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OUTCOME OF MEDICAL MANAGEMENT OF TUBAL GESTATION

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ABSTRACT: AIM: To evaluate the outcome of management of unruptured tubal gestation with Intramuscular Methotrexate. **OBJECTIVE:** To determine whether patients with unruptured tubal gestation can be treated medically with Intramuscular Methotrexate. To evaluate the usefulness of serial measurement of serum β hCG in the medical management.

KEYWORDS: Ectopic tubal gestation, Methotrexate, serum β hcg.

INTRODUCTION: An ectopic pregnancy occurs when a fertilized ovum implants outside the normal uterine cavity. The most common site is the fallopian tube. Ectopic gestation is a common cause of morbidity and occasionally of mortality in women of reproductive age. The etiology remains uncertain although a number of risk factors have been identified. The diagnosis depends on a combination of ultrasound scan and serial serum beta HCG measurement. Ectopic pregnancy is one of the few medical conditions that can be managed expectantly, medically or surgically.

The use of medical management of ectopic gestation has become an accepted alternative to surgical therapy. The most widely used agent is Methotrexate, a folic acid antagonist. The dose of Methotrexate used to treat tubal gestation is relatively low, safe and well tolerated. Single dose of 50mg/m² intramuscularly is generally administered with serial serum beta HCG measurement. Repeat dose of Methotrexate is given if beta HCG level does not fall <15%.

Contraindications to Methotrexate therapy include hemodynamically unstable patients or those with elevated liver enzyme, low white cell count or abnormal renal function. HCG levels are more predictive of success. Studies report success rates of 65- 95%.

A better approach to the management of ectopic tubal gestation has achieved because of improved diagnostic modalities and therefore early diagnosis and treatment. Early diagnosis reduces the risk of tubal rupture and allows more conservative medical treatment to be employed. Preservation of future fertility became possible with the introduction of conservative surgical procedures and with the use of Methotrexate. The main achievement in the treatment of ectopic tubal gestation is the dramatic decrease in mortality rate.

MATERIALS & METHODS: This is a prospective randomised comparative study conducted in an 850 bedded tertiary care centre over a period of 18 months. 25 women admitted with unruptured ectopic tubal gestation satisfying the inclusion criteria were selected without any restriction of age and parity.

INCLUSION CRITERIA:

- Patients with unruptured tubal gestation and hemodynamically stable.
- Ultrasonologically diagnosed ectopic pregnancy with mass size <3.5cm in the greatest diameter.

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- Absent fetal cardiac activity.
- Serum β hCG titre < 10,000 mIU/ml.

ETHICAL CONSIDERATION: All the patients and their relatives were given an explanation of the study and about the investigative and operative procedures with their merits and demerits, expected results and possible complications. If they agreed then the case had been selected for the study. The study did not involve any additional investigation or any significant risk. It did not cause economic burden to the patients. The study was approved by the institutional review board prior to commencement of data collection. Informed consent was taken from each patient and relatives.

CONDUCT OF STUDY: Patients satisfying the criteria were investigated for baseline CBC, LFT, RFT and then administered a single dose of 50mg/m² of Intramuscular Methotrexate – considered as day 1. Serum β hCG titres were obtained on day 4 & 7. Titres were repeated weekly till negative. If β hCG titre did not fall or continued to rise, multiple doses Methotrexate is given to a maximum of 4 dose alternating with Folinic acid.

If the ectopic mass size increase or patient become hemodynamically unstable or β hCG titre rise in spite of multiple dose Methotrexate or sac ruptured, the case was managed surgically.

Patients who respond to medical management remain admitted in the hospital till the full course of Methotrexate is over and as the β hCG starts falling and patient remains clinically stable, they are discharged. Further follow up is in the outpatient clinic with weekly serum β hCG titre till negative.

Analyses of these cases were done to know the outcome of management.

OBSERVATION & RESULT: Total cases 25.

Patient Characteristics:

Age(yrs)	Number	Percentage (%)
20-30	22	88
>30	3	12

TABLE 1: Maternal Age

Parity	Number	Percentage (%)
Primi	10	40
Multi	15	60

TABLE 2: Order of Pregnancy

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Fig. 1: Details of Obsteric History

Case detail(s)	Number	Percentage (%)
Primigravida	10	40
Multi with no h/o abortions or prior ectopic gestation	3	12
Previous h/o abortions	7	28
Previous h/o ectopic gestation	3	12
Multi with h/o both abortion and ectopic	2	8

TABLE 3: Details of Obstetric History

Symptom	Number	Percentage(%)
Amenorrhoea only	7	28
Bleeding PV	13	52
Abdominal pain	5	20

TABLE 4: Mode of presentation

Period of Gestation	Number
4 weeks-≤ 5 weeks	4
5 weeks-≤ 6 weeks	8
6 weeks- ≤7 weeks	8
7 weeks- ≤8 weeks	3
>8 weeks	2

TABLE 5: Period of Gestation

Gestational sac size	Number
No sac	2
1-2 cm size	3
2- 2.5 cm size	12
2.5- 3 cm size	5
3- 3.5 cm size	3

TABLE 6: Ectopic Mass Size

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Serum hCG value	Number of Patients
<1000 mIU/ml	8
1000- 4999 mIU/ml	15
5000- 10000 mIU/ml	2

TABLE 7: Pretreatment hCG Values

Time	Mean β hCG with % fall	Range of β hCG
D1	2611	122-6647
D4	2250	127-9013
D7	529.2(23.5%)	22-4070
D14	68.2(12.8%)	1.2-1012
D21	22.7(33.3%)	0.9-158
D28	1.64(7.2%)	1.34-2.19

TABLE 8: Mean beta hCG values

No. of patients	No of Doses	β hCG at diagnosis	Time of resolution
10(40%)	1	815	14 days
15(60%)	≥ 2	2925	28 days

TABLE 9: Dose of Methotrexate and Time of Resolution

DISCUSSION: Ectopic pregnancy is a major obstetric problem. The exact etiology being unknown it cannot be predicted or prevented. The present study was conducted to see the outcome of medical management of ectopic tubal gestation with Methotrexate. It was noted that 84 % of patients were successfully treated with intramuscular Methotrexate, out of which 40% required single dose and 60% required multiple dose. 16 % underwent surgery due to various reasons, discussed below.

88% of the patients were of the age 20-30 years. 60% of the cases were multigravida. This included those with previous abortions or ectopic pregnancy.

Majority of the cases ie., 16(64%) were diagnosed at the gestational age of 5 – 7 weeks. Early diagnosis is crucial in the medical management of ectopic tubal gestation as the success rate is high in such cases. This is comparable to the study of Lipscomb et al.⁽¹⁾

In the present study the size of the ectopic mass selected was < 3.5 cm. 12 cases were in the group of 2- 2.5 cm size, out of which 2 cases went for surgery as the beta hCG values were rising in spite of multiple dose of Methotrexate. In a study conducted by Stovall TG et al.⁽²⁾ in 1991, they treated 30 patients with unruptured ectopic pregnancy with sac size ≤ 3.5 cm with single dose Methotrexate and they found that 29 patients were treated successfully. This observation is in contrast to our study.

23 out of 25 patients had pretreatment beta hCG level < 5000 IU/L, out of which 8 had <1000 IU/L. 2 patient had beta hCG > 5000 IU/L but ≤ 10000 IU/L, both cases were successfully treated with multidose Methotrexate. This is comparable with Lipscomb study.⁽³⁾ This shows that success rate of medical management is high if the pretreatment beta hCG level is low. Lipscomb et al further stated that the initial level of beta hCG is the best prognostic indicator for treatment success with Methotrexate.

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In the present study 10(40%) out of 25 patients received single dose, of which 6 patients had beta hCG < 1000 IU/L and 3 cases had 1000- 2000 IU/L and 1 case with beta hCG > 3000 IU/L. These patients were followed up with serum beta hCG levels and all resolved within 14 days. This again shows that single dose Methotrexate is effective in patients with initial low beta hCG level. This is comparable to the study by Carla Merisio et al, Khaled B et al and Mamdoh E.^(4,5,6)

Comparison of Overall Success Rate of Present Study with Lipscomb According to Serum hCG Level.⁽³⁾

Beta hCG level	Lipscomb study	Present study
>1000	98.3 %	100 %
1000 -1999	93 %	100 %
2000 – 4999	91.8 %	60 %
5000 – 9999	86.7 %	100 %
TABLE 10		

15(60%) patients received multidose regimen, out of which 4(16%) cases underwent surgery, 2 cases due to persistently high hCG levels, one case because of increasing size of the mass (even though her hCG declined more than 15% on 4th day, patient was complaining of persistent pain abdomen, scan showed increasing size of the sac) and the 4th one because of lack of compliance. The results of present study were comparable with other studies as the cases were selected according to the standard guidelines followed in other places.⁽⁷⁾ It was observed that most of the studies reported to have followed similar selection criteria.⁽⁷⁾

On comparing success following single dose and multidose, our observation was 100% vs. 73% respectively. This was in contrast to the study by Lipscomb.⁽³⁾ 4 of our patients who received multidose underwent surgery.

Overall success rate in the present study was 84% which is comparable with other studies.

Comparison of Success Rate from Different Studies:

Lipscomb et.al ⁽⁸⁾	90 %
Banhart et.al ⁽⁹⁾	89 %
MamdohEskandar et.al ⁽⁶⁾	94.3 %
Khalid B et. al ⁽⁵⁾	86.7%
Carla Merisio et.al ⁽⁴⁾	90 %
Present study	84 %
TABLE 10	

TIME OF RESOLUTION: In all the patients who received single dose, in the present study, the beta hCG became negative in 14 days and in 11 patients who were successfully treated with multidose Methotrexate beta hCG became negative in 28 days. This was earlier than with study of Khaled B et al and Hansa Dhar.^(5,10)

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CONCLUSION:

- The incidence is high among multies especially with history of abortions and ectopic gestation.
- There is a slight increase in the incidence in women on infertility treatment.
- Majority of the cases presented between 5 and 7 weeks of gestation.
- Single dose of Methotrexate was effective in patients with small ectopic mass and low serum β hCG values.
- None of the patients developed major side effects and all of them responded well to the symptomatic treatment.
- Success of treatment depends on correct case selection and perfect counselling.
- S.hCG levels of all the patients returned to normal within 28 days of treatment.
- Methotrexate can be used successfully in the management of ectopic tubal gestation.

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