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Original Research Article

A Clinical Study of Medical Management and Outcome of Un Ruptured Tubal Pregnancy by Using Single Dose of Methotrexate – A Prospective Observational Study in a Tertiary Care Center, Mandya

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Abstract:

Background: Methotrexate is the standard medical management for ectopic pregnancy. Pharmacologically, it is a folic acid antagonist which inhibits DNA synthesis. 90% of appropriately selected un-ruptured none live ectopic pregnancy respond to methotrexate treatment with no further management is required. In the UK, NICE guidance has identified the selection criteria to achieve the best and safest outcome in ectopic pregnancy treatment with methotrexate. Methotrexate also has a role in management of pregnancy of unknown location. Single administration of 50 mg/m2 body surface area is the most widely acceptable regimen for methotrexate in treatment of ectopic pregnancy. Post treatment b-HCG checks at day 0, 4 and 7 are also a widely accepted follow up regimen to ensure satisfactory decline in b-HCG levels. Methotrexate has a role also in managing none tubal ectopic pregnancies where surgical risks are high. Post treatment transient pain is common and represents a clinical challenge as it can also be failed treatment with ruptured ectopic pregnancy.

Materials and Methods: All patients admitted to Mandya Institute of Medical Sciences at Department of Obstetrics and Gynaecology with diagnosis of unruptured tubal pregnancy managed medically between January 2022 and December 2022 were included in this study. The diagnosis of tubal pregnancy was made using both Transvaginal Sonography **(**for Adnexal mass size and Absence of cardiac activity**)** and Initial serum beta β-hCG levels.

Results: The classical triad of tubal pregnancy was present in 11(44%) of patients. 15(60%) cases were found amongst the age group of 20 to 25 years, 14(56%) cases had their initial β-hCG levels <1500 m IU/ml, 4(16%), 3(12%), 4(16%) cases had β-hCG levels of 1500-2500 m IU/ml,2500-3500 m IU/ml, >3500 m IU/ml respectively, 52% of cases had adnexal mass size measuring between 2-3cm, 44% of cases presented with adnexal mass size <2cm, whereas 4% of cases had initial adnexal mass size >3cm, 16 (64%) patients had amenorrhea between 43-56 days, 6 (24%) and 3(12%) cases had amenorrhea of < 42days and >57 days respectively. In this study 21 (84%) were managed successfully by single dose methotrexate and 4 (16%) cases were managed by exploratory laparotomy due to failed medical management.

Conclusion: Early diagnosis using hormonal studies, sonography, and management in an institutional set up can reduce the associated morbidity. Complete resolution was seen in all cases of single dose methotrexate regimen whose mean initial serum β-hCG was 2,275.12 m IU/ml, adnexal mass<2cm and amenorrhea <42days.

Keywords: Methotrexate, folic acid antagonist, un-ruptured, non-live, single administration, serial β-HCG.

Introduction

An ectopic pregnancy occurs when a fertilised ovum implants outside the normal uterine cavity [1-3]. It is a common cause of morbidity and occasionally of mortality in women of reproductive age. Ectopic pregnancy accounts for approximately 2% of all recognized pregnancies [4]. The mean annual rate of ectopic pregnancy is 0.64% in patients of age 15 to 44 years and the incidence is increased from 0.5 to 2 per 100 pregnancies in the past 30 years [5]. The aetiology of ectopic pregnancy remains uncertain although a number of risk factors have been identified6. Its diagnosis can be difficult. In current practice, in developed countries, diagnosis relies on a combination of ultrasound scanning and serial serum beta-human chorionic gonadotrophin (β-hCG) measurements

[7]. Ectopic pregnancy is one of the few medical conditions that can be managed expectantly, medically or surgically [1,3,6]. Methotrexate is the standard medical management for ectopic pregnancy.

Pharmacologically, it is a folic acid antagonist which inhibits DNA synthesis. 90% of appropriately selected un-ruptured none live ectopic pregnancy respond to methotrexate treatment with no further management is required. In the UK, NICE guidance has identified the selection criteria to achieve the best and safest outcome in ectopic pregnancy treatment with methotrexate.

Methotrexate also has a role in management of pregnancy of unknown location. Single administration of 50 mg/m2 body surface area is the most widely acceptable regimen for methotrexate in treatment of ectopic pregnancy. Post treatment b-HCG checks at day 0, 4 and 7 are also a widely accepted follow up regimen to ensure satisfactory decline in β-hcG levels.

Methotrexate has a role also in managing none tubal ectopic pregnancies where surgical risks are high. Post treatment transient pain is common and represents a clinical challenge as it can also be failed treatment with ruptured ectopic pregnancy.

90% of appropriately selected un-ruptured none live ectopic pregnancy respond to methotrexate treatment with no further management is required [8].

Objective

- To study the demographic profile and various clinical manifestations.
- To study the outcome of medically managed cases of un ruptured tubal pregnancies using single dose of intramuscular methotrexate.

Materials and Methods:

Study Design: Prospective Observational study

Study Period: The study will be conducted from the records of January 2022 to December 2022 (1 years) will be analyzed.

Sample Size: All women who have undergone medical management for tubal pregnancy at MIMS during study period (25cases).

Sampling Method: Data will be collected from all available records.

Inclusion Criteria:

- Un-ruptured tubal or other ectopic pregnancy.
- Serum quantitative beta hCG < 5000 IU/L
- Size of ectopic mass < 3.5cm
- Cardiac activity absent.
- Normal liver and kidney function tests (LFT, KFT), and FBS.

Exclusion Criteria: Ruptured Ectopic pregnancy

Method of Data Collection (study tools):

A Prospective Observational study will be conducted over a period of 1 year (January 2022 to December 2022) for patients who have undergone medical management for tubal pregnancy at MIMS willing to participate in the study were included. The diagnosis of tubal pregnancy was made using both Transvaginal Sonography **(**for Adnexal mass size and absence of cardiac activity**)** and Initial serum beta β-hCG levels. On admission after a detailed history, examination, and investigations, the medical management was done according to the findings.

Data Analysis:

The statistical analysis is done by using statistical software (SPSS) . The data is represented as median or frequencies.

Results:

Table 1: Demographic Characteristics

AGE (yrs)		**GRAVIDA**	
20-25	18	PRIMI	8
26-30	6	MULTI	17
>30	1		

Altogether 25 patients were analyzed during the study. The majority age at the time of presentation was 20-25 years. 32 percent of the patients were primigravida and 68 percent were multigravida.

Table 2: Clinical Presentation at the Time of Admission.

Clinical manifestation	**Number**
Triad	11
Pain abdomen	20
Amenorrhea	18
Bleeding PV	12

The classical triad of tubal pregnancy was present in 11(44%) of patients, 20(80%) patients had pain abdomen, 18(72%) had amenorrhea and 12(48%) had bleeding PV.

Table 3: Initial B-Hcg Level at The Time Of Presentation

S. Initial β-hcG level(m IU/ ml)	Cases
<1500	14
1500-2500	4
2500-3500	3
>/=3500	4

In our study group majority of the cases that is 14(56%) cases had their initial β-hCG levels <1500 m IU/ml, 4(16%), 3(12%), 4(16%) cases had β-hCG levels of 1500-2500 m IU/ml, 2500-3500 m IU/ml, >3500 m IU/ml respectively.

Table 4: Adnexal Mass Size

Adnexal mass size	No. of cases
<2 cm	11
2-3 cm	13
>/=3 cm	1

Out of the 25 cases, 52% (13) of cases had adnexal mass size measuring between 2-3cm, 44% (11) of cases presented with adnexal mass size <2cm, whereas 4%(1) of cases had initial adnexal mass size >3cm

Table 5: Days of Amenorrhea.

Days of amenorrhea	No. of cases
< 42 days	6
43-56 days	16
>57 days	3

In this study, 16(64%) patients had amenorrhea between 43-56 days, 6 (24%) and 3(12%) cases had amenorrhea of < 42days and >57 days respectively.

Table 6: Single Dose Regimen: Treatment Outcome

Medically managed	21
Failed medical management (laparotomy)	04
Total cases	25

Total number of cases of ectopic tubal pregnancy from January 2022 to December 2022, 25 cases. Out of these 25 cases, 21 (84%) were managed successfully by single dose methotrexate and 4(16%) cases were managed by exploratory laparotomy due to failed medical management.

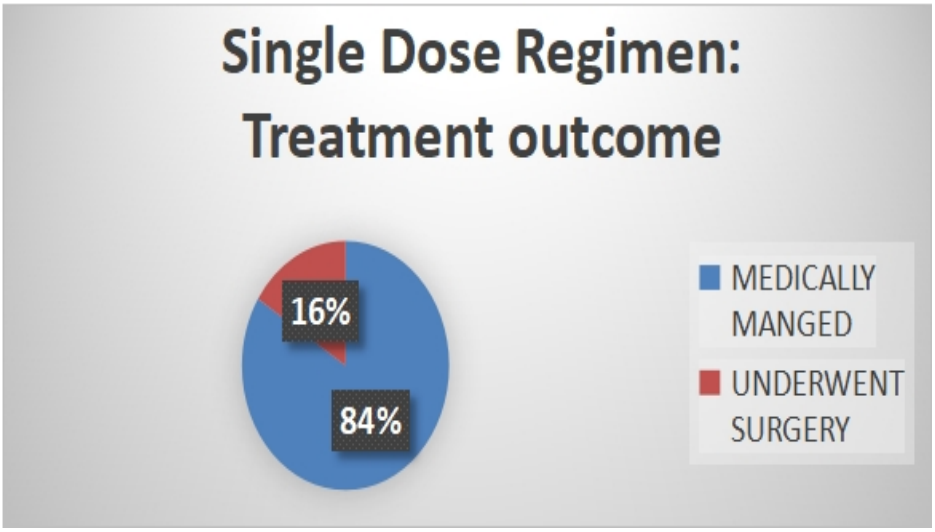

Figure 1: Single dose regimen: treatment outcome

Discussion

This prospective observational study includes all the patients who were diagnosed to have unruptured ectopic pregnancy by Transvaginal sonography (TVS) and serial beta β-hCG levels, and was managed medically with methotrexate.

25 patients with unruptured ectopic pregnancy were enrolled in the study and were observed for outcome of treatment with methotrexate. The mean age of these 25 patients was 24.4years. Maximum patients belong to 20-25 years i.e.60%. The range was 20 to above 30years. Mean gravidity of the patients studied was 1.88. Maximum patients were second gravidas. Mean gestational age of all

patients was 47.76 days. Maximum number of patients had gestational age between 6-8 weeks. Out of the 25 patients who were included in this study, 21 were managed successfully with single dose regimen.

Outcome of Treatment: 25 patients in this study were given single dose of 1mg/kg Inj. Methotrexate intramuscular. However, 21 responded to medical management with methotrexate without any surgical intervention. The end point of treatment i.e. complete resolution in these patients mean fall of β-hCG to <5m UI/ml without any surgical intervention.

Vijay Kalyankar et al study It was a prospective observational study conducted in the department of obstetrics and gynaecology, at Government Medical College, Aurangabad, Maharashtra for a period of 2 years from December 2016 to November 2018 after obtaining clearance from the institutional ethical committee. The magnitude of ectopic pregnancy was 3.95 per 1000 pregnancies. The classical triad of ectopic pregnancy was present in 45.38 % of patients. (89.24%) were managed by surgical methods, by exploratory laparotomy (112) and laparoscopy (6). In surgical management, 64.40% of cases were managed with unilateral salpingectomy, 19.49% cases with bilateral salpingectomy, and 4.23% cases with salpingo-oophorectomy. In 83.90 % of cases, the most common site of ectopic was in the ampullary region. Concluded that surgical management was the mainstay of treatment. The most common site was an ampullary tubal ectopic pregnancy [9]

T Alpana et al study conducted: Hospital based cross-sectional study at Department of Obstetrics and Gynecology, Raja Rajeswari Medical College & Hospital, Bengaluru, Karnataka, India, as per this: A total of 62 patients with ectopic pregnancy were identified and studied. The rate of ectopic pregnancy was 1.26:100 deliveries. The mean age was found to be 26 years and majority of them were multigravida. The most common presenting symptom was abdominal pain. Most patients had tubal ectopic pregnancy (94.2%). Ovarian ectopic occurred in two cases and 1 patient had heterotopic pregnancy. Emergency laparotomy was performed in 39 (62.90%) patients, 3 (5.77%) patients received methotrexate injection while 18 (29.0%) patients were managed by operative laparoscopy. All cases of laparotomy did not require any further procedure.

Out of three cases, 2 (66.66%) cases of medical treatment were successful while only 1 (33.33%) case proceeded to emergency laparotomy. No maternal death occurred. Intensive care unit (ICU) stay was needed in 5 patients. Risk factors were found in 67.3% and most common risk factor was found to be previous pelvic surgeries (56.45%). [10]

Conclusion

Un ruptured tubal pregnancy is a challenge for a obstetrician , which can be managed at tertiary care centers by early diagnosis using sonography [TVS], serum β hCG [serial monitoring] which can reduce the associated morbidity. Out of these 25 cases , 21 (84%) were managed successfully by single dose methotrexate and 4(16%) cases were managed by exploratory laparotomy/laparoscopy due to failed medical management Complete resolution was seen in all cases of single dose methotrexate regimen whose mean initial serum β-hCG was 2,275.12 m IU/ml, adnexal mass<2cm and amenorrhea <42days.

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