RISK FACTOR EPIDEMIOLOGY OF ECTOPIC PREGNANCY AND SUCCESS OF NONSURGICAL MANAGEMENT

Vijayan C.P[1], Sathi M.S[2], Jitha P.J[3]

[1]Additional Professor, Department of Obstetrics and Gynaecology, Government Medical College, Kottayam, Kerala.
[2]Associate Professor, Department of Obstetrics and Gynaecology, Government Medical College, Kottayam, Kerala.
[3]Resident, Department of Obstetrics and Gynaecology, Government Medical College, Kottayam, Kerala.

ABSTRACT

BACKGROUND

Ectopic pregnancies are increasing in number and proportions. Real increase and better detection methods are contributing for this rise. All the cases diagnosed now are not surgical emergencies. Medical management and expectant line of management are possible. Revised clinical guidelines are there for the selection of cases for nonsurgical management. Knowledge about the risk factors is good for prophylaxis and to have a high suspicion about ectopic pregnancy in high-risk individuals. Knowing the success rate is absolutely essential for counselling before starting the therapy.

Aim of the study-

1. To study the risk factor profile of ectopic pregnancies and to compare them with the old data of the study setting.
2. To follow up the cases receiving nonsurgical treatment and to assess the success rate.

MATERIALS AND METHODS

Study Setting- Department of Obstetrics and Gynaecology, Government Medical College, Kottayam. It is a tertiary care centre with 1500 beds and catering for the population of five districts of Kerala.

Study Design- Observational Study

Study Period- This study was completed by eighteen months from April 2014 to September 2015.

RESULTS

219 cases of ectopic pregnancies were diagnosed during the study period. The ratio of this number with the total number of deliveries during that period is 3.48% and this is three times higher than that of the ratio twenty years ago (1.23%). Risk factor profile is also showing changes over this period. 15.1% had medical treatment and 11% had expectant line of therapy. Success rates are 87.87% and 95.65%, respectively.

CONCLUSIONS

Incidence and detection of ectopic pregnancies are increasing and the risk factor profile is changing. In properly selected cases, the success of nonsurgical management is excellent.

KEYWORDS

Ectopic Pregnancy, Risk Factors, Medical Treatment, Methotrexate.

HOW TO CITE THIS ARTICLE: Vijayan CP, Sathi MS, Jitha PJ. Risk factor epidemiology of ectopic pregnancy and success of nonsurgical management. J. Evid. Based Med. Healthc. 2016; 3(83), 4486-4490. DOI: 10.18410/jebmh/2016/952

BACKGROUND

The word ectopic was derived from a Greek word - ektopos - which means out of place. Ectopic pregnancy can occur in a number of abnormal locations other than its normal natural location. It may result in morbidities and mortalities and if untreated may contribute to six percentages of pregnancy-related mortalities.

Financial or Other, Competing Interest: None.
Submission 21-09-2016, Peer Review 28-09-2016,
Acceptance 06-10-2016, Published 15-10-2016.
Corresponding Author:
Dr. Vijayan C. P,
Narayaneeyam, Gandhinagar P.O,
Kottayam-686008, Kerala.
E-mail: vijaycpdr@gmail.com
DOI: 10.18410/jebmh/2016/952

Even though the incidence of ectopic pregnancy is increasing all over the world, the current diagnostic and therapeutic options have resulted in a reduction in the case fatality rate and in the morbidity rate. The various known risk factors are use of intrauterine contraceptive devices, tubal ligation and reconstructive surgeries, medical termination of pregnancies, reproductive tract infections in females and assisted reproductive techniques. It is interesting and useful to know whether there is any change in the pattern of the risk factor profile of ectopic pregnancy over the years. Diagnosis of ectopic pregnancy creates an emergency situation. The implanted ectopic embryo burrows actively into the deeper tissues and vessels and the prostaglandin release or bleeding may cause pain.

In case of severe intraperitoneal haemorrhage, the patient may be presented in shock and vaginal bleeding may or may not be there. Surgical treatment is the main type of management for ectopic pregnancies all over the world. In the present era due to the advancement in the diagnostic methods, lot of less serious types of ectopic pregnancies are diagnosed. Some of them maybe self-perishing and some maybe amenable for medical management. For ectopic pregnancies, surgical treatment offers success. In the case of the subjects managed by nonsurgical methods, some may require surgery later. They can be considered as failures of nonsurgical treatment. The selection of cases for nonsurgical treatment is based on strict criteria. Both the physician and the patient are eager to know the success rate in the nonsurgical treatment of ectopic pregnancy. This knowledge is needed for a proper counselling.

As with any disease process, the aim of the medical profession in relation with ectopic pregnancy is primary prevention, early diagnosis and treatment, disability limitation and rehabilitation. Knowledge of the risk factor profile is good for adopting preventive strategies and to develop high index of suspicion for early diagnosis. The avoidance of surgical treatment will reduce the postoperative morbidities and disabilities arising out of the procedure.

OBJECTIVES

1. To assess the risk factor profile of the ectopic pregnancies and to compare it with that of published data and the previous records of the study setting.
2. To follow up the subjects with ectopic pregnancy receiving nonsurgical management and to evaluate the results.

Study Setting

Department of Obstetrics and Gynaecology, Government Medical College Hospital, Kottayam. This is a tertiary care centre and a teaching hospital with bed strength of 1500. It caters for a population of five revenue districts of Kerala namely, Kottayam, Idukki, Pathanamthitta, Ernakulam and Alappuzha.

Study Period

Eighteen months period from April 2014 to September 2015.

MATERIALS AND METHODS

All subjects with a diagnosis of ectopic pregnancy and admitted to the study setting were included in this series. Clinical methods, ultrasound examination (both abdominal and vaginal) and serum levels of beta subunit of human chorionic gonadotropin (beta hCG) were used for reaching the diagnosis. Information about risk factors was collected along with the case history. The treatment was planned based on the following guidelines.

Surgical Treatment

Once the rupture of the ectopic sac is diagnosed with haemoperitoneum, hypotension and anaemia, surgical treatment was offered. It is the line of treatment if the diameter of the gestational sac is more than 4 cms measured by ultrasonography.

Persisting pain, raising levels of beta hCG, increase in pallor were also indications of surgical treatment. In patients who completed the family and who desired for permanent sterilisation had salpingectomy. If the tube was unruptured and preservation of fertility was needed, salpingostomy was attempted. Salpingectomy was done when the tube was ruptured irrespective of the family status.

Medical Management

Methotrexate was the drug used for the medical management. It is acting because of its antifolate effect and was administered as deep intramuscular injection at the dose of 1 mg per kilogram body weight in a single dose. Before administering methotrexate, complete blood count, liver function tests, serum creatinine, blood group and Rh typing and x-ray chest PA view were done. Intrauterine pregnancy, immunodeficiency, moderate-to-severe anaemia, leucopenia, thrombocytopenia, sensitivity to methotrexate, renal and hepatic dysfunctions and breast feeding were considered as contraindications for methotrexate therapy. The following were the clinical criteria adopted for this treatment.

a. Haemodynamically stable patient.
b. No intrauterine pregnancy on ultrasound examination.
c. Size of the ectopic sac less than 3.5 cms.
d. Absence of foetal cardiac flicker.
e. Serum beta-HCG less than 3000 mIU/mL.
f. No contraindication for the drug methotrexate.
g. Patient willing for regular followup.

Patients who received methotrexate were followed up for a period of four to six weeks. Failure of medical treatment was declared in case of any one of the following.

a. Appearance of adnexal foetal cardiac flickering.
b. Increase in the size and/or volume of gestational sac.
c. Increase in the serum level of beta-HCG.
d. Development of haemoperitoneum.

In all the failure cases, surgical treatment was resorted.

Expectant Line of Treatment

Observation and monitoring of the subject without any active treatment expecting that pregnancy is not growing and will resolve by its own. Criteria for adopting this modality of treatment were:

a. Stable patient.
b. Serum levels of beta-HCG below 1000 mIU/mL.
c. Falling levels of beta-HCG.
d. Adnexal mass less than 3.5 cms.

The points taken as failure of treatment were same as that in case of medical management. Whenever, there was failure in treatment, surgical treatment was resorted. In any

line of treatment, the success of treatment was defined as follows.

a. Asymptomatic patient.
b. Haemodynamically stable.
c. Serum beta-HCG levels below 10 mIU/mL.

RESULTS

Two hundred and nineteen (219) cases of ectopic pregnancies were diagnosed at the study setting during the study period. The total number of deliveries during the same period at the setting was 6290 - making a proportion of 3.48%. Two decades ago this proportion in the same setting was 1.23%.

Mode of Presentation	Number	Percentage
Abdominal pain	158	72.1
Bleeding per vaginum	139	63.5
Giddiness	40	18.3
Shoulder pain	19	8.7
Shock	9	4.1
Accidental detection	52	23.7
Amenorrhoea	157	72

Table 1. Mode of Presentation of Ectopic Pregnancies

[One patient may present with more than one symptom and because of this the number of presentation may not add to 219 and the percentage may not add to hundred].

The risk factors collected from the subjects are listed below in Table 2. It is worth mentioning that nearly half of the subjects were not having any risk factors at the time of presentation. This is a challenge for the primary prevention of ectopic pregnancies.

Risk Factor	Number	Percentage
Previous abortion	71	32.4
Previous LSCS	70	32
Intrauterine contraceptive devise usage	10	4.56
History of tubectomy	36	16.44
Previous uterine surgeries	73	33.33
Previous ectopic pregnancies	26	11.5
Infertility treatment	44	20.1
Artificial reproductive techniques	14	6.4
Pelvic inflammatory disease	29	13.2
Drugs in the second half of pregnancy	9	4
Nulliparity	92	41.6
Peak age group (25-29)	81	36.98
No risk factor identified	109	49.77

Table 2. Risk Factor Profile

[One patient maybe having more than one risk factor and because of this, the total number may not add to 219 and the percentage may not add to hundred.]

One hundred and sixty three patients were treated surgically and the success was good in all of them. There was one who lost followup from this group. Thirty three patients of ectopic pregnancy received medical treatment and there were four failures in this group. Twenty three patients were followed up in the expectant line and there was one failure in that group.

Treatment Mode	Number Received	Number Succeeded	Percentage of Success
Surgical	163	162	99.38
Medical	33	29	87.87
Expectant	23	22	95.65
Total	**219**	**213**	**97.26**

Table 3. Success Rate of Treatment Modalities

DISCUSSION

Ectopic pregnancies are on the increase as demonstrated by the ratio of ectopic pregnancies to deliveries calculated during the corresponding period in the same institution. Over a period of two decades, this ratio went up from 1.23% to 3.48% in the study setting and this shift is demonstrated in other studies as well.[1,2] Modern diagnostic technologies are helping the physician to detect more and more ectopic pregnancies[3,4] and this factor increases the burden of cases with ectopic pregnancy over the caregiver. As far as the clinical presentation of ectopic pregnancy in emergency rooms, there is no difference over the years.[1,5,6] It is observed that 41.6% of patients presenting with ectopic pregnancy are nulliparous women and this shows a definite change in comparison with the previous records of the study setting, which says that it was 31.29% two decades ago. Pradhan et al is reporting that 49% of patients with ectopic pregnancy were nulliparous.[7] The peak age group was between 25 years and 29 years and the mean age was 29.52 and this factor is also comparable with other published studies[7,8] This finding maybe a reflection of the increase in the age at marriage.

A definite change was seen in the following risk factors- previous ectopic pregnancy, history of treatment for infertility, conception by artificial reproductive techniques, increase in the age at marriage and more nulliparous women developing ectopic pregnancy. The above risk factors are related to one another. More number of ectopic pregnancies are being detected by newer diagnostic techniques and this may further rise as an increasing high-risk factor. (Previous ectopic pregnancy increased from 3.4% to 11.5%, history of infertility treatment from 12.2% to 20.1% and ART conception from 4.08% to 6.4% in comparison with

institutional data over the last two decades). These observations are also noted in other published studies.[9,10]

No change was noted in the pattern of risk factors like previous abortions (32.4%), previous uterine surgeries (33.33%) or previous caesarean sections (32%). Even though caesarean section is an increasing risk factor for several other health problems in women, its influence on ectopic pregnancy is static.[11] 16.4% ectopic pregnancies were there following tubectomy and 4.56% were following intrauterine contraceptive device usage.

13.2% of patients gave a history of pelvic inflammatory disease. These risk factors are remaining more or less static over the last two decades. In some of the studies, an increase in the pelvic inflammatory disease is seen and in a report from the Republic of Korea, it is stated that ectopic pregnancy is more common among low socioeconomic group and reproductive tract infections are more common among them.[12] 3.14% patients reported more than one sexual partner and 4% reported drug usage in the second half of the cycle. It is not possible to comment on these risk factors as no previous records were available in respect of them. 49.77% of patients were not having any risk factors. This needs special mention as ectopic pregnancy can occur without any known risk factor.

In the era when all the ectopic pregnancies were diagnosed in the emergency room after rupture, surgical treatment was the only one mode of treatment. This continued for some more time when ectopic pregnancies in unruptured state were detected more frequently. Slowly, the pattern of treatment started changing.[13,14] Medical management using methotrexate[15] and expectant line of management came into existence. When lot of failures was faced, scientific world started thinking about the reasons for such failures.[16,17] These measures brought in strict guidelines for medical and expectant line of therapies. These guidelines were followed in selection of cases and adopting different modes of therapy. 74.4% patients underwent surgical treatment, 15.1% underwent medical treatment and 11% had expectant line of treatment. Success of treatment was defined as an asymptomatic and stable patient with beta-HCG level less than 10 mIU/mL. All cases in the surgical group had success except the one who was lost follow up. Success rate in the medical group was 87.87% and in the expectant group was 95.65%.

CONCLUSIONS

An increase in the proportion of ectopic pregnancies is noted in relation with the number of deliveries over a period of two decades in the study setting. More proportion of cases was detected in nulliparous women. Among the risk factors, an increase was noted in the infertility treatment, recurrence of ectopic pregnancy and assisted reproductive techniques. Previous abortions, uterine surgeries and previous caesarean sections are maintaining the status quo as risk factors. No change was noted in the mean age group of patients and in the presentations. Nearly, half of the patients were not having any risk factors.

Medically treated ectopic pregnancies increased from 4.08% to 15.1% over two decades. The proportion of surgically treated cases came down from 93.88% to 74.4%. Expectant line of treatment was unheard of in the setting two decades ago. 11% cases were managed in the expectant line in this series. All cases were selected using strict criteria and allotted to the respective groups. The success rates were 87.87% and 95.65% in the medical and expectant groups, respectively. These results are in parallel with published information.[18]

REFERENCES

1. Zaidi MT, Ansari MS, Kirmani F, et al. A histoarchitectural study of early human ectopic pregnancy. Biomedical Research 2012;23(1):51-54.
2. Bag TS, Saha DP, Dasgupta N, et al. Time trends in ectopic pregnancy over a decade - a retrospective hospital based study. J Indian Med Assoc 2011;109(10):727-729.
3. Cohen HL, Moore WH. History of emergency ultrasound. J Ultrasound Med 2004;23(4):451-458.
4. Gracia CR, Barnhart KT. Diagnosing ectopic pregnancy: decision analysis comparing six strategies. Obstet Gynaecol 2001;97(3):464-470.
5. Shaw JL, Dey SK, Critchley HO, et al. Current knowledge of the aetiology of human tubal ectopic pregnancy. Hum Reprod Update 2010;16(4)432-444.
6. Tay JI, Moore J, Walker JJ. Ectopic pregnancy. West J Med 2000;173(2):131-134.
7. Pradhan P, Thapamagar SB, Maskey S. A profile of ectopic pregnancy at Nepal medical college teaching hospital. Nepal Med Coll J 2006;8(4):238-242.
8. Gharoro EP, Igbafe AA. Ectopic pregnancy revisited in Benin City, Nigeria: analysis of 152 cases. Acta Obstet Gynaecol Scand 2002;81(12):1139-1143.
9. Pal A, Guptha KB, Sarin R. A study of ectopic pregnancy and high risk factors in Himachal Pradesh. J Indian Med Assoc 1996;94(5):172-173.
10. Lawani OL, Anozie OB, Ezeonu PO. Ectopic pregnancy: a life-threatening gynaecological emergency. Int J Womens Health 2013;5:515-521.
11. O'Neill SM, Khashan AS, Kenny LC, et al. Caesarean section and subsequent ectopic pregnancy: a systematic review and meta-analysis. BJOG 2013;120(6):671-680.
12. Yuk JS, Kim YJ, Hur JY, et al. Association between socioeconomic status and ectopic pregnancy rate in the Republic of Korea. Int J Gynaecol Obstet 2013;122(2):104-107.
13. Yao M, Tulandi T. Current status of surgical and nonsurgical management of ectopic pregnancy. Fertil Steril 1997;67(3):421-433.

14. Lewis-Bliehall C, Rogers RG, Kammerer-Doak DN, et al. Medical vs surgical treatment of ectopic pregnancy. The University of New Mexico's six year experience. J Reprod Med 2001;46(11):983-988.
15. Erdem M, Erdem A, Arslan M, et al. Single-dose methotrexate for the treatment of unruptured ectopic pregnancy. Arch Gynacol Obstet 2004:270(4):201-204.
16. Rabischong B, Tran X, Sleiman AA, et al. Predictive factors of failure in management of ectopic pregnancy with single-dose methotrexate: a general population-based analysis from the Auvergne register, France. Fertil Steril 2011;95(1):401-404.
17. Ustunyurt E, Duran M, Coskun E, et al. Role of initial and day four human chorionic gonadotropin levels in predicting the outcome of single-dose methotrexate treatment in women with tubal ectopic pregnancy. Arch Gynaecol Obstet 2013;288(5):1149-1152.
18. Samartha P, Jefrrey G, Roger L, et al. Medical treatment of ectopic pregnancy: a committee opinion. Fertil Steril 2013;100(3):638-644.