in 1942 by Papanicolaou. Cancer is more common among the women who do not have regular pap-tests. SCC is seen 3.9 and 13 times more in a woman screened once in three years and 10 years, respectively, compared with the ones screened annually (25). In developed countries such as USA, 85% of women have at least one pap-test through their lifetime, but this rate is only 5% in the developing countries (26). We demonstrated that 50 cases (9.2%) out of 5416 CC examinations were unsatisfactory. The main

causes for CC inadequacy were samples obscured by red blood cells and inflammation. An “unsatisfactory” pap-test result (*unsats*) can be caused by a number of factors, including poor sample collection, obscuring inflammation or blood, use of lubricants, or interpretative errors (28). Although this unsatisfactory category constitutes 1% to 2% of all pap-tests, patients with *unsats* are more likely to have histories of abnormalities and are at increased risk of harboring precancer or invasive cervical cancer; therefore it is important to monitor them closely (28,29). Liquid-based cytology significantly reduced the proportion of unsatisfactory specimens from 1.1% to 0.3% and eliminated obscuring blood, poor fixation, cytolysis, and insufficient spreading of cells as causes of unsatisfactory results. All of these

characteristics offer the potential to improve the operational efficiency of cervical cancer screening in Albania.

This paper highlights the abnormalities seen in CC in the Albanian population. Abnormal CC prevalence rate in Albania is lower than that in India and Europe and North America. This might be due to sociocultural differences, lack of population-based studies, or a lower HPV prevalence. Further studies with larger numbers are required to: (i) fully assess the above mentioned factors, especially the role of HPV; (ii) determine the real prevalence of the cervical epithelial abnormalities in Albania, and; (iii) generate knowledge and inform more reliable and evidence-based policies in order to plan for future screening programs.

**Conflicts of interest:** None declared.

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