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

Sheelamoni A
Professor and Head of Department, Department of Obstetrics and Gynaecology, Travancore Medical College, Kollam, Kerala, India

Sheela Thomas
Associate Professor, Department of Obstetrics and Gynecology, Travancore Medical College, Kollam, Kerala, India

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

A comparison between ruptured and unruptured ectopic pregnancy and its association with the risk factors: A single center study

Anaswara T, Sheelamoni A and Sheela Thomas

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Abstract
Background: Rupture of ectopic pregnancy (EP) occurs mainly in the first trimester and is a life-threatening condition. It is a leading cause of maternal morbidity and mortality. Many risk factors had shown significant association with EP. This study aims to find the risk factors associated with ruptured and unruptured EP.
Methodology: This prospective study was conducted among 60 ectopic pregnancy cases during a study period of one and half years. The study population was classified according to the rupture status. The variables assessed were baseline, investigative and operative findings, and risk factors of ectopic pregnancy. Analysis was done to find the association of these factors with rupture status.
Results: Out of the 60 cases, the rupture was present in 35 patients and was absent in 25. Age, parity, and gestational age were not associated with rupture status. Investigative and operative findings are significantly associated with rupture status (Free fluid: p=0.001, Uterine size: p=0.029, Size of sac: p= 0.013, β-hCG: p=0.023, Site of ectopic pregnancy: p=0.001), i.e., abnormalities in these factors shows more chance of rupture in ectopic pregnancy cases. Risk factors such as the history of contraceptive use and sterilization show significance to rupture status (p=0.009 & p=0.006), respectively.
Conclusion: Any women in the reproductive age group who presents with amenorrhea, lower abdominal pain, or bleeding per vaginum should be evaluated for EP, irrespective of the sterilization status and the history of contraceptive use to prevent the rupture and morbidity/mortality associated with the same.

Keywords: ectopic pregnancy, ruptured, unruptured, risk factors

Introduction
Ectopic pregnancy (EP) happens while a fertilized ovum gets implanted anywhere outside the uterine cavity. Rupturing of EP is one of the most important causes of maternal mortality in the first trimester and contributes to maternal morbidity [1]. EP is a challenging situation, as early detection prevents maternal morbidity and mortality. The maternal mortality due to EP was more than 60% 200 years ago, and 80% of EP were not diagnosed before rupture. However, the mortality rate had decreased greatly due to early diagnosis [2].
The previous EP is considered a risk factor for future EP, causing a decline in fertility [3]. This condition can be found in any women in the reproductive age group and accounts for 10-15% of maternal deaths [4]. Factors like tubectomy, pelvic inflammatory disease (PID), spontaneous or induced abortions, infertility, assisted reproductive techniques, history of Copper T insertion, dilatation, and curettage (D and C), previous ectopic pregnancies were all considered as the factors that predispose to EP [5]. Fallopian tubes are the common site for EP, accounting for more than 95% of the cases [6].
Early diagnosis of EP in high-risk women can prevent tubal rupture. A study on the risk factors associated with the rupture of an EP helps identify women at risk, and early detection can save the woman's life through medical or surgical intervention [4]. Hence, it is important to have an early knowledge of the risk factors that leads to the rupture of EP to decrease morbidity, mortality, and hospitalizations. This institutional study aims to compare the risk factors associated with ruptured and unruptured EP.

Materials and Methods
This observational study was conducted among 60 EP cases observed in the Obstetrics Department of Travancore Medical College, Kerala, India, during a study period of one and a

half years from September 2018 to March 2020. The study included all the diagnosed cases of EP admitted to the study setting during the study period and excluded all intrauterine pregnancies. We have classified the subjects according to their rupture status. After the clearance from the Ethics Committee, the need and aim of the study were explained to the patients in detail, and obtained the written consent, and made a detailed history and clinical evaluation. A pretested proforma was used for the collection of the information from the study subjects.

Personal interview using a structured questionnaire was used to collect data on women's prior reproductive history such as previous spontaneous abortions, induced abortions, previous history of ectopic pregnancies. This study assessed the rupture status of the patient as well as the risk factors such as history infertility evaluation and treatment, history of abortion, current or past use of contraceptive measures like oral contraceptive pills (OCP), intrauterine device (IUD), levonorgestrel-releasing intrauterine system (LNG – IUS), EC pills; Dilatation and curettage (D&C), history of ectopic pregnancies, pelvic inflammatory disease (PID) and history of tubal surgeries like sterilization and recanalization.

Statistical Analysis

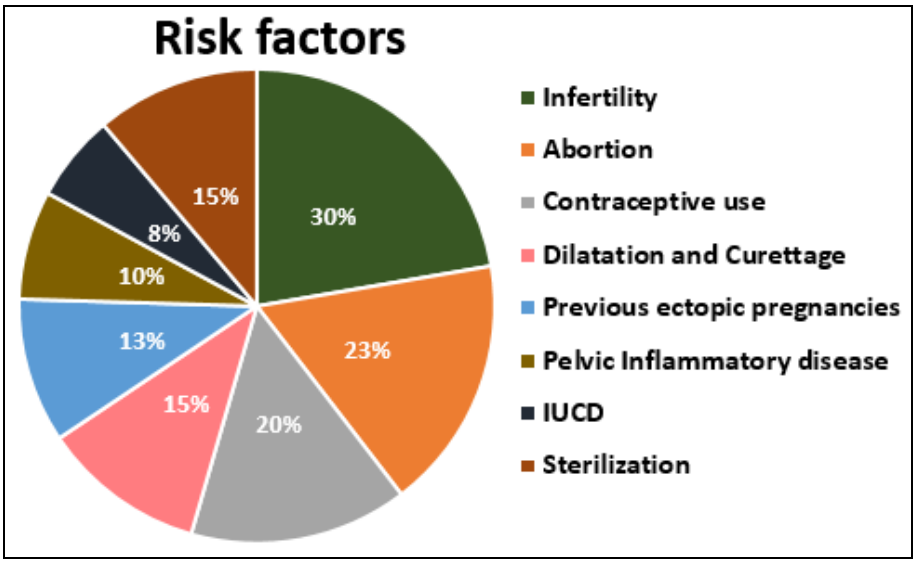
Descriptive statistics were used for the assessment of baseline characteristics of the data. Ordinal data were represented as frequencies and percentages, and continuous data as mean and standard deviation. For the association of rupture status with examination findings and risk factors, Chi-square test or Fisher's exact test were used. A p-value less than 0.05 showed statistical significance. Data were entered in Microsoft Excel datasheet, and Statistical Package for the Social Science (SPSS; ver. 20.0) was used for statistical analysis.

Results

Out of 1304 pregnancies reported, this observational study was conducted in 60 subjects with EP during a study period of one and a half years. The study aimed to compare the rupture and unruptured EPs with their risk factors. Out of the 60 reported EPs, 58.33% were ruptured and 41.66% were unruptured EPs. The overall rate of ruptured EP in this study was 2.68%.

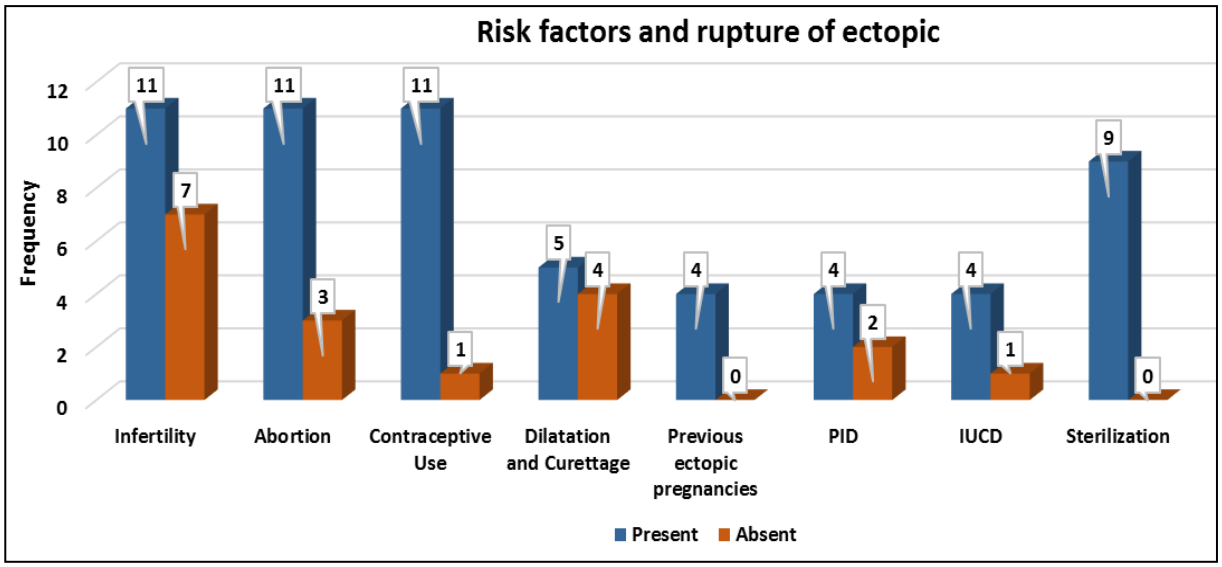
The clinical profile of the study group showed that the range of age varied from 18 to 43 years. The majority of the subjects belonged to 26-35 years, of which 18 (51.4%) in the ruptured group and 17(48.6%) were in the unruptured group. There were fewer subjects in lower and upper age groups. The distribution of parity showed that 18 (30%) were multiparous. Ectopic pregnancy was found in the first conception in 22 (36.7%) patients. Among the study population, 31(51.7%) of the study population belonged to the gestational age of more than seven weeks.

In the present study, 80% of the subjects were having one or the other risk factor. The majority (30%) had a history of infertility, then came a history of abortion (23%), contraceptive use (20%), history of D&C (15%), previous EP (13%), PID (10%), IUCD use (8%), and sterilization (15%) (Graph 1).



Graph 1: Distribution of risk factors of ectopic pregnancy

The multiple bar diagram for the distribution of rupture status and risk factors showed that, among the study subjects with these risk factors, the rupture was present in most cases (Graph 2).



Graph 2: Distribution of cases based on rupture status of ectopic

We have assessed the baseline characteristics such as age, parity, and gestational age with the rupture status. Enough evidence was not present to prove the association between these variables and rupture status. Age showed borderline significance (p=0.056) and others were not significant (p>0.05) (Table 1).

Table 1: Association of baseline characteristics with rupture status

Parameters		Rupture		Chi square value	p value
		Present, n (%)	Absent, n (%)		
Age	16-25	5(45.4%)	6(54.6%)	5.755	0.056
	26-35	18(51.4%)	17(48.6%)		
	36-45	12(85.7%)	2(14.3%)		
Parity	0	9(40.9%)	13(59.1%)	0.082	0.775
	1	12(60%)	8(40%)		
	2	13(76.5%)	4(23.5%)		
	3	1(100%)	0		
Gestational age	5-7 weeks	18(62.1%)	11(37.9%)	1.917	0.456
	8-10 weeks	16(59.3%)	11(40.7%)		
	>10 weeks	1(25%)	3(75%)		

Fisher's exact test

Out of 29 cases with rupture, free fluid was present in 79.3%, and it was statistically significant (p=0.001). Considering the uterine size, the study subjects with normal uterine size showed equally distributed rupture status (50%). Among the study subjects with bulky uterine size, the rupture was present in 81.2%.

This observation was statistically significant (p=0.029). The size of the sac was also significantly associated with rupture status (p<0.023). Out of total 60 patients, 35 had rupture of ectopic. Among the patients with ruptured ectopic, 23 (71.8%) had β-hCG more than 5000 IU/ml. Out of 25 unruptured cases, 9 patients (28.2%) had β-hCG more than 5000 IU/ml, 16 (57.2%) had β-hCG less than 5000 IU/ml and this association was statistically significant (p<0.05).

Considering site of ectopic, Ampullary ectopic was seen in 30 patients of which 24 (80%) had ruptured ectopic and 6 (20%) had unruptured ectopic. Also, 13 patients had ectopic in isthmus of fallopian tube of which 11 had (84.6%) rupture of ectopic pregnancy. There was a statistically significant association between site and rupture of ectopic (p<0.05) (Table 2).

Table 2: Investigative and operative findings with rupture status among the study population

Parameters		Rupture		Chi square value	p value
		Present, n (%)	Absent, n (%)		
Free Fluid	Present	23 (79.3)	6 (20.7)	10.162[b]	0.001*
	Absent	12 (38.7)	19 (61.3)		
Uterine size	Normal	22 (50)	22 (50)	4.714[a]	0.029*
	Bulky	13 (81.2)	3 (18.8)		
	Normal	16(45.7%)	18(72.0%)		
Size of Sac	<4 cm	5(29.4%)	12(70.6%)	8.675[a]	0.013*
	>4 cm	6(60%)	4(40%)		
	No size mentioned	24(72.7%)	9(27.3%)		
βhCG	<5000 IU/ml	12(42.8%)	16(57.2%)	5.173[b]	0.023*
	>5000 IU/ml	23(71.8%)	9(28.2%)		
Site of ectopic pregnancy	Ampullary	24(80%)	6(20%)	28.352[a]	0.001*
	Isthmus	11(84.6%)	2(15.4%)		
	Cornual	0(0.0%)	8(100%)		
	Abdominal	0(0.0%)	1(100%)		
	Not known	0(0.0%)	6(100%)		

a: Fishers exact test, b: Chi square test, p<0.05 shows significance.
βhCG: beta-human chorionic gonadotropin.

We have assessed the significance of risk factors and rupture status in the EP cases. In this analysis, only two factors, history of contraceptive use and sterilization, were significantly associated with the rupture status of EP cases. Out of the 60 cases, only 12 had a history of contraceptive use, 11 (91.7%) were ruptured, and 1 (8.3%) were unruptured. In the unruptured group, the history of contraceptive use was equally distributed. This observation was statistically significant, and we conclude that those with a history of contraceptive use had higher chances of rupture (p=0.009). Sterilization was done in 9 cases, and the rupture was present in all these patients. This finding was also statistically significant (p=0.006). Thus, we have enough evidence to prove the association of these two factors with rupture status (Table 3).

Table 3: Association of risk factors and rupture status among the study population

Parameters		Rupture of Ectopic		Chi square value	p value
		Present	Absent		
Past history of Infertility	Yes	11(61.1%)	7(38.9%)	0.082[b]	0.775
	No	24 (57.1%)	18(42.9%)		
History of Abortion	Yes	11(78.6%)	3 (21.4%)	3.077[a]	0.122
	No	24 (52.2%)	22(47.8%)		
History of Contraceptive Use	Yes	11(91.7%)	1(8.3%)	6.857[a]	0.009*
	No	24(50%)	24(50%)		
Dilatation/ Curettage	Yes	5(55.6%)	4(44.4%)	0.034[a]	0.854
	No	30(58.8%)	21(41.2%)		
Previous ectopic pregnancy	Yes	0	4(100%)	2.897[a]	0.089
	No	35(62.5%)	21(37.5%)		
Sterilization	Yes	9(100%)	0	7.563[b]	0.006*
	No	26(50.9%)	25(49.1%)		
History of Pelvic inflammatory disease	Yes	4(66.7%)	2(33.3%)	0.191[a]	0.662
	No	31(57.4%)	23(42.6%)		
IUCD	Yes	4(80%)	1(20%)	1.053[a]	0.305
	No	31(56.4%)	24(43.6%)		

a: Fishers exact test, b: Chi square test, $p<0.05$ shows significance.
IUCD: Intrauterine contraceptive device.

Discussion

The study was conducted in a tertiary care teaching hospital in South Kerala during a period of one and a half years. The study included 60 patients with EP. The rate of ruptured EP during a period of one and half years was 2.68%. A study conducted by Islam *et al*. involving 6675 patients showed the ruptured ectopic incidence of 0.47% [7], and that conducted by Kohn *et al*. involving 730 patients showed an incidence of 6.71% ruptured cases [8].

Out of the 60 reported ectopic pregnancies, 58.33% were ruptured, and 41.66% were unruptured ectopic pregnancies. The reported rate of ectopic rupture in other studies showed 49 out of 96 (51%), 88 out of 232 (37.9%), 12 out of 39 (31%), and 65 out of 288 (23%) in studies conducted by Kohn *et al*., Goksedef *et al*., Buckley *et al*., and Mol *et al*. respectively(4,8–10). Our institution was a referral center that caters to a vast population in the district of Kollam in Kerala. It might be the reason for the high rate of ruptured cases in this study compared to other studies. Some patients in this study were referred from the peripheral hospitals to the institution's Emergency Department after a rupture. Some studies also showed that most of the ectopic pregnancies were ruptured at the time of presentation [7, 11]. Islam *et al*. stated that the increased rate of ruptured ectopic might be due to late presentation of the patients or failure of early diagnosis, especially in developing countries [7].

The study showed that age had borderline significance with rupture status (p value 0.056). Similar results had been already reported by some other studies [12, 13]. Study conducted by Goksedef *et al*. did not show any statistically significant association between age and parity [4]. As the age advances, the chance of EP increases which also increases the chance of rupture if goes undiagnosed. In the age group 36-45 years, 85.7% of the cases with EP had rupture in this study. Advancing age may increase the risk of exposure to various risk factors of EP and may also change the function of the fallopian tubes that would delay the transport of zygote to the uterine cavity, thereby increasing the risk of EP [14]. The study also showed increased chance of rupture as the parity increases. Most of the rupture occurred between 5-7 weeks of gestation in this study but this was not statistically significant. Study done by Goksedef *et al*., showed that women with gestational age more than 8 weeks were 46.6 times more likely to experience a tubal rupture than with gestational age less than 6 weeks [4].

Ectopic rupture will result in hemoperitoneum resulting in the presence of free fluid. The size of the sac was more than 4 cm in most of the patients with ruptured status. In the group having sac size less than 4 cm, 70.6% did not have a rupture. All these results were statistically significant.

EP with a β-hCG level of more than 5000 IU/ml is indicative of surgical management. Any value below 5000 IU/ml can be initially managed medically [15], and if the β-hCG value increases during subsequent serum analysis, EP may be managed surgically later [16]. In this study, 71.8% of the cases with rupture had β-hCG levels more than 5000 IU/ml. Only 42.8% of the patients had ruptured EP in the group having β-hCG level less than 5000 IU/ml, and this result was statistically significant (p-value 0.023). A study done by Goksedef *et al*. showed that higher β-hCG levels of >5000 IU/ml and higher gestational age had a significant association with increased risk of ectopic rupture [4]. Literature had shown that an EP with the size of sac <4 cm and β-hCG level less than 1000 IU/ml had successful expectant management and spontaneous resolution [17].

In this study, 30 patients had EP in the ampullary region. Out of these 30 EP cases, 24 (80%) were in the ruptured group, and 6 (20%) were in the unruptured group. Isthmus was the ectopic site in 13 patients, of which 11 (84.6%) patients were in the ruptured group, and 2 (15.4%) were in the unruptured group. The site of ectopic could not be determined in 6 patients. Other ectopic sites were cornual (8 patients) and abdominal (1 patient) and these cases were in the unruptured group. Several reports had shown that ampullary pregnancies were most common, followed by isthmus, fimbrial, and corneal [2, 7]. An EP review conducted by Rana *et al*. showed that the fallopian tube is the most common site of EP, with 75-80% in the ampullary region, 10-15% in the isthmic area, and 5% in the fimbrial end [17]. One case in our study showed the abdomen as the site of ectopic. Rana *et al*. had pointed out that an abdominal ectopic is a rare form of EP with a rate of 1.3%. In the review article, Alkatout *et al*. had pointed out that about 3% of the EP can be located in unusual sites like rudimental uterine horn, ovary, abdominal cavity, broad ligament, cervix, or vaginal and had also reported that abdominal EP occurs in only 1% of all EP [2]. The physicians and obstetricians should carefully watch for the symptoms of EP for individual patients. They should consider several criteria to decide on the type of treatment that needs to be catered to each patient.

The study showed the presence of at least one risk factor in 80% of the cases. Some other studies had also shown similar results

[18, 19]. The most common risk factor as per this study was infertility accounting for 30% of the cases, followed by the history of abortion in 23%, history of contraceptive use in 20%, history of D&C in 15%, previous ectopic pregnancies in 13%, PID in 10%, IUCD insertion in 8% and sterilization in 15% of the study population.

As per this study, history of contraceptive use and sterilization has a statistically significant association with ectopic rupture. Other risk factors like infertility, abortion, D&C, previous EP, history of PID, and IUCD use did not significantly correlate with rupture status. Goksedef *et al*., in their study, had reported no significant association between parity, history of PID, IUD use, and cigarette smoking. In another large retrospective study involving 837 patients, a higher incidence of previous EP (33%) was found in the ruptured group [20]. The history of EP should be documented in the medical record to detect the risk factor in their future pregnancies. Diagnosed EP patients should be counseled regarding the chance of recurrence. It is better to advise them to consult an obstetrician early in their future pregnancies [15]. All women with positive pregnancy tests should undergo an ultrasound examination as early as possible to locate an intrauterine/extrauterine gestation for earlier intervention or conservative treatment. Moreover, the possibility of heterotopic pregnancy should also be kept in mind as an intrauterine pregnancy does not rule out its possibility [2]. None of the patients in this study group had heterotopic pregnancy.

In this study, the patients using contraceptives or who underwent sterilization had never doubted the chance of pregnancy. It would have delayed the medical/surgical intervention for their symptoms, resulting in the ectopic rupture. Studies had reported the failure rate of sterilization between 0.1-0.2% [21]. Hence, it is recommended to counsel all women regarding the failure rate of sterilization and to seek medical advice at the earliest in case of any symptoms like lower abdominal pain, bleeding per vaginum, or amenorrhea. No mortality was reported during this study period. However, several studies had reported maternal mortality due to EP and the rate was between 0% to 1.3% [5, 6, 22, 23]. In the United Kingdom, Early Pregnancy Assessment Units (EAPUs) had been set up to provide higher quality and cost-effective early pregnancy care and had shown significant positive effects [24]. However, future studies are essential to evaluate the feasibility and usefulness of such EAPUs in Kerala for the early detection of EP and reduce maternal mortality and morbidity. This is a single-center study. A study conducted in different centers would have given a much clearer picture of the incidence and association of risk factors with rupture status of ectopic. Moreover, a detailed study that includes the patients' socioeconomic status needs to be conducted to check whether any of those factors have any association with the rupture status.

Conclusion

All physicians and obstetricians should keep in mind that any women of reproductive age group, who presents with amenorrhea, lower abdominal pain, or bleeding per vaginum should be evaluated for EP, irrespective of the presence or absence of contraceptive use and sterilization status. This helps in the early detection of EP and reduces maternal mortality and morbidity to a great extent.

References

1. Fylstra DL. Tubal Pregnancy. Obstet Gynecol Surv [Internet] 1998-2021;53(5):320-8. Available from: https://journals.lww.com/obgynsurvey/Abstract/1998/05000/Tubal_Pregnancy__A_Review_of_Current_Diagnosis_and.24.aspx
2. Alkatout I, Honemeyer U, Strauss A, Tinelli A, Malvasi A, Jonat W *et al*. Clinical diagnosis and treatment of ectopic pregnancy. Obstet Gynecol Surv [Internet] 2013-2021;68(8):571-81. Available from: https://journals.lww.com/obgynsurvey/Fulltext/2013/08000/Clinical_Diagnosis_and_Treatment_of_Ectopic.12.aspx
3. Murugesan A, Prabhu K, MMA. Retrospective study of ectopic pregnancies in a tertiary care hospital. Int J Reprod Contraception, Obstet Gynecol [Internet]. 2016 Jan 11 2021;5(8):2537-40. Available from: http://dx.doi.org/10.18203/2320-1770.ijrcog20162225
4. 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.
5. 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] 2010-2021;51(4):160-63. Available from: https://www.nigeriamedj.com/article.asp?issn=0300-1652;year=2010;volume=51;issue=4;spage=160;epage=163;aulast=Udigwe
6. 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):166-70.
7. Islam A, Fawad A, Shah AA, Jadoon H, Sarwar I, Abbasi AUN. Analysis of Two Years Cases of Ectopic Pregnancy. J Ayub Med Coll Abbottabad 2017;29(1):65-7.
8. Kohn MA, Kerr K, Malkevich D, O'Neil N, Kerr MJ, Kaplan BC. Beta-human chorionic gonadotropin levels and the likelihood of ectopic pregnancy in emergency department patients with abdominal pain or vaginal bleeding. Acad Emerg Med 2003;10(2):119-26.
9. Buckley RG, King KJ, Disney JD, Ambroz PK, Gorman JD, Klausen JH. Derivation of a clinical prediction model for the emergency department diagnosis of ectopic pregnancy. Acad Emerg Med [Internet] 1998-2021;5(10):951-60. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1553-2712.1998.tb02770.x
10. Mol BWJ, Hajenius PJ, Engelsbel S, Ankum WM, Van Der Veen F, Hemrika DJ *et al*. Can noninvasive diagnostic tools predict tubal rupture or active bleeding in patients with tubal pregnancy? Fertil Steril 1999;71(1):167-73.
11. Shabab U, Hashmi HA. Different Pattern of Presentation of Ectopic Pregnancy and its Management. J Surg Pakistan [Internet] 2021;18(1):27-40. Available from: https://www.researchgate.net/publication/337075612
12. Nybo Andersen AM, Wohlfahrt J, Christens P, Olsen J, Melbye M. Maternal age and fetal loss: Population based register linkage study. Br Med J [Internet] 2000-2021;320(7251):1708-12. Available from: http://www.bmj.com/
13. Goddijn M, Van Der Veen F, Schuring-Blom GH, Ankum WM, Leschot NJ. Cytogenetic characteristics of ectopic pregnancy. Hum Reprod [Internet]. 1996 Dec 1 2021;11(12):2769-71. Available from: https://academic.oup.com/humrep/article/11/12/2769/714644
14. Shaw JLV, Oliver E, Lee KF, Entrican G, Jabbour HN, Critchley HOD *et al*. Cotinine exposure increases fallopian tube PROKR1 expression via nicotinic AChRα-7: A potential mechanism explaining the link between smoking

and tubal ectopic pregnancy. Am J Pathol 2010;177(5):2509-15.
15. Carusi D. Pregnancy of unknown location: Evaluation and management. Semin Perinatol [Internet] 2019;43(2):95-100. Available from: https://doi.org/10.1053/j.semperi.2018.12.006
16. Elson CJ, Salim R, Potdar N, Chetty M, Ross JA, Kirk EJ. Diagnosis and Management of Ectopic Pregnancy. BJOG An Int J Obstet Gynaecol [Internet] 2016;123(13):e15-55. Available from: http://doi.wiley.com/10.1111/1471-0528.14189
17. Rana P, Kazmi I, Singh R, Afzal M, Al-Abbasi FA, Aseeri A, *et al*. Ectopic pregnancy: A review. Arch Gynecol Obstet. 2013;288(4):747-57.
18. Pal A, Gupta KB, Sarin R. A study of ectopic pregnancy and high risk factors in Himachal Pradesh. J Indian Med Assoc [Internet] 2021;94(5):172-3, 202. Available from: https://europepmc.org/article/med/8855569
19. Pranathi P, Madhavi Y. A clinical analysis of ectopic pregnancies in a tertiary care hospital in Hyderabad. Asian Pacific J Heal Sci [Internet] 2021;5(1):14-24. Available from: www.apjhs.com
20. Latchaw G, Takacs P, Gaitan L, Geren S, Burzawa J. Risk Factors Associated with the Rupture of Tubal Ectopic Pregnancy. Gynecol Obstet Invest [Internet] 2021;60(3):177-80. Available from: https://www.karger.com/Article/FullText/88032
21. Rathod S, Samal SK. Clinical analysis of post sterilization failure cases in a tertiary hospital. Int J Reprod Contraception, Obstet Gynecol 2017;6(8):3294-96.
22. NICE. Ectopic pregnancy and miscarriage guideline 2021. (September). Available from: www.nice.org.uk/guidance/qs69
23. French S, Henry T, Williams E. Evaluation of Waiting Times and Sonographic Findings in Patients with First Trimester Vaginal Bleeding at the University Hospital of the West Indies. Can Emergency Department Ultrasound Make a Difference? West Indian Med J [Internet] 2021;63(3):247-51. Available from: /pmc/articles/PMC4663903/
24. 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] 2021;24(1):106-18. Available from: http://academic.oup.com/humupd/article/24/1/106/4431018