

## THE CERVICAL CANCER AND ITS OBSTETRICAL ANTECEDENTS

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**Keywords:** cervical cancer, parity, number of pregnancies, abortion, contraception

**Abstract.** Cervical cancer is an important public health issue, with a continuously increasing incidence. Identifying the main associated risk factors can lead to useful neutralizing measures, watching closely the risk factors: pregnancy, birth, sperm, genetic or hormone factors. The patients agreed to take part in the study by filling in a questionnaire sheet and after that they were investigated through clinic and paraclinic examinations. The screening was performed in “Elena Doamna” Third Clinic of Obstetrics-Gynecology Iași between 01.01.2001 and 31.12.2007 on a number of 145 women diagnosed with cervical cancer. The increase in the incidence of cervical cancer is associated with the increase of parity, abortions and the intensive use of contraceptive pills; the age when the sexual life begins also influences the incidence of cervical cancer.

### INTRODUCTION

Cervical cancer is diagnosed mainly in its advanced stages, when the treatment applied is sometimes inefficient; improving the clinic and paraclinic means of investigation has the purpose of establishing an early diagnosis; the prevention measures are an important problem, both for each hospital unit and also for the decision factors in the network of medical assistance (4, 5, 11).

### MATERIAL AND METHOD

The study was performed by a team of medical staff, in “Elena Doamna” Third Clinic of Obstetrics-Gynecology Iași, in the period of time between 01.01.2001-31.12.2007, on a number of 145 patients who had been diagnosed with cervical cancer in different stages.

The patients were questioned about their personal physiologic case history: the first menstruation, number of pregnancies and abortions.

They benefited from:

- genital examination and paraclinic examinations (hemoglobin-Hb, hematocrit-Ht),
- abdominal-pelvic ultrasound,
- colposcopy and biopsy,
- they were harvested smears for the bacteriologic and cytologic examination.

### RESULTS AND DISCUSSIONS

The hereditary collateral antecedents show us that over half (64%) of the women with cervical cancer had an increased risk of gynecologic neoplastic disease in the family.

#### ***Number of pregnancies. Parity.***

The increase of susceptibility can suggest the alteration of the nutritional status, the effect of the hormones on the cervix or on the expression HPV (human papilloma virus), or the effect of the trauma on the cervical epithelium during delivery.

Some studies suggest that the most important risk factor is the age when the woman has the first pregnancy and also the number of pregnancies. There is a very close relationship between invasive cancer and the young age of the first pregnancy and this relationship seems to be inter-dependent with the early age of the sexual debut, the presence of HPV and the subsequent births (3, 4, 7, 12, 15).

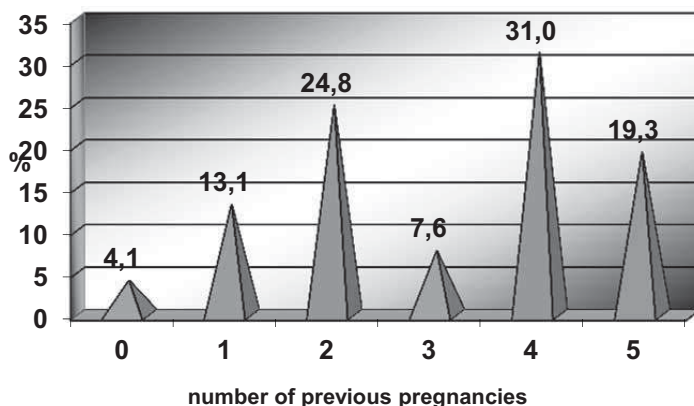
Pregnancy is a state of immunology depression state that favours the subclinic or clinic occurrence of HPV infection and also a physiologic situation that forces the patient to go for a gynecologic consult.

These parameters can have a distinct role in cervical cancer incidence, especially for teenagers. This statement is based on statistical analyses that showed that pregnancy and labour at young ages (14-20 year) represent a risk factor by the gravidic hormonal complex that is possible to be co-carcinogenic, but especially by viral infections and cervical trauma in an area of transformation that is still immature, of cylindro-pavimentous interference. The presence of a big number of pregnancies in the case history when compared with their absence could influence the risk status in cervical cancer (3, 4).

The study made revealed the fact that there is a difference among the number of patients with no pregnancies, one pregnancy or more than 4 pregnancies.

This fact can confirm that the bigger frequency of pregnancies can be an element of unfavorable prognosis in installing the risk of appearance and evolution of cervical cancer.

- no pregnancy - 6 patients-4,14%;
- one pregnancy -19 patients-13,10%;
- two pregnancies -36 patients-24,83 %;
- three pregnancies -11 patients -7,59 %;
- four pregnancies - 45 patients-31,03%;
- multiple pregnancies -28 patients -19,31%



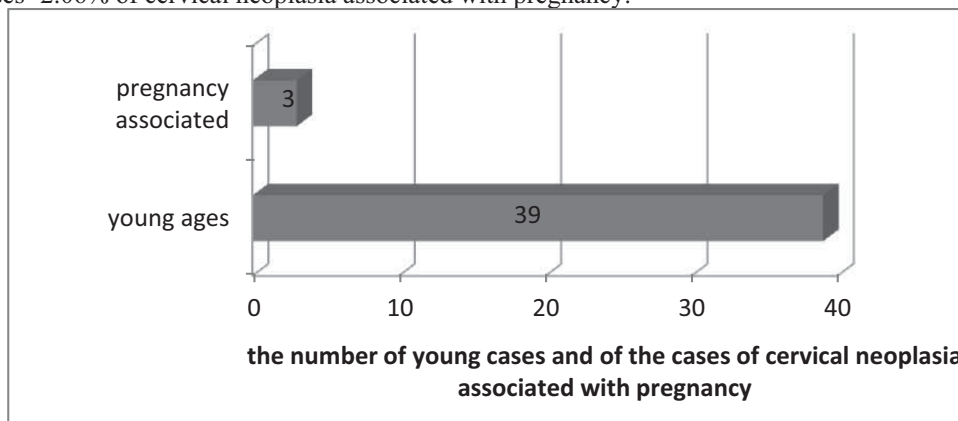
**Fig. 1. The repartition of cases depending on the obstetrical history**

The number of pregnancies seems to influence the incidence of the cervical cancer. A percentage of 57.93% is represented by the patients with a big number of pregnancies. This aspect can be considered as a risk factor both from the point of view of the endocrine changes induced by pregnancy and also from the point of view of an early start in the sexual life.

A bigger percentage of the mothers with twin pregnancies come from the rural area. Hence the conclusion that multiple pregnancies, if considered risk factors for the cervical cancer, act in a more powerful way in the rural area when compared to the urban area, probably because of the inferior quality assistance in child labour than in the case of the urban area.

The importance of the sexual life and of pregnancies in cervical cancer genesis, are explained by the presence of only 6 cases of women with no pregnancy.

Also in 39 cases -26.89% the women had child birth at a very young age and there were 3 cases -2.06% of cervical neoplasia associated with pregnancy.



**Fig. 2. The importance of sexual life and pregnancies in cancer genesis**

Some studies made for detecting the HPV prove the increase of its incidence during pregnancy when compared with the non-puerperal period, thus reflecting a decrease of the cell mediated immunity (6, 8, 13).

A direct effect of pregnancy on the vulnerable cervical epithelium was suggested as a result of the instability of HPV oncogenes that was induced by progesteron. This instability of the viral genome can facilitate the viral DNA HPV integration in the genome of the host, promoting the progression towards malignancy (2, 6, 9).

The nutritional factors during pregnancy can be correlated with the vulnerability of the cervical epithelium, because pregnancy is known as a status with folate depletion. This combination between the increase of HPV expression and the increase of the vulnerability for the transformation zone can explain the increasing risk of cervical neoplasia associated with parity increment (8, 11).

#### **OBSERVATION no 1.**

##### ***Pregnancy + cervical cancer***

The patient N.S., aged 33, is hospitalized for: metrorrhagia, abundant leucorrhoea, back pain.

Personal physiologic case history: first period= 14 years old, regular periods, pregnancies= 2; births= 1, abortions =0.

Vaginal examination with valves – increased volume of the cervix with the external orifice in transversal slot, half open; around the orifice there was an erosion of almost 1,5 cm, more extended towards the right edge; the liquid blood in the vagina was in moderate quantity and it was dark in colour, coming from the uterus.

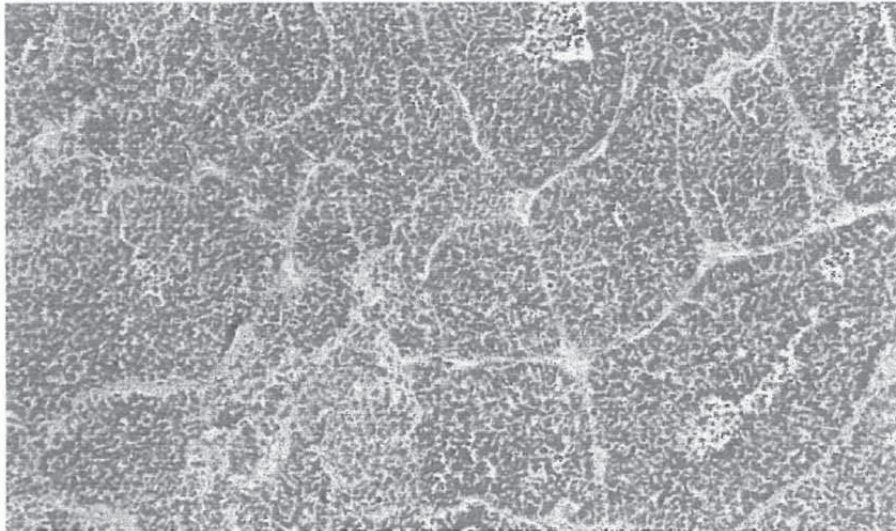
Digital vaginal examination– increased volume of the cervix; increased volume of the uterine body, with the upper limit at 5-6 cm above the pubic symphysis, soft consistency; flexible vaginal cul-de-sacs; free annexes.

Paraclinic examinations:

Hb = 8,5 g%;

Ht = 32 %

- Peripheral blood smear – make anisocytosis with hypochromia, relatively frequent red cells into the target, granulocytes prone to hypersegmentation.
- CDS (cytodiagnostic smear) - type V
- Pelvic-abdominal ultrasound – increased volume of the uterus, 9 weeks pregnancy, annexes can't be visualized, free Douglas cul-de-sac.
- Colposcopy- polyp with a diameter of 8 mm that was ulcerated, situated in an area of rugous mucosa, hyperemic, hemorrhagic, with an aspect of superficial shuffle.
- Biopsy – unkeratinized epidermoid carcinoma with small cells, invasive;
- Lymph nodes- fibrosclerosis, histiomonocytosis; ovaries with stromal hyperplasia, luteinic cyst, atretic cysts; we could see changes in the pregnancy.
- Hystology- pT1N0Mx
- Performed treatment - enlarged Wertheim type colpo-hysterectomy + pelvic lymphadenectomy.



**Fig. 3. Unkeratinized epidermoid carcinoma with small cells**

**OBSERVATION no. 2.**

***Pregnancy + cervical cancer***

The patient M.A. aged 32 was hospitalized for assistance at birth.

Diagnosis when hospitalized: 40 weeks pregnancy, cervical neoplasia.

Personal physiologic antecedents: first menstruation =14 years old, regular menstruations, pregnancies= 1; births= 0, abortions =0..

The pregnancy evolved normally, she had metrorrhagia in moderate quantity in the sixth month of pregnancy and she followed adequate treatment for it etc.

Personal pathologic antecedents: chronic cervicitis.

Genital examination:

Digital vaginal examination - increased volume of the cervix, of increased consistency;  
Vaginal examination with valves - increased volume of the cervix with the external orifice slightly open.

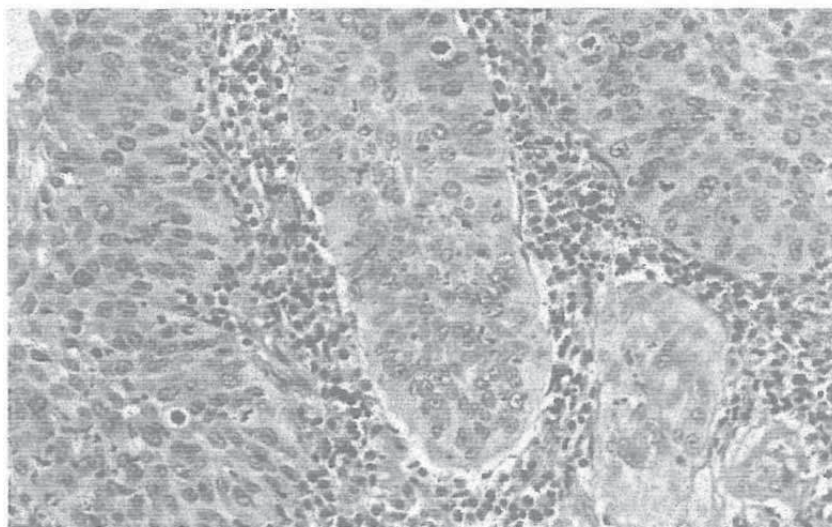
Paraclinic examinations:

- Hb = 11g%;
- Ht = 39%;
- FCD type V

Biopsy – unkeratinized epidermoid carcinoma with big cells, micro-invasive. The anatomico-pathological examination that was made postoperator showed: epidermoid carcinoma - 2mm; lymph nodes – with lympho-monocytary depletion; normal ovaries + salpingitis.

Hystologic – pTis – T1N0M0

Performed treatment – segmento-corporeal C-section surgery followed by enlarged Wertheim type colpo-hysterectomy + pelvic lymphadenectomy.



**Fig. 4. Unkeratinized epidermoid carcinoma with big cells**

Also speaking from the point of view of the significance of the sexual life, we could not find any case of virginity among the 145 cases of cervical cancer studied.

#### ***Abortions***

There are significant differences between the sick women and the witnesses in this respect.

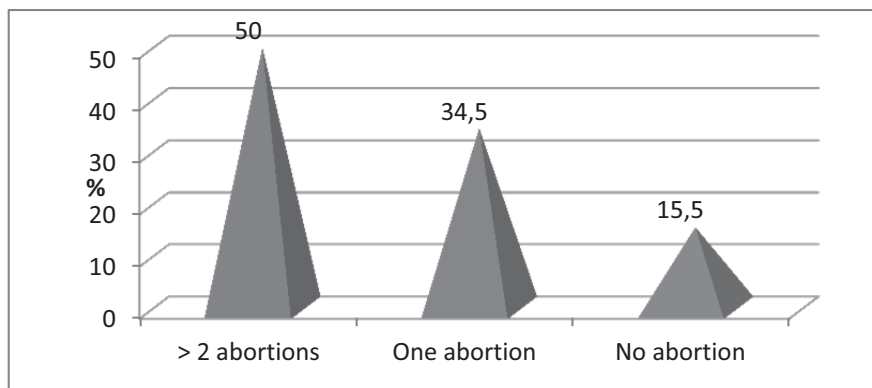
The number of abortions is difficult to be correlated with cervical neoplasia it is almost impossible to know for sure the exact number of abortions for the general population or even for the considered group because many of the women do not say the truth about it.

We studied pregnancies, births, quality of obstetrical assistance and abortions and we have found out that the obstetrical history of the sick women with cancer is significantly and under many aspects higher than in the case of the witnesses, but also that *it is not the number of births*



*the one generating a high risk factor of getting sick, but rather the low quality of the assistance in delivery.*

However, cervical neoplasia also appears in women who had a C-section when delivering the baby or in cases where the cervix remained malignant post-partum and where the role of the traumatic-cicatricial factor lacks. In these cases we will have to consider one or many of the outer factors we have mentioned before or eventually intrinsic factors.



**Fig. 5. Prevalence of obstetrical trauma by abortion patients with cervical cancer**

#### ***Hormonal factors***

The oncogenic risk of the long term use of oral contraceptive pills is very controversial. Many studies have shown an increased incidence of dysplasias in women who used oral contraceptive pills (1, 3).

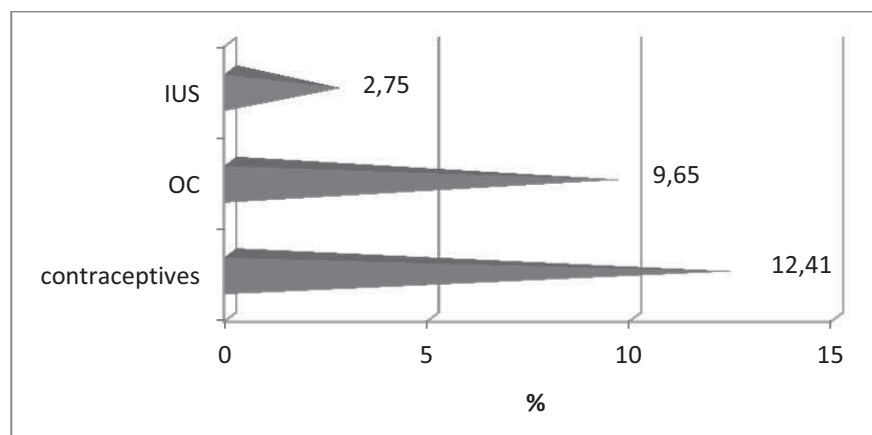
This difference concerning the risk of getting cervical cancer was assumed to have been caused by the characteristics of the sexual behaviour and also to a possible direct effect of oral contraceptive pills (OC) on the cervical metaplastic epithelium.

Women who take oral contraceptive pills frequently are subjected to screening more often, thus increasing the possibility of detecting the pre-invasive cervical lesions. But they do not use blocking methods and increase the risk of being exposed to sexually, transmitted carcinogenic agents.

The possible effect of the oral contraceptive pills on the cervical epithelium could not be demonstrated and neither could the way in which it might influence the risk of cervical cancer. For some women the risk can be increased by the activity of OC on the immature metaplastic processes. Also the OC cause a decrease in the levels of blood folate, causing megaloblastic changes in the cervical epithelial cells, which would increase the incidence of cervical cancer.

The relatively poor association between OC and cervical cancer is not strong enough to recommend the ending of OC consumption in women diagnosed with pre-malignant diseases. It is possible for the contraceptive agents to interfere in the more advanced stages of the carcinogenesis.

The small number of cases that used a contraceptive method (18 cases-12.41% out of which 14 women – 9.65% used OC and 4-2.75% IUS) is not significant.



**Fig. 6. Cases that used a contraceptive method**

An explanation could be the fact that, until 1989, any contraceptive method was officially banned, and after that, after abortions were legalized, the population was educated gradually in order to accept a contraceptive method and for a long time women preferred abortion as a method of family planning instead of another contraceptive method.

The data in the specialized literature reveal a slightly increased risk of getting cervical cancer to the people who use hormonal contraceptives – either by changing the position of the squamo-cylindrical junction, or by changing the sexual behaviour (6, 14).

On the other hand, oral contraceptive pills (used for more than 5 years) would increase the risk of cervical cancer even after the statistic removal of other factors that might be convergent, for example the sexual behaviour, especially for adenocarcinoma. The mechanism could be to amplify the transcription of HPV and to transform the cells infected with HPV (the genome segments that control these mechanisms having hormonal receptors for estrogen and progesteron).

## CONCLUSIONS

The obstetrical antecedents in patients with cervical cancer are more frequent than in witnesses.

The higher frequency of pregnancies is an unfavorable element of prognosis for installing the risk of appearance and evolution of cervical cancer.

The number of abortions is difficult to be correlated with cervical neoplasia because many of the women did not state the real number of abortions.

We noticed a reduced frequency of the patients who used a contraceptive method when studying the women in the study group (12.41%)

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