

Clinical Analysis of Ectopic Pregnancies in a Tertiary Care Centre in Southern India: A Six-Year Retrospective Study

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ABSTRACT

Introduction: Ectopic Pregnancy (EP) is a life-threatening emergency commonly encountered by medical practitioners where diagnosis can often be missed. Any woman in the reproductive age group, presenting with lower abdominal pain or vaginal bleeding must raise the suspicion of an ectopic pregnancy to prevent mortality and morbidity.

Aim: To review all cases of EP and determine the incidence of EP. To study the high risk factors and know the types of clinical presentation, methods of diagnosis, outcome and complications.

Materials and Methods: This was a retrospective cohort study, conducted at a tertiary care medical teaching hospital in Pondicherry, India. Medical records of all women with an EP between 2009 and 2015 were retrieved. Demographic data, parity, risk factors, clinical features, mode of management and need for blood transfusion was noted. Main outcome measures studied were the incidence of EP, risk factors, mortality and morbidity in these women.

Statistical Analysis: Data was entered in Microsoft Excel spreadsheet and analysed using SPSS software version 19.0. For categorical variables, data was compiled as frequency and percent. For continuous variables, data was calculated as mean \pm SD.

Results: Seventy-two EP were diagnosed during the six-year period with an incidence of 9.1/1000 pregnancies. Majority of women were aged 21-30 years (51.39%), 27.8% women were nulliparous. The most common risk factors were previous abortion (36.1%) and pelvic surgery (37.50%). Fifteen cases (20.8%) were diagnosed in women who had tubectomy. The classic triad of lower abdominal pain, amenorrhoea and vaginal bleeding was seen in 29(40.3%) cases. Ultrasonography was required to arrive at a diagnosis in 28(38.9%) cases. Urine pregnancy test was positive in 100% of cases. Majority (94.4%) were tubal ectopic pregnancies. Medical management with methotrexate alone benefitted 10(13.89%) of patients while another four required surgery for failed medical management. More than half of the patients (59.7%) required blood transfusion and two (2.8%) had transfusion related acute lung injury. No deaths were noted.

Conclusion: Common risk factors for EP must be identified. Use of transvaginal ultrasonography and human chorionic gonadotropin assay have revolutionised the management of EP and serve as valuable adjuncts to early diagnosis and management.

Keywords: Amenorrhoea, Maternal mortality, Risk factors, Tubal pregnancy, Ultrasonography, Vaginal bleeding

INTRODUCTION

Ectopic Pregnancy (EP) is a pregnancy implanted outside the cavity of the uterus. It is well recognised as a life-threatening emergency in early pregnancy. The incidence of EP is around 1-2% in most hospital based studies [1-6].

Diagnosis requires a high index of suspicion as the classic triad of amenorrhoea, abdominal pain and vaginal bleeding is not seen in majority of cases. Women may present with non-specific symptoms, unaware of an ongoing pregnancy or even present with haemodynamic shock. The contribution of EP to the maternal mortality rates in developing countries including India is not precisely known, with data from few studies indicating 3.5-7.1% maternal deaths due to EP [7,8].

The purpose of this study was to appraise all the cases of EP managed at a tertiary care centre over a period of 6 years and, to determine the incidence, risk factors, clinical presentation, management and morbidity associated with EP.

MATERIALS AND METHODS

This retrospective study was conducted at Pondicherry Institute of Medical Sciences, a 650 bedded, tertiary care teaching hospital in south India. The study was approved by the Institute Ethics

Committee. The case records of patients diagnosed with EP between October 2009 and September 2015 were retrieved from the medical records department. Patient characteristics like age, parity and risk factors for EP were noted. Mode of diagnosis, management modality, complications and need for blood transfusion were also recorded. The primary outcome measures studied were incidence of EP, their risk factors, mortality and morbidity in these women.

Data was entered in MS excel spreadsheet and analysed using SPSS software version 19.0. For categorical variables, data was compiled as frequency and percent. For continuous variables, data was calculated as Mean \pm SD.

RESULTS

Over the six-year period, 7832 pregnancies were diagnosed, among whom 72 pregnancies were extra-uterine. The incidence of EP was 9.1/1000 pregnancies or one in 108 pregnancies. Majority of the women were aged 21-30 years [Table/Fig-1]. The most common risk factors were previous abortion (36.1%) and pelvic surgery (37.5%). Among the women who underwent pelvic surgery, 15 women had undergone tubectomy and two women had a tubal recanalization.

The classic triad of amenorrhoea, vaginal bleeding and lower abdominal pain was present in 29(40.3%) cases. Acute abdominal pain was the most common complaint, seen in 59 (81.9%) women;

although a history of preceding amenorrhoea was present in 67 (93.1%)-women. The other symptoms at presentation were vomiting and syncope. Cervical motion tenderness was elicited on pelvic examination in 58.3% cases.

A spot urine pregnancy test was performed in all cases and was found to be positive in 100% cases. A diagnosis of EP was made on clinical findings alone in 44(61.1%) women. However, ultrasonography was useful in making the diagnosis in 25 more cases. Ultrasonography was inconclusive in three cases, which needed a diagnostic laparoscopy to arrive at a diagnosis. The mean gestational age at diagnosis was 7.1 weeks. The site of ectopic was fallopian tubes in 68 cases (94.4%).

Patients who were haemodynamically stable, had a gestational sac size measuring less than 4cm by transvaginal ultrasonography, serum beta hCG (human Chorionic Gonadotropin) levels less than 10,000 U/ml and no free fluid in the pelvic cavity, were managed medically. Ability for regular follow-up was ensured before medical treatment. Fourteen (19.4%) women were managed medically with methotrexate. Nine of them had a single dose of methotrexate, while five needed a multiple dose regimen. Four of the 14 women, required surgery following failed medical management. Among the 62 women managed surgically, 47 were ruptured at the time of diagnosis, with haemoperitoneum seen intraoperatively. Mean haemoglobin at admission was 9.6 ± 1.9 g/dL. More than half of the women needed blood transfusion (59.7%) and two women had transfusion related acute lung injury. Mean duration of hospital stay was 6.6 ± 2.9 days. No deaths were noted. Admission to intensive care unit was required either due to haemodynamic instability or owing to complications like atelectasis and Transfusion Related Acute Lung Injury (TRALI). Abdominal wound infection was seen in four cases [Table/Fig-2].

Characteristics	n=72	%
Age (Mean=29.67±6.06; 18-42yrs)		
18-20 years	2	2.7
21-30 years	37	51.4
31-40 years	29	40.3
>40 years	4	5.6
Parity		
0	20	27.8
1	25	34.7
2	23	31.9
3	2	2.8
4	2	2.8
Risk factors		
History of abortions (≥1)	26	36.1
History of previous ectopic pregnancy	3	4.2
History of pelvic surgery	27	37.5
History of infertility	13	18.1
History of PID	11	15.3
History of intrauterine contraceptive device	3	4.2
Symptoms		
Amenorrhoea	67	93.1
Vaginal bleeding	36	50
Abdominal pain	59	81.9
Signs		
Haemodynamic shock	19	26.4
Abdominal tenderness	54	75.0
Cervical motion tenderness	42	58.3
Diagnostic modality		
Clinical alone	44	61.1
Ultrasonography	25	34.7
Laparoscopy	3	4.2
Site		
Tubal	68	94.4
Cervical	1	1.4
Cornual	1	1.4
Unknown location	2	2.8

[Table/Fig-1]: Patient characteristics.

DISCUSSION

EP accounts for 3.5-7.1% of maternal mortality in India [7,8]. The incidence of EP was 0.91% in our study. This is in agreement with

Morbidity	n=72	%
ICU admission	6	8.3
Bowel injury	1	1.4
Wound infection	4	5.6
Atelectasis	1	1.4
Transfusion related acute lung injury	2	2.8

[Table/Fig-2]: Morbidity following ectopic pregnancy

most studies from developing countries where incidence ranged from 0.56-1.5% [1-3,5,6,9,10]. It is a significant cause of mortality in the first trimester. Timely referral to a higher centre is imperative in order to reduce mortality and morbidity.

The classical triad of abdominal pain, amenorrhoea and vaginal bleeding was seen in 40.3% of our cases. Other studies have reported this triad to be present in 28-95% women [1,11,12], clearly indicating that this is not a presenting feature in most cases. A history of amenorrhoea was present in 93.1% of our cases, but this may not come to light unless specifically enquired into.

Mean gestational age at diagnosis of EP was 7.1 weeks in our study, while Khaleeque et al., reported 6 weeks at diagnosis [2]. Singh et al., reported that 52% of their cases did not have preceding amenorrhoea [1]. Women may be unaware of an ongoing pregnancy and hence may not anticipate a pregnancy complication. Such women are most often seen first at a primary health centre or by a general practitioner and hence, the importance of careful history-taking cannot be overemphasised.

In our study, history revealed presence of at least one risk factor in 66.7% of the women, similar to other studies [1,2,13]. Among the risk factors, previous pelvic surgery was the most common (37.5%), followed by previous abortions (36.1%) in our study. Studies from various regions have reported a similarly high incidence of previous abortions, but contrary to our study previous abortions were the most common risk factor for EP in these studies [1-3,6,9,12,14,15]. The reason for previous pelvic surgery being the most common risk factor in our study could be attributed to the high caesarean section (33.6%) and tubal sterilisation (57.4%) rates in our state [16]. Singh et al., also reported prior tubal surgery as the most common (40%) risk factor in their study which is again a reflection of their high acceptance (57.4%) of tubal sterilisation as a method of family planning [1,16]. Hence a pregnancy test must be performed in all cases irrespective of their sterilisation status. Pregnancy must not be ruled out in women on such pretext.

History of Pelvic Inflammatory Disease (PID) was seen in 15.3% of our patients, similar to that reported by Singh et al., and Mufti et al., in their studies [1,15]. However, researchers from Nigeria have reported PID in 27-35.5% of their patients making it the most common risk factor for EP in that region. This high prevalence has been attributed to high polygamy rates in Nigeria [3,5,6].

Although clinical examination may raise suspicion of an EP, relying on clinical signs and symptoms alone would have missed the diagnosis in 38.9% of our cases. Ultrasonography was useful in diagnosing most of these cases, with the exception of three cases which needed laparoscopy for diagnosis. Culdocentesis, abdominal paracentesis and laparoscopy were used frequently in the past to aid diagnosis [3,5,6,17], but have been replaced by ultrasonography due to its non-invasive nature. Availability of point of care ultrasonography is of utmost importance in avoiding delay in diagnosis. This may not require gynaecologic specialists as physicians in community practice may be able to acquire comparable skills as residency graduates through a two-week intensive ultrasonography-dedicated training, as suggested by Jiang et al., in their study [18].

Most of the cases (86.1%) were managed surgically and a salpingectomy was performed. A recent study concluded that laparoscopic surgical management was not better than a laparotomy in terms of the tubal patency and intrauterine pregnancy rates [19]. Most studies reported a similarly high rate of surgical management [2,3,6,9,20]. In contrast, surveys from the United Kingdom by Taheri et al., and van den Berg et al., reported a falling trend in the number of cases managed surgically (98% to 62% and 50% to 27% respectively), over the last two decades [21,22]. This was attributed to the establishment of Early Pregnancy Assessment Units (EPAU) where EP is likely to be diagnosed at an early stage when medical management is still plausible.

The fallopian tubes were the most common seat of EP (94.4%). Most studies reported a higher incidence of EP in the right tube [1,3,6,10,23], while we found 72.2% of tubal ectopic pregnancies on the left side. In developing countries, majority of patients are diagnosed after tubal rupture. Our centre being a tertiary level referral centre, 65.3% of the women had ruptured ectopic pregnancies and presented with a haemoperitoneum, while some studies have reported 70-100% of ectopic pregnancies which were ruptured at diagnosis, mostly due to late referrals. Forty-three (59.7%) women needed blood transfusion, which was similar to that in other studies [2,9,10,20]. Udigwe et al., reported a 94.4% need for blood transfusion, as all women presented with a ruptured ectopic pregnancy and underwent a laparotomy and salpingectomy. Mean duration of hospital stay was 6.6 ±2.9 days. Udigwe et al., similarly reported that 94.4% of their patients had a hospital stay of less than 8 days, while 5.6% of the women needed prolonged hospitalisation upto 14 days [3].

There were no deaths due to EP during the period of our study. Maternal mortality due to EP was reported to be between 0% and 1.3% in various studies [2,3,5,6,9,20]. Mortality is mostly due to haemorrhage following rupture of the EP due to delayed referrals and diagnosis. National Institute for Health and Clinical Excellence has estimated that two-thirds of maternal deaths due to ectopic pregnancies in the UK may have been associated with inadequate care [24].

Prevention and treatment of PID and encouraging women to undergo an early transvaginal ultrasonography to confirm the location of pregnancy is likely to prevent late diagnosis. This will also allow medical management or fertility sparing conservative surgical management. Setting up Early Pregnancy Assessment Units has been shown to result in higher quality and cost-effective care, and to have a positive effect on early pregnancy care in the UK [22]. Future studies are required to evaluate usefulness of such EPAUs and feasibility of setting them up in India.

Ultrasonography being the mainstay for evaluating EP, its availability at the point of care will also help majority of patients by allowing safe and timely discharge of patients presenting to emergency departments with clinical suspicion of an EP [25]. Future research may be directed at assessing the impact of training doctors at primary and secondary levels of healthcare with two-week intensive ultrasonography courses, on the mortality and morbidity associated with EP.

Horne et al., suggested the use of serum Placental Growth Factor (PGF) to differentiate between intrauterine and ectopic pregnancies and concluded that serum PIGF was undetectable in women with tubal ectopic pregnancies and reduced, or undetectable, in miscarriage compared to viable intrauterine pregnancies [26]. Cabar et al., attempted to correlate the levels of serum Vascular Endothelial Growth Factor (VEGF) and ultrasonographic features in EP and concluded that serum VEGF was raised in ectopic pregnancies with cardiac activity [27]. Future studies are required to assess clinical utility of these markers.

LIMITATION

Our study is limited by its retrospective nature. Further, we were unable to estimate the duration of delay in diagnosis and referral and its effect on morbidity.

CONCLUSION

Culdocentesis and laparoscopy have been superseded by non-invasive transvaginal ultrasonography and highly sensitive and accurate beta hCG assays for diagnosis of EP. Timely diagnosis and management in early pregnancy units with point of care ultrasonography can reduce the morbidity and mortality due to ectopic pregnancy. In conclusion, identifying underlying risk factors, availability of point of care ultrasound, complimented by availability of beta hCG assay and timely intervention will help reduce the morbidity and mortality due to EP.

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REFERENCES

- [1] 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.
- [2] Khaleeqe F, Siddiqui RI, Jafarey SN. Ectopic pregnancies: A three year study. *J-Pak Med Assoc.* 2001;51(7):240-42.
- [3] Udigwe GO, Umeononihu OS, Mbachu II. Ectopic pregnancy: a 5 year review of cases at nnamdi-azikiwe university teaching hospital (NAUTH) Nnewi. *Niger Med J.* 2010;51(4):160.
- [4] Kirk E, Bottomley C, Bourne T. Diagnosing ectopic pregnancy and current concepts in the management of pregnancy of unknown location. *Hum Reprod Update.* 2014;20(2):250-61.
- [5] Panti A, Tanko B, Yakubu A, Egongu S, Ikechukwu N, lukman O. Ectopic pregnancy at UsmanuDanfodiyo University Teaching Hospital Sokoto: A ten year review. *Ann Niger Med.* 2012;6(2):87.
- [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] Shah P, Shah S, Kuty RV, Modi D. Changing epidemiology of maternal mortality in rural India: time to reset strategies for MDG-5. *Trop Med Int Health.* 2014;19(5):568-75.
- [8] Yadav K, Namdeo A, Bhargava M. A retrospective and prospective study of maternal mortality in a rural tertiary care hospital of Central India. *Indian J Community Health.* 2013;25(1):16-21.
- [9] 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>
- [10] 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.
- [11] Jabbar FA, Al-Wakeel M. A study of 45 cases of ectopic pregnancy. *Int J GynaecolObstet Off Organ Int Fed Gynaecol Obstet.* 1980;18(3):214-17.
- [12] Jani R, Munshi D, Jani S, Munshi S. Study of 50 cases of modern management of ectopic pregnancy. *Int J ReprodContraceptObstet Gynecol.* 2014;3(2):374-79.
- [13] Pal A, Gupta KB, Sarin R. A study of ectopic pregnancy and high risk factors in Himachal Pradesh. *J Indian Med Assoc.* 1996;94(5):172-73, 202.
- [14] Shobeiri F, Tehrani N, Nazari M. Trend of ectopic pregnancy and its main determinants in Hamadan province, Iran (2000-2010). *BMC Res Notes.* 2014; 7:733.
- [15] Mufti S, Rather S, Mufti S, Rangrez RA, Wasiqa K. Ectopic pregnancy: An analysis of 114 cases. *JK-Pract.* 2012;17(4):20-23.
- [16] National Family Health Survey-4 [Internet]. 2016 [cited 2016 Apr 19]. Available from: http://rchiips.org/nfhs/factsheet_nfhs-4.shtml
- [17] Tancer ML, Delke I, Veridiano NP. A fifteen year experience with ectopic pregnancy. *SurgGynecol Obstet.* 1981;152(2):179-82.
- [18] Jang TB, Kaji AH. A 2-week elective experience provides comparable training as longitudinal exposure during residency for pelvic sonography. *J Ultrasound Med Off J Am Inst Ultrasound Med.* 2015;34(2):221-24.
- [19] Saranovic M, Vasiljevic M, Prorocic M, Macut ND, Filipovic T. Ectopic pregnancy and laparoscopy. *ClinExpObstet Gynecol.* 2014;41(3):276-79.
- [20] Cornelius AC, Onyegbule A, Onyema null, Uchenna ET, Duke OA. A five year review of ectopic pregnancy at Federal Medical Centre, Owerri, South East, Nigeria. *Niger J Med J Natl AssocResid Dr Niger.* 2014;23(3):207-12.
- [21] Taheri M, Bharathan R, Subramaniam A, Kelly T. A United Kingdom national survey of trends in ectopic pregnancy management. *J ObstetGynaecol J Inst ObstetGynaecol.* 2014;34(6):508-11.
- [22] van den Berg MMJ, Goddijn M, Ankum WM, van Woerden EE, van der Veen F, van Wely M et al. Early pregnancy care over time: should we promote an early pregnancy assessment unit? *Reprod Biomed Online.* 2015;31(2):192-98.

- [23] Okmen F, Zeybek B, Akdemir A, Ergenoglu AM, Yeniel O, Ulukus M. Is there a relationship between age and side dominance of tubal ectopic pregnancies? A preliminary report. *Ginekol Pol.* 2014;85(9):677–81.
- [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 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]. 2014 Jul 21 [cited 2015 Nov 17]; Available from: <http://myspot.mona.uwi.edu/fms/wimj/article/1854>
- [26] Horne AW, Shaw JL, Murdoch A, McDonald SE, Williams AR, Jabbour HN, et al. Placental growth factor: a promising diagnostic biomarker for tubal ectopic pregnancy. *J Clin Endocrinol Metab.* 2011;96(1):E104–08.
- [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;103(3):734–37.

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