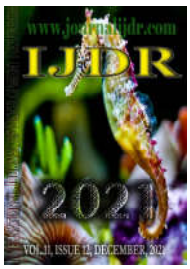
ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 11, Issue, 12, pp. 52889-52893, December, 2021
https://doi.org/10.37118/ijdr.23334.12.2021



RESEARCH ARTICLE OPEN ACCESS

PELVIC INFLAMMATORY DISEASE AS A MAJOR RISK FACTOR FOR ECTOPIC PREGNANCY

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ARTICLE INFO

Article History:

Received 08th September, 2021
Received in revised form
27th October, 2021
Accepted 11th November, 2021
Published online 30th December, 2021

Key Words:

Ectopic Pregnancy.
Sexually Transmitted Infections.
Women.

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ABSTRACT

Introduction: Pelvic Inflammatory Disease can cause an inflammation of the acute or chronic type as a result of Sexually Transmitted Infections caused mainly by Neisseria gonorrhoeae and Chlamydia trachomatis. And since one of the consequences of PID is to block the uterine tubes, preventing the embryo from passing and implanting in the uterus, thus generating an ectopic pregnancy that can lead to the loss of the uterine tubes and even death. **Objective:** To verify Pelvic Inflammatory Disease in scientific evidence as one of the main risk factors for ectopic pregnancy. **Methodology:** Integrative Literature Review conducted between November 2020 and February 2021 using the electronic databases National Library of Medicine National Institutes of Health PubMed and MEDLINE and the electronic journal Acervo Health. Studies published in full in Portuguese and English in the last five years (2016-2021) were included, while monographs, dissertations and case reports were excluded. **Results:** It was evidenced in the scientific literature that women who had already contracted some PID had a 12% to 15% chance of having ectopic pregnancy and that it is one of the main factors associated with the onset of ectopic pregnancy. The PID presented with one of the main consequences the salpingitis that is one of the precursor factors of ectopic pregnancy. **Conclusion:** It is necessary to have knowledge about clinical and epidemiological aspects of PID and ectopic pregnancy in women. It becomes fundamental for the prevention of future cases, as well as for an adequate management according to the particularities of each patient, highlighting also the importance of other studies that complement the information obtained and expand the approach regarding PID and ectopic pregnancy to effect changes in the existing reality.

Citation: ***Maria Nauside Pessoa da Silva, Aimê Viilenuev de Paula Guedêlha, Daniel Campelo Rodrigues, Davi Sodré, Thayná Cunha Bezerra, Maria Valneide Gomes Andrade Coelho et al.*** "Pelvic inflammatory disease as a major risk factor for ectopic pregnancy*", International Journal of Development Research*, 11, (12), 52889-52893.

INTRODUCTION

Pelvic inflammatory disease (PID) is a common infection associated with significant complications, including infertility, chronic pelvic pain, ruptured tubo-ovarian abscess, and ectopic pregnancy. And when diagnosis is delayed, the disease can present with nonspecific signs and symptoms and when identified, PID is usually treated ineffectively (Charles and Taku, 2016). The occurrence of PID is common and has a high cost to healthcare services.

In the United States, the annual incidence of 750,000 to 800,000 cases and presents direct costs of 2 billion a year (Sweet, 2011). Most patients with PID have mild to moderately severe disease and are treated on an outpatient basis (Mitchell, Prabhu, 2013). Only a small percentage of patients progress to severe or complicated disease. Although the direct morbidity and mortality rate is low, treatment prevents subsequent infertility, pelvic scarring, chronic pelvic pain, and ectopic pregnancy (Macaluso, Wright, 2010). Pelvic Inflammatory Disease can cause an acute or chronic type of inflammation as a result of Sexually Transmitted

Infections. In 85% of cases, PID can be caused by sexually transmitted bacteria and the main etiological agents of the disease are the bacteria Neisseria gonorrhoeae or Chlamydia trachomatis (MOLENAAR, SINGER, OUBURG, 2018). Approximately 10% to 15% of women with endocervical Neisseria gonorrhoeae and Chlamydia trachomatis will develop PID. However, gonorrheal infection is among the most frequent causes and the most severe form of PID (Di Tucci *et al*, 2018). Chlamydia infection can cause PID, however it is less likely to cause symptoms and therefore is more likely to result in subclinical PID and being subclinical may produce few or no symptoms, but can still have long-term adverse consequences (Risser, Risser, Risser, 2017). If not diagnosed early and treated, PID can lead to infertility, ectopic pregnancy, chronic pelvic pain, or tubo-ovarian abscess formation (Sweet, 2011; Khan, Rizvi, 2006). The consequences of PID can cause interruption of the embryo's passage through the uterine tubes preventing it from passing and implanting in the uterus, thus generating an ectopic pregnancy (Sweet, Wiesenfeld, 2006; Soper, 2008). The ectopic pregnancy is a complication of pregnancy, in which the fetus settles outside the uterus, and may implant in the fallopian tubes, heterotopic, in the abdominal cavity, in the previous cesarean section scar, cervical or ovarian. The causes of this pregnancy can be from a previous c-section, the use of IUD, Chlamydia or even endometriosis. There are also other risk factors such as age over 35 years, in vitro fertilization, tubal malformation, multiple sexual partners, infertility, pelvic inflammation, among others (Sedicias, 2017).

Ectopic pregnancy (EG) is a medical emergency that can evolve to tubal rupture, the most frequent location (96-98%), causing life-threatening internal bleeding or injury to the fallopian tube. Its prevalence has been increasing, a fact attributable to incomplete treatment of sexually transmitted diseases and the increase in the practice of assisted reproduction (Arenas, 2011; Samith, Ivan, Germán, 2010). The incidence of ectopic pregnancy has increased in recent decades due to several factors. On the one hand, the dosage of the beta subunit of chorionic gonadotrophin, the more accurate ultrasound scanners, and the use of gynecological endoscopy have facilitated the diagnosis. In Brazil, mortality from ectopic pregnancy is among the hemorrhagic causes. According to data from the State of São Paulo between the years 1991-1995, the maternal mortality rate due to all causes ranged from 43.7 to 49.6 per 100,000 live births (Fernandes, 2004). Since maternal mortality is associated with a greater number of risk factors and also with high-risk pregnancies, ectopic pregnancy being one of them, this study becomes very useful. Thus, the aim of the study was to verify Pelvic Inflammatory Disease (PID) as one of the main risk factors for ectopic pregnancy according to the scientific literature.

METHODOLOGY

This is an Integrative Literature Review (ILR), a methodology that consists of the organization, cataloging and synthesis of the results presented in the materials selected for analysis, facilitating interpretation (Botelho; Cunha; Macedo, 2011). This method was the search for data in secondary sources, however, adopting the same rigor and clarity of a primary study. For this, the steps were adopted: identification of the theme and formulation of the research question, preparation of the criteria for inclusion and exclusion of articles, construction of an instrument for collecting relevant data from the articles found, evaluation and analysis of the articles selected in the research, interpretation and discussion of the results obtained and presentation of the review (Mendes; Silveira; Galvão, 2008). The question that guided this research was: What is the scientific evidence on Pelvic Inflammatory Disease as one of the main risk factors for ectopic pregnancy?

The research was conducted between November 2020 and February 2021 using the electronic databases National Library of Medicine National Institutes of Health PubMed, MEDLINE and the electronic journal acervo saúde. The following descriptors were used in the search for articles: ectopic pregnancy, Pelvic Inflammatory Disease, Associated factors. Inclusion criteria were defined as: studies available in full in Portuguese and English published in the last five years (2016-2021) and excluded monographs, dissertations and case reports. We identified 980 publications and excluded 958 according to the inclusion criteria and for being duplicate studies. Fourteen studies were also excluded for not meeting the proposed objectives. The integrative review was operationalized with eight studies. The instrument for operationalizing the selection of studies was applied. All articles were read in their entirety; then, a table was drawn up containing: article identification number, article title, authors, journal of publication, year of publication, type of article, and database and/or electronic library where it was available. For the evaluation of the studies, the Qualitative Textual Analysis was used, which is developed through a process of fragmentation of the material read (MORAES and GALIAZZI, 2016).

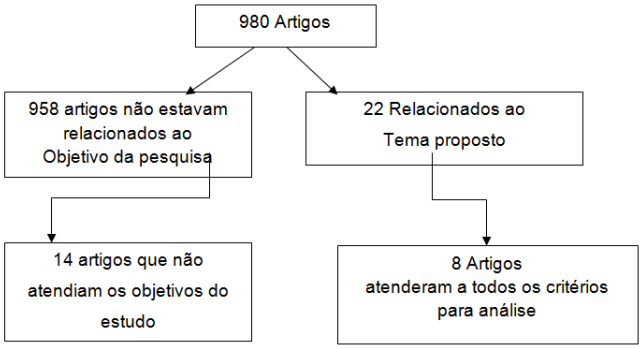

Figure 1. Analytical diagram of the bibliographic survey. Teresina, 2021

RESULTS AND DISCUSSION

Of the eight articles selected for Integrative Review, 7 were published in the English language, with the majority four published in 2020. PubMed was the database with the largest number of articles with four, followed by MedLine with three. As for the methodological approach, four articles used quantitative method.

Association of Pelvic Inflammatory Disease with ectopic pregnancy: Cheong *et al*., (2014) put that women who have already contracted some PID have a 12% to 15% chance of having ectopic pregnancy in the future. Acute pelvic inflammatory disease is a public health problem due to the fact that it is associated with major medical complications (infertility, ectopic pregnancy and chronic pelvic pain) as well as high cost healthcare. Hence the importance of early diagnosis and appropriate and rapid onset treatment strategies to prevent or even minimize long-term sequelae. According to Gontijo *et al*., (2015), PID has been associated with the occurrence of sterility, premature delivery, ectopic pregnancy, cervical cancer, puerperal infections, chronic pelvic pain and recurrent upper tract infections. In the study by Colombel, Shin , Gibson (2019) showed that women with PID were aged between 20 and 24 years, 18% would develop chronic pain, 8.5%, ectopic pregnancy and 16.8% would experience infertility. Infertility can also result from PID, regardless of whether the patient is symptomatic or asymptomatic of pelvic infection. Infection can cause severe damage to the fallopian tubes, including the loss of fallopian tube ciliary epithelial cells and their occlusion.

Table 1. Description of the studies included in the Integrative Review, according to title, author, year of publication, database and type of research. Teresina, 2021

N	Título	Autores	Ano	Base de dados/ revista eletrônica	Abordagem metodológica
01	Pelvic inflammatory disease: diagnosis and treatment in the emergency department	Charles Walter Bugg, Taku Taira, Milana Zaurova	2016	PUBMED	Revisão Sistemática
02	Pelvic Inflammatory Disease: Diagnosis, Management, and Prevention	Amy Curry, Tracy Williams, Melissa L Penny	2019	PUBMED	Randomizado
03	Manejo clínico de DIP / DIPA doença inflamatória pélvica e de repetição: uma revisão narrativa	Francisca Amanda de Souza Mesquita, Adelaide Gomes Martins, Sabrina Cabral Rego, Paula Barros Pereira	2020	Revista Eletrônica Acervo Saúde	Revisão Narrativa
04	Association between pelvic inflammatory disease, infertility, ectopic pregnancy and the development of ovarian serous borderline tumor, mucinous borderline tumor and low-grade serous carcinoma	Stewart, L M; Stewart, C J R; Spilsbury, K; Cohen, P A; Jordan, S.	2020	MEDLINE	Estudo de Coorte
05	Pelvic Inflammatory Disease	LindseyK. Jennings, Diann M. Krywko	2020	PUBMED	Sem identificação
06	Pregnancy and fertility-related adverse outcomes associated with Chlamydia trachomatis infection: a global systematic review and meta-analysis.	Tang, Weiming; Mao, Jessica; Li, Katherine T; Walker, Jennifer S; Chou, Roger; Fu, Rong; Chen, Weiying; Darville, Toni; Klausner, Jeffrey; Tucker, Joseph D.	2020	MEDLINE	Revisão Sistemática e Metanálise
07	Brazilian Protocol for Sexually Transmitted Infections 2020: pelvic inflammatory disease]. / Protocolo Brasileiro para Infecções Sexualmente Transmissíveis 2020: doença inflamatória pélvica.	Menezes, Maria Luiza Bezerra; Giraldo, Paulo Cesar; Linhares, Iara Moreno; Boldrini, Neide Aparecida Tosato; Aragón, Mayra Gonçalves.	2021	MEDLINE	Sem identificação
08	Study of Risk factors and treatment modalities of ectopic pregnancy	Shruthi Andola, R Ramesh Kumar, Ratnamala M Desai, SA Krutika	2021	PUBMED	Estudo Transversal

The effects on fertility can be pronounced, with some studies indicating a 5-fold increase in infertility in women with a history of PID. Also in the same study, it was shown that there is an increased risk of ectopic pregnancy after PID, with damage primarily to the fallopian tubes. And the ectopic pregnancy rate after PID is approximately 7.8%, while the non-PID ectopic rate is 1.3% (Jennings, Krywko, 2021). According to Fehring, Bouchard, Meyers (2018), patients with PID can develop chronic pain, ectopic pregnancy, or infertility. About 25% had chronic pelvic pain, usually due to adhesions, 10-50% impaired fertility, usually caused by scars and adhesions in the fallopian tubes. And as a final problem, ectopic pregnancy that can occur in 15-60% of women, due to damage to the fallopian tubes. Pelvic infection is the most frequent gynecologic cause of emergency medical services visits with the number of visits around 350,000 per year in the United States, with 70% of cases occurring in adolescent patients. Despite its relative frequency, pelvic infection can pose a diagnostic dilemma because symptoms are often mild and nonspecific and may not direct the clinician to the correct diagnosis (Goyal. 2013). Among the main consequences of PID is salpingitis, defined as inflammation of one or both fallopian tubes, the most common initial acute form. The incidence of salpingitis continues to increase worldwide. The predominant affected population is young women. Among the spectrum of pathological conditions of PID, salpingitis is associated with the highest risk of infertility and is responsible for the majority of ectopic pregnancies (Haggerty *et al*, 2004).

In cases of salpingitis, the fallopian tubes become edematous and congested. As acute suppurative salpingitis occurs, the tubal lumen fills with pus, which subsequently leaks into the peritoneal cavity and covers the serosal surface of the uterus and ovary. This event results in inflammation of the peritoneal structures. The tubal fimbriae may adhere to the ovary, resulting in salpingo-oophoritis or tubo-ovarian complex. In tubo-ovarian complex, although the ovaries and fallopian tubes partially adhere to each other, they still remain widely separated (Kim *et al*, 2009). The clinical manifestations of salpingitis are diverse, ranging from no symptoms to severe pelvic pain, with a weak correlation between symptom intensity and the severity of tubal inflammation. Although direct laparoscopy is the reference standard for diagnosing salpingitis, the use of this procedure is limited due to its invasive nature and high cost (Potter, Chandrasekhar, 2008). Many women who develop PID do not experience any symptoms or seek any treatment, so it is detected only when problems occur in pregnancy or develop chronic pelvic pain (Mitchell *et al*., 2013). According to Shetty, Shetty (2014), the prevalence of ectopic pregnancy is 1-3% worldwide.3 Ectopic pregnancy is the leading cause of first trimester pregnancy-related death (Mufti *et al*, 2012). The possible causes of increased incidence of ectopic pregnancy are pelvic inflammatory disease (PID), use of intrauterine contraceptive device, increased age induced by smoking (Kumar, *et al*, 2010).

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