



## Role of Conservative Management in Ectopic Pregnancy: A Prospective Study

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### Abstract

**Introduction:** Ectopic pregnancy is a life threatening emergency in young age females. Incidence of ectopic pregnancy is increasing worldwide. All cases of ectopic pregnancy were classically managed by surgery, later medical management with Methotrxate was established in selective cases, Current study explores the feasibility of conservative management in cases of ectopic pregnancy.

**Materials and Methods:** This is a prospective case control study conducted at Sree Avittom Thirunal Hospital, Govt. Medical College, Trivandrum, Kerala, South India- a major tertiary care hospital. A total of 250 patients including 125 cases of ectopic pregnancy diagnosed by USS and serial Bhcg assay and 125 controls of early intrauterine gestation confirmed by USS as controls were included in this study. Data collected with structured questionnaire regarding risk factors as well ongoing treatment and investigations.

**Results:** The findings revealed that advanced maternal age, prior adverse pregnancy outcome and infertility as well as infertility treatment as risk factors for ectopic pregnancy. The study clearly established the role of conservative approach in haemo dynamically stable patients with Bhcg less than 2500 and stable USS features.

**Keywords:** Ectopic pregnancy, Risk factors, Bhcg, USS, Conservative management.

### Background

Ectopic Pregnancy (EP) is a life-threatening emergency situation in women of reproductive age group. It remains the leading cause of maternal mortality as well as morbidity in the first trimester of pregnancy. Ectopic pregnancy accounts for almost 5% of early gestational age maternal deaths. Over the past decade, incidence of ectopic pregnancy has increased and various factors like wide range of contraceptive options and their failure is a major causative factor. A previous history of EP is considered a major risk factor for subsequent recurrence. The classical

treatment for ectopic pregnancy is surgical management which includes salpingo-oophorectomy or salpingotomy<sup>(1)</sup>.

The other modality of treatment of ectopic pregnancy is medical management utilizing Methotrxate, a folic acid antagonist. This method is proved to be effective in patients with an unruptured tubal ectopic pregnancy who are haemodynamically stable and have minimal symptoms and a low volume free intra peritoneal fluid on ultrasound scan.<sup>(2)</sup> Intramuscular methotrexate is the most widely used and successful medical therapy for ectopic pregnancy

and is generally administered in a single-dose protocol<sup>(3)</sup>. In ectopic pregnancy, the drug prevents the proliferation of cytotrophoblast cells, reducing cell viability and  $\beta$ -hCG secretion and thus progesterone support for the pregnancy. This facilitates the resolution of the ectopic pregnancy and tissue remodelling<sup>(4)</sup>.

Is there a role for conservative treatment in ectopic pregnancy without resorting to either surgery nor medical management? In this study we tried to assess whether there is a role for conservative treatment in ectopic pregnancy especially in women with unruptured ectopic pregnancy and low serum B-hcg values. Through this study we are trying to identify whether there is any role for conservative treatment in ectopic pregnancy conducted at Sree Avittom Thirunal Hospital, Govt. Medical College, Trivandrum - A major tertiary care referral hospital in Kerala, South India. Eventually, analysis of this study will help in deciding treatment of clinically stable patients with unruptured ectopic pregnancy and low serum B-hcg values.

### Materials and Methods

This is a prospective case-control study conducted at Sree Avittom Thirunal Hospital, Govt. Medical College, Trivandrum, Kerala. The study protocol was approved by the Institutional Research Committee and State Board of Medical Research

Medical College, Trivandrum. Written informed consent was obtained from all participants before interview.

During the study period of 12 months from March 2013 to February 2014, a total of 250 patients were included; 125 patients diagnosed as EP by menstrual history, symptoms, physical examination and confirmed by serial beta-HCG and transvaginal ultrasound and 125 women with ultrasound confirmed early intrauterine pregnancy as control, were enrolled in the study.

Data was collected using a structured questionnaire by personal interview regarding women's socioeconomic status, prior reproductive history such as previous spontaneous abortions, induced abortions, previous h/o ectopic pregnancies, h/o infertility treatment and its details. Data regarding USS findings, serum B-hcg values initial as well as follow up, patients symptom score, response to treatment were collected and analyzed. Data were analyzed by using SPSS software, qualitative data analyzed by Chi-square test and quantitative data analyzed by using t-test. P value of  $< 0.05$  was considered statistically significant. Logistic regression analysis was performed including variables with significant P value. Adjusted odds ratio was calculated, which gave an additional dimension to the study which becomes significant at the community level.

### Results

**Table 1** Socio – Demographic Profile of Participants

Profile		Ectopic Pregnancy (N = 125)		Intrauterine Pregnancy (N = 125)		OR (95%, CI)	P Value
		N	%	N	%		
		Age	>30	32	25.6		
	<30	93	74.4	116	92.8		
Education	Upto 10 <sup>th</sup>	44	35.2	47	37.6		0.693
	Plus Two and Higher	81	64.8	78	62.4		
Occupation	House wife	116	92.8	114	91.2		0.641
	Employed	9	7.2	11	8.8		
SES	Upper Lower / Lower	73	58.4	61	48.8		0.128
	Lower Middle / Upper Middle	52	41.6	64	51.2		
Residence	Rural	83	66.4	94	75.2		0.126
	Urban	42	33.6	31	24.8		

Risk of EP is found to increase with advancing age (> 30 years), which was statistically significant (OR 4.44, 95% CI 2.02 - 9.75, P value < 0.001).

**Table 2** Reproductive History of Participants

		Ectopic Pregnancy		Intrauterine Pregnancy (N = 125)		OR (95%, CI)	P Value
		N	%	N	%		
Gravida	Multi	60	48.0	30	24.0	2.92(1.70-5.02)	<0.001
	Primi	65	52.0	95	<0.01		
Previous H/O ectopic		8	6.4	1	0.8	8.48(1.04-68.83)	0.017
Previous spontaneous abortion		10	8.0	2	1.6	5.35(1.15-24.93)	0.018
Previous MTP		10	8.0	2	1.6	5.35(1.15-24.93)	0.018
History of infertility		23	18.4	10	8.0	2.59(1.18-5.71)	1.015
Previous MTP		23	18.4	16	12.8		0.222
History of Infertility		22	17.6	3	2.4	8.69(2.53-29.85)	<0.001

Under reproductive history multiparity is strongly related to risk of EP, even though the number of multi's were less in the study group (OR 2.92, 95% CI 1.70 - 5.02, P value < 0.001). Adverse

pregnancy outcomes such as spontaneous abortion, induced abortion and previous h/o EP also shows a significant association with a P value < 0.05.

**Table 3** Relation between Causes of Infertility and Ectopic Pregnancy

Causes	Ectopic Pregnancy		Intrauterine Pregnancy (N = 125)		OR (95%, CI)	P Value
	N	%	N	%		
Total infertility	23	18.4	10	8.0	2.59(1.18-5.71)	0.015
Male factor	3	2.4	2	1.6		0.651
PCOS	10	8.0	2	1.6	5.35(1.15-24.93)	0.018
Tubopertoneal	8	6.4	1	0.8	8.48(1.04-68.83)	0.017
Ovulation induction	6	4.8	2	1.6	3.211(1.31-7.90)	0.151
OI + IUI	14	11.2	5	4.0	3.027(1.05-8.68)	0.032
Unexplained	2	1.6	5	4.0		0.250

History of infertility as well as infertility treatment was associated with high risk of ectopic as per many reports. Our study also showed similar results (p value - 0.015) compared to multiparous women. Women with tuboperitoneal factors like endometriosis and peritubal adhesions (p value 0.017) and polycystic ovaries (p value 0.0218) are also found to be significantly correlated with increased incidence of EP. Ovulation induction with clomiphene citrate alone does not show an increased risk (p value 0.151), while ovulation induction followed by intrauterine insemination seems to significantly increase the risk (p value 0.032).

Uss findings	Ectopic pregnancy (Numbers)	Ectopic pregnancy (Percentage)
Ruptured ectopic	26	20.8
Unruptured ectopic	92	73.6
Impending rupture	7	05.6
total	125	100

All patients with ruptured ectopic as well as impending rupture on USS were managed by surgery. Among study group 73.6 % of patients presented with unruptured ectopic pregnancy which contributes to the factor that more number of patients being managed by conservative approach.

B-hcg valued	Ectopic pregnancy (Numbers)	Ectopic pregnancy (Percentage)
<200	0	0
200-500	2	1.6
500-1000	14	11.2
1000-2500	61	48.8
2500-5000	22	17.6
5000-10,000	15	12
10,000-20,000	9	7.2
>20,000	2	1.6

Almost half of patients (48.8%) had B-hcg value less than 2500. Patients with B-hcg value more than 5000 were managed by surgery except 1 case, which was managed medically.

Treatment underwent	Ectopic pregnancy (Numbers)	Ectopic pregnancy (Percentage)
Medical	24	19.2
Conservative	5	4.8
Surgical	45	36
Total	125	100

In this study 44.8 % of patients were conservatively managed with expectant approach.

### Discussion

In the present study we tried to establish the role of conservative treatment in ectopic pregnancy. Among the 125 patients of EP, those with ruptured ectopic pregnancy as diagnosed by trans vaginal USS and those patients with very high B-hcg values as per serum assay were treated by surgical management. Surgical management also done for patients with impending rupture of ectopic pregnancy as per USS evaluation as well as for sterilization failure cases also. For patients with EP after sterilization we did a bilateral salpingo - oophorectomy and unilateral salpingo-oophorectomy for patients who wishes to retain their fertility. Salpingostomy was successful in 3 patients who are under infertility treatment.

Patients who were haemodynamically stable and with B-hcg values less than 2,500 and USS showing unruptured EP were willing for conservative management when we explained them regarding the possible expectant management and chances of its failure and then

the need for either medical / surgical management. Also explained those regarding chances of emergency surgery in case of ruptured EP. Among such 56.8 % patients 3 were not willing for expectant management and we did surgery for 2 and intravenous methotrxate for the other patient. All patients were followed up with 48 hourly serial B-hcg value and USS. Those who showed increasing B-hcg value or increasing size of EP on USS were taken for surgery/ medical management. Medical management was preferred for patients who are not willing for surgery and for those subset of patients with rising B-hcg value but no progressive change in USS. Methotrxate 1mg/kg was given as intramuscular injection single dose and followed up with B-hcg value on day 7. If the fall of B-hcg is less than 64% from previous value one additional dose of Methotrxate also administered. Patient was followed up with B-hcg and when value was less than 5 miu/ml, we discharge patient.

Expectant management was successful in 44.8% patients. All patients were followed up with serial B-hcg value and USS. Patient discharged once B-hcg value was less than 5 miu/ml.

Conservative management of ectopic pregnancy was particularly useful for patients who are on infertility treatment and for patients who wishes to retain their fertility. From patient part, patient was more satisfied with conservative approach as the important organ (fallopian tube) for fertilization was still retained. Before recommending conservative approach as a routine management in low risk cases of ectopic pregnancy, further studies should explore the increased risk of recurrent EP after conservative approach

### Conclusion

Ectopic pregnancy is a major medical and emotional problem in a woman's reproductive life. Although several risk factors for ectopic pregnancy are known, the cause for a large proportion of EP still remains to be studied. Even though surgical management was the definitive treatment for ectopic pregnancy current study

establishes the role of conservative management in patients who are haemodynamically stable and with Bhcg value less than 2500 and USS showing no signs of rupture/ impending rupture.

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