ETHICAL AND DEMOGRAPHICAL ISSUES IN SCREENING FOR CERVICAL CANCER – AN OUTLINE IN NORTH EASTERN REGION OF ROMANIA

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ETHICAL AND DEMOGRAPHICAL ISSUES IN SCREENING FOR CERVICAL CANCER – AN OUTLINE IN NORTH EASTERN REGION OF ROMANIA (Abstract): Aim: This study complements the national screening program for cervical cancer, implemented in Romania. Material and Methods: Inclusion criteria for this program of active detection of cervical cancer are women aged 25 to 64 years and exclusion criteria were other age groups and the diagnosis confirmed of cervical cancer. The testing was free and used the method of colored cervical smear Pap. Results: In 2013, 23,680 women were tested, that means only 10.13% of the total female population eligible for screening. In 2014, the test group was 6337 (one smear required retesting), of which 5852 were negative results and 484 positive results. Squamous cell abnormalities were detected in 433 women (6.84% of total group who attended the screening). Cervical smears with atypical squamous lesions were present at the most women included in the screening, regardless of age group (67.43%). The screening detected 21 lesions HSIL (4.84%), 2 HSIL with suspicion of invasion (0.46%) and 5 lesions of squamous carcinoma (1.15%). Conclusions: The presence of a small number of people compared to the female population eligible to the test screening may show the need for a better spread of notions about the screening and the afferent national program, for the population in northeastern Romania, considering the ethical issues that this test assumes. Keywords: CERVICAL SCREENING, CANCER, ETHICS, CERVICAL SMEAR, HUMAN PAPILLOMAVIRUS.

Cervical cancer is the fourth in frequency between the woman’s malignancy worldwide and the seventh of all cancers in both sexes, with 528,000 new cases detected in 2012, as GLOBOCAN reported. Regarding mortality, it is estimated 266,000 annual deaths worldwide in 2012, representing 7.5% of all deaths in women (1).

In the European region, Romania ranks first in the incidence and the mortality of cervical cancer. Regarding the incidence, it was 39.4‰ in 2012, according to GLOBOCAN, with 4343 new cases registered, a standardized age rate of 28.6 and a cumulative risk (0-74) 2.8. The distribution by age showed that the most affected were women 50-54 years (83.3‰), then those 55-59 years (80.9‰) (2).
There is a regional variation in the incidence of cervical cancer, with higher rates of over 30% of women in Maramures, Hunedoara, Arad, Constanta, Timis, Mehedinți, compared with rates below 10% recorded in Ilfov, Bucharest and Vrancea (3).

Regarding the mortality, its values were 17.3% in 2012, according to GLOBOCAN, with 1909 deaths, a standardized age rate of 10 and a cumulative risk (0-74) 1.2. Most deaths were recorded among women in the 70-74 years age group (39.2%), then those 65-69 years (38.2%) (2).

Cervical Intraepithelial Neoplasia (CIN) is a precancerous condition that may exist in one of three stages: CIN1, CIN2 and CIN3. If it is untreated, CIN2 or CIN3 (together CIN2 +) can progress to cervical cancer (4).

It is estimated that approximately 1-2% of women have CIN2 + every year. This rate is reported to be close to 10% of HIV-positive women (5).

Standard screening test is colored cervical smear Pap, and when cytology results are positive for CIN, the diagnosis is based on subsequent colposcopy, biopsy of suspicious lesions, followed by treatment only when CIN2 + lesions was confirmed by histopathology. This traditional method of screening requires high-skilled human resources and a substantial amount of laboratory equipment. In countries with low and medium socioeconomic level, because of the high cost of such screening programs based on cytology, national coverage is very low. Further, the monitoring of women with positive cytologic test and their subsequent testing by colposcopic and biopsy requires resources and trained personnel, which is a major problem in many such regions. Other blockages in cytology-based screening programs includes long distances between the woman's residence and equipped hospitals or clinics. An alternative approach to the detection and the treatment of lesions of CIN may be the method "Screening and Treatment" ("screen-and-treat"), where the treatment decision is based on a screening test rather than a histologically confirmed diagnosis of CIN2 + (4).

Molecular epidemiology data showed in 1991 that human papilloma viruses (HPV) are the main etiologic agent of cervical cancer, however, only in 1997 was established this fact. The study of HPV carcinogenic role continues to be a priority in research on the molecular biology of cervical cancer, especially as the number of viral genotypes identified and characterized is rising. According to a study of the female population in the North-East of Romania (Iasi), HPV16 was the prevalent oncogenic genotype (43.12%), followed by HPV18 (10.34%) and HPV31 (10.34%), and the distribution of age groups showed that the percentage of HPV positive patients was approximately the same (65% in the 17-29 years, 66.15% in the 30-39 years and 70.83% in the 40+ years). The authors of this study concluded that, although cytological screening test will not be replaced by HPV, the results on genotypes circulating will be used to develop an algorithm for effective monitoring and proper management of this type of infection (6).

Cervical Neoplasia has a progressive development, slight dysplastic changes progressing to severe dysplasias, then to carcinoma *in situ*, and without therapeutic intervention, to an invasion of squamous cell carcinoma. Screening is one of the methods of prevention (in the literal sense
of the word, screening is a protection against the danger), being a test of orientation that allows presumptive identification of the people affected previously by unknown diseases or who are exposed to risk factors. The success of screening methods and the increase of women's compliance on cervical cancer measures of prevention encourages the health systems makers to make these methods more accessible (7).

MATERIAL AND METHODS

The study comes as a complement to The National Screening Program for Cervical Cancer, implemented in Romania. Criteria for inclusion in this program of active detection of cervical cancer are women aged between 25 and 64 years and criteria for exclusion were the other age groups and the confirmed diagnosis of cervical cancer. Testing was free and used the cervical colored smear Pap method.

The program started in October 2012, and the number of women tested by the end of that year was 2915. In 2013, 23,680 women were tested, compared with eligible women population for cervical screening, of 233.615 (census provided by those networks validated until the present and it has been included in the budget estimates for 2013, as it stated in official documents of the Iasi Regional Oncology Institute) (10.13% of the total tested).

Total group of patients tested in 2014 was 6337 (1 smear required retesting), of which 5852 results were negative and 484 results were positive. In the first quarter were tested 2355 women (37.16% of the total group), in the second quarter were tested 1713 women (27.03%) and in the third quarter were tested 1119 women (17.66%) and in the last quarter of 2014 were tested 1150 women (18.15%).

The statistical analysis was performed using these software: MS Excel 2010 and EPI/INFO 7.

RESULTS

The distribution by age of the women group who presented at the IRO, for cervical smear collection indicated a preponderance of women by 40-44 years (936 - 14.77%) and 35-39 years (927 - 14.63%), and the least represented age group was the women by 50-54 years (587 - 9.26%) (fig. 1).

![Fig. 1. Age histogram](image-url)
Of all smears examined, 8.29% were positive for various neoplastic and atypical lesions (485 patients). The distribution by age groups of positive smears showed a predominance in women by 40-44 years and 55-59 years (15.87% each). Of the total harvested smears, the positive ones had the highest frequency in women by 55-59 years (9.64% of total smears collected at this age group) and 50-54 years (8.35%) (fig. 1, tab. I).

Squamous cell abnormalities were detected in 433 women (6.84% of total screening group). Cervical smears with atypical squamous lesions were present in the most women included in the screening, regardless of age group (67.43%). Even at 25-29 years, they (ASC-US) accounted for 56.51% of all smears. They were most often present in women by 55-59 years (73.91%). LSIL were present in 9.69% of the total group, and most often in women by 55-59 years (11.59%). It is noted that LSIL with atypical HPV (8.77% of total) were most often present in young women by 25-29 years (34.21%). The screening detected 21 HSIL lesions (4.84%), 2 HSIL with suspicion of invasion (0.46%) and 5 squamous cell carcinoma lesions (1.15%) (fig. 2).

**TABLE I**

<table>
<thead>
<tr>
<th>Indicador pentru leziuni intraepiteliale sau malignitate</th>
<th>Grupa de vârstă (ani)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25-29</td>
<td>30-34</td>
</tr>
<tr>
<td>Negativ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nr.</td>
<td>777</td>
<td>745</td>
</tr>
<tr>
<td>%</td>
<td>94.19</td>
<td>93.95</td>
</tr>
<tr>
<td>Pozitiv</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nr.</td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td>%</td>
<td>5.81</td>
<td>6.05</td>
</tr>
<tr>
<td>Total</td>
<td>825</td>
<td>793</td>
</tr>
</tbody>
</table>

**Fig. 2.** Results of cervical screening

With reference to abnormalities of glandular cells (ACG), the harvested cervical smears showed 51 lesions (0.8% of all women participating in screening),
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being more common in women by 35-39 years. Was found a case of adenocarcinoma in the 60-64 years age group and 2 anomalies in the favor of neoplasia (ACG-FN). However, most of these lesions types were ACG endocervical - NOS (significance unspecified) - 56.86% of ACG total lesions (fig. 3).

Fig. 3. Age group distribution of the anomalies of squamous epithelial cells in Pap’s test of the patients

DISCUSSION

The mission facing doctors specialists and family physicians, refers to presenting the benefits of the screening test, the patients included in the list or who come to medical examination. However, must be considered that the Pap test of cervical smear can have false negative results or false positive results or can be inconclusive, therefore, when planning to guide the patient to screening, doctors should reflect the ethical responsibilities of this test (8, 9).

Some researchers in social psychology and in ethics have mentioned the existence of a degree of emotional involvement of patients, reflected in particular by increased anxiety related to performing cervical screening. False positive results can cause importantly distress to patients, including on unnecessary treatment, the false negative results may cause emotional changes when diagnosis will be made later, and the false assurance of the woman that it would be in a state of full health. These negative effects of screening are probably quite frequent and can be the cause of anxiety and a long-term distress. To minimize these problems, the patient should be well informed and involved in cognitive processes to really take the best decision regarding the test screening (8, 10).

It was found that the reduction in incidence and mortality rates of cervical cancer was more pronounced in women who were tested for HPV compared to those who carried out only cytology followed by colposcopy. Treatment may still be overestimated in groups with high prevalence of HPV and therefore, this can get greater harm at the individual level. Adding col-
colposcopy, however, require a second visit to the specialist. However, in countries where there is already an adequate strategy for high quality screening, cytology (done in women with ASC-US or other more advanced lesions) is followed by colposcopy, regardless that the HPV test was previously performed (4).

The general reaction of women to a positive test screening or HPV testing was one of distress, anxiety and anger. Women have described that they felt shocked at receiving the news that they had a genital infection, that had previously acknowledged a little or not at all, due to lack of symptoms. This was combined with anxieties about the risk of cancer and concerns about further investigation or treatment for cervical intraepithelial neoplasia (CIN) and about fertility. These problems have been common in the groups of women with abnormal Pap smears, even in the absence of HPV testing. Some women described the degree of anxiety associated with intrusive thoughts and somatic reactions in the period in which they received their first screening test result. Much of the concern that arose related to the test result was positive was on the issue of sexual transmission of infection, this distress affecting their social, emotional and behavioral dimensions. Shock, embarrassment to the partner, feeling of shame and blaming, the stigma of having a sexually transmitted disease were common reactions in women with a positive Pap test, they used terms such as unclean, dirty, embarrassing, disgusting, immoral. Searching of a case and trying to understand what caused the positive result was a frequently behavior in women with abnormal Pap smear. Some women described the feeling of annoyance that a previous partner would be infected with a serious and carcinogenic virus, others can be considered guilty of acquiring infection because of negligence or an previously promiscuous behavior. Other women may accuse breach of trust in a partner who subsequently proved unfaithful. However, most of these women finally say that the source of the infections is another one, such as a previous partner (11, 12, 13).

The social, cultural, especially economic, religious and historical differences under the pressure whose live the women from anywhere in the world, reflect deeply on the issues and the ethical dilemmas that they carry with them when they are put in a position to consult a doctor on a gynecologist or gynecologic oncologist problem. The doctor must learn to recognize the social and ethical particularities of the community it cares for. These issues include the right to knowledge (the right to know), and inequalities in health insurances and services from that the patient can benefit (14).

Contrary to many significant advances purchased, the cervical cancer screening still may be associated with adverse events in national screening programs, requiring a balanced view of risk - the benefit of participating women. Thus, Weller notes that it would be appropriate to cover the following areas: social inequality, informed choice, the cost of screening when screening did not go well, given the new challenges of HPV testing and HPV vaccination (15).

Adding the answers to these dilemmas in a time capsule, along with the successes and the shortcomings of the program, known from past and present, can be interesting to anticipate the exciting directions and the ethical challenges that cervical
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cancer screening will be up to future generations.

CONCLUSIONS
Through our study, we found that a small number of people compared to the female population eligible, was present at the screening test, which shows the need for better spread of notions screening and the national program related, on the North-East Romania population, taking into account the ethical issues of this test.

REFERENCES