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TUBAL ECTOPIC PREGNANCY AND THE DETERMINANTS OF ITS DIFFERENT TREATMENT OPTIONS

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ABSTRACT

Objective: To find out the determinants affecting the different management options of tubal ectopic pregnancy.

Methodology: This cross sectional study was carried out in the Unit A of the department of obstetrics and gynecology, Hayatabad Medical Complex, Peshawar from December 2014 to March 2018. All the patients admitted with clinical/ultrasound diagnosis of tubal ectopic pregnancy were included in the study through convenient sampling technique after informed consent. Patients having other early pregnancy problems which would mimic tubal ectopic pregnancy and those having any medical contraindications to Methotrexate were excluded. A pre-designed performa was used to collect the data, which was analyzed using SPSS v.22.0.

Results: The mean age of the sample (n=78) was 27.0±7.8 years. Maximum patients were multigravida (n=41, 52.6%), followed by primigravida (n=25, 32.0%). In treatment modalities, maximum of the cases (n=43, 55.1%) were managed medically via methotrexate with success rate of 93.0%, while 18 (23.1%) cases were managed conservatively with success rate of 83.3%, and 17 (21.8%) of the cases were managed surgically with 100% success rate. The maximum size of adnexal mass was found to be as 8.6×7, 10×7, and 8×6 in three management options, i.e., conservative, medical and surgical respectively, while in the same categories, maximum Beta-Human Chorionic Gonadotropin (β-hCG) level was found to be as 978, 43220, and 29844 mIU/ml respectively.

Conclusion: Hemodynamic instability and rising β-hCG were the core determinants in the management of tubal ectopic pregnancy. The size of the adnexal mass and the initial β-hCG did not affect the management.

Key Words: Ectopic pregnancy; βhCG; Methotrexate; Laparotomy; Ultrasound.

INTRODUCTION

In ectopic pregnancy, the fertilized ovum gets implanted outside the uterine cavity. Tubal ectopic is the most common type of ectopic pregnancy.¹ Ectopic pregnancy is one of the most important causes of maternal mortality during 1st trimester. With the advent of high resolution transvaginal ultrasound and serial Beta-Human Chorionic Gonadotropin (β-hCG), the morbidity and mortality due to ectopic pregnancy has declined.^{1,2} In developed countries early pregnancy assessment units (EPAU) have been developed for the management of early pregnancy complications under specialist cover.³ Although, methotrexate has revolutionized the management of ectopic pregnancy, but still there is role of surgery in the management of ectopic pregnancy. Both open laparotomy and laparoscopy are used depending on the availability, skills of the operating surgeon, and condition of the patient.⁴ β-hCG can be detected in the maternal blood as early as 8-10 days after ovulation. Generally, in early pregnancy the β-hCG levels double every 1.4-2.1 days and reaches peak level of 50000-100000 by 8-10 weeks of pregnancy. It is the discriminatory zone being used

to differentiate normal intrauterine pregnancy from ectopic pregnancy. But this discriminatory zone should be used with caution and in conjunction with the clinical findings, to avoid unnecessary intervention.^{5,6}

Ectopic pregnancy can be managed conservatively (expectantly), medically, or surgically. Patients who are clinically unstable will require emergency surgery either laparotomy or laparoscopy.⁷ Patients having β-hCG ≤ 1000 i.u, and which is falling by 13% every 48 hours and who are clinically stable can be managed conservatively, while patients having β-hCG ≤ 1500 i.u with an adnexal mass not greater than 3.5 cm who are haemodynamically stable and have no contraindication for methotrexate and able to follow strict surveillance, can be managed with methotrexate.⁸

For medical management, majority of the studies have given a cutoff value for upper limit at which medical treatment can be initiated.⁹ Our study aimed at looking at the outcome of medical management given to all hemodynamically stable patients with β-hCG greater than 1000 i.u irrespective of the size of adnexal mass. We, however, followed the same international standards for conservative and surgical management of tubal ectopic pregnancy.

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Because of scarcity of local data regarding these variations in the management of ectopic pregnancy, we decided to conduct this study.

METHODOLOGY

This cross sectional study was conducted in the Unit A of the department of obstetrics and gynaecology, Hayatabad Medical Complex, Peshawar from December 2014 to March 2018 after getting institutional ethical approval. Patients admitted with clinical/ultrasound diagnosis of tubal ectopic pregnancy were included in the study based on convenient sampling. An informed written consent was taken from all of the patients enrolled in the study. Patients having any other early pregnancy problems, which would mimic the tubal ectopic pregnancy e.g., miscarriages, ectopic pregnancies other than tubal ectopic, those having any medical contraindications to methotrexate (e.g., thrombocytopenia, leukopenia, elevated liver enzymes or high creatinine levels) were excluded from the study.

Patients who were haemodynamically unstable were prepared for emergency laparotomy, irrespective of β -hCG levels or ultrasound findings. Those patients who were haemodynamically stable were then selected for either conservative or medical management depending on the β -hCG levels, irrespective of ultrasound findings. Patients having β -hCG \leq 1000 mIU/ml were managed conservatively as in patient. These patients were then followed with β -hCG after 48 hours. If β -hCG levels were falling then these patients were managed conservatively with weekly monitoring of β -hCG level till full recovery. If there isn't any fall in the β -hCG level (β -hCG level remains same on 2 occasions) or showing a rising pattern, then such patients were shifted to medical treatment.

Patients having β -hCG $>$ 1000 mIU/ml irrespective of ultrasound findings and also were haemodynamically stable were managed medically. Injection Methotrexate 50 mg as blanket dose was given Intramuscular (after base line investigation). Patients were then followed on day 4 and 7 with β -hCG. If fall in β -hCG levels was \geq 30% on day 7 as compared to day 4, then these patients were

managed conservatively with weekly β -hCG follow up. But if the fall was \leq 30% then 2nd dose of Methotrexate 50mg intramuscular was given to such patients and β -hCG was repeated on day 4 and 7 again. Methotrexate doses were repeated till \geq 30% fall of β -hCG. Patients having plateau β -hCG levels on 2 occasions or those who become haemodynamically unstable were then shifted to surgical treatment. Patients requiring more than 3 doses of methotrexate were given injection Folinic acid 15mg intramuscular 36 hours after the last dose. In all cases, β -hCG was done from a single laboratory using monoclonal assay technique and results were expressed in mIU/ml. Abdominal ultrasound was performed by consultant ultrasonologist using 6.5MHz probe.

Data was collected on a predesigned proforma, and then analyzed using descriptive statistics in the form of frequencies and percentages using SPSS v.22.0.

RESULTS

A total of 78 cases were included in the study. Mean age of the patients was

27.0 \pm 7.8 years. Most of the patients were multigravida (n=41, 52.6%). The details are given in Table 1. Eighteen (23.1%) cases were managed conservatively, 43 (55.1%) cases were treated with methotrexate and 17 (21.8%) patients were haemodynamically unstable and underwent emergency laparotomy. The details including success rate are given in Table 2. The details of minimum and maximum size of adnexal mass and maximum and minimum levels of β -hCG in all the three management options, i.e., conservative, medical and surgical, are given in Table 3.

DISCUSSION

This study has investigated the major determinants of different treatment options in tubal ectopic pregnancy.

Previous studies have shown that β -hCG level \leq 1500 mIU can be managed conservatively.^{3,8} In our study the success of conservative management was 83.33%. A study has documented 10.3% success rate in patients having β -hCG level \leq 1500mIU in conservatively managed group.⁹ In another

Table No 1: Demographic details of the sample (n= 78)

Variables		Frequency (percentages)
Age(years)	\leq 20	20 (25.7%)
	21-30	32 (41.0%)
	\geq 31	26 (33.3%)
Gravidity	Primigravida	25 (32.0%)
	Multigravida	41 (52.6%)
	Grand multigravida	12 (15.4%)

Table No: 2 Outcome of different treatment options (n= 78)

Treatment Option	Total*	Successful*	Failed*
Conservative	18 (23.1%)	15 (83.3%)	3 (16.7%)
Medical	43 (55.1%)	40 (93.0%)	3 (7.0%)
Surgical	17 (21.8%)	17 (100%)	0

*The percentages in the total column are depicting the percentage from the whole while the percentages in the successful and failed column are calculated in respect to their respective groups.

Table No 3: Size of adnexal mass and β -hCG levels of treatment options (n= 78)

Treatment Option	Minimum size of adnexal mass (cm)	Maximum size of adnexal mass (cm)	β hCG Minimum level (mIU/ ml)	β hCG Maximum level (mIU/ ml)
Conservative	1.2 \times 0.9	8.6 \times 7	86	978
Medical	2.2 \times 2	10 \times 7	1030	43220
Surgical	2 \times 2	8 \times 6	683	29844

study 21% success rate has been reported with initial β -hCG levels ≥ 1500 mIU.¹⁰ Korhonen et al has documented 15% success rate when the initial β -hCG value was ≥ 2000 mIU.¹¹ The high success rate in our study (83.33%) may be because the cut of value of β -hCG in conservatively managed patients was ≤ 1000 mIU. Three patients in our study had failed conservative management because of rising β -hCG levels.

This study recorded a success rate of 93.04% in medically managed patients. There was no upper cut off value for β -hCG level and size of the adnexal mass, except haemodynamically of the patient, based on which surgical intervention was planned. Although in the literature it has been documented that success of medical treatment depends on β -hCG levels. However, a study has documented that β -hCG levels do not affect the success of methotrexate treatment.¹² Methotrexate can be given at higher levels of β -hCG, but it will need more doses of methotrexate, long term follow up and more chances of emergency surgery.^{13,14}

Barnart et al has shown 89% success rate with methotrexate treatment.¹⁵ Another study reported 83.33% success with methotrexate, they have also documented that a fall of $>15\%$ in the β -hCG values between Day 4 and Day 7, which might predict the treatment success rate with a sensitivity of 83.33% and a positive predictive value of 84.51%.⁹ The success of single dose methotrexate is affected by β -hCG levels, size of the adnexal mass, presence of yolk sac and cardiac activity.¹⁶ American Society for Reproductive Medicine (ASRM) in its guideline has suggested that single dose methotrexate is associated with high failure rates when given at high β -hCG levels.¹⁷ Jaspan et al has reported that 88.4% cases responded to single dose methotrexate, but they have included only those patients having adnexal mass less than 3.5cm.¹⁸ In our study, 93.04% patients responded to a single dose of methotrexate and only 3 (6.96%) patients required more than 3 doses of methotrexate or even surgical intervention. Requirement of multiple dose methotrexate in our study may be because of difference in the selection of patients. Our patients were having higher level of β -hCG and larger size of ad-

nexal mass. This study also revealed 100% successful management via surgical intervention which is approximately the same in other studies reported in the literature.^{6,11}

Management of ectopic pregnancy depends on the initial β -hCG levels, patient's hemodynamic condition, fertility desires, compliance with long-term follow-up, size of the adnexal mass and the presence of fetal cardiac activity.^{9,16} In our study, the success of medical treatment was not affected by the size of the adnexal mass but such patients required multiple doses of methotrexate.

CONCLUSION

Hemodynamic instability and rising β -hCG were the core (factors to determine the mode of treatment for a patient with ectopic pregnancy) determinants in the management of tubal ectopic pregnancy. The size of the adnexal mass and initial β -hCG did not affect management option of ectopic pregnancy.

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Author's Contribution

RK drafted the proposal, collected the data, analyzed the results and wrote the manuscript. BR conceived the idea, helped in designing the study, acquisition of the data and gave intellectual input in the writing of the paper. Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

Authors declared no conflict of interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.