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Incidence rate and prevalence of major risk factors for ectopic pregnancy in the Pakistani population: mini-review

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ABSTRACT

Ectopic pregnancy is the complication of pregnancy in which the product of conception implants outside the uterine cavity *i.e.* in the uterine tubes, cervix, ovaries and abdomen. It is life-threatening emergency and a major cause of maternal morbidity and mortality. The incidence rate is 0.5%-1.5% of all pregnancies. Even though its incidence rate is drop off when compared with earlier decades, it is still the foremost causes of maternal morbidity and mortality in the first trimester of pregnancy, especially in developing countries. In Pakistan, it varies from 1:1 124 to 1:130 pregnancies. Risk factors associated to ectopic pregnancy are pelvic inflammatory disease, past history of miscarriages, age, parity, infertility, previous ectopic pregnancy, induction of ovulation and intrauterine device usage. The aim of this study is to review the published literature concerning the disease knowledge and major risk factors associated to ectopic pregnancy in Pakistan.

1. Introduction

Pakistan is one of those countries that have the highest fertility rates, exceeding four children per woman. Its area is approximately 800 000 km^2 and it is larger than either Turkey or Chile[1]. Taking into consideration its size and extensiveness, growing population, there is a surprising death of information about ectopic pregnancy incidence, although more is known about its risk factors. In Pakistan, incidence of ectopic pregnancy varies from 1:1 124 to 1:130 pregnancies[2]. Incidence rate is raising and has go up from 4.9/1 000 pregnancies in 1970 to 9.6/1 000 pregnancies in 1992 (Royal College of London, 1999)[3]. The reason for the increasing incidence has not been fully evaluated[4]. We, therefore, reviewed the published literature concerning the disease knowledge, incidence and the major risk factors associated to ectopic pregnancy in Pakistan.

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2. Ectopic pregnancy

Ectopic pregnancy is a complication of pregnancy in which the fertilized ovum implants outside the endometrium and endometrial cavity[5], *i.e.* in the uterine tubes, ovaries, and abdomen. An ectopic pregnancy is a life threatening emergency, and if not treated, it can produce adverse effect[6]. In an ectopic pregnancy, generally the fertilized embryo holds on to the lining of the Fallopian tube and penetrates into the nearby vessels and causes bleeding. Heavy intratubal bleeding sometimes threatens the health or life of the woman. In ectopic pregnancy, heavy bleeding occurs earlier than usual, if embryo invades into the nearby Sampson artery.

Usually, in most of the cases, ectopic pregnancies will resolve, without treatment. However, surgery is required in cases where the Fallopian tube has ruptured. This intervention may be done by a larger incision, known as a laparotomy.

Ectopic pregnancy can be classified as tubal pregnancy in which the embryo implants in the Fallopian tubes[7]. Non-tubal ectopic pregnancy is a type in which pregnancies occur in the ovary, cervix, or in abdomen. This type of pregnancy is usually detected by transvaginal ultrasound examination. In heterotopic pregnancy, two eggs fertilized, one implants outside the endometrial cavity and the other inside[8]. Persistent ectopic pregnancy is the growth of trophoblastic tissues after a surgically removal of ectopic pregnancy. This happens because some trophoblastic tissue, deeply embedded, left after the surgical removal and continues to grow, giving a rise in human chorionic gonadotropin levels[9]. In pregnancy of unknown location pregnancy is test positive, but on transvaginal ultrasonography no pregnancy has been visualized[10].

Early signs and symptoms include abdominal pain, vaginal bleeding or spotting, nausea, vomiting and diarrhea[10]. Risk factors associated to ectopic pregnancy are pelvic inflammatory disease (PID), use of an intrauterine device, intrauterine surgery (*e.g.* dilatation and curettage), smoking, tubal surgery previous ectopic pregnancy, infertility and tubal ligation[11]. Women with PID are increased risk of ectopic pregnancy. PID damages the hair like cilia that are located on the internal surface of the Fallopian tubes. These cilia bring the fertilized ovum to the uterus[12]. Transvaginal ultrasonography alone, ultrasonography and β-human chorionic gonadotropin, laparoscopy or laparotomy can be done to confirm an ectopic pregnancy. Early treatment of an ectopic pregnancy is done with methotrexate injection, considering alternative to surgical treatment[13]. If hemorrhage has already occurred, keyhole surgery can be used either to remove the tube containing the ectopic pregnancy or open surgery to preserve the tube. Open surgery will be done to increase the chances of a normal pregnancy in the future, although it also increases the risk of another ectopic pregnancy[14].

3. Incidence of ectopic pregnancy in Pakistan

The incidence of ectopic pregnancy, over the past 30 years has increased dramatically in most developed and developing countries. It is estimated that annual incidence rates vary between 100 and 175 per 100 000 women age between 15 and 44[15]. The Centre for Disease Control reports that the incidence of ectopic pregnancies is 1 in 70 pregnancies[16] while in Pakistan it varies from 1:1 124 to 1:130 pregnancies[2]. It is estimated that the incidence rate of ectopic pregnancy is increasing and has go up from 4.9/1 000 pregnancies in 1970 to 9.6/1 000 pregnancies in 1992[3].

The frequency of ectopic pregnancy was determined by Khaleeque *et al.* during the period 1997 to 1999 at Ziauddin Medical University Hospital, North Nazimabad campus, Karachi[17]. Out of 3 252 patients, 43 were admitted with ectopic pregnancy during this period. Frequency of ectopic pregnancy over the 2-year study period was 1.3% of total 3 252 pregnancies[17].

Over a period of 2 years, a cross-sectional analytical study was conducted by Mahboob and Mazhar in the Department of Obstetrics & Gynaecology Unit II, MCH Centre, Pakistan Institute of Medical Sciences, Islamabad in the year 2004 to 2005. Fifty-two patients diagnosed with ectopic pregnancy presenting to the Department of Gynaecology and Obstetrics during this 1-year period[13].

Another descriptive study was carried out at Gynecology Unit II Liaquat University Hospital Hyderabad in the year 2006 to 2008. During this period total maternity admissions were 8 016 out of these 62 cases were diagnosed with ectopic pregnancy giving an incidence of 0.8% or 1:129 in this region[18].

4. Risk factors attributing ectopic pregnancy

Several number of researchers conducted a study to determine the frequency of risk factors, clinical features and diagnostic modalities of ectopic pregnancy in Pakistan hospitals. We reviewed the published literature concerning the major risk factors associated to ectopic pregnancy in Pakistan.

Ehsan and Mehmood conducted a study to determine the incidence, risk factors, diagnostic features, and clinical management of ectopic pregnancy in a prospective review of 62 cases admitted to Jinnah Postgraduate Medical Center in Karachi, Pakistan, in 1989-1990[19]. The incidence of ectopic pregnancy during the 18-month study period was 1:174 births or 5.7/1 000 live births. The exact cause was unknown in 30 cases (48.3%); however, PID was implicated in 10 cases (16.1%), 10 women (16.1%) had a past history of dilatation and evacuation for incomplete abortion, 4 women (6.4%) had undergone another type of pelvic surgery, 3 women (4.8%) had an intrauterine device *in situ*, and 1 woman (1.6%) had recurrent ectopic pregnancy. The most common clinical presentations were abdominal pain (100%), amenorrhea (80.6%), syncope (61.2%), vaginal bleeding (48.3%), and nausea and vomiting (35.4%)[19].

Khaleeque *et al.* did a retrospective analysis of patients admitted with ectopic pregnancy at Ziauddin Medical University Hospital from 1st January 1997 to 31st December 1999[17]. Total numbers of pregnancies were 3 252. Out of these 43 patients were admitted with ectopic pregnancies. Thirty-nine were patients evaluated. It was shown that frequency of ectopic pregnancy was 1.3%. Majority of patients were in the age group of 21-30 years(74%).

Multiparous women were more suffered in ectopic pregnancy (61%), among which five patients had a history of previous abortions followed by dilatation and evacuation[17]. Previous abortions are usually associated with slightly increased risk for ectopic pregnancy[20], four patients were infertile and were taking clomiphene citrate for ovulation induction. Another study was conducted by Shah and Khan at Department of Obstetrics and Gynaecology, Civil Hospital, Karachi from January 2002 to December 2003[21]. The aim of the study was to describe the clinical features and risk factors in ectopic pregnancy. The most frequent presenting symptom was abdominal pain in 37 (97.3%) patients whereas history of amenorrhea and vaginal bleeding were found in 28 (73.6%) and 22 (57.8%) patients, respectively. The most common risk factors were infertility, tuberculosis, previous ectopic pregnancy and previous tubal surgery in one (2.6%) patient[21].

Furthermore, Qazi *et al.* conducted a descriptive study on 50 cases of tubal pregnancy at Khyber Teaching Hospital Peshawar from September 2002 to December 2003[22]. Among the etiologic factors the most frequent was, PID (14%), previous ectopic (4%), ovulation induction (4%) and intra uterine contraceptive device insertion (2%). Common clinical presentations were abdominal pain (90%), amenorrhea (84%), vaginal bleeding (70%) and shock (32%). Clinical signs raising suspicion of tubal rupture were shock (36.3%), anemia (86.3%) and irregular mass in pouch of douglas (88.6%)[22].

Hassan *et al*. observed the risk factors, clinical pattern and management of ectopic pregnancy at Gynecological Unit II, Liaquat University of Medical and Health Sciences, Hyderabad during January 1st 2006 to April 1st 2008[18]. All patients with confirmed diagnosis of ectopic pregnancy were included in the study. Total pregnancies were 8016 with 62 cases of ectopic pregnancy giving an incidence of 0.8% or 1:129. PID (35.4%), previous abdominal pelvic surgery (26%), previous ectopic (6.4%) and infertility (35.4%) were seen as the major risk factors for ectopic pregnancy. Common clinical pattern was abdominal pain, amenorrhea and collapse[18].

Afroza and Akram find out the causative factors for rising rate of ectopic pregnancy in young women[2]. The study was conducted at Maula Bakhsh Teaching Hospital (Obstetrical and Gynaecological Unit), Sargodha. The study period was from January 2008 to December 2008. All patients who were presented in labour room emergency and gynaecological out patients department with confirmed diagnosis of ectopic pregnancy on ultrasonography were included in the study. The study showed frequency of ectopic pregnancy was too high compared to international studies. Rising rate of ectopic pregnancy was frequent among young, nulliparous women which was secondary to PID[2].

Cheema *et al*. determined risk factors for ectopic pregnancy in patients presenting in Lahore General Hospital, Lahore from 01-08-2009 to 01-08-2010[23]. It was a descriptive study in which 56 patients with ectopic pregnancy were included. They concluded that the maximum numbers of patients were between 20-29 years of age (60%). While 57% patients were multigravida (P2 or more). Common risk factors associated with ectopic pregnancy were PID (25%) previous ectopic pregnancy (10.7%), previous surgery (10.7%) and smoking (21.4%). Infertility and use of intra uterine contraceptive device was found in 12.5% and 7.1% alternatively[23].

Shabab and Hashmi determined the clinical presentations and the management options for ectopic pregnancy at Department of Obstetrics and Gynecology, Liaquat National Hospital Karachi, from 13th August 2011 to 12th August 2012[24]. During the study period the gynecological admissions were 1126 and 1618 deliveries conducted. Forty patients were of ectopic gestations accounting for 2.4% of all deliveries and 3.5% of all gynecological admissions. The peak age was 20-30 years old. Cases of ectopic pregnancy were found more among primigravida, *i.e.* 45%. Abdominal pain was the most common presenting complains in 92.5% whereas history of amenorrhea present in 75% and vaginal bleeding was found in 45% of patients. Identifiable risk factors were present in 52.5% of cases, the most frequent was previous miscarriages in 22.5%, whereas infertility treatment 10%, previous ectopic pregnancy 5%, PID 5%, tubal ligation 5% and previous cesarean section 5%[24].

Shafquat *et al*. find out the involvement of age, parity, and duration of subfertility as risk factors for ectopic pregnancy[5]. This study was of 3-year period from 1st January 2009 to 31st December 2011 and conducted in Gynae C Unit, Lady Reading Hospital, Peshawar, Pakistan, including 150 cases of ectopic pregnancy. It was observed that ectopic pregnancy found in 64 (42.6%) patients aged 26-35 years old, 49 (32.6%) patients were 15-25 years of age and 37 (24.6%) were>35 years old. It was most frequent among multipara 71 (47.3%) as compared to primipara 52 (34.66%), and grand multipara 27 (18.8%). Subfertility of 2-5 years was frequent in 56 (37.3%) patients, 6-10 years in 72 (48%), and 11-15 years in 22 (14.6%). They, therefore, concluded that the contributing risk factors leading to ectopic pregnancy are age, parity, and duration of subfertility, especially the age group 26-35 years, multiparity and subfertility duration of 6-10 years[5].

Khan *et al*. conducted a study to determine the frequency, risk factors, clinical features and diagnostic modalities of ectopic pregnancy in Ayub Teaching Hospital, Abbottabad, from January 2003 to December 2012[25]. This was a 10-year study. There were 255 cases of ectopic pregnancy out of 25010 pregnancies during the study period and the frequency was 1.01%. The most common predisposing factor to ectopic pregnancy was PID (43.13%) while 37.64% had previous

abortions. Recurrent ectopic pregnancy was in range of 9.01% of patients while 27.05% had history of previous pelvic surgeries. The incidence of ectopic pregnancy in their study was found to be 10.1 per 1 000 deliveries[25].

5. Worldwide incidence of ectopic pregnancy

The incidence of ectopic pregnancy in western countries now going to decrease, generally because of accessibility of modern diagnostic techniques, which makes timely diagnosis before tubal rupture, occurs in over 70% of cases[26]. In France, the incidence of ectopic pregnancy was 2.0%[27], 2.8% in Finland[28] and 2.2% in the United States. Another study of 18-year period in America reported an increasing incidence from 0.45% to 1.68%[29]. In England the incidence is 1.24%. In most of Europe and North America, the incidence of ectopic pregnancy is reported to be 2% of livebirths[12]. A study in Norway showed that the incidence of ectopic pregnancy in that country increased during 1976 and 1993 from 1.4% to 2.2%[30]. The incidence of ectopic pregnancy increased in England and Wales, by five times between 1966 and 1996 from 0.3% to 1.6% of livebirths[26]. The incidence also increased in the United States from 1.9% to 2.3% of livebirths between 1981 and 1991[31]. In another study conducted in the United States, it reported that the annual incidence of ectopic pregnancy raised from 0.37% of pregnancies in 1948 to 1.97% in 1992[32]. At the Yanbe Industrial City in the Kingdom of Saudi Arabia the incidence was found to be 1 in 171 deliveries that is 0.58% from 2005 to 2008[33]. The incidence of ectopic pregnancy in India is 1 in 161 (0.6%) deliveries[34]. In African developing countries, a majority of studies have reported an ectopic pregnancy rate is 1%-3%, which is ten times higher than that of reported in industrialized countries[35].

6. Future prospects and conclusion

Ectopic pregnancy is a major health issue among women of childbearing age[26]. If it is not diagnosed properly and timely, it can become a life-threatening situation[26]. PID, previous abortion and history of infertility are the main risk factors for ectopic pregnancy in Pakistan. Increased incidence of sexually transmitted infections and perilous abortions leads to increased risk of ectopic pregnancy. Some factors involved in the prompt treatment of ectopic pregnancy such as late presentation, poverty, ignorance, non-accessibility of modern diagnostic methods[36]. Community based health education programme are therefore urgently needed, which give awareness regarding contraception, sex education, PID, prevention and treatment of sepsis after abortion and puerperal phase. It has a key role in maternal morbidity and mortality and early wastages during the first trimester of pregnancy, because of the late diagnosis, late seeking for medical help with attendant risk of tubal rupture and haemorrhage[37]. Emphasis should be given on prevention and timely diagnose of ectopic pregnancy so that to give the patients better opportunities for tubal conservative treatment. Timely diagnosed and use of modern diagnostic tools will improve maternal morbidity and mortality. Health education of women during gestational age on safe sex and obliteration of unsafe abortion and early treatment of pelvic infections will prove useful as preventive measures[38].

In our set up PID is a common risk factor because majority of women conduct deliveries at home due to low paying capacity or going for an induced abortion of unwanted pregnancy to dai (mid-wife) ending up in chronic pelvic infection. Other risk factors include history of infertility, pelvic surgery, previous history of ectopic pregnancy and ovulation induction. So by reducing and identifying the risk factors and evaluating the patient through ultrasonographic examination at the earliest 6 weeks, it is possible to improve the prognosis so far as the morbidity and mortality of ectopic pregnancy. Prevention of PID and establishment of early pregnancy units are the other areas to be focused on. It is suggested that aggressive screening and awareness programs should be arranged. Risk factors predisposing to high incidence of ectopic pregnancy should be identified and dealt with. Ectopic pregnancy registry system should be introduced by government.

Conflict of interest statement

We declare that we have no conflict of interest.

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