Pelvic Inflammatory Disease, A Perturbing Trigger to Infertility:
A Systematic Review

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Abstract

Introduction: Pelvic inflammatory disease is comprehensively termed for cervicitis, endometritis, salpingitis, pelvic peritonitis, and tubo-ovarian abscess. Diagnosis is initially by clinical assessment, confirmed by laboratory investigations and imaging modalities. PID is usually ignored by patients and clinicians eventually leading to infertility. Purpose: The goal of this systematic review is to evaluate relation of PID with infertility and role of imaging modalities for diagnosis. Method: During October 2020 we searched Google scholar, pubmed, Medscape research articles from 2010 -2020. Conclusion: Pelvic inflammatory disease is second most common cause of infertility while diagnostic ultrasonography plays a limited role to diagnose.

Keywords: Pelvic inflammatory disease, infertility, endometritis, hydro salpinx, Tubal factor infertility and Sonographic evaluation.

DOI: 10.7176/JHMN/82-08
Publication date: November 30th 2020

Introduction:
Pelvic Inflammatory Disease is collectively termed for infections involving female genital tract comprising of cervix, uterine endometrium, ovaries, fallopian tubes, and pelvic peritoneum. Organisms thought to be culprit are *Chlamydia trachomatis* and *Neisseria gonorrhea*, which are cause of sexually transmitted diseases (STI,) but clinical disease is not associated with only these organisms. It is difficult to diagnose Pelvic Inflammatory Disease due to variable clinical presentations ranging from subclinical PID to severe disease that may need surgical interventions. Presentation of acute PID without clinical signs and symptoms is defined as subclinical PID. CDC 2015 Sexually Transmitted Diseases Treatment Guidelines gave minimal clinical criteria to offer conjunctural treatment for PID to sexually active woman or woman at risk for STIs who had been through lower abdominal or pelvic pain and on clinical examination either cervical motion tenderness or uterine tenderness or adnexal tenderness was experienced. Additional standards include oral temperature more than 101F (38.3C), friable cervix, cervical mucopurulent discharge. Vaginal fluid showing abundance of white blood cells on microscopy. Erythrocyte sedimentation rate and C-reactive proteins with raised values, *Neisseria gonorrhea* and *Chlamydia trachomatis* documented by laboratory. Last but not the least is Specific diagnostic criteria comprising of Transvaginal ultrasound or magnetic resonance imaging exhibiting thickening of fluid filled tubes with or without free fluid in pelvis, or tubo ovarian complex, pelvic infections manifested by Doppler,Laparoscopic findings revealing PID and evidence of endometritis on histopathology of endometrial biopsy.

Mostly bacteria are the cause of inflammation in PID [3]. *Chlamydia trachomatis*, *Neisseria gonorrhea*, Streptococcus species, Enterococcus faecalis are the responsible microorganisms.

PID evolved subsequently in About 10% of women previously infected by *Chlamydia trachomatis*. Bacterial vaginosis (BV) may also be responsible for tubal factor infertility by its mechanism of reduction of lactobacilli, raising vaginal pH and stimulating growth of anaerobic vaginal organisms [2].

Females considered at high risk of PID are of young age (30 years), single status, multiple sex partners, lower socioeconomic status, with reluctance of seeking medical advice, use of intrauterine contraceptive device, previously experienced interventionary methods of endometrial biopsy or hysteroscopy or HSG (Hystero-Salpinography).

PID is a noteworthy public health problem. most of the cases go unreported and about two third of cases remained unnoticed. We are unable to determine the actual incidence of PID due to lack of reliable diagnostic techniques as well as asymptomatic nature of the disease. In United States more than one million women are affected by an episode of acute PID every year [4]. Approximately, more than 100,000 women have to put up with infertility each year [4].

Methods:

Search strategy
We searched Google Scholar, PubMed, Medline, Medscape, Cochrane. All words like Pelvic Inflammatory Disease, Infertility, sonographic evaluation, hydro salpinx, endometritis, tubal factor infertility were used.
Study selection
We studied 30 articles and then excluded prospective, case control and case reports from data. We applied additional methodological filter for paper selection and searched articles published between 2010-2020. 19 articles were selected for systematic review. Articles containing data from South Asia were preferred.

Systematic Review
In 2010 a study was conducted by Nousheen Aziz for Laparoscopic Evaluation of female factors in Infertility by a case series of all primary and secondary infertile women. It revealed 21.9% of primary and 33.3% of secondary infertility is due to Tubal Blockage (PID) (14).

In 2013 Shraddha K Shetty investigated 50 women with primary and secondary infertility for tubal disease by laparoscopy and concluded 44% of primary and 50% of secondary infertility is due to nonspecific pelvic inflammatory disease. The study revealed that ensuing incidents of PID subsequently increased the risk of infertility (5). In 2014 Zhao W.-H. conducted a retrospective analysis to spot the reason of pelvic inflammatory disease (PID) and infertility in north china. Shanxi, He stipulated 4,540 cases of infertility 1922 (42.3%) cases were distinguished with PID. His results showed incidence for nonspecific PID was 57.9% and 42.1% for Genital Tuberculosis. He concluded tubal infertility is eventual outcome of PID (6).

In 2015 a retrospective study was mediated by Babita Kumari in the Department of Microbiology, Patna Medical Collage, Patna. She selected 150 cases for this study from wards and OPD of the Department of Obstetrics and Gynecology PMCH, Patna in time period of 13 months i.e. August 2013 to September 2014. Cases with symptoms of raised temperature, chronic pelvic pain, and abnormal vaginal discharge were selected. women seeking treatment for infertility were also included who were of age group 26-35 yrs. Aspirate from pouch of Douglas and High vaginal swab were taken to examine. Study revealed that 48.24% cases were reported for PID and 55.55% for infertility illustrating strong relation with the optimum reproductive life (7).

In 2015 Jasmina Begum conducted a retrospective study of 135 patients aged of 19 -40 years at Department of Obstetrics and gynecology MGMCRl Pudcherry by combined Hysterolaparoscopy and 2nd commonly abnormality detected was Pelvic inflammatory disease i.e. 18.5% (8).

In 2016, Chayachinda Chenchit conducted a retrospective cohort study in patients hospitalized with pelvic inflammatory disease (PID) and predicted the prevalence of adverse reproductive outcomes in them. The criteria for this study was sexually active aged 14–40 years’ women admitted with PID or Tubo ovarian abscess for a period of 7 years from January 2004 to December 2011.

69 [IQR 51–93] months duration follows up unfolded that out of 94 patients, 24 (25.5%) linked up to the criteria of infertility, 15 (16.0%) suffered recurrent PID and 13 (13.8%) experienced chronic pelvic pain. For live births the only negative predictor factor was TOA (aOR 0.23, 95%CI 0.07–0.79, p = .019) (9).

A retrospective study was conducted by Sairem Mangolngabi Chanu, for duration of 2 years i.e. July 2014 to June 2016. He evaluated 151 patients and presumed primary and secondary infertility 58.28% and 41.72% respectively. Abnormal findings were assessed in 37.5% of primary infertility group and 49.2% of secondary infertility group. Adnexal adhesions (pelvic inflammatory disease) were most common finding (10).

In 2017 KHOURI described Ultrasound is considered first line imaging modality in the evaluation of fallopian tubes and techniques to distinguish between chronic and acute pelvic inflammatory disease as well as infertility. He also mentioned employing modern ultrasonography such as color Doppler and three dimensional imaging and salpingocentesis in clinical practice (11).

Dr Rahat Akhtar conducted a cross sectional study in department of Obstetrics and Gynecology Nishter Hospital Multan in 2017 on sub-fertile women to know THE factors frequently leading to tubal impetency. Pelvic vaginoscopy was assigned for evaluation and 27.4% patients of infertility were summed up due to Pelvic inflammatory disease (12).

In 2017, Nafeesa Binti Hussain from BGC Trust Medical College Department of Obstetrics & Gynecology, Chittagong in 2017 conducted a study on infertile women of reproductive age over one-year period. It was an interesting effort to diarize TVS findings in patients complaining infertility. Among the 100 cases 75% cases were documented with primary infertility and 25% with secondary infertility. Out of 100 cases undergone TVS study illustrated results were as following, chronic pelvic inflammatory disease was 14(14%)of cases, free fluid in pelvic/abdominal cavity was in 7 (7%) cases, while 5(5%) showed endometritis, tubo-ovarian mass was 2(2%) and 2% share was from intrauterine and intra pelvic adhesions (13).

C Casper D J den Heijer in 2019 conducted retrospective study at Clinical Practice Research Datalink GOLD database, 2000-2013.12-25 years aged women were specified who had previous Chlamydia trachomatis (CT) diagnosis. Objective of the study was to estimate the risk of pelvic inflammatory disease (PID) infertility and ectopic pregnancy due to this infection.857324 women were analyzed on the basis Chlamydia Trachomatis test. The study divulged that risk of PID is increased in CT-positive women (adjusted hazard ratio [aHR], 2.36; 95% confidence interval [CI], 2.01 – 2.79) with the consequence of infertility (aHR, 1.85; 95% CI, 1.27-2.68) (14).
In 2020 Afshan Majeed conducted a study in Quetta that the difficulty to conceive is seen as a major problem among families especially in Pakistan. The study was designed to get the measure of different causes of female infertility in different ethnic groups of Baluchistan, using ultrasonography technique and supporting information. 100 infertile females of the age ranging from 20-45 yrs were divided into 5 groups with difference of 5yrs i.e. 20-25and so on. Her study deduced that diagnostic Ultrasonography is worthwhile and instructive to find the causes, analysis and to administer the treatment of female infertility. Study showed that the Tubal factor infertility which is blocking of fallopian tubes, is one the most common cause of females to not conceive and recognized in approximately 30%-35% of women putting up with infertility. The most prevailing rationale of tubal factor infertility is pelvic inflammatory disease (PID) (15).

In 2017 Patrik M Bavoil presented an interesting hypothesis based upon recent, historical and circumstantial evidences that prevalence of Chlamydia trachomatis is increasing due to rising practice of oral sex as the infectious organism produced in GI tract and reached to rectum. It can infect female urogenital tract by its chronic contamination which may lead to serious sequelae of Chlamydia infection in women i.e. pelvic inflammatory disease eventually resulting in tubal factor infertility (19).

Discussion
PID is a dynamic problem and continuous increase in the number is observed from 2009-2012, in acute cases of PID early diagnosis and intervention is drastically important (17). Because endometrial secretary transformation is violated in patients with infertility associated with pelvic inflammatory disease (16).

The long term complications of PID were linked with disease severity, delay in treatment and recurrence of infection. Repeated episodes worsens the sequel of PID so important goal is prevention of recurrent PID (17).

Clinicians should get alert for adequate long term care and cure of PID and TOA due to elevated prevalence of its adverse sequel. (8)
Chlamydia and gonorrhea are the most common known causes of PID. Annual screening of chlamydia and gonorrhea should be practiced to avert PID that may eventually reduce the burden of infertility (18).

Patient education about personal hygiene, proper sanitation and cleanliness is necessary. Public health interventions to use of adequate measures for intra uterine contraceptive devices and sex education play a role to reduce rate of PID (1).

Conclusion
Infertility was reported 4 fold higher prevalent among women of 18-29 years of age group with history of PID (18) so special attention should be paid by health authorities towards its early diagnosis and prevention (3). Such potential cost-effective approaches should be implemented which could be employed in real-world settings (1).

Acknowledgements
The authors are grateful to the institute of Radiological Sciences and Medical Imaging Technology, University of Lahore.

Compliance with Ethical Standards
There is no violation of human or animal rights.

Recommendation:
A strong requisite is documented for further involvement and progress of diagnostic and interventional ultrasonography for the early diagnosis and cure for PID.

Conflict of Interest
Authors confirm that this manuscript has no conflict of interest.

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