MANAGEMENT OF ECTOPIC PREGNANCY: A TWO-YEAR STUDY

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Background: Ectopic pregnancy is the most important cause of maternal mortality and morbidity in the first trimester. Over the past few decades, the management of ectopic pregnancy has been revolutionized; various modalities of treatment are currently in practice. The purpose of this study was to determine the frequency of these modes of treatment of ectopic pregnancy and their outcome. **Methods:** Fifty two patients diagnosed to have ectopic pregnancy at MCH Center unit II in the year 2004 and 2005 were included in the study. A cross-sectional analytical study was done. Four modes of treatment were given according to patient's condition, ultrasound findings and ß-hCG levels; these were laparotomy, operative laparoscopy, methotrexate injection and conservative management. The outcome measures included success of each treatment modality, need for second mode of treatment in each group and duration of hospital stay. **Results:** A total number of 52 patients with ectopic pregnancy were identified and studied. The rate of ectopic pregnancy was 1:100 deliveries. Emergency laparotomy was performed in 30 (57.9%) women, 15 (28.8%) received methotrexate injection. Seven women (13.3%) were managed conservatively and operative laparoscopy was not used as primary treatment in any of the patient. All cases of laparotomy did not require any further procedure. Twelve out of fifteen (80%) cases of medical treatment were successful while one (6.7%) proceeded to emergency laparotomy, one (6.7%) to operative laparoscopy and one (6.7%) to laparoscopy preceding laparotomy. Five out of seven patients (71.4%) on conservative treatment did not require any further intervention while two (28.6%) of them resolved with methotrexate injection. The duration of hospital stay in laparotomy, medically treated and conservatively managed groups was 6.5, 5.9 and 1.7 days respectively. **Conclusion:** In the institutional setting ectopic pregnancy accounted for 1% of total deliveries. More than half of all women with ectopic pregnancy presented with acute abdomen and required emergency laparotomy. About 40% women could be managed with non-surgical modalities with 80% success for methotrexate injection and 71% for conservative treatment in the present study.

Keywords : Ectopic pregnancy, methotrexate, laparoscopy.

INTRODUCTION

Ectopic pregnancy is a pregnancy in which the fertilized ovum implants outside the uterine cavity. Its incidence has increased from 0.5 per 100 pregnancies thirty years ago, to the present day of 2 per 100 pregnancies[1,2]. The Centre for Disease Control (CDC) reports that the incidence of ectopic pregnancies is 1 in 70 pregnancies[3] while in Pakistan it varies from 1:112[4] to 1:130 pregnancies[5]. Heterotopic pregnancy, although rare in spontaneous conceptions (1/3000-4000), can be seen in up to 3% of pregnancies resulting from assisted reproduction[6].

In first trimester, ectopic pregnancy is the most important cause of maternal mortality and morbidity[7]. Prior to 1883, no women ever underwent a deliberate and successful operation for a ruptured ectopic pregnancy when Trait did it for the first time. Surgical treatment may either be an open laparotomy or laparoscopic depending on the surgeon's skill, equipment availability and condition of the patient[8].

Over the past few decades, the management of ectopic pregnancy has been revolutionized. This has resulted in emergence of several non-surgical options to what had once been thought to be a solely surgically treatable condition. An earlier diagnosis can be made with transvaginal ultrasound and quantitative ß-hCG. This increases the chances of success of medical treatment and minimizes the morbidity, mortality and financial burden created by this health problem[8,9].

Non-surgical management has an established role in the treatment of ectopic pregnancy[10,11] but little data are available on national scale. In the tertiary care hospital where this study was conducted, facilities for all four modes of treatment of ectopic pregnancy were available i.e. laparotomy, laparoscopy, medical treatment and conservative management. Therefore this study was conducted using all the treatment modalities according to set protocols.

MATERIAL AND METHODS

Over a period of two y ears, a cross-sectional analytical study was conducted in the department of Obstetrics & Gynaecology Unit II, MCH centre, Pakistan Institute of Medical Sciences, Islamabad. Fifty-two patients diagnosed to have ectopic pregnancy presenting to the department of Gynaecology and Obstetrics, were included in the study.

All cases of ectopic pregnancy diagnosed on the basis of history, examination and specific investigations were treated by one of the four treatment modalities. Informed consent was taken and

data were recorded on a proforma. According to set inclusion criteria patients presenting with haemodynamic shock, having ß-hCG levels >6000 mIU/ml or those suspected to have ruptured tubal pregnancies were treated with immediate laparotomy.

Stable patients with intact tubal pregnancy, ß-hCG level <6000 mIU/ml, mass size <6 cm or with contraindication to methotrexate (i.e. leukopenia, thrombocytopenia, or elevated serum liver enzymes or creatinine) were to be planned for laparoscopy.

Inclusion criteria for conservative management were ß-hCG level 1000-2000 mIU/ml & falling, pregnancy diameter <2cm, no evidence of rupture and minimally symptomatic patients.

Women who were minimally symptomatic with ß-hCG =5000 mIU/ml, pregnancy diameter <5 cm, non-viable pregnancy and no signs of rupture were treated with methotrexate injection.

Single intramuscular injection of methotrexate (1 mg/kg body weight) was given to eligible patients. A second dose was given to those cases in which more than 10-15% fall of ß-hCG level did not occur in 48 hours or size of the mass further increased after a lapse of seven days.

Possible signs of methotrexate toxicity like stomatitis, gastritis, dermatitis, pleuritis, leucopenia, thrombocytopenia, raised hepatic enzymes and raised blood urea and creatinine levels were noted carefully. Patients on methotrexate were warned that the therapy might fail in 5- 10% of cases. Moreover the failure of medical therapy could result in surgery, which might be elective or emergency. Coitus was prohibited until serum ß-hCG was undetectable. Folic acid was avoided during treatment phase.

Success of a mode of treatment meant complete resolution associated with that mode i.e., return of ß-hCG level to 10 mIU/ml without any need for further intervention.

Outcome measures were proportion of cases diagnosed as ectopic pregnancy out of total deliveries and success of eliminating ectopic pregnancies by indicated methods. Duration of hospital stay and the need for alternative methods of management were additional variables studied.

Data were entered into SPSS version 11 and analyzed. The outcome measures of various regimens were compared for differences on clinical and statistical significance using chi square/ Fisher Exact Test for qualitative data and t- test for numerical data. A p- value of 0.05 or less was taken as significant.

RESULTS

Fifty-two women presented with ectopic pregnancy out of total 5220 deliveries at MCH Centre Unit-II during the specified study period (making a proportion of 1%). The mean age of women was 28yr±4.8 years. Of these, 16 were primigravida, 27 were multigravida and 9 were grand multigravida. Seven (14%) were clomiphene-induced pregnancies, 6(11.5%) had history of IUCD use, while 8 (15.4%) had previous pelvic surgery. Thirty patients had adnexal masses on ultrasonography and in 20 of these the mass was in right adnexa.

Thirty (58%) patients underwent emergency laparotomy. Twenty-two of them had haemoperitonium and were haemodynamically unstable. Two laparotomies were done for abdominal pregnancies. One patient had heterotopic pregnancy; therefore laparotomy was done for ruptured right tubal pregnancy besides intact healthy intrauterine pregnancy of 77 days.

None of the patients underwent primary operative laparoscopy as no one fulfilled the inclusion criteria for this procedure. Among the rest of 22 (42.1%) patients, 15 (28.8%) had methotrexate injection, and 7(13.3 %) were allocated to conservative management (i.e., no treatment). Variables such as age, gravidity, parity, gestational age, duration since last child birth and use of contraception were comparable in all groups of patients ($p>0.05$)

Seven women were managed conservatively. The day 0 ß-hCG levels range was 78-2004 mIU/ml (884.7±815). Six of them had adnexal masses on ultrasound. The mean adnexal mass size was 2.83 cm (±1.2) which exceeds the range of inclusion criteria for conservative management. It was because of a single patient who had resolving ectopic pregnancy with mass size of 5 cm but very low ß-hCG (just 78mIU/ml) & was asymptomatic and therefore allocated to the conservative group. Excluding this patient, mean mass size was 1.7±0.2 (range 1.4-2cm) in accordance with the set inclusion criteria.

The mean gestational age was 51.8± 21.4 days for women who were offered medical treatment. Adnexal mass size range was 2-5 cm (mean 3.35±1.2). Ten (67%) patients responded well to single dose of methotrexate while five (33.3%) required its 2nd dose. Regarding the side- effects of methotrexate, stomatitis was observed in one patient and increase in abdominal pain in another. However, the course of treatment was uneventful in the remaining patients.

All cases undergoing laparotomy did not require a secondary procedure meaning 100% success rate. Twelve out of fifteen (80%) cases undergoing medical treatment were successful while one (6.7%) proceeded to emergency laparotomy, one (6.7%) to operative laparoscopy and one (6.7%) to laparoscopy preceeding laparotomy. Five out of seven patients (71.4%) on conservative treatment did not require any further intervention while two (28.6%) of them were cured with methotrexate injection.

The comparison of success rate was found statistically significant when conservative and medical groups were compared with laparotomy group (p-value 0.032 & 0.03 respectively). When medical and conservative groups were considered, success rates were comparable i.e., p=0.65.

Mean duration of hospital stay in laparotomy, medical and conservative groups was 6.5, 5.9 and 1.7 days respectively. It was statistically significant when conservative group was compared with medical and laparotomy groups ((p value < 0.01). Comparison of laparotomy group with medical group was not found to be statistically significant (p value >0.05). (Table 1)

Table-1: Distribution of cases by duration of hospital stay (n=52)

Mode of Treatment	Days (Mean ± SD)
Conservative	1.7±1.5
Methotrexate	5.9±3.2
Laparotomy	6.5±1.1

One patient in the laparotomy group had serious morbidity. She was referred from a private hospital, bled massively on the way, had laparotomy, was put on ventilator, weaned off later and discharged in satisfactory condition.

DISCUSSION

The incidence of ectopic pregnancy has remained static in recent years i.e. 11.1/1000 pregnancies[11,12,13,14]. In this study the rate was found to be 10/1000 deliveries, which is comparable. Ectopic pregnancy affects young women. The mean age was found to be 28 years and majority of them were multigravida. The commonest presenting symptom was abdominal pain (100%). These results are comparable with other studies.[13,14,15]

Thirteen maternal deaths resulted from ectopic pregnancy in U.K during the period of 1997-99[11]. In this study there was no mortality but one had serious morbidity requiring ICU care, which is comparable with a local study. It is may be because of the fact that in our country many maternal mortalities go unnoticed because of illiteracy or lack of medical facilities.

Historically, the treatment of ectopic pregnancy was emergency laparotomy and salpingectomy. Nowadays laparoscopic treatment is being considered the gold standard in hemodynamically stable patients particularly where expertise is available. To minimize the morbidity, mortality and financial burden created by this rapidly growing health problem, non surgical alternatives are increasingly being investigated[12,16].

In this study seven (14%) patients were treated conservatively, 15 (28%) with medical treatment, 30 (58%) by laparotomy while none of them had laparoscopy as primary treatment as none of the patients fulfilled its inclusion criteria.

Five observational studies have shown that 44-69% of pregnancies of unknown location resolve spontaneously with conservative management[6,11], which is comparable with this study (71%). Conservative management is an option for clinically stable, asymptomatic women with an ultrasound diagnosis of ectopic pregnancy and decreasing serum ß-hCG, initially < 1000-2000mIU/ml[11]. Another seven observational studies were reviewed and a total of 478 women were treated conservatively. Conservative management was successful in 318 (67%) women. Intervention has been shown to be required in 23-29% of cases[11] which is comparable with this study i.e. 29%.

Conservative management was found to be more successful (88%) when initial ß-hCG level was <1000 mIU/ml[11,16] while in this study it was found to be 75%. This study is also comparable with another study published in 1992, where success rate of conservative management was found to be 69% but in that study the inclusion criteria were mass size <4 cm & falling ß-hCG levels [17].

Tanaka et al first described the successful resolution of ectopic pregnancy with systemic methotrexate in 1982[12,18]. Forty-five percent of all ectopic pregnancies can be managed with methotrexate and it effectively treats ectopic pregnancy in 82-90% of selected cases.[18,19,20,21] In a review by Slaughter and Grimes of 17 studies including 400 patients, the overall success rate was 90%. Approximately 5% patients required surgery for failed treatment[6] as compared to 15 % in another study[21]. The success rate of methotrexate in this study is comparable with other series (80% vs. 77 - 90%). A second injection of methotrexate was required in 5 (33.3%) patients in this study. In a large series of 120 patients treated with single intramuscular dose of methotrexate, Stovall and Ling needed to use a second dose in only 3.3% of cases, however in some series as many as 15-25% of patients required more than one dose[20,21]. Patients with lower serum ß-hCG concentrations before treatment with methotrexate were significantly more likely to require only a single dose compared with those with higher levels (specially >3000-4000 mIU/ml)[20,21,22,23].

It is important to counsel the patients for prolonged follow up, need for 2nd injection or laparotomy and distinct likelihood of increased pelvic pain[22]. In most series more than half of all patients experienced increase in pelvic pain after methotrexate administration. This was not associated with increased risk of rupture but increased the risk of unnecessary

intervention[6,22]. The result of this study is quite different where only one (2%)patient complained of it.

Laparoscopic surgery has been compared with open surgery in 228 women in 3 randomized controlled trials. Laparoscopic procedures were associated with shorter operation time, less intraoperative blood loss, shorter hospital stay and lesser analgesic requirement[11]. However, this is the preferred mode of treatment when expertise is available and patients fulfill the inclusion criteria for laparoscopy.

Rate of persistent ectopic pregnancy after laparotomy with tube- conserving surgery is 3-5% while after laparoscopy it is 3-20%[11,15]. The results depend on the selection of patients for different treatment modalities. In this study, no patient had persistent ectopic pregnancy.

Only one case of recurrence was noted in this study comparable with another study conducted in France (one out of 77 cases) [15].

CONCLUSION

In the institutional setting ectopic pregnancy accounted for 1% of total deliveries. More than half of all women with ectopic pregnancy presented with acute abdomen and required emergency laparotomy. About 40% women could be managed with non-surgical modalities with 80% success for methotrexate and 71% for conservative treatment.

REFERENCES

1. Hankins GD, Clark SL, Cunningham FG, Gilstrap LC. Ectopic pregnancy. In: Dilmond E; Gilstrap. Operative obstetrics. New York: Appleton & Lange; 1995:437-56.
2. Lehner R, Kucera E, Jirecek S, Egarter C, Husslein P. Ectopic pregnancy. Arch Gynecol Obstet 2000; 263: 87-92.
3. Hill GA, Herbert CM. Ectopic pregnancy. In: Herbert CM, Textbook of gynaecology. Philadelphia: WB Saunders 1993; 242-60.
4. Mazhar SB, Mahmood G, Parveen F. Systemic methotrexate for the treatment of ectopic pregnancy larger than 3.5 cms. The XVIth Asian and Oceanic Congress of Obstetrics and Gynaecology. June 14-19th, Kuala Lumpur, Malaysia 1998; 17-20.
5. Khawaja NP, Rehman R, Durrani Z. Ectopic pregnancy at gynaecology unit II Sir Ganga Ram Hospital, Lahore; study of fifty cases. Pak J Obstet Gynecol 1998; 11: 61-5.
6. Symonds I M. Modern management in ectopic pregnancy, Current obstetricians & gynecology 1998; 8:27-31.
7. Akbar N, Shami N, Anwar S, Asif S. Evaluation of predisposing factors of tubal pregnancy in multigravidas versus primigravidas. J Surg PIMS 2002; 25: 20-3.
8. Braun RD. Surgical management of ectopic pregnancy. Online 2005. e medicine. [cited 2005 Oct 27].Available from: URL:http://www.emedicine.com/med/topic 3316.htm-94k.
9. Sowter MC, Farquhar CM, Petrie KJ, Gudex G. A randomized trial of comparing single dose systemic methotrexate and laparoscopic surgery for the treatment of unruptured tubal pregnancy. Br J Obstet Gynecol 2001; 108:192-203.
10. Grudzinskas JG. Miscarriage, ectopic pregnancy and trophoblastic disease. In: Edmonds DK. Dewhurst's textbook of obstetrics and gynaecology for postgraduates. 6th ed. Oxford: Blackwell Science 1999; .61-75.
11. The management of tubal pregnancy. Royal college of obstetricians and gynecologists guidelines 2004;21:1-10.
12. Lozean AM, Potter B. Diagnosis and management of ectopic pregnancy. Am Fam Physician 2005; 72:1707-14.
13. Bangash N, Ahmed H. A study of 65 cases of ectopic pregnancy during one year period in military hospital. Pak Armed Forces Med J 2004; 54:205-8.
14. Wasim T. Proportionate morbidity and risk factors of ectopic pregnancy. Ann King Edward Med Coll 2004;10:298-300.
15. Ben Hmid R, Mahjoub S, Mourali M, El Houssaini S, Zeqhal D, Zouari F, et al. Management of ectopic pregnancy. Tunis Med 2006; 84:238-41.
16. Korhoren J, Stenman UH, Ylostalo P. Methotrexate with expectant management of ectopic pregnancy. Obstet Gynecol 1996; 88:775-8.
17. Ylostal P, Cacciatore B, Sjoberg J. Expactant management of ectopic pregnancy. Obstet Gynecol 1992; 80:345-8.
18. Mazhar SB, Mahmud G, Rarveen F. Systemic methotrexate for the treatment of ectopic pregnancies. J Obstet Gynaecol Res 1999; 80:44-5.
19. Barnhart KT, Gosman G, Ashby R, Sammel M. The medical management of ectopic pregnancy; a meta-analysis comparing single dose and multidose regimens. Obstet Gynecol 2003; 101:778-84.
20. Soliman KB, Saleh NM, Omran AA. Safety and efficacy of systemic methotrexate in the treatment of unruptured tubal pregnancy. Saudi Med J 2006; 27:1005-10.
21. Dilbaz S, Caliskan E, Dilbaz B, Deqirmenci O, Haberal A. Predictors of methotrexate treatment failure in ectopic pregnancy. J Reprod Med 2006; 51:87-93.
22. OlofssonI J, Sundtrom I, Ottander U, Kjellberj L, Damber MG, Clinical and pregnancy outcome following pregnancy; a prospective study comparing expectancy, surgery and systemic methotrexate treatment. Aeta Obstet Gynecol Scanol 2001; 80:744-9.
23. Stovall TG, Ling FW. Single dose methotrexate;an expanded clinical trial. Am J Obstet Gynecol 1993; 168:1759-63.

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