

# Aspirin use in obstetrics and gynecology: a comprehensive review of applications and considerations

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## ABSTRACT

*Aspirin, known for its anti-inflammatory and antiplatelet properties, has found widespread applications in Obstetrics and Gynecology. This research provides a concise overview of the multifaceted use of aspirin in these medical fields, outlining key considerations and current perspectives. In obstetrics, low-dose aspirin has emerged as a preventive strategy against preeclampsia, a hypertensive disorder with potentially life-threatening consequences for both mother and fetus. This review delves into the evidence supporting aspirin's role in preeclampsia prevention, including dosage considerations and identification of high-risk populations. Antiphospholipid syndrome (APS) and recurrent miscarriage pose unique challenges in pregnancy. The review discusses the use of aspirin, often in combination with anticoagulants, as a management strategy for these conditions, exploring the ongoing debates and evolving perspectives on its efficacy. Fertility treatments, particularly in vitro fertilization (IVF), have seen the exploration of aspirin's potential benefits in improving uterine blood flow and enhancing implantation. Additionally, this review touches upon aspirin's role in gynecological contexts, including pain relief for menstrual disorders, management of inflammatory conditions, and its potential implications in cancer prevention, especially in ovarian and endometrial cancers. In general, the review underscores the need for standardized guidelines, considering the diverse applications of aspirin in Obstetrics and Gynecology. It emphasizes the importance of individualized patient assessments to tailor aspirin therapy based on specific medical conditions and risk factors. In conclusion, this review provides a comprehensive overview of the diverse applications of aspirin in Obstetrics and Gynecology, offering insights into current perspectives, ongoing debates, and the need for further research to refine guidelines and optimize patient care.*

**Keywords:** aspirin, obstetrics, gynecology, pregnancy, prostaglandins, inhibition of cyclooxygenase (COX)

## INTRODUCTION

Aspirin, with the generic name acetylsalicylic acid, is a medication that belongs to the class of drugs known as nonsteroidal anti-inflammatory drugs (NSAIDs). It is widely used for its analgesic, anti-inflammatory, and antipyretic properties. Aspirin acts by inhibiting the production of prostaglandins, which are involved in inflammation, pain, and fever [1].

In addition to its role in pain relief and inflammation reduction, aspirin is also known for its antiplatelet effects [2]. It inhibits the aggregation of platelets, which are blood cells involved in clot formation. This property makes aspirin commonly prescribed for preventing the events that lead to the formation of blood clots.

It is important to use aspirin according to recommended dosages and guidelines, as excessive or inap-

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appropriate use can lead to adverse effects, including various type of bleeding [3].

## METHODOLOGY

### Identification of research

In the PubMed, Scopus, and Web of Science databases, the literature related to aspirin use in Obstetrics and Gynecology was searched. Search keywords: aspirin, obstetrics, gynecology, Pregnancy, prostaglandins, and inhibition of cyclooxygenase (COX).

Keywords are combined with Boolean operators (AND/OR): (“Aspirin” AND “Pregnancy” AND “Aspirin” OR “Prostaglandins” AND “Aspirin” OR “Inhibition of Cyclooxygenase (COX)” OR “Aspirin” AND “Obstetrics and Gynecology”).

Inclusion criteria: medical studies published in English, from 2012 to 2023; original quantitative studies and full-text studies on the patient's aspirin use as the population of interest.

Exclusion criteria: Studies published outside medical journals, studies published in languages other than English, and studies with limited access were excluded.

### Selected research

The studies were selected by the criteria for the literature review. Thirty-two studies were included in the current review. To prevent and reduce prejudices in the process of selecting studies, a professor in the field of Obstetrics and Gynecology was contacted. Disagreements were discussed and resolved with full agreement by both researchers.

### Pharmacokinetics and pharmacodynamics of aspirin

#### Pharmacokinetics of Aspirin

**Absorption:** The absorption process begins as soon as the aspirin reaches the acidic environment of the stomach. Aspirin is rapidly and almost completely absorbed after oral administration. The absorption occurs in the stomach and small intestine. Absorption can be delayed if the aspirin is taken with food, as the presence of food in the stomach may slow down the process [4,5].

**Distribution:** Once absorbed, the aspirin enters the bloodstream and is distributed throughout the body. Aspirin is known to cross the blood-brain barrier and the placenta, potentially affecting the central nervous system and the developing fetus [5].

**Metabolism:** Once in the bloodstream, aspirin undergoes metabolism primarily in the liver. The main metabolic pathway involves hydrolysis, where aspirin is broken down into its active form, salicylate. This active metabolite, salicylate, is responsible for many of the pharmacological effects of aspirin.

Salicylate is further metabolized in the liver by conjugation with glycine to form salicyluric acid, and with glucuronic acid to form salicyl acyl glucuronide. These metabolites are less active than salicylate and are eventually excreted in the urine.

The enzyme responsible for the hydrolysis of aspirin to salicylate is esterase. It's important to note that the metabolism of aspirin can saturate at higher doses, leading to a decrease in the rate of clearance and an increase in plasma levels of the drug [6].

**Elimination:** The elimination half-life of aspirin is relatively short, typically around 2 to 3 hours. Elimination occurs through renal excretion of the metabolites, with some elimination in the form of unchanged aspirin. The effects of a single dose can last longer due to the irreversible acetylation of platelet cyclooxygenase, impacting the platelet function for the lifespan of the platelets (7-10 days). This prolonged effect on platelets is important for aspirin's role in preventing blood clot formation [5].

Overall, the absorption and metabolism of aspirin are crucial factors in determining its pharmacokinetics and therapeutic effects. Individual variations in these processes can influence the drug's efficacy and potential side effects [4,6].

#### Pharmacodynamics of Aspirin

**Inhibition of COX Enzymes:** Aspirin irreversibly inhibits the cyclooxygenase (COX) enzymes, particularly COX-1. COX enzymes are involved in the synthesis of prostaglandins, which mediate inflammation, pain, and fever. Inhibition of COX results in reduced production of prostaglandins, leading to anti-inflammatory, analgesic, and antipyretic effects [7,8].

**Antiplatelet Effects:** Aspirin's irreversible inhibition of COX-1 has an antiplatelet effect. It prevents the formation of thromboxane A<sub>2</sub>, a prostaglandin that promotes platelet aggregation and blood clot formation. This antiplatelet effect is crucial in reducing the risk of the events leading to blood clots forming [9].

**Analgesic and Anti-Inflammatory Effects:** By reducing the production of prostaglandins, aspirin alleviates pain and inflammation. It is effective in treating mild to moderate pain and various inflammatory conditions [10].

**Antipyretic Effects:** Aspirin's ability to lower fever is attributed to its action on prostaglandins involved in the regulation of body temperature [11].

Understanding both the pharmacokinetics (absorption, distribution, metabolism, and elimination) and pharmacodynamics (effects on the body) of aspirin is essential for optimizing its therapeutic use while minimizing potential side effects. Individual variations in these processes, as well as factors like dose and frequency of administration, can impact the overall effectiveness and safety of aspirin.

## MECHANIS OF ACTION OF ASPIRIN

The mechanism of action of aspirin (acetylsalicylic acid) involves its ability to inhibit the activity of an enzyme called cyclooxygenase (COX). There are two isoforms of this enzyme: COX-1 and COX-2.

**Inhibition of Cyclooxygenase (COX):** Aspirin irreversibly acetylates (adds an acetyl group to) the COX enzymes, particularly COX-1. This covalent modification inhibits the activity of COX by preventing it from converting arachidonic acid into prostaglandins. Prostaglandins are signaling molecules in the body that play a key role in inflammation, pain, and fever.

**Anti-Inflammatory Effects:** By inhibiting COX-1 and COX-2, aspirin reduces the production of prostaglandins. Prostaglandins are responsible for promoting inflammation, causing pain and swelling. Therefore, by suppressing their synthesis, aspirin exerts anti-inflammatory effects.

**Analgesic Effects:** The reduction in prostaglandin levels leads to a decrease in pain perception. Aspirin is effective in relieving mild to moderate pain, such as headaches, muscle aches, and joint pain.

**Antipyretic Effects:** Aspirin's inhibition of prostaglandins also helps to lower fever. Prostaglandins play a role in the regulation of body temperature, and by reducing their production, aspirin helps bring down elevated temperatures.

**Antiplatelet Effects:** Aspirin's acetylation of COX-1 also has an antiplatelet effect. Platelets play a crucial role in blood clotting, and aspirin's antiplatelet action makes it useful in preventing the formation of blood clots. This property makes aspirin commonly prescribed for preventing the events that lead to the formation of blood clots.

It's important to note that the irreversible inhibition of COX by aspirin distinguishes it from other NSAIDs, which typically exert reversible inhibition. Aspirin's effects on COX last for the lifespan of the platelets which is about 7-10 days, leading to its classification as an irreversible COX inhibitor [7,8,12-14].

## ASPIRIN USE IN OBSTETRICS AND GYNAECOLOGY

Aspirin has several applications in Obstetrics and Gynecology, and its use is based on its pharmacological properties, particularly its antiplatelet and anti-inflammatory effects [9,15].

Low-dose aspirin (typically 81 mg/day) is prescribed to women at high risk of developing preeclampsia. This preventive use is usually recommended for women with a history of preeclampsia, chronic hypertension, renal disease, diabetes, or multiple gestations.

Some studies suggest that aspirin may be beneficial in certain cases of recurrent miscarriage, particularly when associated with antiphospholipid syndrome (APS). Antiphospholipid antibodies can increase the risk of blood clots, and aspirin's antiplatelet effects may be helpful.

Women with antiphospholipid Syndrome (APS), a condition characterized by abnormal blood clotting, may be treated with aspirin to prevent blood clots and improve outcomes in pregnancy.

Aspirin is sometimes used in fertility treatments, particularly in women undergoing in vitro fertilization (IVF). It is thought that aspirin may improve blood flow to the uterus, potentially enhancing implantation.

Aspirin can be used for pain relief and fever reduction in women experiencing menstrual pain (dysmenorrhea) or other gynecological conditions associated with inflammation.

The applications of aspirin in Obstetrics and Gynaecology will be specifically described below [9,15,16].

### Aspirin use in obstetrics

The use of aspirin in obstetrics is often aimed at preventing or managing certain pregnancy-related conditions.

#### Prevention of Preeclampsia

Preeclampsia is a hypertensive disorder that can occur during pregnancy and is characterized by high blood pressure and damage to organs. Low-dose aspirin (typically 81 mg per day) is sometimes prescribed to women at high risk of developing preeclampsia. This is often recommended for women with a history of preeclampsia, chronic hypertension, renal disease, diabetes, or multiple gestations [17,18].

#### Management of Antiphospholipid Syndrome (APS)

Women with APS, an autoimmune condition that increases the risk of blood clots, may be prescribed aspirin to reduce the risk of blood clot formation. Aspirin, along with heparin, is commonly used in APS to prevent thrombosis and improve pregnancy outcomes [19-22].

#### Recurrent Miscarriage

In cases of recurrent miscarriage, particularly when associated with antiphospholipid antibodies, aspirin may be considered. It is often used in conjunction with other interventions, such as heparin [23].

#### Improving Uterine Blood Flow

Aspirin may be considered in situations where there are concerns about inadequate blood flow to the uterus, potentially impacting fetal development. It is thought that aspirin's antiplatelet effects could enhance blood flow.

#### Fetal Growth Restriction

Some healthcare providers may consider aspirin therapy for women at risk of fetal growth restriction.

Aspirin's potential to improve blood flow to the placenta may be beneficial in certain cases [24].

It's important to note that the decision to use aspirin during pregnancy should be made in consultation with a healthcare provider. The benefits and risks must be carefully assessed based on the individual's medical history, risk factors, and the specific circumstances of the pregnancy.

While low-dose aspirin is generally considered safe for use in pregnancy, there are situations where its use may be contraindicated, such as in cases of hypersensitivity, bleeding disorders, or certain gastrointestinal conditions. Additionally, the timing, dosage, and duration of aspirin therapy will be determined based on the specific medical conditions and recommendations from the healthcare provider.

### Aspirin use in gynecology

In Gynaecology, aspirin may be used for various purposes, mainly related to its anti-inflammatory and antiplatelet properties.

#### Dysmenorrhea

Aspirin is commonly used for pain relief in Gynecology, particularly for menstrual pain (dysmenorrhea). It helps alleviate cramping and discomfort associated with menstruation [25].

#### Inflammation and Inflammatory Conditions

Gynecological conditions characterized by inflammation, such as pelvic inflammatory disease (PID) or certain types of pelvic pain, may be managed with aspirin for its anti-inflammatory effects [26].

#### Fertility Treatment

Aspirin has been explored in fertility treatments, especially in the context of in vitro fertilization (IVF). It is sometimes prescribed to improve blood flow to the uterus, potentially enhancing implantation [27].

#### Prevention of Recurrent Pregnancy Loss

In cases of recurrent pregnancy loss associated with certain immune or clotting disorders, aspirin may be considered as part of a treatment plan. This use is often in conjunction with other medications, such as heparin.

#### Cardiovascular Protection

In postmenopausal women or women with cardiovascular risk factors, aspirin may be recommended for cardiovascular protection. It is used to reduce the risk of heart attacks and strokes [28].

#### Cancer Prevention

Some studies suggest a potential role for aspirin in reducing the risk of certain gynecological cancers, including ovarian and endometrial cancers. However, the use of aspirin for cancer prevention is an evolving area of research and is not yet firmly established [29,30].

Aspirin, like any medication, should be used under the guidance of a healthcare provider. It is important to consider individual health factors, medical history, and potential interactions with other medications. While aspirin is generally well-tolerated, it can have side effects such as gastrointestinal irritation and an increased risk of bleeding, especially at higher doses.

Women who are pregnant or trying to conceive should consult with their healthcare provider before using aspirin, as its use during pregnancy requires careful consideration based on individual circumstances.

## DISCUSSION

The use of aspirin in Obstetrics and Gynecology is a topic of significant discussion and research. Aspirin, a commonly used medication with anti-inflammatory and antiplatelet properties, plays a crucial role in various aspects of women's health [31,32].

One of the primary discussions revolves around the use of low-dose aspirin for the prevention of preeclampsia. The decision to prescribe aspirin is based on individual risk factors and medical history. While studies support its efficacy, questions remain about the optimal dosage, timing, and specific criteria for identifying high-risk individuals [15,17,18].

The use of aspirin in women with antiphospholipid syndrome (APS) to prevent blood clots and improve pregnancy outcomes is one other topic. The combination of aspirin with anticoagulants like heparin is often prescribed, but the optimal regimen and duration remain areas of investigation [19-22].

Aspirin is sometimes prescribed in cases of recurrent miscarriage, particularly when antiphospholipid antibodies are present. However, the evidence supporting its use in improving pregnancy outcomes in this context is still debated [16,23].

The role of aspirin in fertility treatments, such as IVF, is a topic of interest. Some studies suggest potential benefits in terms of improving blood flow to the uterus, but more research is needed to establish clear guidelines and determine the subset of patients who might benefit [27].

Emerging research explores the potential of aspirin in preventing Gynecological cancers, particularly ovarian and endometrial cancers. However, the balance between potential benefits and risks, such as gastrointestinal bleeding, needs careful consideration [29,30].

Aspirin's use for cardiovascular protection in postmenopausal women, especially those with risk factors, is a point of ongoing discussion. The balance between its cardiovascular benefits and potential side effects is a complex issue that requires individualized risk assessment [28].

The safety of aspirin use during pregnancy, its potential impact on fetal development, and the risk of

bleeding complications are important considerations. The potential for gastrointestinal irritation and bleeding in certain populations also requires careful evaluation.

The development of clear guidelines for aspirin use in obstetrics and gynecology is an ongoing effort. Standardization of recommendations, taking into account individual patient characteristics, is crucial to ensuring consistent and evidence-based care.

## CONCLUSION

In summary, while aspirin is widely used in obstetrics and gynecology for various indications, there are areas where further research is needed to refine guidelines, determine optimal regimens, and understand the

balance between benefits and potential risks. As with any medical intervention, the decision to use aspirin should be based on a thorough assessment of individual patient factors and consideration of the latest evidence.

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