LOW DOSE ASPIRIN IN THE PREVENTION OF PRETERM BIRTH

By

Dr. CHITTARI SWETHAMRUTHA

DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SURGERY

IN

OBSTETRICS AND GYNAECOLOGY

Under the Guidance of
DR. SHEELA S R
Professor
Department of Obstetrics and Gynaecology

And Co-Guidance of
DR. K N V PRASAD
Professor
Department of Pediatrics

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY
SRI DEVARAJ URS MEDICAL COLLEGE
TAMAKA, KOLAR 563101

ALMA MATER

Sri Devaraj URS Medical College

R.L.JALAPPA HOSPITAL AND RESEARCH CENTRE

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I,hereby declare that this dissertation entitled **"LOW DOSE ASPIRIN IN THE PREVENTION OF PRETERM BIRTH"** is a bonafide and genuine research work carried out by me, **Dr. CHITTARI SWETHAMRUTHA**, in partial fulfillment of the requirement for the degree of Masters of Surgery (MS) in Obstetrics and Gynaecology, under the guidance of **Dr. SHEELA SR**, Professor, Department of Obstetrics and Gynecology, Sri Devaraj URS Medical College, Tamaka, Kolar.

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Place: Kolar

SIGNATURE OF THE GUIDE

Dr. SHEELA S R
Professor,

Department Obstetrics and Gynaecology
SDUMC, Kolar.

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

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SIGNATURE OF THE CO-GUIDE

Dr. K N V PRASAD

Professor,

Department of Pediatrics

SDUMC, Kolar.

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Dr MUNIKRISHNA.M

Professor & HOD
Department of Obstetrics and Gynaecology

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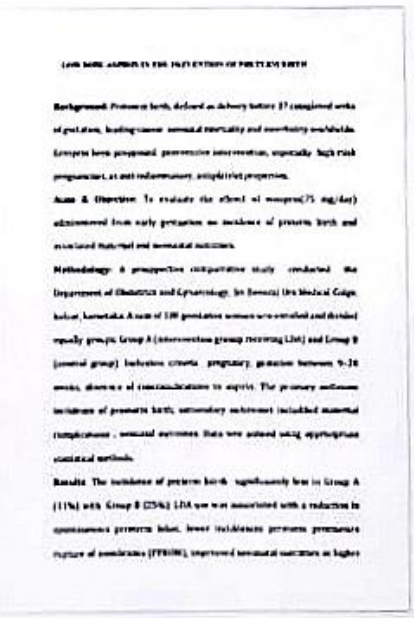

LOW DOSE ASPIRIN IN THE PREVENTION OF PRETERM BIRTH

Background: Preterm birth, defined as delivery before 37 completed weeks of gestation, leading cause neonatal mortality and morbidity worldwide. Interest been peripheral preventive intervention, especially high risk pregnancies, at anti-inflammatory, antiplatelet properties.

Aims & Objectives: To evaluate the effect of aspirin(75 mg/day) administered from early gestation on incidence of preterm birth and associated maternal and neonatal outcomes.

Methodology: A prospective comparative study conducted the Department of Obstetrics and Gynaecology, Sri Devaraj Urs Medical Colge, kolar, karnataka. A sum of 100 gestation women were enrolled and divided equally groups; Group A (intervention group receiving LDA) and Group B (control group). Inclusion criteria pregnancy, gestation between 9-26 weeks, absence of contraindications to aspirin. The primary outcome incidence of preterm birth, secondary outcomes included maternal complications , neonatal outcomes. Data were analysed using appropriate statistical methods.

Results: The incidence of preterm birth significantly low in Group A (11%) with Group B (25%). LDA use was associated with a reduction in spontaneous preterm labor, lower incidences previous premature rupture of membranes (PPROM), improved neonatal outcomes as higher

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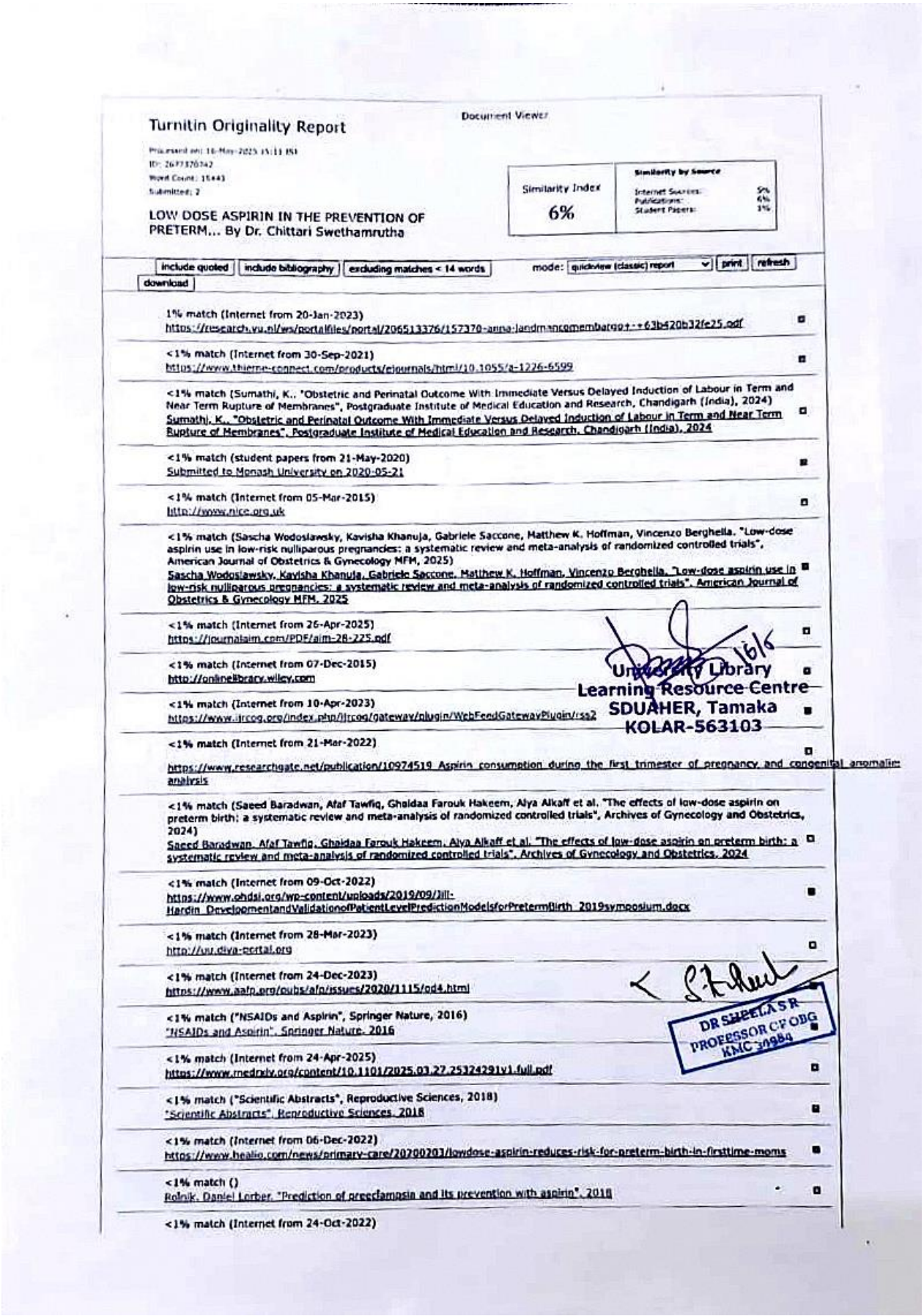

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DATE **DR. CHITTARI SWETHAMRUTHA**

PLACE

LOW DOSE ASPIRIN IN THE PREVENTION OF PRETERM BIRTH

ABSTRACT

Background: Preterm birth, defined as delivery before 37 completed weeks of gestation, is a leading cause of neonatal morbidity and mortality worldwide. Low-dose aspirin (LDA) has been proposed as a preventive intervention, especially in high-risk pregnancies, due to its anti-inflammatory and antiplatelet properties.

Aims & Objective: To evaluate the effect of low-dose aspirin (75 mg/day) administered from early pregnancy on the incidence of preterm birth and associated maternal and neonatal outcomes.

Methodology: A prospective comparative study was conducted at the Department of Obstetrics and Gynaecology, SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA. A total of 100 pregnant women were enrolled and divided equally into two groups: Group A (intervention group receiving LDA) and Group B (control group). Inclusion criteria included pregnant women with gestational age between 9–20 weeks, and absence of contraindications to aspirin. The primary outcome was incidence of preterm birth; secondary outcomes included maternal and neonatal outcomes. Data were analyzed using appropriate statistical methods.

Results: The incidence of preterm birth was significantly lower in Group A (11%) compared to Group B (25%). LDA use was associated with a reduction in spontaneous preterm labor, and improved neonatal outcomes such as higher birth weight and reduced NICU admissions. No significant increase in maternal adverse effects was observed with aspirin use.

Conclusion: Prophylactic administration of low-dose aspirin from early pregnancy is effective in reducing the incidence of preterm birth without significant adverse effects. The findings support the inclusion of LDA in antenatal care protocols for women at risk of preterm delivery.

Keywords: Low-dose aspirin, preterm birth, pregnancy, neonatal outcome, antenatal care

LIST OF ABBREVIATIONS

Glossary	Abbreviations
LDA	Low Dose Aspirin
LMIC	Low and Middle Income Countries
COX	Cyclooxygenase
RCT	Randomised controlled Trial
PTB	Preterm Birth
sPTB	Spontaneous Preterm Birth
iPTB	Indicated Preterm Birth
HPA	Hypothalamo – Pituitary Adrenal Axis
IL-1	Interleukin-1
IL-6	Interleukin-6
TNF-Alpha	Tumor Necrosis Factor Alpha
MMPs	Matrix Metalloproteinases
PROM	Premature Rupture of Membranes
ACTH	Adrenocorticotropic Hormone
CRH	Corticotropin Releasing Hormone
CAPs	Contraction Associated Proteins
IUGR	Intrauterine Growth Restriction
NO	Nitric Oxide
TXA2	Thromboxane A2
PGI2	Prostacyclin
RDS	Respiratory Distress Syndrome
HMD	Hyaline Membrane Disease
NICU	Neonatal Intensive Care Unit
CPAP	Continues Positive Airway Pressure
PVL	Periventricular Leukomalacia
CLD	Chronic Lung Disease
ICH	Intracranial Hemorrhage
WML	White Matter Lesion

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INTRODUCTION

INTRODUCTION

Preterm birth, defined as birth before 37 weeks 'gestation, claims the lives of approximately 1 million children every year.[1] Women who have had a previous preterm birth (medically indicated or with spontaneous onset) are at increased risk for preterm birth in their subsequent pregnancy.[2–4]

Low-dose aspirin use has been shown to reduce the risk for preeclampsia, a pregnancy condition characterized by hypertension and organ injury. In addition, low-dose aspirin use has been shown to protect against preterm birth among women at risk for developing preeclampsia.[5]There is also a growing body of evidence suggesting that low-dose aspirin use could be associated with a reduced risk for preterm birth and in particular, spontaneous preterm birth among women without major risk factors for preeclampsia.[6–8]Still, there is insufficient evidence regarding the use of low-dose aspirin in pregnant women with a previous preterm birth. The low-dose aspirin in the prevention of recurrent spontaneous preterm labour (APRIL) study, a randomized controlled trial with 406 participants, reported a small but nonsignificant reduction in preterm birth among women with a previous spontaneous preterm birth using low-dose aspirin.[9]However, the study was only powered to detect a difference in preterm birth >35% between groups, and the included population had a lower-than-expected preterm birth rate. A larger study is needed to investigate whether low-dose aspirin use can prevent recurrent preterm birth.[10,11]

Preterm birth is the leading cause of neonatal mortality and morbidity. Low dose aspirin use reduces the risk for preterm birth among women at risk of developing preeclampsia, however, it is unclear whether low-dose aspirin may reduce the risk of recurrence in both induced and spontaneous preterm birth.Every year, an estimated 15 million babies are born preterm (before 37 completed weeks of gestation). Preterm birth complications are the leading cause of death among children under 5 years of age, responsible for approximately 1 million deaths in 2015. Three-quarters of these deaths could be prevented with current, cost-effective interventions. Across countries, the rate of preterm birth ranges from 5% to 18% of babies born.[12,13]

So, present study was conducted to assess the effect of low dose aspirin in prevention of preterm birth

AIMS & OBJECTIVES

AIM & OBJECTIVES

- Primary-To study the efficacy of low dose aspirin in prevention of preterm birth.
- Secondary-To determine the feto-maternal outcome.

REVIEW OF

LITERATURE

REVIEW OF LITERATURE:

2 INTRODUCTION TO PRETERM BIRTH AND ITS GLOBAL IMPACT

Preterm birth, defined as birth before 37 weeks of gestation, is a significant global health concern. It remains the leading cause of neonatal morbidity and mortality, contributing to long-term health complications, developmental delays, and economic burdens on healthcare systems and families.[14]Despite advances in obstetric care, the incidence of preterm birth has not decreased substantially, making it a priority for maternal and neonatal health interventions. Various factors contribute to preterm birth, including maternal health conditions, genetic predisposition, infections, uteroplacental insufficiency, and environmental influences. Addressing this complex issue requires a multifaceted approach, including pharmacological, behavioral, and healthcare system interventions. One pharmacological strategy that has gained significant attention is the use of low-dose aspirin (LDA) to prevent preterm birth, particularly in high-risk populations.[15]

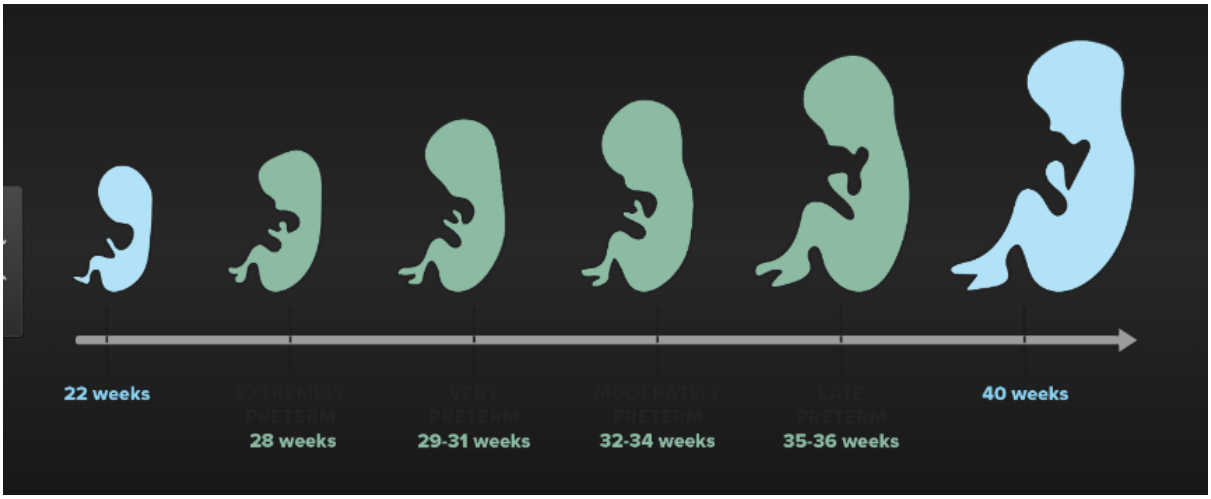


Figure 1: Overview of Preterm Birth

Overview of Preterm Birth and Its Global Impact

Preterm birth affects approximately 10% of all births worldwide, with higher rates in low- and middle-income countries (LMICs). It is responsible for nearly 1 million neonatal deaths annually, making it the single largest cause of under-five mortality. Even among those who survive, preterm birth is associated with an increased risk of neurodevelopmental impairments, respiratory complications, feeding difficulties, and long-term metabolic disorders. Premature infants often require prolonged hospitalization, specialized neonatal care, and ongoing medical attention throughout childhood, leading to considerable healthcare costs and emotional stress for families.[16]

There are sub-categories of preterm birth, based on gestational age: [17]

- extremely preterm (less than 28 weeks)

- very preterm (28 to 32 weeks)
- moderate to late preterm (32 to 37 weeks).

Induction or caesarean birth should not be planned before 39 completed weeks unless medically indicated.

The causes of preterm birth are multifactorial, involving both spontaneous and medically indicated deliveries. Spontaneous preterm labor and premature rupture of membranes account for the majority of cases, while conditions such as preeclampsia, intrauterine growth restriction, and placental abruption often necessitate early delivery for maternal or fetal indications. Despite extensive research, predicting and preventing preterm birth remains challenging. Effective interventions are crucial to improving maternal and neonatal outcomes, reducing healthcare costs, and addressing health disparities, particularly in resource-limited settings where access to advanced neonatal care is limited.[18,19]

Importance of Prevention Strategies

Given the significant burden of preterm birth, prevention strategies are essential. These strategies range from lifestyle modifications and early prenatal care to pharmacological interventions and public health policies. Several approaches have been explored, including cervical cerclage, progesterone supplementation, lifestyle modifications (such as smoking cessation and stress reduction), and improved maternal nutrition. However, these interventions have varying degrees of success and are often not universally applicable to all at-risk populations.[20]

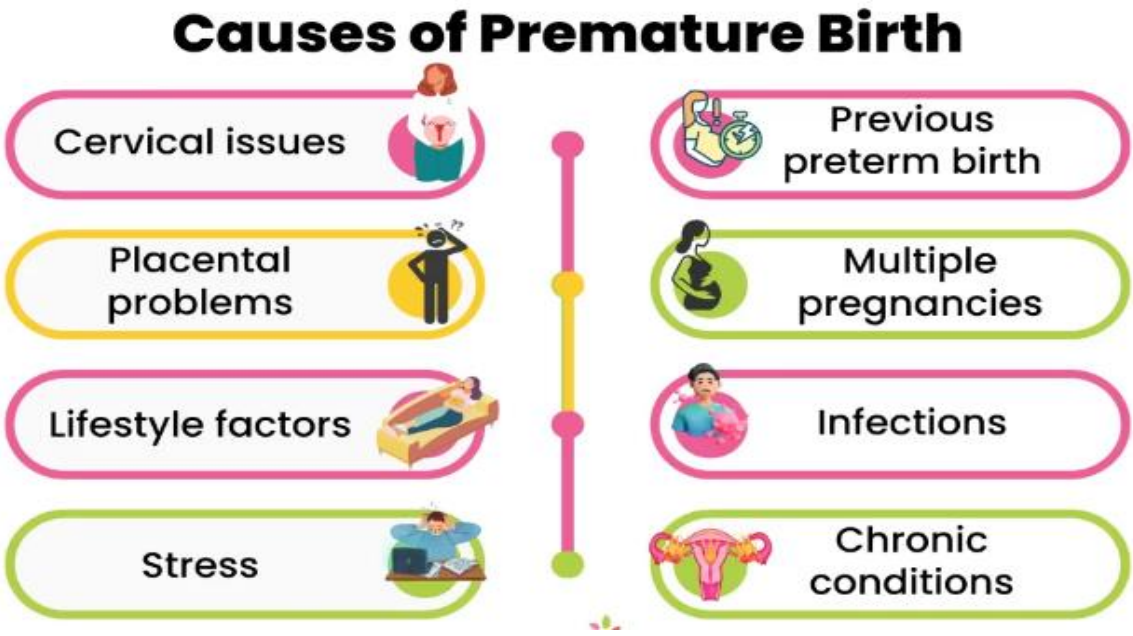


Figure 2: Causes of Premature Birth

One of the most promising pharmacological interventions for preterm birth prevention is the use of low-dose aspirin. Originally used for cardiovascular disease prevention, aspirin's potential benefits in pregnancy have been recognized due to its antiplatelet, anti-inflammatory, and vasodilatory properties. Over the years,

research has demonstrated that aspirin can help prevent preeclampsia—a major risk factor for preterm birth—by improving placental blood flow and reducing systemic inflammation. More recent evidence suggests that aspirin may have broader benefits in preventing spontaneous preterm labor, making it a valuable tool in maternal-fetal medicine.[21,22]

Role of Low-Dose Aspirin (LDA) in Obstetric Care

Low-dose aspirin (typically 75–150 mg per day) is increasingly recommended for pregnant individuals at high risk of preterm birth, particularly those with a history of preeclampsia, chronic hypertension, diabetes, or previous preterm delivery. The rationale behind its use lies in its ability to modulate key pathophysiological pathways involved in pregnancy complications.[23]

Aspirin inhibits cyclooxygenase (COX) enzymes, leading to a reduction in thromboxane A2 (a vasoconstrictor and platelet aggregator) while maintaining prostacyclin production, which promotes vasodilation and blood flow. This balance is particularly beneficial in pregnancy, where placental insufficiency and endothelial dysfunction contribute to adverse outcomes. By improving placental perfusion and reducing systemic inflammation, aspirin may decrease the likelihood of conditions such as preeclampsia, fetal growth restriction, and spontaneous preterm labor.[24]

Several large-scale randomized controlled trials (RCTs) and meta-analyses have evaluated the efficacy of aspirin in reducing the risk of preterm birth. Studies such as the ASPRE trial and the PARIS study have provided compelling evidence that early initiation of aspirin (before 16 weeks of gestation) significantly lowers the incidence of preeclampsia and preterm birth. Additionally, aspirin appears to be safe for both mother and baby when used at appropriate doses, with minimal risks of adverse effects such as gastrointestinal discomfort or bleeding complications.[25]

Despite the growing body of evidence supporting aspirin's role in preterm birth prevention, challenges remain in its implementation. Many high-risk individuals do not receive aspirin therapy due to lack of awareness, inconsistent healthcare provider recommendations, or concerns about safety. Furthermore, variations in guidelines across different countries and healthcare systems contribute to discrepancies in practice. Addressing these barriers requires education, standardized protocols, and improved access to prenatal care to ensure that eligible individuals benefit from this low-cost, widely available intervention.[26–29]

2.1 PATHOPHYSIOLOGY OF PRETERM BIRTH

Preterm birth (PTB), defined as birth before 37 weeks of gestation, remains a significant global health challenge due to its association with increased neonatal morbidity and mortality. PTB can be categorized into spontaneous preterm birth (sPTB) and medically indicated preterm birth (iPTB), each with distinct underlying mechanisms. While sPTB is primarily linked to premature activation of labor pathways, iPTB often results from maternal or fetal complications necessitating early delivery. Understanding the pathophysiology of PTB is essential for developing effective preventive strategies, including pharmacological interventions such as low-dose aspirin. This section explores the key mechanisms underlying PTB, emphasizing the roles of inflammation, vascular dysfunction, and placental insufficiency.[30,31]

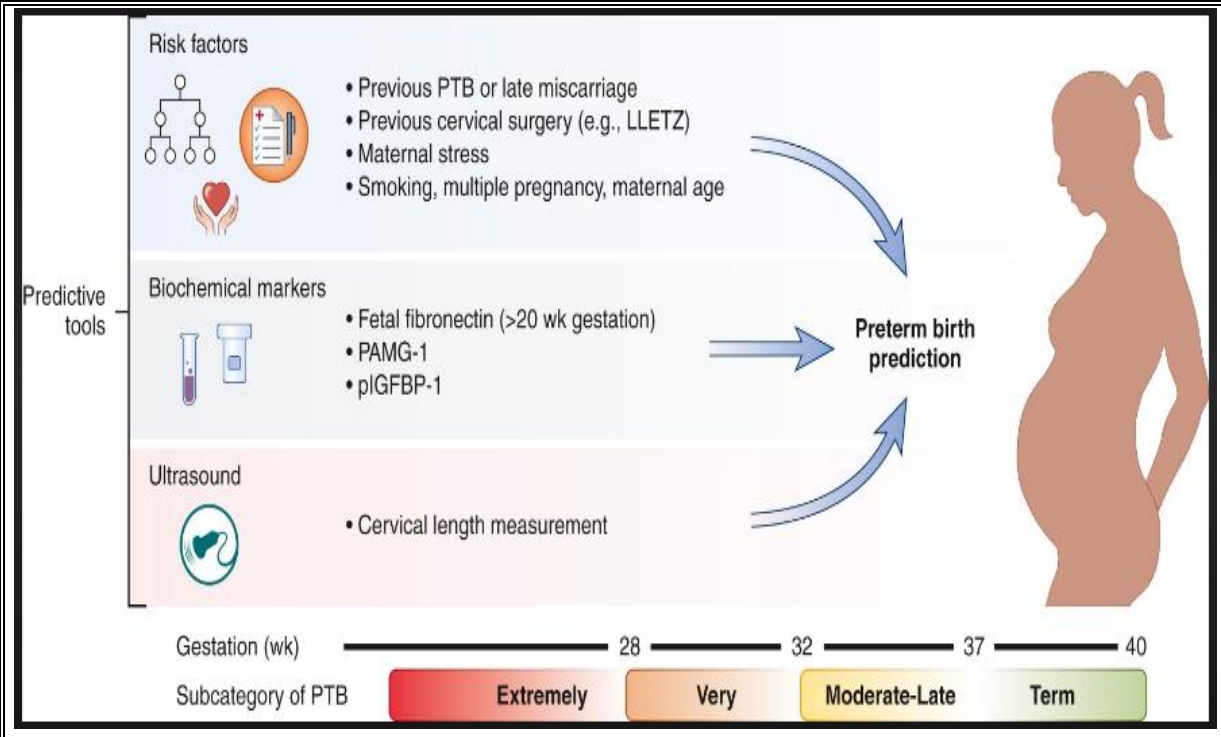


Figure 3: Pathophysiology Of Preterm Birth

Underlying Mechanisms of Spontaneous Preterm Birth

Spontaneous preterm birth (sPTB) is a multifactorial process influenced by genetic, environmental, infectious, and immunological factors. The primary mechanisms implicated in sPTB include inflammation and infection, premature activation of the hypothalamic-pituitary-adrenal (HPA) axis, uterine overdistension, and cervical insufficiency.[32]

1. Inflammation and Infection

Inflammation is a key driver of sPTB, with intrauterine infection being a leading cause. Bacterial infections, particularly those involving the genital tract (e.g., bacterial vaginosis, chorioamnionitis), can trigger an inflammatory cascade that leads to preterm labor. Microbial invasion of the amniotic cavity results in the release of pro-inflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α). These cytokines activate pathways leading to:[33–36]

- Increased prostaglandin production, which promotes uterine contractions.
- Degradation of fetal membranes through matrix metalloproteinases (MMPs), causing premature rupture of membranes (PROM).
- Cervical remodeling and ripening due to inflammatory-mediated collagen degradation.

Ureaplasma urealyticum and Mycoplasma hominis are commonly implicated pathogens in intrauterine infections associated with PTB. Notably, sterile inflammation (non-infectious inflammation) can also contribute to PTB through damage-associated molecular patterns (DAMPs) that activate the immune response.

2. Premature Activation of the HPA Axis

Maternal or fetal stress can lead to early activation of the hypothalamic-pituitary-adrenal (HPA) axis,

resulting in elevated levels of corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), and cortisol. Increased CRH levels stimulate the production of prostaglandins, which enhance uterine contractility and cervical ripening. In addition[36–39]

- Cortisol increases fetal lung maturity but also promotes inflammation and premature membrane rupture.
- Elevated CRH has been associated with preterm labor in response to maternal psychological stress, malnutrition, and infections.

3. Uterine Overdistension

Overdistension of the uterus, seen in multiple gestations, polyhydramnios, and uterine abnormalities, triggers mechanical and biochemical pathways leading to PTB. Stretching of the myometrium increases the expression of contraction-associated proteins (CAPs) such as connexin-43 and oxytocin receptors, which enhance uterine contractility. Additionally, excessive mechanical stress can activate inflammatory pathways and promote the release of prostaglandins, leading to labor initiation.[40]

4. Cervical Insufficiency and Remodeling

Cervical insufficiency, characterized by premature cervical dilation and effacement, is a known risk factor for PTB. The cervix undergoes biochemical changes, including[40–42]

- Increased matrix metalloproteinase (MMP) activity, leading to collagen breakdown.
- Enhanced pro-inflammatory cytokine expression, promoting cervical softening.
- Reduced progesterone activity, impairing cervical integrity and delaying labor suppression.

Women with a history of cervical insufficiency, prior cervical surgeries, or short cervical length (<25 mm) are at increased risk of PTB.

Underlying Mechanisms of Indicated Preterm Birth

Medically indicated preterm birth (iPTB) occurs when early delivery is necessary to prevent adverse maternal or fetal outcomes. The major conditions necessitating iPTB include preeclampsia, intrauterine growth restriction (IUGR), placental abruption, and fetal distress,[43]

1. Preeclampsia and Hypertensive Disorders

Preeclampsia, a disorder characterized by hypertension and end-organ dysfunction, is a leading cause of iPTB. The pathophysiology involves abnormal placentation, endothelial dysfunction, and excessive maternal inflammatory response. Key features include[42–44]

- Defective trophoblast invasion, leading to inadequate spiral artery remodeling.
- Reduced placental perfusion and ischemia, triggering oxidative stress and systemic endothelial activation.
- Increased circulating anti-angiogenic factors (e.g., soluble fms-like tyrosine kinase-1 [sFlt-1]), which impair vascular function and fetal growth.
- Maternal systemic inflammation, contributing to cardiovascular and renal complications necessitating preterm delivery.

2. Intrauterine Growth Restriction (IUGR)

IUGR, defined as fetal growth below the 10th percentile for gestational age, often results from placental

insufficiency. The primary mechanisms include[43–45]

- Impaired placental angiogenesis, leading to decreased nutrient and oxygen transfer.
- Dysregulated maternal-fetal hemodynamics, as seen in abnormal umbilical artery Doppler findings (e.g., absent or reversed end-diastolic flow).
- Chronic fetal hypoxia, which triggers fetal adaptive responses but can lead to acidosis and stillbirth if prolonged.

Delivery is indicated when fetal compromise is detected, necessitating iPTB.

3. Placental Abruption

Placental abruption, the premature separation of the placenta from the uterine wall, is a life-threatening condition requiring urgent delivery. It is associated with[35,40,42]

- Chronic maternal hypertension
- Placental ischemia and vascular malperfusion
- Inflammatory processes that weaken placental attachment

Severe cases result in fetal distress, maternal hemorrhage, and disseminated intravascular coagulation (DIC), necessitating immediate preterm delivery.

Role of Inflammation, Vascular Dysfunction, and Placental Insufficiency in PTB

Several overlapping pathological pathways contribute to PTB, involving inflammation, vascular dysfunction, and placental insufficiency.

1. Inflammation as a Central Driver of PTB

Inflammation plays a pivotal role in both sPTB and iPTB. Infection-induced or sterile inflammation can trigger labor by[42–45]

- Stimulating prostaglandin synthesis, leading to uterine contractions.
- Increasing oxidative stress, promoting placental dysfunction.
- Activating immune cells (e.g., macrophages, neutrophils) that degrade fetal membranes.

2. Vascular Dysfunction and Endothelial Injury

Conditions such as preeclampsia and chronic hypertension contribute to endothelial dysfunction, impairing placental perfusion. The release of anti-angiogenic factors like sFlt-1 and soluble endoglin (sEng) reduces nitric oxide (NO) availability, exacerbating vasoconstriction and placental ischemia.[45]

3. Placental Insufficiency and Its Consequences

Placental insufficiency results in fetal growth restriction, chronic hypoxia, and metabolic disturbances, all of which increase the risk of PTB. Reduced placental villous density, impaired trophoblast invasion, and abnormal placental metabolism are hallmarks of placental insufficiency leading to early delivery.[44]

2.2 THEORETICAL FRAMEWORKS FOR PRETERM BIRTH PREVENTION

Preterm birth, defined as delivery before 37 weeks of gestation, remains a significant cause of neonatal morbidity and mortality worldwide. A complex interplay of biological, genetic, and environmental factors contributes to preterm labor, making its prevention a major focus of obstetric research. Among the numerous strategies proposed, the use of low-dose aspirin (LDA) has gained considerable attention due to its potential to mitigate several pathophysiological mechanisms linked to preterm birth. This section

explores the theoretical frameworks underlying preterm birth prevention, emphasizing biological and clinical theories that support aspirin use, including the inflammation, thrombosis, and endothelial dysfunction theories.[46,47]

Biological and Clinical Theories Supporting Aspirin Use

The rationale for using low-dose aspirin in preventing preterm birth is primarily rooted in its well-established pharmacological properties. Aspirin, an acetylsalicylic acid derivative, exerts its effects mainly through inhibition of cyclooxygenase (COX) enzymes, leading to reduced production of prostaglandins and thromboxane A2. These mediators play crucial roles in platelet aggregation, inflammation, and vascular function, all of which are implicated in preterm birth. The application of aspirin in obstetrics is supported by three main theoretical frameworks[48]

1. Inflammatory Theory of Preterm Birth

Inflammation is a key driver of spontaneous preterm labor and preterm premature rupture of membranes (PPROM). Various maternal and fetal triggers, including infections, autoimmune responses, and oxidative stress, can initiate an inflammatory cascade leading to uterine contractions, cervical ripening, and membrane rupture.[49]

Role of Aspirin in Inflammation Regulation:[50–52]

- Aspirin exerts anti-inflammatory effects by inhibiting COX-2, reducing prostaglandin synthesis, and modulating the immune response.
- It helps suppress pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which are commonly elevated in women who deliver preterm.
- Aspirin can mitigate maternal systemic inflammation, which is often heightened in conditions such as preeclampsia and fetal growth restriction, both of which are associated with an increased risk of preterm birth.

Clinical Evidence: Studies have demonstrated that pregnant women with elevated inflammatory markers who receive LDA have a lower incidence of preterm labor, suggesting its role in downregulating inflammatory pathways that contribute to early parturition.[43]

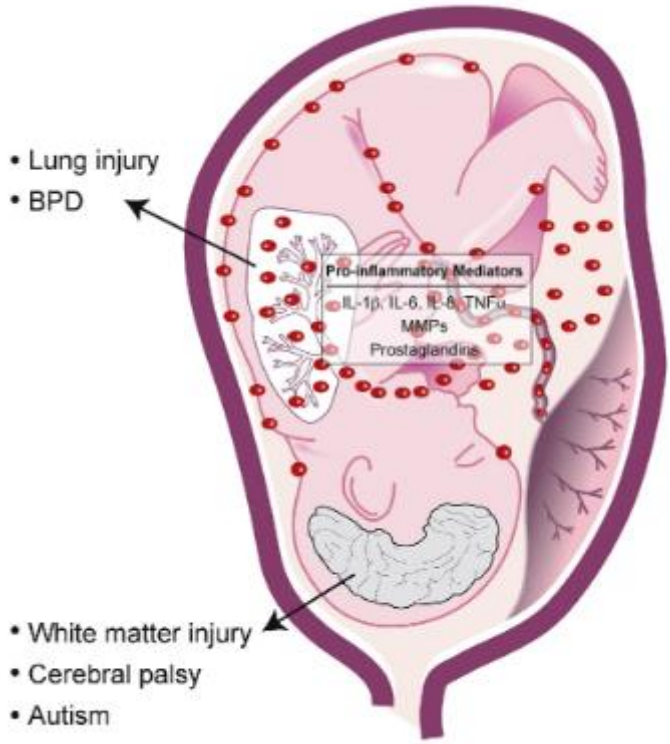


Figure 4: Inflammatory Theory of Preterm Birth

2. Thrombosis Theory of Preterm Birth

Abnormal placentation and uteroplacental insufficiency are well-established contributors to preterm birth. Placental vascular complications, including microthrombosis and impaired trophoblastic invasion, can lead to fetal hypoxia and placental dysfunction, ultimately triggering preterm labor.[53]

Role of Aspirin in Thrombosis Prevention[14,54,55]

- Aspirin is a potent antiplatelet agent that inhibits thromboxane A2, a key promoter of platelet aggregation and vasoconstriction.
- By reducing platelet adhesion and thrombus formation, aspirin improves placental perfusion and reduces the risk of ischemia-related complications.
- It enhances trophoblast invasion and remodeling of spiral arteries, which are crucial for optimal placental blood flow.

Clinical Evidence: Low-dose aspirin has been widely recommended for women at high risk of preeclampsia, a disorder characterized by placental thrombosis and endothelial dysfunction. The reduction in preeclampsia rates observed with aspirin use indirectly supports its role in preventing preterm birth by improving placental function.[56]

3. Endothelial Dysfunction Theory of Preterm Birth

Endothelial dysfunction plays a central role in the pathogenesis of conditions that predispose to preterm birth, including preeclampsia, intrauterine growth restriction (IUGR), and chronic hypertension. Impaired endothelial function leads to reduced nitric oxide (NO) bioavailability, increased oxidative stress, and

heightened vascular resistance.[57]

Role of Aspirin in Endothelial Protection:[45,58,59]

- Aspirin enhances endothelial function by increasing NO production, leading to improved vasodilation and placental blood flow.
- It reduces oxidative stress by modulating free radical generation and improving antioxidant defenses.
- Aspirin's ability to prevent endothelial activation and damage may contribute to prolonging pregnancy by maintaining vascular stability.

Clinical Evidence: Numerous studies have linked aspirin use to improved maternal endothelial function and lower rates of hypertensive disorders in pregnancy. These benefits suggest that aspirin plays a protective role against endothelial-related complications that can precipitate preterm birth.[60]

Integrating the Theoretical Frameworks

While each of these theories provides a distinct perspective on the mechanisms leading to preterm birth, they are interconnected in practice. Inflammation, thrombosis, and endothelial dysfunction often coexist, particularly in high-risk pregnancies. Aspirin's broad pharmacological profile allows it to address these overlapping pathways, making it a valuable intervention for preventing preterm birth.[59]

For example, in pregnancies complicated by preeclampsia, aspirin not only reduces the risk of thrombosis but also exerts anti-inflammatory effects and improves endothelial function. Similarly, in women with a history of preterm birth due to infection-induced inflammation, aspirin may mitigate the inflammatory response while simultaneously improving placental blood flow.[60]

2.3 MECHANISM OF ACTION OF LOW-DOSE ASPIRIN

Low-dose aspirin (LDA) exerts its primary therapeutic effects through its well-documented antiplatelet and anti-inflammatory properties. Aspirin is an acetylated salicylate that functions as an irreversible inhibitor of cyclooxygenase (COX) enzymes, which play a crucial role in prostaglandin and thromboxane synthesis.[61]

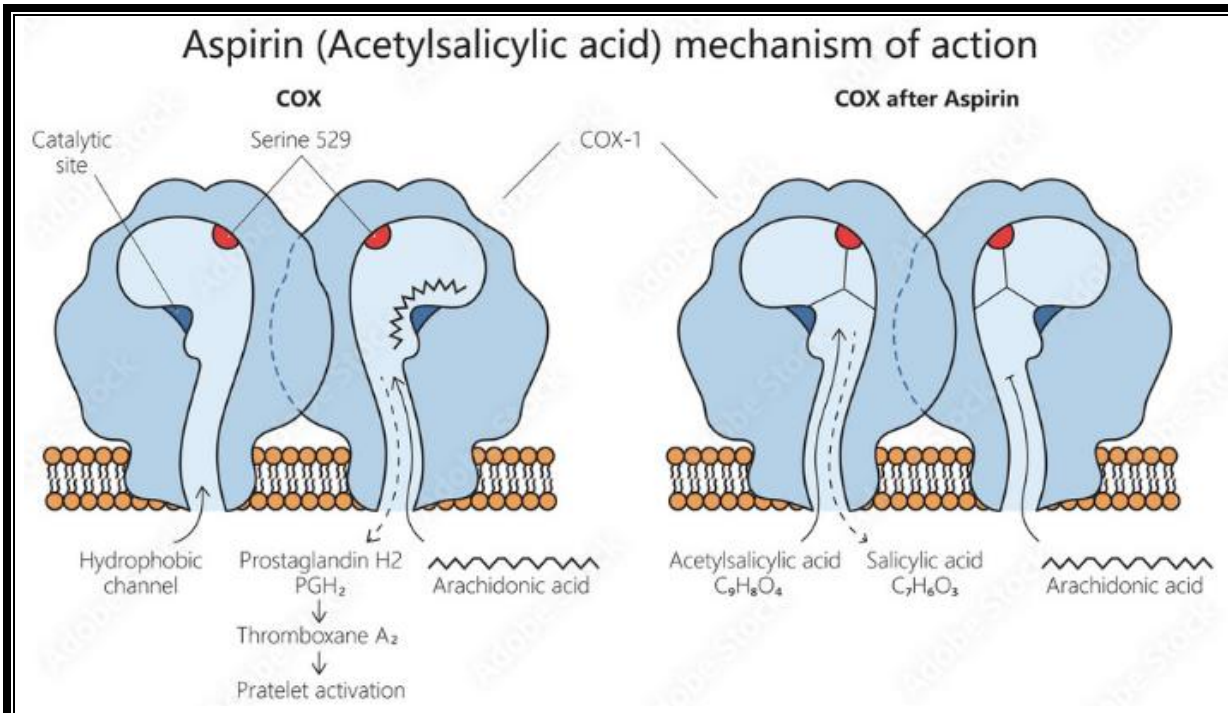


Figure 5: Low-dose aspirin (LDA)

Antiplatelet Effects of Low-Dose Aspirin

Aspirin's antiplatelet action is primarily mediated through the inhibition of cyclooxygenase-1 (COX-1) in platelets. COX-1 is responsible for the conversion of arachidonic acid to thromboxane A2 (TXA2), a potent vasoconstrictor and platelet aggregator. By irreversibly acetylating COX-1, aspirin prevents TXA2 synthesis, thereby reducing platelet aggregation and improving blood flow. This effect is particularly important in pregnancy, where abnormal platelet activation and aggregation have been linked to preeclampsia and placental dysfunction, conditions that significantly contribute to preterm birth.[62]

Unlike other cells in the body, platelets are anucleate, meaning they lack the ability to synthesize new proteins, including COX-1. Therefore, the inhibition of COX-1 by aspirin lasts for the entire lifespan of the platelet (approximately 7–10 days). This prolonged effect ensures sustained antithrombotic activity, which is beneficial in conditions characterized by hypercoagulability, such as pregnancy-induced hypertension and preeclampsia.[63]

Low-dose aspirin preferentially inhibits COX-1 over cyclooxygenase-2 (COX-2), the latter of which is responsible for the synthesis of prostacyclin (PGI2), a vasodilatory and anti-aggregatory prostaglandin. At low doses (typically 60–150 mg daily), aspirin selectively inhibits platelet-derived TXA2 without significantly affecting endothelial PGI2 production. This selective inhibition helps maintain a balance between vasoconstriction (TXA2) and vasodilation (PGI2), ultimately enhancing placental perfusion and reducing the risk of placental ischemia, which can contribute to preterm birth.[64]

Anti-Inflammatory Effects of Low-Dose Aspirin

In addition to its antiplatelet effects, aspirin exerts powerful anti-inflammatory actions through COX-2 modulation and direct effects on inflammatory pathways. Chronic inflammation plays a significant role in the pathogenesis of preterm birth, as infections, placental dysfunction, and systemic maternal inflammation

are known triggers of early labor.

Aspirin inhibits COX-2-mediated production of prostaglandins (PGE2 and PGF2α), which are involved in cervical ripening, uterine contractions, and fetal membrane rupture—all key processes in the initiation of labor. By reducing prostaglandin synthesis, aspirin delays the onset of labor and lowers the risk of spontaneous preterm birth.[65]

Moreover, aspirin modulates immune responses by reducing the activation of inflammatory cells, such as monocytes, macrophages, and neutrophils. It inhibits nuclear factor kappa B (NF-κB), a transcription factor that regulates the expression of pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β). These cytokines contribute to the inflammatory cascade associated with preterm labor, chorioamnionitis, and fetal inflammatory response syndrome. By suppressing inflammatory pathways, aspirin helps protect against excessive immune activation that could otherwise precipitate preterm birth.[14]

Effects on Placental Blood Flow and Trophoblast Function

A well-functioning placenta is essential for fetal growth and the maintenance of pregnancy to term. Impaired placental blood flow, as seen in conditions such as preeclampsia and intrauterine growth restriction (IUGR), is a major risk factor for preterm birth. Low-dose aspirin plays a crucial role in improving placental hemodynamics by influencing vascular function and trophoblast behavior.[66]

Improvement of Uteroplacental Blood Flow

Aspirin enhances uteroplacental blood flow through several mechanisms:

1. Reduction of Vasoconstriction: By inhibiting TXA2, aspirin prevents excessive vasoconstriction, thereby reducing vascular resistance in the uteroplacental circulation. This leads to improved blood flow to the placenta and, consequently, better oxygen and nutrient delivery to the fetus.[67]
2. Increased Vasodilation: Aspirin preserves endothelial prostacyclin (PGI2) function, which promotes vascular relaxation and maintains normal placental perfusion. PGI2 also counteracts platelet aggregation, reducing the likelihood of placental microthrombosis that could restrict fetal blood supply.[68]
3. Prevention of Spiral Artery Remodeling Defects: Proper transformation of the maternal spiral arteries is critical for ensuring adequate placental perfusion. In preeclampsia and IUGR, inadequate invasion of trophoblast cells into these arteries results in high-resistance blood flow, leading to placental hypoxia. Aspirin enhances spiral artery remodeling by modulating inflammatory and thrombotic pathways, leading to improved maternal-fetal circulation and a reduced risk of placental dysfunction.[69]

Trophoblast Function and Placental Development

Trophoblasts are specialized cells of the placenta that play key roles in implantation, immune modulation, and nutrient exchange between the mother and fetus. Dysfunctional trophoblast invasion has been implicated in the pathogenesis of preeclampsia, fetal growth restriction, and preterm birth. Low-dose aspirin influences trophoblast function through the following mechanisms[70]

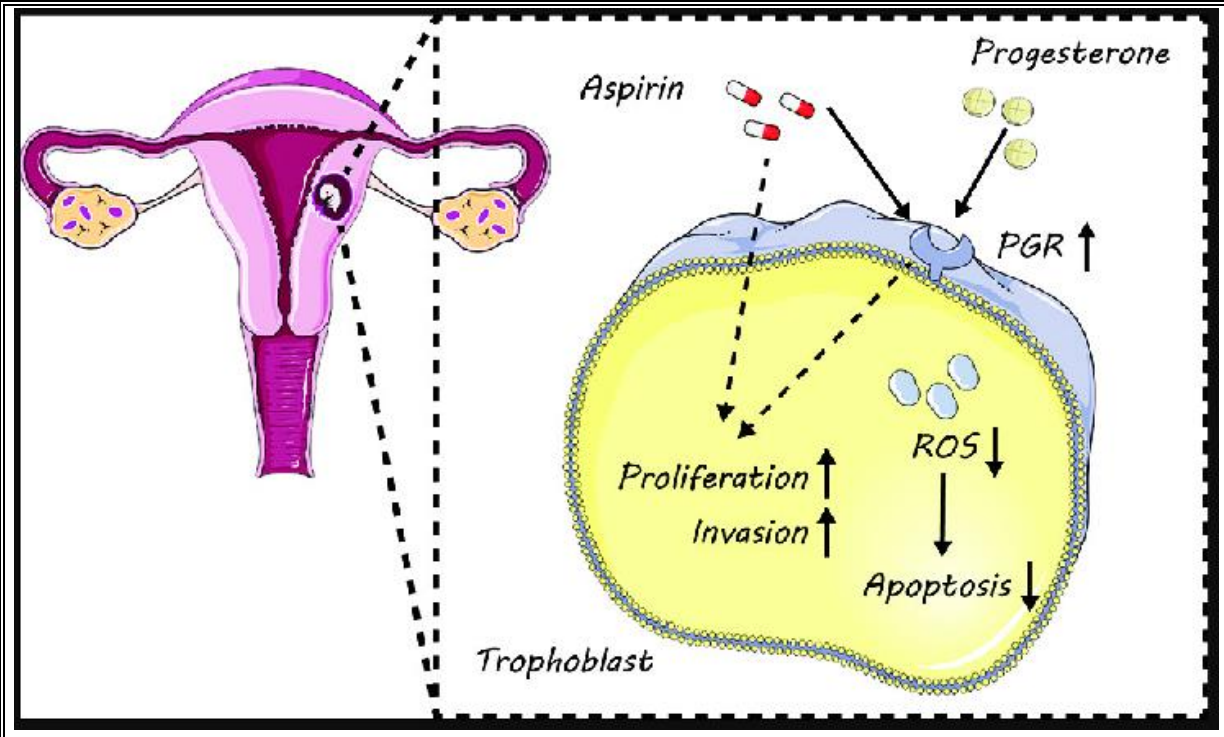


Figure 6: Effect Of Aspirin

1. Promotion of Trophoblast Migration and Invasion: Adequate trophoblast invasion into the maternal endometrium is necessary for proper placental development. Studies suggest that aspirin enhances trophoblast invasion by modulating matrix metalloproteinases (MMPs), enzymes that facilitate extracellular matrix breakdown, allowing for deeper placental anchoring.[71]
2. Reduction of Oxidative Stress: Aspirin decreases the production of reactive oxygen species (ROS) in the placenta, which helps prevent oxidative damage to trophoblasts. High oxidative stress is a known contributor to placental dysfunction and has been linked to preterm birth.[72]
3. Regulation of Immune Tolerance: Successful pregnancy requires a delicate balance between maternal immune tolerance and defense against infections. Aspirin has been shown to modulate the maternal immune response, enhancing the expression of regulatory T cells (Tregs) that promote fetal tolerance while reducing inflammatory immune responses that could trigger preterm labor.[73]
4. Prevention of Microvascular Thrombosis in the Placenta: In pregnancies complicated by preeclampsia or IUGR, microvascular thrombosis in the placenta can lead to placental insufficiency and fetal distress. By reducing platelet aggregation and enhancing endothelial function, aspirin helps maintain adequate placental circulation, lowering the risk of complications that could necessitate preterm delivery.[74–76]

Problems associated with preterm birth are related to difficulty in extrauterine function due to immaturity of organ system.[27,77,78]

1. Respiratory.

a. Perinatal depression in the delivery room due to hypoxic ischemia perinatal conditions

b. RDS due to surfactant deficiency and pulmonary immaturity

Respiratory distress syndrome (RDS), formerly known as hyaline membrane disease (HMD), describes a disease typical of preterm infants that is caused by insufficient pulmonary surfactant in alveoli. Pulmonary surfactant is a complex mixture of phospholipids, neutral lipids, and surfactant-specific proteins that is synthesized, packaged, and secreted from alveolar type II cells of the lung.[77]

In the alveolar spaces and small respiratory bronchioles that have poor structural support, surfactant sits at the air-liquid interface over the residual and protective liquid layer overlying the epithelium and disrupts the surface tension generated by the lung liquid. This surface tension is forceful enough to promote alveolar collapse at low lung volumes and to oppose reinflation of atelectatic airspaces.[77]

Absent or insufficient surfactant due to developmental immaturity of alveolar type II cells or spontaneous or inherited mutations of surfactant-related genes, or inactivation of surfactant due to inflammation, chemical modification, or lung injury, result in high surface tension and atelectasis. Preterm infants are particularly prone to RDS because alveolar type II cells do not develop until early in the third trimester, and their number and capacity to produce surfactant increase throughout the third trimester. Advances in preventive and rescue treatment strategies, including antenatal glucocorticoids, exogenous surfactant, and continuous positive airway pressure (CPAP), have greatly reduced the impact of RDS on neonatal morbidity and mortality.[27,79]

c. Apnea due to immaturity in mechanisms controlling breathing

Apnea is pathologic (an apneic spell) when absent airflow is prolonged (usually 20 seconds or more) or accompanied by bradycardia (heart rate <100 beats per minute) or hypoxemia that is detected clinically (cyanosis) or by oxygen saturation monitoring. Bradycardia and desaturation are usually present after 20 seconds of apnea, although they typically occur more rapidly in the small premature infant. As the spell continues, pallor and hypotonia are seen, and infants may be

unresponsive to tactile stimulation. The level or duration of bradycardia or desaturation that may increase the risk of neurodevelopmental impairment is not known.[27]

d. Eventual development of chronic lung disease (CLD) of prematurity also referred to as bronchopulmonary dysplasia

The need for supplemental oxygen is based on oxygen saturation (SpO2) during a room air challenge performed at 36 weeks' PMA (or 56 days for infants >32 weeks' PMA) or before hospital discharge. Persistent SpO2 <90% is the cutoff below which supplemental O2 should be considered. Immature lung substrate. The lung is most susceptible before alveolar septation begins. Injury at this stage may lead to an arrest of alveolarization and simplified lung structures that are the hallmark of new BPD.[27]

2. Neurologic[78]

Preterm infants have a higher risk of neurologic problems including the following:

a. Perinatal depression

Physiology involves the release of endogenous catecholamines leading to normal or increased SVR clinically manifested by pallor, mottled appearance, and poor perfusion and myocardial dysfunction. The baby is likely to be euvolemic and may have associated pulmonary hypertension.

b. ICH

c. Periventricular leukomalacia

PVL is a lesion found predominantly in the preterm newborn and is the neuropathologic lesion underlying much of the cognitive, motor, and sensory impairments and disabilities in children born prematurely. The true incidence of this lesion is not known, largely because detection of the mild form of this lesion is difficult using conventional neuroimaging and because the threshold for determining clinically important signal abnormality in the cerebral white matter has not been rigorously defined. WMI is a term used increasingly in place of the traditional term PVL or periventricular leukoencephalopathy, although the term PVL is still commonly used. WMI is a somewhat broader term than PVL in that it denotes the diffuse lesion of the cerebral white matter

that extends beyond the periventricular regions defined in initial neuropathologic and ultrasonographic studies and is most often a noncystic lesion.[79]

3. Cardiovascular.

Preterm infants may present with cardiovascular problems including the following:

a. Hypotension

i. Hypovolemia

ii. Cardiac dysfunction

iii. Sepsis-induced vasodilation

b. Patent ductus arteriosus is common and may lead to pulmonary overcirculation and diastolic hypotension

4. Hematologic.

Conditions for which preterm infants are at higher risk include the following:

a. Anemia

Premature babies may be quite comfortable with hemoglobin levels of 6.5 to 7.0 mg/dL. The level itself is not an indication for transfusion. Growing premature infants may manifest a need for transfusion by exhibiting poor weight gain, apnea, tachypnea, or poor feeding. Sick infants (e.g., with sepsis, pneumonia, or bronchopulmonary dysplasia) may require increased oxygen-carrying capacities and therefore need transfusion. Transfusion Despite efforts to adopt uniform transfusion criteria, significant variation in transfusion practices among neonatal intensive care units (NICUs) has been reported.[78]

b. Hyperbilirubinemia

5. Nutritional.

Preterm infants require specific attention to the content, caloric density, volume, an route of feeding, including parental nutrition when indicated.

6. Gastrointestinal.

Premature infants are at increased risk for necrotizing enterocolitis; formula feeding is an additional risk factor; a mother's own breast milk appears to be protective.

7. Metabolic.

Problems, especially in glucose and calcium metabolism, are more common in preterm infants.

8. Renal.

Immature kidneys are characterized by low glomerular filtration rate as well as an inability to process water, solute, and acid loads. Therefore, fluid and electrolyte management require close attention.

9. Temperature regulation.

Preterm infants are especially susceptible to hypothermia; iatrogenic hyperthermia can also be a problem.

10. Immunologic. Because of deficiencies in both humoral and cellular response, preterm infants are at greater risk for infection than are term infants.

11. Ophthalmologic. Retinopathy of prematurity may develop in the immature retina of infants <32 weeks or with birth weight <1,500 g

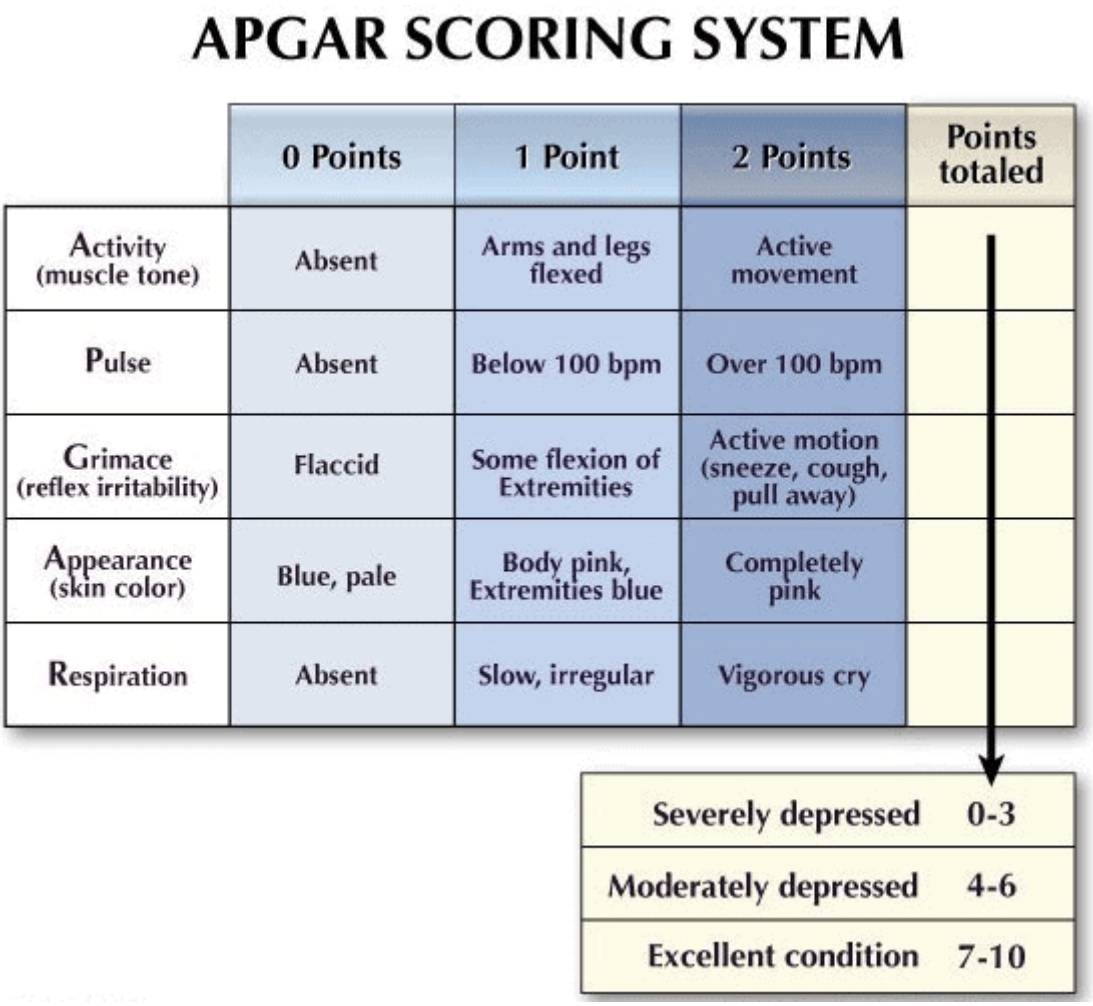
MANAGEMENT OF THE PRETERM INFANT[77]

1. Immediate postnatal management

a. Delivery in an appropriately equipped and staffed hospital is preferable. Risks to the very premature or sick preterm infant are greatly increased by delays in initiating necessary specialized care.

b. Resuscitation and stabilization require the immediate availability of qualified personnel and equipment. Anticipation and prevention are always preferred over reaction to problems already present.

Figure 7: APGAR Scoring System



Resuscitation efforts at delivery are designed to help the newborn make the respiratory and circulatory transitions that must be accomplished immediately after birth: The lungs expand, fetal lung fluid is cleared, effective air exchange is established, and the right-to-left circulatory shunts terminate. The critical period for these physiologic changes is during the first several breaths, which result in lung expansion and elevation of the partial pressure of oxygen (PO_2) in both the alveoli and the arterial circulation.

Elevation of the PO_2 from the fetal level of approximately 25 mm Hg to values of 50 to 70 mm Hg is associated with (i) decrease in pulmonary vascular resistance, (ii) decrease in right-to-left shunting through the ductus arteriosus, (iii) increase in venous return to the left atrium, (iv) rise in left atrial pressure, and (v) cessation of right-to-left shunt through the foramen ovale. The end result is conversion from fetal to transitional to neonatal circulatory pattern.

Adequate systemic arterial oxygenation results from perfusion of well-expanded, well-ventilated lungs and adequate circulation. Adequate oxygen delivery and maintenance of proper temperature are immediate postnatal goals.

Minimizing immediate heat loss by drying and providing warmth, thereby decreasing oxygen consumption by the neonate. Establishing normal respiration and lung expansion by clearing the upper airway and using positive pressure ventilation if necessary. Increasing arterial PO2 by providing adequate alveolar ventilation. The routine use of added oxygen is not warranted, but this therapy may be necessary in some situations. Supporting adequate cardiac output.[80]

2. Neonatal management[80]

a. Thermal regulation should be directed toward achieving a neutral thermal zone; that is, environmental temperature sufficient to maintain body temperature with minimal oxygen consumption. For the small preterm infant, this will require either an overhead radiant warmer (with the advantages of infant accessibility and rapid temperature response) or a closed incubator (with the advantages of diminished insensible water loss).

Premature infants experience increased mechanisms of heat loss combined with decreased heat production capabilities. These special problems in temperature maintenance put them at a disadvantage. Compared with term infants, premature infants have , A higher ratio of skin surface area to weight, Highly permeable skin which leads to increased transepidermal water loss , Decreased subcutaneous fat with less insulative capacity, Less-developed stores of brown fat and decreased glycogen stores, Poor vasomotor control, Challenges with adequate caloric intake to provide nutrients for thermogenesis and growth, Limited oxygen delivery if pulmonary conditions coexist.

Humidification of incubators has been shown to reduce evaporative heat loss and decrease insensible water loss, typically used for patients <1,200 g or 30 to 32 weeks' gestation for the first 10 to 14 days after birth. Risks and concerns for possible bacterial contamination have been

addressed in current incubator designs which include heating devices that elevate the water temperature to a level that destroys most organisms. Notably, the water transforms into a gaseous vapor and not a mist, thus eliminating the airborne water droplet as a medium for infection.[80]

b. Oxygen therapy and assisted ventilation

c. Fluid and electrolyte therapy must account for relatively high insensible water loss while avoiding overhydration and maintaining normal glucose and plasma electrolyte concentrations. Allow a 5% to 15% weight loss over the first 5 to 6 days.Then, adjust fluids to maintain stable weight until an anabolic state is achieved and growth occurs. Frequently assess response to fluid and electrolyte therapy during the first 2 days of life. Physical examination and urine output and SG and serum electrolyte determinations may be required initially as frequently as every 6 to 8 hours in infants <1,000 g.

d. Nutrition may be complicated by the inability of many preterm infants to tolerate enteral feedings, necessitating treatment with parenteral nutrition. When enteral feedings are tolerated, ineffective suck and swallow usually necessitate gavage feeding.

e. Hyperbilirubinemia, which is inevitable in less mature infants, can usually be managed effectively by careful monitoring of bilirubin levels and early use of phototherapy. In the most severe cases, exchange transfusion may be necessary.[80]

f. Infection may be the precipitant of preterm delivery. If an infant displays signs or symptoms that could be attributed to infection, the infant should be carefully evaluated for sepsis (e.g., physical exam, +/− CBC, +/−blood culture). There should be a low threshold for starting broad-spectrum antibiotics (e.g., ampicillin and gentamicin) until sepsis can be ruled out. Consider antistaphylococcal antibiotics for VLBW infants who have a central venous catheter, have undergone multiple procedures, or have remained for long periods in the hospital and are at increased risk for nosocomial infections.

g. Patent ductus arteriosus in preterm infants with birth weight >1,000 g often requires only conservative management with fluid restriction (usually 110 to 130 mL/kg/day) and supportive

care. Supportive care includes a neutral thermal environment, adequate oxygenation to minimize demands on left ventricular (LV) function, use of positive end-expiratory pressure (PEEP) to improve gas exchange in infants with respiratory compromise, and maintenance of the hematocrit at 35% to 40% to help increase pulmonary vascular resistance and reduce left-to right shunting.[80]

In smaller infants, a prostaglandin antagonist such as indomethacin or ibuprofen may be necessary. In the most symptomatic infants or those for whom medical therapy is either contraindicated or fails to close the ductus, surgical ligation may be necessary.

Outcome & Long-term problems of preterm birth.[81]

Preterm infants are vulnerable to a wide spectrum of morbidities. The risk of morbidity and mortality declines steadily with increasing GA.

1. Neurologic disability

a. Major handicaps (cerebral palsy, developmental delay)

b. Cognitive dysfunction (language disorders, learning disability, hyperactivity, attention deficits, behavior disorders)

c. Sensory impairments (hearing loss, visual impairment)

2. Retinopathy of prematurity

3. Chronic lung disease (CLD)

4. Poor growth.

Preterm infants are at risk for a wide range of growth problems. Although it is imperative for clinicians to visually assess the size and growth rate of individual infants, there is considerable controversy on which growth charts to use, and thus there are several approaches to monitoring infant growth.

Because extrauterine preterm infants grow at a different rate than their intrauterine fetal counterparts, some argue that a different measure may be needed to assess fetal growth than is used to follow longitudinal preterm infant growth. Although more accurate, the use of multiple growth charts can become confusing and complex.

A simpler approach is to use the same growth curve to assess fetal growth (size at birth) and preterm infant longitudinal growth. Using the simpler approach, one must recognize that the preterm infants are not likely to achieve the same growth rates as term infants

5. Increased rates of childhood illness and readmission to the hospital.

When can a premature baby go home from the hospital?

General goals for discharge may include the following:

• Serious illnesses are resolved

• Stable temperature

• Taking all feedings by breast

• No recent apnea or bradycardia

• Parents are able to provide care including medications and feedings

2.4 EVIDENCE FROM RANDOMIZED CONTROLLED TRIALS (RCTS)

Preterm birth, defined as birth before 37 weeks of gestation, remains a significant public health challenge worldwide, contributing to neonatal morbidity and mortality. Among various preventive strategies, the use of low-dose aspirin (LDA) has gained substantial interest due to its potential role in improving placental function and reducing the risk of preterm birth, particularly in high-risk pregnancies. Numerous randomized controlled trials (RCTs) have been conducted to assess the efficacy of LDA in preventing preterm birth. These trials provide valuable insights into the optimal dosage, timing, and the specific populations that benefit most from LDA therapy.[82]

Major RCTs Evaluating Low-Dose Aspirin for Preterm Birth Prevention

Several landmark RCTs have investigated the role of LDA in reducing the incidence of preterm birth, with varying outcomes based on study design, population characteristics, and intervention protocols. Some of the most influential trials include[83]

1. The Collaborative Low-dose Aspirin Study in Pregnancy (CLASP) Trial

One of the earliest large-scale RCTs evaluating aspirin in pregnancy, the CLASP trial enrolled over 9,000 women with risk factors for preeclampsia or fetal growth restriction. Participants were randomized to receive either 60 mg of aspirin daily or a placebo. The results showed no significant reduction in overall preterm birth rates but suggested a modest benefit in certain subgroups, such as women with a history of hypertensive disorders.[84]

2. The Maternal-Fetal Medicine Units (MFMU) Network Trial

This trial focused on women with a history of preeclampsia and found that LDA (81 mg daily) significantly reduced the incidence of preeclampsia and preterm birth before 34 weeks. The study supported the

hypothesis that aspirin improves placental function, leading to better pregnancy outcomes in high-risk women.[85]

3. The ASPRE Trial

A pivotal study, the Aspirin for Evidence-Based Preeclampsia Prevention (ASPRE) trial, examined the effect of LDA (150 mg daily) in pregnant women identified as high risk for preeclampsia using a combination of maternal history, biophysical markers, and biochemical screening. The trial demonstrated a 62% reduction in preterm preeclampsia and a significant decrease in early preterm birth (<34 weeks). These findings reinforced the idea that aspirin is most effective when initiated early in pregnancy and at higher doses than traditionally used.[86]

4. The APOSTEL IV Trial

This Dutch multicenter RCT evaluated LDA (80 mg daily) in women with a history of spontaneous preterm birth. While the study did not show a statistically significant reduction in overall preterm birth rates, it did highlight potential benefits in specific subgroups, particularly those with underlying vascular or inflammatory conditions.[87]

5. The WHO Multicountry Trial

A large-scale trial conducted by the World Health Organization examined the effects of LDA (75 mg daily) in low- and middle-income countries. The study found a modest reduction in preterm birth rates, with the most significant benefits observed in women at high risk for preeclampsia and fetal growth restriction.[88]

Dosage Considerations

The optimal dosage of LDA for preterm birth prevention has been a topic of extensive research. Early studies primarily used doses ranging from 60 to 81 mg daily, based on cardiovascular research and concerns about bleeding risks. However, more recent evidence suggests that higher doses, such as 100-150 mg daily, may be more effective in preventing preterm birth, particularly in women at high risk for preeclampsia.[83–85]

- Low Dose (60-81 mg): Initially used in early trials, these doses showed some benefit but may be suboptimal for all high-risk populations.
- Moderate Dose (100-150 mg): The ASPRE trial demonstrated significant benefits with 150 mg, supporting higher doses in high-risk women.
- High Dose (>150 mg): Some studies suggest that even higher doses could be beneficial in severe cases of placental dysfunction, but safety concerns remain.

Timing of Initiation[84–86]

The timing of aspirin initiation plays a crucial role in its effectiveness. The prevailing consensus is that aspirin should be started before 16 weeks of gestation for maximal benefit, as this is when placental development is most susceptible to aspirin's effects.

- Before 16 weeks: Most effective in reducing preeclampsia and early preterm birth.
- Between 16-20 weeks: Some benefit observed, though less than in earlier initiation.
- After 20 weeks: Limited efficacy; not routinely recommended for preterm birth prevention.

Population Considerations[84–88]

The effectiveness of LDA varies based on maternal risk factors, including:

- High-risk women (history of preeclampsia, chronic hypertension, or fetal growth restriction): Strong evidence supports LDA use.
- Women with spontaneous preterm birth history: Mixed evidence, with benefits seen in some subgroups.
- Low-risk populations: Routine LDA use is not recommended due to limited benefits.
- Women with multiple gestations: Conflicting data, with some trials showing a modest reduction in preeclampsia but not preterm birth.

PAST STUDIES

Bujold E, Roberge S, Tapp S, Giguère Y (2011)hypothesized that early aspirin prophylaxis could be a preventive measure against preterm birth, based on growing evidence linking defective placentation to preeclampsia, intrauterine growth restriction (IUGR), and spontaneous preterm birth. They emphasized that preeclampsia and IUGR share a common pathophysiology with preterm birth, primarily involving uteroplacental ischemia. This ischemia disrupts normal placental function, increasing the likelihood of pregnancy complications that can lead to early delivery. The study referenced a meta-analysis of low-dose aspirin trials that demonstrated a significant reduction in the incidence of preeclampsia and IUGR when aspirin was initiated early in gestation. Interestingly, the same meta-analysis suggested that aspirin use was also associated with a reduction in preterm birth rates, although the exact mechanism remained unclear. The authors pointed out that while these findings were promising, most trials included in the meta-analysis did not differentiate between spontaneous and indicated preterm births, making it difficult to determine whether aspirin directly prevented spontaneous preterm labor or simply reduced medically indicated preterm births due to preeclampsia and related conditions. Bujold et al. (2011) concluded that further large-scale studies were needed to explore the direct impact of low-dose aspirin on spontaneous preterm birth, as the available evidence, although compelling, remained inconclusive.[89]

Silver R, Ahrens K, Wong L, et al. (2015)conducted a secondary analysis of the Effects of Aspirin in Gestation and Reproduction (EAGeR) trial to evaluate whether preconception use of low-dose aspirin (81 mg) influenced preterm birth rates. This trial initially aimed to assess aspirin's role in improving pregnancy outcomes in women with a history of pregnancy loss, but the researchers analyzed its effects on preterm birth as well. The study randomized women into two groups: one receiving daily low-dose aspirin and folic acid, and the other receiving a placebo with folic acid. Results indicated that overall preterm birth rates were lower in the aspirin group (4.1%) compared to the placebo group (5.7%), although this difference did not reach statistical significance. However, the aspirin group exhibited a notable reduction in spontaneous preterm births (1.1% vs. 2.2%), suggesting a potential protective effect against early labor onset. The study further analyzed subgroups and found that in women with a recent pregnancy loss, aspirin use was associated with a significantly lower risk of preterm birth (3.8% vs. 9.7%). While the study was underpowered for definitive conclusions, the findings suggested a potential benefit of preconception aspirin

use in reducing spontaneous preterm birth, particularly in women with a history of pregnancy loss. The authors emphasized the need for further research to confirm these observations and to determine the optimal timing and dosage of aspirin for preterm birth prevention.[82]

Xu T, Zhou F, Deng C, et al. (2015)conducted a meta-analysis of 29 randomized controlled trials to evaluate the efficacy and safety of low-dose aspirin in preventing preeclampsia and its complications, including preterm birth. The analysis included studies that assessed aspirin use in high-risk pregnancies, particularly in women at risk for preeclampsia and IUGR. The results demonstrated that aspirin significantly reduced the incidence of preeclampsia (OR 0.71, 95% CI 0.57–0.87), severe preeclampsia (OR 0.37, 95% CI 0.23–0.61), and preterm birth (OR 0.81, 95% CI 0.75–0.88). The study found that aspirin was more effective when initiated before 16 weeks of gestation, highlighting the importance of early intervention. Furthermore, the meta-analysis showed that aspirin significantly reduced the risk of IUGR (OR 0.80, 95% CI 0.71–0.90), reinforcing its potential benefits for fetal development. However, the study also noted an increased incidence of placental abruption (OR 1.35, 95% CI 1.05–1.73), raising concerns about the safety of widespread aspirin use. Despite this, the authors concluded that low-dose aspirin was an effective strategy for preventing preeclampsia, preterm birth, and IUGR in high-risk pregnancies, supporting its inclusion in clinical guidelines for maternal care. The study emphasized the need for further research to refine risk stratification criteria and optimize aspirin therapy for different patient populations.[90]

Allshouse A, Jessel R, Heyborne K (2016)conducted a secondary analysis of the Maternal-Fetal Medicine Units High-Risk Aspirin trial to investigate the effects of low-dose aspirin on preterm birth phenotypes. The study categorized preterm births into three groups: medically indicated, spontaneous preterm labor, and preterm premature rupture of membranes (PPROM). Among the 1,789 women randomized, 30.5% delivered before 37 weeks, with 18.5% classified as indicated preterm births, 5.8% as spontaneous, and 6.2% due to PPROM. The researchers observed a trend suggesting that aspirin use was associated with a lower risk of spontaneous preterm labor and PPROM-related preterm births (OR 0.826, 95% CI 0.620–1.099), although the results did not reach statistical significance. Conversely, aspirin did not appear to impact the rate of medically indicated preterm births (OR 0.999, 95% CI 0.787–1.268). The findings aligned with previous research suggesting that aspirin might have a protective effect against spontaneous preterm birth, possibly through mechanisms involving improved placental function and reduced systemic inflammation. However, the study was limited by its sample size and inability to establish a definitive causal relationship between aspirin use and reduced preterm birth rates. The authors recommended larger randomized controlled trials to confirm their findings and to explore the biological pathways through which aspirin may exert its effects on pregnancy outcomes.[91]

Visser L, de Boer MD, de Groot CD, et al. (2017)conducted the APRIL study, a multicenter randomized placebo-controlled trial designed to evaluate the cost-effectiveness of low-dose aspirin in preventing recurrent spontaneous preterm labor. The study recruited women with a singleton pregnancy and a history of spontaneous preterm birth, randomizing them to receive either 80 mg of aspirin daily or a placebo from 8 to 16 weeks of gestation until 36 weeks. The primary outcome was the incidence of preterm birth before

37 weeks, with secondary outcomes including neonatal complications, intrauterine growth restriction, and healthcare costs. The trial aimed to enroll 406 women to detect a 35% reduction in preterm birth rates, from 36% to 23%. Preliminary findings suggested that aspirin was associated with a modest reduction in preterm birth, but the effect did not reach statistical significance. Despite the lack of conclusive evidence, the study highlighted the potential for aspirin to be a cost-effective intervention for reducing recurrent preterm birth, given its low cost and safety profile. The authors emphasized the need for further research to determine whether aspirin should be incorporated into routine clinical practice for women at high risk of recurrent spontaneous preterm birth.[92]

Visser L, de Boer MD, de Groot CD, et al. (2017) In a related study, Visser et al. (2017) further examined the effects of low-dose aspirin in preventing recurrent spontaneous preterm labor. This study reinforced the findings from the initial APRIL study, emphasizing the potential role of aspirin in mitigating preterm birth risk in women with a history of spontaneous early deliveries. The researchers analyzed subgroup data and found that aspirin appeared to be more effective in women with a history of extremely early preterm births (before 32 weeks) compared to those who had experienced late preterm births. This suggested that aspirin might be particularly beneficial for pregnancies at the highest risk of early delivery. However, due to the relatively small sample size, the study was underpowered to make definitive clinical recommendations. The authors called for larger, multicenter trials with diverse populations to validate their findings and to explore additional interventions that could be combined with aspirin for enhanced preterm birth prevention.[93]

Andrikopoulou M, Purisch SE, Handal-Orefice R, Gyamfi-Bannerman C. 2018 Low-dose aspirin has been widely studied for its potential benefits in preventing spontaneous preterm birth, particularly among nulliparous women without comorbidities. This secondary analysis of a randomized, placebo-controlled trial explored whether low-dose aspirin (60 mg) administered between 13 and 25 weeks of gestation could reduce the risk of spontaneous preterm birth. The study included 2,543 women, with 1,262 receiving low-dose aspirin and 1,281 receiving a placebo. Baseline characteristics were similar between the groups, except for marital status. The primary outcome was spontaneous preterm birth before 34 weeks, while secondary outcomes included spontaneous preterm birth before 37 weeks and overall preterm birth rates. The results demonstrated that the spontaneous preterm birth rate before 34 weeks was significantly lower in the aspirin group (1.03%) compared to the placebo group (2.34%), with an adjusted odds ratio (OR) of 0.46 (95% confidence interval [CI], 0.23–0.89). However, no significant differences were observed for preterm birth before 37 weeks or overall preterm birth rates between the two groups. These findings suggest that low-dose aspirin may offer a protective effect against early spontaneous preterm birth in low-risk, nulliparous women. Given the substantial impact of preterm birth on neonatal morbidity and mortality, further research is warranted to explore the optimal dosage, timing, and population that would benefit most from low-dose aspirin prophylaxis.[94]

Alashwah AA, Bayoumy H, Abou-gamrah A, Gomaa M. 2018 This study investigated the combined use of low-dose aspirin and 17α-hydroxyprogesterone for the prevention of spontaneous preterm birth compared to 17α-hydroxyprogesterone alone. Conducted as a double-blinded, randomized, placebo-

controlled clinical trial at Ain Shams University Maternity Hospital, the study enrolled 400 women at risk for preterm birth. After exclusions, 240 participants were randomized into two intervention groups. The primary outcome was preterm birth, defined as birth before 37 weeks, while secondary outcomes included neonatal complications such as bronchopulmonary dysplasia, periventricular leukomalacia, and intraventricular hemorrhage. The study found no significant differences between the groups in maternal age, parity, body mass index, cervical length, or prior history of preterm labor. The incidence of preterm premature rupture of membranes (PPROM) was also similar between the groups. However, the combined aspirin and progesterone group showed a modest but not statistically significant reduction in overall preterm birth rates. Additionally, no significant differences were observed in neonatal intensive care unit (NICU) admissions, neonatal birth weight, Apgar scores, or neonatal complications such as respiratory distress syndrome or neonatal sepsis. The findings suggest that while aspirin and progesterone may have potential benefits in preterm birth prevention, further randomized controlled trials with larger sample sizes are necessary to confirm their efficacy and safety.[95]

Cui Y, Zhu B, Zheng F. 2018A systematic review and meta-analysis were conducted to assess the efficacy of low-dose aspirin administered at or before 16 weeks of gestation in preventing preterm and term preeclampsia, as well as associated maternal and neonatal complications. A comprehensive search of multiple databases identified 10 randomized controlled trials (RCTs) involving 3,168 participants. The meta-analysis found that low-dose aspirin significantly reduced the risk of preeclampsia overall (risk ratio [RR] = 0.67, 95% CI: 0.57–0.80), with an even greater effect on preterm preeclampsia (RR = 0.35, 95% CI: 0.13–0.94). However, no significant reduction was observed for term preeclampsia (RR = 1.01, 95% CI: 0.60–1.70). Additionally, aspirin reduced the risk of maternal complications, including gestational hypertension and preterm birth, as well as neonatal adverse outcomes such as intrauterine growth restriction (IUGR) and stillbirth. The study concluded that early initiation of low-dose aspirin in women at risk of preeclampsia provides substantial benefits, particularly in reducing preterm preeclampsia and associated complications. These findings support current guidelines recommending aspirin prophylaxis for high-risk pregnant women.[96]

Landman A, Oudijk M. 2019 This commentary examined the role of low-dose aspirin as a potential preventive therapy for spontaneous preterm birth. It referenced a study by Andrikopoulou et al., which demonstrated that low-dose aspirin significantly reduces spontaneous preterm birth in nulliparous women. The authors emphasized that preterm birth remains a leading cause of neonatal morbidity and mortality and that current interventions, such as progesterone supplementation, have not sufficiently reduced its incidence. They highlighted that uteroplacental ischemia plays a crucial role in the etiology of spontaneous preterm birth, similar to its role in preeclampsia. Since aspirin has been shown to reduce the risk of preeclampsia through its antiplatelet and anti-inflammatory properties, it is hypothesized that it may also lower the risk of spontaneous preterm labor. The commentary stressed the need for further randomized trials to confirm these findings and to determine the most effective aspirin dosage and timing for preterm birth prevention.[97]

Hoffman M, Goudar S, Kodkany B, et al. 2020 The ASPIRIN (Aspirin Supplementation for Pregnancy

Indicated Risk Reduction in Nulliparas) trial was a large, multicountry, randomized, double-blind, placebo-controlled trial that assessed the effects of low-dose aspirin (81 mg) on preterm birth in nulliparous women with singleton pregnancies. Conducted across seven community sites in six countries, the trial enrolled 11,976 women aged 14 to 40 years who were randomized to receive either aspirin or placebo starting between 6 weeks 0 days and 13 weeks 6 days of gestation, continuing until 36 weeks 7 days. The primary outcome was the incidence of preterm birth before 37 weeks. The results showed that preterm birth occurred in 11.6% of women in the aspirin group compared to 13.1% in the placebo group (RR = 0.89, 95% CI: 0.81–0.98, p = 0.012). Additional findings included significant reductions in perinatal mortality (RR = 0.86, 95% CI: 0.73–1.00, p = 0.048), fetal loss (RR = 0.86, 95% CI: 0.74–1.00, p = 0.039), and early preterm delivery before 34 weeks (RR = 0.75, 95% CI: 0.61–0.93, p = 0.039). The study concluded that low-dose aspirin effectively reduces preterm birth and perinatal mortality in nulliparous women from low- and middle-income countries. These findings suggest that aspirin could be a simple and cost-effective intervention for reducing the global burden of preterm birth.[6]

Speer LM. 2020 A review article in American Family Physician discussed the benefits of low-dose aspirin (81 mg) in reducing preterm birth among nulliparous patients with singleton pregnancies, particularly in resource-poor settings. The article summarized findings from the ASPIRIN trial and emphasized that routine use of low-dose aspirin, starting as early as six weeks of gestation, resulted in a statistically significant reduction in the incidence of preterm birth. The review highlighted that aspirin's anti-inflammatory and antithrombotic properties may play a role in improving uteroplacental blood flow, thereby reducing the risk of spontaneous preterm birth. The author also addressed concerns regarding the safety of aspirin use during pregnancy, noting that the available evidence suggests a low likelihood of serious maternal or fetal complications. The review concluded that given the simplicity, affordability, and efficacy of aspirin, it should be considered a standard preventive measure in pregnant women at risk of preterm birth.[98]

Berger R, Kyvernitakis I, Maul H. (2021):discusses the high rate of preterm birth in Germany (8.6%) compared to other European nations and emphasizes the need to refine current prevention strategies. The authors classify preterm births into two major categories: spontaneous preterm birth, which includes cases due to premature rupture of membranes or spontaneous labor, and iatrogenic preterm birth, often linked to conditions like preeclampsia and intrauterine growth restriction. They explore the hypothesis that low-dose aspirin (LDA) might help reduce the incidence of spontaneous preterm birth, not just iatrogenic cases. Their analysis relies on a selective literature search up to April 2020, focusing on randomized trials studying aspirin's role in preventing spontaneous preterm birth. Secondary analyses of existing trials targeting preeclampsia prevention suggest that LDA may significantly reduce spontaneous preterm birth rates across both high-risk and low-risk populations. They specifically reference the ASPIRIN trial conducted in six developing countries, where 81 mg of aspirin, initiated before 14 weeks of gestation, lowered the overall preterm birth rate by approximately 11%. This reduction was statistically significant (11.6% in the aspirin group vs. 13.1% in the placebo group, RR 0.89; 95% CI: 0.81–0.98, p = 0.012). The authors conclude that further large-scale trials are needed to determine whether routine aspirin prophylaxis

should be considered for all pregnant women starting no later than 12 weeks of gestation.[99]

Landman A, de Boer MD, Visser L, et al. (2022):evaluate the effectiveness of low-dose aspirin in preventing recurrent spontaneous preterm labor, particularly among women with a history of spontaneous preterm birth. Conducted as the APRIL study, this randomized, multicenter, double-blinded, placebo-controlled trial included participants from multiple tertiary and secondary care hospitals across the Netherlands. The study population consisted of women with singleton pregnancies who had experienced a previous spontaneous preterm birth between 22 and 37 weeks. Participants were randomized to receive either 80 mg of aspirin daily or a placebo, starting between 8 and 16 weeks of gestation and continuing until 36 weeks or delivery. The primary outcome measured was preterm birth occurring before 37 weeks. Secondary outcomes included neonatal complications such as bronchopulmonary dysplasia, periventricular leukomalacia, intraventricular hemorrhage, necrotizing enterocolitis, retinopathy of prematurity, culture-proven sepsis, and perinatal death. A total of 406 women were enrolled, with 204 allocated to aspirin and 202 to placebo. Among the aspirin group, 21.2% experienced preterm birth, compared to 25.4% in the placebo group (RR 0.83, 95% CI 0.58–1.20, p = 0.32), indicating a non-significant trend toward reduction. However, in women with at least 80% adherence to medication, the incidence of preterm birth was lower (19.2% vs. 24.8%, RR 0.77, 95% CI 0.48–1.25, p = 0.29). The authors note that the study was underpowered due to lower-than-expected preterm birth rates. They conclude that while low-dose aspirin did not significantly reduce preterm birth in this cohort, a modest benefit cannot be ruled out, warranting further research.[9]

Hodgetts Morton V, Stock S. (2022): The study presents an in-depth analysis of the potential of low-dose aspirin to prevent preterm birth. They highlight preterm birth as the leading cause of neonatal mortality and lifelong disability, creating a substantial burden on healthcare systems. Although aspirin prophylaxis is well-established for preventing hypertensive disorders in pregnancy, recent meta-analyses suggest that it may also play a role in reducing the incidence of spontaneous preterm birth. The authors discuss the results of a reanalysis of data from trials originally focused on preeclampsia prevention, which found a small but statistically significant reduction in spontaneous preterm birth among women who took aspirin. The study references the APRIL trial, which aimed to assess aspirin's effectiveness in reducing recurrent spontaneous preterm birth. The trial enrolled women with a history of spontaneous preterm birth between 22 and 36 weeks and randomized them to receive either 80 mg of aspirin daily or a placebo. Although aspirin was associated with a modest reduction in recurrent preterm birth (21% in the aspirin group vs. 25% in the placebo group), the results were not statistically significant. The authors emphasize that the trial was underpowered, limiting its ability to provide a definitive answer. They conclude that while aspirin's potential in preventing spontaneous preterm birth remains an open question, further well-powered studies are necessary to explore this possibility in greater detail.[10]

Sadaf M, Saleem A, Farkhanda T, et al. (2023):conducted a randomized controlled trial to evaluate the effectiveness of low-dose aspirin in preventing preterm birth in women with a history of spontaneous preterm delivery. The study included 172 patients who met the inclusion criteria and were randomly assigned to two groups: one receiving 75 mg of aspirin daily and the other serving as a control group. The

primary outcome measured was the incidence of preterm birth, defined as delivery occurring before 37 weeks of gestation. The researchers monitored participants every eight weeks to assess medication adherence and any potential side effects. The results showed that in the aspirin group, 11.6% of women experienced preterm birth compared to 36.0% in the control group ($p = 0.001$), indicating a statistically significant reduction. The relative risk of preterm birth in the aspirin group was 1.801 times lower than in the control group. The authors conclude that aspirin, when initiated before 14 weeks of gestation, significantly reduces the likelihood of spontaneous preterm birth in women with a history of previous spontaneous preterm delivery. They recommend further large-scale studies to validate these findings and explore optimal dosing strategies.[100]

Mirzamoradi M, Dehghani Z, Azadi P, et al. (2023):conducted a pilot randomized clinical trial to assess the efficacy of low-dose aspirin in preventing preterm delivery among women with a history of spontaneous preterm birth. The study included 107 participants, with 54 assigned to the aspirin group (receiving 80 mg daily until 36 weeks of gestation) and 53 assigned to the control group (receiving standard care without aspirin). The primary outcome was the incidence of preterm birth before 37 weeks. The results indicated that 19% of women in the aspirin group experienced preterm birth compared to 34% in the control group ($p = 0.069$), which, while indicative of a trend toward benefit, did not reach statistical significance. Notably, among women experiencing spontaneous labor, the preterm birth rate was significantly lower in the aspirin group (45%) compared to the control group (80%) ($p = 0.022$). The authors conclude that while aspirin did not significantly reduce overall preterm birth rates, it may have a protective effect in cases of spontaneous labor. They emphasize the need for larger, well-powered studies to confirm these findings and determine the most effective aspirin regimen for preventing preterm birth.[101]

Sanad HZ, El-Lakwa E, Masaod E, et al. (2024):conducted a randomized controlled clinical trial to assess the efficacy and safety of low-dose aspirin in combination with vaginal progesterone for preventing spontaneous preterm birth. The study was conducted at Samanoud General Hospital and included 127 pregnant women who were randomly assigned to three groups: one receiving aspirin alone, one receiving vaginal progesterone alone, and one receiving both treatments. The primary outcome measured was preterm birth occurring before 37 weeks, with a particular focus on early preterm birth before 34 weeks. The results showed that the combination therapy group had a significantly lower incidence of preterm birth before 34 weeks ($p = 0.024$), whereas there were no significant differences between groups in the overall preterm birth rate before 37 weeks. The authors conclude that vaginal progesterone combined with low-dose aspirin, when initiated at 14–16 weeks and continued until 36 weeks, significantly reduces early preterm birth. They highlight that both medications are safe for use during pregnancy and recommend further studies to explore their combined effectiveness in larger populations.[102]

MATERIALS & METHODS

1. Study Design

The study was designed as a prospective cohort study to evaluate the efficacy of low-dose aspirin in preventing preterm birth. The cohort consisted of pregnant women meeting the inclusion criteria, who were followed from early pregnancy until delivery. The study aimed to establish a correlation between aspirin administration and gestational outcomes by comparing outcomes between aspirin users and non-users.

2. Study Setting

The study was conducted at the Department of Obstetrics and Gynaecology, RL Jalappa Hospital, Kolar. This tertiary care hospital, affiliated with Sri Devaraj Urs Medical College, served as the primary recruitment and data collection site. The hospital provided comprehensive obstetric and neonatal care, ensuring a controlled environment for conducting the study.

3. Study Duration

The study was carried out over an 18-month period, spanning from July 2023 to December 2024. The duration was selected to allow for adequate patient recruitment, follow-up, and analysis of pregnancy outcomes.

4. Participants - Inclusion and Exclusion Criteria

Inclusion Criteria:

- Pregnant women with gestational age >9 weeks
- History of second-trimester abortion
- Previous history of preterm pregnancy
- Multiple pregnancies
- Diagnosis of preeclampsia
- Gestational diabetes mellitus

Exclusion Criteria:

- Presence of uterine anomalies
- Cervical incompetence
- History of preterm premature rupture of membranes

5. Study Sampling

A non-probability purposive sampling method was employed to recruit participants. Eligible pregnant women presenting to the outpatient department were assessed based on inclusion and exclusion criteria. Those fulfilling the criteria were invited to participate in the study and provided informed consent.

6. Study Sample Size

The sample size was determined using a standard formula to achieve statistical significance. Based on prior

literature and expected effect size, a total of 100 pregnant women were recruited. The sample size calculation accounted for possible dropouts and ensured adequate statistical power for detecting differences in preterm birth rates between study groups.

- **Sample size(n)**

$$n = \frac{\left[z\alpha \sqrt{(1+1/m)\bar{p}(1-\bar{p})} + z\beta \sqrt{\frac{po(1-po)}{m} + p1(1-p1)} \right]^2}{(po-p1)2}$$

$$\text{Where } \bar{p} = \frac{p1+mpo}{m+1}$$

$$n_c = \frac{n}{4}\left[1 + \sqrt{1 + \frac{2(m+1)}{nm|po-p1|}}\right]^2$$

7. Study Groups (if applicable)

Participants were categorized into two groups:

- **Intervention Group**: Pregnant women receiving low-dose aspirin (75 mg daily) until 36 weeks of gestation.
- **Control Group**: Pregnant women not receiving aspirin, managed according to standard obstetric protocols(delivered were taken from case record register)

8. Study Parameters

The study focused on both maternal and fetal parameters:

- **Maternal Parameters:** Incidence of preeclampsia, ICU admissions, maternal mortality, HELLP syndrome, placental abruption, and eclampsia.
- **Fetal Parameters:** Gestational age at birth, intrauterine fetal death, fetal growth restriction, prematurity, neonatal intensive care unit (NICU) admission, and neonatal mortality within the first week of life.

9. Study Procedure

Eligible participants were identified and provided with detailed information about the study. After obtaining informed consent, a thorough history was recorded, including demographic details, obstetric history, and medical conditions. Participants in the intervention group were prescribed low-dose aspirin (75 mg daily) from the time of recruitment until 36 weeks of gestation.

Routine antenatal investigations were performed, including complete blood count, urine routine, liver function tests, renal function tests, and coagulation profile. Follow-up visits were scheduled throughout pregnancy to monitor adherence, side effects, and pregnancy progression. Delivery outcomes were documented for all participants.

10. Study Data Collection

Data were collected using a structured proforma, which included demographic details, obstetric history, laboratory findings, and pregnancy outcomes. Data entry was performed in an Excel spreadsheet for systematic recording. Follow-ups were conducted through regular hospital visits, and delivery details were recorded upon admission for labor.

11. Data Analysis

Statistical analysis was performed using SPSS software version 26. Categorical data were described using frequency and percentages and analyzed using the chi-square test. Continuous variables were presented as mean and standard deviation, with statistical comparisons conducted using Z-tests or ANOVA, as appropriate. A p-value of <0.05 was considered statistically significant.

12. Ethical Considerations

Ethical approval was sought and obtained from the Institutional Ethical Committee prior to study initiation. Written informed consent was obtained from all participants after explaining the study objectives, procedures, risks, and benefits. Confidentiality of participant data was maintained, and no financial burden was placed on participants. The study adhered to the principles of the Declaration of Helsinki for ethical biomedical research.

RESULTS AND ANALYSIS

RESULT AND ANALYSIS

Group A - Cases who dealt with ecosprin

Group B - Cases who dealt without ecosprin

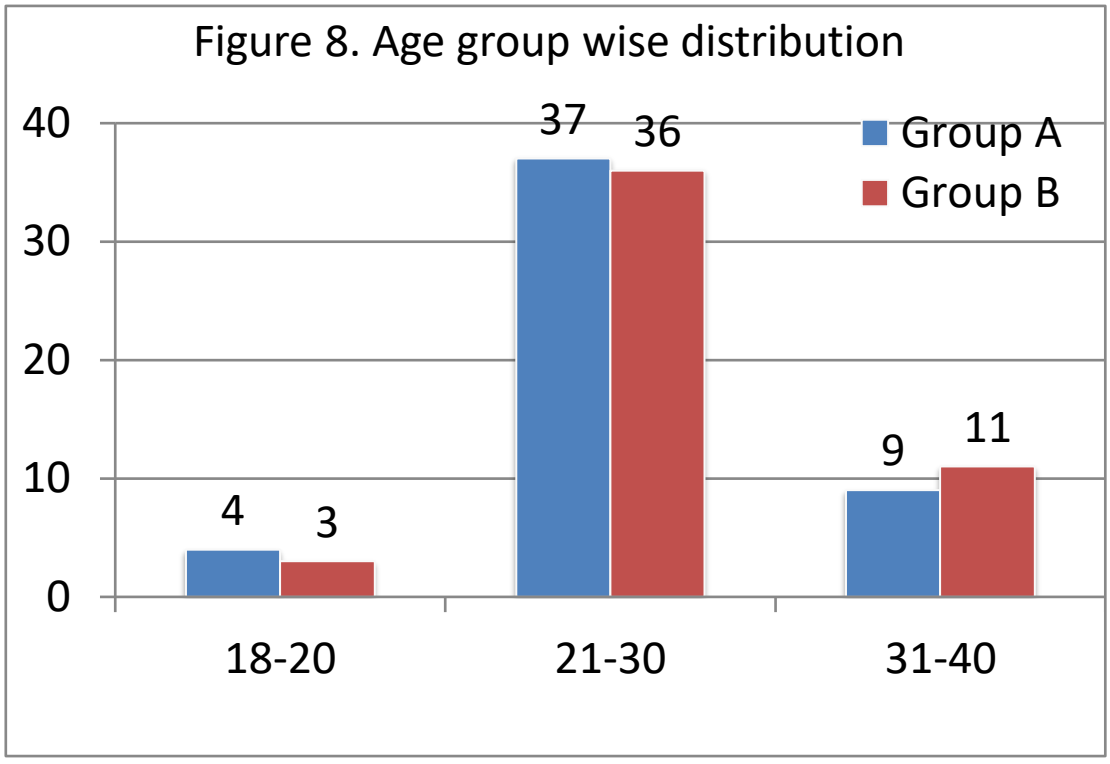


Table 1. Age group wise distribution

Age group (in years)	Group A	Group B	P value
18-20	4 (4%)	3 (3%)	0.002
21-30	37(37%)	36(36%)	
31-40	9(9%)	11(11%)	
Mean age	25.9 + 4.4 years	27.1 + 4.7 years	0.002

The mean age of study participants was 25.9 + 4.4 years in group A and 27.1 + 4.7 years in group B. In group A, 37(37%) cases and in group B 36(36%) cases were belonged to age group of 21-30 years. On applying chi square test, there was association between age of both groups.[table 1 & Figure 8]

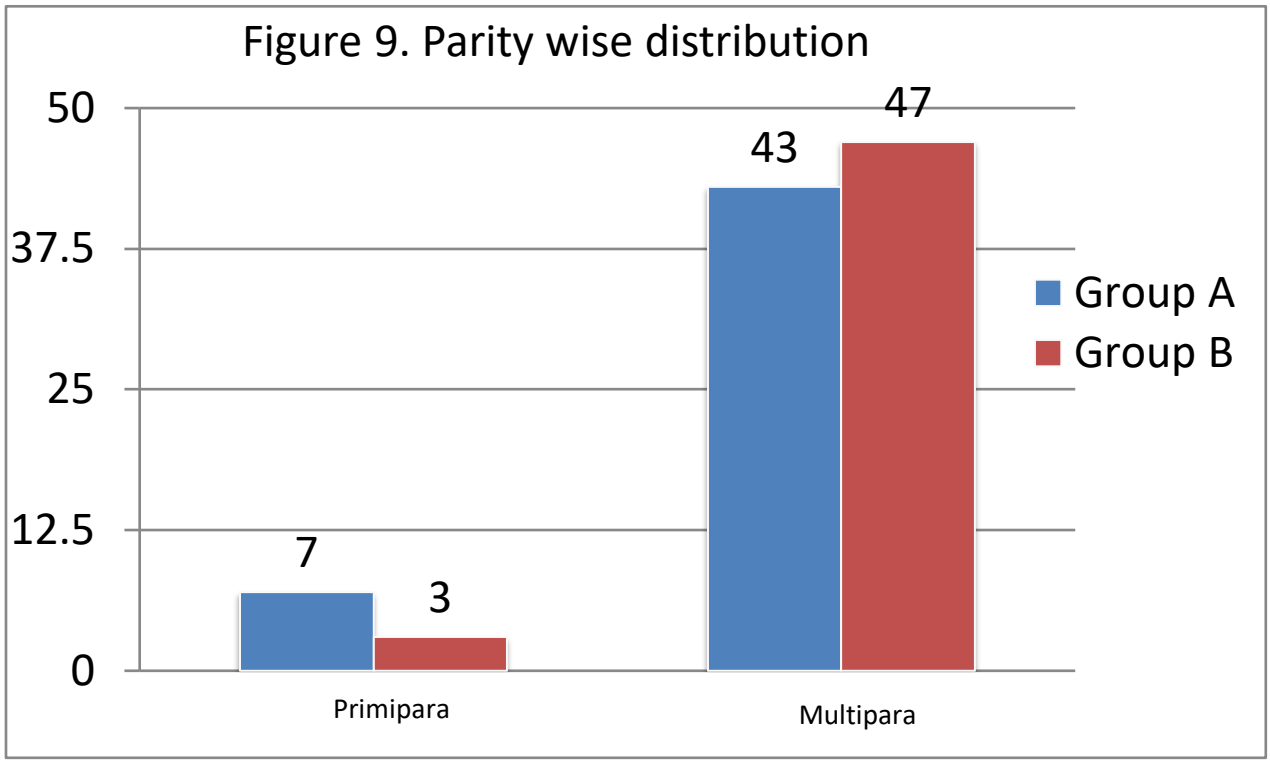


Table 2. Parity wise distribution

Parity	Group A	Group B	P value
Primipara	7 (7%)	3 (3%)	0.321
Multipara	43 (43%)	47 (47%)	

Out of total , in group A, 7 cases were primipara and 43 cases were multipara. In group B, 3 cases were primipara and 47 cases were multipara. On applying chi square test there was no association between parity and ecosprin given to study participants.[Table 2 & Figure 9]

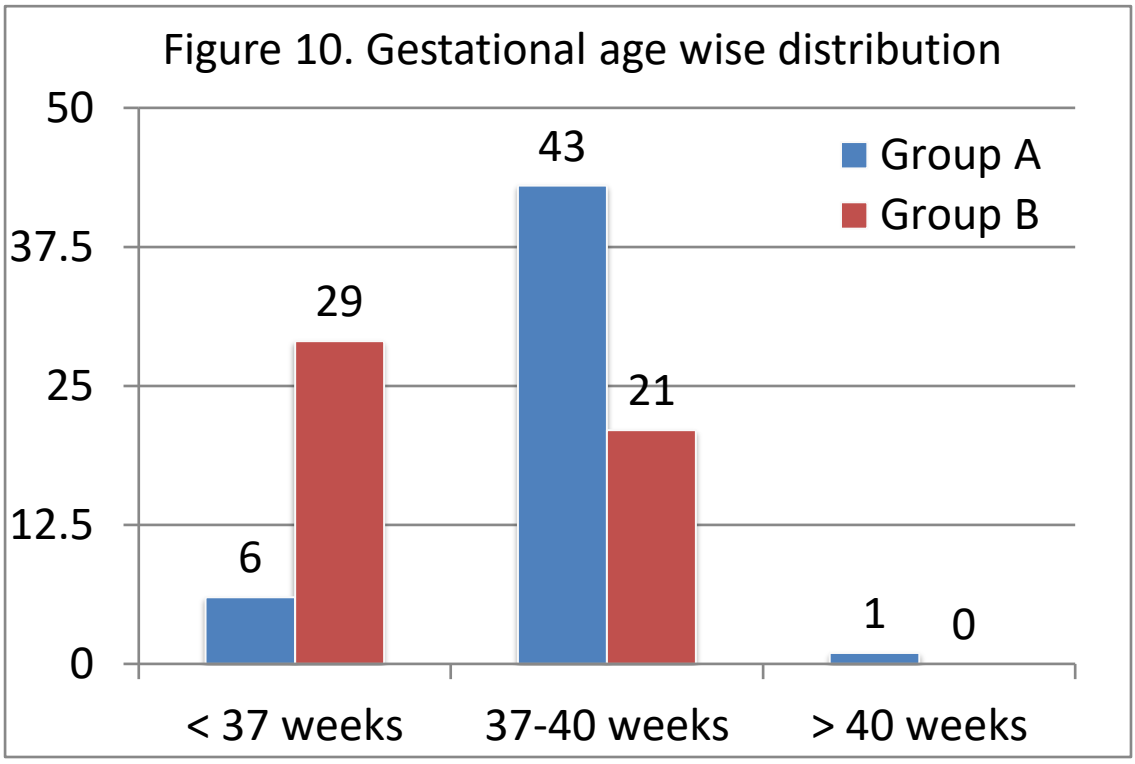


Table 3. Gestational age wise distribution

Gestational age	Group A	Group B	P value
< 37 weeks	6 (6%)	29(29%)	0.00007
37-40 weeks	43 (43%)	21 (21%)	
> 40 weeks	1(1%)	0 (0%)	

In group A, total 6 cases had less than 37 weeks of gestational age and only 1 case had more than 40 weeks of gestational age. In group B, total 29 cases had less than 37 weeks of gestational age and no case had more than 40 weeks of gestational age. On applying chi square test, there was an stastically significant association found between gestational age and ecosprin given to study participants. [Table 3 & Figure 10]

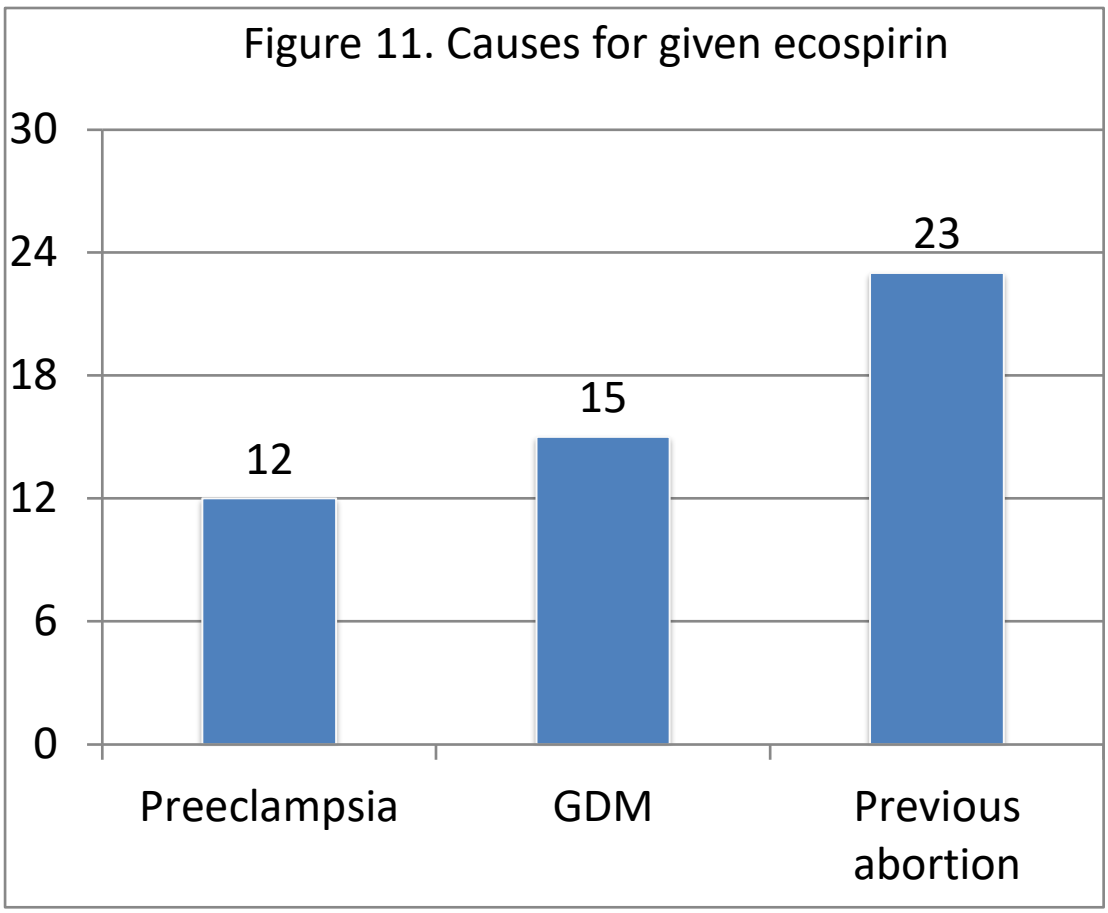


Table 4. Causes for given ecosprin to study participants (n=50)

Causes	Frequency	Percentage
Preeclampsia	12	24
GDM	15	30
Previous second trimester abortion	23	46

Out of total, 12 cases had preeclampsia, 15 cases had GDM and 23 cases had previous second trimester abortion among study participants. [Table 4 & Figure 11]

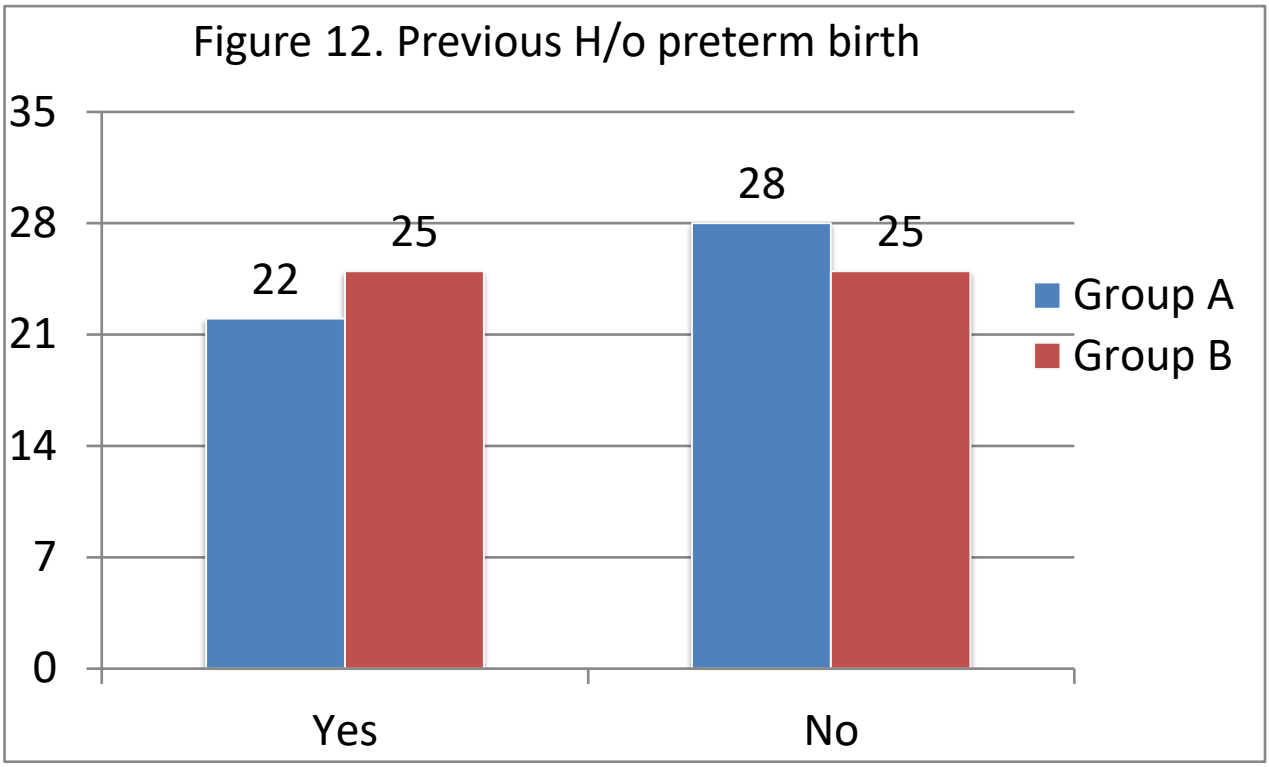


Table 5. Previous H/o Preterm birth wise distribution

Previous H/o Preterm birth	Group A	Group B	P value
Yes	22 (22%)	25 (25%)	0.547
No	28 (28%)	25 (25%)	

In group A, 22(22%) cases had h/o preterm birth and in group B, 28(28%) cases had history of preterm birth. On applying chi square test, there was no association found between previous history preterm birth among both groups. [Table 5 & Figure 12]

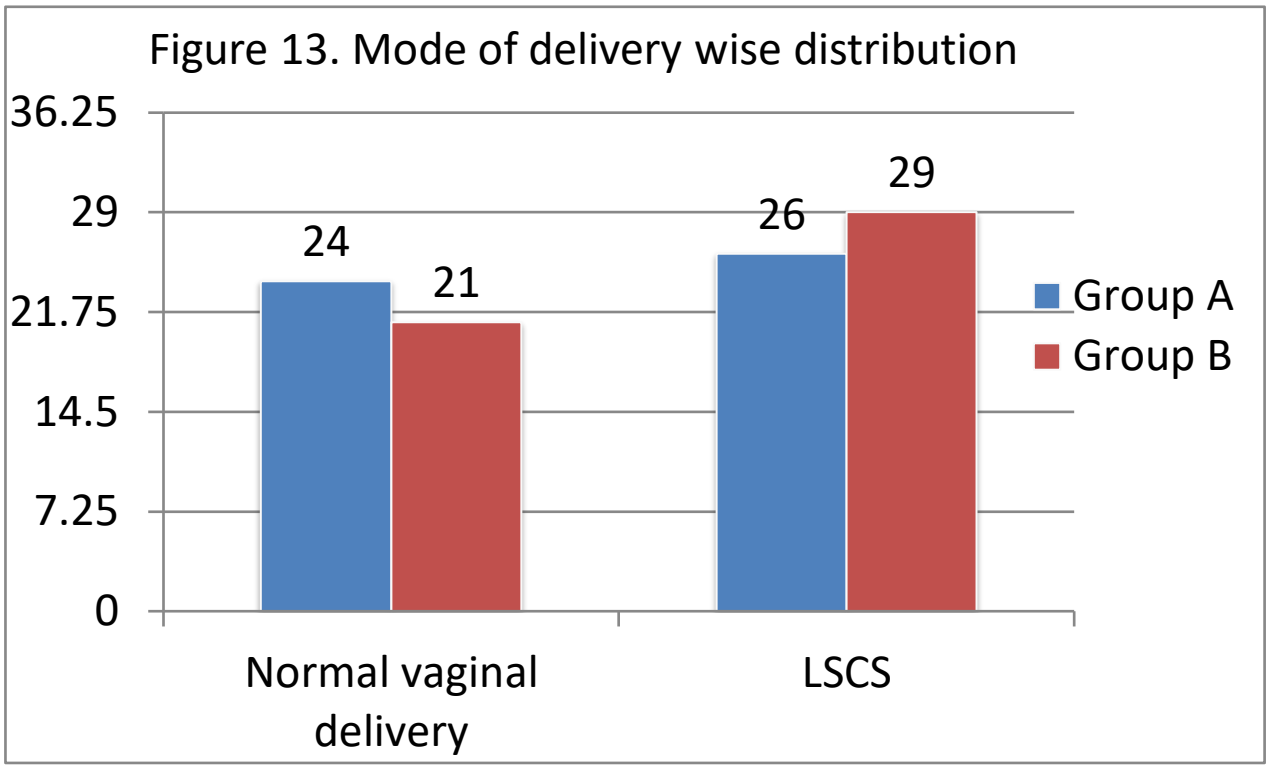


Table 6. Mode of delivery wise distribution

Mode of Delivery	Group A	Group B	P value
Normal vaginal delivery	24 (24%)	21 (21%)	0.546
LSCS	26 (26%)	29 (29%)	

Among the study participants, in group A, 24% cases had normal vaginal delivery and 26% cases had LSCS mode of delivery.in group B, 21% cases had normal vaginal delivery and 29% cases had LSCS mode of delivery. On applying chi square test, there was no association found between mode of delivery among both groups. [Table 6 & Figure 13]

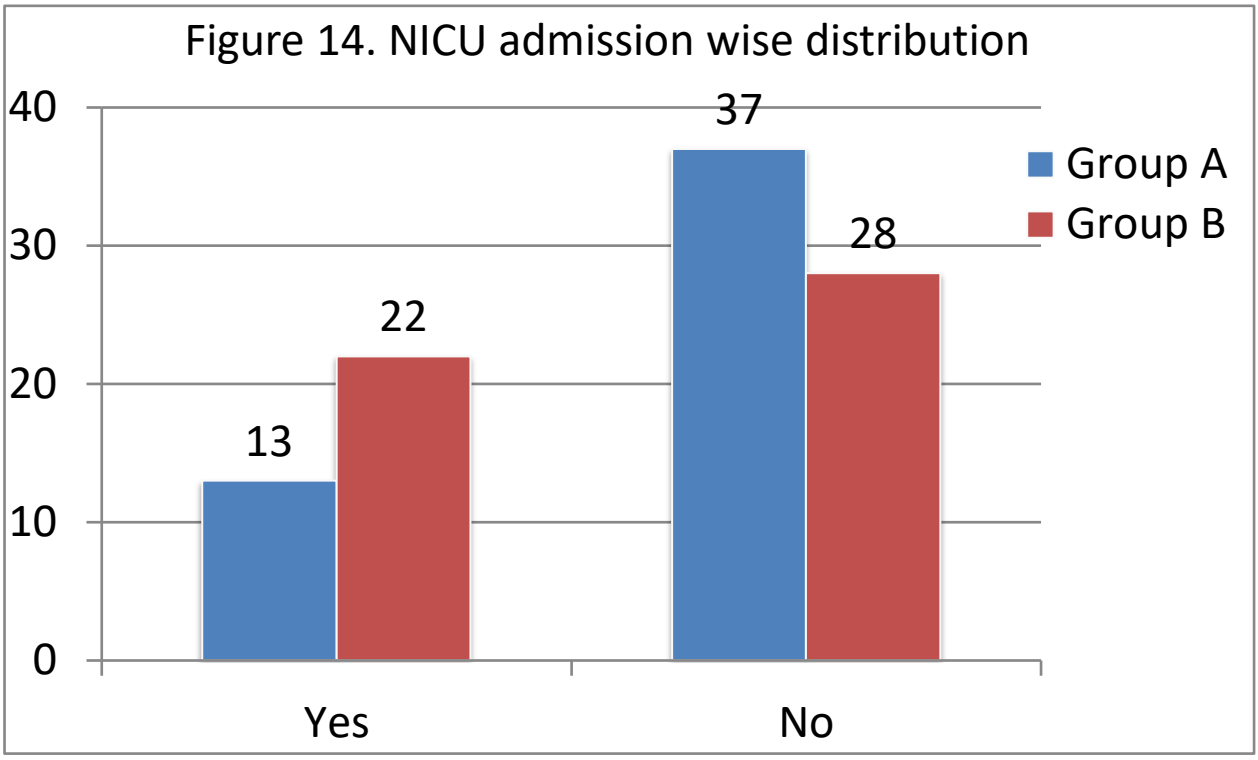


Table 7. NICU admission wise distribution

NICU admission	Group A	Group B	P value
Yes	13 (13%)	22 (22%)	0.0491
No	37 (37%)	28 (28%)	

In group A, 13 cases and in group B 22 cases had required NICU admission. On applying chi square test, there was an association between ecosprin given and NICU admission among study participants. [Table 7 & Figure 14]

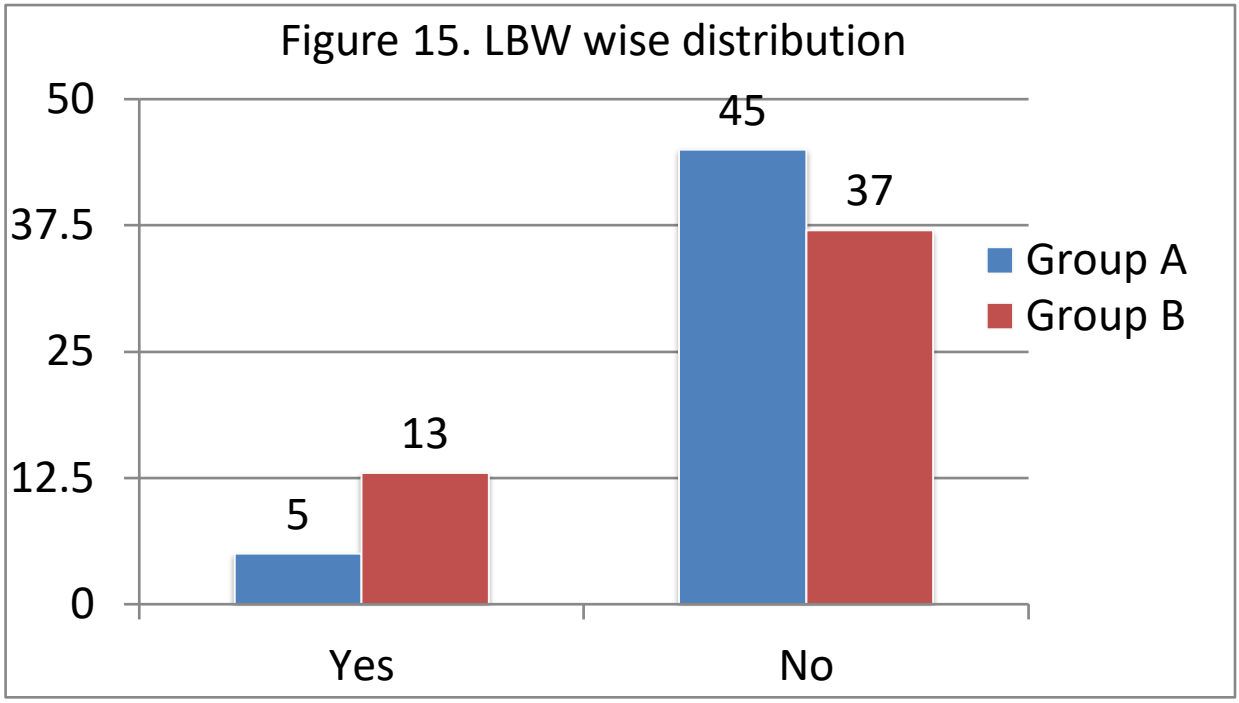


Table 8. LBW wise distribution

LBW	Group A	Group B	P value
Yes	5 (5%)	13 (13%)	0.037
No	45 (45%)	37 (37%)	

In group A, 5 cases had LBW babies and in group B, 13 cases had LBW babies. On applying chi square test, there was an association found between LBW and ecosprin given to study participants. [Table 8 & Figure 15]

Figure 16. Respiratory distress wise distribution

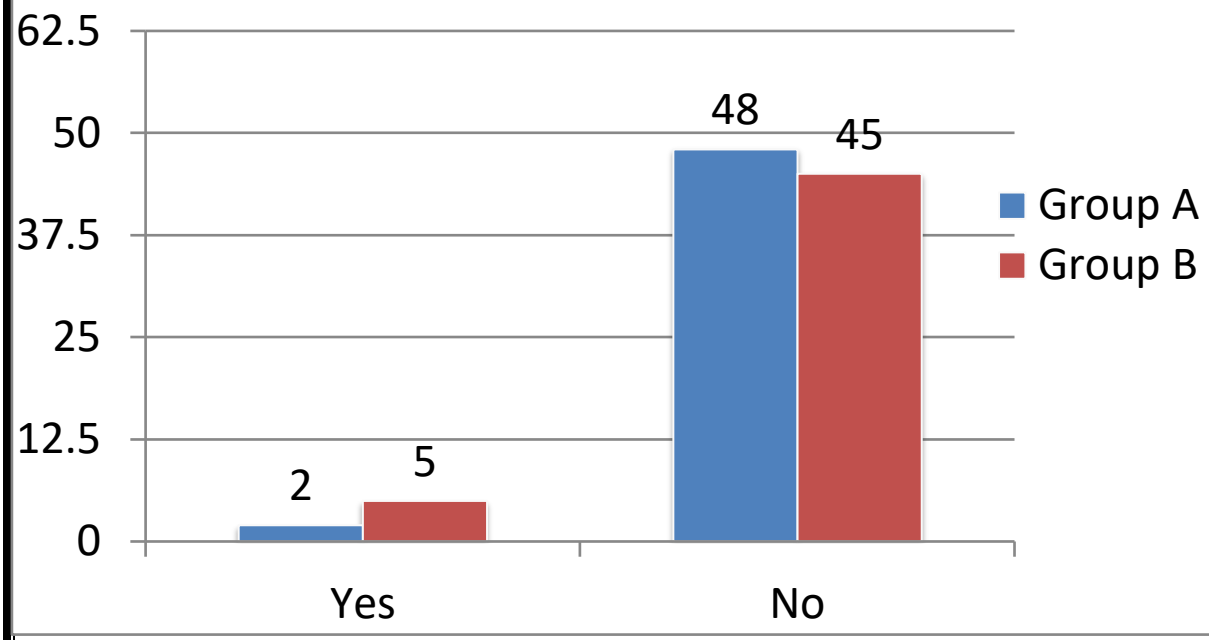


Table 9. Respiratory distress wise distribution

Respiratory distress	Group A	Group B	P value
Yes	2 (2%)	5 (5%)	0.239
No	48 (48%)	45 (45%)	

In group A, 2 cases had respiratory distress and in group B, 5 cases had respiratory distress. On applying chi square test, there was no association between respiratory distress and ecosprin given to study participants. [Table 9 & Figure 16]

Table 10. Mean APGAR score

Duration	Group A	Group B	P value
1 min	7.1 + 1.2	6.9 + 1.7	0.265
5 min	9.5 + 1.2	7.1 + 1.3	0.041

The mean Apgar score at 1 minute of duration was 7.1 + 1.2 in group A and 6.9 + 1.7 in group B. The mean Apgar score at 5 minute of duration was 9.5 + 1.2 in group A and 7.1 + 1.3 in group B. On applying Z test, there was a stastically significant mean APGAR score difference found at 5minutes duration among both groups. [Table 10]

Figure 17. Multiple gestation wise distribution

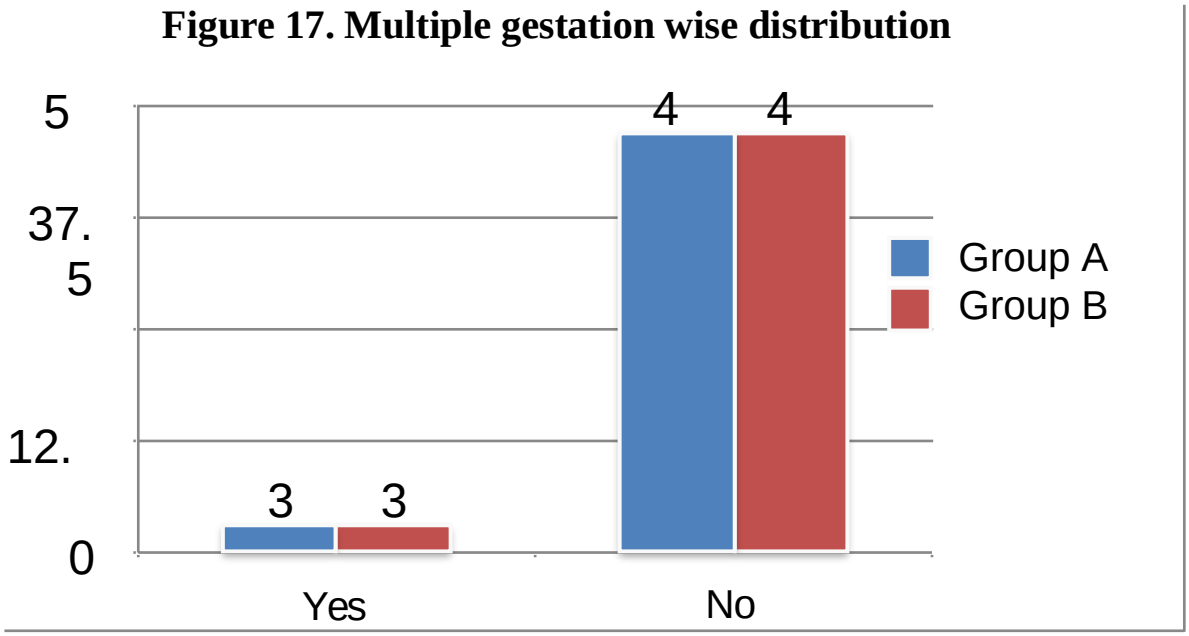


Table 11. Multiple gestation wise distribution

Multiple gestation	Group A	Group B	P value
Yes	3 (3%)	3 (3%)	1
No	47 (47%)	47 (47%)	

Among the study participants, in Group A, 3 cases and in group B, 3 cases had multiple gestation. On applying chi square test, there was no association found between multiple gestation among both groups. [Table 11 & Figure 17]

DISCUSSION

Discussion

The present study aimed to evaluate the effectiveness of low-dose aspirin in preventing preterm birth among pregnant women with known risk factors. The participants were divided into two groups, with Group A receiving aspirin and Group B serving as the control group.

Demographic distribution by age indicated that the majority of participants in both groups were aged 21–30 years, which is consistent with the peak reproductive age range. Although a statistically significant difference in mean age was observed (p=0.002), this likely had minimal clinical relevance. Previous studies have shown that maternal age outside the 20–35 range is associated with an increased risk of preterm birth, but both groups in this study largely fell within the safe range.[3]

Parity distribution showed that most participants were multiparous, with no significant difference between groups (p=0.321). Prior research identifies multiparity as a complex risk factor that can be protective in some contexts but risky in others depending on maternal health status.[2]

The most compelling evidence supporting aspirin's role was the significant reduction in preterm births <37 weeks in Group A (6%) compared to Group B (29%) . This finding is consistent with earlier meta-analyses indicating that aspirin reduces the risk of spontaneous preterm birth before 34 and 37 weeks.[8]

Group A included women with conditions such as preeclampsia (24%), GDM (30%), and previous abortions (46%), conditions known to elevate preterm birth risk. Aspirin's efficacy in such cases may stem from its anti-inflammatory and antithrombotic effects, improving placental perfusion.[103]

While the history of previous preterm birth was slightly higher in Group B (28%) compared to Group A (22%) , the difference was not statistically significant (p=0.547), suggesting that prior preterm delivery was evenly distributed and not a confounding factor.

The mode of delivery did not differ significantly between groups (p=0.546), indicating that aspirin use did not influence the decision for vaginal delivery versus cesarean section. This aligns with evidence that aspirin's effect is more preventive than interventional in labor progression.[104]

Significantly fewer NICU admissions were recorded in Group A (13%) compared to Group B (22%) (p=0.0491), reinforcing aspirin's potential in improving neonatal outcomes. Aspirin may reduce the incidence of complications like preeclampsia, a major contributor to NICU admissions.[5]

Low birth weight was also significantly less frequent in the aspirin group (5% vs. 13%, p=0.037), consistent with aspirin's role in promoting fetal growth by enhancing uteroplacental blood flow.[94]

Although fewer cases of respiratory distress were observed in Group A (2%) compared to Group B (5%), the difference was not statistically significant (p=0.239). This trend, however, aligns with the reduced preterm birth rate, which is a major risk factor for neonatal respiratory complications.[104]

Finally, a significantly higher mean Apgar score at 5 minutes was observed in Group A (9.5 ±1.2) versus Group B (7.1 ±1.3) (p=0.041), suggesting better immediate neonatal health outcomes associated with aspirin use. This is supported by studies linking maternal aspirin use to improved placental function and neonatal vitality.[105]

Strength of the Study

This study provides valuable insights into the potential role of low-dose aspirin (Ecosprin) in preventing preterm birth. One of its key strengths is its comprehensive approach, covering a wide range of maternal characteristics, including gestational age, gravida status, previous pregnancy history, and maternal health conditions. The study's large sample size of 100 participants ensures that the results are statistically relevant and provide a broad representation of the target population. Furthermore, the inclusion of both term and preterm birth groups allows for meaningful comparisons of Ecosprin's effectiveness in preventing preterm labor. The study's clear

focus on neonatal outcomes, such as Apgar scores and birth weight, further strengthens its applicability to clinical practice, as these outcomes are directly linked to the effectiveness of any prenatal intervention.

Implications

The findings of this study suggest that low-dose aspirin may be a beneficial intervention for reducing preterm birth rates, especially for women at high risk, such as those with previous preterm births or underlying health conditions like preeclampsis,gestational diabetes. The improvement in birth weight and the reduction in early preterm births have significant implications for both maternal and neonatal health. If these results are replicated in larger trials, low-dose aspirin could be integrated into standard care for at-risk pregnancies, offering a cost-effective and non-invasive option for preventing preterm birth and related complications. Additionally, the study underscores the need for personalized treatment approaches, taking into account maternal history and health conditions.

Recommendations

Based on the results of this study, it is recommended that low-dose aspirin be considered for women at high risk of preterm birth, particularly those with a history of previous preterm deliveries or conditions like preeclampsia and gestational diabetes. Healthcare providers should assess the individual risk profiles of patients and consider early intervention with low-dose aspirin as part of a broader strategy to prevent preterm birth. Further studies are needed to determine the optimal timing, dosage, and duration of treatment to maximize benefits. Additionally, patient adherence to the regimen should be closely monitored to ensure efficacy.

LIMITATION

Limitations

Despite its strengths, the study has several limitations. First, the sample size of 100 participants, while adequate for initial findings, may not be large enough to draw definitive conclusions. A larger cohort would help to further validate the results and ensure that the observed effects are statistically significant across a wider population. Additionally, the study did not differentiate between spontaneous and medically indicated preterm births, which could have provided more granular insights into the mechanisms of Ecosprin's effectiveness. Another limitation is the lack of long-term follow-up on neonatal health beyond birth, which could provide more information on the lasting effects of Ecosprin use on child development and health outcomes.

Future Aspects

Future research should focus on conducting large-scale randomized controlled trials with diverse populations to further assess the effectiveness of low-dose aspirin in preventing preterm birth. These studies should include both high-risk and low-risk groups, and also differentiate between spontaneous and medically indicated preterm births to better understand the specific mechanisms involved. Additionally, research should explore the optimal timing for initiating aspirin therapy, as well as its long-term effects on both maternal and neonatal health. Given the promising results of this study, further investigation into the combined use of low-dose aspirin with other preventive measures, such as progesterone supplementation, should also be considered.

CONCLUSION

Conclusion

This prospective cohort study investigated the role of low-dose aspirin (Ecosprin) in the prevention of preterm birth among high-risk pregnant women. The results demonstrated that low-dose aspirin significantly reduced the incidence of preterm delivery before 37 weeks of gestation, with only 6% of cases in the aspirin group experiencing preterm birth compared to 29% in the control group ($p=0.00007$). Additionally, the aspirin group showed a statistically significant reduction in NICU admissions ($p=0.0491$) and incidence of low birth weight ($p=0.037$).

Although no significant difference was observed in respiratory distress or mode of delivery between the groups, the mean Apgar score at 5 minutes was notably higher in the aspirin group, suggesting improved neonatal outcomes.

The findings support the hypothesis that low-dose aspirin has a beneficial effect in reducing preterm births and improving perinatal outcomes among women at risk due to factors such as previous preterm birth, preeclampsia, and gestational diabetes. However, further large-scale randomized controlled trials are warranted to validate these results and establish standardized guidelines for the use of aspirin in such high-risk pregnancies.

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ANNEXURES

PROFORMA
LOW DOSE ASPIRIN IN THE PREVENTION OF PRETERM BIRTH

NAME: AGE:
UHID NO: ADDRESS:

I.PNO:
DATE/TIMEOFADMISSION:
DATE/TIMEOFDISCHARGE:
CHIEFCOMPLAINTS:
OBSTETRICAL HISTORY: Booked/ Unbooked/ Referred
Married Life: Consanguinous marriage: Yes/ No
Obstetrical Score:
MENSTRUAL HISTORY:
LMP:
EDD: cEDD:
POG:
PAST HISTORY:
PERSONAL HISTORY:
FAMILY HISTORY:

GENERAL PHYSICAL EXAMINATION:
Pallor/ Icterus/ Cyanosis/ Clubbing/ Lymphadenopathy/ Edema
Pulse: RR:
BP:
RS: Temp:
CNS: CVS:
Per Abdomen:
Per Speculum:
Per Vagina:
PROVISIONAL DIAGNOSIS:
INVESTIGATIONS:
BLOOD GROUP

- URINE ROUTINE

Date	**HB(gm%)**	**PCV(%)**	**WBC(th/cubicmm)**	**Platelet (th/cubicmm)**	**RBC(mil/cubicmm)**

Coagulation profile: PT/ APTT/ INR

OUTCOME
Primary-Gestational age at delivery: preterm/term/post term
Secondary-Mode of delivery: vaginal/ caesarean/ instrumental
Perinatal outcome : Birth weight/APGAR Score/ NICU admission

NEONATAL AT BIRTH				
GESTATIONAL AGE	WEIGHT	CONGENITAL ANOMALY	CARE	
			ROUTINE	NICU

NICU DAY-1 TO DAY-7

		DAY -1	**DAY -2**	**DAY -3**	**DAY -4**	**DAY -5**	**DAY -6**	**DAY -7**
RESPIRATORY STATUS	**O_2**							
	Tachypnea							
CVS STATUS	**Tachycardia**							
	Cyanosis							
SEPSIS (Fever)	**Present**							
	Absent							
NEUROLOGICAL STATUS	**Tone**							
	Reflex							
HAEMOTOLOGICAL STATUS	**Anemia**							
	Leucopenia							
	Thrombocytopenia							
	Coagulation Profile							

INFORMED CONSENT FORM

I Mrs._____ have been explained in my own understandable language, that I will be included in a study which is "**LOW DOSE ASPIRIN IN THE PREVENTION OF PRETERM BIRTH**."

I have been explained that my clinical findings, investigations will be assessed and documented for study purpose.

I have been explained my participation in this study is entirely voluntary, and I can withdraw from the study any time and this will not affect my relation with my doctor or the treatment for my ailment.

I have been explained about the interventions needed possible benefits and adversities due to interventions, in my own understandable language.

I have understood that all my details found during the study are kept confidential and while publishing or sharing of the findings, my details will be masked.

I have principal investigator mobile number for enquiries.

I in my sound mind give full consent to be added in the part of this study.

Signature of the patient: Signature of the witness:
Name: Name:
Date:
Place: Relation to the patient:

ಮಾಹಿತಿನೀಡಿದಒಪ್ಪಿಗೆನಮೂನೆ

ನಾನು ಶ್ರೀಮತಿ____ ನನ್ನ ಸ್ವಂತ ಅರ್ಥವಾಗುವ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಿದ್ದೇನೆ, "ಪೂರ್ವ ಜನನದ ತಡೆಗಟ್ಟುವಿಕೆಯಲ್ಲಿ ಕಡಿಮೆ ಡೋಸ್ ಆಸ್ಪಿರಿನ್" ಎಂಬ ಅಧ್ಯಯನದಲ್ಲಿ ನನ್ನನ್ನು ಸೇರಿಸಲಾಗುವುದು.ನನ್ನ ಕ್ಲಿನಿಕಲ್ ಸಂಶೋಧನೆಗಳು, ತನಿಖೆಗಳನ್ನು ಮೌಲ್ಯಮಾಪನ ಮಾಡಲಾಗುತ್ತದೆ ಮತ್ತು ಅಧ್ಯಯನ ಉದ್ದೇಶಕ್ಕಾಗಿ ದಾಖಲಿಸಲಾಗುತ್ತದೆ ಎಂದು ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನನ್ನ ಭಾಗವಹಿಸುವಿಕೆಯು ಸಂಪೂರ್ಣವಾಗಿ ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ ಎಂದು ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ ಮತ್ತು ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಬಹುದು ಮತ್ತು ಇದು ನನ್ನ ವೈದ್ಯರೊಂದಿಗಿನ ನನ್ನ ಸಂಬಂಧ ಅಥವಾ ನನ್ನ ಕಾಯಿಲೆಯ ಚಿಕಿತ್ಸೆಯ ಮೇಲೆ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ.ನನ್ನ ಸ್ವಂತ ಅರ್ಥವಾಗುವ ಭಾಷೆಯಲ್ಲಿ ಮಧ್ಯಸ್ಥಿಕೆಗಳಿಂದಾಗಬಹುದಾದ ಪ್ರಯೋಜನಗಳು ಮತ್ತು ಪ್ರತಿಕೂಲತೆಗಳ ಅಗತ್ಯವಿರುವ ಮಧ್ಯಸ್ಥಿಕೆಗಳ ಬಗ್ಗೆ ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಪತ್ತೆಯಾದ ನನ್ನ ಎಲ್ಲಾ ವಿವರಗಳನ್ನು ಗೌಪ್ಯವಾಗಿ ಇರಿಸಲಾಗಿದೆ ಮತ್ತು ಸಂಶೋಧನೆಗಳನ್ನು ಪ್ರಕಟಿಸುವಾಗ ಅಥವಾ ಹಂಚಿಕೊಳ್ಳುವಾಗ, ನನ್ನ ವಿವರಗಳನ್ನು ಮರೆಮಾಚಲಾಗುತ್ತದೆ ಎಂದು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.ವಿಚಾರಣೆಗಾಗಿ ನಾನು ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿಯ ಮೊಬೈಲ್ ಸಂಖ್ಯೆಯನ್ನು ಹೊಂದಿದ್ದೇನೆ.ಈ ಅಧ್ಯಯನದ ಭಾಗದಲ್ಲಿ ಸೇರಿಸಲು ನನ್ನ ಉತ್ತಮ ಮನಸ್ಸಿನಲ್ಲಿ ನಾನು ಸಂಪೂರ್ಣ ಒಪ್ಪಿಗೆಯನ್ನು ನೀಡುತ್ತೇನೆ.

ರೋಗಿಯ ಸಹಿ:
ಸಾಕ್ಷಿಯ ಸಹಿ:
ಹೆಸರು:
ಹೆಸರು:
ದಿನಾಂಕ:
ಸ್ಥಳ:
ರೋಗಿಗೆ ಸಂಬಂಧ:

PATIENT INFORMATION SHEET

STUDY TITLE: LOW DOSE ASPIRIN IN THE PREVENTION OF PRETERM BIRTH

STUDY SITE: R.L Jalappa Hospital and Research Centre, Tamaka, Kolar. This is to inform you that, you require low dose aspirin, for making the diagnosis and extent of the pregnancy and for planning of the treatment,predicting adverse maternal and fetal outcome in pregnant patients.

We are conducting this study to predict severity and adverse maternal and fetal outcome of this condition.

If you are willing you will be enrolled in this study and we will send relevant investigations which are required for diagnosis and treatment.

This will facilitate identifying the extent of severity of Preterm births and help predict abnormal maternal and fetal outcome ,thus can be used as an adjunct to assist in clinical decisions.You are free to opt- out of the study at any time if you are not satisfied or apprehensive to be a part of the study. Your treatment and care will not be compromised if you refuse to be a part of the study. The study will not add any risk or financial burden to you if you are part of the study. In case of any complication during surgery patient will be treated accordingly.

Your identity and clinical details will be confidential. You will not receive any financial benefit for being a part of the study. You are free to contact Dr. CHITTARI SWETHAMRUTHA or any other member of the above research team for any doubt or clarification you have.

Dr. CHITTARI SWETHAMRUTHA
Mobile no:
E-mail id:

ರೀಗಿಯಮಾಹಿತಿಯಹಾಳೆ

ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ: ಪ್ರಸವಪೂರ್ವ ಜನನದ ತಡೆಗಟ್ಟುವಿಕೆಯಲ್ಲಿ ಕಡಿಮೆ ಡೋಸ್ ಆಸ್ಪಿರಿನ್ಸ್ಟಡಿ ಸೈಟ್: ಆರ್.ಎಲ್ ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರ, ಟಮಕ, ಕೋಲಾರ. ಗರ್ಭಾವಸ್ಥೆಯ ರೋಗನಿರ್ಣಯ ಮತ್ತು ವ್ಯಾಪ್ತಿಯನ್ನು ಮಾಡಲು ಮತ್ತು ಚಿಕಿತ್ಸೆಯ ಯೋಜನೆಗಾಗಿ, ಗರ್ಭಿಣಿ ರೋಗಿಗಳಲ್ಲಿ ತಾಯಿಯ ಮತ್ತು ಭ್ರೂಣದ ಪ್ರತಿಕೂಲ ಫಲಿತಾಂಶವನ್ನು ಊಹಿಸಲು ನಿಮಗೆ ಪ್ರಿಕ್ಲಾಂಪ್ಸಿಯಾ ಅಗತ್ಯವಿರುತ್ತದೆ ಎಂದು ಇದು ನಿಮಗೆ ತಿಳಿಸುತ್ತದೆ.ಈ ಸ್ಥಿತಿಯ ತೀವ್ರತೆ ಮತ್ತು ಪ್ರತಿಕೂಲ ತಾಯಿಯ ಮತ್ತು ಭ್ರೂಣದ ಫಲಿತಾಂಶವನ್ನು ಊಹಿಸಲು ನಾವು ಈ ಅಧ್ಯಯನವನ್ನು ನಡೆಸುತ್ತಿದ್ದೇವೆ.ನೀವು ಸಿದ್ದರಿದ್ದರೆ ನೀವು ಈ ಅಧ್ಯಯನಕ್ಕೆ ದಾಖಲಾಗುತ್ತೀರಿ ಮತ್ತು ರೋಗನಿರ್ಣಯ ಮತ್ತು ಚಿಕಿತ್ಸೆಗೆ ಅಗತ್ಯವಿರುವ ಸಂಬಂಧಿತ ತನಿಖೆಗಳನ್ನು ನಾವು ಕಳುಹಿಸುತ್ತೇವೆಇದು ಪ್ರೀಕ್ಲಾಂಪ್ಸಿಯಾದ ತೀವ್ರತೆಯ ಪ್ರಮಾಣವನ್ನು ಗುರುತಿಸಲು ಸಹಾಯ ಮಾಡುತ್ತದೆ ಮತ್ತು ಅಸಹಜ ತಾಯಿಯ ಮತ್ತು ಭ್ರೂಣದ ಫಲಿತಾಂಶವನ್ನು ಊಹಿಸಲು ಸಹಾಯ ಮಾಡುತ್ತದೆ, ಹೀಗಾಗಿ ವೈದ್ಯಕೀಯ ನಿರ್ಧಾರಗಳಲ್ಲಿ ಸಹಾಯ ಮಾಡಲು ಸಹಾಯಕವಾಗಿ ಬಳಸಬಹುದು. ನೀವು ತೃಪ್ತರಾಗದಿದ್ದರೆ ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹೊರಗುಳಿಯಲು ನೀವು ಮುಕ್ತರಾಗಿದ್ದೀರಿ. ಅಥವಾ ಅಧ್ಯಯನದ ಭಾಗವಾಗಲು ಭಯಪಡುತ್ತಾರೆ. ನೀವು ಅಧ್ಯಯನದ ಭಾಗವಾಗಲು ನಿರಾಕರಿಸಿದರೆ ನಿಮ್ಮ ಚಿಕಿತ್ಸೆ ಮತ್ತು ಕಾಳಜಿಗೆ ಧಕ್ಕೆಯಾಗುವುದಿಲ್ಲ. ನೀವು ಅಧ್ಯಯನದ ಭಾಗವಾಗಿದ್ದರೆ ಅಧ್ಯಯನವು ನಿಮಗೆ ಯಾವುದೇ ಅಪಾಯ ಅಥವಾ ಆರ್ಥಿಕ ಹೊರೆಯನ್ನು ಸೇರಿಸುವುದಿಲ್ಲ. ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯ ಸಮಯದಲ್ಲಿ ಯಾವುದೇ ತೊಡಕುಗಳ ಸಂದರ್ಭದಲ್ಲಿ ರೋಗಿಗೆ ಅನುಗುಣವಾಗಿ ಚಿಕಿತ್ಸೆ ನೀಡಲಾಗುತ್ತದೆ.ನಿಮ್ಮ ಗುರುತು ಮತ್ತು ಕ್ಲಿನಿಕಲ್ ವಿವರಗಳು ಗೌಪ್ಯವಾಗಿರುತ್ತವೆ. ಅಧ್ಯಯನದ ಭಾಗವಾಗಿರುವುದರಿಂದ ನೀವು ಯಾವುದೇ ಹಣಕಾಸಿನ ಪ್ರಯೋಜನವನ್ನು ಪಡೆಯುವುದಿಲ್ಲ. ನಿಮ್ಮಲ್ಲಿರುವ ಯಾವುದೇ ಸಂದೇಹ ಅಥವಾ ಸ್ಪಷ್ಟೀಕರಣಕ್ಕಾಗಿ ಡಾ. ಚಿತ್ತಾರಿ ಶ್ವೇತಾಮೃತ ಅಥವಾ ಮೇಲಿನ ಸಂಶೋಧನಾ ತಂಡದ ಇತರ ಸದಸ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಲು ನೀವು ಮುಕ್ತರಾಗಿದ್ದೀರಿ

ಡಾ. ಚಿತ್ತಾರಿ ಶ್ವೇತಾಮೃತ

ಮೊಬೈಲ್ ನಂಬರ್ :

ಈ ಮೇಲ್ ಇಡ್ :

MASTER CHART

SNo	Name of the Patient	Age	Gravida	GestationalAge	Previous	PreviousVa	GDM	Pre-eclamps	PreviousA	MultiplePregnancy	Previoushistoryo	ModeofDelivery	Baby Motherside	BabyNICU	Birthweight	ApgarScore	Ecosprin	Remarks
1	Sushmitha	24	G3A2	38+3					Yes			Vaginal	Yes		2.9	1'7/10,5'9/10	Yes	
2	Shruthi	20	G3P2L1D1	37+1	Yes						Yes	C-Section	Yes		3.3	1'7/10,5'9/10	Yes	
3	Ramya	25	Primi	40			Yes					C-Section		Yes-IDM Care	2.92	1'7/10,5'9/10	Yes	
4	Parvathi	27	G3P1L1A1	39	Yes				Yes			C-Section	Yes		2.6	1'7/10,5'9/10	Yes	
5	Sathya	34	G6P3L1A2D2	37	Yes		Yes		Yes		Yes	C-Section		Yes-Respiratory Distress	2.26	1'7/10,5'9/10	Yes	
6	Nayana	24	G2P1L1	38	Yes		Yes				Yes	C-Section		Yes-IDM Care	2.64	1'7/10,5'9/10	Yes	
7	Shireesha	23	G2P1L1	37+5		Yes					Yes	Vaginal	Yes		2.72	1'7/10,5'9/10	Yes	
8	Nohira	21	G2P1L1	37+1	Yes						Yes	C-Section			2.58	1'7/10,5'9/10	Yes	
9	Veena	34	G3P1L1A1	37		Yes					Yes	Vaginal	Yes		3.24	1'7/10,5'9/10	Yes	
10	Poornima	24	G3P2L2	39		Yes					Yes	Vaginal	Yes		3.12	1'7/10,5'9/10	Yes	
11	Meena	25	G3A2	40+2					Yes			C-Section	Yes		2.72	1'7/10,5'9/10	Yes	
12	Chaitra	21	Primi	37						DCDA-Twins		C-Section		Yes-Preterm Care,LB	2.1,1.9	1'6/10,5'8/10	Yes	

														W				
13	Lakshmi	33	G2P1L1	37		Yes		Yes				Vaginal	Yes		2.32	1'7/10,5'9/10	Yes	
14	Asphia	20	G2P1L1	37+4		Yes		Yes			Yes	Vaginal	Yes		2.26	1'7/10,5'9/10	Yes	
15	Yamuna	21	G2P1L1	40		Yes					Yes	Vaginal	Yes		2.84	1'7/10,5'9/10	Yes	
16	Jayanthi	27	G3P2L2	34+3	Yes			Yes		DCDA-Twins	Yes	C-Section		Yes-Preterm Care,LBW	1.64, 2.08	1'6/10,5'8/10	Yes	
17	Jyothi	26	G4P2L2A1	34+2				Yes			Yes	C-Section		Yes-Preterm Care,LBW	1.66	1'6/10,5'8/10	no	
18	Swathi	31	G3P1L1A1	37+3					Yes			C-Section	Yes		2.08	1'6/10,5'8/10	Yes	
19	Ruchitha	24	G2P1L1	38+5	Yes						Yes	C-Section	Yes		2.96	1'7/10,5'9/10	Yes	
20	Sumiya	27	G4P2L2A1	37+4	Yes						Yes	C-Section	Yes		2.23	1'7/10,5'9/10	Yes	
21	Madhavi	21	Primi	39+2				Yes				Vaginal	Yes		2.44	1'7/10,5'9/10	Yes	
22	Rama	30	Primi	37+1			Yes					C-Section		Yes-IDM Care	2.94	1'7/10,5'9/10	Yes	
23	Varalakshmi	34	G6P2L2A3	38+6	Yes				Yes			C-Section	Yes		2.64	1'7/10,5'9/10	Yes	
24	Vani	27	Primi	38				Yes				Vaginal	Yes		2.44	1'7/10,5'9/10	Yes	
25	Sreelakshmi	27	G3P2L1D1	39+1	Yes				Yes		Yes	C-Section	Yes		2.3	1'7/10,5'9/10	Yes	

26	Padmasree	31	G2P1L1	37+3	Yes		Yes					C-Section		Yes-IDM Care	3.38	1'7/10,5'9/10	Yes	
27	Sahana	21	G2A1	38+5					Yes			Vaginal	Yes		2.64	1'7/10,5'9/10	Yes	
28	Pavitra	29	G2P1L1	37+6	Yes						Yes	C-Section	Yes		2.36	1'7/10,5'9/10	Yes	
29	Saniya	19	Primi	40+1				Yes				C-Section	Yes		2.86	1'7/10,5'9/10	Yes	
30	Aiyesha	25	G4P3L2D1	35		Yes					Yes	Vaginal	Yes		1.42	1'6/10,5'8/10	Yes	
31	Manjula	20	G2P1L0	35+4		Yes		Yes			Yes	C-Section		Yes-Respiratory Distress	2.32	1'6/10,5'8/10	Yes	
32	Pavitra	22	Primi	38+2				Yes				Vaginal	Yes		2.76	1'7/10,5'9/10	Yes	
33	Manjula	38	Primi	36+6				Yes				C-Section		Yes-Preterm Care,LBW	1.9	1'6/10,5'8/10	no	
34	Nayana	26	G3P1L1A1	38+4		Yes	Yes		Yes			Vaginal		Yes-IDM Care	3.22	1'6/10,5'8/10	Yes	
35	Sulthana	29	G2P1L1	35+6	Yes		Yes					C-Section		Yes-IDM Care	3.1	1'7/10,5'9/10	Yes	
36	Roja	29	G4P3L1D2	40+1		Yes		Yes			Yes	Vaginal	Yes		3	1'7/10,5'9/10	Yes	
37	Trisha	22	G2A1	38+2				Yes	Yes			C-Section	Yes		2.7	1'7/10,5'9/10	Yes	
38	Farzana	26	G4P3L3	37+5							Yes	Vaginal	Yes		3.1	1'7/10,5'9/10	Yes	
39	Chandrika	23	G3A2	38					Yes	DCDA-Twins		C-Section		Yes-Preterm	1.86, 2.3	1'7/10,5'9/10	Yes	

														Care,LBW				
40	Revathi	26	G2A1	38+4					Yes			Vaginal	Yes		2.98	1'7/10,5'9/10	Yes	
41	Arbin Taj	24	G3P1L0A1D1	38+3	Yes				Yes		Yes	C-Section	Yes		2.38	1'7/10,5'9/10	Yes	
42	Manasa	23	G4A3	38					Yes			Vaginal	Yes		3.16	1'7/10,5'9/10	Yes	
43	Nandini	32	G3P1L1A1	36+5		Yes			Yes		Yes	Vaginal	Yes		2.74	1'7/10,5'9/10	Yes	
44	Nagamani	32	G4P1L0A2	37		Yes		Yes	Yes			Vaginal		Yes-Preterm Care,LBW	1.84	1'6/10,5'8/10	Yes	
45	Bhumika	21	G2A1	39+1					Yes			Vaginal	Yes		2.7	1'7/10,5'9/10	Yes	
46	Amrutha	23	G3P1L1A1	40+1	Yes				Yes			C-Section	Yes		3.2	1'7/10,5'9/10	Yes	
47	Nandini	38	G4P1L1A2	39+4	Yes				Yes			C-Section	Yes		2.54	1'7/10,5'9/10	Yes	
48	Navyasree	26	G3P1L1A1	38+3		Yes			Yes			Vaginal	Yes		3.12	1'7/10,5'9/10	Yes	
49	Chandana	27	G2P1L1	38+1	Yes			Yes				C-Section	Yes		3.18	1'7/10,5'9/10	no	
50	Shabnam	19	G2P1L1	40+2		Yes					Yes	Vaginal	Yes		3.06	1'7/10,5'9/10	No	
51	Manjula	29	G3P2L1D1	35+6		Yes					Yes	Vaginal		Yes-Preterm Care,LBW	2.18	1'7/10,5'9/10	No	
52	Bibi Rani	21	G2P1L1	38+4		Yes					Yes	Vaginal	Yes		3.24	1'7/10,5'9/10	No	

53	Asha	19	G2P1L1	35+4							Yes	Vaginal		Yes-Preterm Care,LBW	1.94	1'6/10,5'8/10	No	
54	Meghana	27	G3P1L1A1	37+4	Yes				Yes			C-Section	Yes		2.7	1'7/10,5'9/10	No	
55	Silpa	31	G2P1L1	38+1		Yes					Yes	Vaginal	Yes		3.22	1'7/10,5'9/10	No	
56	Asma	26	G3P2L2	37+2	Yes						Yes	C-Section	Yes		2.52	1'7/10,5'9/10	No	
57	Veena	25	G4P1L1A2	34+5		Yes			Yes			Vaginal		Yes-Respiratory Distress	2.28	1'7/10,5'9/10	No	
58	Suma	25	G4P1L1A2	39+4		Yes			Yes			Vaginal	Yes		2.72	1'7/10,5'9/10	No	
59	Neeva	33	G5P4L3D1	36+4		Yes					Yes	Vaginal	Yes		2.18	1'7/10,5'9/10	No	
60	Pavitra	23	G2P1L1	33+5		Yes		Yes				C-Section		Yes-Preterm Care,LBW	1.38	1'6/10,5'8/10	No	
61	Nandini	26	G2P1L1	38+6	Yes						Yes	C-Section	Yes		2.92	1'7/10,5'9/10	No	
62	Saniya	20	G2A1	38+2					Yes			Vaginal	Yes		2.4	1'7/10,5'9/10	No	
63	Kavana	26	G2P1L1	36+1	Yes			Yes			Yes	C-Section	Yes		2.22	1'7/10,5'9/10	No	
64	Sharada	31	G4P2L2A1	38		Yes					Yes	Vaginal	Yes		2.7	1'7/10,5'9/10	No	
65	Dharani	23	G5P1L1A3	37+6	Yes				Yes			C-Section	Yes		2.98	1'7/10,5'9/10	No	

66	Aliya	22	G2P1L1	33+5	Yes						Yes	C-Section		Yes-Preterm Care,LBW	1.76	1'6/10,5'8/10	No	
67	Bharathi	27	G2P1L1	36+1		Yes		Yes			Yes	Vaginal		Yes-Respiratory Distress	2.8	1'6/10,5'8/10	No	
68	Bharathi	27	G3P1L1A1	35+2	Yes				Yes			C-Section		Yes-Preterm Care,LBW	2.12	1'6/10,5'8/10	No	
69	Kavya	29	G3P1L1A1	36+2	Yes				Yes			C-Section	Yes		3.12	1'7/10,5'9/10	No	
70	Sravani	25	G3P2L2	32+4		Yes					Yes	Vaginal		Yes-Preterm Care,LBW	2	1'6/10,5'8/10	No	
71	Seema	26	G3P1L0A1D1	34+4		Yes			Yes		Yes	Vaginal		Yes-Preterm Care,LBW	1.82	1'6/10,5'8/10	No	
72	Silpa	28	G4P2L2A1	39+1		Yes			Yes			Vaginal	Yes		3.22	1'7/10,5'9/10	No	
73	Poornima	23	G2P1L2	38+3		Yes					Yes	C-Section	Yes		2.72	1'7/10,5'9/10	No	
74	Nayana	24	G3P2L2	40		Yes					Yes	Vaginal		Yes-Respiratory Distress	2.8	1'6/10,5'8/10	No	
75	Preethi	21	G2P2L1	34+5	Yes					DCDA-Twins	Yes	C-Section		Yes-Preterm Care,LBW	1.64, 1.56	1'6/10,5'8/10	No	

76	Nandini	22	G2P1L1	36		Yes					Yes	C-Section	Yes		2.42	1'7/10,5'9/10	No	
77	Jasmin	25	G3P2L2	37+1	Yes			Yes			Yes	C-Section	Yes		3.24	1'7/10,5'9/10	No	
78	Mamatha	36	G2P1L1	34+5	Yes		Yes					C-Section		Yes-IDM Care	3.12	1'7/10,5'9/10	No	
79	Suman Taj	25	G5P4L4	37		Yes					Yes	Vaginal	Yes		2.4	1'7/10,5'9/10	No	
80	Aiyesha	31	G4P3L3	35		Yes					Yes	Vaginal		Yes-Preterm Care,LBW	1.8	1'7/10,5'9/10	No	
81	Anjum	33	G5P2L2A2	38+3	Yes	Yes			Yes			C-Section	Yes		2.6	1'7/10,5'9/10	No	
82	Amala	33	G3P3L2	34		Yes					Yes	Vaginal		Yes-Respiratory Distress	2.08	1'7/10,5'9/10	No	
83	Simran	24	Primi	35			Yes	Yes				Vaginal		Yes-IDM Care	3.18	1'7/10,5'9/10	No	
84	Lavanya	27	G2P1L1	36	Yes					MCDA-Twins		C-Section		Yes-Preterm Care,LBW	1.54, 2.3	1'7/10,5'9/10	No	
85	Sumalatha	30	G3P1L1A1	35+6	Yes				Yes			C-Section		Yes-Respiratory Distress	2.6	1'6/10,5'8/10	No	
86	Farzana	33	G4P3L2D1	37		Yes					Yes	Vaginal	Yes		3.1	1'7/10,5'9/10	No	
87	Komala	26	G4P1L1A2	36	Yes				Yes			C-Section	Yes		2.6	1'7/10,5'9/10	No	
88	Shabina	27	G2A1	37+3					Yes			C-Section	Yes		2.36	1'7/10,5'9/1	No	

																0		
89	Fiza	22	G2P1L1	35+6	Yes						Yes	C-Section		Yes-Preterm Care,LBW	2.18	1'6/10,5'8/10	No	
90	Sumitra	28	G3P1L1A1	37	Yes				Yes			C-Section	Yes		2.6	1'7/10,5'9/10	No	
91	Safiha	26	Primi	37+1						MCDA-Twins		C-Section		Yes-Preterm Care,LBW	2.1,2.2	1'6/10,5'8/10	No	
92	Heena	26	G3P2L2	34+6	Yes						Yes	C-Section	Yes		2.6	1'7/10,5'9/10	No	
93	Chaitra	24	G2A1	35+6					Yes			C-Section	Yes		2.7	1'7/10,5'9/10	No	
94	Sumitra	30	G4P1L1A2	36+2	Yes		Yes		Yes			C-Section		Yes-IDM Care	2.62	1'6/10,5'8/10	No	
95	Surekha	24	G2A1	35+4			Yes		Yes			Vaginal		Yes-IDM Care	2.56	1'7/10,5'9/10	No	
96	Leelavathi	35	G3P1L1A1	36+4	Yes				Yes			C-Section	Yes		2.4	1'7/10,5'9/10	No	
97	Annapoorna	40	G2A1	36+2				Yes	Yes			C-Section	Yes		3.5	1'7/10,5'9/10	No	
98	Divya	22	G3P1L1A1	41					Yes		Yes	vaginal	yes		2.9	1'7/10, 5'9/10	Yes	
99	Ambika	28	G4P1L1A2	40+4		Yes			Yes			vaginal	yes		3.1	1'7/10,5'9/10	Yes	
100	Bhavana	26	G2A1	40+2					Yes			vaginal	yes		3.2	1'7/10,5'9/10	Yes	