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ECTOPIC PREGNANCY TREATMENT – OPTIONS IN OBSTETRICS AND GYNECOLOGY CLINIC SIBIU

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Abstract: *Ectopic pregnancy has a general incidence of up to 1-2%, being a frequent cause of morbidity in the patient of fertile age, being a pathology that endangers fertility, future health and rarely the vital prognosis of the patient. The aim of the study is to present the therapeutic possibilities and their results on a cohort of 135 patients during a period of 3 years, hospitalized in the Sibiu Obstetrics and Gynecology Clinic with the diagnosis of ectopic pregnancy. Materials and methods: A number of 135 patients were diagnosed in a period of 3 years. Epidemiological data and the results of medical or surgical, classic or laparoscopic treatment were analysed. Results: both conservative, medical and surgical treatment methods are favourable. Sometimes the failure of medical treatment requires surgical treatment. Conclusions: the most common way to resolve ectopic pregnancy, for hospitalized patients, is surgical treatment.*

INTRODUCTION

Ectopic pregnancy is a relatively frequent pathology, the incidence is described in the literature as being between 1-2% of all pregnancies.(1) It is an important cause of morbidity among patients of childbearing age, with an impact on fertility and last but not least on vital prognosis, being responsible for up to 5-6% of maternal mortality.(2) Mortality is increased in countries with difficult access to the secondary medical system (hospitals), the treatment of the pathology being, in an important proportion, surgical.

The most frequent location of the pregnancy is the fallopian tube, but it can be located practically anywhere: at the level of the ovaries, abdominal cavity, in the uterus cervix and rare variants with the pregnancy implanted at the interstitial level of the uterus, at the level of the uterine diverticulum or in the rudimentary horns of malformed uterus.(3)

AIM

Multiple therapeutic possibilities for ectopic pregnancy with different indications and limitations, advantages and disadvantages for each of the treatment methods are described in the literature.

The aim of the study is to present the therapeutic possibilities and their results on a cohoLaurart of 135 patients during a period of 3 years, hospitalized in the Sibiu Obstetrics and Gynecology Clinic with the diagnosis of ectopic pregnancy.

MATERIALS AND METHODS

The study was elaborated as a retrospective evaluation of the ectopic pregnancy admitted to the Sibiu Obstetrics and Gynecology Clinic over a 4-year period between 2019-2022 were analysed and a number of 135 cases of ectopic pregnancy were diagnosed.

The data were obtained from the computer database of the hospital and the following epidemiological parameters were analysed: age, distributed over the analysed years, location in the fallopian tube and the method of diagnosis. The mode of admission, the treatment, the condition at discharge were also evaluated.

RESULTS

The distribution over the 4 years can be seen in table no.1. In 2021, a number of 53 cases were registered, which represents 39.25% of the total, and the minimum was recorded in 2022 with 17 cases (12.59% of the total) because the 2022 was not completely evaluated.

Table no. 1. The distribution of the patients according to the year

Year	Number of cases	%
2019	28	20,74%
2020	37	27,40%
2021	53	39,25%
2022	17	12,59%
Total	135	100%

One of the important parameters to be evaluated is the period of amenorrhea until the diagnosis can be done. The greater the amenorrhea, the less the possibility of drug treatment, and the solution of the pathology is a surgical one, affecting the integrity of the fallopian tube with the ectopic pregnancy. The amenorrhea period until presentation of the patient is presented in table no. 2.

Table no. 2. The amenorrhea period until diagnosis

Weeks of amenorrhea	Number of patients	Percentage
4	1	0,74%
5	5	3,70%
6	20	14,81%
7	16	11,85%
8	5	3,70%
9	3	2,22%
10	1	0,74%
14	1	0,74%
Unspecified	83	61,48%

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The age for developing an ectopic pregnancy is the age of maximum fertility, when patients try to procreate. Advanced age, over 35 years predisposes to ectopic pregnancy. We have analysed the incidence of cases by age group. The maximum incidence is reported in the age group between 26-35 years, with a percentage of 57.77% of the total. The distribution of the patients according to the age is presented in table no. 3.

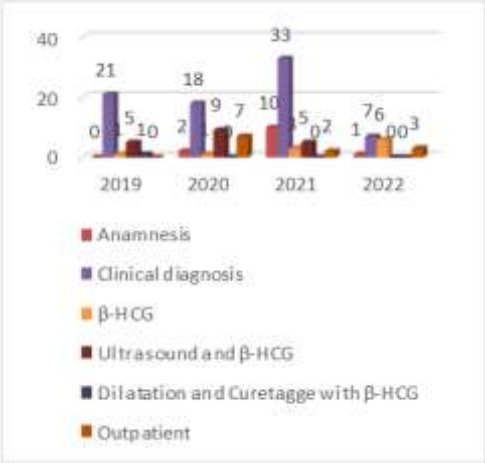
Table no. 1. The distribution of the patients according to the age

Age group	Number of cases	Percentage
Below 18 years old	4	2,96%
19-25 years	28	20,74%
26-35 years	78	57,77%
Above 35 years	25	18,51%

Usually the methods of diagnosis were the measurement of β-HCG in dynamics or trans-vaginal ultrasound. To these were added the anamnesis, the general and local objective examination and other laboratory analyses. Dilation and curettage followed by β-HCG in dynamics was also o method for exclusion of missed abortion and differential diagnosis. Some patients presented with the diagnosis already established in the outpatient clinic, most of the time in a specialized service. The data are presented in figure no. 1.

From the total number of cases, a percentage of 52.59% (71 cases) were found of right tube and 42.22% (57 cases) on the left tube.

Figure no. 1. The modality of diagnostic according to the year



Among the risk factors described for tubal pregnancy, some of them were discovered in the investigated patients: scarred uterus after cesarean section, previous ectopic pregnancy, uterine fibroids, use of intrauterine devices, assisted human reproduction, age over 40, smoking, chronic pelvic infections . An analysis of the number of cases for the associated factors are presented in table no. 4.

Table no. 4. Risk factors fund for the ectopic pregnancy patients

Risk factors	No. of cases	Percentage
Scarred uterus	8	5,92%
Chlamydia infection	2	1,48%
Fibroids	3	2,22%
Previous ectopic pregnancy	2	1,48%
C&D	1	0,74%
IUD	4	2,96%
Assisted human reproduction	1	0,74%
Smoking	3	2,22%
Advanced maternal age	7	5,18%
Total	**31**	**22,96%**

The therapeutic possibilities for the diagnosed ectopic pregnancies were: administration of methotrexate, either in a single dose or repeated depending on the evolution of β-HCG titers, surgical treatment (open surgery, laparoscopic salpingectomy and laparoscopic salpingotomy) associated with different other surgical operations such as myomectomy, adnexectomy, adhesion removal, etc. The data are presented in figure no. 2 for uncomplicated pregnancies and in figure no. 3 for complicated pregnancies.

Figure no. 2. The treatment possibilities in uncomplicated ectopic pregnancy

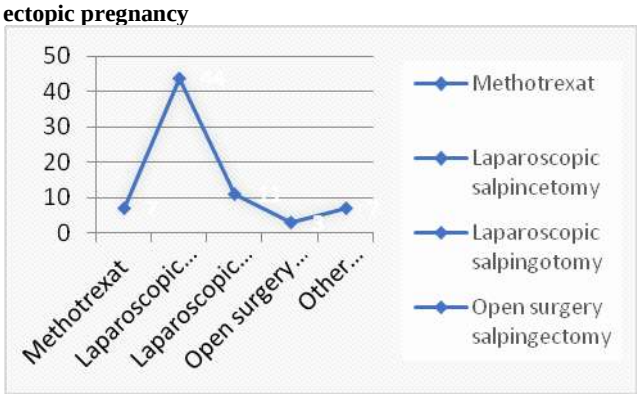
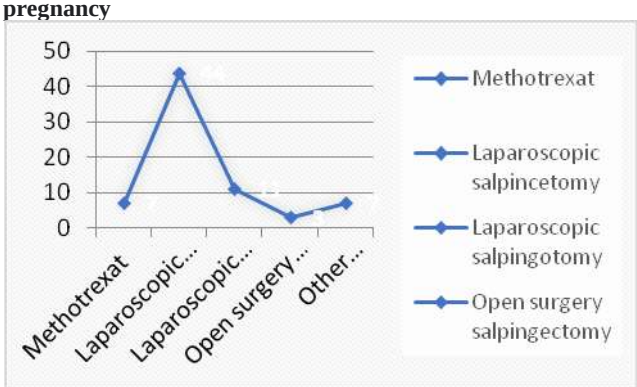


Figure no. 3. The treatment possibilities in complicated ectopic pregnancy



The average duration of hospitalization was 4.66 days. The length of hospitalization depends significantly on the length of time from the suspicion of ectopic pregnancy until the final diagnosis, the chosen treatment modality, the duration being longer in medical, conservative treatment and shorter in surgical treatment, also influenced by the presence of associated risk factors and associated pathology, the patient's condition at presentation, and the postoperative evolution.

DISCUSSIONS

Considering the average number of births in the Sibiu Obstetrics and Gynecology Clinic, which varies between 2000 and 2500 births per year, the percentage of ectopic pregnancies diagnosed in the clinic is similar to the data in the literature, between 1 and 2% of all pregnancies.(1)

A parameter analyzed in the study is that of the gestational age, calculated after the period of amenorrhea. Gestational age is very important for choosing the treatment method. The conservative therapeutic possibilities are suitable only for small gestational ages, the older the gestational age, the more likely is the treatment of an ectopic pregnancy complicated with hematocele or even rupture.(4) It is observed that the most frequently encountered gestational age is 6-7 gestational weeks. With the exception of cases in which the pregnancy is determined by assisted human reproduction treatment, it is

unlikely to actively investigate for the detection of a pregnancy before 1 week of amenorrhea.(5)

With regard to the distribution of patients by age, it is natural that the maximum incidence of the pathology should be around the age of 25-35 years (57.77%), this being the average age at which couples try to procreate. Of course, the incidence is relatively high and after this age, advanced maternal age is an independent risk factor in increasing the incidence of ectopic pregnancy. The same trend can be found in the data from the literature.(6)

Regarding the risk factors for ectopic pregnancy, 3 of them deserve special attention: scarred uterus, antecedents of ectopic pregnancy and advanced maternal age.

The scarred uterus implies, at the level of the scar, an area with the endometrium with significantly modified qualities in order to implant the pregnancy. The presence of a scarred uterus is a risk factor for ectopic pregnancy consistently recognized in the literature.(7,8,9) This is frequently the place of implantation of the pregnancy and mostly results in pathological placentas such as the spectrum of placenta accreta. If the location of the scar is in the uterine cavity, the evolution is most often towards placenta paevia. If the localization is at the cervical level, there will be a pregnancy with cervical localization, one of the most severe possibilities of the evolution of an ectopic pregnancy due to the importance of hemorrhage and the significant risk of hysterectomy with the loss of the uterus and reproductive capacity.(10)

One of the important risk factors for ectopic pregnancy is the previous ectopic pregnancy. The implantation process involves significant invasion in the depth of the tissue which is physiologically limited in the normal endometrium. Implantation in other areas of the genital sphere that does not have an endometrium implies, regardless of the method of solving the ectopic pregnancy (treatment with Methotrexate or conservative surgery), a healing process with scar tissue, with areas of stenosis at the level of the tubes or uterine scar tissue as was described in the previous paragraph. They predispose to a new ectopic pregnancy in the next pregnancy.(11,12)

Advanced maternal age represents a risk factor for ectopic pregnancy through a multitude of pathological aspects that accompany advancement in age. The risks that advanced maternal age brings are represented by the presence of a scarred uterus, often after myomectomy, history of repeated pregnancy loss, pelvic inflammatory disease and, last but not least, genetic pathology with an increased risk of ectopic implantation of embryos.(13,14)

Conservative, medical treatment of ectopic pregnancy can be done with Methotrexate. Methotrexate administration is cost effective compared to surgical treatment.(15) The beginnings of drug treatment of ectopic pregnancy date back to the 1980s and it has been proven that it leads relatively quickly to the resolution of the trophoblast and the healing of the ectopic pregnancy. The main limitations are gestational age and more studies show that it can also be used successfully in pregnancies in which cardiac activity appears.(16) Methotrexate can be administered orally, intravenously, intramuscularly or injected directly into the gestational sac under laparoscopic control in case of cornual ectopic pregnancy or cervical. Before the administration of the treatment, it is necessary to collect a complete set of analyzes including the blood count, serum creatinine, B-HCG, liver markers, blood group and Rh.

The usual dose is 50 mg/m2 body surface and after the initial collection of β-HCG will then be collected on days 4 and 7 after methotrexate administration. Approximately 14-20% of patients will require a repeat dose if the β-HCG level falls by less than 15% after administration of methotrexate. A maximum of 4 doses of methotrexate can be administered, and the multiple therapy will be accompanied by the simultaneous administration of Leucovorin (folinic acid), an antagonist of methotrexate to reduce the severe adverse effects that can occur with multiple doses of methotrexate.(17) The main side effect of Methotrexate administration is neutropenia.

The upper limit of β-HCG values at which Methotrexate can be administered is 3500 IU/l, which is also the reason why the number of pregnancies treated in the clinic is relatively low. The patient must present herself relatively quickly for diagnosis in order to be able to access drug treatment.

The surgical treatment of choice for ectopic pregnancy is laparoscopy. It is a minimally invasive technique that does not require large incisions in the abdominal wall and, secondarily, reduced healing processes with reduced frequency and severity of complications.(18) The main laparoscopic procedures are, depending on the size of the pregnancy, its complicated or uncomplicated aspect, the obstetric history and the patient's desire to preserve her reproductive capacity salpingectomy and salpingotomy with trophoblast evacuation and rigorous hemostasis. The main treatment method used in the clinic is laparoscopic surgery, but sometimes this technique is not accessible during the guards, or the skills of the operator do not allow the laparoscopic approach. There are a multitude of studies that highlight the advantages of minimally invasive surgery compared to classic, open surgery, its value in surgical trauma, postoperative recovery and cost effectiveness being unanimously recognized.(19,20)

The average duration of hospitalization was 4.66 days. The length of hospitalization is significantly influencing the costs for each patient. The duration is significantly longer in medical, conservative treatment and shorter in surgical treatment, also influenced by the presence of associated risk factors and associated pathology, the patient's condition at presentation, and the postoperative evolution.

The advantages of the rapid dosing of beta HCG and its dynamic monitoring lead to a much earlier diagnosis of pregnancy and the possibility of administering Methotrexate, which is cost effective and in certain health systems can be administered and monitored as an outpatient basis. However, the administration of Methotrexate is not without risks and side effects and with a failure rate that reaches up to 25% of cases with the need for emergency hospitalization, rescue for surgical treatment in case of complications. According to data from the literature, ectopic pregnancy represents a significant burden on health systems, for example, in the United States of America, approximately 100,000 patients are managed annually with a total cost of up to $1 Billion.(21,22)

CONCLUSIONS

1. Ectopic pregnancy is a pathology frequently diagnosed and treated in the Sibiu Obstetrics and Gynecology Clinic, the incidence being similar to that in the literature
2. The main treatment methods used are the administration of Methotrexate and laparoscopic surgery
3. The average duration of hospitalization is similar to that of the studies found in the literature

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