

CHARACTERIZATION OF THE CLINICAL PROFILE IN TUBARIC ECTOPIC PREGNANCY IN TERESOPOLIS IN THE YEAR 2020

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Abstract: Introduction: Tubal ectopic pregnancy is a major health problem among women of childbearing age, accounting for approximately 1-2% of all pregnancies in the general population. It is considered the leading cause of maternal death in the first trimester, accounting for approximately 2.7% of all pregnancy-related deaths. **Goals:** To know the profile of patients diagnosed with tubal ectopic pregnancy at the Hospital das Clinicas de Teresópolis Constantino Ottaviano, in the year 2020. **Method:** A bibliographic survey was carried out, followed by a quantitative-descriptive field research, with an analysis of 1620 records of interest. Of these, 23 had a diagnosis of tubal ectopic pregnancy and, after exclusion criteria, 22 medical records were admitted for analysis of the variables predefined in the form. After completing this stage, a retrospective study was carried out in order to identify prevalent elements and their relationships, and a characterization of these patients was outlined. **Results:** Higher incidence of white women, between 25 and 30 years old, complaining of bilateral abdominal pain, associated with vaginal bleeding, with tubal rupture and good general condition, diagnosed with transvaginal ultrasound and treated with exploratory laparotomy with salpingectomy. **Conclusion:** From this study, it was possible to trace the epidemiological profile of women who had tubal ectopic pregnancy at the HCTCO in 2020, but the lack of information reported in the medical records affected the accuracy of the analysis and outcome of this research.

Keywords: Ectopic Pregnancy, Tubal Pregnancy, Epidemiological Profile.

INTRODUCTION

Ectopic pregnancy (EG) is defined as blastocyst implantation that occurs externally to the endometrial lining of the uterine cavity.¹ Tubal pregnancy (TG) accounts for

approximately 95% of EG cases, of which more than 70% occur in the ampulla, followed by 25% in the isthmic zone and 2% in the interstitial zone.² Other sites affected by GE involve the ovaries, cesarean section scar, peritoneal cavity and the broad ligament.³

EF is a major health problem among women of childbearing age, accounting for approximately 1-2% of all pregnancies in the general population.⁴ It is considered the leading cause of maternal death in the first trimester⁵, having been responsible for approximately 2.7% of all pregnancy-related deaths⁶. When related to an unstable condition, it becomes a medical emergency, requiring urgent surgical treatment.⁷ In addition to the direct influence on mortality, GE also reduces maternal fertility rates and considerably increases the chances of recurrence.⁸

Despite advances in diagnostic and treatment techniques, the incidence of GT has been increasing lately. This may be associated with the increased occurrence of pelvic inflammatory diseases, especially those caused by *Chlamydia trachomatis*, the use of contraceptive methods such as IUDs and oral contraceptives, and assisted reproduction.⁹ In addition, GT is also associated with other risk factors, such as smoking, infertility, history of miscarriage, age over 40 years and multiple sexual partners.¹⁰

In order for there to be a reduction in morbidity and mortality caused by GT, there must be an association between early diagnosis and the most appropriate management, before tubal rupture occurs and the installation of a hemodynamically unstable maternal condition. The classic triad of symptoms of an EG includes amenorrhea, genital bleeding, and/or pelvic pain, which can be bilateral or in the right or left iliac fossa.¹¹ Added to this, other symptoms may be present, such as nausea, vomiting, pain radiating to the shoulder, dizziness and fainting.³ In addition

to symptoms and assessment of risk factors, quantitative measurement of the human chorionic gonadotropin hormone (hCG) and transvaginal ultrasound in the diagnosis of GT help in early diagnosis, reducing the need for laparoscopy and allowing a more conservative approach¹⁰.

Taking into account that GT is an important health problem in women of childbearing age, being one of the main responsible for maternal morbidity and mortality in an important portion of pregnancies in the general population and conferring a medical emergency when not properly and early diagnosed, it is important to draw a profile of women with a higher incidence of this clinical condition, characterizing their particularities and generalities, so that health services can be better prepared to deal with such a situation, optimizing the diagnosis and enabling a more adequate treatment. and less invasive.

THEORETICAL FOUNDATION

The fallopian tubes (UT) are the most common site of EG. They are bilateral tubular structures that communicate the ovaries with the uterine cavity, functioning as a conduit for the transport of the oocyte, and are made up of four anatomical segments. Its origin is in the uterine horn with the interstitial portion, which consists of an intramural region, and becomes the isthmus, which is formed by a thick muscular wall and a narrow lumen. This continues in the ampulla, the longest portion, with the largest lumen and thinner walls, where most fertilization takes place. The most distal part of the TU is the infundibulum, a fimbriate portion whose mucosa has projections that maintain contact with the ipsilateral ovary to capture the oocyte released at each menstrual cycle.^{12,13}.

The most affected TU site in ectopic pregnancy is the ampulla, followed by the isthmus zone. This location is important

to determine the extent of the lesion and, consequently, the prognosis. A little more than half of pregnancies located in the ampulla occur intraluminal and, in most of these cases, the muscular layer is preserved. In the isthmus, pregnancies are extraluminal or both intraluminal and extraluminal, with more extensive ruptures of the tubal wall occurring.¹⁴

Histologically, TU are formed by an inner mucosa composed of longitudinal cilia, a muscular middle layer and the outer serosa, also known as muscular mucosa, which comprises an inner circular layer and an outer longitudinal layer. The combination of ciliary movement, muscle contraction, and fluids secreted at this site promote egg transport along the TU.¹⁵.

As the TUs do not have a submucosal layer in their wall, interposing between the epithelium and the muscular layer, the access of the blastocyst to the muscular layer and its implantation become easier. This lower resistance also provides for earlier penetration of the trophoblast.¹³.

GT has a multifactorial cause. The mechanism involved in its occurrence seems to be strongly associated with anatomical and/or functional changes that prevent the migration of the fertilized egg through this organ, including obstruction, motility deficiency, ciliary dysfunction and the influence of chemotactic molecular substances that stimulate and facilitate tubal implantation. of the blastocyst, such as lectin, integrin, prostaglandins, growth factors, cytokines and modular proteins¹⁶. Thus, any factor that somehow damages the fallopian tubes can contribute to the occurrence of a GT.¹⁷ Although most women diagnosed with GT do not have identified risk factors, it is known that its etiology may be influenced by a number of risk factors.¹⁸

The history of previous EG seems to be the main factor related to its recurrence, so

that a woman with two previous diagnoses of EG is up to 10 times more likely to have the same clinical picture^{8,19}. Surgeries in TU, such as salpingoplasty and tubal ligation, were associated with greater risks of obstruction, thus increasing the chances of GT¹³.

The presence of inflammation in the TU occurs in up to 90% of the GT, being 6 times more prevalent in the tubes involved in this clinical condition when compared to the unaffected ones. Infection by *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, an important cause of tubal inflammation, damages the ciliary system of TU and stimulates the production of the PROKR2 protein, which has chemotactic properties that facilitate blastocyst implantation in this location, increasing the risk of GT by up to 4 times, this risk being increased with each successive episode¹⁸.

Smoking increases the risk for GT by up to 4 times, due to a relationship with decreased tubal mobility due to ciliary dysfunction, impaired immunity, which is related to tubal damage, delayed ovulation and change in smooth muscle contractility^{20,21}.

Despite reducing the chances of both intrauterine and extrauterine contraception, when a pregnancy occurs in women who use some contraceptive methods, there is an increased risk of this pregnancy occurring in TUs. IUD use was present in 4% of GT cases and progesterone contraceptive pills increase their risk due to a reduction in tubal motility²².

There is also a relationship between the age at which women become pregnant and the increase in GT rates, due to tubal dysfunction caused by hormonal changes.²³ The risks for this condition increase by up to 3 times in pregnancies that occur in women aged between 35 and 44 years when compared to women between 15 and 25 years of age.²⁴

As GT remains undiagnosed, the development and growth of the blastocyst

implanted in the TU wall increases the risk of tubal rupture, resulting in hemorrhage and hemodynamic instability. The main risk factors related to this condition are women over 35 years of age, ovulation induction and a serum hCG level greater than 1000 mIU/mL²⁵. This outcome occurs in 20 to 35% of cases and is associated with a higher maternal mortality rate⁴.

Greater access to care resulting from advances in diagnosis and treatment has reduced mortality rates resulting from tubal rupture by up to 10 times in the last 3 decades. However, GT remains the main cause of maternal death related to early pregnancy, accounting for approximately 9% of fatalities. The risk of mortality increases by 50-fold in GT when compared to first-trimester abortions, and by 10-fold when considering third-trimester birth deaths¹⁸.

GT is mainly diagnosed between the 6th and 9th week of pregnancy, through a combination of clinical findings, transvaginal ultrasound (TVUS) and serial assessment of hCG levels. Any sexually active woman of childbearing age who experiences vaginal bleeding or abdominal pain must be evaluated for EG screening. Pregnant women who have high risk factors for this condition must also be investigated, even if asymptomatic.²⁶

The clinical picture of GT begins with abdominal or pelvic pain located on the side of the affected tube, due to its distension as the pregnancy progresses. The rupture of the tube and involvement of the peritoneum trigger a more acute and generalized pain, and other symptoms such as syncope, vomiting, pain radiating to the shoulders and hemorrhagic shock may be present, with hemodynamic instability that manifests as dyspnea, hypotension and tachycardia^{26,27}

USGTV has a sensitivity of 73-93% for the diagnosis of GT, depending on the gestational age and the examiner's skill. She is able to

confirm an intrauterine pregnancy when a hyperechoic ring structure containing an embryo or yolk sac is visualized.²⁶. Thus, a GT is admitted when there is no clear ultrasound evidence of intrauterine pregnancy, associated with extrauterine findings, such as a heterogeneous mass in the UT with or without a hyperechoic “ring sign” or a fetal pole with or without cardiac activity. The presence of echogenic fluid at the bottom of the rectouterine excavation is indicative of hemorrhage and is present in up to 50% of cases¹⁷.

Unlike its absolute value, the behavior of hCG levels taken serially is important in the diagnosis of GT, with a sensitivity of 74-100%²⁶. In normal pregnancy, serum hCG levels double every 48 hours. If this increase is smaller or if the value doubles in this time interval and reaches a level greater than 3,500 mIU/mL, but associated with the absence of ultrasound evidence of an intrauterine pregnancy, the diagnosis of GT is very likely¹⁷.

GT diagnosed in asymptomatic patients with intact UT can be managed through expectant, drug treatment, with methotrexate, or surgical treatment, with salpingostomy or salpingectomy. The choice of method must be considered according to the patient's expectations regarding future pregnancies, clinical picture, ultrasound findings and hCG levels. Patients diagnosed with ruptured GT are included in medical emergencies and must be urgently transferred for surgical intervention²⁸.

GOALS

PRIMARY

To know the profile of patients diagnosed with tubal ectopic pregnancy at the Hospital das Clínicas de Teresópolis Constantino Ottaviano (HCTCO) in 2020.

SECONDARY

- Carry out the characterization of women who had tubal ectopic pregnancies by collecting data on their sociodemographic profiles, clinical conditions, diagnoses and outcomes.

- Identify whether there are more incident variables in this clinical picture, aiming to optimize their identification and facilitate the planning of evidence-based procedures and protocols, specifically aimed at the clientele of this health service.

METHODS

The present study was carried out for the Course Completion Work - TCC, of the Medicine graduation of the Serra dos Órgãos University Center - UNIFESO. This was done from a bibliographic survey, which included articles and books, for a better understanding of the subject studied and to obtain the necessary theoretical basis for this research. It was decided to carry out a quantitative-descriptive field research, with a direct search for data in the population and place of interest, in which the collected and evaluated elements allowed the analysis of its main variables.²⁹

The research project was submitted to Plataforma Brasil and, after approval by the Research Ethics Committee - CEP, generating opinion n° 4,903,561, the following stages of this work began. The selection process of the target population was done by means of a non-probabilistic sampling for convenience, in which the sample was chosen deliberately, by identifying a number of patients who meet the criteria for inclusion in this study³⁰. Thus, data collection was carried out in person in the obstetrics sector of the HCTCO, through the analysis of procedure books, in which all the patients admitted to the institution for this sector are gathered. This step was followed by the identification of patients who initially fit

into this research, whose admission diagnosis was tubal ectopic pregnancy in 2020, to be sent to the hospital's medical records sector, which requested the scanned file for the responsible company. From this, several times were scheduled for the face-to-face analysis of documents and gathering of information following the pre-defined variables in the form in Appendix 1.

In all, 1620 medical records were analyzed, which correspond to all patients admitted to the gynecology and obstetrics service of the HCTCO in 2020. Of these, 23 had a diagnosis of EG. One patient had hospitalization recorded in his medical record as canceled, with no further information reported, which made his analysis unfeasible. Therefore, 22 medical records were considered for this study, which minimally met the previously formulated inclusion criteria.

After completing this stage, a retrospective study was carried out, in which the generalities and specificities observed were evaluated, in order to identify prevalent elements and their relationships. This was carried out through a descriptive statistical analysis, in which elements of the same nature were synthesized to obtain a global view of the variation of this information.³¹ Finally, based on this study, a characterization of these patients was drawn up, in order to assist in the creation of more specialized and effective protocols in the face of this situation.

INCLUSION CRITERIA

Female patients, covering all variants included in the sociodemographic data, such as age group and race, who were diagnosed with tubal ectopic pregnancy at the HCTCO obstetrics service in 2020.

EXCLUSION CRITERIA

- Patients who had an ectopic pregnancy in a location other than the fallopian tubes;

- Patients diagnosed with this condition in a year other than 2020;
- Patients whose medical records present incomplete information, compromising the standardization of data from this research.

RESULTS

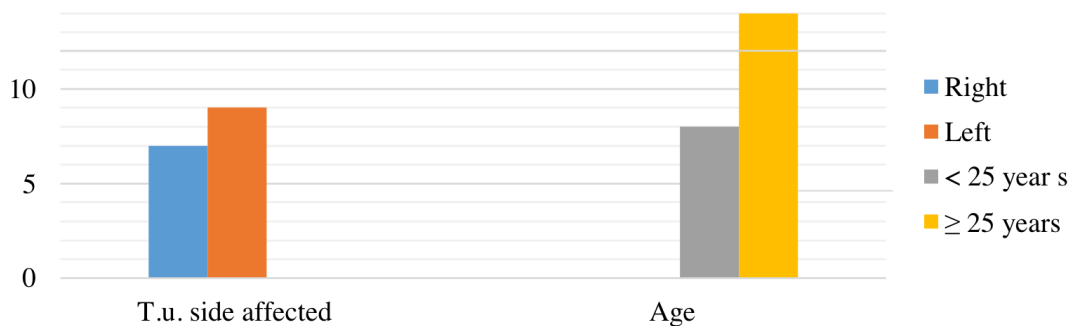
During the period from 01/01/2020 to 12/31/2020, 1620 patients were admitted to the gynecology and obstetrics service of the HCTCO, 23 of them diagnosed with EG (1.4%). Among the cases analyzed, all patients had ectopic pregnancy located in the TU. All cases were diagnosed via TVUSG, with the exception of 1, in which the method used was computed tomography (CT), considering that the main diagnostic hypothesis at the time had not been GE, due to the nonspecificity of the symptoms presented. The average age of women at diagnosis was 26.9 years, with slightly more than half (54.5%) being 25 years of age or older. Most patients were white (59%), followed by brown women. No other races have been reported. In addition, the vast majority (72.6%) did not have GT in their first pregnancy and the left side of the UT was slightly more affected (54.5%). Tube rupture occurred in 72.7% of the admitted cases, mainly in women over 25 years old (mean 27.7) and 56.2% occurred on the left side (graph 1). Despite this, only 1 patient was admitted to the service with signs of hemodynamic instability, requiring intraoperative red blood cell transfusion. The mean value of hCG was 2958.3mIU/ml (Table 1).

The mean gestational age at the time of diagnosis of GT was 6 weeks and 4 days, with most women (38.4%) having 7 weeks of gestation. In two cases, the gestational age was less than 3 weeks, with one of them counting 5 days and the other 14 days, from the date of the last menstrual period reported by the patients (Table 2). In most cases (90%), the patients

	Number of women	Average (Variation)	Percentage (%)
Age:		26.9 (17-42)	
- < 25 years	10		45.4
- ≥ 25 years	12		54.5
Color:		-	
- White	13		59.0
- Brown	9		40.9
It moves to:		2.6 (1-6)	
- G1	6		27.2
- ≥ G2	10		45.4
- ≥ G4	6		27.2
TU Side:		-	
- Left	12		54.5
- Right	10		45.4
Rupture:		-	
- Yes	16		72.7
- No	6		27.2
hCG (mUI/ml)		2958.3 (3.58-	
- < 1000	4	9428)	40.0
- ≥ 1000	6		60.0

Table 01: Demographic and gynecological-obstetric data analyzed in patients admitted with GT.

Source: HCTCO medical records.



Graph 01: Characteristics present in cases of TU rupture 15.

Source: HCTCO medical records.

Gestational Age	Number of women	Percentage (%)
- < 3 weeks	2	15.3
- 4 weeks	1	7.6
- 5 weeks	4	30.7
- 6 weeks	0	0
- 7 weeks	5	38.4
- 8 weeks	1	7.6

Table 02: Gestational age at the time of TG diagnosis.

Source: HCTCO Records.

did not have any comorbidity reported in the medical records, with the exception of two, one with systemic arterial hypertension and the other with rheumatic fever. In another case, the patient had undergone tubal recanalization 45 days ago. Only one patient had a history of previous EG and another had a history of repeated spontaneous abortions (3).

The most prevalent clinical picture at the time of TG diagnosis involved the presence of abdominal or lower abdomen pain, associated with bleeding, corresponding to 55% of the cases. Pain in the lower abdomen was present in almost all patients, accounting for 95%. Of these, 20% of women reported unilateral pain located on the side of the affected tube. The other symptoms can be seen in graph 2.

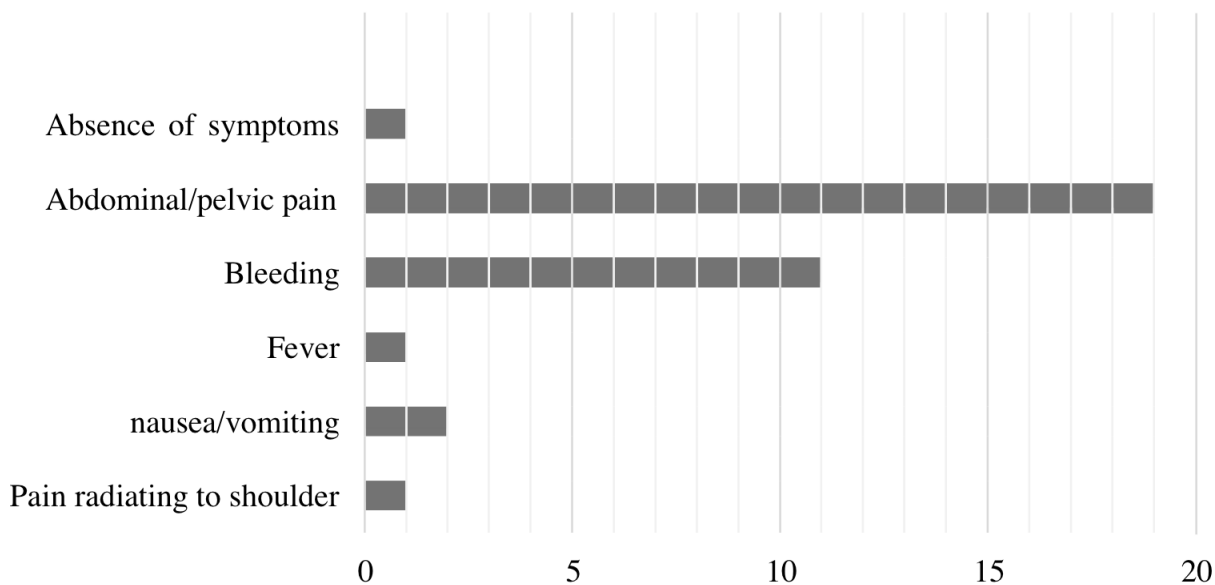
Exploratory laparotomy with salpingectomy was the most used therapeutic method, totaling 86.3% of cases. The others were managed with the administration of Methotrexate, 50mg, intramuscular, single dose. Of these, 2 patients returned to the service with persistence of symptoms, with

subsequent submission to exploratory laparotomy. The mean length of hospital stay was 1.9 days, with a range of 1 to 3 days.

DISCUSSION

When compared with the total number of patients admitted to the obstetrics sector in 2020, the incidence of GT found in this study was 1.4%. This value is in agreement with the literature, as demonstrated by the Centers for Disease Control and Prevention (CDC) and The American College of Obstetricians and Gynecologists (ACOG), in addition to several authors, such as Berg et al., Farquhar et al, Marion et al. and Peterson et al., who point out the occurrence of this diagnosis in approximately 1-2% of all pregnancies.^{4,6,9,17,20}

All studies found for this research, such as those by Fernandes et al. and Marion et. Al, demonstrate that the most affected site in EG are the fallopian tubes, accounting for approximately 95% of cases.^{2,17} These data confirm the findings of this research, in which the percentage of patients with pregnancies in the fallopian tubes was 100%



Graph 02: Clinical picture presented by patients with GT.

Source: HCTCO Records.

of the cases. Another factor considered in the studies involves the portion of the UT affected, but this data was not recorded in any of the medical records included in this study, making its analysis impossible.

The age of women appears in studies as an important risk factor for GT, with a 3- to 8-fold increase in the chances of this diagnosis occurring in women aged 35 years or older.^{17,24} However, this study noted a higher prevalence of TG in women aged 25-30 years, with only 9% of cases occurring at ages above 35 years, differing from published data.

Regarding the prevalence of GT in different races, few articles in which the topic was addressed were published. These pointed to an up to 40% higher risk of this condition happening in non-white women.^{32,33} In contrast to this result, the present study found that more than half of the women admitted with the diagnosis were white.

According to published studies, such as those by Fernandes et al., Taran et al. and the CDC, the rupture of the affected fallopian tube occurs in approximately one to two thirds of documented cases and the chances of this outcome occurring are higher in women over 35 years of age.^{2,4,25} Accordingly, in this study, rupture was also observed in the vast majority of patients, but this age was not a risk factor, since the mean age in this situation was approximately 27 years.

Of the patients considered in this study, only 1 of them required blood transfusion due to signs and symptoms of shock. It is known that hemodynamic instability triggered by the rupture of the fallopian tube is one of the main causes of maternal mortality in first trimester pregnant women and that its occurrence involves approximately 20% of cases of GT^{2,5}, which corroborates the result found.

Regarding hCG, its dosage has value in the diagnosis of GT when performed serially.²⁶ However, this practice does not seem to

be adopted by the service where this study was developed, with this test having been performed or recorded in less than half of the patients and, when performed, it was collected only once. The mean hCG value found of 2958.3 mIU/ml was lower than that reported in studies, which accounted for approximately 3,500 mIU/ml of absolute value as having a positive predictive value for the diagnosis.¹⁷

The increase in access to health services has reduced the gestation time elapsed at the time of TG diagnosis, which is important for positive prognoses. Thus, this situation occurs approximately between the sixth and ninth week of pregnancy, as shown by Marion et al. and Hendriks et al.^{17,26} This data was similar to that found in this study, whose mean gestational age at admission was 6-7 weeks.

The main risk factor associated with the recurrence of GT is the history of previous GT, as demonstrated by ACOG and Shawn et al.^{16,19} This study, however, could not observe this variable, since in only one of the cases the patient had a history of GT. Thus, this information would need to be evaluated through the follow-up of the patients in this study, in order to verify a possible future diagnostic repetition.

Another risk factor reported in published studies includes a previous history of spontaneous abortions, as shown by Fernandes et al., Chow et al. and Elito et al.^{2,7,34} Of the cases considered in this study, only one had a history of three miscarriages prior to diagnosis. However, this positive association is not unanimous among the authors, as shown in the work by Gaskins et al.²⁰

The main symptoms presented by the patients found in this study are in agreement with published studies. Farquhar et al., Marion et al., Hendriks et al. and Scibetta et al., agree in saying that most women arrive at the health service with mainly abdominal pain and

bleeding, which corroborates the data shown here.^{9,17,26,27}

Therapeutic conduct involving conservative treatment, with a single dose of Methotrexate, occurred in 20% of the cases, and in 66% of these the patient underwent surgery after a few days. This result is in disagreement with the study by Farquhar et al., which showed that the success rate of this method reaches more than 85%.⁹ The article by Sowter et al. corroborates this result, attesting that the need for surgery after Methotrexate administration ranged from 4 to 15%.³⁵ The length of stay of the patients was in line with the studies, which showed a period of up to three days for at least half of the women.²

STUDY LIMITATIONS

The medical records of the institution chosen to carry out this study are digitized by an outsourced company and their analysis must be carried out by sending a report containing the name of the patients of interest or the identification number of their records, so that the responsible company make them available for on-site study. The selection of these documents must be done through the analysis of physical books filled in by those responsible at the time, which contain the initial diagnosis of all patients admitted to the gynecology and obstetrics sector of the hospital in a certain period. In addition to missing important information, such as the diagnosis itself, and the manual review of patient by patient taking a large amount of time, which could be optimized through a search through computerized systems, there was a lack of organization by the responsible sector, since, as informed, some requested books were lost and were only found after a period, which is crucial for the conclusion of this work due to the stipulated deadline.

Initially, the form for collecting data from medical records, whose variables this research

is based on to carry out the characterization of the profile of the object of study, contained additional information to the final form, which was actually used. As part of the objectives idealized in this work, there is the delineation of a profile of patients with characteristics found to be more incidents, so that the identification and conduct of this diagnosis can be optimized, which includes the research of risk factors that increase the chances of a same diagnosis later, such as the use of IUDs and oral contraceptives, previous pelvic surgeries and habits such as smoking.

However, filling in the medical records during the hospitalization of the admitted patients was done, in most of them, in an insufficient way, omitting important information, without which the deepening and relevance of this research is unfeasible. In addition to risk factors, other essential variables were absent in a series of documents, such as gestational age and hCG value at the time of therapeutic intervention, decisive information in the choice of conduct, side and portion of the fallopian tube affected and symptoms presented by the patient. Therefore, some variables had to be excluded from the original form and it was not possible to comply with one of the proposed exclusion criteria, which postulates the disregard of medical records that do not contain all the predefined information considered necessary for this study.

CONCLUSIONS

From this work, the epidemiological characterization of the profile of patients diagnosed with GT at the HCTCO during the year 2020 showed a higher incidence of white women, between 25 and 30 years old, who arrive at the service with a main complaint of abdominal or lower abdominal pain, bilateral, associated with vaginal bleeding. Most are admitted with tubal rupture, but

in good general condition, with no signs of hemodynamic instability. The diagnostic confirmation is made mainly through TVUS, and the hCG dosage is little used. Few patients have a previous history of EG or miscarriages, and the other risk factors could not be evaluated. The main outcome of this situation is exploratory laparotomy with

salpingectomy of the affected tube, even when the therapeutic method used is Methotrexate. Patients spend approximately 2 days in the hospital until discharge from the service. It is noteworthy the difficulty of deepening this study to improve its applicability, due to the lack of data and standardization in the analyzed records.

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APPENDIX 1

Form for collecting data from medical records:

Sociodemographic data:

Initials of the name:
Age:
Origin:
Color (breed):
Profession:

Gynecological-obstetric data:

Pregnancy:
Gestational age at diagnosis:
Diagnostic method:
Beta-hCG value:
Side of the fallopian tube:
GT route: Yes () No ()
Symptoms:
Physical exam:
Laboratory test:
Previous GE: Yes () No ()
Place:
Date:
End:
Therapeutic method:
Length of stay:
Comorbidities: