

Comparison of Successful Outcome in Medical Versus Expectant Management in Patients with Unruptured Tubal Pregnancy Having β -Hcg 1000-3000 IU/L

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ABSTRACT

Objective: To compare the successful outcome in medical versus expectant management in patients with unruptured tubal pregnancy having β -hcg 1000-3000 IU/L.

Materials & Methods: In this randomized controlled trial, total 90 patients of ectopic pregnancy having age 18-40 years and having size of ectopic mass < 4cm were selected from the Department of Obstetrics & Gynecology Combined Military Hospital, Bahawalpur from March 20 to September 20. Group A included patients in which expectant management was done while Group B included the patients in which medical management (single intramuscular injection of methotrexate in a dose of 50mg/m²) was done. After one week, successful outcome was compared between the both groups.

Results: Total 90 women with tubal ectopic pregnancy were selected for this study. Comparison of successful outcome between the both study groups was done. Mean age of the patients was 31.66 \pm 6.44 years, mean gestational age was 7.83 \pm 2.33 weeks and mean β -hcg levels 1565.45 \pm 517.89 IU/L. In study group A, outcome was found successful in 40 (88.89%) patients and 31 (68.89%) patients of group B was found with successful outcome. After applying chi-square test, difference of successful outcome between the both groups was found statistically significant with p value 0.037.

Conclusion: This study concluded that expectant management is associated with better outcome (β -hcg levels negligible i.e. <10 IU/L and complete resolution on ultrasonography (absence of adnexal mass, pelvic free fluid, gestational sac) within one week) as compared to medical management in women with tubal ectopic pregnancy having β -hcg between 1000-3000 IU/L

Keywords: Ectopic pregnancy, methotrexate, expectant, resolution.

INTRODUCTION

A condition known as ectopic pregnancy (EP) occurs when the fertilized egg grows outside the uterine cavity,¹ during the first trimester, maternal morbidity and mortality are highly to occur due to EP. About 0.5-2% pregnancies globally have EP,² if not timely managed it can become a critical condition. Morbidity and mortality related to EP can be reduced by early and proper treatment. A diagnosis is necessary to find out when a woman has early pregnancy bleeding.³ Early pregnancy units (EPU) are essential for diagnosis of early pregnancy with access to fast immunoassay of serum hCG and high resolution transvaginal ultrasonography (TVS).

More than 90% of EPs can actually be presented on TVS.⁴ In result to which asymptomatic women have frequent benign conditions so that they can also use nonsurgical methods. Previously it resulted in a life threatening condition in immediate need of surgery for EPs.⁵⁻⁶ Non-surgical management like expectant and medical treatment, have become a focus of research as laparoscopies are not more performed as gold standard for the diagnosis of EPs.⁷ Trio D et al⁸ in their study has shown success rate (complete resolution) of 88% with expectant management (EM) in cases of EP with β -hcg <1000 IU/L while Dhar H et al² has shown this success rate of 65% with single dose of methotrexate.

Surgical management (laparoscopic route or mini-laparotomy) may be provided in cases of ruptured ectopic pregnancy.⁹ In most of the cases, laparoscopy is

recommended approach. Patients of cornual ectopic pregnancy and hemodynamically unstable cases were usually managed with laparotomy.¹⁰ In literature, many studies reported that in cases of EP, Postoperative adhesions are higher in laparotomy as compared to laparoscopic management. Furthermore, In addition to it, less need of analgesia and low blood loss has been seen in laparoscopy.^{10,11}

The aim of this study was to evaluate whether single dose of methotrexate or expectant management is associated with successful outcome in un-ruptured tubal ectopic pregnancy having β -hcg between 1000-3000 IU/L and the better modality should be advised for these particular women. Furthermore, for the management of women with un-ruptured tubal ectopic pregnancy having β -hcg between 1000-3000 IU/L, evidence for selection of medical versus expectant management is scarce and no local data available on this in our general population, so this study would also give better management plan for our population in order to avoid tubal injury and improve fertility outcome.

Operational Definitions

Tubal Ectopic Pregnancy: any pregnancy within the fallopian tubes and were diagnosed on ultrasonography as presence of a thick, brightly echogenic, ring like structure is located outside the uterus, with a gestational sac (thick, echogenic rim surrounding a sonolucent center corresponding to the trophoblastic decidual reaction

surrounding the chorionic sac) without cardiac activity and also having β -hcg between 1000-3000 IU/L, was considered positive.

Medical Management: All patients were given single intramuscular injection of methotrexate in a dose of 50mg/m².

Expectant management: In the expectant management, patients were monitored till one week. Monitoring consisted of serial β -hcg measurements and ultrasonography according to the local protocol.

Outcome: was considered successful if patient had β -hcg levels negligibly reduced and complete resolution on ultrasonography (absence of adnexal mass, pelvic free fluid, gestational sac) within one week and was considered unsuccessful if patient had β -hcg levels >3000 IU/L and no complete resolution within one week.

MATERIAL AND METHODS

After permission from Local Ethical Committee, 90 women with tubal ectopic pregnancy (as per-operational definition) having β -hcg levels between 1000-3000 IU/L, having age from 18-40 years and having size of ectopic mass < 4cm were selected from the Department of Obstetrics & Gynecology Combined Military Hospital, Bahawalpur from March 20 to September 20.

Patients with non-tubal ectopic pregnancy, patients having β -hcg >1000 IU/L and >3000 IU/L, ectopic mass >4 cm, patients with ruptured ectopic pregnancy assessed on ultrasound, hemodynamically unstable patients, presence of fetal cardiac activity, coexistent viable intrauterine pregnancy (heterotropic pregnancy), patients with hepatic

or renal failure and patients with known hypersensitivity to methotrexate were excluded from the study.

After taking informed, written consent from each patient selected patients were equally divided into group A and B randomly. Group A included patients in which expectant management was done while Group B included the patients in which medical management (single intramuscular injection of methotrexate in a dose of 50mg/m²) was done.

Outcome was measured after one week in term of success/unsuccessful and entered in pre-designed preform along with demographic profile of the patients.

Statistical analysis was conducted by SPSS version 20.0. Mean and SD was calculated for β -hcg levels, age (years) and gestational age (weeks). Outcome (successful/unsuccessful) was presented by frequency and percentages.

Difference of frequency of successful outcome between the both study groups was detected by applying chi-square test. Stratification in relation to age, gestational age and β -hcg levels was done and chi-square test was applied to detect the effect of these on successful outcome. P value ≤ 0.05 was considered as statistically significant.

RESULTS

Total 90 women with tubal ectopic pregnancy were selected for this study. Comparison of successful outcome between the bot study groups was done. Mean age of the patients was 31.66 \pm 6.44 years, mean gestational age was 7.83 \pm 2.33 weeks and mean β -hcg levels 1565.45 \pm 517.89 IU/L.

Table 1: Comparison of successful outcome between the both groups

Group	OUTCOME		Total	P value
	Successful	Unsuccessful		
A (expectant management)	40 (88.89%)	5 (11.11%)	45	0.037
B (medical management)	31 (68.89%)	14 (31.11%)	45	

Table 2: Comparison of successful outcome between the both groups for age

Group	OUTCOME		Total	P value
	Successful	Unsuccessful		
Age group 18-30 years				
A (expectant management)	16 (80%)	04 (20%)	20 (44.45%)	0.4351
B (medical management)	09 (64.29%)	05 (35.72%)	14 (31.12%)	
Age group 31-40 years				
A (expectant management)	20 (80%)	05 (20%)	25 (55.56%)	0.1548
B (medical management)	19 (61.29%)	12 (38.71%)	31 (68.89%)	

Table 3: Comparison of successful outcome between the both groups gestational age

Group	OUTCOME		Total	P value
	Successful	Unsuccessful		
Gestational age group ≤ 6 weeks				
A (expectant management)	18 (94.73%)	01 (5.27%)	19 (42.23%)	0.6071
B (medical management)	18 (85.70%)	03 (14.30%)	21 (33.34%)	
Gestational age group >6 weeks				
A (expectant management)	19 (86.35%)	03 (13.65%)	22 (48.89%)	0.0032
B (medical management)	08 (40.0%)	12 (60.0%)	20 (44.45%)	

Table 4: Comparison of successful outcome between the both groups for β -hcg levels

Group	OUTCOME		Total	P value
	Successful	Unsuccessful		
β -hcg levels 1000-2000 IU/L				
A (expectant management)	30 (83.34%)	06 (16.67%)	36 (80%)	0.0184
B (medical management)	19 (55.89%)	15 (44.11%)	34 (75.56%)	
β -hcg levels >2000-3000 IU/L				
A (expectant management)	07 (77.78%)	02 (22.23%)	9 (20%)	1.000
B (medical management)	08 (72.73%)	03 (27.28%)	11 (24.45%)	

In study group A, outcome was found successful in 40 (88.89%) patients and 31 (68.89%) patients of group B was found with successful outcome. After applying chi-square test, difference of successful outcome between the both groups was found statistically significant with p value 0.037. (Table 1)

Two age groups was made i.e. age group 18-30 years and age group 31-40 years. In age group 18-30 years, total 20 (44.45%) patients of group A and 14 (31.12%) patients of group B belonged to study group A and B. Outcome was found successful in 16 (80%) patients of study group A while in 09 (64.29%) patients of study group B. difference of successful outcome between study group A and B was not significant ($P = 0.4351$). In age group 31-40 years, out of 25 (55.56%) patients of study group A, successful outcome was noted in 20 (80%) patients. Among the 31 (68.89%) patients of study group B, treatment was found successful in 19 (61.29%) patients. But the difference of successful outcome between the both groups was found statistically insignificant with p value 0.1548. (Table 2)

Division of patients according to gestational was done and two groups were created, ≤ 6 weeks group and > 6 weeks group. In gestational age group ≤ 6 weeks, study group A and B consisted on 19 (42.23%) patients and 21 (33.34%) patients respectively. Total 18 (94.73%) patients of study group A and 18 (85.70%) patients of study group B found with successful outcome. Difference of successful outcome between the both groups was found statistically insignificant with p value 0.6071. In > 6 weeks group, total 22 (48.89%) patients belonged to study group A and 20 (44.45%) patients belonged to study group B. Outcome was found successful in 19 (86.35%) patients of study group A while in 08 (40.0%) patients of study group B. Difference of successful outcome between the both study group was statistically significant with p value 0.0032. (Table 3)

Among 36 (80%) patients of study group A and 34 (75.56%) patients of study group B, β -hcg levels were between 1000-2000 IU/L. In 30 (83.34%) patients of study group A while in 19 (55.89%) patients of study group B, treatment was found successful. Difference of successful between the both groups was statistically significant with p value 0.0184. β -hcg levels of 9 (20%) patients of study group A and 11 (24.45%) patients of study group B were between > 2000 -3000 IU/L. outcome was found successful in 07 (77.78%) patients and 08 (72.73%) patients of study group A and B respectively. But the difference was statistically insignificant with p value 1.000. (Table 4)

DISCUSSION

Increase in the incidence of EP is partially attributed to improve the ability for early diagnosis of EP. Complete or tubal abortion were the consequences of EP's further including remaining undetectable and spontaneous reabsorption which occurred in the past.¹² In very early cases of EP's, un-necessary medical or surgical intervention were questioned by some researchers whom advised expected management for selected patients. Clinical dilemma can occur while differentiating patients of proliferative EPs from patients having spontaneous

resolution of EPs.¹³

The objective of present study was to compare the successful outcome between medical and expectant management in patients with unruptured tubal pregnancy having β -hcg 1000-3000 IU/L. Outcome was found successful in 40 (88.89%) patients of study group A (expectant management) and in 31 (68.89%) patients of study group B (medical management). After applying chi-square test, difference of successful outcome between the both groups was found statistically significant with p value 0.037. Trio D et al⁸ in his study has shown success rate (complete resolution) of 88% with expectant management in patients with ectopic pregnancy having β -hcg < 1000 IU/L while Dhar H et al² has shown this success rate of 65% with single dose of methotrexate. Results of both studies were in agreement with our study. Initial β -HCG levels are the best predictor of medical treatment success. Lipscomb et al reported success rate with medical treatment as 90% when β -HCG levels < 5000 mIU/mL.¹⁴ Srivichai et al recruited 106 patients with EP, they found success rate as 90.6% while treated with methotrexate.¹⁵ But in our study success rate of patients treated with methotrexate was 68.89%, which is higher than our study. Merisio et al also treated their 11 patients of EP with methotrexate. In their series treatment was found successful in 90% patients.¹⁶ In published literature, success rate of medical management of EP ranges from 67-100%.¹⁷ In one study by Mahboob et al, total 15 women with EP having initial β -hcg levels equal to 5000 mIU/ml were selected and treated with methotrexate (single dose). Treatment was found successful in 80% patients.¹⁸ In published literature, success rate of expectant management of EP was between 48-100%.¹⁹⁻²³ In one study total 118 patients of EP were managed expectantly and found success rate as 63.5% which is similar to our findings.²⁴

CONCLUSION

This study concluded that expectant management is associated with better outcome (β -hcg levels negligible i.e. < 10 IU/L and complete resolution on ultrasonography (absence of adnexal mass, pelvic free fluid, gestational sac) within one week) as compared to medical management in women with tubal ectopic pregnancy having β -hcg between 1000-3000 IU/L. So, we recommend that expectant management should be preferred in women with tubal ectopic pregnancy having β -hcg between 1000-3000 IU/L in order to avoid tubal injury and improve fertility outcome.

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