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	RETROSPECTIVE STUDY OF TUBAL ECTOPIC PREGNANCY AT TERTIARY CARE CENTRE, ANDHRA PRADESH		KEY WORDS: Absence of menstruation, Maternal mortality, Risk factors, Tubal pregnancy, Ultrasonography, Vaginal bleeding
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ABSTRACT	Introduction: Ectopic Pregnancy [EP] poses a substantial medical challenge, often eluding timely detection and potentially leading to life-threatening consequences. When women of reproductive age present with lower abdominal pain or vaginal bleeding, it's essential to maintain a high level of suspicion for ectopic pregnancy to mitigate associated mortality and morbidity risks. Objective: This study seeks to provide a comprehensive examination of Ectopic pregnancy cases, with a primary focus on determining its incidence. It also aims to explore high-risk factors, describe various clinical presentations, elaborate on diagnostic methods, analyse outcomes, and evaluate complications linked to EP. Materials and Methodology: Conducted at a tertiary care medical teaching hospital in Andhra Pradesh, India, this retrospective cohort study involved a thorough review of medical records spanning the period from January 2022 to December 2022. The study meticulously compiled essential data, including parity, risk factors, clinical manifestations, modes of management, and the requirement for blood transfusion. The primary endpoints of this investigation encompassed the incidence of Ectopic pregnancy, identification of risk factors, and an exploration of the mortality and morbidity profiles within the study population. Findings: Over one-year timeframe of this study, a total of seventy-six cases of EP were identified, resulting in an incidence rate of 9 per 1000 pregnancies. The majority of women within the study population fell within the age range of 20-25 years, constituting 50% of the cases. Notably, 13% of the women were nulliparous. The most commonly identified risk factors were a history of previous surgery (37%) and prior pelvic surgery (37.50%). Intriguingly, fifteen cases (20.8%) were diagnosed in women who had previously undergone tubal ligation. The classic triad of lower abdominal pain, amenorrhea, and vaginal bleeding was observed in 45 (59.2%) cases. The pivotal role of ultrasonography in the diagnostic process was highlighted, as it played a crucial role in diagnosing 41 (53.9%) cases. It's important to note that urine pregnancy tests yielded positive results in 100% of the cases. Regarding management, medical intervention with methotrexate alone proved successful for 3 patients, while an additional four necessitated surgical intervention due to the ineffectiveness of medical management. Importantly, over half of the patients (73%) required blood transfusions, with no experiencing transfusion-related acute lung injury. Remarkably, 2 deaths were recorded during the course of this study. Conclusion: It is imperative to identify common risk factors associated with EP. The integration of transvaginal ultrasonography and human chorionic gonadotropin assays has notably transformed the landscape of EP management, offering invaluable tools for early diagnosis and intervention.		
	INTRODUCTION Ectopic pregnancy stands as a formidable challenge in the realm of obstetrics and gynaecology, demanding vigilant clinical attention. This perplexing condition occurs when a fertilized ovum implants outside the uterine cavity, with grave consequences potentially including the rupture of the ectopic site, culminating in life-threatening internal haemorrhage. The rupture of an ectopic pregnancy mandates immediate medical intervention, underscoring the critical significance of a nuanced understanding of this clinical entity. The prevalence of ectopic pregnancy has shown a disconcerting upward trajectory, encompassing approximately 1.4% to 2.4% of all pregnancies worldwide [1][2]. While advances in early pregnancy detection and diagnostic methodologies have made significant strides in the recognition of ectopic pregnancies, there remains an imperative to explore the multifaceted clinical nuances of this condition, including its diverse risk factors, intricate clinical presentation, nuanced management strategies, and potential complications [3]. Ectopic pregnancies are a poignant example of the clinical art of medicine, where timely diagnosis and intervention can make the difference between life and death. These pregnancies often manifest with nonspecific symptoms, such as lower abdominal pain, vaginal bleeding, and shoulder tip pain, which can mimic other gynaecological conditions, making early diagnosis a formidable clinical challenge.		
	Therefore, this research article aims to delve deeper into the clinical intricacies of ectopic pregnancies, emphasizing their risk factors, myriad clinical presentations, intricate management approaches, and potential complications.		
	MATERIALS & METHODS: This retrospective investigation was carried out at a tertiary care teaching hospital located in the southern region of India. Ethical approval for the study was obtained from the Institute Ethics Committee. The medical records department was the source of patient data, encompassing cases diagnosed with ectopic pregnancies (EP) spanning from January 2022 to December 2022. Information regarding patient characteristics such as age, parity, and EP risk factors was meticulously collected. Furthermore, the study documented the diagnostic methods employed, various management approaches, complications that arose, and the necessity for blood transfusions. The primary objectives of this research were to assess the incidence of EP, identify associated risk factors, and evaluate the mortality and morbidity rates among affected women. Data were meticulously entered into an MS Excel spreadsheet and subjected to analysis using SPSS software version 19.0. Categorical variables were expressed as frequencies and corresponding percentages, whereas continuous variables were represented as Mean ± SD.		
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RESULTS

Over a one-year timeframe, a total of 8400 pregnancies came under scrutiny, and among this cohort, 76 instances were diagnosed as extra-uterine pregnancies (EP). This translated to an incidence rate of 9.048 per 1000 pregnancies, or approximately one in every 111 pregnancies. The prevailing age group among these women fell within the 20 to 25-year range, as illustrated in Table/Figure-1. The most frequently encountered risk factors comprised a history of prior pelvic surgeries (37%) and pelvic inflammatory disease (15%). Among those who had undergone pelvic surgery, 26 individuals had opted for tubal ligation, while two women had undergone tubal recanalization.

Table 1 :Patient characteristics.

Characteristics	N=76	%
Age (years)		
20-25	38	50
26-30	28	37
31-35	8	10
>35	2	3
Parity		
0	10	13
1	15	20
2	46	60.5
3 and above	5	6.5
Risk Factors		
History of previous ectopic pregnancy	3	3.9
History of pelvic surgery	28	37
History of infertility	6	7.8
History of PID	21	27.6
History of intra uterine contraceptive device	3	3.9
No risk factor noted	5	6.5
Symptoms		
Amenorrhoea	70	93
Vaginal bleeding	60	78.9
Abdominal pain	55	72.3
Triad of symptoms	45	59.2
Signs		
Shock	20	26.3
Abdominal tenderness	53	69.7
Cervical motion tenderness	47	61.8
Adnexal tenderness	47	61.8
Pallor	65	85.5
Hemoperitoneum	53	69.7
Diagnostic modality		
Clinical alone	35	46
ultrasonography	41	53.9
laparoscopy	0	4.2

Among the cases studied over a one-year period, 45 instances (59.2%) exhibited the classic triad of symptoms, including amenorrhea, vaginal bleeding, and lower abdominal pain. Amenorrhoea was the most frequently reported complaint, observed in 70 women (93%). A history of vaginal bleeding was noted in 60 women (78.9%). Examination revealed cervical motion tenderness in 61.8% of the cases.

In all cases, a spot urine pregnancy test was conducted and yielded positive results without exception. Diagnosis of ectopic pregnancy (EP) relied solely on clinical findings in 35 women (46%). However, ultrasonography played a pivotal role in diagnosing an additional 41 cases. On average, the gestational age at diagnosis was 7.1 weeks.

Medical management was considered for patients who met specific criteria, including hemodynamic stability, gestational sac size less than 4cm by transvaginal ultrasonography, serum beta HCG levels below 10,000 U/ml,

and the absence of free pelvic fluid. Compliance with regular follow-up was ensured before initiating medical treatment. Out of the total, 4 women (5.2%) underwent medical management with methotrexate. This group included three individuals who received a single dose of methotrexate, while one required a multiple-dose regimen. one of the 4 women ultimately required surgical intervention after unsuccessful medical management. Among the 73 women managed surgically, 64 were found to have ruptured ectopic pregnancies, leading to intraoperative hemoperitoneum. The mean haemoglobin level at admission was 9.6 ± 1.9 g/dL. A significant proportion of patients (73%) required blood transfusions, with four women experiencing febrile illness. The average duration of hospitalization was 6.6 ± 2.9 days, and no fatalities occurred. Admission to the intensive care unit was necessary in some cases, either due to hemodynamic instability or complications such as atelectasis. Additionally, two cases exhibited abdominal wound infections [Table/Fig-2].

Table 2: Morbidity and mortality associated with ectopic pregnancy

Complications	No cases	percentage
Wound infection	2	3%
Anemia	55	73%
Febrile illness	4	6%
ICU admission	4	6%
TRALI	Nil	Nil
Mortality	2	3%

DISCUSSION:

Ectopic pregnancies (EP) contribute significantly to maternal mortality in India, comprising 3.5-7.1% of such cases [7,8][4,5]. Our study reported an EP incidence of 0.9%, consistent with findings from various developing countries where the incidence typically ranges from 0.56% to 1.5% [1-3,5,6,9,10] [6-8,9,10,11,12]. EP poses a notable risk in the first trimester, underscoring the importance of prompt referral to advanced medical facilities to mitigate mortality and morbidity.

While 59.2% of our cases presented with the classic symptom triad—abdominal pain, amenorrhea, and vaginal bleeding—other studies reported varying percentages, ranging from 28% to 95% [1,11,12] [6,13,14]. This indicates that this triad is not a predominant feature in most cases. Surprisingly, 93% of our cases acknowledged a history of amenorrhea, though this detail may remain concealed unless explicitly inquired.

Our study revealed an average gestational age at EP diagnosis of 7.1 weeks, slightly higher than the 6-week diagnosis reported by Khaleeque et al. [2] [7]. Additionally, Singh et al. noted that 52% of their cases lacked preceding amenorrhea [1] [6]. These findings highlight the potential lack of awareness among some women regarding their ongoing pregnancies, contributing to delayed identification of pregnancy complications. Such cases often first come to the attention of primary healthcare centres or general practitioners, emphasizing the significance of thorough medical histories.

Among our cases, 93.4% had at least one identifiable risk factor, consistent with findings in prior research [1,2,13] [6,7,15]. Notably, prior pelvic surgery emerged as the most common risk factor (37%), followed closely by PID (27.6%) in our study. In contrast to our findings, several studies reported previous abortions as the primary risk factor for EP [1-3,6,9,12,14,15] [6-8,10,11,14,16,17]. This variation may be attributed to the higher prevalence of caesarean sections (33.6%) and tubal sterilization (57.4%) in our region [16]. Singh et al. also identified prior tubal surgery as the predominant (40%) risk factor in their study, reflecting the high acceptance (57.4%) of tubal sterilization as a family

planning method [1,16] [6,18]. Hence, a thorough pregnancy evaluation is essential in all cases, irrespective of sterilization status.

History of Pelvic Inflammatory Disease (PID) was reported in 27.6% of our patients, in line with findings by Singh et al. and Mufti et al. [1,15] [6,17]. Conversely, Nigerian researchers noted PID in 27-35.5% of their patients, making it the most prevalent risk factor for EP in that region, possibly linked to higher polygamy rates [3,5,6] [8,9,10].

While clinical examination may raise suspicion of EP, relying solely on clinical signs and symptoms would have resulted in missed diagnoses in 53.9% of our cases. Ultrasonography played a pivotal role in diagnosing the majority of these cases, with no necessitating laparoscopy for confirmation. In the past, culdocentesis, abdominal paracentesis, and laparoscopy were frequently used to aid diagnosis, but ultrasonography's non-invasive nature has now made it the primary diagnostic tool [3,5,6,17] [8,9,10,19]. Availability of point-of-care ultrasonography is crucial to avoid diagnostic delays. This may not necessarily require gynaecologic specialists, as physicians in community practice can acquire comparable skills through intensive two-week ultrasonography training, as suggested by Jang et al. [18] [20]. Surgical management was the choice in the majority (86.1%) of cases in our study, typically involving salpingectomy. However, recent research suggests that laparoscopic surgical management is not superior to laparotomy in terms of tubal patency and intrauterine pregnancy rates [19]. Most studies have reported a similarly high rate of surgical management [2,3,6,9,20] [7,8,10,11,21]. In contrast, surveys from the United Kingdom have reported a decline in surgical management cases (from 98% to 62% and 50% to 27%, respectively) over the past two decades, attributed to the establishment of Early Pregnancy Assessment Units (EPAU) where early EP diagnosis is likely [21,22] [22,23].

The fallopian tubes were the most common site of EP in our study (100%). While most studies report a higher incidence of EP in the right tube, our findings indicated 72.2% of tubal ectopic pregnancies on the left side. In developing countries, the majority of patients are diagnosed after tubal rupture. Our tertiary-level referral centre saw 65.3% of women with ruptured ectopic pregnancies, often presenting with hemoperitoneum. This contrasts with studies reporting 70-100% of ectopic pregnancies ruptured at diagnosis, largely due to late referrals. Approximately 73% of our cases required blood transfusion, consistent with other studies [2,9,10,20] [7,11,12,21]. Udigwe et al. reported a 94.4% need for blood transfusion, as all their cases presented with ruptured ectopic pregnancies, underwent laparotomy, and received salpingectomy. The mean duration of hospital stay in our study was 6.6 ± 2.9 days. Udigwe et al. similarly reported that 94.4% of their patients had hospital stays of less than 8 days, while 5.6% required prolonged hospitalization of up to 14 days [3][8].

During our study period, there were 2 recorded deaths attributed to EP. Maternal mortality rates due to EP have been reported between 0% and 1.3% in various studies [2,3,5,6,9,20] [7,8,9,10,11,21]. Most EP-related mortalities result from haemorrhage following rupture due to delayed referrals and diagnosis. The National Institute for Health and Clinical Excellence estimated that inadequate care was associated with two-thirds of maternal deaths due to EP in the UK [24][24].

Prevention and treatment of PID, along with encouraging early transvaginal ultrasonography to confirm pregnancy location, can aid in preventing late diagnoses. This approach may also allow for medical management or fertility-sparing conservative surgical procedures. Establishing Early Pregnancy Assessment Units (EPAUs) has been shown to

enhance the quality and cost-effectiveness of care, positively impacting early pregnancy management in the UK [22] [23]. Future research should assess the feasibility and effectiveness of setting up such EPAUs in India.

Given that ultrasonography plays a central role in evaluating EP, its availability at the point of care can facilitate safe and timely discharge of patients presenting to emergency departments with suspected EP [25][25]. Future research could explore the impact of training doctors at primary and secondary healthcare levels through intensive two-week ultrasonography courses on EP-related mortality and morbidity.

Furthermore, research is needed to assess the clinical utility of markers such as serum Placental Growth Factor (PGF) and Vascular Endothelial Growth Factor (VEGF) in differentiating intrauterine and ectopic pregnancies, as suggested by Horne et al. and Cabar et al. [26,27] [26,27].

Limitations:

We acknowledge that our study's retrospective design imposes inherent limitations. Additionally, we encountered challenges in quantifying the extent of the delay in diagnosing and referring cases and its potential impact on morbidity.

CONCLUSION:

The diagnostic methods of culdocentesis and laparoscopy have been surpassed by non-invasive transvaginal ultrasonography and the implementation of highly sensitive and precise beta HCG assays for diagnosing EP. The early identification and management of EP within specialized early pregnancy units equipped with point-of-care ultrasonography hold significant potential for diminishing the morbidity and mortality associated with ectopic pregnancies. To conclude, the key strategies for reducing the morbidity and mortality related to EP encompass the identification of underlying risk factors, the widespread availability of point-of-care ultrasound, the complementation of beta HCG assays, and the timely implementation of interventions.

REFERENCES:

- Shaw JL, Dey SK, Critchley HO, Horne AW. Current knowledge of the aetiology of human tubal ectopic pregnancy. *Hum Reprod Update*. 2010 Jul-Aug;16(4):432-44. doi: 10.1093/humupd/dmp057. Epub 2010 Jan 12. PMID: 20071358; PMCID: PMC2880914.
- Farquhar CM. Ectopic pregnancy. *Lancet*. 2005 Aug 13-19;366(9485):583-91. doi: 10.1016/S0140-6736(05)67103-6. PMID: 16099295.
- Barnhart KT, Sammel MD, Gracia CR, Chittams J, Hummel AC, Shaunik A. Risk factors for ectopic pregnancy in women with symptomatic first-trimester pregnancies. *Fertil Steril*. 2006 Jul;86(1):36-43. doi: 10.1016/j.fertnstert.2005.12.023. Epub 2006 May 30. PMID: 16730724.
- Shah P, Shah S, Kuttu RV, Modi D. Changing epidemiology of maternal mortality in rural India: time to reset strategies for MDG-5. *Trop Med Int Health*. 2014 May;19(5):568-75. doi: 10.1111/tmi.12282. Epub 2014 Feb 18. PMID: 24533443.
- Yadav, Kalpana, Arpita Namdeo, and Meena Bhargava. "A retrospective and prospective study of maternal mortality in a rural tertiary care hospital of Central India." *Indian Journal of Community Health* 25.1 (2013): 16-21.
- Singh S, Mahendra G, Vijayalakshmi S, Pukale RS. Clinical study of ectopic pregnancy in a rural setup: A two year survey. *Natl J Med Res*. 2014;4(1):37-39.
- Khaleeq F, Siddiqui RI, Jafarey SN. Ectopic pregnancies: a three year study. *J Pak Med Assoc*. 2001 Jul;51(7):240-3. PMID: 11558214.
- Udigwe GO, Umeonihui OS, Mbachu II. Ectopic pregnancy: a 5 year review of cases at nnamdiakiziwe university teaching hospital (NAUTH) Nnewi. *Niger Med J*. 2010;51(4):160.
- Panti A, Tanko B, Yakubu A, Egondu S, Ikechukwu N, Lulman O. Ectopic pregnancy at Usmanu Danfodiyo University Teaching Hospital Sokoto: A ten year review. *Ann Niger Med*. 2012;6(2):87.
- Igwembe A, Eleje G, Okpala B. An appraisal of the management of ectopic pregnancy in a nigerian tertiary hospital. *Ann Med Health Sci Res*. 2013 Apr;3(2):166-70. doi: 10.4103/2141-9248.113655. PMID: 23919183; PMCID: PMC3728856.
- Shetty S, Shetty A. A clinical study of Ectopic Pregnancies in a Tertiary care hospital of Mangalore, India. *Innov J Med Health Sci [Internet]* 2014 [cited 2015 Oct 12];4(1) Available from: <http://innovativejournal.in/index.php/ijmhs/article/view/600>
- Baria D, Thaker R, Patel M, Shah S, Shah P, Jani S. Analysis of ectopic pregnancy at a tertiary care hospital: one year study. *Int J Reprod Contracept Obstet Gynecol*. 2013;2(4):621.
- Jabbar FA, Al-Wakeel M. A study of 45 cases of ectopic pregnancy. *Int J Gynaecol Obstet*. 1980;18(3):214-7. doi: 10.1002/j.1879-3479.1980.tb00285.x. PMID: 6109659.

- 14) Jani R, Munshi D, Jani S, Munshi S. Study of 50 cases of modern management of ectopic pregnancy. *Int J Reprod Contracept Obstet Gynecol*. 2014;3(2):374-79.
- 15) Pal A, Gupta KB, Sarin R. A study of ectopic pregnancy and high risk factors in Himachal Pradesh. *J Indian Med Assoc*. 1996 May;94(5):172-3. PMID: 8855569.
- 16) Shobeiri F, Tehrani N, Nazari M. Trend of ectopic pregnancy and its main determinants in Hamadan province, Iran (2000-2010). *BMC Res Notes*. 2014 Oct 17;7:733. doi: 10.1186/1756-0500-7-733. PMID: 25326269; PMCID: PMC4283128.
- 17) Mufti S, Rather S, Mufti S, Rangrez RA, Wasiqa K. Ectopic pregnancy: An analysis of 114 cases. *JK-Pract*. 2012;17(4):20-23.
- 18) National Family Health Survey-4 [Internet]. 2016 [cited 2016 Apr 19]. Available from: http://rchiips.org/nfhs/factsheet_nfhs-4.shtml
- 19) Tancer ML, Delke I, Veridiano NP. A fifteen year experience with ectopic pregnancy. *Surg Gynecol Obstet*. 1981 Feb;152(2):179-82. PMID: 6451944.
- 20) Jang TB, Kaji AH. A 2-week elective experience provides comparable training as longitudinal exposure during residency for pelvic sonography. *J Ultrasound Med*. 2015 Feb;34(2):221-4. doi: 10.7863/ultra.34.2.221. PMID: 25614394.
- 21) Cornelius AC, Onyegbule A, Onyema, Uchenna ET, Duke OA. A five year review of ectopic pregnancy at Federal Medical Centre, Owerri, South East, Nigeria. *Niger J Med*. 2014 Jul-Sep;23(3):207-12. PMID: 25185377.
- 22) Taheri M, Bharathan R, Subramaniam A, Kelly T. A United Kingdom national survey of trends in ectopic pregnancy management. *J Obstet Gynaecol*. 2014 Aug;34(6):508-11. doi: 10.3109/01443615.2014.910181. Epub 2014 Apr 25. PMID: 24766292.
- 23) van den Berg MM, Goddijn M, Ankum WM, van Woerden EE, van der Veen F, van Wely M, Hajenius PJ. Early pregnancy care over time: should we promote an early pregnancy assessment unit? *Reprod Biomed Online*. 2015 Aug;31(2):192-8. doi: 10.1016/j.rbmo.2015.04.008. Epub 2015 May 8. PMID: 26099443.
- 24) Ectopic pregnancy and miscarriage. NICE Quality standard [Internet]. National Institute for Health and Clinical Excellence; 2014 [cited 2016 Feb 6]. Available from: <https://www.nice.org.uk/guidance/qs69/resources/ectopic-pregnancy-and-miscarriage-2098796040133>
- 25) French S, Henry T, Williams EW. 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*. 2014 Jun;63(3):247-51. doi: 10.7727/wimj.2013.230. Epub 2014 Jun 11. PMID: 25314282; PMCID: PMC4663903.
- 26) Horne AW, Shaw JL, Murdoch A, McDonald SE, Williams AR, Jabbour HN, Duncan WC, Critchley HO. Placental growth factor: a promising diagnostic biomarker for tubal ectopic pregnancy. *J Clin Endocrinol Metab*. 2011 Jan;96(1):E104-8. doi: 10.1210/jc.2010-1403. Epub 2010 Nov 3. PMID: 21047920; PMCID: PMC3017520.
- 27) Cabar FR, Pereira PP, Schultz R, Francisco RP, Zugaib M. Association between ultrasound findings and serum levels of vascular endothelial growth factor in ampullary pregnancy. *Fertil Steril*. 2015 Mar;103(3):734-7. doi: 10.1016/j.fertnstert.2014.12.100. Epub 2015 Jan 7. PMID: 25577466.