THE ROLE OF RISK FACTORS IN THE INCIDENCE AND RECURRENCE OF ECTOPIC PREGNANCY

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ABSTRACT
The increase in the incidence of ectopic pregnancy in the last 20 years, with the serious compromise of the woman's obstetric future and the life-threatening complications caused by it, makes ectopic pregnancy a very current problem, frequently encountered in Obstetrics-Gynecology clinics.

The aim of this study is to compare how risk factors and management can influence the incidence and the risk of recurrence of ectopic pregnancy.

This paper presents a prospective case-control study for 65 patients, who have been diagnosed serologically and ultrasonically. In the present study, the most common risk factors involved were: pelvic inflammatory disease (46%), ectopic pregnancy (20%), smoking (85%), abortions (55%), and abdominal surgery (43%). In the group of patients studied, patients required surgical and medical treatment, and also a management of expectation.

The risk factors that influence recurrence were smoking (100%), pelvic inflammatory disease (84.6%), abortions (53.8%), abdominal surgery (46%). By the type of surgery (laparoscopy or laparotomy), the risk of recurrence varies between 6 and 10% and does not seem to be influenced by it.

Keywords: incidence of ectopic pregnancy, recurrence of ectopic pregnancy, anxiety after ectopic pregnancy

INTRODUCTION

In recent years, there has been an increase in the incidence of ectopic pregnancy in women of reproductive age, explained by the existence of many risk factors underlying its occurrence and whose share has increased recently. Both physiological and pathological history are among the risk factors for ectopic pregnancy (1,2).

Complications resulting from voluntary termination of pregnancy, infections, as well as post-abortion endometritis can cause irreversible morphological lesions that favor, in the future, the occurrence of ectopic pregnancy. Specialized studies show that personal pathological history of ectopic pregnancy increases the risk of a new ectopic pregnancy (3). Appendectomy, cholecystectomy, tubal ligation, tubal plasies, pelvic interventions (ovarectomies, myomectomies), as well as cesarean operations result in the appearance of intra-abdominal adhesions that can change the tubal anatomy, favoring the appearance of ectopic pregnancies (4). The risk of ectopic pregnancy is doubled by the use of tobacco. Nicotine alters the number and affinity of adrenergic receptors, alters tubal motility and inhibits ciliary activity (5). In vitro fertilization and the use of ovulation stimulators cause endocrine imbalances (6,7).

Immunological tests in conjunction with ultrasound (transabdominal and transvaginal) can make the diagnosis very accurately. All women in the reproductive period who have the Crossen triad (abdominal pain, metrorrhagia and amenorrhea) should undergo paraclinical tests to confirm or refute the diagnosis of ectopic pregnancy (8).

Curative behavior includes both medical treatment and conservative or radical surgical therapy. From the point of view of surgery, the treatment is classified into classic and laparoscopic interventions, and from the point of view of the integrity of the female genital tract, the interventions can be
conservative (linear salpingostomy and tubal evacuation of the conception product).

The study aims to compare how the risk factors and treatment methods can influence the recurrent risk, reducing anxiety.

**MATERIAL AND METHOD**

This paper presents a prospective case-control study, conducted in the Bucharest Maternity Hospital - Bucharest between January 1, 2018 and December 31, 2018.

During the study, 65 patients with ectopic pregnancy were hospitalized. The diagnosis was established on the basis of clinical examination and specialized investigations, in accordance with current protocols.

Several parameters were evaluated: age, parity, risk factors, location, treatment, psychological impact of ectopic pregnancy on patients.

Inclusion criteria were:
- Pregnancy test positive;
- The absence of ultrasound images of intrauterine sac, or extraterine ovarian sac with or without embryonic elements, or equivocal intrauterine ultrasound images;
- hospitalized patients;
- Treatment-compliant patients.

All data were collected from hospitalization sheets and have been processed using Microsoft Excel. All data obtained were processed while maintaining the confidentiality of patients’ personal data. Every patient that was enrolled in our study signed an informed consent, and the study was approved by the Ethical Committee.

**RESULTS**

As the youngest patient was 18 years old and the oldest 44 years old, the group of patients was divided into age groups.

In the study group there is an incidence of 3.8% of ectopic pregnancy in relation to the number of births in the evaluated period (65 ectopic pregnancies per 1,693 births).

The evaluation of the data shows a much lower incidence of ectopic pregnancy after 40 years (9%) and before 20 years (6%) compared to other age groups.

The first physiological antecedent that was followed in this case was multiparity. Thus, in the studied group there were 24 nulliparous, 22 primiparous and 19 multiparous.

The vast majority of risk factors for ectopic pregnancy are included in the pathological history. Among these risk factors, the present study assessed number of abortions, number of ectopic pregnancies, number of abdominal surgeries, smoking, using of ovulation stimulants, sexually transmitted diseases.

Number of abortions – 55% of patients had a history of one or more abortions.

| Number of abortions | Number of cases | Percentages |
|---------------------|----------------|-------------|
| 0                   | 29             | 44.61%      |
| 1                   | 12             | 18.46%      |
| 2                   | 6              | 9.23%       |
| 3                   | 8              | 12.30%      |
| ≥4                  | 10             | 15.38%      |
| Total               | 65             |             |

Number of ectopic pregnancies in the history – The presence of ectopic pregnancy in a personal pathological history in 20% (13 cases) of hospitalized patients.

Abdominal surgeries – The present study highlights the presence of a history of abdominal surgery (mostly appendectomy and cesarean section) in 30 patients (43%).

| Intervention                              | Number of cases | Percentages |
|-------------------------------------------|-----------------|-------------|
| Cesarean section                          | 17              | 26%         |
| Other interventions                       | 11              | 16%         |
| Cesarean section and other interventions   | 10              | 15%         |
Smoking – A worryingly large number of patients in the study, 55 (85%), used tobacco and only 10 (15%) were non-smokers.

Ovulation stimulators – Of the total group of 65 patients, three patients (4.61%) used ovulation stimulants.

**TABLE 4. Risk factors in the occurrence of ectopic pregnancy**

| Risk factors                        | Number of cases | Percentages |
|-------------------------------------|-----------------|-------------|
| Abdominal surgery                   | 28              | 43.07%      |
| Pelvic inflammatory disease         | 30              | 46.15%      |
| Sexually transmitted diseases       | 4               | 6.15%       |
| Smoking                             | 55              | 84.61%      |
| Ovulation stimulants                | 3               | 4.61%       |
| Abortions                           | 36              | 55.38%      |
| Nulliparous                         | 24              | 36.92%      |
| Ectopic pregnancies in the history  | 13              | 20%         |

Among the risk factors for ectopic pregnancy, smoking is the most common culprit in the etiology (55 cases), followed by abortions, pelvic inflammatory disease and surgery, while sexually transmitted diseases (4 cases) and ovulation stimulants (3 cases) were the least common.

In the group of patients studied, the localization was predominantly tubal and a pregnancy with ovarian localization. No abdominal pregnancies were reported. At the same time, there was a case of hemoperitoneum in a patient with a uterine curettage on request performed previously (7 days before) for 7 weeks of pregnancy. In that case we could not classify as heterotopic pregnancy, not having sufficient anatomical-pathological data for this.

**TABLE 5. Anatomical location of ectopic pregnancy**

| Anatomical location | Number of cases | Percentages |
|---------------------|-----------------|-------------|
| Ampullary           | 20              | 30.76%      |
| Infundibular        | 32              | 49.23%      |
| Interstitial        | 2               | 3.07%       |
| Isthmic             | 5               | 7.69%       |
| Corneal             | 1               | 1.53%       |
| Ovarian             | 1               | 1.53%       |
| Cervical            | 2               | 3.07%       |
| Post-cesarean scar  | 2               | 3.07%       |

The investigations used to confirm the diagnosis of ectopic pregnancy in the Bucur Maternity Clinic are ultrasound and βHCG dosing.

The therapeutic management of ectopic pregnancies diagnosed in patients in the study group is mainly surgical (69% of patients), followed by medical management (25%), pregnancy aspiration (4%) and expectation management (2%).

At the level of the studied group, 13 cases from 65 were recurrent. How risk factors influenced the recurrence of ectopic pregnancy in these cases is reflected in table 6.

**TABLE 6. The recurrence of ectopic pregnancy according to risk factors**

| Risk factors                        | Number of cases | Percentages |
|-------------------------------------|-----------------|-------------|
| Smoking                             | 13              | 100%        |
| Pelvic inflammatory disease         | 11              | 84.61%      |
| Abortions                           | 7               | 53.84%      |
| Abdominal surgery                   | 6               | 46.15%      |

The recurrence of ectopic pregnancy depending on treatment is 16% (11 patients) after surgical therapy and 3% (2 patients) after medical therapy.

**TABLE 7. The recurrence of ectopic pregnancy depending on treatment**

| Treatment            | Number of cases | Percentages |
|----------------------|-----------------|-------------|
| Salpingectomy        | 5               | 7%          |
| Salpingostomy        | 6               | 9%          |
| Methotrexate         | 2               | 3%          |

According to the type of intervention it is 6% (4 patients) after laparoscopic intervention and 10% (7 patients) after laparotomy. The risk of recurrence of ectopic tubal pregnancy does not seem to be influenced by the surgical procedure.

The present study revealed in 95% (61 cases) the presence of mild anxiety, especially in patients with recurrence of ectopic pregnancy.

**TABLE 8. Anxiety after ectopic pregnancy**

| Anxiety                  | Number of cases | Percentages |
|--------------------------|-----------------|-------------|
| First ectopic pregnancy  | 48              | 73.84%      |
| Recurrent ectopic pregnancy | 13              | 20%         |
| Total                    | 61              |             |

It is imperative to support the patient and family, provide informational materials on the consequences of ectopic pregnancy and future fertility, display an empathic attitude, encourage the patient to express doubts, fears, and the involvement of the psychologist and patient support groups on supporting the patient and her family.

**DISCUSSIONS**

The discussions are generated following the comparative study carried out between the group of evaluated patients hospitalized in Bucur Maternity and the specialized literature.
The occurrence of ectopic pregnancy in the studied group of patients is predominantly in primiparous and multiparous patients (a total of 41 cases) compared to nulliparous patients (24 cases), and as an age range the study showed that ectopic pregnancy is a frequent pathology of reproductive age. In this case our results were not similar to those of other studies. (9)

In the present study, the most common risk factors involved in the etiopathogenesis of this condition were: smoking, abortions, a history of pelvic inflammatory disease, abdominal surgery and ectopic pregnancy. The risk factors included in our study were similar to those highlighted in the literature (10-15). Due to the diverse etiopathogenesis of ectopic pregnancy, prevention should address the risk factors involved in its occurrence: active and correct treatment of inflammation and genital infections, eradication of endometriosis, treatment of sexual hormonal disorders, combating induced abortions, avoidance of gynecological adhesions in surgery conservative, as well as a rigorous selection of cesarean-terminated births (16).

As a location of the ectopic pregnancy, the tubal location predominates in 91% of cases (59 patients), the non-tubal location amounting to 9% (6 patients), in accordance with the literature (17,18).

The risk of recurrence of ectopic pregnancy appears to be influenced by the mode of treatment, similar to the literature (19). In our study, recurrence of ectopic pregnancy was 16% (11 patients) after surgical therapy and 3% (2 patients) after medical therapy.

According to the type of intervention -laparoscopic or laparotomy -the risk of recurrence of ectopic tubal pregnancy does not seem to be influenced by the surgical procedure. Other studies reveal a lower risk for laparoscopy (20,21).

The diagnosis of ectopic pregnancy can have a major impact on a woman’s mental health, especially if the conception took place after much effort. Pregnancy loss can have devastating effects on physical and mental health by needing the unconditional support of family, partner, friends and the support provided by medical staff. Post-traumatic stress is all the greater as the woman has suffered a recurrence of ectopic pregnancy, which significantly reduces the chances of a later conception (22,23). Published studies on the psychological impact of ectopic pregnancy on patients are few, the medical world being focused on the discovery of new treatment methods and surgical techniques for early detection and treatment with minimal physical consequences of ectopic pregnancy, leaving in second place, somehow, the assessment of posttraumatic stress felt by the patient. These studies showed that psychological morbidity is higher in patients who have had ectopic pregnancy compared to patients who have had an abortion, with anxiety and even depression persisting even 3 months after the triggering event (20% showing signs of anxiety, and 5% signs of depression (24,25).

CONCLUSIONS

Even if the study group was not numerically significant, most of the evaluated indicators were in line with the results published in the literature.

Ectopic pregnancy is the leading cause of maternal death during the first trimester of pregnancy. A better understanding of risk can help prevent its occurrence.

With earlier diagnosis, medical therapy with methotrexate can be offered and surgery avoided in some women, though the best regimen remains unclear. In the surgical management of ectopic pregnancy, the benefits of salpingectomy over salpingostomy are uncertain. Although there have been advances in the management of ectopic pregnancy there are still questions to be answered.
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