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Suspected Ectopic Pregnancies and the Outcome in a Tertiary Care Hospital in South India

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Abstract

Background: *Ectopic pregnancy is potentially lethal obstetric emergency, early diagnosis of unruptured ectopic pregnancy is of paramount importance..During the past decade, transvaginal ultrasonography has given an earlier and clearer picture of early pregnancies, by ruling out ectopic pregnancy if intra uterine pregnancy is identified or it may strongly suggest an ectopic pregnancy if an adnexal mass is seen or in the presence of pelvic fluid. However in 15% of cases the report may be indeterminate, that is empty uterus, ectopic pregnancy not ruled out. It is this cohort of women with suspected Ectopic pregnancy that forms the subject of this study.*

Aim of the study *was to study the outcome of pregnancies with indeterminate early pregnancy pelvic ultrasounds, admitted with clinical suspicion of ectopic pregnancy.*

Methodology*: This is a retrospective cohort study conducted for 1 year in Sree Avittom Thirunal hospital, Government Medical College, Trivandrum, a tertiary care center.*

Statistical tests used are mean, SD, Percentage, chi square and Odds Ratio to assess association of the selected parameters with the Ectopic pregnancy.

Results: *The study identified 109 women admitted with clinical suspicion of ectopic pregnancy and were followed up of which 99 patients met the inclusion criteria.Of the 99 patients 26 were ectopic pregnancies, 34 were spontaneous miscarriages, and 39 were viable intra utrine pregnncy. The overall mean age of the patients at presentation was 26.87yrs. The majority of patients were in 25 - 29 yrs age group, which was also true for ectopic pregnancy and spontaneous abortions, but not for the patients in Intra Uterine pregnancy group where the maximum number of patients were in the g group of 20 – 24 yrs.(X^2 =12.4,P =0.001).*

There was more number of referred cases in all the three categories.60% 0f the suspected ectopic pregnancy were referred. Among the cases that were eventually ectopic pregnancy 65.38 had been referred. The association of gravidity and outcome was found significant with Chi-square =20.58; P =0.008. The majority of patients in Intra Uterine group were primi gravidas. The overall incidence of prior miscarriage in our study population was around 21%.History of Infertility was also studied and in this there were 14 (14.14%) patients with infertility. In the ectopic pregnancy group,19,2% gave history of treatment for infertility while 80.8% did not have history of infertility treatment. 11.53% of patients with ectopic pregnancy had a history of previous ectopic.

Conclusion: *Early detection of ectopic pregnancy is of paramount importance. Early detection can be challenging and a number of early ectopic pregnancies are missed at the initial medical examination. Documentation of risk factor is an essential part of history-taking, and asymptomatic clinic patients with risk factors may benefit from routine early imaging. However, more than half of identified ectopic pregnancies are in women without known risk factors.*

Keywords-*Ectopic Pregnancy, Beta Human Chorionic Gonadotropin; Transvaginal ultrasonography.*

Introduction

An ectopic pregnancy occurs when a fertilized ovum implants outside the normal uterine cavity.[2,4] It is a common cause of morbidity and occasionally of mortality in women of reproductive age

Ectopic Pregnancy was earlier diagnosed with clinical examination findings and history. But today the transvaginal ultrasonography and immunoassays of serum beta HCG levels is more discerning in patients with suspected ectopic pregnancy.

The diagnosis of ectopic pregnancy is increasing both as a result of early diagnosis and owing to true increased incidence of the disease. Despite the high frequency of this condition, early detection can be challenging and a number of early ectopics are missed at the initial medical examination. Although the incidence of ectopic pregnancy in the general population is about 2 % , the prevalence of ectopic pregnancy in pregnant patients presenting to an emergency department with first trimester bleeding or pain or both is 6 % to 16 %.[1,2] Thus greater suspicion and a lower threshold for investigations are justified.

The emergence of transvaginal ultrasonography has marked a new era in diagnosis and decision making. The simplicity and non-invasiveness soon transformed ultrasound into a principal imaging tool.

Normal Intrauterine Pregnancy

A normal gestational sac, an ovoid collection of fluid adjacent to the endometrial stripe, can be visualized by means of the transvaginal probe at a gestational age of about 5 weeks. Radioimmuno assays of HCG can detect pregnancy as early as12 days post conception. The ability to document an intra uterine pregnancy by ultrasound has lagged behind by two to three weeks. The hormonal environment in ectopic pregnancy produces such an intrauterine fluid collection that mimics a gestational sac, and hence called the "pseudo gestational sac". Therefore a sac alone cannot confirm intrauterine pregnancy. Once the sac is implanted within the endometrium, its position relative to the endometrial wall changes, producing the 'intradecidual-sac sign' and then the 'double decidual-sac sign'.[6] The yolk sac appears during the fifth week and the cardiac activity at 6-6.5 weeks.[6]

The proportion of accurate preliminary ultrasound diagnosis in detecting intrauterine pregnancy was significantly higher in subjects who presented with beta-HCG levels above 1500 mIU/ml compared with levels below 1500 mIU/ml.[7]

Ectopic Pregnancy

The spectrum of sonographic findings in ectopic pregnancy is broad and the diagnosis of ectopic pregnancy is usually based on one of the following grey- scale appearances[8].

1. An in homogenous mass or 'Blob sign' adjacent to the ovary and moving separately from the ovary.
2. A mass with a hyper-echoic ring around the gestational sac or 'Bagel sign'.
3. A gestational sac with a foetal pole with cardiac activity, i.e. a viable extra uterine pregnancy.
4. A gestational sac with a foetal pole without cardiac activity, i.e. a non-viable extra uterine pregnancy.

Materials and Methods

This is a retrospective study conducted Sree Avittom Thirunal Hospital, Department of Obstetrics and Gynaecology, Govt. Medical College, Trivandrum , a tertiary care setting.

Duration – One year

Inclusion Criteria: Patients with clinical suspicion of ectopic pregnancy, admitted to ectopic room of Sree Avittom Thirunal Hospital during this study period with a positive urine pregnancy test and indeterminate pelvic ultrasound findings are included in the study. Patients were selected from the register maintained in this ward.

Exclusion Criteria: Patients with missing data till a final diagnosis was arrived were excluded.

Patients who conceived with IVF-ET were excluded s the transfer of multiple embryos could influence the beta HCG levels

Sample Size: During the study period 109 patients were admitted with a positive urine pregnancy test and indeterminate pelvic ultrasound findings, of which 10 patients were excluded from the study because of incomplete follow up. There was no instance of tubal rupture while on follow up.

Study Variables

Data collected included potential predictors such as the age, place of residence, socioeconomic status, gravidity, parity, number of previous ectopic pregnancy, number of previous spontaneous abortions, number of previous induced abortions, history of pelvic inflammatory disease (requiring hospital admissions), history of documented tubal pathology, history of using intra uterine devices, history of abdominal or pelvic surgery, history of treatment for infertility or artificial reproductive technologies.

Data regarding clinical signs and symptoms at presentation were also collected, length of gestation at presentation and ultrasound features were also collected. For all patients with indeterminate scans, the final outcome category was assigned as follows:

Category 1: Ectopic pregnancy

Category 2: Non viable pregnancy- spontaneous miscarriage and cases of failing or self resolving pregnancy of unknown location

Category 3: Viable intra uterine pregnancy

The data was collected using a proforma and subsequently entered using Microsoft excel sheet, and data analysis was done with SPSS software

Observation and Results

During the period of study 99 patients met the inclusion criteria of which 26 were ectopic pregnancies, 34 were spontaneous miscarriages, and 39 were viable intra utrine pregnncy

Fig:1. Outcome of patients with suspcted ectopic pregnancy.

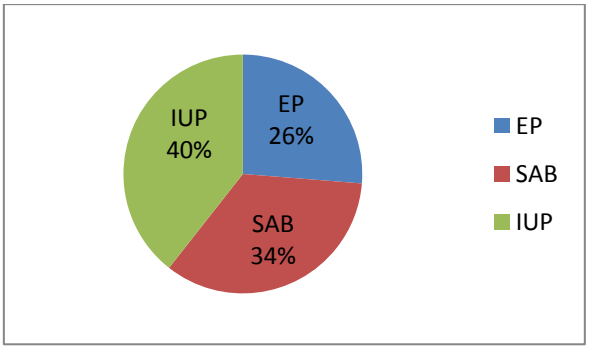


Table:1 Mean age of the patients

	No	Mean Age in yrs	Std Deviation
EP	26	28.58	3.797
SAB	34	28.88	4.125
IUP	39	23.97	3.558
TOTAL	99	26.87	4.453

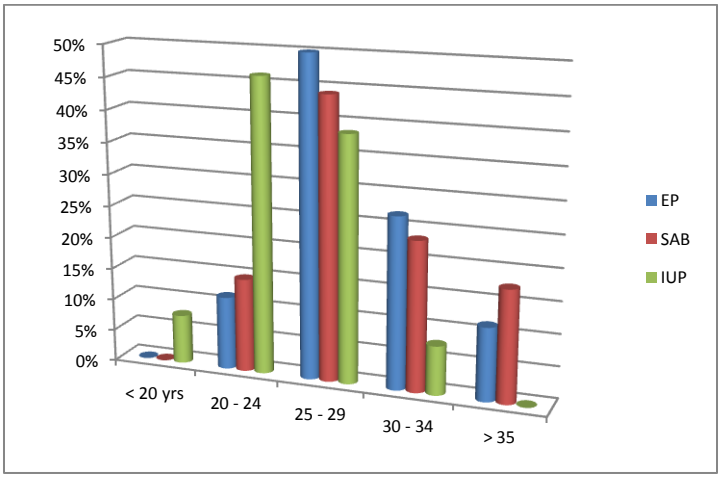
The overall mean age of the patients at presentation was 26.87yrs.

Table: 2 Age Distribution within each category.

	< 20 yrs	20 - 24	25 - 29	30 - 34	≥ 35	TOTAL
EP	0%	11.50%	50%	26.90%	11.50%	100%
SAB	0%	14.70%	44.10%	23.50%	17.60%	100%
IUP	7.70%	46.20%	38.50%	7.70%	0%	100%

The distribution is statistically significant *Chi-square =12.4, P =0.001*

Fig: 2 Distribution of Age in each category



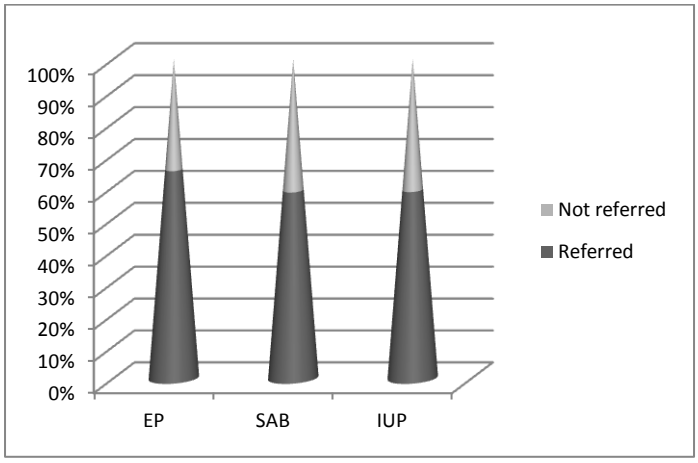
The majority of patients were in 25 - 29 yrs age group, which was also true for ectopic pregnancy and spontaneous abortions, but not for the patients in Intra Uterine pregnancy group where the maximum number of patients were in the g group of 20 – 24 yrs.(X^2 =12.4,P =0.001)

Table: 3 Referral status and outcome

Referral status and outcome			
	Referred	Not referred	Total
EP	17(65.4%)	9(34%)	26(100%)
SAB	20(58.8%)	14(41.2%)	34(100%)
IUP	23(59%)	16(41.0%)	39(100%)
Total	60(60%)	39(40%)	99(100%)

There was more number of referred cases in all the three categories.60% 0f the suspected ectopic pregnancy were referred.

Fig: 3 Referral patern



Among the cases that were eventually ectopic pregnancy 65.38 had been referred.

Table: 4 Distribution according to Gravidity

Gravida	G1	G2	G3	G4	G5	Total
EP	7(26.9%)	10(38.5%)	7(26.9%)	1(3.8%)	1(3.8%)	26(100%)
SAB	11(32.4%)	10(29.4%)	12(35.3%)	1(2.9%)	0	34(100%)
IUP	27(69.2%)	9(23.1%)	2(5.1%)	1(2.6%)	0	39(100%)

The association of gravidity and outcome was found significant with *Chi-square =20.58; P=0.008.* The majority of patients in Intra Uterine group were primi gravidas.

The overall incidence of prior miscarriage in our study population was around 21%. Statistically significant association of previous history of abortions either spontaneous or induced was not obtained in this study.

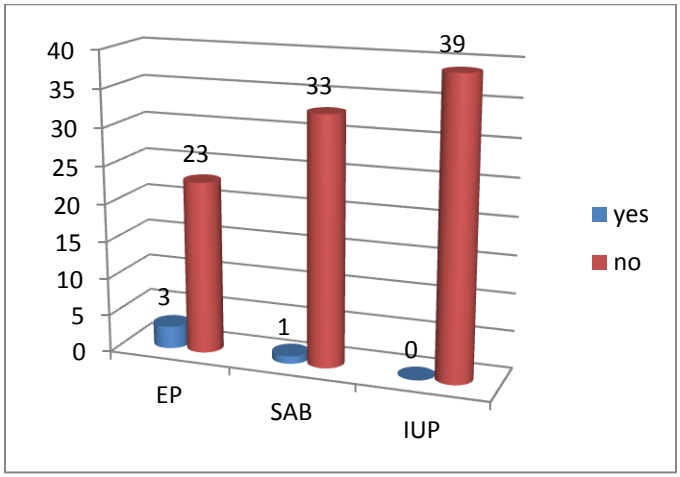
History of Infertility and Outcome was also studied and in this study there were 14 (14.14%) patients with infertility. In the ectopic pregnancy group, 19,2% gave history of treatment for infertility while 80.8% did not have history of infertility treatment. A similar distribution was noted in both the other groups and hence the association was not statistically significant. Increased risk of infertility is for patients with tubal factor but this could not be studied as patients who conceived with Artificial reproductive techniques were excluded from this study.

Table: 5 History of previous ectopic pregnancy and outcome

H/o previous ectopic	Yes	No
EP	3(11.53%)	23(88.46%)
SAB	1(2.94%)	33(97.05%)
IUP	0	39(100%)
Total	4(4.04%)	95(95.95%)

11.53% of patients with ectopic pregnancy had history of previous ectopic.

Fig: 4 Past history of ectopic pregnancy.



Comparing the ectopic prgnancy as one group and non ectopics as the other group, History of ectopic prgnancy is found to be a statistically significant risk factor for ectopic prgnancy with *Chi-square =5.11 ; P =0.024.*

The number of patients with previous ectopic prgnancy were not large enough in this study population to get a significant result on the influence of treatment modality in the previous ectopic prgnancy.

However in ectopic prgnancy group 42.3% gave history of prior adominal surgery, while 57.7% did not have history of prior adominal surgery.This was found to be statistically significant for ectopic prgnancy with *Chi-square =8.235 ; P =0.016.*

11 out of 26 patients in ectopic prgnancy group had previous abdominal surgery; of which 6 had

previous tubal surgery. whereas only 2 in spontaneous abortion group and none in intra uterine prgnancy group had previous tubal surgery.This oservation is statistically significant risk factor for ectopic prgnancy with *Chi-square =5.238 ; P =0.022; odds ratio:12* making tubal ligation and partial salphingectomy important risk factor for ectopic prgnancy.

Table: 6 History of Pelvic inflammatory disease.

histoty of PID	yes	no
EP	1(3.8%)	25(96.2%)
SAB	2(5.9%)	25(94.1%)
IUP	1(2.6%)	25(97.4%)
Total	4(4%)	25(96%)

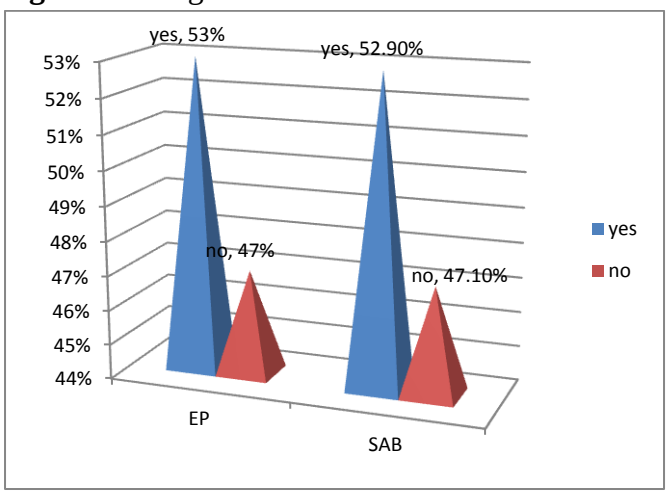
No statistical significance was noted as only patients with history of hospital admission for PID was included.

Table:7 Bleeding PV as presenting complaint

Bleding pv	yes	no
EP	14(53%)	12(47%)
SAB	18(52.9%)	16(47.1%)

More than 50% 0f Ectopic as well as abortion group had bleding per vaginum.

Fig: 5 Bleeding PV and outcome



Bleding per vaginum was the predominant symptom in abortion group. In ectopic pregnancy group 53% presented with irregular bleeding per vaginum. 11.5% of patients in ectopic group were asymptomatic but had indeterminate scans that caused suspicion of ectopic.

Discussion

The outcome of patients with suspected ectopic pregnncy with n indeterminte scan was that of the 99 patients who met the inclusion criteria 26 were ectopic pregnancies, 34 were spontaneous misc-arriages, and 39 wre viable intra utrine pregnncy. That is 26% of the patients with indeterminte scans in early pregnancy turned out to ectopic pregnancy

The risk of ectopic pregnancy increases with advancing maternal age, in a study by Farquhar CM. on Ectopic pregnancy; age over 35 years was found to be a significant risk factor.[12] In this study the majority of patients were in 25 - 29 yrs age group, which was also true for ectopic pregnancy and spontaneous abortions, but not for the patients in Intra Uterine pregnancy group where the maximum number of patients were in the g group of 20 – 24 yrs. (X^2 =12.4,P =0.001). The mean age for Intra Uterine pregnancy group was lower than for ectopic pregnancy and spontaneous abortions. Hypotheses for this association include the higher probability of exposure to most other risk factors with advancing age, increase in chromosomal abnormalities in trophoblastic tissue and age-related changes in tubal function delaying ovum transport, resulting in tubal implantation.[18]

Though no age is immune to ectopic pregnancy advancing maternal age, with increasing gravidity and parity is associated with increased risk for poor pregnancy outcomes including ectopic and abortions. Studies by Gracia, Sammel et al 2005 and Thonneau et al 2002 have shown the association of < 20 years and > 35 years to be associated with poor pregnancy outcome.60% of the patients in this study were referred cases. Among the cases that were eventually ectopic pregnancy 65.38% had been referred.

The overall prevalence of prior miscarriage in this study population was around 21% consistent with quoted incidence of 17% to 22% in a study by Barnhart et al and Poland et al.

Women with a previous history of ectopic pregnancy also have an increased risk, which increases further in proportion to the number of previous ectopic pregnancies. In one study the OR

for having an ectopic pregnancy was 12.5 after one previous ectopic pregnancy and 76.6 after two.[18]

In this study 11.53% of patients with ectopic pregnancy had history of previous ectopic, where as there was none with history of previous ectopic in Intra Uterine pregnancy group, and comparing the ectopic prgnancy as one group and non ectopics as the other group, History of ectopic prgnancy is found to be a statistically significant risk factor for ectopic prgnancy with Chi-square =5.11 ; P =0.024.

Ectopic pregnancy is more common in women attending infertility clinics[14] even in the absence of tubal disease. In this study the ectopic pregnancy group, 19,2% gave history of treatment for infertility while 80.8% did not have history of infertility treatment. A similar distribution was noted in both the other groups and hence the association was not statistically significant In addition, the use of ART increases the rate of ectopic pregnancies. In vitro fertilisation (IVF) is associated with an ectopic pregnancy risk of 2-5% and it may be higher than this where there is tubal disease. Indeed the first IVF pregnancy, before the first IVF live birth, was a tubal ectopic pregnancy[4]. Increased risk of infertility is for patients with tubal factor but this could not be studied as patients who conceived with Artificial reproductive techniques were excluded from this study.

Prior damage to the Fallopian tube is an important risk factor for ectopic pregnancy. These factors include any previous pelvic or abdominal surgery, and pelvic infection[11] .Chlamydia trachomatis has been linked to 30-50% of all ectopic pregnancie[6]. The exact mechanism of this association is not known but it has been proposed that in addition to distortion of tubal architecture, it may to be due to an effect on the tubal microenvironmen[13].

11 out of 26 patients in ectopic prgnancy group had previous abdominal surgery; of which 6 had previous tubal surgery, whereas only 2 in spontaneous abortion group and none in intra uterine prgnancy group had previous tubal surgery.This oservation is statistically significant risk factor for ectopic prgnancy with *Chi-square =5.238; P =0.022; odds ratio:12* making tubal ligation and partial salphingectomy important risk factor for ectopic prgnancy. In this study a positive history of Pelvic inflmmatory disease was considered only if there was history of hospitalisation and treatment. Hence due to a small sample size a statistically significant associtionws not obtained.

Regarding clinical presentation Patients with an ectopic pregnancy commonly present with pain and vaginal bleeding between 6 and 10 weeks' gestation[4]. However, these are common symptoms in early pregnancy, with one third of women experiencing some pain and/or bleeding[22,23]. The pain can be persistent and severe and is often unilateral. However unilateral pain is not always indicative of ectopic pregnancy as, in early pregnancy, a prominent painful ovarian corpus luteum cyst is common. Here in the ectopic group, 53.8% presented with irregular bleeding per vaginum, 23.1% had abdominal pain and 11,5% had both.

During the period of study 99 patients met the inclusion criteria of which 26 were ectopic pregnancies, 34 were spontaneous miscarriages, and 39 were viable intra utrine pregnancy

Conclusion

The worst outcome in a patient with a suspected ectopic pregnancy is ectopic pregnancy which is a major cause for maternal mortality and morbidity in the first trimester. Hence early detection and proper management is essential and therefore knowledge of the associated risk factors helps identify women at higher risk in order to facilitate early and more accurate diagnosis. Diagnosis of ectopic pregnancy has improved significantly due to advances in ultrasound technology, rapid and sensitive serum hormone assays.

However, it remains difficult to diagnose an ectopic pregnancy from risk factors, history and examination alone. Clinicians should be suspicious of pregnancy in any such woman who presents with abdominal or pelvic symptoms and should always bear in mind the possibility of

ectopic pregnancy in any woman of reproductive age who presents with any of the symptoms mentioned above. Early diagnosis reduces the risk of tubal rupture and allows more conservative medical treatments to be employed.

Recommendation

Ectopic pregnancy is a common and serious problem, with a significant morbidity rate and the potential for maternal death. Early diagnosis of ectopic pregnancy reduces the risk of tubal rupture and allows more conservative medical treatments to be employed. Ultrasonography should be the initial investigation for symptomatic women in their first trimester; when the results are indeterminate, the serum β human chorionic gonadotropin (β-hCG) concentration should be measured. Serial measurement of β-hCG and progesterone concentrations may be useful when the diagnosis remains unclear.

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