

“Anticipating the occurrence of tubal ectopic pregnancy in the absence of history of pelvic inflammatory disease”-a short communication

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Short communication

Ectopic pregnancy (EP) results when the developing blastocyst becomes implanted at a site other than endometrium of the uterine cavity. Although in US and Europe only 1-2 pregnancies are ectopic, EP is the cause of 75% of maternal deaths in the 1st trimester and 9-13% of all pregnancy related deaths.^{1,2} This situation is far worse in the developing world with EP fatality rates being 10 times greater than in developed world.³ Though its incidence has reduced in the past 25 years, which is true for the African-American populations.¹ Since the time from conceiving to that of tubal rupture is little, with it reporting within 6-8 weeks of conception, it is highly important for pediatricians, family medicine doctors besides obstetrician and gynaecologists to be alert regarding this diagnosis. Cause of EP mainly relates to the damage of fallopian tube mucosa that has been exposed to both manifest and occult sexually transmitted infections (STIs), and thus incidence of EP is greater in populations who have higher risk of STIs. Periadnexal adhesions and fimbrial agglutination are often seen at the time of laparoscopy done to confirm along with treat EP. A recent study in Australia has shown that the incidence of PID has increased from 2009 till 2014 and this is increasing EP rates.⁴

Gaskins, et al.,⁵ further emphasized on the importance of STIs being a major cause, with epidemiological and experimental strong evidence showing that other risk factors exist and EP might occur within apparently normal fallopian tubes. A Prospective study where lifestyle and reproductive factors that were associated with other risk factors associated with greater risk of EP in 22,356 women who participated in the Nurses' Health Study II from 1990-2009. They analyzed a huge dataset comprising of 41,440 pregnancies, that was contributed by nurses whose history one can rely on regarding their reproductive history. The EP incidence was 1% in their study as seen in earlier studies. Current smokers had 1.73 times (95% confidence interval [CI] 1.28-2.32 times) the risk of EP as compared with never smokers. People who had smoked earlier had 1.22 times the risk that after 10 years was similar to that of never smokers. While alcohol intake of >10g/d was associated with 1.5 times the risk in never consumers, that was a new finding. Also in utero exposure of diethyl stilboestrol (DES), current IUD use, previous history of tubal ligation and infertility history contributed to greater risk for EP. Women who used oral contraceptives before the age of 16 years had greater risk of EP though this risk was correlated with riskier sexual habits which increased risk of STIs.⁵ Though most of these factors barring alcohol use are not new, they help in giving a stronger emphasis on the findings of previous case control studies having limited sample size and tends to label recall or selection bias in those studies.⁵

Gatkins et al.,⁵ suggested that both cigarette smoking and alcohol

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intake may lead to EP by changing the motility of normal fallopian tubes. For this hypothesis was previously presented by experiments done in laboratory animals.⁶ In women having EP low serum estradiol (E2) and progesterone (P) levels have been seen. It is not clear whether this implicates the formation of a defective corpus luteum at ovulation or changed bioactivity of HCG produced by the blastocyst? These sex steroids are known to play a role in the oviductal motility is it possible that these low levels alter the tubal transport of the fertilized egg leading to delayed embryo transport within the fallopian tubes.⁷

Another query is those women who present with EP with no risk factors initially? Medical History might be unreliable as laparoscopically previous pelvic infection is found many times without patient realizing its occurrence. A high occurrence of Chlamydia trachomatis has been found in women who develop EP without history of STI. Ahmed et al showed that pelvic chlamydial infection predisposes to EP by up regulating integrin $\beta 1$ to promote Embryo-tubal Attachment.⁸ Further glycosylation dependent galectin receptor interactions promote Chlamydia trachomatis infection.⁹ Also a high incidence of C. trachomatis has been observed in women suffering from EP without a history of an STI, and it has been shown that antibodies to Chlamydia trachomatis, 70-kDa heat shock protein might play a role in the pathogenesis of tubal mucosal damage. Some experiments by Bladeau et al in rabbits whose oviducts have extensive fimbria, like in humans support an etiology of EP without the damage of fallopian tubes. Importance of cumulus oophorus which surrounds the ovulated egg in the transport from the ovary into the tubal ostium. Once there is enzymatic removal of the cumulus, this cumulus free eggs show delayed transport into the oviduct. Thus they hypothesized that the highly negatively charged glycosaminoglycans present in the cumulus interact with the ciliated fimbria, aiding in the egg's transport. The cumulus oophorus formation varies widely between human oocytes recovered at follicular aspiration for in vitro fertilization. Thus one thinks that is it possible that result of abnormal formation of the cumulus oophorus near the time of ovulation case a sporadic EP-rest?¹⁰

With the use of methotrexate, accepted as the approved medical treatment for EP, the incidence of surgical treatment has markedly reduced in view of early diagnosis of EP. Once surgery has to be done salpingectomy is the procedure of choice if fallopian tube is ruptured or near rupture, or shows evidence of previous pelvic infection at the time of laparoscopy? Initially when linear salpingostomy technique got developed, basis was that tubal conservation would increase the chances if intrauterine pregnancy in future without increasing the incidence of recurrent EP. This has been confirmed by a number of case controlled studies. Two recent prospective randomized studies where salpingectomy vs salpingostomy were compared, along with In a recent meta-analysis, no differences in the subsequent fertility was found between the 2 groups.¹¹ Basically the decision of using either of the technique was not on the basis of intraoperative findings, but done randomly. The fallopian tubes EP was in a regressive phase, or more easily evacuated from the fallopian tubes, or was actively invading or the size in fallopian tubes was not taken into account. Also how skilled the operator was and his operative quality might have played a role as salpingostomy needs >surgical skill. In fallopian tubes than the simpler salpingectomy. Further conformatory hysterosalpingography was not gone to ensure patency of both the tubes following the procedure.

Thus basically the study by Gaskins et al.,⁵ further emphasizes the fact that EP may occur in normal fallopian tubes, with the absence of previous STI does not rule out the diagnosis. Thus knowing the factors that might =>EP development help in anticipation and early diagnosis, preventing catastrophic haemorrhage to develop, aid in medical methotrexate treatment that might prevent both cost and risk associated with surgery Further help in choosing conservative surgery is there knowing EP may develop in normal fallopian tubes.

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Conflicts of interest

Author declares that there are no conflicts of interest.

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