

An evaluation of management modalities and outcomes of ectopic pregnancy

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ABSTRACT

Objectives: To describe the role of early diagnosis, outcomes of medical and surgical management of ectopic pregnancy. **Methods:** A prospective observational study was conducted for one and half years, on women with an ectopic pregnancy. Demographic, medical, gynecological and obstetric details were noted. Standard criteria were followed for conservative management and the others underwent surgery. Outcomes studied included status of rupture of the tube, presence or absence of shock, need for blood transfusion, operative procedure performed, post-operative morbidity, time for resolution of beta-hCG and success of medical management. Appropriate statistical analysis was performed using percentages and chi-square tests. **Results:** 40 patients were studied in the time period with an average of 27.6 years. There were more multigravidae (78%) in the study, and majority of the patients (80%) had at least one risk factor. Larger proportion of patients presented with ruptured ectopic status (55%), and they belonged to a more advanced gestational age. Though medical management was offered in 40% of the patients initially, 15% required conversion to surgical management. **Conclusions:** Ectopic pregnancy continues to be a problem with significant morbidity. Multigravidae of younger presenting at a later gestational age appear to have a higher magnitude of the problem.

Keywords: Ectopic pregnancy, beta-hCG, conservative management, methotrexate, first trimester.

Ectopic pregnancy is defined as “Implantation of a fertilized ovum or blastocyst in a location other than in the endometrial lining of the uterine cavity”. The abnormal implantation grows and draws its blood supply from the abnormal implantation site. Enlargement of the gestational sac predisposes it for organ rupture. Ectopic pregnancy can lead to massive haemorrhage, leading to morbidity and mortality in first trimester, which can be prevented by early diagnosis and managed by either medical or surgical intervention. Ectopic pregnancy has most features of being a

life-threatening condition, and patients typically present in the emergency department.¹ The first recorded case of ectopic pregnancy is believed to have been first described by Albus in way back in 963 AD. The incidence of ectopic pregnancy is on the raising trend. The incidence of ectopic pregnancy was 28.1/1000 deliveries in one study in India.² Park et al reported a rate of 34 per 1000 deliveries in South Korea.³ In a 12-year study period in Ireland, Campillo et al noticed a rise from 12.8/1,000 deliveries (2005) to 17.7/1,000 deliveries (2016).⁴

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This can be attributed to the increase in number of infertility patients undergoing Assisted Reproductive Technology (ART), an elevation in the number of sterilization procedures and tubal recanalization also. Those undergoing ART are at a definite high risk of ectopic pregnancy.⁵ While tubal ectopic pregnancy forms the most common site, rarely even abdominal locations have been described.⁶ Early diagnosis of ectopic pregnancy is now possible due to availability of accurate beta hCG value and performance of transvaginal ultrasound (TVS). It is now becoming established that early diagnosis of the condition is important for both maternal survival and conservation of reproductive capacity.⁷

There are constant improvements in the recommendations and criteria regarding ultrasonographic evaluation of ectopic pregnancy, and this can help in earlier identification of the same.⁸ In this context, it is important to understand the real-world experiences with the life-threatening condition of ectopic pregnancy. With this in mind, this study was conducted with following objectives -

- To describe the role of early diagnosis of ectopic pregnancy with management and outcomes
- To describe the outcome of medical management of ectopic pregnancy.
- To describe the outcome of surgical management ectopic pregnancy

Methodology

This was a prospective observational study conducted in the department of Obstetrics and Gynaecology of a tertiary care hospital in urban India, with institutional ethics committee clearance. Women fulfilling the inclusion and exclusion criteria were recruited for the study for a duration of one and half years (January 2017 to June 2018). Their consent for participation in the study was obtained.

All women diagnosed with ectopic pregnancy by TVS and serum beta hCG were included in the study. Those with pregnancy of unknown location and heterotopic pregnancy, those with malignancies with potential for beta-hCG secretion potential and those who expressed refusal to consent for participation in study were excluded from the study. A detailed gynecological history, menstrual history and obstetric history was obtained. Previous history of ectopic pregnancy, tubectomy, tubal recanalization or previous pelvic or abdominal surgeries were elicited and noted. A general physical examination was performed and details regarding features of shock, pallor, presence of shock, restlessness, cold and clammy extremities were noted. Pulse

rate, respiratory rate, blood pressure and temperature were recorded. Abdominal examination was done to note guarding, rigidity and tenderness. Examination was done to look for presence of mass, signs of free fluid in peritoneal cavity and other contributory findings. Vaginal examination was done to look for tenderness on movement of the cervix, size of the uterus, mobility and consistency, presence of mass in any of the fornices.

Blood grouping, Rh typing, haemoglobin with complete blood count, urine pregnancy test, bleeding time and clotting time, transvaginal ultrasonography, beta hCG, liver function tests and renal function tests were obtained. Patient's management was individualized based on the well established (below mentioned) criteria.

Criteria for Medical Management

- Hemodynamically stable, without active bleeding.
- Sac size of less than 4 cms without cardiac activity
- Beta hCG < 3000IU/l
- No clinical signs of hemoperitoneum.

Patients fitting into the above mentioned criteria were managed conservatively- either with expected management or medical management. In expectant management, no intervention was performed. In Medical management, injection methotrexate was given. Patients who failed medical management (failure in reduction of beta hCG levels by 15% after injection methotrexate doses) or hemodynamic instability were treated surgically.

Patients who did not fit into the criteria of medical management, hemodynamically unstable, presence of distension and guarding of abdomen, intraperitoneal haemorrhage, rupture of an ectopic mass, high Beta hCG levels or had contraindication for medical treatment were managed surgically. All the surgical procedures were performed under general anaesthesia. The procedure done, site of ectopic pregnancy, hemoperitoneum, requirement of blood transfusion were noted. Postoperative status of the patient including development of fever, abdominal pain, distension of the abdomen and presence or absence of wound sepsis, need for ICU was noted. Patients were discharged with an advice to come for follow up after a week.

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square test or Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance

to identify the mean difference between two quantitative variables. Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram. P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Results

In this study, 40 patients who were diagnosed and treated of ectopic pregnancy were studied during a study period of one and half year from January 2017 to June 2018 at VIMS &RC, Bangalore.

Table 1: Age distribution

| Age group | Number (%) |
|-----------|------------|
| 20-25yrs | 14 (35%) |
| 26-30yrs | 20 (50%) |
| 31-35yrs | 6 (15%) |
| Total | 40 |

As shown in the table no 1, maximum patients belonged to the age group 26 to 30 years. The youngest age was 20 years and oldest was 35, with average age of 27.6 years. Out of 40 patients with ectopic pregnancy 31 patients were multigravida's (78%) and 9 patients were primigravida (22%). The composite distribution of parity with age distribution is presented in figure no 1. As can be seen older primigravidae and younger multigravidae were more common than the other groups. Majority of the ectopic gestations were seen on the right side (57.5%) than on the left side (42.5%).

Table 2: Detailed distribution of risk factors

| Single Risk Factors 23(57%) | Two risk factors 7(23%) |
|--------------------------------|----------------------------|
| Tubectomy | D&C + Appendicectomy 2(5%) |
| Dilatation and curettage (D&C) | D&C + IUCD 1(2.5%) |
| IUCD | D&C + PID 2(5%) |
| PID | Tubectomy +TB 2(5%) |
| Previous ectopic | Appendectomy + |
| TB | Ovarian cystectomy 2(5%) |

D&C – Dilatation & curettage, IUCD – Intrauterine contraceptive device, PID – Pelvic inflammatory disease, TB – Tuberculosis.

Among all the risk factors considered, tubectomy was identified as the common risk factor. 6 out of 40 patients had tubectomy (15%) and 2 patients had tubectomy with TB (5%). 2 patients had PID and were treated previously for the same. 2 patients had previous history of ectopic pregnancy

Table 3: Physical examination findings with respect to condition of the tube

| Category | Ruptured | Unruptured | P value |
|----------|------------|------------|---------|
| Pallor | 18 (81.8%) | 4 (18.2%) | <0.001 |
| Shock | 3 (100.0%) | 0 | 0.098 |
| None | 1 (5.6%) | 17(94.4%) | <0.001 |

and were operated. 20% patients had no risk factors. Dilatation & curettage was identified as single factor in 10% of the cases. Surgical procedures like appendicectomy

associated with D&C is seen in 2 patients. Other details are presented in table number 2.

Table 4: Comparison of Hb and baseline beta HCG in ruptured and unruptured

| Parameters | Hb(g/dl) | Baseline Beta HCG |
|-------------|----------------|--------------------|
| Ruptured | 7.6053 ± 1.85 | 69581.74 ± 3757.21 |
| Un ruptured | 10.3905 ± 1.46 | 18740.67 ± 3571.2 |
| Composite | 9.0675 ± 2.16 | 42890.18 ± 4434.79 |
| P value | <0.001 | <0.001 |

Presence of pallor was significantly associated with the nature of tube having ruptured status (table 3). As seen in table 4, there was a significant correlation between beta HCG, hemoglobin and status of rupture. It is inferred that lower hemoglobin and higher baseline beta HCG are essential components of a ruptured ectopic state.

Unruptured ectopic pregnancy was likely to be noted at 4-5 weeks, and with advancing gestational age, the likelihood of being ruptured increased; and this difference was statistically significant, as shown in table number 5. Though in both ruptured and unruptured groups,

Table 5: Distribution of subject according to gestational age and condition of the fallopian tube

| Gestational age | Ruptured | Unruptured | Total | P value <0.001 |
|-----------------|-----------|------------|-----------|------------------|
| 4-5weeks | 1 (5.3%) | 15(71.4%) | 16(40%) | Unpaired t-test, |
| 6-7weeks | 11(57.9%) | 4(19%) | 15(37.5%) | Statistically |
| 8-9weeks | 7(36.8%) | 2(9.5%) | 9(22.5%) | significant |
| Total | 19 | 21 | 40 | difference |

multigravidae were more common, there was no statistically significant difference (p value 0.457, table 6). It is inferred that there is no influence of parity on resultant rupture status of the tube. 43.75% patients had received one dose of MTX and 56 % (9) of patients had received 2 doses of MTX. Out 40 patients, 16 patients had medical management. 62.5% (10) of patients had successful management whereas 37.5% (6) patients needed laparotomy. There was no statistically significant time taken for beta hCG to normalise and Outcome of medical management (p value=0.392, table number 7). In 40% of the patients who had successful medical management beta hCG decreased in 2-3 weeks and 20 % patients it decreased in 4 weeks. It is inferred that in the appropriate candidate, medical management is not inferior to surgical management with respect to reduction in beta-HCG.

In most of the cases (18), unilateral salpingectomy was done. whereas salphingo-oophorectomy was done in 7 cases and salpingostomy was done in 5 cases. 4 out of 30 patients underwent laparoscopic procedure, of which two were partial salpingectomy. Ampullary was the most common. There was no significant difference (p-value= 0.569) between the

location and the occurrence of rupture. There were 3 cases of extra-tubal ectopic gestation (ovarian).

Table 6: Distribution of subject according to parity and condition of the fallopian tube

| Gravida status | Ruptured | Unruptured | Total |
|----------------|------------|------------|------------|
| Primigravida | 3 (15.8%) | 6 (28.6%) | 9 (22.5%) |
| Multigravida | 16 (84.2%) | 15 (71.2%) | 31 (77.5%) |
| Total | 19 | 21 | 40 |

Table 7: Time taken for beta hCG to normalise and outcome of medical management

| Time taken for beta-hCG normalization | Laparotomy needed | | Total |
|---------------------------------------|-------------------|-----------|-----------|
| | No | Yes | |
| 2weeks | 4 (40%) | 2 (33.3%) | 6 (37.5%) |
| 3weeks | 4(40%) | 3 (50%) | 7(43.8%) |
| 4weeks | 2(20%) | 0 | 2 (12.5%) |
| 5weeks | 0 | 1(16.67%) | 1(6.3%) |
| Total | 10 | 6 | 16 |

Table 8: Distribution of subject in surgical management according to site and condition of fallopian tube

| Location | Ruptured | Unruptured | Total |
|---------------------|-------------|-------------|-------------|
| Ampullary | 13 (68.4%) | 8 (72.7%) | 21 (70.0%) |
| Fimbrial | 2 (10.5%) | 0 | 2 (6.7%) |
| Isthmal | 2 (10.5%) | 1 (9.1%) | 3 (10.0%) |
| Isthmal + Ampullary | 1 (5.3%) | 0 | 1 (3.3%) |
| Ovary | 1 (5.3%) | 2 (18.2%) | 3 (10.0%) |
| Total | 19 (100.0%) | 11 (100.0%) | 30 (100.0%) |

The presence of haemoperitoneum and the number of cases received blood transfusion was found to be the same that is 73.3%. There were no mortalities in this case series. There were only 3 cases of ICU admission, only for post-operative observation. The average duration of stay in the hospital was 6 days. There were no re-admissions. There was one wound gape, which required re-suturing.

Discussion

In this study, 40 patients who were diagnosed and treated of ectopic pregnancy were studied during a study period of one and half year. In our study, the most common age group was in the 26-30 years group, which formed almost half. The corresponding number in the same group, in the study by Kharat et al⁹ was 65%. In the study by Murugesan et al,¹⁰ the age group of 21-30 years formed 78% of the study subject. In ours, it constitutes 85%. Whereas in the study by Zuber et al,¹¹ it was 65% and in a study by Nethra et al,¹² it was 63%. In our study, multigravidae constituted 78%. This is almost identical to the study by Nethra et al and issimilar to the study by Kharat et al, who reported 82.5% multigravidae. Whereas in the study by Hanji et al, there was a very high 95% multigravidae. In our study, we specifically noted that younger multigravidae were particularly affected. However, this distribution has not been compared in other similar studies.

We found tubectomy as a prominent risk factor (15%). This is similar to the study by Nethra et al (14%). However, Kharat et al found it only 1.5% of the pregnancies, while Zuber et al found it in 7.1%. Quite contrastingly, Murugesan et al found tubectomy as a risk factor in 28%. Previous ectopic was seen in 5% of our cases. This is similar to the study by Hanji et al,¹³ who also noticed it in 5.3%, Zuber et al (4.6%) and Murugesan et al (5.48%). This is different from the findings of Kharat et al, who found it in a much lesser 2.6%. We found IUCD as a risk factor in 12.5%, while Zuber et al found it in 9.4%. The occurrence was much lesser in the study by Kharat (3.6%) and in the study by Murugesan et al (1.36%). Tuberculosis was seen as a risk factor in 7.5% in our study, whereas none of the other studies had specified tuberculosis to be a risk factor. Most other studies have identified PID to be a risk factor in a few cases, Zuber (14%), Murugesan (10%), Kharat (14%). It is not clear whether tuberculosis formed a subset of PID in these study groups. Dilatation and curettage was identified as risk factor in 10% of the cases, which was similar to the findings of Kharat et al (8.6%). Hanji et al and Murugesan et al reported a previous abortion as a risk factor, seen in 15.8% and 19.17% respectively. In these, it was not specified if a surgical method of evacuation was performed. No risk factor was found in 12.5% of the patients. While Hanji et al (26%) and Murugesan et al (28%) reported a higher rate of “no risk factor found”, in the study by Kharat et al, it was much higher, at 52.6%.

Ruptured ectopic gestation was seen in 55% of our cases, which is slightly more than that of the findings in the study by Zuber et al (45%). However, Kharat et al (68.5%) and Murugesan et al (65%) found a much higher proportion of ruptured ectopic gestation.

Presence of pallor was a consistent finding with ruptured ectopic, which is a consistent finding across most studies. While only 3 out of 40 patients were brought in a state of shock, the reported rate in prior studies is much higher. Rashmi et al had reported that almost 40% of the patients had been brought in a state of shock. This could be explained by the improvement in facilities such as transport, and an overall improvement in awareness. However, a little more than 50% of the patients directly required surgical management, suggesting that there continues to be a delay in the time of presentation of the patient.

In the study by Murugesan et al, maximum patients were seen in the 6th to 8th week of gestation (65%). Our study notes that as the gestational age increases, the possibility of it

being a ruptured ectopic gestation, increases. While maximum number of cases occur after the 6th week, it is suggested that an earlier identification of an ectopic gestation can result in the possibility of a medical management rather than a surgical management. A detailed analysis of the incidence of rupture with increasing gestational has not been done by other similar studies.

Though in both ruptured and unruptured groups, multigravidae were more common, it is noted that the while taking both age and parity into account, the younger multigravidae have the highest risk for ruptured ectopic gestation. It is inferred that those multigravidae who are young should be more vigilantly advised to undergo an early scan for identification of an abnormally located gestational sac. For unknown reasons, there is a slightly more common occurrence of ectopic gestations on the right side, rather than the left. Findings of our study (57%) was similar to that of most other similar studies- pusuloor et al (53%), Kharat et al (53%) and Murugesan et al (58%). The required of blood transfusion in our study was 73.3%, which was similar to the findings of the study by Pulusoori et al (68%).¹⁴ In the studies by Hanji et al (42%), Murugesan et al (48%) it was much lesser, whereas in the study by Kharat et al, it was much higher (87%).

The successful outcome of a medical management depends on the gestational age at which the patient presents and the beta-hCG value at the time of presentation. In our study, out 40 patients, 16 patients had medical management initially. 62.5% (10) of patients had successful management. The remaining 6 (37.5%) needed laparotomy. In the other similar studies reported, the preference for medical management has remained very poor. For example, in the study by Murugesan et al (2 patients out of 82 patients), Zuber et al (2 out of 42 patients), Kharat et al (0 out of 194 patients), Hanji et al (0 out of 19 patients) and Gaddagi et al (0 out of 37 patients). Compared to these studies, the success rate of medical management in our study appears much better. 4 out of 30 patients underwent laparoscopic procedure, of which two were partial salpingectomy. In the study by Murugesan et al, 20% of the patients underwent laparoscopy. In the study by Zuber et al and Pusuloori et al, only one patient each had undergone laparoscopy. All the other similar studies reported have also reported use of laparotomy as the route for the procedure. In many institutions, like ours, laparoscopy is available only during the routine working hours, and not during emergency hours.

This may be a reason for the reduced number of laparoscopy compared to laparotomies.

In our study, ampullary was the most common (70%). This was similar to the finding by Murugesan et al (67%). Though in their respective studies, the proportion of ampullary ectopic was highest, the actual proportion was lesser than in our study, Zuber et al (45%), Kharat et al (44%), Pulusoori et al (42%) and Hanji et al (31%). Ovarian ectopic gestations are quite rare, with a one in 1000 occurrence. However, we had 3 cases in this study, which was more than expected. In most of the cases (18), unilateral salpingectomy was done. whereas salphingo-oophorectomy was done in 7 cases (17.5%) and salphingostomy was done in 5 cases (12.5%). Salpingectomy is the most preferred procedure in most of the other studies also- Hanji et al (68%), Pulusoori et al (86%), Kharat et al (91%), and Murugesan et al (96%). In the study by Zuber et al, the proportion was lesser (40%), with a preference for conservative procedures.

Conclusion

The outcomes of ectopic pregnancy in this population has been presented. Younger multigravidae appear to have higher occurrence of ectopic pregnancy. Tubectomy, IUCD insertion and past history of tuberculosis are consistent risk factors for ectopic pregnancy. Earlier identification of the ectopic pregnancy favours medical conservative management. Though there may be requirement for conversion to surgical method, there is scope for a higher utilization of medical management. Salpingectomy remains the most preferred technique for surgical management of ectopic pregnancy. Overall morbidity can be improved by earlier identification using transvaginal ultrasound and beta-hCG.

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