

# The Modern Chemical Theory of Ovarian Cancer Origin

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*Because of its histological and embryological complex development, the ovary can be the source of a large variety of tumors, ovarian cancer being the fifth female neoplasia as a frequency. A major clinical significance is that the ovarian tumor is asymptomatic for a long period of time. Ovarian proliferative pathology raises a number of important issues from both theoretical and practical point of view. The change in the therapeutic attitude, especially in the areas of surgery and chemotherapy, has led in the last decades to an improvement in the survival rate. Our retrospective study included the analysis of 64 patients with ovarian cancer. Ovarian neoplasms should have a multidisciplinary approach with individualized treatment for each patient. The long-term survival remains, however, the detection of the tumor at an early stage, the undetectment in the initial stages leading to a survival rate of 5 years less than 20%.*

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Because of its histological and embryological complex development, the ovary can be the source of a large variety of tumors, ovarian cancer being the fifth female neoplasia as a frequency. A major clinical significance is that the ovarian tumor is asymptomatic for a long period of time [1- 3].

The characteristic of ovarian tumors is underlined by the following findings: it shows a high degree of macroscopic polymorphism, starting from the periphery towards the center of the tumor and microscopically, sometimes in the same section encountering a multitude of aspects [4-6]. The incidence of the disease is increasing, the history and clinical aspects are nonspecific, and the varied nature of the patients, early diagnosis is difficult or even impossible to consider [7-9].

The staging is based on clinical, anatomopathological and surgical criteria. Surgery is followed by numerous relapses if it is not combined with the specific oncology [10-12].

Ovarian cancer should be resolved, if the situation so permits, by surgery [13-16]. Their confusing clinical appearance, diagnostic difficulties (many of them being confirmed only intraoperatively), histogenesis, the wide variety of anatomic-pathological forms, the staging and treatment of malignant ovarian tumors remain issues that must be solved by oncology gynecology [17- 19].

According to the chemical theory of ovarian oncogenesis, the transformation of normal cells into blastoma cells is caused by carcinogenic substances that enter the body from outside or are formed in the human body as a result of changes in metabolism [20-22].

Carcinogenic substances act slowly, not initially causing obvious changes in the tissues. Only after a fairly long latent

period occurs tumor growth phenomena, sometimes in places other than the one where the substances are administered [23- 26].

## Experimental part

### Material and methods

The study was conducted on a group of 64 patients admitted to the Obstetrics-Gynecology Clinic of the Clinical Hospital in Galati. All the cases were diagnosed with ovarian cancer in the period January 2014-December 2017.

The data obtained were statistically processed and consist of the objectification of risk factors, clinical diagnostic criteria, histopathological type and surgical technique applied. The statistical processing of this material, following the mentioned criteria, provides a basis for discussion on the complex problem of malignant ovarian tumors.

## Results and discussions

We divided the group into two large age groups with an increased incidence of ovarian cancer: group I represented the number of cases between 41-71 years, in which 36 cases were recorded, representing 56.25% of the total cases studied and group II aged 18-40 years represents a total of 28 cases and 43.75%, which is comparable to the percentage of cases recorded in the first group.

Ovarian cancer is the 9th neoplasia in terms of incidence in women and the fifth cause of death in women. The lifetime risk of a female invasive ovarian cancer is 1 to 71 and the risk of death is 1 to 95.

We tried to focus our risk factors on our cases, the results being shown in table 1.

Age	Limits average	18-76 years -46 years
Origin	rural	36 cases
	urban	28 cases
Marital status	married	60 cases
	unmarried	4 cases
Nulliparous		34 cases
Significant gynecological history		20 cases

**Table 1**  
RISK FACTORS IN OUR CASES

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There are two hypotheses regarding ovarian carcinogenesis, namely that of *Fathalla's uninterrupted ovulation* in 1971 and the *action of gonadotrophins*.

Ovulation that occurs between 20-29 years seems to have the most impact on risk factors. For each year of ovulation the cancer risk increases by 6%, and in the period 20-29 years by 20%. For each year of ovulation inhibited with combined oral contraceptives, the risk decreases by 8%, with the use period being significant.

Nuliparity, early menarche, late menopause increase the risk cancer, while women with high parity have a lower incidence of ovarian cancer, each birth gives a 10-16% reduction in risk, the effect diminishing over time. The interrupted pregnancies also provide protection.

Lactation reduces risk by suppressing ovulation, the effect being stronger in the months immediately following birth, reducing the risk by 1% for each lactation month. Reversed effect was reported for prolonged breastfeeding.

Ovarian cancer is a condition that does not respect an age limit, occurring at any age, but reaching a maximum incidence in women over 45 years old, pre- or post-menopausal. It seems that with the end of genital function, the ovary suffers, in a high percentage, processes of potentially malignant cell degeneration [27- 29].

The risk factors confirmed in the aetiology of ovarian cancer are age and genetic risk. The distribution by age group of the patients belonging to the studied group is shown in table 2.

**Table 2**  
AGE DISTRIBUTION OF PATIENTS

Age (years)	Case numbers	%
Under 20	2	3.12
21-30	8	12.50
31-40	18	28.12
41-50	8	12.50
51-60	14	21.87
61-70	8	12.50
over 71	6	9.39

In the literature, the highest percentage of cases is considered to be between 40-60 years, this age interval being considered as a risk factor [30-33]. On our cases, the incidence at these ages was 22 cases, representing 34.1% versus 60-70% as the percentage of published statistics in the literature.

In the second age group of the study group, 18 cases representing 64.28% were aged between 31-40 years. This makes us affirm that malignant ovarian tumors are constantly increasing in number in younger ages, causing a mutation in incidence towards the third decade of life. We therefore believe, based on the increased incidence at this age, that the maximum incidence is considered to be between 30-60 years, on our group representing 40 cases with a percentage of 62.50%.

On our studied group, we can say that the incidence of ovarian cancer by age group has three periods:

- Under 30 years, with low incidence;
- From 31 to 60 years of age when the incidence of ovarian cancer reaches its peak;
- After 61 years, when the incidence is again decreasing.

The study of the distribution of cases according to the patient origin shows, unlike other statistics, that in our clinic the number of the patients from the rural area (36-56.25%) was higher than in the urban area (28-43.75%).

The incidence of ovarian cancer is believed to be higher in unmarried, nulliparous women, as well as in those with a significant gynecological history (considered as risk factors).

12 cases had no pregnancy -18.75%, 18 cases, one pregnancy-28.12%; 16 cases, two pregnancies-25.00%; 6 cases, three pregnancies - 9.37%; 6 cases, four pregnancies - 9.37%; 6 cases, five pregnancies - 9.37%.

Because 46 cases representing 71.87% had a low number of pregnancies or were nuliparous, we can consider these parameters as risk factors.

The gynecological history, like menstruation disorders and surgeries on uterus were present in 20 patients (31.25%).

Menarche at 81.40% of the patients appeared at the age of 13-14 years.

Initial symptoms presented by the patients of our casuistry at admission were: abdominal pain 56 cases (87.50%), abdomen enlargement, 16 cases (25.00%), metrorrhagia, 12 cases (18.75%), lumbar pain, 10 cases (15.62%), fetid leucorrhoea, 8 cases (12.50%), palpable transabdominal pelvic formation 2 cases (3.12%), weight loss, 2 cases (3.12%), urine retention 2 cases (3.12%), fever 2 cases (3.12%).

Monosymptomatic manifestations were found in 38 cases (59.37%), being abdominal pain, metrorrhagia and leukorrhoeic leakage. 30 cases were polysymptomatic (46.87%), the associations of symptoms being: abdominal pain with abdominal volume increase, abdominal pain with metrorrhagia, abdominal pain with lumbar pain and metrorrhagia.

By reporting these symptoms to the time elapsed from their appearance to the presentation to the physician of the patients, it was found a time period between two weeks and two years.

The occurrence of malignancy signs: the fixation of the ovarian tumor, the folding of the Douglas recess, the intensive pain produced by the compression of the nerve tracts or the infiltration of the rectum, the bladder, ascites in some of our cases allowed for a certain diagnosis of cancer, but gave the patients a minimum chance of postoperative survival [34-38].

**Table 3**

DIAGNOSIS AT ADMISSION

Diagnosis at admission	Cases number
Ovar tumor	22
Pelvic tumor	14
Malign ovarian tumor	8
Extensive ovarian tumor	2
leiomyoma of uterus	12
pelvic peritonitis	2
Cystic metritis	4

In 32 cases (50%) preoperative diagnostic errors were in the order of frequency: pelvic tumor, fibromatous uterus, pelvic piperitonitis, cystic metritis.

Noteworthy, however, that these errors also address disorders of the genital sphere, which, have very close symptomatic symptoms [39- 42].

On our studied group, two large lots are distinguished:

- a lot with 24 cases detected in advanced stages (III and IV);

- an even larger lot of 38 cases that were detected in stage I.

- Stage II was present in only 2 cases.

The results of the study of these elements are shown in table 4.

Histological types of tumors was based on the *Histological Classification of Ovarian Tumors* (WHO) model.

In our study group, the type of tumor most commonly encountered was represented by epithelial tumors, which

**Table 4**

THE ELEMENTS THAT HAVE BEEN TAKEN INTO ACCOUNT FOR THE STAGING OF OVARIAN CANCER IN THE STUDIED GROUP

Intraoperative	Number of cases	%
ascites	14	21.87
vegetation on the surface	16	25.00
vegetation intracystic	4	6.25
subdiaphragmatic metastases	24	37.50

accounted for 84.90% of the total anatomopathological formations.

The type of surgery was performed according to the appearance of the lesion and the local conditions, the presence or absence of metastases, and the age of the patient (table 5).

**Table 5**

TYPES OF INTERVENTIONS IN CASE STUDIES

Types of interventions	Cases numbers	%
tumorectomy	10	15.60
unilateral anexectomy	6	9.30
bilateral anexectomy	10	15.60
subtotal hysterectomy + tumorectomy	4	6.20
subtotal hysterectomy + bilateral anexectomy	12	18.70
total hysterectomy + unilateral anexectomy	4	6.20
total hysterectomy + bilateral anexectomy	10	15.60
total laparotomy + biopsy	8	12.40

Surgical treatment was completed with chemotherapy and radiotherapy and postoperative evolution was good. Using this radio-chemo-surgical complex treatment, survival over 3 years was achieved in most patients.

Surgical treatment, as the initial and main treatment method, should provide a more accurate assessment of the lesions and staging, maximum possible excision, fixation of the adjuvant therapeutic protocol and prognosis [43 - 48].

## Conclusions

Observations made on the presented group regarding the high percentage of cases diagnosed at an early stage did not overlap with the literature data, constituting a histological surprise. Because the group presented is relatively small, the results obtained on the risk factors do not allow us to define a clear opinion on their significance in the etiopathogenesis of ovarian cancer, but the presence of some to a fairly large number of our cases makes us not ignore them.

Treatment should be multifactorial, chemotherapy and radiotherapy being adjuvant methods currently used.

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