

# Reproductive Performance After Medically Managed Tubal Ectopic Pregnancies

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## Abstract:

The early diagnosis of an ectopic pregnancy, with the help of a transvaginal ultrasound (tvs) and serum Beta-hCG levels, has drawn our interest to a conservative management protocol. Ectopic pregnancies (EP) meeting the criteria for medical management can be treated with systemic methotrexate. This is emerging as a safe alternative to surgical treatment. The aim of my study was to investigate the effectiveness of systemic methotrexate in routine clinical practice and also to assess reproductive performance on follow up.

**Keywords:** Ectopic pregnancy, medical management of ectopic pregnancy, Methotrexate, Reproductive outcome, Tubal patency

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## I. Introduction:

Ectopic is derived from Greek word ektopos meaning 'away from a place'. Ectopic pregnancy is a pregnancy where the fertilised egg or the blastocyst gets implanted to any other place apart from the uterine endometrium. It is one of the most dreaded emergencies in gynecology and its modern management is one of the medicine's greatest success stories. In the last few decades varieties of surgical treatment have been tried to manage ectopic pregnancy and one method is claimed to be better than others. However, there is also a conservative approach with medical management with methotrexate being one such modality. The early diagnosis of an ectopic pregnancy, with the help of a transvaginal ultrasound (tvs) and serum Beta-hCG levels, has enabled us to effectively manage ectopic pregnancies meeting criteria for medical management with the use of systemic methotrexate. This is emerging as a safe alternative to surgical treatment. Reproductive performance and fertility should be kept in mind during selection of the choice of management. The purpose of this study was to investigate the effectiveness of systemic methotrexate in routine clinical practice and also to assess reproductive performance on follow up.

## II. Aims And Objectives:

To assess the reproductive performance after medically managed tubal ectopic pregnancies with systemic methotrexate.

## III. Methodology:

Total 39 vitally stable patients presenting to Obstetrics and Gynaecology department, MGM hospital Kalamboli over the last 5 years, diagnosed as having EP mass  $\leq 4$ cm by trans-vaginal sonography with no cardiac activity or evidence of rupture and B-hCG level  $< 5000$  IU/l were included in this retrospective study. Their treatment modality whether surgical or medical was elicited. Systemic methotrexate 50mg IM was administered as a single dose after basic investigations to all patients satisfying the selection criteria. Serum beta hcg levels were repeated weekly till non pregnant levels achieved. They were subjected to an HSG 6 months post beta hcg levels were non-pregnant to document tubal patency and followed up for subsequent pregnancies or repeat EP. These were taken as outcome measures revealing relative rate of subsequent fertility. Few cases whose beta-hcg was done on day 4, showed a rise. Hence weekly beta hcg levels were assessed.

#### IV. Results:

Our study period was from Jan'2011 to Jan'2016. Of the 39 patients diagnosed as an EP, satisfying all criteria, the success rate of medical management was 84% (32 patients), 16% (7 patients) required surgical intervention where operative finding of opposite tube was not recorded. 40% of the medically treated cases failed to follow up. 46.8% Of the follow up patients were willing for follow up HSG, patency of the diseased tube was 66.7% (10/15) after 6 months of non-pregnant beta hcg levels. In total subsequent pregnancy rate was 57.8% (11/19) and rate of repeat ectopic was 5.2% (1/19). Medically treated patient group according to beta hcg and size of ectopic mass and for Beta hcg as a marker of outcome patients were divided in 2 groups with beta hcg levels less or more than 2500 IU/L. Only 2 out of 24 patients in group with beta hcg <2500 required surgical intervention whereas 5 out of 15 patients with beta hcg >2500 needed surgery. Based on the size of ectopic mass only 2 out of 21 patients with EP mass less than 2.5cm required surgical intervention whereas 5 out of 18 patients with EP mass >2.5cm eventually needed a surgery

Results – Study Period Jan 2011 – Jan 2016

- Total patients 39
- Medical treatment Success 32 (84%)
- Surgical intervention 07 (16%)
- Failed to follow up cases 13 (40.6%)
- Follow up cases 19 (59.3%)
- Willing for HSG 15/19 (78.9%)
- HSG patency of diseased tube 10/15 (66.7%)
- Subsequent pregnancy rate followed till January 2018 11/19 (57.8%)
- Rate of repeat ectopic 1/19 (5.2%)

#### Beta hCG and Outcome of Treatment:

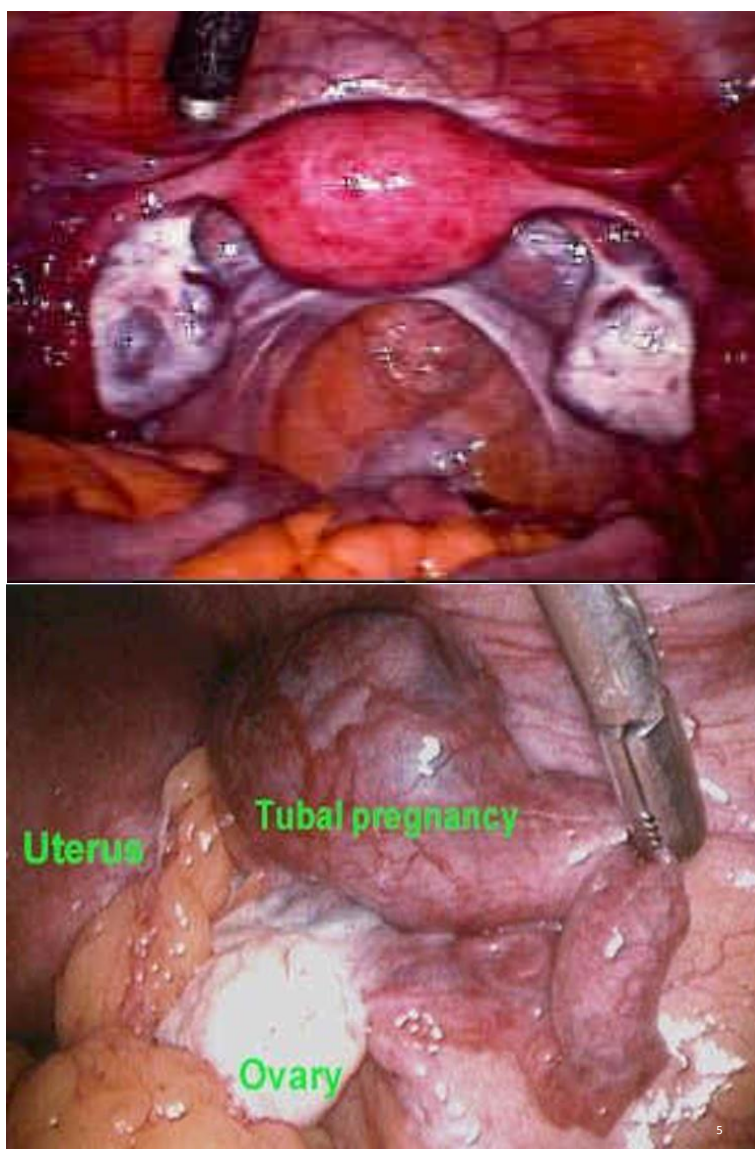
Initial beta hCG	No of patients	Successful medical treatment	Surgical intervention
2500 IU/L or less	24 (61.5%)	22 (91.6%)	2 (8.4%)
>2500 IU/L	15 (38.45)	10 (66.6%)	5 (33.4%)
Total	39	32 (84%)	7 (16%)

#### Size of Ectopic and the Outcome:

Size of Pregnancy	No of patients	Successful medical tt	Surgical intervention
2.5cm or less	21 (53.9%)	19 (90.4%)	3 (14.2%)
>2.5cm	18 (46.1%)	13 (72.3%)	4 (22.3%)
Total	39	32 (84%)	7 (16%)

## V. Discussion:

Ectopic pregnancy is one of leading cause of maternal morbidity and mortality. Even though mortality associated with ectopic pregnancy have reduced with newer and improved diagnosis, the majority (80%) of maternal first trimester deaths, and 10- 15% of all pregnancy related deaths, are related to haemorrhage from ruptured ectopic pregnancy. The incidence of EP is around 1-2% in most hospital-based studies.<sup>1</sup> 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 ectopic pregnancy. The results of this study show that systemic single dose methotrexate is a safe treatment option in unruptured EP with a reasonably high success rate and good probability of tubal patency. Patency of the diseased tube was 66.7% (10/15) after 6 months of non-pregnant beta hcg levels. In total subsequent pregnancy rate was 57.8% (11/19) and rate of repeat ectopic was 5.2% (1/19). Initial beta hCG levels less than 2500 IU/L respond well to medical management given the size of ectopic mass by TVS should be less than 2.5cm.



With these criteria 8 more cases were treated between March 2016 to March 2017 with no failure seen.

In a study investigating future fertility status of 158 women who received MTX for tubal EP, the cumulative intrauterine pregnancy and EP rates were 57.5% and 66.9%, and 15.4% and 23.7% after 1 and 2 years, respectively. In Cox regression analysis, after adjustment for factors associated with fertility, only previous history of infertility was associated with poor reproductive performance. The authors suggest that fertility is associated with the previous medical history of the patient rather than the treatment for EP

In a similar study by Stovall et al<sup>11</sup> Nineteen of 23 patients who had hysterosalpingograms demonstrated patency in the ipsilateral tube. Fourteen patients desired pregnancy; 11 of 14 (78.6%) were successful, with 10 of

11 (90.9%) having an intrauterine pregnancy, whereas one of 14 (9.1%) were extrauterine gestations. The mean time from first attempt to achieving pregnancy was 2.3 (1 to 4) months.

Whereas in a study by Elito Junior J et al<sup>iii</sup> the patency of the ipsilateral tube was 84% after methotrexate treatment and 78% after expectant management. In addition, contralateral tubal patency was 97% after methotrexate treatment, 92% after expectant management and 83% after salpingectomy.

In a study by Talwar et al<sup>iv</sup> MTX is successfully used for the treatment of unruptured EPs as an effective, safe and non-invasive method with minimal or no side effects.

In present study, it took 25-35 days for Beta-hCG to become normal. Ideal time for anatomical regression being 1-6 months. HSG patency being 66.7% hence it shows a positive result for future pregnancies with 11 intrauterine pregnancies that occurs subsequently without needing any intervention.

One study assessing compliance of methotrexate therapy noted that only 45.5% of patients completed follow-up, defined as documented resolution of hCG from the serum. Only 19.7% completed "appropriate" follow-up, which was defined as returning day 4, day 7 and weekly until hCG levels declined to zero. A total of 24% of patients in this group required surgery.<sup>v</sup>

In another study twenty-five patients (21%) failed methotrexate therapy and required surgical treatment, and 11 (9%) pregnancies were ruptured. Primary treatment was surgical in 275 (69%) patients: 172 (63%) underwent laparoscopies and 103 (37%) laparotomies. Success rates were significantly lower for medical therapy as compared to laparoscopic treatment (79% vs. 90%, odds ratio 2.2, 95% confidence interval 1.1, 4.3; P = .02). No discriminating predictors of successful treatment with methotrexate were identified.<sup>vi</sup>

In present study only 2 out of 21 patients with EP mass less than 2.5cm required surgical intervention whereas 5 out of 18 patients with EP mass >2.5cm eventually needed a surgery.

## VI. Conclusion:

The early diagnosis of an ectopic pregnancy, with the help of a transvaginal ultrasound (tvs) and serum BhCG levels, has drawn our interest to a conservative management protocol. Ectopic pregnancies meeting the criteria for medical management can be treated with systemic methotrexate and is emerging as a safe alternative to surgical treatment. No matter what modality of management used, preservation of fertility should also be an area of focus. Successful viable pregnancies have been reported after all the modalities of management of ectopic pregnancy however our study was concerned with influence of medical management of ectopic pregnancy on subsequent fertility. The results of this study show that systemic single dose methotrexate is a safe treatment option in unruptured EP with a 66.7% high success rate and good probability of tubal patency thus enabling better reproductive performance in future.

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