EJMO

DOI: 10.14744/ejmo.2024.37551
EJMO 2024;8(1):9–14

Review

Acute Pelvic Inflammatory Disease

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Abstract

Pregnant women of reproductive age continue to be a major public health concern. It is linked to serious long-term consequences such as tubal factor infertility, pregnancy, and persistent pelvic discomfort. Furthermore, the treatment of acute PID and its consequences incurs significant healthcare expenses. Preventing these long-term consequences requires doctors to have a high index of suspicion in order to make an early diagnosis and devise treatment methods based on the understanding of the microbiologic etiology of acute PID. A polymicrobial infection is widely regarded as the cause of acute PID. In many cases, sexually transmitted organisms such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are present, while microbes from the endogenous vaginal and cervical flora are usually associated with PID. This comprises anaerobic and facultative bacteria, which are related to bacterial vaginosis. *Mycoplasmas* of the vaginal tract, most notably *Mycoplasma genitalium*, have lately been linked to acute PID. As a result, treatment regimens for acute PID should include wide spectrum coverage that is effective against these pathogens.

Keywords: Pelvic inflammatory disease (PID), Genital tract inflammation, Sexually Transmitted Disease (STD).

Cite This Article: *Dolui S, Manna S, Mandal A. Acute Pelvic Inflammatory Disease. EJMO 2024;8(1):9–14.*

A serious sexually transmitted disease known as pelvic inflammatory disease. Usually affects sexually active female adolescents and young adults.[1] Every year, around 800,000 US women are diagnosed with PID or pelvic inflammatory disease. The US Centres for Disease Control and Prevention (CDC) project that more than a million women experience an episode of PID each year, taking into account any occurrences of PID that have gone unreported. The prevalence of PID is concerning given its serious potential effects, which include tubal fertility issues, ectopic pregnancy, and chronic pelvic pain (CPP). There is a higher risk of PID-related complications when PID instances are ignored, misdiagnosed, or improperly or poorly handled.[2] The sexually transmitted pathogens *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (GC), in particular, are estimated to represent the root of more than 85% of PID cases. *Haemophilus influenza, Gardnerella vaginalis*, and anaerobes like *Peptococcus* and *Bacteroides species* are additional microbes linked to PID. A sexually engaged woman at risk of STDs should begin presumptive antibiotic therapy if PID is suspected based on the minimal clinical criteria, according to the CDC's suggested diagnostic criteria: motion discomfort in the cervical region, adnexal soreness, or uterine tenderness.[3] In the NHANES 2013-2014, the rate of self-reported lifelong PID was 4.4% among 1,171 sexually active reproductive-age women. This suggests that approximately 2.5 million women in the country between the ages of 18 and 44 have ever received a PID diagnosis (95% CI = 1.8-3.2 million). In order to ascertain the incidence of self-reported PID in a nationally representative population, our studies made use of data from the NHANES' 2013–2014 cycle.[4] Significant progress has been made in the past 25 years in

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Submitted Date: October 17, 2023 **Revision Date:** November 29, 2023 **Accepted Date:** January 21, 2024 **Available Online Date:** March 06, 2024

understanding acute PID pathophysiology, etiology, and therapy. As a result, our strategy for treating acute PID has undergone significant paradigm modifications. In the past, *Neisseria gonorrhoeae* was thought to be the sole causative agent of PID. Today, a wide range of antibiotic regimens are used to treat acute PID since the polymicrobial etiology of PID is well documented.[5]

Definition: The term "pelvic inflammatory disease" (PID) refers to the acute clinical state brought on by an infection of the endometrium, fallopian tubes, and/or surrounding structures by germs that have ascended from the cervix and/or vagina. *Neisseria gonorrhoeae (N. gonorrhoeae)* and/or *Chlamydia trachomatis (C. trachomatis)* infections of the lower vaginal tract, which then spread to the uterus, fallopian tubes, and ovaries, are frequently the cause of this condition. Various vaginal-cervical endogenous bacteria cause PID to frequently develop into a polymicrobial infection.[6]

Epidemiology: In the U.S., about one million PID cases are diagnosed annually, with adolescent females accounting for about one-third of those instances. Initial PID office visits have been steadily declining until 2014 when a growing trend was noted. Due to variations in monitoring among nations and areas, variations in the prevalence of PID, and the difficulty of telling cervicitis from overt PID, obtaining precise PID epidemiologic data can be problematic.[7]

Microbial Aetiology: PID typically happens when bacteria infect the uterus, fallopian tubes, and ovaries after ascending from the lower genital tract.[8]

The etiology of pelvic inflammatory disease involves the following factors:

- Bacterial migration: Microorganisms that infect the cervix cause damage to the endocervical canal and the disintegration of the mucus plug, which helps the infection progress.[8]
- Sexually transmitted infections (STIs): *N gonorrhea* was the pathogen that was most frequently isolated in early PID research, and it continues to have a higher propensity to produce severe symptoms than other infections.[8]
- Other organisms: Numerous additional bacteria, including *Chlamydia trachomatis, Mycoplasma hominis, Mycoplasma genitalium*, and others, cling to spermatozoa, possibly assisting in their ascent via the genital tract.[8]
- Multiple sexual partners: The likelihood of getting STIs, particularly those that cause PID, increases when one engages in sexual activity with several partners. There is a chance of getting exposed to new bacterial strains with every new sexual partner.[9]
- Young age: PID has an increased chance of occurring in adolescents and young women. This could be caused by a number of things, such as increased cervical ectopy, which increases the cervix's susceptibility to infection by causing the cervical lining to stretch onto the vaginal section of the cervix.[9]

Pathophysiology: Classic PID is an infection that develops in the cervical-vaginal region and progresses to the upper genital tract, resulting in a constellation of symptoms such as acute salpingitis, perihepatitis, endometritis, oophoritis, pelvic peritonitis, and/or tubo-ovarian abscess. The pathogenesis is a complicated interplay of genetic, immunological, and bacterial virulence factors, and our understanding of the immunopathological routes from infection to PID and tubal scarring is insufficient at the moment.[10] The majority (60–80%) of cases of PID in people under the age of 25 are caused by STIs such as *Gonorrhea and Chlamydia*, which are the most significant causal organisms linked with PID. In order to ascend into the endometrium, fallopian tubes, and peritoneal cavity, one or both of the original infections and vaginal flora must first induce damage to the epithelium. Acute pelvic inflammatory illness is more common in women who use intrauterine devices (IUDs), however, there is no proven link between the use of an IUD and future infertility (Table 1) (Fig. 1).[11]

Clinical Presentation

Acute PID manifests as a wide range of symptoms, from over-clinical infection to unrecognized (subclinical) illness. Subclinical PID was detected in 13% of females with PID in a sample of endometrial biopsies (Table 2).[12]

Table 1. Microbes associated with in pelvic inflammatory disease[4]

Chlamydia trachomatis
Neisseria gonorrhoeae
Gardnerella vaginalis
Haemophilus influenzae
Bacteroides species (B. fragilis, bivius, disiens)
Mycoplasma genitalium
Group B streptococcus (S. agalactiae)
Coliforms (Enterobacteriaceae)
Peptostreptococcus
Streptococcus faecalis
Ureaplasma urealyticum
Neisseria meningitides
Mycoplasma hominis
Enterococcus
Cytomegalovirus
Other *anaerobes*

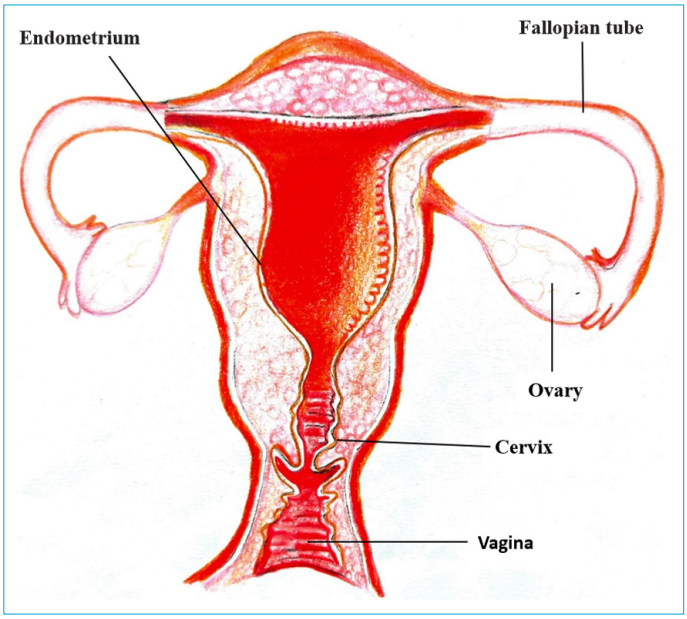

Figure 1. Female reproductive system.

Table 2. Common signs and symptoms associated with PID[12]

Common signs and symptoms associated with PID	
Symptoms	**Signs**
Lower abdomen discomfort or agony	Abdominal tenderness/guarding/ rebound
Vaginal discharge	Adnexal tenderness
Dyspareunia	Cervical excoriation
Abnormal vaginal bleeding	Raised temperature

Clinical Assessment and Differential Diagnosis

PID is difficult to diagnose since the symptoms and indications can vary greatly. Even when endometrial infection and inflammation are clearly present, pelvic discomfort, the most prevalent symptom of PID, may be minimal or non-existent in some women. The most serious form of PID is gonorrheal, whereas Chlamydial PID is more likely to be subclinical with little or no symptoms but with potentially harmful long-term effects. One-third of PID-positive females with endometrial biopsies had subclinical PID, according to the study.[13] Practically speaking, PID must be taken into consideration when a sexually active woman visits a clinic or emergency room complaining of lower abdominal or pelvic pain. Other conditions that must be ruled out include appendicitis, ectopic pregnancy, ovarian torsion, intrapelvic bleeding, rupture of an adnexal mass, endometriosis, and gastroenteritis. The criteria included in both the Australian STI Management Guidelines and the European Guideline for the Management of PID served as guidance for PID diagnosis.[14]

The following are important aspects of the physical examination:

- Enquiring about your medical history, sexual history, and current symptoms, as well as your overall health.
- Examining the cervix with a vaginal speculum and checking for friability and cervical discharge with a mucopurulent swab.[8]
- BV, leukorrhea, and/or Trichomonas vaginalis are all examined microscopically in a sample of cervical vaginal discharge.[8]
- Examine the patient manually for cervical mobility, uterine or adnexal tenderness, and pelvic lumps.[8]

Laboratory Testing: Since PID is a clinical diagnosis, test results or imaging procedures are often not required but may be useful in making the diagnosis or determining the severity of the condition. Sometimes excessive white blood cell (WBC) levels are useful in confirming an acute PID diagnosis. However, leukocytosis is seen in only 60% of individuals with acute PID.[14] A high leukocyte count (10,000 cells/mL) exhibited a 41% sensitivity and 76% specificity for the presence of endometritis in the PEACH study, which included women who had pelvic discomfort, stomach pain, and signs of lower genital tract inflammation.[15]

Imaging Studies: Additionally, PID can be directly treated using ultrasonography as a diagnostic tool. Among women with clinically confirmed PID, a finding of thicker, fluid-filled tubes provides an 85% sensitivity and 100% specificity for endometritis.[8] When doing interventional treatment to drain pelvic abscesses, computed tomography (CT) should only be used to gauge the severity of this infection in the abdominal cavity.[16]

- Other Diagnosis Tests
- Blood Test
- Urine Test
- Ultrasound Test
- Testing for STIs.
- Laparoscopy
- Endometrial Biopsy

Pelvic Examination: During a pelvic exam, your doctor puts two gloved fingers within your vagina. Your physician can inspect your uterus, ovaries, and other organs while pressing down on your belly (Fig. 2).

Specificity of CDC Diagnostic Criteria:

In accordance with the Centres for Disease Control and Prevention's (CDC) guidelines, PID is clinically diagnosed.

Minimum diagnostic criteria is given below (Table 3):

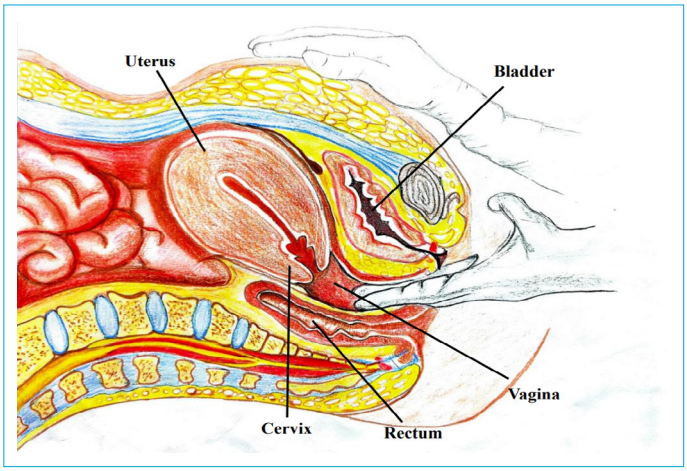

Figure 2. Pelvic Examination.

Treatment of Acute PID: The creation of efficient treatment plans is necessary to prevent the serious long-term effects linked to PID. Although PID may be asymptomatic, it is important to have a quick diagnosis and follow recognized methods such as those recommended by the WHO in 2001 or the CDC in 2015. Additionally, accelerated partner treatment (EPT) principles are recommended. PID frequently results in irreparable damage to the female reproductive system; as a result, immediate antibiotic therapy is required to avoid any scarring of the reproductive tract.[18] Once a PID presumptive diagnosis has been obtained, empirical therapy should start. The CDC advises hospitalization for certain patient subgroups, such as pregnant women, those who do not respond well to outpatient antibiotic therapy, those who cannot tolerate an outpatient oral regimen, women who have a severe illness, such as nausea and vomiting or a high fever, and those with tubo-ovarian abscesses. Broad-spectrum antibiotics are used in the treatment of PID in accordance with CDC recommendations (Table 4).[19]

The following medicines were included in these in-patient regimens:

- Clindamycin and aminoglycosides (clinical cure rate 92%, microbiological cure (97%).
- Doxycycline with cefoxitin (clinical cure 93%, micro-biological cure 98%).
- Doxycycline with cefotetan (clinical cure 94%, microbiological cure 100%).
- Ciprofloxacin has a 94% clinical cure rate and a 96% microbiological cure rate.

Prevention: Over the past few decades, a number of STI/PID testing programs have been used globally, such as the yearly *C. trachomatis* screening program that the U.S. has advised. In order to reduce the incidence and consequences of PID, gonorrhea and chlamydia infections should be screened for and treated as they account for more than half to three-quarters of PID. Preventing PID often falls under one of two categories: 1) preventing the initial PID episode; and 2) preventing the disease from returning. Given the link between recurrent STIs like C. trachomatis and infertility, women who have experienced one episode of PID should take precautions against STI infection.24 Early STI detection is necessary for PID prevention, which calls for enhanced provider adherence to CDC and US Preventive Screening Task Force recommendation.[20] In a managed care organisation, over 1000 women

Table 3. Specificity of CDC Diagnostic criteria[17]

CDC criteria for PID diagnosis		
Minimum Requirements (At Least 1 Is Required for Diagnosis)	**Additional Requirements (Support PID Diagnosis)**	**Final Requirements (Confirm PID Diagnosis)**
• Discomfort in the cervical motion	• A fever in the mouth more than 101F/38.3C	• Endometritis is shown histopathologically.
• Uterine tenderness	• Abnormal discharge from the cervix or vaginal area	• Imaging demonstrating thicker, fluid-filled tubes, with or without pelvic free fluid or the tubo-ovarian complex
• Adnexal tenderness	• White blood cells on a wet saline mount (>10 polymorphonuclear leukocytes per high-power field)	• Doppler investigations reveal a pelvic infection.
	• Higher than normal erythrocyte sedimentation rates (>15 mm/h)	• Laparoscopy revealed intra-abdominal abnormalities compatible with PID.
	• Elevated C-reactive protein	
	• Elevated white blood cell count higher than 10,000 cells/mL	
	• laboratory proof of Chlamydia trachomatis or Neisseria gonorrhoeae infection	

Adapted from Workowski KA, Berman S. Sexually transmitted diseases treatment guidelines, 2010. MMWR Recomm Rep 2010;59 (RR-12):1–110.

Table 4. CDC PID treatment recommendations for 2015, including antibiotic regimens[19]

Parenteral treatment	
Regimen A	Cefotetan 2 g IV every 12 hours in addition to doxycycline 100 mg PO or IV every 12 hours
Regimen B	Doxycycline 100 mg PO or IV every 12 hours in addition to Cefoxitin 2 g IV every 6 hours
Regimen c	Clindamycin 900 mg IV every 8 hours and gentamicin 2 mg/kg loading dose IV or IM followed by 1.5 mg/kg every 8 hours (can substitute single daily dosage of 3–5 mg/kg)
Alternate Regimen	Doxycycline 100 mg orally or intravenously every 12 hours in addition to 3 g of ampicillin/sulbactam every 6 hours
Oral treatment	
Regimen A	Metronidazole 500 mg PO BID for 14 days + Ceftriaxone 250 mg IM in a single dosage + Doxycycline 100 mg PO BID for 14 days.
Regimen B	Doxycycline 100 mg PO BID for 14 days, metronidazole 500 mg PO BID for 14 days, and Cefoxitin 2 g IM and probenecid 1 g PO in a single dosage.
Regimen c	Doxycycline 100 mg PO BID for 14 days, followed by 14 days of metronidazole 500 mg PO BID, all as part of a third-generation cephalosporin

Reproduced from the 2015 CDC Treatment Guidelines for Sexually Transmitted Diseases. Department of Health and Human Services, Atlanta, Georgia; 2015.3 Trials have demonstrated the short-term therapeutic efficacy of azithromycin 500 mg IV daily for one or two doses with 250 mg PO for five to six days, alone or in combination with a 12-day course of metronidazole. Following any signs of clinical improvement, parenteral regimens should be continued for 24 hours before switching to an oral regimen to finish the 14-day treatment period. CDC stands for the US Centres for Disease Control and Prevention; BID stands for twice daily; PID stands for pelvic inflammatory illness. IM stands for intramuscular. By mouth, PO.

were compared to over 1600 women getting standard care after being randomly assigned to receive an invitation for a chlamydia screening. Medical professionals may also advise screening using a "self-taken swab" that is performed by the individual being tested, in which case nucleic acid amplification technology is used to examine the swab in order to identify both C. trachomatis and *N. gonorrhea*. The Prevention of Pelvic Infections (POPI) experiment, conducted most recently in England, recruited sexually active women under the age of 27 and randomly assigned them to early or delayed chlamydia screening. the first screening group, chlamydia prevalence was 5.4%, and during the course of the trial, 15 of 1191 people (1.3%) developed PID. 5.9% of those in the delayed group tested positive for chlamydia a year after their enrolment swab was checked.[21]

Awareness: Adolescents are much more at risk of acquiring PID and its accompanying difficulties, according to research on PID in younger groups. One study found that adolescents and young women between the ages of 17 and 21 were twice as likely to be diagnosed with PID as other age groups, with women under the age of 19 accounting for one in five instances of PID. Adolescents are likely to have a secondary, increased risk of PID due to a confluence of behavioural and biological variables. Teenagers had a higher propensity for several sexual partners, short-lived, and frequently monogamous partnerships.[21]

Conclusion

The adverse reproductive effects linked to acute PID must be avoided or at least minimised, which calls for early identification and appropriate antibiotic therapy. To achieve these objectives, doctors must grasp the vast range of clinical symptoms in acute PID, have a high level of suspicion for the diagnosis, and be familiar with the polymicrobial aetiology of acute PID.

The polymicrobial character of this infection should be taken into consideration when developing treatment plans for women having acute PID. N. gonorrhea, C. trachomatis, anaerobic and aerobic bacteria typical to the endogenous vaginal flora, and genital mycoplasmas, notably *M. genitalium*, are among the microorganisms found in the upper genital tract of women with acute PID. The CDC does not advise coverage for *M. genitalium*, despite the fact that its potential function is yet unknown.[2] These needs can be satisfied by a number of antibiotic regimens (Table 3).

Disclosures

Acknowledgments: Our foremost acknowledgment goes to Indian Academy Degree College Autonomous, Bengaluru, India.

Ethics Committee Approval: Ethics committee approval was not requested for this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

Authorship Contributions: Concept – S.D.; Supervision – S.D.; Literature search – S.D., S.M., A.M.; Writing – S.D.; Critical review – S.D., S.M., A.M.

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