

Pelvic Inflammatory Disease (PID) Management in *Corona Virus Disease 2019 (COVID-19)* Pandemic Era

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Abstract

Objective: This article aims to review pelvic inflammatory disease management during the coronavirus disease 2019 pandemic

Method: We conducted a search for scientific articles through PubMed and Google Scholar, using the terminologies of “PID AND COVID-19”, “Pelvic Inflammatory Disease”; “Pelvic Inflammatory Disease AND COVID-19”, “PID Management AND COVID-19”, “Pelvic Inflammatory Disease Management AND COVID-19”, and “PID AND Pandemic” in English and Indonesian from 2019-2020.

Result: There were a total of 25 scientific articles from PubMed and Google Scholar within 2019-2020 that were included as the source of this review

Conclusion: There is no difference between the management of pelvic inflammatory disease during and before the pandemic. The mode of medical services and follow up tends to be conducted virtually. Technology-based services for pelvic inflammatory disease during the corona virus disease 2019 pandemic are promising and have been proven to be an effective method, therefore virtual-based pelvic inflammatory disease services may be safely applied. However, if there is any indication of emergency found during the telemedicine services, a face-to-face consultation or emergency room visit should be recommended.

Key words : COVID-19, Pelvic Inflammatory Disease, SARS-CoV-2

Tatalaksana Radang Panggul selama Era Pandemi Virus Corona 2019 (COVID-19)

Abstrak

Tujuan: Melakukan kajian mengenai tatalaksana dari penyakit radang panggul selama pandemi penyakit *coronavirus* 2019

Metode: Kami melakukan pencarian artikel ilmiah melalui PubMed dan Google Scholar menggunakan terminologi “PID AND COVID-19”, “Pelvic Inflammatory Disease”; “Pelvic Inflammatory Disease AND COVID-19”, “PID Management AND COVID-19”, “Pelvic Inflammatory Disease Management AND COVID-19”, and “PID AND Pandemic” dalam Bahasa Inggris dan Indonesia dari tahun 2019-2020.

Hasil: Ditemukan sebanyak 25 publikasi ilmiah dari pencarian di PubMed dan Google Scholar pada tahun 2019-2020 yang digunakan sebagai sumber kajian ilmiah ini.

Kesimpulan: Tatalaksana penyakit radang panggul sebelum dan selama pandemi tidak berubah. Metode pelayanan kesehatan dan *follow up* cenderung dilakukan secara virtual. Pelayanan kesehatan berbasis teknologi untuk penyakit radang panggul selama pandemi penyakit *coronavirus* 2019 menjanjikan dan telah terbukti sebagai metode yang efektif, sehingga pelayanan kesehatan untuk penyakit radang panggul secara virtual dapat diaplikasikan secara aman. Jika ditemukan adanya indikasi kegawatdaruratan selama pelayanan *telemedicine*, pasien sebaiknya melakukan konsultasi tatap muka atau mengunjungi instalasi gawat darurat.

Kata kunci : COVID-19, penyakit radang panggul, SARS-CoV-2

Introduction

Coronavirus Disease 2019 (COVID-19) is a recent disease which spread globally and has been announced as a pandemic by the World Health Organization (WHO). The disease was reported for the first time in Wuhan, Hubei province of China at the end of 2019. The agent of this disease is a virus named *Severe Acute Respiratory Syndrome-Corona Virus-2* (SARS COV-2). This agent has a similar structure with the causative agent of previous SARS and *Middle East Respiratory Syndrome* (MERS) disease. Clinically, the disease mostly appears as a respiratory tract infection and acute lung infection such as pneumonia. In Indonesia, COVID-19 was reported for the first time in February 2020.^{1,2}

Epidemiology studies found that this pandemic carries a high incidence and fatality rate. Based on online data, until September 19th, 2020 globally, 30.685.257 people have been infected with the fatality rate of 4%. Among them, nearly a quarter of cases were in the United States of America. While in Indonesia, the incidence until the same date was 236,519 people and the fatality rate was 3.9%, similar to global mortality rate. Recent active cases were 99% mild to moderate; only 1% was critical disease.³

Case definition in Indonesia has been changed over the time. At the beginning, the disease was classified clinically and based on the history of contact into asymptomatic people, people under observation, and patient on monitoring. Nowadays, it has been classified into suspect, probable, and confirmed, following the classification of WHO. Other classification is based on the need of treatment into mild, moderate, and severe. The severe cases are associated with Acute Respiratory Disease Syndrome (ARDS) or cytokine storm. The elderly and patients with cardiorespiratory or metabolic comorbidities have a higher risk to develop into this severe disease.^{1,2,4,5}

The virus is transmitted mainly through respiratory droplets and close contact. The wide clinical spectrum of the disease, especially asymptomatic infected people may make the transmission easier.⁴ As it is transmitted easily, medical service is the setting with high risk of transmission.

One of the common problems that leads patients to seek medical care in everyday medical practice is Pelvic Inflammatory Disease (PID). PID is prevalent among sexually active people. About 1 million cases of PID were diagnosed in USA every year and twenty percent or more involved adolescent.⁶ For the reason of transmission, the pandemic has changed the pattern of life widely.

Medical services are considered as high risks settings of transmissions so, all of the medical services must follow the health protocols that were made locally or nationally. These protocols were made in order to prevent the risk of transmission to both the medical staffs and patients. Therefore, this article aims to review about management of pelvic inflammatory disease in COVID-19 era.

Method

This review was based on scientific articles found through PubMed and Google Scholar with a time frame from 2019 through 2020.

Terminology used in scientific articles search are "PID AND COVID-19", "Pelvic Inflammatory Disease"; "Pelvic Inflammatory Disease AND COVID-19", "PID Management AND COVID-19", "Pelvic Inflammatory Disease Management AND COVID-19", and "PID AND Pandemic" in English and Indonesia language. There were a total of 25 scientific articles found and included in this review.

Results

PID is a clinical course which results from an ascending infection from endocervix to upper

reproductive organs which may develop into oophoritis, salpingitis, endometritis, parametritis, tubo-ovarian abscess, or even more severe into pelvic peritonitis.^{7,8}

There are numerous causative agents of PID known. Those agents are *C. trachomatis*, *N. gonorrhoeae*, *Gardnerella vaginalis*, Group B *Streptococcus* (*S. agalactiae*, *Neisseria meningitidis*, *Mycoplasma genitalium*, *Mycoplasma hominis*, *Bacteroides species* (*B. fragilis*, *B. bivius*, *B. disiens*), *Streptococcus faecalis*, *Ureaplasma urealyticum*, *Haemophilus influenzae*, *Coliforms* (*Enterobacteriaceae*), *Enterococcus*, *Cytomegalovirus*, *Peptostreptococcus*, *Other anaerobes*.^{7,8}

Generally, *Chlamydia trachomatis* or *Neisseria gonorrhoeae* are the most prevalent agents. *Chlamydia trachomatis* accounts for about 14-35% of cases and 25–50% for *Neisseria gonorrhoeae*. Interestingly, those two common agents are less likely to be found in older women.⁷

Clinical symptoms suggesting to the diagnosis of PID are pain on lower abdomen (typically bilateral), dyspareunia (commonly deep), abnormal cervical or vaginal discharge (often purulent), abnormal vaginal bleeding such as menorrhagia, inter-menstrual bleeding, post-coital bleeding and secondary dysmenorrhea. History of sexual activity that should be noticed includes new partner, contraception used, and menstrual period history.⁸

The signs commonly found were fever (>38°C) (more common in moderate to severe cases), adnexal tenderness on bimanual vaginal examination or cervical motion tenderness, and lower abdominal tenderness (usually bilateral).⁸

PID can be symptomatic and asymptomatic. The positive predictive value of clinical diagnosis is only 65-90% compared to laparoscopic diagnosis.⁸ Absence of vaginal or endocervical pus cell 95% excludes the diagnosis of PID, but its

presence has poor positive predictive value.⁹ Ultrasound (US) examination may be helpful in confirming abscess and hydrosalpinx, but lack significance for uncomplicated PID.¹⁰ Increase of blood flow in doppler US is associated with infection but less specific. MRI and CT scan are preferred to exclude other causes, but not routinely indicated.⁸

Pregnancy and other causes should be excluded first before confirming the diagnosis and starting the treatment. Some differential diagnosis should be taken into consideration such ectopic pregnancy, complication of an ovarian cyst, acute appendicitis, endometriosis, urinary tract infection, irritable bowel syndrome, and functional pain.⁸

Delaying the treatment for PID is associated with an increased risk of ectopic pregnancy, infertility, and pelvic pain. Aerobic and anaerobic bacteria are usually isolated from upper genital tract with PID. Therefore, broad spectrum antibiotics are required to cover those agents.⁷

In outpatient setting, the regimen of 1 gram ceftriaxone intramuscularly (single dose) followed by metronidazole 400 mg every 12 hours and doxycycline 100 mg every 12 hours for 14 days orally is recommended. Second line regimen includes ofloxacin and metronidazole or moxifloxacin only orally for 14 days. For pregnant and breastfeeding women, parenteral therapy is advised although no evidence has proven its safety. Ceftriaxone, erythromycin, and metronidazole intravenously may be recommended, followed by two weeks completion after clinical response. But, in early pregnancy antibiotic administration has to outweigh between risk and benefit.⁶⁻⁸

Some complications may develop such as adhesion, abscess, peritonitis and severe pelvic infection. In this case, surgical management may be needed to perform adhesiolysis and draining the pelvic abscess. Laparotomy and laparoscopic surgeries are

commonly done.⁷

COVID-19 is infection disease caused by SARS COV-2. The disease has been spreading globally since early 2020. This agent was firstly identified in China on the end of 2019.¹⁻³ The causative is a single stranded RNA virus, not only found in human but also in other mammals. This virus belongs to the coronavirus family which causes respiratory, gastrointestinal, and neurological diseases.¹¹

During early infection, the targeted cell is nasal epithelial, bronchial epithelial, and pneumocytes. Infection occurs through the binding between the structural spike protein (S) of virus and *Angiotensin-Converting Enzyme-2* (ACE-2) receptor. *Type 2 transmembrane serine protease* (TMPRSS2) of host cell cleaves ACE-2 and activates the SARS-CoV-2 S protein that promotes the entrance of virus into host cell.¹¹

Respiratory droplet and close contacts are the main transmission routes. According to the report from WHO, SARS-COV-2 spread through the nasal and oral droplets. It is capable to float in the air (in form of aerosol).¹¹ Some evidences reveal oral-fecal transmission of pathogen. This evidence is supported by the findings of virus on fecal specimen and gastrointestinal manifestation of COVID-19.¹²⁻¹³ Prolonged exposure by infected patient (more than 15 minutes within 6 feet) or shorter time for symptomatic patient are associated with a higher risk of transmission.¹¹ In inanimate surfaces, the virus was found to remain red for some days. The virus has been identified for 3–4 days after inoculation in permeable surface. However, the virus decays rapidly within 24–48 hours.¹⁴

The incubation period varies from 2–14 days with a median period of 5-6 days. Viral shedding begins two until three days prior to onset of symptoms and the peak of viral load in upper respiratory tract is around the onset of symptoms.¹⁴

COVID-19 has a wide spectrum of

clinical severity. According to its severity, 81% were mild, 14 were severe, and 5% have critical manifestation (such as multiple organ failures, septic shock, and respiratory failure).¹⁵

The symptoms which appeared were fever (up to 90%), shortness of breath (53%–80%), dry cough (60%–86%), fatigue (38%), myalgia (15%–44%) and nausea, or vomiting or diarrhea (15%–39%).¹¹ Anosmia and ageusia maybe an atypical sole symptom in 3% of patients.²

Most of the hospitalized patients are associated with the patients' comorbidities. Twenty five percent of infected patients have comorbidity/s, but on the hospitalized, patient they account for 60%–90% of cases.¹¹

The standard diagnosis of COVID-19 is based on RT-PCR SARS-CoV-2 RNA detection from isolated virus on respiratory sample. The sensitivity of this method was around 33% until 80%, varies accordingly to the clinical course. Higher sensitivity was observed on the third day of onset.¹¹ Sample from bronchoalveolar lavage has a higher sensitivity compare to sputum, nasal swab, and pharyngeal swab samples.¹¹

Serological tests may assist on directing the diagnosis. However, this examination is doubted and the test performance, accuracy, and validity are variable. The presence of this antibody does not guarantee protection because not all of the antibodies produced have a neutralizing effect.¹¹

Laboratory findings include elevated C-reactive protein, lymphopenia, mild thrombocytopenia, prolonged prothrombin time, elevated D-Dimer value, and elevated liver function test. Meanwhile for imaging, the typical characteristic of COVID-19 is diffuse, peripheral ground glass opacity.¹⁶

There are two targets in managing COVID-19; supportive care (respiratory support) and targeting the virus (and the host response). Reason for the first target is that more than 75% hospitalized patients need

oxygen supplementation. Patients that are unresponsive to conventional oxygen therapy, may need heated high-flow nasal canula or intubation. Low pressure 4–8 ml/kg (based on predicted body weight) and less than 80 mmHg of plateau pressure is recommended.¹⁷

The second target of therapy is the virus itself and the host response.

Antiviral (such as remdesivir), targeted immunomodulatory therapies (e.g. Tocilizumab), anti-inflammatory agents (eg. Dexamethason), antibody (e.g Convalescent plasma), anticoagulant (e.g Heparin), and antifibrotics (e.g Tyrosine kinase inhibitor) are used in clinical practice. Each modality has a different efficacy in every stage of disease. Viral inhibitor may more effective in early infection, immunomodulatory agent may benefit for preventing the disease progression, and anticoagulant aims to prevent thromboembolic complications.¹¹

There are wide clinical complications which occur in COVID-19. About 17%–35% need to be treated in Intensive Care Unit (ICU). The most common indication is respiratory failure. Other complications that may occur are acute kidney injury (9%), liver dysfunction (19%), bleeding and coagulation (10%–25%), and septic shock (6%).¹¹

In this Pandemic Era, primary care and outpatient care are always held with minimal contact in order to prevent the risk of transmission. As the technology rapidly grows and its services are widely available in the society, digital care may be a promising alternative to deliver health services.¹⁸

The transformation of this tele-health has a multitude of barrier such as reimbursement system, accreditation and also the human factors. A report in USA said that only one fifth of states need payment parity between telemedicine and in-person services. The other challenges in performing this system is the maturation of technology used and the regulation for data protection and privacy.¹⁹ A large study may be needed to evaluate its

effectiveness and efficiency.

In addition, Artificial Intelligence (AI) may also be a potential solution for diagnosis and treatment of COVID-19. AI has been used to extract knowledge of drug that may be advantage as the treatment of COVID-19. If the pandemic is prolonged and continues to further, this modality is promising in delivering the health services temporarily during pandemic.²⁰ There are still limited studies regarding the use of AI in diagnosing PID, however one study in Nigeria investigated the use of AI model to diagnose PID using a set of data. It used a soft computing technique to predict the presence of PID based on the available symptoms. The accuracy of the AI program used in diagnosis PID was 96.1%, thus there may be a chance to use this technology in the future. However, further study and development of a standardized AI technology still need to be done.²¹

The emergency of PID had been decreased over the time. Kreisel et al, (2017) reported that since 2006 to 2013 PID's emergency decreased 4.3% annually. The decrease mainly occurs in upper income and less likely in non-health insurance holder.²² This data may be promising in Indonesia as this country has better economic status and national health coverage. But in opposite, as longer the pandemic exists, the higher economical issue will happen Thus, the PID will potentially increase as the pandemic goes.

Discussion

Prevention is better for community PID problem during COVID-19 pandemic.

To apply this prevention, the risk factors like targets of intervention should be known. Some risk factors of PID in the young women are issues of confidentiality, lower education, ineffectiveness of follow up the youth with PID, and the lack of interest in the youth to

sexual education that stresses safer sex and the use of condoms.⁶ These problems are the potential targets of intervention, especially in this pandemic in order to minimize health care contacts. In addition, health promotion may be easier to be conducted virtually. Nowadays, the aspect of technology devices needed to deliver this strategy is not a problem in youth. Study has found that 95% of adolescents and young adults who are sexually active have mobile phone and internet access.²³

One study of Technology-Enhanced Community Health Nursing Intervention (TECH-N) revealed a positive effect. Intervention with text messaging support and audio computer-assisted interview decreased the rate of *C. trachomatis* and *N. gonorrhoea* positivity compare to control group (rate of decrease 25.6% vs 10.4%, P=0.02). Condom use also tends to increase higher in the intervention group (15.7% to 36.6% vs 18.8% to 29.6%), even though it is not statistically significant. The adherences to standard care was also higher in the interventional group compare to the standard care group. The problem of this study is that it is conducted in younger age (18.8 ±2.5 years), so that it is still changing for older age.²³ But, trend of data of emergency visit decreases over age.

The incidence observed was higher in 15-29 years compare to older age.²⁴ There is no consensus or study found that stated a change of PID treatment in the COVID-19 era. The changes are mostly focused on the mode of medical services delivery and target of intervention, which emphasized that the prevention and follow up of PID were done virtually. The virtual-based management of PID during pandemic might not carry a significant health hazard because the rate of emergency visits was quite low (less than 1%).²¹ However, if the doctor found any emergency indication based on the telemedicine services, the patient will be recommended to have a face-to-face

consultation or to visit the emergency room immediately. Several gynaecological cases that need an emergency treatment or face-to-face consultation are suspected ovarian torsion, ectopic pregnancy, acute PID (eg. Tubo-ovarian abscess requiring surgery), and heavy vaginal bleeding. The telemedicine algorithm for gynecological cases is shown in Figure 1.²⁴

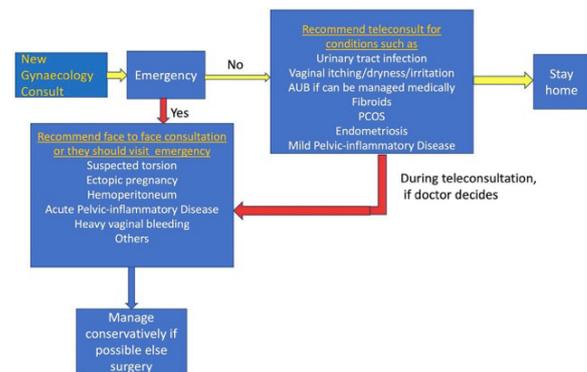


Figure 1 Telemedicine Algorithm for Gynecological Cases in COVID-19 Pandemic Era.²⁴

Conclusion

The management of PID is suitable to be done through a technology-based services in COVID-19 pandemic era due to its low rate emergency visit. PID is also more common in younger age population, most of whom already have cellphones and internet access, thus the technology-based services can be applied. However, if there is any indication of emergency found during the telemedicine services, a face-to-face consultation or emergency room visit should be recommended.

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