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ABSTRACT

Introduction: Ectopic pregnancy is the commonest gynecological emergencies. If not treated timely, it places major morbidity upon future fertility and family. Ectopic pregnancy presents a major health problem for women of childbearing age. The increased incidence of ectopic pregnancy has been partially attributed to improved ability in making an earlier diagnosis. Anything that hampers the migration of the embryo to the endometrial cavity could predispose women to ectopic gestation. The most logical explanation for the increasing frequency of EPs is previous pelvic infection; however, most patients presenting with an EP have no identifiable risk factor.

Objective: To determine the frequency of fertility outcome (intrauterine pregnancy and extrauterine pregnancy) in patients having history of ectopic pregnancy.

Materials and Methods: A total of 92 patients having history of ectopic pregnancy were included in the study in a consecutive manner and assessed for fertility outcome in terms of extrauterine or intrauterine pregnancy. The study utilized descriptive cross sectional study design. The study settings was department of gynecology, Lady Reading Hospital, Peshawar. The study duration was from 1st January 2019 to 31st December 2020.

Results: The mean age of the sample was 30.3 $\pm$ 6.1 years. The mean parity of the sample was 2.1 $\pm$ 1.5, mean BMI was 26.4 $\pm$ 3.5kg/m^2 and mean gestational age at presentation was 6.7 $\pm$ 2.1 weeks. With regards to fertility outcome, 39.1% women had extrauterine pregnancy and 60.9% had intrauterine pregnancy. Extrauterine pregnancy though less than intrauterine is still a significant problem in the study's population with previous history of ectopic pregnancy.

Recommendation: The study recommend more research projects particularly interventional studies for proper management of ectopic pregnancy and reduce the burden of extrauterine pregnancies so that even with history of ectopic pregnancy, term delivery can be assured.

Keywords: Ectopic pregnancy amenorrhea, extrauterine pregnancy, intrauterine pregnancy, fertility outcome, parity

INTRODUCTION

Ectopic pregnancy (EP) is the most common gynecological emergencies. If not treated timely, it places major morbidity upon future fertility and family.[1] pregnancy in which fertilized egg grows outside uterus usually in one of the fallopian tubes. Ectopic pregnancy presents a major health problem for women of childbearing age.[2,3] The increased incidence of ectopic pregnancy has been partially attributed to improved ability in making an earlier diagnosis. [4] In the 1980s and 1990s, medical therapy for ectopic pregnancy was implemented; it has now replaced surgical therapy in many cases. [4] In a study, the IUP rate was 40.3%, which is lower than the results of other studies.[6] Multiple factors contribute to the relative risk of EP in women with infertility. Anything that hampers the migration of the embryo to the endometrial cavity could predispose women to ectopic gestation. The most logical explanation for the increasing frequency of EPs is previous pelvic infection; however, most patients presenting with an EP have no identifiable risk factor.[7] During recent decades, the diagnosis and efficacy of treatment of EP has progressed significantly.[8] In modern obstetrics, ectopic pregnancy (EP) is a life- and fertility-threatening condition, and it remains one of the leading causes of maternal morbidity and mortality.[9] The findings reveal that the following factors were associated with increased risk of EP, including: Maternal age, spouse's cigarette smoking, gravidity, prior spontaneous abortions, history of EP, tubal blockage, use of intrauterine device (IUD), tubal damage, first pregnancy interval and history of infertility.[10] In another study, 849 EPs were surgically managed (758 primary EPs and 91 recurrent EPs). Recurrent EPs were significantly older than primary EPs (32.2 ± 5.08 vs. 30.5 ± 5.83 years, $p < 0.05$). They presented at a significantly earlier gestation (5.99 ± 1.08 vs. 6.52 ± 1.81 weeks, $p < 0.05$) and with a significantly lower primary βHCG (3176 ± 7350 vs. 6243 ± 12,282, $p < 0.05$). Recurrent EPs were significantly more likely to have a positive history of tubal or pelvic surgery (61.5 % vs. 3.5 %, $p < 0.05$ and 53.8 vs. 14 %, $p < 0.05$). At surgery, primary EPs had a significantly greater volume of hemoperitoneum (592 ± 850 vs. 249 ± 391 ml, $p < 0.05$), whereas recurrent EPs were significantly more likely to have contralateral pathology (31.1 vs. 9.8 %, $p < 0.05$).

Regression analysis showed that the parameters of age, gestational age at presentation, first βHCG level, positive history of previous tubal surgery and previous ectopic pregnancy differ in women at risk of a recurrent EP when compared to women not at risk of a recurrent ectopic (AUC, 0.844).[11] In one another study, three hundred and twenty-eight women treated between April 1994 and March 1997 who had not been using an IUCD at the time of the ectopic pregnancy and were trying to become pregnant. Interviews by telephone every 6 months for 2 years and once yearly thereafter. Cumulative pregnancy rate. Two hundred fifteen (65.5%) women became pregnant after a mean of 5 months. One hundred eighty-two (84.7%) pregnancies were intrauterine; 22 (10.2%) were recurrent ectopic pregnancies; and in 11 women (5.1%), it was too early to define implantation. The cumulative intrauterine pregnancy rate was 56% at 1 year and 67% at 2 years. After applying Cox regression, three factors associated with fertility seemed to decrease reproductive performance: age > 35 years, history of infertility, and anterior tubal damage. More than half of the women treated for ectopic pregnancy spontaneously conceived and had a normally progressive pregnancy at 1 year. Fertility depends more on established patient characteristics than characteristics of ectopic pregnancy itself or treatment thereof.[12]

The aim of this study was to determine the fertility outcomes in patient having history of ectopic pregnancy in our local population. This study will help in drafting recommendations for future

research which is warranted in this field. This study will help increase knowledge of local health researchers on reproductive health of these women in our local population of Khyber Pakhtunkhwa.

MATERIALS AND METHODS

The study utilized descriptive cross sectional study design. The study settings was department of gynecology, Lady Reading Hospital, Peshawar. The study duration was from 1st January 2019 to 31st December 2020. Total sample size was 92 keeping 40.3% proportion of IUP as fertility outcome in patients having history of EP level of confidence 95%, margin of error 10% and 5% level of significance calculated on WHO formula for sample determination. The sampling technique used was non probability consecutive sampling.

Sample selection

Inclusion criteria

Women with age between 20- 40 years. Women of any parity and gravidy/all primi gravida and multi gravida. Women with a history of EP confirmed on medical history / women with previous history of ectopic pregnancy.

Exclusion Criteria

Patients using any contraceptive method. Patients who have undergone salpingectomy or hysterectomy. Patients who had received medical treatment with methotrexate and patients receiving in vitro fertilization/ patients with past history of medical illness like tuberculosis.

Data collection procedure

After taking informed consent from the patient ensuring confidentiality and permission from hospital ethical committee and research committee of CPSP was included in the study. Data was collected from all women presented to department of gynecology in Lady Reading Hospital Peshawar in OPD/labor room with history of ectopic pregnancy confirmed by past obstetrical history. Complete gynecological examination, reproductive health, type of conception (e.g spontaneous contraception, ovulation induction) was recorded. Patients with extra-uterine pregnancy and IUPs was taken into account regardless of the outcome. All the above information including age, parity, gestational age, weight, height, BMI and fertility outcomes such as extra-uterine pregnancy (Ectopic Pregnancy) and Intrauterine Pregnancy was recorded on a pre-designed proforma attached to this synopsis.

DATA ANALYSIS

Data was entered and analyzed in SPSS Version 22.0. Mean and standard deviation was calculated for quantitative variables like age, height, weight, BMI, gestational age, parity and gravidy. Frequencies and percentages was calculated for fertility outcomes (ectopic pregnancy and intrauterine pregnancy). Fertility Outcomes such as extra-uterine pregnancy (ectopic pregnancy) and intrauterine pregnancy was stratified with age, height, gestational age, parity, gravidy, weight and BMI in order to see the effect modification. Post stratification chi square test was applied keeping P value $\leq$ 0.05 as significant. All the results was presented in the form of tables and graphs.

RESULTS

The study was conducted on 92 patients with ectopic pregnancy and assessed for fertility outcome. The mean age of the sample was 30.3 ± 6.1 years. The mean parity of the sample was 2.1 ± 1.5, mean BMI was 26.4 ± 3.5kg/m^2 and mean gestational age at presentation was 6.7 ± 2.1 weeks. Table 1 elaborates patients' demographic data regarding age, parity, gestational age and BMI. With regards to fertility outcome, 39.1% women had extrauterine pregnancy and 60.9% had intrauterine pregnancy as shown in table 1.

Table 1: Demographic characteristics and fertility outcome after Ectopic pregnancy (N=92)

Demographic characteristics		Frequency	Percentage (%)
AGE	20-30 years	50	54.3
	> 30-40 years	42	45.7
	Total	92	100.0
PARITY	Primiparous	21	22.8
	Multipara	71	77.2
BMI(kg/m^2)	20-25.5 BMI	49	53.3
	> 25.5-29.9 BMI	22	23.9
	> 29.9-32 BMI	21	22.8
GESTATIONAL AGE	4-7 weeks Gestational age	58	63.0
	> 7-10 weeks Gestational age	34	37.0
FERTILITY OUTCOME	Extrauterine pregnancy	36	39.1
	Intrauterine pregnancy	56	60.9

Table 2: Age wise stratification of fertility outcome

Age groups	Fertility outcome		P value
	Extrauterine pregnancy	Intrauterine pregnancy	
20-30 years	22 (44.0%)	28 (56.0%)	0.298
30-40 years	14 (33.3%)	28 (66.7%)	
Total	36 (39.1%)	56 (60.9%)	

Table 3: Parity wise stratification of fertility outcome

Parity	Fertility outcome		P value
	Extrauterine pregnancy	Intrauterine pregnancy	
Primiparous	4 (19.0%)	17 (81.0%)	0.032
Multipara	32 (45.1%)	39 (54.9%)	
Total	36 (39.1%)	56 (60.9%)	

Table 4: BMI wise stratification of fertility outcome

BMI(in kg/m^2)	Fertility outcome		P value
	Extrauterine pregnancy	Intrauterine pregnancy	
20-25.5	21 (42.9%)	28 (57.1%)	0.053
> 25.5-29.9	4 (18.2%)	18 (81.8%)	
> 29.9-32	11 (52.4%)	10 (47.6%)	
Total	36 (39.1%)	56 (60.9%)	

Table 5: Gestational age wise stratification of fertility outcome

Gestational age	Fertility outcome		P value
	Extrauterine pregnancy	Intrauterine pregnancy	
4-7 weeks	20 (34.5%)	38 (65.5%)	0.233
> 7-10 weeks	16 (47.1%)	18 (52.9%)	
Total	36 (39.1%)	56 (60.9%)	

DISCUSSION

The current incidence of ectopic pregnancy is difficult to estimate from available data because inpatient hospital treatment of ectopic pregnancy has decreased and multiple health care visits for a single ectopic pregnancy have increased. Furthermore, since the incidence is expressed as the number of ectopic pregnancies/1000 pregnancies, the denominator is difficult to determine accurately as early pregnancy failures that do not result in delivery or hospitalization, are often not counted. Ectopic pregnancy still accounts for 4% to 10% of pregnancy-related deaths and leads to a high incidence of ectopic site gestations in subsequent pregnancies 13. Precise physiological impact of advanced maternal age on ectopic pregnancy risk is unclear[14]. It is highly improbable that ectopic may be more common with advancing age due to an increase in chromosomal abnormalities in the trophoblastic tissue[15].

Age wise stratification has shown that a good fertility outcome of 66.7% is noticed inpatients in the age group of30 to 40 years whereas more chance of a repeat ectopic in age group of 20 to 30 years(44%) in different studies the risk of recurrence in those who have had a previous ectopic pregnancy reaches 10–27%, patients who had two previous ectopic pregnancies via natural conception and treated with salpingectomy or salpingectomy were found to have a 10-fold increased risk of further REP as compared to those with one prior Results of population-based studies of pregnancy outcomes after a prior tubal EP are encouraging, and independent of treatment modality[16]. The rates of IUP have been shown to be similar following salpingectomy and salpingectomy in several large series[17.] The future fertility outcomes after ectopic have also been studied after various managements of ectopic pregnancy and it doesn't seem to be affected by the different managements and the various sites of ectopic pregnancy [18].No difference in the rate of fertility, the risk of future tubal ectopic pregnancy or tubal patency rates was found between the different management methods based on low-quality evidence.[19] Expectant management was associated with the highest cumulative incidence in terms of intrauterine CP and LB, and to the shortest time interval between the index EP and the intrauterine CP as compared to MTX and surgery, although statistically significant differences were reported only compared to the surgical approach.

A good fertility out come in the form of intrauterine pregnancy (81%) was noted in primiparous patients as compared to multiparous women. Regarding gestational age at ectopic, it was observed that the lesser the gestational age at which ectopic pregnancy occurred, the more is the chance of a better fertility outcome .there was65.5%chance of intrauterine pregnancy at four to seven weeks of gestation. BMI wise stratification has revealed that 81.8% of patients who had subsequent intrauterine pregnancy were in the BMI range of 25.5-29.9. In comparison with the normal BMI group, the rate of EP was significantly increased in the low BMI group[20] .In a study regarding analysis of fertility after ectopic it was found that The cumulative intrauterine pregnancy rate was 56% at 1 year and 67% at 2 years and the three major factors associated with a poor fertility outcome were age > 35 years, prior history of infertility, and the tubal damage[21].

The study reveals a good fertility outcome in the form of intrauterine pregnancy in majority of primiparas in the average BMI ranges of 25.5-29.9. A better outcome would be expected at lower gestational ages of ectopic pregnancy especially less than 7 weeks gestation. Thus an earlier diagnosis of ectopic at an ealier gestational age, with prompt management of ectopic may improve future prospects of pregnancy.

CONCLUSION

Extrauterine pregnancy though less than intrauterine is still a significant problem in local population with history of ectopic pregnancy. The future good fertility outcome in the form of intrauterine pregnancy is expected in more than 81% cases in primiparas in the average BMI ranges. A better outcome would be expected at lower gestational ages of ectopic pregnancy especially less than 7 weeks gestation.

RECOMMENDATION

Patients with higher risk of subsequent ectopic pregnancy are to be more vigilantly monitored to exclude future ectopic pregnancy to and reduce the burden of extrauterine pregnancies so that even with history of ectopic pregnancy, term delivery can be assured.

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