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Medical Management Of Ectopic Pregnancy: A Study From North Kashmir Medical College

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Abstract

Background: Ectopic pregnancy is a commonest cause of maternal morbidity and mortality in the first trimester of pregnancy.

Aims And Objectives: The study was done to evaluate medical management of ectopic pregnancy.

Material And Methods: A cohort study was conducted by department of Obstetrics and Gynaecology at GMC Baramulla over a period of2 year on 65 unruptured ectopic pregnancies who were treated with methotrexate injection**.**

Results: Out of 65 unruptured ectopic pregnancies, 62 (95.4%) were successfully treated with medical treatment which included methotrexate in 59 and expectant treatment in remaining six. Failure rate was 4.6% (3/65) patients who underwent laparotomy. Success of medical treatment was dependent on pretreatment β-hCG (≤4102.5 mIU/mL), period of gestation (≤5 weeks), size of gestational sac (≤3 cm) above which the failure rate increases. No correlation was seen between fall of β-hCG from day 4 to 7 and the success rate. Meantime to resolution of β-hCG seen was 4.3±1.25 weeks. Mean duration of hospital stay was 8.85±1.603 days. Single dose regimen of methotrexate was given to all patients and only 1/60 patients required second dose of methotrexate for suboptimal decrease of β-hCG.

Conclusions: The result showed that pretreatment β-hCG level and masses with small diameters were good predictors for success of medical treatments.

Keywords: Ectopic pregnancy, Methotrexate, 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. The aetiology of ectopic pregnancy remains uncertain although a number of risk factors have been identified.[4] 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.[5] Ectopic pregnancy is one of the few medical conditions that can be managed expectantly, medically or surgically.[1,3,6]

In clinically stable patients medical management is a safe and effective option whereas patients who are not eligible for medical management or present with ruptured ectopic pregnancy or failed medical management are to be surgically dealt.[7]

Methotrexate is a folate antagonist, which acts to block DNA synthesis by inactivating the enzyme dihydrofolate reductase. Methotrexate acts on rapidly dividing cells at the implantation site, most notably

trophoblast cells.[8] (2). The use of methotrexate to treat ectopic pregnancy was first cited in 1982.[9] (4) In 1991, a one-dose protocol was proposed, but this protocol is a misnomer as often more than one dose is often needed. Their protocol consisted of 50 mg/m^2 of methotrexate administered on day 0. Serial hCG values are drawn and compared between days 4 and 7 post treatment. Treatment is considered successful if a 15% drop in hCG level is noted between days 4–7. However, a second dose is administered on day 7 if a 15% drop is not observed and the patient remains an appropriate candidate for medical management. Thirty patients were enrolled in this study and 29/30, or 96.7%, patients were successfully treated. The quantitative hCG range for these patients was 30–16,700 mIU/ml. Five out of 6 patients who had ectopic pregnancies with cardiac activity were also successfully treated.[10]—[9]

Table 1:Methotrexate regimens used to treat ectopic pregnancy Modified from Barnhart et al[11].[8]

Protocol	Dose MTX	Regimen	hCG measurement	Treatment success	When to administer additional dose
Multidose	1 mg/kg and 0.1 mg/kg LEU	Alternate daily doses of each	Days 0, 1, 3, 5, 7	hCG declines 15% from previous value	2nd, 3rd or 4th dose given if hCG does not decline 15% from previous value. Maximum 4 doses
Single dose	50 mg/m^2	Day 0	Days 0, 4, 7	hCG declines 15% between Day 4 and 7	Second dose on Day 7 if hCG does not decline 15%
Two dose	50 mg/m^2	Day 0 and Day 4	Days 0, 4, 7	hCG declines 15% between Day 4 and 7	Second course on Day 7 if hCG does not decline 15%

MTX = Methotrexate, LEU = Leucovorin

Table 2: Selection of appropriate candidate for medical management of ectopic pregnancy[12].[3]

Contraindicated	Good Candidate	Poor Candidate
• Hemodynamically unstable • Suspected ruptured EP • Sensitivity to MTX • Intrauterine pregnancy • Breastfeeding • Active pulmonary disease • Renal disease • Chronic liver disease • Preexisting blood dyscrasia • Immunodeficiency • Peptic ulcer disease • Unable to comply with visits	• Hemodynamically stable • Low hCG (< 5000 mIU/ml) • Small mass (<3.5 cm) • Unruptured mass • No embryonic cardiac activity • Certainty that there is no IUP • Willingness for follow-up • No known sensitivity to MTX	• High hCG (>5000 mIU/ml) • Large mass (>3.5 cm) • Embryonic cardiac activity present • Significant abdominal pain • IUP has not been ruled out • Questionable ability to return for all outpatient visits

Volume 5, Issue 6; November-December 2022; Page No 799-804

Contraindicated	Good Candidate	Poor Candidate
and follow-up		

EP = ectopic pregnancy, IUP = intrauterine pregnancy, MTX = methotrexate

Material And Methods:

This study was conducted by Dept, of Obstetrics and Gynaecology at GMC Baramulla which is a referral centre for whole of north Kashmir. The study was conducted over a period of 2 year from Sep. 2020 to Aug. 2022.

Patients attending the outpatient department who were diagnosed as ectopic pregnancy were recruited for the study. The diagnosis of ectopic pregnancy was done by transvaginal ultrasonography and serial serum β-hCG. Inclusion criteria for the study was unruptured tubal ectopic pregnancy, hemodynamically stable patient, absent cardiac activity, and serum β-hCG in the range from 1500 to 10,000 mIU/mL. Patients having non-tubal ectopic pregnancy, ruptured tubal ectopic pregnancy, and hemodynamically unstable patients were excluded from the study. In addition, patient with deranged laboratory parameters, immunodeficiency, active pulmonary disease, lactating women, and not willing to follow-up were also excluded from the study.

A single dose MTX protocol for patients who were haemodynamically stable with absence of cardiac activity in the ectopic with normal liver and renal function tests. All the patients fulfilling the above criteria were given a single IM injection of MTX 50 mg/M^2 on day [0]. Serum b-HCG levels were repeated on day 4,7 and weekly after that. If b-HCG dropped by 15% on day 7 compared to day 0 the treatment was considered successful and in case were a 15% drop in b-HCG was not observed they were planned for a second dose. In patients who had signs and symptoms of ruptured ectopic were managed surgically.

Results:

This study was conducted by department of Gynaecology and Obstetrics GMC Baramulla over a period of two years.Total no. of deliveries were 13168 out of which 124 were ectopic giving an incidence of 0.94 cases/1000 deliveries. Out of 124 patients who were diagnosed as ectopic 59 were managed surgically and 65 were medically managed. Out of 65 patients who were managed medically, 5 were managed conservatively and single dose MTX was given to 60 patients. 2 patients required second dose and 3 patients had ruptured ectopic after receiving MTX. The mean age of the patients was…..

Table 1. Number of cases

Total number of ectopic pregnancy(%)	Medically managed (%)	Surgically managed (%)	P value
124(100)	65(52.4)	59(47.5)	0.589 (Non Sig)

Volume 5, Issue 6; November-December 2022; Page No 799-804

Fig: Management of cases

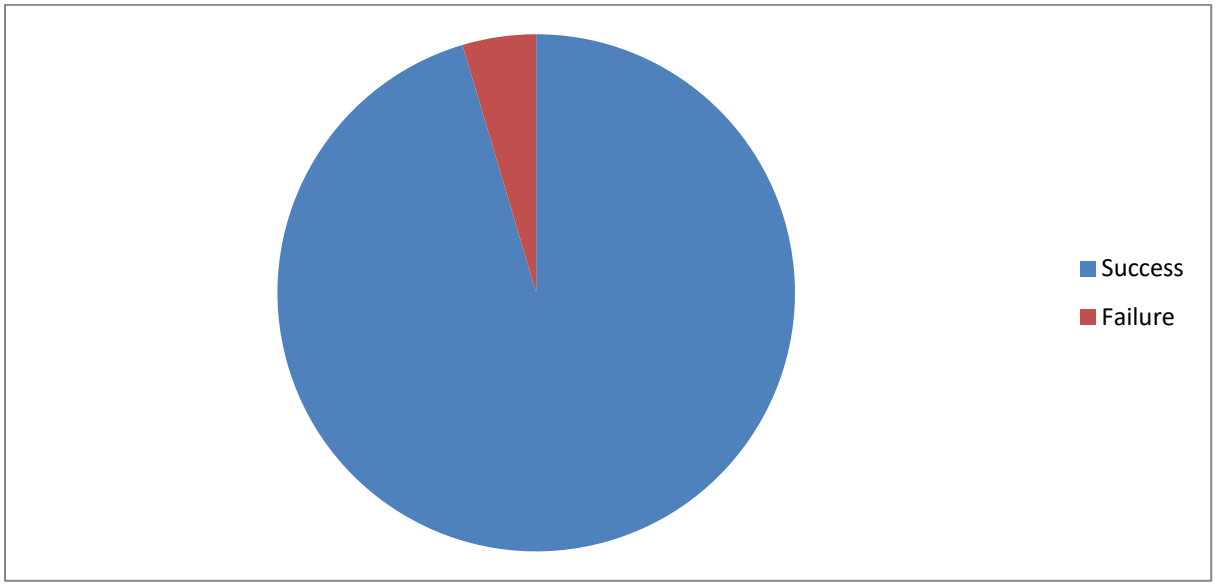

Table 2. Distribution of cases as per outcome

Outcomeijpik[o	Number of cases	Percenttage(%)	P value
Success	62	95.4%	Less than 0.005
Failure	3	4.6%	
Total	65	100%	

Fig:Cases as per out come

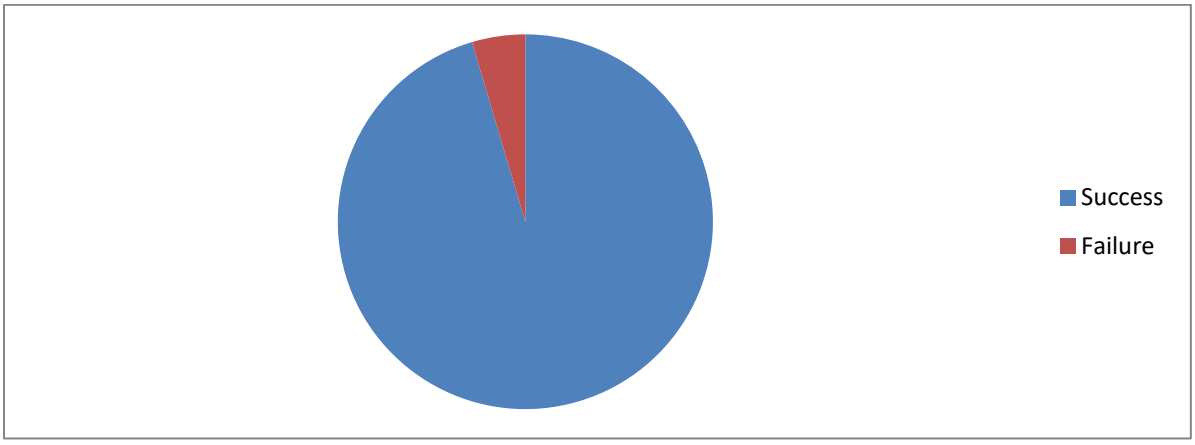

Table 3:B-hcg levels

b-HCG level	No. of cases	Percentage
200-1000	42	64.6
1001-2500	13	20

Volume 5, Issue 6; November-December 2022; Page No 799-804

2501-5000	5	7.6
5001-7500	3	4.6
7501-10000	2	3

Table 3: Size of ectopic

Size of ectopic	No. of patients (%)	Outcome		P value
		Success n(%)	Failure n (%)	
<4	50(76.9%)	49(98.0%)	1(2.0%)	<.005 (Sig)
>/= 4	15(23.0%)	13(86.6%)	2(13.3%)	0.004 (Sig)

Table 4. Average time of b-HCG resolution

Time in weeks	No. of cases	Percentage	P value
3-4 week	21	32.3%	<0.005
4-6 week	38	58.4%	
>6 week	6	9.2%	

Table 5. Reason for failure

Reason for failure	Number of cases	Percentage	P value
Haemodynamic instability	1	33.3	0.563
Severe pain	2	66.6	

Discussion:

Various studies have reported success of methotrexate in 65 to 95% of the cases ,as Orozco et al. [16] in their prospective study, demonstrated a global success rate of 88.1% ,similar findigs were also reported by Stovall TG et.al [10] ,these findings are consistent with our present study with success rate of 95.4%..

Henry MA[17] et.al also reported use of single dose of methotrexate in managent of ectopic pregnancy with success rate of 85%,these findings are also consistent with our present study.

While as the most important parameter for drug therapy with methotrexate in ectopic pregnancy is beta-hCG.it is known that success rates decline with increasing beta-hCG levels,as reported in a systemic study of 503 patients by Menon et [18] .that rates of treatment failure were statistically greater if the initial values of beta-hCG exceed 5,000 mIU/ml,these findings were consistent as reported in our present study.

Besides this,regarding size of the mass evaluated on transvaginal ultrasound with respect to treatment with methotrexate some administer drug treatment in masses with a diameter up to 3.5 cm [12] ,while others extend the use for masses larger than 3.5 cm

Volume 5, Issue 6; November-December 2022; Page No 799-804

[19,7] ,these findings are in concurrence as reported in our present study.

These above studies are evidence points to a growing trend in the choice of conservative treatment for ectopic pregnancies(EP)

Conclusion:

This study was conducted by department of gynae and obstetrics at GMC Baramulla from sep 2020 to august 2022. A total of 124 patients were diagnosed as ectopic out of which 65(52.4)% were managed conservatively . The result showed that pretreatment β-hCG level and masses with small diameter were good predictors for success of medical treatments.

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Volume 5, Issue 6; November-December 2022; Page No 799-804