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Introduction:

Ectopic pregnancy (EP) is defined as any pregnancy in which embryo implantation occurs outside the uterine cavity such as endometrium and endometrial cavity that is in the cervix, uterine tubes, ovaries, abdominal or pelvic cavities.^{1,2} It is the one of the life-threatening emergency in pregnancy. The real concern is its increasing prevalence with subsequent impairment of fertility.

The incidence of EP with contraception is decreasing in present days while incidence of EP without contraception is increasing in contrast.² The prime objectives of the present study are to understand the epidemiology, important risk factors as well as the mode of treatment of EP cases.³Ectopic gestation or pregnancy is the leading cause of pregnancy related maternal

death during first trimester. ¹ EP was first described in the 11th century. Presently the Worldwide estimated incidence of EP is between 1-2% of all pregnancies. ² It is reported that EP is the leading cause of maternal mortality in Africa accounting 0.5-2.3% of all deaths. In South East Asia incidence of EP is 1.48%.⁴ Highest incidence of EP is reported from African countries i.e. 0.5-2.3% of live birth, while low incidence is reported from Asia and Middle East i.e. 0.4-0.6% of live birth. The incidence of EP is 0.5%-1.5% of all pregnancies in Pakistan.⁵

The common sites of EP are fallopian tubes (approximately 97%), for tubal pregnancies, ampulla is the most common site of implantation (80%), followed by the isthmus (12%), fimbria (5%) and others (3%). With 3% of ectopic developed extra tubal, sites of implantation include the cervix, ovary, corneal region of the uterus, and abdominal cavity. Risk factors for ectopic pregnancy are pelvic inflammatory disease, smoking, previous ectopic pregnancy, age, parity, infertility, use of intrauterine device, surgical history and past history of miscarriages.¹

Methodology:

We designed the case control study with cases (n=50) and controls (n=50) during May 2017 to 30 July 2017 at Muhammad Medical College Mirpurkhas, Nishtar Hospital Multan, Victoria Hospital Bahawalpur and Civil Hospital Khanewal. Sample achieved using non-probability convenience sampling. Ethical approval from Muhammad Medical College and gatekeeper permission from other hospital was sought. For this study, we defined "case" as "a pregnant woman with confirmed extra uterine ectopic gestation". The control group comprises of pregnant women with confirmed normal intrauterine pregnancy. Clinically an ectopic pregnancy was suspected if a woman presented with a short period of amenorrhea indicating possible pregnancy, abdominal pain and or bleeding per vagina or sign and symptoms of shock. The diagnosis of an ectopic pregnancy was confirmed through an ultrasound (transabdominal and transvaginal) examination and serum beta HCG level. We retrieved records of women with ectopic pregnancy from electronic database for this study. Information on various aspects focusing on the epidemiology, socio demographic profile, presence or absence of risk factors for EP, were collected either from the patient or from the accompanying relative. Informed verbal consent was obtained from each of the willing participant or from their accompanying person. Each participant was given right to left study at any time. Epidemiological variables like age, religion, number of family members, monthly family income, per capita income (PCI) as well as obstetrical variables such as gravida, parity, last child birth, last menstrual period was considered for this study. Data to have information for past history of pelvic inflammatory disease (PID), sexually transmitted infection (STI), ectopic pregnancy, infertility, any surgery, medical illness, abortion, use of oral contraceptive pill (OCP), use of OCP at conception were collected. Data entered in an excel sheet and analyzed using statistical formula as applicable. The association between EP and risk factors was

measured by odds ratio (OR), 95% confidence interval (CI) and p value were obtained by using SPSS 22.0 (licensed) software. P value of < 0.05 considered as significant. Fisher's exact value was considered if any cell value found less than 5. The baseline characteristics of women with intrauterine and those with EP were compared using one-way analysis of variance (ANOVA) for continuous variables and a chi-square or fisher's exact test for categorical variables.

Results:

The mean age of study population was 22.53 years. One third (40%) of ectopic occurred among 20 to 25 years age-group corresponding to several other studies 8-10 closely followed by the under 25 years group (40%). The average income of the family was PKRs. 25935.80/- per month. The case (n=50) & control (n=50) were almost similar in age, education, residence, age of marriages and parity. The age range of all study participants was between 15 years to 35 years. Age divided into 4 subgroups to study the effects i.e. 15 to 20 years, 21 to 25 years, 26 to 30 years and 31 to 35 years. The mean age of study population was 22.53 ±SD 5.69 years. Most of the participants (40.6%) were from younger age group that is 20 to 25 years, it may simply be the reflection of the fact that it is the most common child bearing age group in Pakistan. Only three women were from upper socio-economic class indicating the economic disparity in the society. We found significant association between current ectopic pregnancy and previous ectopic pregnancy (OR 15.47, CI 95% 1.92-124.3, p=0.00), previous history of pelvic inflammatory diseases (OR 13.5, CI 95% 5.09-35.83, p=0.01), smoking (OR 15.47, CI 95% 1.92-124.3, p=0.00), history of endometriosis (OR 4.04, CI 95% 1.22-13.47, p=0.00), use of intrauterine contraceptive device (IUCD) OR 5.41, CI 95% 1.66-17.65, p=0.00), and previous cesarean section (OR 2.42, CI 95% 1.04-5.63, p=0.02).

Table 1: Comparison of age groups between cases and controls

Age group (years)	Case	Control	Chi Square	p value
15-20	9 (18%)	6 (12%)	7.2	0.06
21-25	20 (40%)	11 (22%)		
26-30	16 (32%)	20 (40%)		
31-35	5 (10%)	13 (26%)		

Table 2: Comparison of parity between cases and controls

Parity	Case	Control	Chi Square	p value
Primary	09 (18%)	15 (30%)	5.1	0.2
Gravida II	07 (14%)	12 (24%)		
Gravida III	27 (54%)	16 (32%)		
Gravida IV	06 (12%)	06 (12%)		
Gravida V (+)	01 (2%)	01 (2%)		

Table 3: Comparison of residence between cases and controls

Residence	Case	Control	Chi Square	p value
Rural	29 (58%)	28 (56%)	0.04	0.8
Urban	21 (42%)	22 (44%)		

Table 4: Comparison of age groups when married between cases and controls

Age Group (years)	Case	Control	Chi Square	p value
10-15	05 (10%)	09 (18%)	15.9	0
16-20	18 (36%)	33 (66%)		
21-25	22 (44%)	06 (12%)		
26-30	05 (10%)	02 (4%)		

Table 5: Comparison between previous C. Sections of cases and controls

Previous C-section	Case	Control	Odds ratio	95% CI	p value
Yes	23 (46%)	13 (26%)	2.42	1.04-5.63	0.02
No	27 (54%)	37 (74%)			

Table 6: Comparison of past history of endometriosis between cases and controls.

H/O Endometriosis	Case	Control	Odds ratio	95% CI	p value
Yes	13 (26%)	04 (08%)	4.04	1.22-13.43	0
No	37 (74%)	46 (92%)			

Table 7: Comparison of use of emergency contraception between cases and controls

Use of emergency contraception	Case	Control	Odds ratio	95% CI	p value
Yes	16 (32%)	04 (08%)	5.41	1.66-17.65	0
No	34 (68%)	46 (92%)			

Table 8: Comparison of history of previous C. section between cases and controls

History of previous C section	Case	Control	Odds ratio	95% CI	p value
Yes	13 (26%)	05 (10%)	3.16	1.03-9.69	0.02
No	37 (74%)	45 (90%)			

Discussion:

This study is probably the first to recruit participants simultaneously from Multan, Khanewal, Bahawalpur and Mirpurkhas. The cases were collected from the regional register of the study hospitals. During period of the study, 50 cases of ectopic pregnancy were selected by convenience sampling. In current study, the frequency of ectopic pregnancy was much higher than that seen in developed countries.² Even this figure may be fallaciously low as many mothers with ectopic pregnancy might have died in the outskirts areas due to delayed diagnosis, lack of transport and medical support as well as dearth of health care practitioners. Transvaginal ultrasound scan is the best test to diagnose ectopic pregnancy² but there are villages where no

ultrasound scan machine is available. Therefore, mostly diagnoses of EP is based upon clinical features, consequently many cases misdiagnosed or ignored due to lack of ancillary laboratory and ultrasound facilities. The ultrasound machine with expert sonologist was not even available in the study hospitals twenty-four hours and throughout the week, therefore many cases might have been referred to tertiary care as significant number of obstetrics patients report during night time. Moreover, other cause of delay in diagnosis includes; majority of patients were not aware of the pregnancy, few had been seen by health provider but falsely reassured and few regarded the symptoms not serious enough to ask for care.² Identification of these risk factors for ectopic pregnancy shall help in early detection and appropriate management in an individual case and it may help in devising a comprehensive preventive strategy for ectopic pregnancy³. By identifying this risk factor, modification in cigarette smoking, use of IUD and interval between pregnancies may effectively reduce the risk of ectopic pregnancy. EP continues to be the leading cause of first-trimester maternal death. Since 1970, the frequency of EP has increased six-fold, and currently reported to be 2% of all pregnancies.⁴ The clinical features of cases during this study followed the global pattern and includes abdominal pain, amenorrhea, and vaginal bleeding. According to Ashraf Moini⁵ the most frequent presenting complaints (58.6%) was amenorrhea of 6-10 weeks, while Shah and Khan⁶ found abdominal pain as the most common (97.3%) presenting feature, followed by history of amenorrhea (73.6%) and vaginal bleeding (57.8%); these findings are in agreement with the results of current study where 60% presented with abdominal pain and vomiting, amenorrhea in 73.6% and vaginal bleeding in 57.8% of the patients. Strikingly 10% of the patients in current study presented with complain of burning micturition, a symptom which apparently has no connection with the ectopic pregnancy. In the study by Karki and Saha⁷, 14% had history of ectopic pregnancy; while in current study 24% women had previous EP having an Odds of 15.5 and p value of 0. This figure of 24% is more in agreement with study of Aziz et al.⁸ Among participants of the present study 72% of patients presented with ectopic pregnancy having had pelvic inflammatory disease; Odds of developing ectopic pregnancy in patients with pelvic inflammatory diseases is 13.5 (p=0.01) as only 16% patients gives history of PID among control group. Almost identical figure has been reported in published literature⁹⁻¹¹. In a study by Kevin C. Worley et al¹² smoking was one of the risk factors for EP as it delays passage of the fertilized ovum into the uterine cavity by altering the tubal motility. The result of current study endorsed this finding as odds of ectopic pregnancy among smoker is 15.5 when compared to nonsmokers; as 36% of patients having ectopic pregnancy were smoker. Identical results have been reported by other national and international studies^{13,14}.

Limitation of the study:

The completeness of documentation was the major strength of current study. It is, however, possible that there may be differences in the determination of exposures pertaining to risk factors by different clinicians.

Conclusions:

Identification of risk factors helps in early and appropriate management. For ectopic pregnancy risk factors modification, such as cigarette smoking, use of IUD and sufficient interval between ectopic pregnancy and subsequent pregnancy can help to reduce the prevalence of ectopic pregnancy with overall reduction in pregnancy related morbidity and mortality. Current research will be useful to help in executing and implementing preventive measures among females of province of Sindh and Punjab by providing adequate education and awareness at grass root level.

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