

International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622
© Gynaecology Journal
www.gynaecologyjournal.com
2021; 5(3): 12-16
Received: 12-02-2021
Accepted: 16-04-2021

Anaswara T
Senior Resident, Department of
Obstetrics and Gynaecology, ESI
Super Speciality Hospital
Asramom, Kollam, Kerala, India

Ancy T Jacob
Associate Professor, Department of
Obstetrics and Gynaecology,
Travancore Medical College
Kollam, Kerala, India

Corresponding Author:
Ancy T Jacob
Associate Professor, Department of
Obstetrics and Gynaecology,
Travancore Medical College
Kollam, Kerala, India

Clinical profile and risk factors of ectopic pregnancy: A Prospective study from a tertiary care center in Kerala

Anaswara T and Ancy T Jacob

DOI: <https://doi.org/10.33545/gynae.2021.v5.i3a.897>

Abstract

Background: Ectopic pregnancy is a life-threatening condition that every obstetrician and gynecologist encounter during their clinical practice. Accurate diagnosis is crucial to prevent mortality in women. The study aims to determine the clinical profile and risk factors of ectopic pregnancy.

Methodology: This prospective observational study was conducted in 60 diagnosed cases of EP during a study period of one and half year. All diagnosed EP cases during the study period were included and all intrauterine pregnancies excluded. Clinical characteristics and medical management of patients obtained through a structured questionnaire. Descriptive statistics used for data analysis.

Results: The incidence of EP in relation to intrauterine pregnancy in the present study is 4.6 in 100. Abdominal pain was the most significant symptom in 63.3% of patients. Risk factors (one or more) observed in 80% of the study population. Majority had history of infertility (30%), history of contraceptive use in 20%, history of abortion (25%), previous D&C in 15% and sterilization in 15%. 58.3% of the cases were ruptured. Ectopic pregnancy was medically managed in 17 cases (28.3%) and surgically managed in 43 cases (71.7%).

Conclusion: Every physician attending a woman in the reproductive age group presenting with abdominal pain should have a high index of clinical suspicion of EP unless proved otherwise irrespective of the presence or absence of amenorrhea or whether sterilized or not. An EPAU setup, similar to the one in UK, is the need of hour in Kerala as the diagnosis of EP can be picked up at an early stage and timely managed to reduce mortality in women.

Keywords: ectopic pregnancy, ectopic rupture, clinical profile, risk factors, life-threatening

Introduction

Ectopic pregnancy (EP), a life-threatening situation, is faced by every practicing obstetrician and gynecologist during their practice. It significantly risks the woman's life and fertility as it damages the fallopian tubes along with or without ovaries [1]. It is considered the leading cause of morbidity or mortality during the first trimester [2], and its incidence varies with population and accounts for 1-2% of all pregnancies [3, 4]. The factors contributing to early detection of EP before rupture are a high index of suspicion for EP, serial hormone assays, and transvaginal ultrasonography. A decline in the mortality rate due to EP rupture can be achieved by early diagnosis and timely treatment.

Any sexually active or pregnant woman who presents with abnormal vaginal bleeding may be at the risk of EP regardless of the presence of abdominal pain. Much knowledge on the risk factors helps to identify the women with EP. Women with a previous history of EP have a higher chance of recurrence and should be kept in close follow-up even in the absence of symptoms. Close monitoring and early treatment help to lessen the morbidity and mortality in pregnant women. The risk factors include previous EP, sexually transmitted diseases, tubal infections, pelvic adhesions, intrauterine device, conception resulting from assisted reproduction, history of tubal surgery, tubal sterilization, cigarette smoking and in-utero exposure to diethylstilbestrol [5]. EP can be diagnosed with human chorionic gonadotropin (hCG) assays, ultrasonographic examinations, and at times with uterine curettage [6]. It is crucial to diagnose unruptured EP as when ruptured it is a medical emergency. This study aims to determine the clinical profile and risk factors of EP.

Materials and Methods

This prospective observational study was conducted in the obstetrics and gynecology department

of Travancore Medical College Kollam, Kerala, during a study period from October 2018 to March 2020. As the cases were rare, we used a non-probability convenient sampling method to collect samples. The study included all the diagnosed EP cases admitted to the study setting during the study period and excluded all intrauterine pregnancies. A total of 60 diagnosed cases of EP were enrolled in the study. A detailed explanation of the study's need and aim were explained to the patients, and informed written consent was obtained. A detailed history was taken, and clinical evaluations were done. A pretested proforma was used to collect the information from the study subjects.

Data was collected using a structured questionnaire by personally interviewing each patient regarding their reproductive history such as previous spontaneous abortions and/or induced abortions, previous history of ectopic pregnancies, detailed history of infertility evaluation and treatment if any, current or past use of contraceptive measures like oral contraceptive pills (OCP), intrauterine device (IUD), levonorgestrel-releasing intrauterine system (LNG – IUS), emergency contraception (EC) pills; sexual history and treatment of pelvic inflammatory disease (PID) and sexually transmitted diseases (STDs) and history of tubal surgeries like sterilization and recanalization.

Statistical Analysis

Data were entered in Microsoft Excel data sheet and Statistical Package for the Social Science (SPSS; ver. 20.0) was used for statistical analysis. Ordinal data was represented in the form of frequencies and percentages. Continuous data was represented as mean and standard deviation.

Results

This study aims to assess the clinical profile of ectopic pregnancy. The incidence of EP in relation to intrauterine pregnancy in the present study is 4.6 in 100. A total of 60 cases during the study period was included in the study and the observations are as follows.

Clinical Profile of Study Population

The age distribution of study population varied from 18-43 years. The maximum number of ectopic gestations was found in the age group, 26-30 years. Least number of ectopic pregnancies were in the age group of 15-20 years and 40-45 years (Table 1). Majority of the cases (56 %) belonged to the low socio-economic status and 41.7% of the study population are from a middle socio-economic status and 1.7% of them belonged to the high socio-economic status.

Table 1: Age distribution of the study population

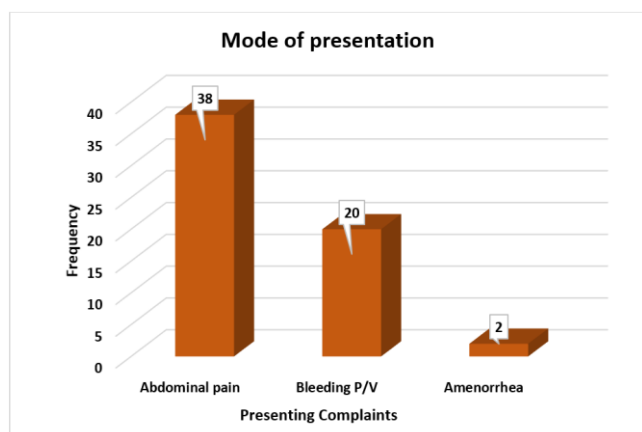
Age group	Frequency	Percentage
16-25	11	18.4
26-35	35	58.2
36-45	14	23.4
Total	60	100.0

Upon reviewing the reproductive status of the study population, 63.3 % were multiparous and ectopic pregnancy was found in the first conception in 22 patients. Among the study population 51.7% of the study population belonged to gestational age of more than 7 weeks (Table 2).

Table 2: Distribution of cases based on parity and gestational age

Parameters	No: of cases	Percentage
Parity		
Primi	22	36.7%
1	20	33.3%
2	17	28.3%
3	1	1.7%
Gestational Age		
5-7 weeks	29	48.33%
8-10 weeks	27	45%
>10 weeks	4	6.67%

The typical triad of amenorrhea, abdominal pain and bleeding were observed in a few cases. Abdominal pain was the most significant symptom in 63.3% of patients. Other symptoms were giddiness, nausea and vomiting, syncopal attacks in 36.1% (Graph 1).



Graph 1: Distribution of study subjects based on Mode of presentation

In the present study 80% of the subjects had one or the other risk factors. Majority had history of infertility (30%), history of abortion (25%), history of contraceptive use in 20%, previous D&C in 15% and sterilization in 15%. Other risk factors included previous history of ectopic pregnancy (13.3%), pelvic inflammatory disease (10%), history of IUCD use (8.3%). Previous history of endometriosis was found in 6.7% cases and PCOD was found in 8.3%.

It is observed that, 8(13.3%) had a history of ovulation induction, 8(13.3%) had a history of Intra uterine Insemination, 2(3.3%) had a history of IVF. Increased risk of EP was noted among women whose pregnancies resulted from ovulation induction, especially with clomiphene citrate.

Scientific method of contraception was used by 20% of the population. 13.3 % of the cases were sterilized and 6.7% were using Copper T as a method of contraception and the other 80% were using nonscientific methods of contraception like natural methods, withdrawal methods etc. (Table 3).

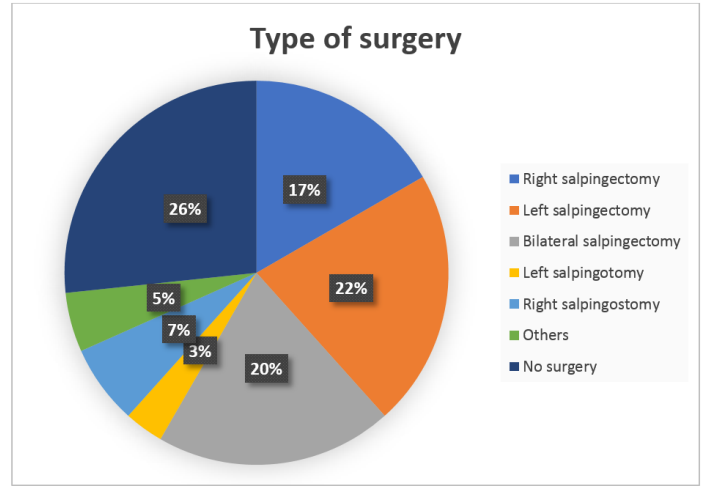
Table 3: Clinical characteristics of the study population

Clinical Parameters	Frequency	Percentage
History of Abortion	15	25%
History of ectopic pregnancies	8	13.3%
Use of Intra Uterine Device	5	8.3%
History of contraception use	12	20%
History of D & C	9	15%
Sterilization done or not	9	15%
History of infertility	18	30%
History of endometriosis	4	6.7%
History of PCOD	5	8.3%

Lab reports in this study showed a hemoglobin < 9 mg/dl in 8(13.3%), 26(43.3%) had high total count. 2 cases had negative urine pregnancy test but was later diagnosed with ectopic pregnancy. Beta hCG discriminatory level for rupture of ectopic was taken as 5000 IU/L. Out of total 60 patients, 35 cases had ruptured ectopic of which 23(65.7%) had Beta HCG more than 5000. Out of 25 unruptured cases 9 patients (36%) had Beta HCG > 5000 IU/L, 16 had Beta HCG < 5000 IU/L.

Out of total 60 ectopic pregnancies 40 (66.7%) had ectopic in the right side. Ultrasound and surgical findings showed that 58.3% of the cases were ruptured, 41.7% of them were unruptured. In the majority of the cases (55%), gestational sac could not be accurately measured due to rupture and a gestational sac of <4 cm was found in 28.3%. 53.3% had ectopic in the ampullary area of fallopian tube, (21.7%) in isthmic region, cornual in 13%, pregnancy of unknown origin in 11.7%. Out of 60 patients, 48 % had >500 ml blood loss, those with no blood loss are the ones who had medical management. Three of the patients had > 2 litre blood loss. Blood transfusion was given in 66.6% of cases. Out of 60 patients 43.3% patients had less than 2 units blood transfusion. 15 % had 4 units transfusion.

(Table 4).



Graph 3: Distribution of type of surgery among the study population

Discussion

This is a hospital-based prospective observational study conducted from October 2018 to March 2020 and aims to find out the clinical profile of EP in a tertiary care teaching hospital in Kerala. The incidence of EP in relation to intrauterine pregnancy in the present study is 4.6 in 100. It is higher than most other studies in developing countries, where it ranges from 0.56-1.5% [7, 8]. The incidence of EP in India had been reported by the Indian council of medical research (ICMR 1990) in a multi-centric case-control study. It was 3.12 per 1000 pregnancies or 3.86 per 1000 live births in the hospital reported pregnancies [9]. The present study's increased incidence may be because most of the cases in this study are referred from peripheral hospitals, our hospital being a tertiary care center. There is a wide variation in the incidence of EP reported in Western and Indian studies. This is because incidence varies from place to place, and the incidence is calculated based on variables such as total admissions, live births, intrauterine pregnancies, etc. The increase in incidence may be due to several factors like the increased prevalence of pelvic infections, increased tubal surgeries, increased incidence of infertility, and better facilities for diagnosis and treatment.

Pal et al. showed that the incidence was maximum in the 26-30 years of age group (37.6%) [10]. Some other studies showed that most of the patients in their study belonged to 21-30 age groups [11-13]. However, the exact pathological factors of maternal age on EP risk are unclear.

EP can happen at any time in the life of a female, from menarche to menopause. In the present study, 56.7% of the cases belonged to 21-30 years. This is almost similar to many other studies from developing countries. Women are more sexually active in this age group and get more predisposed to sexually transmitted diseases, PIDs, and their complications. Contrary to this, some studies from the USA [14] reported an increased EP incidence with advancing age. In India, women enter into their married life earlier and end their reproduction earlier.

In the present study, EP was seen predominantly with higher birth order. Coste et al. revealed that increasing parity increases tubal implantation possibility [15]. But Svirsky et al. and Stovall et al. showed no special relationship with parity, but a few studies reported a reduction in the incidence of EP with increasing parity [16-17]. In the study conducted by ICMR on EP, most women were young and had low parity [9].

Of the classical triad of EP symptoms, i.e., abdominal pain, amenorrhea, and vaginal bleeding is associated with EP. Some studies had reported that this triad is present in 28-29% of the

Table 4: Distribution of ultrasound and surgical findings of ectopic pregnancy

Characteristics	Frequency	Percentage
Side of ectopic on laparotomy	Right	40 (66.7%)
	Left	20 (33.3%)
Ruptured	Present	35 (58.3%)
	Absent	25 (41.7%)
SAC Size	<4cm	17 (28.3%)
	>4cm	10 (16.7%)
	No size mentioned	33 (55%)
Site of ectopic pregnancy	Ampullary	32 (53.3%)
	Isthmic	13 (21.7%)
	Cornual	8 (13.3%)
	Others	1 (1.7%)
	Not known	6 (10%)
Amount of blood loss	<500 ml	19 (31.7%)
	500-1 litre	10 (16.7%)
	1-1.5 litre	12 (20.0%)
	1.5-2 litre	4 (6.7%)
	2-2.5 litre	3 (5.0%)
	No	12 (20.0%)

Ectopic pregnancy was medically managed in 17 cases (28.3%) and surgically managed in 43 cases (71.7%). Of these medically managed cases 4 cases had tubal rupture which was later surgically managed. Significantly more cases had unilateral salpingectomy (38.4%) followed by bilateral salpingectomy (20%) and the least were salpingotomy (3.3%) (Graph 3).

study population [18-20]. In our study population, 64% of the patients presented with abdominal pain, which may not come into light unless they inquire explicitly. In the present study the most frequent gestational age at diagnosis of EP was >7 weeks. Pusuloori et al. also had similar findings in their research [21]. Some studies already mentioned that at least one of the risk factors for EP was found in 80% of the women [10, 18, 21]. This study also revealed similar findings. Among the risk factors, history of infertility (30%), history of abortions (25%) and history of contraception (20%) were the most common, followed by the history of sterilization (15%) in our study. In the present study, infertility accounted for 30% of cases of EP. Ectopic pregnancies were found to follow a period of infertility. Some studies had already shown the history of infertility as a risk factor for EP [23].

Only 5 patients had used IUD in this study. Literature had shown a link between the use of IUD insertion and EP [23]. But it was also reported that the use of contraceptives lessens unwanted pregnancies as well as ectopic pregnancies [24]. In the present study, 15% of the cases were sterilized. In India, 62% of the females prefer tubal sterilization over all other contraceptive use, but this procedure may fail even several years after the procedure.

Pelvic inflammatory disease, a significant predisposing risk factor for EP, was found in 6 patients contributing to about 10% of the study population in this study. Similar results were shown by the survey done by Marchbanks *et al.* [23].

In present study history of abortion within the past one and a half years was found in 25% of the patients. Studies have shown that previous abortions can be a risk factor for EP due to tubal dysfunction or damage following the induced abortion [15, 25]. Previous ectopic gestation was seen in 3.3% of the cases, and the finding was in agreement with the results of other studies [25, 26].

Our data clearly showed a higher Beta HCG level in patients with ruptured EP than those without rupture. The study showed that patients with Beta HCG levels >5000 mIU/ml had a higher chance of rupture. Goksedef et al. showed that Beta HCG >5000 IU/ml is a significant risk factor for tubal rupture [27]. Several other studies showed no relation between Beta HCG levels and ruptured ectopic [28, 29].

USG and operative findings in this study showed that the fallopian tubes were the most common seat of EP (88%) in the present study and showed that 66.7% of tubal ectopic pregnancies on the right side. The finding is almost in concurrence with other studies that reported a higher incidence in the right tube [30, 31]. Forty (66.6%) women needed a blood transfusion, and were reported in other studies [13]. Udigwe *et al.* also reported a 94.4% need for blood transfusion as they had to undergo a laparotomy and salpingectomy following ruptured EP [30].

In the present study, 73.3% of the cases were managed surgically, mainly salpingectomy and 26.7% of the patients were medically managed. Laparotomy was done for 75 % of cases (including 4 cases from the medically managed group, as they had a rupture later) and laparoscopy was done in 3% cases. Most studies had shown a similar higher rate for surgical management of EP [22, 30]. The tubal rupture occurrence in EP ranges from 18.0% to 64.5% [32]. No deaths due to EP were reported during the study period. Studies have reported maternal mortality between 0-1.3% due to EP [22, 30, 31, 33]. The mortality was mainly due to hemorrhage that follows the rupture, delayed referrals, and wrong diagnosis.

In the United Kingdom, there is a fall in the surgical management of EP [34, 35]. The reduction in the number may be

due to Early Pregnancy Assessment Units (EPAU), where the diagnosis of EP can be made at an early stage and is medically managed. In developing countries, most patients are being diagnosed after tubal rupture. Our center being a tertiary level referral center, 58.3% of the women had ruptured ectopic pregnancies and presented with a hemoperitoneum.

Conclusion

Every physician attending a woman in the reproductive age group presenting with abdominal pain should have a high index of clinical suspicion of EP unless proved otherwise irrespective of the presence or absence of amenorrhea or whether sterilized or not. EP is still a matter of great concern as the correct diagnosis is crucial. EPAU like setup in Kerala is thus necessary as EP can be diagnosed early thereby reducing the number of ruptured ectopic and hence decreasing the morbidity and mortality associated with EP.

References

1. Soren M, Patnaik R, Sarangi BK. A clinical study on ectopic pregnancy. *Int J Res Med Sci* [Internet] 2017;5(11):4776. Available from: <https://www.msjonline.org/index.php/ijrms/article/view/4106>
2. Sivalingam VN, Duncan WC, Kirk E, Shephard LA, Horne AW. Diagnosis and management of ectopic pregnancy [Internet]. Vol. 37, *Journal of Family Planning and Reproductive Health Care*. British Medical Journal Publishing Group, 2011, 231-40. Available from: <http://jfprhc.bmj.com/>
3. Shaw JLV, Dey SK, Critchley HOD, Horne AW. Current knowledge of the aetiology of human tubal ectopic pregnancy [Internet]. Vol. 16, *Human Reproduction Update*. 2010, 432-44. Available from: <https://academic.oup.com/humupd/article-abstract/16/4/432/801230>
4. Varma R, Gupta J. Tubal ectopic pregnancy [Internet]. Vol. 2009, *BMJ clinical evidence*. BMJ Publishing Group, 2009. Available from: <http://pmc/articles/PMC2907783/>
5. Schrage S, Potter BE. Diethylstilbestrol Exposure - American Family Physician [Internet]. *American Family Physician*. 2004, 69. Available from: www.aafp.org/afp.
6. Holman JF, Tyrey EL, Hammond CB. A contemporary approach to suspected ectopic pregnancy with use of quantitative and qualitative assays for the β -subunit of human chorionic gonadotropin and sonography. *Am J Obstet Gynecol* 1984;150(2):151-7.
7. Mehta DD, Kukadiya DSB, Guru DM, Pandya DN. Ectopic tales of kachcch: A study of ectopic pregnancies. *Int J Clin Obstet Gynaecol* [Internet]. 2019;3(5):10-6. Available from: <https://doi.org/10.33545/gynae.2019.v3.i5a.323>
8. Asah-Opoku K, Oppong SA, Ameme DK, Nuamah MA, Mumuni K, Yeboah AO *et al.* Risk factors for ectopic pregnancy among pregnant women attending a tertiary healthcare facility in Accra, Ghana. *Int J Gynecol Obstet* [Internet]. 2019;147(1):120-5. Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1002/ijgo.12928>
9. Anand P, Datey S, Gaur LN, Gupta N., Kumar S, Mehta S *et al.* Multi Centre Case control Study of Ectopic pregnancy in India [Internet]. *Journal of Obstetrics and Gynaecology* 1990, 425-30. Available from: https://jogi.co.in/articles/files/filebase/Archives/1990/jun/1990_425_430_Jun.pdf
10. Pal A, Gupta KB, Sarin R. A study of ectopic pregnancy

- and high risk factors in Himachal Pradesh. *J Indian Med Assoc* [Internet]. 1996;94(5):172–3, 202. Available from: <https://europepmc.org/article/med/8855569>
11. Jacob S, Nath AG. Ectopic pregnancy, risk factors, infertility, contraception. *Chang TRENDS RISK FACTORS ECTOPIC PREGNANCY- A CASE Control STUDY* [Internet]. 2017;6(12780):831-6. Available from: https://jemds.com/abstract.php?at_id=12780
 12. Murugesan A, Prabhu KMM. A retrospective study of ectopic pregnancies in a tertiary care hospital. *Int J Reprod Contraception, Obstet Gynecol* [Internet]. 2016;5(8):2537-40. Available from: <http://dx.doi.org/10.18203/2320-1770.ijrcog20162225>
 13. Shetty S, Shetty A. A Clinical Study of Ectopic Pregnancies in a tertiary Care Hospital of Mangalore, India. *Innov J Med Heal Sci* [Internet]. 2014;4:305-9. Available from: <https://www.researchgate.net/publication/274717335>
 14. Hoover KW, Tao G, Kent CK. Trends in the diagnosis and treatment of ectopic pregnancy in the United States. *Obstet Gynecol* [Internet]. 2010;115(3):495-502. Available from: <https://journals.lww.com/00006250-201003000-00005>
 15. Coste J, Job-spira N, Fernandez H. Risk factors for spontaneous abortion: A case-control study in france. *Hum Reprod* [Internet]. 1991;6(9):1332-7. Available from: <https://academic.oup.com/humrep/article/6/16139/Risk>
 16. Svirsky R, Maymon R, Vaknin Z, Mendlovic S, Weissman A, Halperin R, et al. Twin tubal pregnancy: A rising complication? *Fertil Steril*. 2010;94(5):1910.e13-1910.e16.
 17. Stovall TG, Ling FW, Cope BJ, Buster JE. Preventing ruptured ectopic pregnancy with a single serum progesterone. *Am J Obstet Gynecol*. 1989;160(6):1425-31.
 18. Pranathi P, Madhavi Y. A clinical analysis of ectopic pregnancies in a tertiary care hospital in Hyderabad. *Asian Pacific J Heal Sci* [Internet]. 2018;5(1):14-24. Available from: www.apjhs.com
 19. Jabbar FA, Al-Wakeel M. A study of 45 cases of ectopic pregnancy. *Int J Gynecol Obstet* [Internet]. 1980;18(3):214–7. Available from: <http://doi.wiley.com/10.1002/j.1879-3479.1980.tb00285.x>
 20. Verma I, Priya P, Chugh C, Kaur H, Sood D. Clinical presentation and outcome of ectopic pregnancies in a tertiary care rural hospital. *Int J Reprod Contraception, Obstet Gynecol* [Internet]. 2019;8(2):692. Available from: <http://dx.doi.org/10.18203/2320-1770.ijrcog20190307>
 21. Pusuloori R, Arora KD. A comparative study of ectopic pregnancy at a tertiary care centre. *Int J Reprod Contraception, Obstet Gynecol* [Internet]. 2018;7(2):694. Available from: <http://dx.doi.org/10.18203/2320-1770.ijrcog20180196>
 22. Zuber I, Chaurasia V. Spectrum of ectopic pregnancy in tertiary care centre. *Int J Reprod Contraception, Obstet Gynecol* [Internet]. 2018;7(4):1435. Available from: www.ijrcog.org
 23. Marchbanks PA, Coulam CB, Annegers JF. An association between clomiphene citrate and ectopic pregnancy: A preliminary report. *Fertil Steril* [Internet]. 1985;44(2):268-70. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0015028216487492>
 24. Bouyer J, Coste J, Shojaei T, Pouly JL, Fernandez H, Gerbaud L et al. Risk factors for ectopic pregnancy: A comprehensive analysis based on a large case-control, population-based study in France. *Am J Epidemiol* [Internet]. 2003;157(3):185-94. Available from: <https://academic.oup.com/aje/article-lookup/doi/10.1093/aje/kwf190>
 25. Rose J, Annamma T, Arun M. Ectopic Pregnancy 5 years' experience. *J Obstet Gynecol India* [Internet]. 2002;52(4):55-8. Available from: https://jogi.co.in/articles/files/filebase/Archives/2002/julaug/2002_55_58_JulAug.pdf
 26. Narayanan R, Lillian S., Liao S. Aetiology of Ectopic Tubal Gestation-An Analysis. *J Obstet Gynaecol India*, 1981, 559-662. Available from: https://jogi.co.in/articles/files/filebase/Archives/1983/oct/1983_659_662_Oct.pdf
 27. Goksedef BPC, Kef S, Akca A, Bayik RNE, Cetin A. Risk factors for rupture in tubal ectopic pregnancy: Definition of the clinical findings. *Eur J Obstet Gynecol Reprod Biol*. 2011;154(1):96-9.
 28. Galstyan K, Kurzel RB. Serum beta-hCC titers do not predict ruptured ectopic pregnancy. *Int J Fertil Womens Med* [Internet]. 2006;51(1):14-6. Available from: <https://europepmc.org/article/med/16596903>
 29. Heller DS, Kesavan S, Goldsmith LT. Risk factors for rupture of tubal ectopic pregnancy. *J Gynecol Surg* [Internet]. 2014;30(6):344-6. Available from: <https://www.liebertpub.com/doi/abs/10.1089/gyn.2014.0050>
 30. Udigwe, Umeononihu O, Mbachu I. Ectopic pregnancy: A 5 year review of cases at Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi. *Niger Med J* [Internet]. 2010;51(4):160. Available from: <https://www.nigeriamedj.com/article.asp?issn=0300-1652;year=2010;volume=51;issue=4;spage=160;epage=163;aulast=Udigwe>
 31. Igwegbe A, Eleje G, Okpala B. An appraisal of the management of ectopic pregnancy in a Nigerian tertiary hospital. *Ann Med Health Sci Res*. 2013;3(2):166.
 32. Bickell NA, Bodian C, Anderson RM, Kase N. Time and the risk of ruptured tubal pregnancy. *Obstet Gynecol* [Internet]. 2004;104(4):789-94. Available from: <http://journals.lww.com/00006250-200410000-00024>
 33. Panti A, Tanko B, Yakubu A, Egongdu S, Ikechukwu N, Lukman O. Ectopic pregnancy at Usmanu Danfodiyo University Teaching Hospital Sokoto: A ten year review. *Ann Niger Med* [Internet]. 2012;6(2):87. Available from: <http://www.anmjournals.com/text.asp?2012/6/2/87/108128>
 34. Taheri M, Bharathan R, Subramaniam A, Kelly T. A United Kingdom national survey of trends in ectopic pregnancy management [Internet]. Vol. 34, *Journal of Obstetrics and Gynaecology*. Informa Healthcare, 2014, 508-11. Available from: <https://www.tandfonline.com/doi/abs/10.3109/01443615.2014.910181>
 35. Van den Berg MMJ, Dancet EAF, Erlikh T, van der Veen F, Goddijn M, Hajenius PJ. Patient-centered early pregnancy care: A systematic review of quantitative and qualitative studies on the perspectives of women and their partners. *Hum Reprod Update* [Internet]. 2018;24(1):106-18. Available from: <https://academic.oup.com/humupd/article/24/1/106/4431018>