International Journal of Pharmaceutical Drug Design
IJPDD (JANUARY, 2024)
Website: https://ijpdd.org/
Vol.-1, Issue-2
Page No: 39-50

Exploring Pregnancy Complications and Interventions: A Comprehensive and In-Depth Analysis for Enhanced Understanding and Medical Approaches

Km. Shiva[1], Km. Bhumika[2], Jiyaul Hak[3], Mukesh Kumar[4], Suraj Mandal[5]

[1]NGI College of Pharmacy, Neelkanth Group of Institutions, Near SVBP University, Modipuram, Meerut, 250001, U.P., India

[2]Department of Pharmacy, IIMT College of Medical Sciences, IIMT University, O-Pocket, Ganganagar, Meerut, 250001, U.P., India

Article History

Received : 18/12/2023
Revised : 07/01/2024
Accepted : 15/01/2024

Abstract:

Physical, hormonal, and emotional changes accompany pregnancy, which is a transforming and important time in a woman's life. While the majority of pregnancies go off without a hitch, a sizable percentage experience difficulties that endanger both the expectant woman and the growing fetus. The vast range of pregnancy difficulties are covered in this thorough review, from common problems like gestational diabetes and preeclampsia to uncommon ailments like placental abruption and ectopic pregnancies, the variety of treatments and management techniques accessible to medical practitioners to ensure both mother and child's wellbeing throughout difficult pregnancies. It looks at prenatal care, diagnostic techniques, and treatment approaches including bed rest, medication, and surgery. The necessity of collaborative decision-making with expectant women and the relevance of diverse healthcare teams in developing individualized treatment strategies are both highlighted. Moreover, the value of ongoing study and technology development in enhancing outcomes for high-risk pregnancies. It draws attention to the potential benefits of cutting-edge innovations in early identification, monitoring, and management of pregnancy problems, including telemedicine and artificial intelligence.

Keywords: pregnancy, woman's life, treatment strategies, medication, high-risk pregnancies

***Corresponding Author**

Km. Shiva

NGI College of Pharmacy, Neelkanth Group of Institutions, Near SVBP University, Modipuram, Meerut, 250001, U.P., India

Email: rajputshiva026@gmail.com

1. Introduction

Each year, there are more than 200 million pregnancies in the world. These pregnancies are unplanned in almost 40% of cases. Unwanted is different from intended. Every couple should have the option to determine how many children they want to have and when they are ready to conceive. For the 40% of unplanned deliveries, early prenatal care is essential to preventing poor perinatal outcomes and issues. Pregnancy can be identified and unwanted and unexpected pregnancies averted at routine checkups, sports checks, well-woman exams, crises, and acute visits (Schaefer, Hilfiker-Kleiner, and Keil 2023)(Wastnedge et al. 2021). Women may have a higher probability of receiving early prenatal care if they use these chances for a pregnancy test. All women of reproductive age should consume 400–800 mcg of folate per day to prevent neural tube abnormalities. The American College of Obstetrics and Gynecology (ACOG) and the United States Preventive Task Force (USPTF) award this recommendation an A since most women arrive beyond the critical period of

organogenesis. The main variables in defining a healthy pregnancy and reproductive life include preventing, recognizing, and treating preconception health issues, pregnancy readiness, early prenatal care, and minimizing risks during the perinatal and interconceptional periods (Jamieson and Rasmussen 2022)(Neuberger 2022). Women who visit for checks in between treatments frequently worry about abdominal discomfort, atypical uterine bleeding, and irregular menstruation. Women with functioning reproductive systems must take a pregnancy test to rule out pregnancy. The gold standard for prenatal diagnosis is the quantitative beta HCG radioimmunoassay. Most healthcare practitioners in emergency, ambulatory, or episodic care settings use urine HCG testing for the first screen (Pishko and Marshall 2022)(Mehedintu et al. 2021). The quantitative HCG test is often carried out in conjunction with an examination and an ultrasound to determine if a pregnancy is normal or abnormal, to correlate gestational age with the last period that was normal, or to offer suggestions for managing a possible miscarriage. Once a woman's pregnancy has been confirmed, she should schedule her first prenatal checkup. Every couple need to give the opportunity to evaluate their readiness for parenthood and make a choice. It is necessary to talk about the many forms of contraception, including oral contraceptives, condoms, implants, injections, intrauterine devices, and options for sterilization (Lambonmung, Acheampong, and Langkulsen 2023). The benefits and drawbacks of non-coercive family planning should be fully disclosed during teaching and counseling sessions. For couples who have just concluded a pregnancy, education must include the risks of short-interval pregnancies. Couples should be informed about contraceptive choices before, during, and after pregnancy. Prenatal care recommendations are generally established. Family physicians, midwives, and obstetricians all offer regular prenatal care. Every doctor provides the patient and her companion with whatever particular care they have requested or needed. Women with high-risk preconception conditions must have a team examination at the beginning of the preconception period or upon entrance in every Centre. Clinicians, educators, and nurses should be aware of the referral services offered both locally and on-site at the clinic. Standardized policies and procedures on the core requirements for prenatal care and pregnancy management, education, and care should be in place at the facility or within the health system. Family physicians and midwives should maintain open channels of communication with high-risk doctors for high-risk patients throughout the whole pregnancy (Braunthal and Brateanu 2019)(Chilaka and Konje 2021)(Cudalba et al. 2021).

2. Early Pregnancy Complications:

Beginning on the day a woman typically gets her period and lasting until the end of the twelfth week of pregnancy, the first trimester, sometimes referred to as early pregnancy, begins.

During this time and before a pregnancy is confirmed, the majority of women are aware of the symptoms linked with pregnancy. Mood fluctuations, nausea, breast soreness, and exhaustion are a few of the most typical early indicators that show up throughout the first trimester of maternity. There may be additional symptoms in the first 12 weeks, but they can sometimes be more serious and need careful observation, prompt and effective medical care.

When HG complicates a pregnancy, inpatient care should be given. The following standards are applied when admitting women who have hyperemesis:

- Incapacity to use anti-emetics or medications.
- Related conditions including urinary tract infections.
- Persistent nausea and vomiting despite antiemetic's, along with ketonuria and/or weight loss of above 5%.

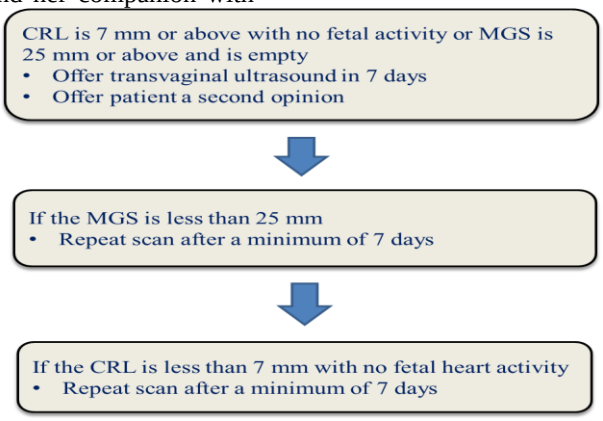

Figure 1: Management of miscarriage according to ultrasound finding

2.1. Early embryo death and ectopic conception:

Vaginal bleeding can indicate an ectopic or molar pregnancy, despite the 20% miscarriage risk associated with it. Ectopic pregnancy happens when a fertilized ovum implants outside of the uterus. Estimates of the occurrence of ectopic pregnancy in the US range from 1% to 2%, but this might be an underestimate given that the ailment is frequently treated in offices where data is not kept track of (Creanga et al. 2011)(Marion and Meeks 2012).

All expectant mothers who report with vaginal bleeding and are hemodynamically stable should be provided a diagnostic transvaginal ultrasound screening. The measures of the mean gestation sac (MGS) and crown rump length (CRL) on the ultrasound scan, as seen in Figure 1, are used to diagnose early embryonic death. Over the past three decades, the fatality rate from ruptured ectopic pregnancy has consistently decreased, accounting for 2.7% of pregnancy-related deaths from 2011 to 2013 (Creanga et al. 2017).

It is important to urge women who have vaginal bleeding and a viable intrauterine pregnancy during a scan to come back for additional evaluation if their bleeding gets worse or lasts longer than 14 days. She should begin or resume prenatal care if the bleeding stops (Ankum et al. 1996)("ACOG Practice Bulletin No. 193: Tubal Ectopic Pregnancy" 2018).

The patient should be informed of the available treatment options once it has been determined that the bleeding is due to early embryonic death in the first trimester. When there is no history of coagulopathies, infection, higher risk of bleeding, or bad pregnancy experience, the first-line treatment option should be administered to expectant mothers for 7–14 days. Oral and written instructions on what to anticipate and how to receive help in an emergency should be given to women. When a patient wears an intrauterine device (IUD), the total pregnancy rate (including ectopic) is less than 1%. Nonetheless, the incidence of an ectopic pregnancy might reach 53% in the uncommon event that a woman becomes pregnant while wearing an IUD (Backman et al. 2004)(Hardeman and Weiss 2014).

Table 1: Risk factors for Ectopic or Early pregnancy

S. no.	Risk Factors for Ectopic or Early pregnancy
1.	35 years or older
2.	Smoking cigarettes
3.	Documented pathology of the fallopian tubes
4.	Infertility
5.	Pelvic inflammatory disease
6.	Pregnancy with an implanted intrauterine device
7.	Ectopic pregnancy in the past
8.	Past fallopian tube operations

2.2. Miscarriage:

Preconceptions around miscarriage are pervasive, and many women, men, and medical professionals seem to have preconceptions about it (Banno et al. 2020)(Bardos et al. 2015).

Women may think, for instance, that miscarriages are uncommon, that lifting large things or using contraceptives in the past may have contributed to them, or that there are no proven ways to stop miscarriages. Miscarriage can also lead to isolation since many women may decide not to tell their partner, family, or close friends about the loss of their pregnancy. Couples have voiced concerns about routine clinical care given by uncaring healthcare professionals (Brier 1999)(Betts, Dahlen, and Smith 2014)(MacWilliams et al. 2016). The different ways that different countries and international organizations define miscarriage affect estimates of the risk and prevalence of it. Miscarriage is typically defined as the loss of an intrauterine pregnancy before to viability; however, there are differences in the diagnosis of pregnancy and the specific definitions of viability and intrauterine pregnancy. The limits of viability can be established using fetal weight or gestational age. The gestational threshold for viability might range from 20 and 28 weeks of pregnancy, depending on the area. According to the WHO, a miscarriage is when a fetus (embryo) weighs less than 500 g or is extracted at a gestational age of about 22 weeks (Faraji et al. 2022)(World Health Organization (WHO). 1992).

2.3. Miscarriage risk:

The likelihood of miscarriage is affected by the greater gestational age or fetal weight limit, as well as whether the denominator includes all fetuses discovered by blood or urine -hCG concentrations or simply pregnancies detected by ultrasonography. Preclinical losses—pregnancy lost before to ultrasound diagnosis—will raise the miscarriage rate if they are included. The miscarriage rate has increased because more sensitive β-hCG testing has made it possible to identify pregnancies as early as 22 days after the previous menstrual cycle. This has also made it possible to diagnose very early miscarriages that may

have gone undiagnosed otherwise. Lastly, a population's demographic characteristics will influence the likelihood of miscarriages, with the distribution of female age having a significant impact (Himmelberger, Brown, and Cohen 1978)(Armstrong, McDonald, and Sloan 1992)(Nybo Andersen et al. 2000)(Linnakaari et al. 2019)(Rossen, Ahrens, and Branum 2018)(B. T. Nguyen, Chang, and Bendikson 2019). International comparisons are challenging since relatively few nations, like Denmark, publish their yearly miscarriage rate. The woman's age and the quantity of previous losses have a big impact on the chance of miscarriage. The risk of miscarriage is lowest for women between the ages of 20 and 29 (12%), and highest for those over the age of 45 (65%) (Appendix p 4). The risk of miscarriage is lowest in women without a history of losses (11%), and it increases by around 10% for each additional loss, reaching 42% in women with three or more prior losses.

3. Gestational Diabetes:

Even though Carrington first used the phrase "gestational diabetes" in 1957 (Carrington, Shuman, and Reardon 1957). It wasn't until John O'Sullivan's books in 1961 that it became well known (O'SULLIVAN 1961). Nonetheless, the phenomenon of hyperglycemia during pregnancy was seen previously. Since then, the diagnosis of gestational diabetes mellitus (GDM) has been surrounded by complexity and disagreement, in part because of the extremely wide criteria that was first supported (Metzger and Coustan 1998). As a result, the term "GDM" was used to describe a broad range of hyperglycemia, from glucose levels typical of overt diabetes (or, in rare instances, even newly diagnosed type 1 diabetes mellitus, or T1DM) found in early pregnancy (20 weeks of gestation) to mild impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) found in late pregnancy. For instance, in the USA, IGT, IFG, or impaired glycated hemoglobin (HbA1c) levels are indicators of detectable pre-diabetes in people aged 20 to 22. Of those, 29.3% had overt diabetes (Menke, Casagrande, and Cowie 2018). Since there isn't a single diagnostic procedure or set of diagnostic standards for GDM that is universally acknowledged internationally, making comparisons across national boundaries can be difficult.

However, the International Association of Diabetes in Pregnancy Study Groups (IADPSG) 2010 criteria7 was accepted by the WHO in 2013 (Colagiuri et al. 2014).

3.1. Intervention in Gestational Diabetes:

Diet and physical activity treatments were included in the majority of evaluations, while interventions encouraging breastfeeding were included in six of them(Morton, Kirkwood, and Thangaratinam 2014)(Feng et al. 2018)(Ali, Pathak, and Mandal 2023). From four weeks to three years, the length of the treatments varied significantly (Jones, Fraley, and Mazzawi 2017). In order to reduce the risk of perinatal morbidities and protect newborns from the harmful metabolic consequences of being born LGA or SGA, the global standards suggest beginning a personalized medical food plan and physical activity as soon as GDM is detected (Volkova, Davidenko, and Degtyareva 2021)("Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes-2021" 2021). However, certain pregnant GDM patients who require pharmacological treatment might be unable to utilize insulin properly or safely due to financial limitations, linguistic or cultural obstacles, a fear of needles, or a lack of storage options. Oral antidiabetic medicines would be an alternative in these circumstances (Hamelin, Yan, and Stiell 2018).

4. Gestational Hypertension:

Between 5 and 10% of pregnancies are complicated by pregnancy-related hypertension disorders, which raise the danger of morbidity and mortality for the mother, fetus, and infant. (Regitz-Zagrosek et al. 2018). A systolic blood pressure (SBP) of at least 140 mmHg and/or a diastolic blood pressure (DBP) of at least 90 mmHg are required to be considered hypertensive during pregnancy when checked twice. During the first trimester of a typical pregnancy, the blood pressure gradually decreases because there is less systemic vascular resistance. It reaches a low point between weeks 22 and 24 of gestation, then begins to increase once again at week 28 and reaches preconception levels by week 36 (Shen et al. 2017). Hypertension brought on by pregnancy is bad for a woman's long-term cardiovascular health. An extensive population study (1970–2010) revealed that in the past forty years, the prevalence of chronic hypertension in pregnancy increased by about thirteen times (Ananth et al. 2019). Women who are pregnant have a lower threshold for severe hypertension because they are more prone than non-pregnant women to acquire hypertensive encephalopathy. Despite revisions to the diagnosis of hypertension in the general population (BP 130-139/80-89 mmHg is now considered stage 1 hypertension), the criteria for diagnosing hypertension in pregnancy have not changed in recent years ("Correction to: Systematic Review for the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/ APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice

Guidelines (Hypertension (2018) 71 (E116-E135) DOI: 10.1161/HYP.0000000000000067)" 2018).

4.1. Intervention in Gestational Hypertension:

Adverse pregnancy outcomes are frequently caused by hypertensive diseases; preeclampsia accounts for 15% of premature births and increases morbidity and death rates for both the mother and the fetus (Brouwers et al. 2018). Resistance training and aerobic exercise are common types of exercise during pregnancy. Women who exercise aerobically when pregnant can improve their cardiopulmonary function, prevent chronic diseases, and stop gaining too much weight (Ramírez-Vélez et al. 2011)(Ramírez-Vélez et al. 2013). Resistance training aims to energize expectant mothers, increase muscular strength, and enhance general health. According to a randomized controlled trial, women who engaged in strength training and aerobic exercise had significantly lower incidences of hypertension and gestational diabetes mellitus (GDM) during pregnancy than those who did neither (E. White, Pivarnik, and Pfeiffer 2014). Moderate exercise has been shown to ameliorate maternal endothelial dysfunction and induce placental angiogenesis, according to 2013 ACOG recommendations.

Pregnant women in high-risk groups for gestational hypertension may find it more affordable to engage in moderate exercise under medical supervision. However, other sports—like basketball, rugby, skiing, horseback riding, and gymnastics—are dangerous because players might get hit and fall. It should be noted that pregnant women who experience any of the symptoms listed below should stop exercising right away and seek immediate medical care for both the mother and the fetus. These symptoms include vaginal bleeding, headaches, dizziness, chest pain, muscle weakness, early labor, decreased fetal movement, early rupture of membranes, calf pain or swelling, and difficulty breathing. Expectant moms should take it easy before starting up again.

5. Preterm Labor

Preterm delivery is the primary cause of infant mortality and a considerable portion of all birth-related short- and long-term disease. Spontaneous preterm labor is the cause of more than half of premature births. This review's subject is how it is managed. Preterm delivery is connected with a variety of maternal traits, but the cause is typically unclear. However, in the early instances, intrauterine infection is playing a more significant role (Spencer, Simpson, and Bonney 2022)(Browne, Linfert, and Perez-Jorge 2020). Similar to how discouraging it is that the majority of attempts to halt premature labor after it has started have failed, the majority of measures to avoid preterm labor have also not been effective. Therefore, preventing traumatic deliveries and reducing infant difficulties by utilizing corticosteroids and antibiotics to prevent group B streptococcal neonatal sepsis are the most important components of therapy (Griggs et al. 2020)(Yeni, Rismawati, and Hasanuddin 2020). Giving birth in a hospital with a newborn intensive care unit and an experienced resuscitation team will result in the best possible neonatal outcomes. There is limited proof of the effectiveness of obstetric techniques such bed rest, hydration, sedation, home uterine activity monitoring, oral terbutaline after successful intravenous tocolysis, and tocolysis without the concomitant use of corticosteroids in stopping or managing premature labor (Songthamwat, Na Nan, and Songthamwat 2018)(Q. H. V. Nguyen et al. 2021). A preterm birth is one that occurs between 37 and more than 20 weeks into the pregnancy, according to the World Health Organization. In Europe, preterm birth rates range between 5% and 7%, but they are over 11% in the US. In wealthy nations, prematurity continues to be a major contributor to newborn morbidity and mortality, accounting for 60 to 80% of baby deaths without congenital abnormalities. Early preterm delivery is receiving more attention as a result of the low risk of newborn morbidity and death in the close term period. Despite making up only 1% to 2% of all births, babies born in this gestational age range account for 60% of perinatal deaths and close to 50% of all long-term neurological illness (Hosny et al. 2020)(Phung et al. 2022)(Patel and Ludmir 2019).

5.1 Intervention in Preterm Labor

While premature labor is evident, the following goals are frequently considered while taking treatment measures: 1) to stop or reduce the number and severity of contractions, delaying delivery; and 2) to enhance fetal health before an early birth. This section reviews a number of contemporary obstetric treatment methods that promise to achieve these goals (Kao et al. 2019)(MacDorman et al. 2022). One of the most popular treatments or preventative measures for suspected preterm labor is bed rest. In fact, it is advised for a variety of ailments connected to pregnancy. In 20% of pregnancies in the US, bed rest was recommended for at least one week, according to a poll. Oral or intravenous hydration is another popular technique used for the initial management of preterm labor. Some doctors use this technique to distinguish between real and fake premature labor (Maasoumi et al. 2023)(Spencer, Simpson, and Bonney 2022)(IRCT20201024049128N2 2020). Water may be beneficial in treating preterm labor for a number of reasons. First, at least in animals, hydration decreases the synthesis of antidiuretic hormone via the Henry-Gauer reflex. Second, premature laboring women may have lower-than-average plasma volumes (H. White et al. 2019).

6. Embryo Previa

Placenta previa is the term for a placenta that covers or is relatively close to the internal os (the aperture into the uterus) of the cervix. The placenta often implants in the upper uterine lining. In placenta previa, the placenta is either entirely or partially housed within the lower uterine segment (Jauniaux et al. 2019)(Wasim et al. 2020). Four classifications have traditionally been used to classify placenta previa.

1. 1. Complete placenta previa, which is when the placenta completely encases the internal os.
2. Partial placenta previa, in which the placenta partially encases the internal os. As a result, this circumstance only arises when the internal os is somewhat dilated.
3. Marginal placenta previa, this does not hide the core os, but only reaches it.
4. The placenta is low-lying and only enters the internal os; it does not reach the lower uterine area.

Maternal mortality happens in 0.03% of placenta previa cases in the US. Women with placenta previa may endure severe emotional distress due to frequent hospital stays and recurrent bleeding in the second trimester. Additionally linked to a rise in preterm births, perinatal death, and morbidity is placenta previa (Jenabi, Salimi, Bashirian, et al. 2022)(Fan et al. 2021). According to reports, as the pregnancy proceeds, more than 90% of low-lying placentas that were discovered in the beginning will move away from the cervix and out of the lower uterine area. Despite the use of the phrase "placental migration," the majority of experts do not think the placenta travels. Instead, it is believed that the placenta trophotropically expands towards a fundus with greater blood flow, whereas the placenta overlaying a cervix with worse blood flow may atrophy (Jain, Bos, and Bujold 2020)(Jansen et al. 2022)(Zhang et al. 2020).

6.1. Intervention in Placenta Previa

A vaginal examination and an emergency caesarean delivery were once the only treatments for placenta previa. It was believed that the mother would pass away during the initial bleeding, which frequently began in the early third trimester. Preterm birth had a major role in the high perinatal mortality from placenta previa, which might be considerably reduced by careful expectant care and delivery as close to mature as is practical. However, this seldom ever happened when there was no intervention (NCT05688111 2023). It is advisable to hospitalize women with placenta previa who are having intense uterine contractions or bleeding. One to two wide-bore intravenous cannulas should be inserted to get an accurate blood count, type, and screen. Investigations into coagulation are pointless if there isn't significant bleeding or another issue. At least four acceptable units of packed red blood cells and coagulation factors must be available from the blood bank in a timely manner. Rh immune globulin should be provided to Rh-negative females (Jansen et al. 2022). Since the mother could require greater doses of Rh immune globulin, a Kleihauer-Bettke test for fetal-maternal transfusion quantification should also be performed in Rh negative women. Steroids should be administered to expectant mothers between 24 and 34 weeks gestation to promote the development of the fetal lung, frequently when the mother is sent to the hospital for bleeding. To discuss the care of the infant, the patient and her family should make an appointment with a neonatologist (Park and Cho 2020).

7. Abrupt Placentation

In around 1% of instances, placental abruption—early separation of the placenta—leads to difficulties during delivery. With a focus on incidence, temporal trends, and risk factors, the review's goal is to summarize the epidemiology of placental abruption (Bruinsma et al. 2022)(Y. Li et al. 2019).

Despite the fact that placenta previa usually causes some degree of placental separation, these circumstances are not typically thought of as abruptions in the true sense. It is possible for a rupture to be "revealed," in which case blood escapes past the cervix into the vagina and passes through the decidua and membranes. The less common "concealed" abruption, which doesn't have any obvious external bleeding, causes blood to accumulate behind the placenta (Tikkanen 2011)(Roberge, Bujold, and Nicolaides 2018). The placenta might separate completely from the uterine wall, in which case the fetus typically dies, or it can separate partially, removing only a portion of the placenta from the uterine wall. Placental abruption has a wide spectrum of clinical importance, from little bleeding with little to no consequences to catastrophic abruption leading to fetal death and considerable maternal morbidity. Disruption may be the cause of 10% or more preterm births. The danger to the fetus depends on both the severity of the abruption and the gestational age at which it occurs; nevertheless, the mother is most at risk from a severe abruption. In contrast to all other births, which had a perinatal mortality rate of 8.2 per 1,000, pregnancies complicated by abruption had a perinatal death rate of 119 per 1,000 births, according to a population-based cohort analysis of 7,508,655 pregnancies in the United States. These prior results are supported by more recent U.S. statistics (Jenabi, Salimi, Ayubi, et al. 2022)(Bączkowska et al. 2021)(Ichizuka et al. 2021).

7.1. Intervention in Placental Abruption

Placental abruption treatment is influenced by the appearance, gestational age, and degree of maternal and fetal damage. Given the wide variety of

presentations, it is essential to tailor management to each particular circumstance. More active care may not be required in cases of milder abruption, but it is preferred in cases of severe abruption. Regardless of gestational age, it is feasible to allow the patient to give birth vaginally in cases of acute abruption with fetal death if the mother is stable and there are no other contraindications (Neilson 2003)(Yang, Lee, and Lee 2022). Usually, labor moves along rapidly and the uterus is forcefully contracting. Amniotomy are frequently sufficient to accelerate labor. When a live fetus has an abruption during or just before term, prompt delivery is indicated. The main question is whether vaginal delivery is feasible without significant morbidity or fetal or maternal death. When there are signs of fetal compromise but delivery is not imminent, it is crucial to have a caesarean birth as soon as possible since total placental separation can occur at any time (Dick and Brotman 2022)(Dick and Brotman 2022)(JP 2003).

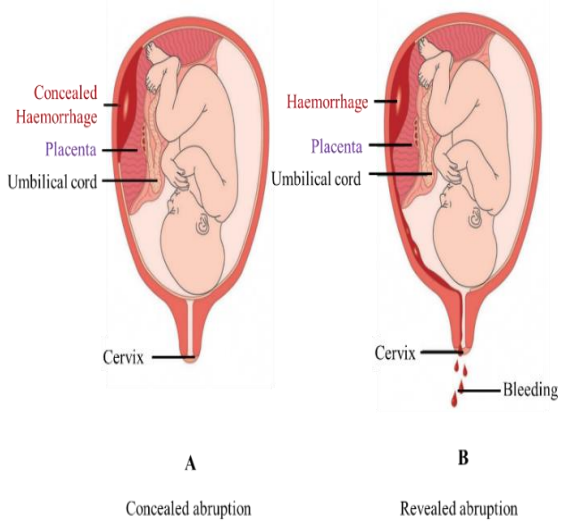

Fig 2: A. Despite the absence of vaginal bleeding, blood accumulates beneath the placenta. **B.** Blood leaks from the cervix and vagina via the spaces between the membrane

8. Fetal Growth Restriction

In addition to the genetically programmed growth potential, normal fetal development is influenced by maternal, fetal, placental, and environmental variables. The multisystem impacts of placental dysfunction augment the already high baseline mortality and morbidity. Preterm fetal growth restriction (FGR) caused by iatrogenic prematurity increases perinatal mortality and morbidity when the delivery date is uncertain (Nowakowska et al. 2022)(Meler et al. 2021). Questions concerning delivery timing in the near future are less crucial. However, approximately 50% of unexplained stillbirths are attributable to the difficulties in diagnosing term FGR. To improve these statistics, accurate diagnosis, proper surveillance, and confidence in the timing of therapies are all considered crucial factors. Effective first-trimester trophoblastic adhesion results in a low impedance and high capacitance circulatory interface between the fetal and maternal circulations, as well as a carrier system for vital nutrients (Özgen et al. 2022)(da Costa et al. 2022). Despite the placental unit's effectiveness in healthy pregnancies, the fetus is vulnerable to food deprivation when placental dysfunction sets in. Since the placenta takes a specific amount of the nutrient stream (70 percent of the glucose and 40 percent of the oxygen given to the uterus), feeding the fetus can only be done with the excess nutrients that are left over after placental needs have been met (Healy et al. 2019). While placental nutrition is maintained, even minor placental dysfunction can restrict blood flow and nutrients to the fetus. When uterine perfusion is reduced to less than 0.6 mL/Kg/min, the supply of fetal glucose and amino acids is noticeably reduced. The insulin and insulin-like growth factor-1 endocrine axis as well as hepatic glucose metabolism are down regulated as a result of this decrease in substrate availability. Final results include delayed longitudinal growth, reduced liver size, and redistribution of gluconeogenic amino acids resulting from endogenous protein synthesis. When fatty acid transport is inhibited, the availability of precursor molecules for many bioactive chemicals decreases. These changes significantly contributed to the development of FGR (McCowan, Figueras, and Anderson 2018)(Ankert et al. 2021)(Zur et al. 2020).

8.1. Fetal Growth Restriction Intervention

The timing of procedures in the perinatal treatment of FGR is determined by the balance of fetal and neonatal dangers. The biggest difficulty with term FGR is identifying the at-risk fetus, thus infant risks are minor. There are no randomized trials of elective delivery once the diagnosis of FGR has been made close to delivery (Valenzuela et al. 2022)(Bettiol et al. 2021). Even while risk indicators like FGR may necessitate delivery as early as 37 weeks, statistics on prospective stillbirth risk from a huge US cohort suggest that this is not the case. This shows that a low threshold for delivery should be used for these fetuses. Possible delivery criteria include documented lung maturity, complete fetal development arrest, oligohydramnios, abnormal BPS, and UA AEDV. Things get more difficult in preterm FGR that

manifests before 34 weeks, when deterioration may occur fast and where prematurity-related morbidity is significantly greater than in comparably developed counterparts (Wang et al. 2022)(Colson et al. 2021)(Cottrell et al. 2017).

9. Conclusion

The problems and tactics involved in protecting the welfare of both pregnant mothers and their growing fetuses have been thoroughly explained in this thorough survey of pregnancy issues and interventions. While most pregnancies go off without a hitch, pregnancy is a magnificent but difficult journey, and occasionally problems arise that call for specialized care and attention. This review has emphasized the wide spectrum of pregnancy difficulties, from common but less understood problems like placental abruption and ectopic pregnancies to well-known disorders like gestational diabetes and preeclampsia. To provide pregnant women with the best treatment and support, healthcare professionals must be knowledgeable about the complexities of these illnesses. The interventions and management techniques examined here also highlight the dynamic character of prenatal care and the value of adjusting therapies to the unique requirements of each patient. It emphasizes cooperation between obstetricians, nurses, sonographers, and other healthcare providers, highlighting the critical significance of a multidisciplinary approach in providing the best results for high-risk pregnancies.

References:

1. "ACOG Practice Bulletin No. 193: Tubal Ectopic Pregnancy." 2018. *Obstetrics and Gynecology*. https://doi.org/10.1097/AOG.0000000000002560.
2. Ananth, Cande V., Christina M. Duzyj, Stacy Yadava, Marlene Schwebel, Alan T.N. Tita, and K. S. Joseph. 2019. "Changes in the Prevalence of Chronic Hypertension in Pregnancy, United States, 1970 to 2010." *Hypertension*. https://doi.org/10.1161/HYPERTENSIONAHA.119.12968.
3. Ankert, Juliane, Tanja Groten, Mathias W. Pletz, Sasmita Mishra, Gregor Seliger, Silvia M. Lobmaier, Clarissa Prazeres da Costa, et al. 2021. "Fetal Growth Restriction in a Cohort of Migrants in Germany." *BMC Pregnancy and Childbirth*. https://doi.org/10.1186/s12884-021-03620-z.
4. Ankum, W. M., B. W.J. Mol, F. Van der Veen, and P. M.M. Bossuyt. 1996. "Risk Factors for Ectopic Pregnancy: A Meta-Analysis." *Fertility and Sterility*. https://doi.org/10.1016/s0015-0282(16)58320-4.
5. Armstrong, B. G., A. D. McDonald, and M. Sloan. 1992. "Cigarette, Alcohol, and Coffee Consumption and Spontaneous Abortion." *American Journal of Public Health*. https://doi.org/10.2105/AJPH.82.1.85.
6. Backman, Tiina, Ilkka Rauramo, Sakke Huhtala, and Markku Koskenvuo. 2004. "Pregnancy during the Use of Levonorgestrel Intrauterine System." *American Journal of Obstetrics and Gynecology*. https://doi.org/10.1016/j.ajog.2003.07.021.
7. Bączkowska, Monika, Magdalena Zgliczyńska, Jan Faryna, Ewa Przytuła, Błażej Nowakowski, and Michał Ciebiera. 2021. "Molecular Changes on Maternal–Fetal Interface in Placental Abruption—a Systematic Review." *International Journal of Molecular Sciences*. https://doi.org/10.3390/ijms22126612.
8. Banno, Chihiro, Mayumi Sugiura-Ogasawara, Takeshi Ebara, Shoko Ide, Tamao Kitaori, Takeshi Sato, Kiwamu Ando, and Yoko Morita. 2020. "Attitude and Perceptions toward Miscarriage: A Survey of a General Population in Japan." *Journal of Human Genetics*. https://doi.org/10.1038/s10038-019-0694-1.
9. Bardos, Jonah, Daniel Hercz, Jenna Friedenthal, Stacey A. Missmer, and Zev Williams. 2015. "A National Survey on Public Perceptions of Miscarriage." *Obstetrics and Gynecology*. https://doi.org/10.1097/AOG.0000000000000859.
10. Bettiol, Alessandra, Laura Avagliano, Niccolò Lombardi, Giada Crescioli, Giacomo Emmi, Maria Letizia Urban, Gianni Virgili, Claudia Ravaldi, and Alfredo Vannacci. 2021. "Pharmacological Interventions for the Prevention of Fetal Growth Restriction: A Systematic Review and Network Meta-Analysis." *Clinical Pharmacology and Therapeutics*. https://doi.org/10.1002/cpt.2164.
11. Betts, Debra, Hannah G. Dahlen, and Caroline A. Smith. 2014. "A Search for Hope and Understanding: An Analysis of Threatened Miscarriage Internet Forums." *Midwifery*. https://doi.org/10.1016/j.midw.2013.12.011.
12. Braunthal, Stephanie, and Andrei Brateanu. 2019. "Hypertension in Pregnancy: Pathophysiology and Treatment." *SAGE Open Medicine*. https://doi.org/10.1177/2050312119843700.
13. Brier, Norman. 1999. "Understanding and Managing the Emotional Reactions to a Miscarriage." *Obstetrics and Gynecology*. https://doi.org/10.1016/S0029-7844(98)00294-4.
14. Brouwers, L., A. J. van der Meiden-van Roest, C. Savelkoul, T. E. Vogelvang, A. T. Lely, A. Franx, and B. B. van Rijn. 2018. "Recurrence of Pre-Eclampsia and the Risk of Future Hypertension and Cardiovascular Disease: A Systematic Review and Meta-Analysis." *BJOG: An International Journal of Obstetrics and Gynaecology*. https://doi.org/10.1111/1471-0528.15394.
15. Browne, Paul C., Jennifer B. Linfert, and Emilio Perez-Jorge. 2020. "Successful Treatment of Preterm Labor in Association with Acute COVID-19 Infection." *American Journal of Perinatology*. https://doi.org/10.1055/s-0040-1709993.
16. Bruinsma, Marieke A.W., Marjon A. de Boer, Sandra Prins, and Carolien N.H. Abheiden. 2022. "Does Placental Abruption Cause Neonatal Anemia?" *Acta Obstetricia et Gynecologica Scandinavica*. https://doi.org/10.1111/aogs.14376.
17. Carrington, Elsie R., Charles R. Shuman, and Helen S. Reardon. 1957. "Evaluation of the Prediabetic State during Pregnancy." *Obstetrics and Gynecology*.

https://doi.org/10.1097/00006250-195706000-00008.
18. Chilaka, Victor N., and Justin C. Konje. 2021. "HIV in Pregnancy – An Update." *European Journal of Obstetrics and Gynecology and Reproductive Biology*. https://doi.org/10.1016/j.ejogrb.2020.11.034.
19. Colagiuri, Stephen, Maicon Falavigna, Mukesh M. Agarwal, Michel Boulvain, Edward Coetzee, Moshe Hod, Sara J. Meltzer, et al. 2014. "Strategies for Implementing the WHO Diagnostic Criteria and Classification of Hyperglycaemia First Detected in Pregnancy." *Diabetes Research and Clinical Practice*. https://doi.org/10.1016/j.diabres.2014.02.012.
20. Colson, Arthur, Pierre Sonveaux, Frédéric Debième, and Amanda N. Sferruzzi-Perri. 2021. "Adaptations of the Human Placenta to Hypoxia: Opportunities for Interventions in Fetal Growth Restriction." *Human Reproduction Update*. https://doi.org/10.1093/humupd/dmaa053.
21. "Correction to: Systematic Review for the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/ APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines (Hypertension (2018) 71 (E116-E135) DOI: 10.1161/HYP.0000000000000067)." 2018. *Hypertension*. https://doi.org/10.1161/HYP.0000000000000077.
22. Costa, Danyella Santana da, Marcos Aurélio Santos da Costa, Renatha Claudia Barros Sobreira, Bruno Mendes Tenório, Débora Farias Leite, and Fernanda da Chagas Ângelo Mendes Tenório. 2022. "Placenta and Fetal Growth Restriction: A Review." *Journal of Morphological Sciences*. https://doi.org/10.51929/jms.39.431.2022.
23. Cottrell, Elizabeth, Teresa Tropea, Laura Ormesher, Susan Greenwood, Mark Wareing, Edward Johnstone, Jenny Myers, and Colin Sibley. 2017. "Dietary Interventions for Fetal Growth Restriction – Therapeutic Potential of Dietary Nitrate Supplementation in Pregnancy." *Journal of Physiology*. https://doi.org/10.1113/JP273331.
24. Creanga, Andreea A., Carrie K. Shapiro-Mendoza, Connie L. Bish, Suzanne Zane, Cynthia J. Berg, and William M. Callaghan. 2011. "Trends in Ectopic Pregnancy Mortality in the United States: 1980-2007." *Obstetrics and Gynecology*. https://doi.org/10.1097/AOG.0b013e3182113c10.
25. Creanga, Andreea A., Carla Syverson, Kristi Seed, and William M. Callaghan. 2017. "Pregnancy-Related Mortality in the United States, 2011-2013." *Obstetrics and Gynecology*. https://doi.org/10.1097/AOG.0000000000002114.
26. Cudalba, Delia Ioana, Brindusa Ana Cimpoca-Raptis, Anca Marina Ciobanu, Corina Gica, Radu Botezatu, Nicolae Gica, Gheorghe Peltecu, and Anca Maria Panaitescu. 2021. "Pneumonia in Pregnancy." *Romanian Journal of Medical Practice*. https://doi.org/10.37897/RJMP.2021.S3.8.
27. Davenport, Baylea N., Rebecca L. Wilson, and Helen N. Jones. 2022. "Interventions for Placental Insufficiency and Fetal Growth Restriction." *Placenta*. https://doi.org/10.1016/j.placenta.2022.03.127.
28. Dick, Maurice H, and Monique Brotman. 2022. "Placental Abruption and Partial Placental Prolapse During Induction of Labor in a 31-Year-Old Female With Intrahepatic Cholestasis of Pregnancy: A Case Report." *Cureus*. https://doi.org/10.7759/cureus.23995.
29. Fan, Dazhi, Huishan Zhang, Jiaming Rao, Dongxin Lin, Shuzhen Wu, Pengsheng Li, Gengdong Chen, et al. 2021. "Maternal and Neonatal Outcomes in Transverse and Vertical Skin Incision for Placenta Previa: Skin Incision for Placenta Previa." *BMC Pregnancy and Childbirth*. https://doi.org/10.1186/s12884-021-03923-1.
30. Faraji, Azam, Mojgan Akbarzadeh-Jahromi, Shima Bahrami, Sayeh Gharamani, Hadi Raeisi Shahraki, Maryam Kasraeian, Homeira Vafaei, Marjan Zare, and Nasrin Asadi. 2022. "Predictive Value of Vascular Endothelial Growth Factor and Placenta Growth Factor for Placenta Accreta Spectrum." *Journal of Obstetrics and Gynaecology*. https://doi.org/10.1080/01443615.2021.1955337.
31. Feng, Lijun, Qunli Xu, Zhefang Hu, and Hongying Pan. 2018. "Lactation and Progression to Type 2 Diabetes in Patients with Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis of Cohort Studies." *Journal of Diabetes Investigation*. https://doi.org/10.1111/jdi.12838.
32. Griggs, Kellie M., Debra A. Hrelic, Nina Williams, Michelle McEwen-Campbell, and Rebecca Cypher. 2020. "Preterm Labor and Birth: A Clinical Review." *MCN The American Journal of Maternal/Child Nursing*. https://doi.org/10.1097/NMC.0000000000000656.
33. Groom, Katie M., and Anna L. David. 2018. "The Role of Aspirin, Heparin, and Other Interventions in the Prevention and Treatment of Fetal Growth Restriction." *American Journal of Obstetrics and Gynecology*. https://doi.org/10.1016/j.ajog.2017.11.565.
34. Hadden, D. R. 2008. "Prediabetes and the Big Baby." *Diabetic Medicine*. https://doi.org/10.1111/j.1464-5491.2007.02331.x.
35. Hamelin, Alexandra L., Justin W. Yan, and Ian G. Stiell. 2018. "Emergency Department Management of Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic State in Adults: National Survey of Attitudes and Practice." *Canadian Journal of Diabetes*. https://doi.org/10.1016/j.jcjd.2017.05.005.
36. Hardeman, Julia, and Barry D. Weiss. 2014. "Intrauterine Devices: An Update." *American Family Physician*.
37. Healy, Patricia, Sanne J. Gordijn, Wessel Ganzevoort, Irene M. Beune, Ahmet Baschat, Asma Khalil, Louise Kenny, et al. 2019. "A Core Outcome Set for the Prevention and Treatment of Fetal GROwth Restriction: DeVeloping Endpoints: The COSGROVE Study." *American Journal of Obstetrics and Gynecology*. https://doi.org/10.1016/j.ajog.2019.05.039.
38. Himmelberger, David U., Byron Wm Brown, and Ellis

N. Cohen. 1978. "Cigarette Smoking during Pregnancy and the Occurrence of Spontaneous Abortion and Congenital Abnormality." *American Journal of Epidemiology*. https://doi.org/10.1093/oxfordjournals.aje.a112645.

39. Hosny, Alaa El Dien M.S., Mohsen N. Fakhry, Waleed El-Khayat, and Mona T. Kashef. 2020. "Risk Factors Associated with Preterm Labor, with Special Emphasis on Preterm Premature Rupture of Membranes and Severe Preterm Labor." *Journal of the Chinese Medical Association*. https://doi.org/10.1097/JCMA.0000000000000243.
40. Ichizuka, Kiyotake, Satoshi Toyokawa, Tsuyomu Ikenoue, Shoji Satoh, Junichi Hasegawa, Tomoaki Ikeda, Nanako Tamiya, et al. 2021. "Risk Factors for Cerebral Palsy in Neonates Due to Placental Abruption." *Journal of Obstetrics and Gynaecology Research*. https://doi.org/10.1111/jog.14447.
41. IRCT20201024049128N2. 2020. "Comparison of Probiotics in the Prevention of Preterm Labor." *Http://Www.Who.Int/Trialsearch/Trial2.Aspx?TrialID=IRCT20201024049128N2*.
42. Jain, Venu, Hayley Bos, and Emmanuel Bujold. 2020. "Guideline No. 402: Diagnosis and Management of Placenta Previa." *Journal of Obstetrics and Gynaecology Canada*. https://doi.org/10.1016/j.jogc.2019.07.019.
43. Jamieson, Denise J., and Sonja A. Rasmussen. 2022. "An Update on COVID-19 and Pregnancy." *American Journal of Obstetrics and Gynecology*. https://doi.org/10.1016/j.ajog.2021.08.054.
44. Jansen, Charlotte H.J.R., Charlotte E. van Dijk, C. Emily Kleinrouweler, Jacob J. Holzscherer, Anouk C. Smits, Jacqueline C.E.J.M. Limpens, Brenda M. Kazemier, Elisabeth van Leeuwen, and Eva Pajkrt. 2022. "Risk of Preterm Birth for Placenta Previa or Low-Lying Placenta and Possible Preventive Interventions: A Systematic Review and Meta-Analysis." *Frontiers in Endocrinology*. https://doi.org/10.3389/fendo.2022.921220.
45. Jauniaux, Eric, Lene Grønbeck, Catey Bunce, Jens Langhoff-Roos, and Sally L. Collins. 2019. "Epidemiology of Placenta Previa Accreta: A Systematic Review and Meta-Analysis." *BMJ Open*. https://doi.org/10.1136/bmjopen-2019-031193.
46. Jenabi, Ensiyeh, Zohreh Salimi, Erfan Ayubi, Saeid Bashirian, and Amir Mohammad Salehi. 2022. "The Environmental Risk Factors Prior to Conception Associated with Placental Abruption: An Umbrella Review." *Systematic Reviews*. https://doi.org/10.1186/s13643-022-01915-6.
47. Jenabi, Ensiyeh, Zohreh Salimi, Saeid Bashirian, Salman Khazaei, and Erfan Ayubi. 2022. "The Risk Factors Associated with Placenta Previa: An Umbrella Review." *Placenta*. https://doi.org/10.1016/j.placenta.2021.10.009.
48. Jones, Emily J., Hannah E. Fraley, and Julianne Mazzawi. 2017. "Appreciating Recent Motherhood and Culture: A Systematic Review of Multimodal Postpartum Lifestyle Interventions to Reduce Diabetes Risk in Women with Prior Gestational Diabetes." *Maternal and Child Health Journal*. https://doi.org/10.1007/s10995-016-2092-z.
49. JP, Neilson. 2003. "Interventions for Treating Placental Abruption." *Cochrane Database of Systematic Reviews*.
50. Kao, Mei Hua, Pi Feng Hsu, Sheng Fang Tien, and Chie Pein Chen. 2019. "Effects of Support Interventions in Women Hospitalized With Preterm Labor." *Clinical Nursing Research*. https://doi.org/10.1177/1054773817744323.
51. Lambonmung, Augustine, Charity Asantewaa Acheampong, and Uma Langkulsen. 2023. "The Effects of Pregnancy: A Systematic Review of Adolescent Pregnancy in Ghana, Liberia, and Nigeria." *International Journal of Environmental Research and Public Health*. https://doi.org/10.3390/ijerph20010605.
52. Li, Xue Lian, Dan Feng Du, Shang Jie Chen, Sai Hua Zheng, Arier C. Lee, and Qi Chen. 2016. "Trends in Ectopic Pregnancy, Hydatidiform Mole and Miscarriage in the Largest Obstetrics and Gynaecology Hospital in China from 2003 to 2013." *Reproductive Health*. https://doi.org/10.1186/s12978-016-0181-5.
53. Li, Yang, Yuan Tian, Ning Liu, Yang Chen, and Fuju Wu. 2019. "Analysis of 62 Placental Abruption Cases: Risk Factors and Clinical Outcomes." *Taiwanese Journal of Obstetrics and Gynecology*. https://doi.org/10.1016/j.tjog.2019.01.010.
54. Linnakaari, R., N. Helle, M. Mentula, A. Bloigu, M. Gissler, O. Heikinheimo, and M. Niinimäki. 2019. "Trends in the Incidence, Rate and Treatment of Miscarriage - Nationwide Register-Study in Finland, 1998-2016." *Human Reproduction*. https://doi.org/10.1093/humrep/dez211.
55. Maasoumi, Raziyeh, Farzaneh Dastaran, Fatemeh Faghihiniya, Shima Haghani, and Shadi Sabetghadam. 2023. "The Effect of Spiritual Self-Care Intervention with a Blended Learning Approach on Anxiety in Women with Preterm Labor: A Randomized Controlled Trial." *International Journal of Community Based Nursing and Midwifery*. https://doi.org/10.30476/IJCBNM.2023.96119.2106.
56. MacDorman, Marian F., Marie Thoma, Eugene Declercq, and Elizabeth A. Howell. 2022. "The Relationship between Obstetrical Interventions and the Increase in U.S. Preterm Births, 2014-2019." *PLoS ONE*. https://doi.org/10.1371/journal.pone.0265146.
57. MacWilliams, Kate, Jean Hughes, Megan Aston, Simon Field, and Faith Wight Moffatt. 2016. "Understanding the Experience of Miscarriage in the Emergency Department." *Journal of Emergency Nursing*. https://doi.org/10.1016/j.jen.2016.05.011.
58. "Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes-2021." 2021. *Diabetes Care*. https://doi.org/10.2337/dc21-S014.
59. Marion, Laura L., and George Rodney Meeks. 2012. "Ectopic Pregnancy: History, Incidence, Epidemiology, and Risk Factors." *Clinical Obstetrics and Gynecology*. https://doi.org/10.1097/GRF.0b013e3182516d7b.
60. McCowan, Lesley M., Francesc Figueras, and Ngaire H. Anderson. 2018. "Evidence-Based National

Guidelines for the Management of Suspected Fetal Growth Restriction: Comparison, Consensus, and Controversy." *American Journal of Obstetrics and Gynecology*. https://doi.org/10.1016/j.ajog.2017.12.004.

61. Mehedintu, Claudia, Oana Maria Ionescu, Mihaela Plotogea, Antoine Edu, Mihaela Bujor, Andreea Carp-Veliscu, Mihai Dumitrascu, Florica Sandru, and Mona Khraibani. 2021. "Smoking and Pregnancy." *Romanian Journal of Medical Practice*. https://doi.org/10.37897/RJMP.2021.S6.9.
62. Meler, Eva, Leticia Benítez, Judith Martínez, and Francesc Figueras. 2021. "Fetal Growth Restriction." In *Perinatology: Evidence-Based Best Practices in Perinatal Medicine*. https://doi.org/10.1007/978-3-030-83434-0_37.
63. Menke, Andy, Sarah Casagrande, and Catherine C. Cowie. 2018. "Contributions of A1c, Fasting Plasma Glucose, and 2-Hour Plasma Glucose to Prediabetes Prevalence: NHANES 2011–2014." *Annals of Epidemiology*. https://doi.org/10.1016/j.annepidem.2018.07.012.
64. Metzger, Boyd E., and Donald R. Coustan. 1998. "Summary and Recommendations of the Fourth International Workshop- Conference on Gestational Diabetes Mellitus." In *Diabetes Care*. https://doi.org/10.2337/diab.34.2.s123.
65. Mirabelli, Maria, Eusebio Chiefari, Vera Tocci, Emanuela Greco, Daniela Foti, and Antonio Brunetti. 2021. "Gestational Diabetes: Implications for Fetal Growth, Intervention Timing, and Treatment Options." *Current Opinion in Pharmacology*. https://doi.org/10.1016/j.coph.2021.06.003.
66. Morton, Suzanna, Samantha Kirkwood, and Shakila Thangaratinam. 2014. "Interventions to Modify the Progression to Type 2 Diabetes Mellitus in Women with Gestational Diabetes: A Systematic Review of Literature." *Current Opinion in Obstetrics and Gynecology*. https://doi.org/10.1097/GCO.0000000000000127.
67. NCT05688111. 2023. "Tranexamic Acid as an Intervention in Placenta Previa." *Https://Clinicaltrials.Gov/Show/NCT05688111*.
68. Neilson, James P. 2003. "Interventions for Treating Placental Abruption." *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD003247.
69. Neuberger, Francesca E.M. 2022. "Pregnancy." In *The Liver in Systemic Disease: A Clinician's Guide to Abnormal Liver Tests*. https://doi.org/10.1002/9781119802181.ch7.
70. Nguyen, Brian T., Erica J. Chang, and Kristin A. Bendikson. 2019. "Advanced Paternal Age and the Risk of Spontaneous Abortion: An Analysis of the Combined 2011–2013 and 2013–2015 National Survey of Family Growth." In *American Journal of Obstetrics and Gynecology*. https://doi.org/10.1016/j.ajog.2019.05.028. Gupta, V., Kumar, S. and Agrawal, R., 2023. An Innovative Sintering Technique in Pharmaceutical Industry. International Journal of Pharmaceutical Drug Design.
71. Aijaz, M., Ahmad, M., Ansari, M.A. and Ahmad, S., 2023. Antimicrobial Resistance in a Globalized World: Current Challenges and Future Perspectives. International Journal of Pharmaceutical Drug Design.
72. Biswas, K. and Chaurasia, V., 2023. A review on floating drug delivery system: an inventive approach in gastro-retentive system. International Journal of Pharmaceutical Drug Design.
73. Ali, S.A., Ali, S. and Jahan, I., 2023. Allergies to Infections: Understanding the Spectrum of Conjunctivitis. International Journal of Pharmaceutical Drug Design.
74. Sridivya, C., Paturi, G., Gugulothu, S., Rajitha, E., Jatoth, M., Suram, R., Jatoth, T. and Ramisetty, P., 2023. A novel antibiotic to treat bacterial conjunctivitis–besifloxacin. International Journal of Pharmaceutical Drug Design.
75. Biswas, K., 2023. A review on emulgel in the treatment topical application. International Journal of Pharmaceutical Drug Design.
76. Bhumika, K., Mandal, S. and Shiva, K., 2023. Intermetatarsal Bursitis: A case report (With Accompanying Images). International Journal of Pharmaceutical Drug Design.
77. Mandal S, Vishvakarma P. Nanoemulgel: A Smarter Topical Lipidic Emulsion-based Nanocarrier. Indian J of Pharmaceutical Education and Research. 2023;57(3s):s481-s498.
78. Mandal S, Jaiswal DV, Shiva K. A review on marketed Carica papaya leaf extract (CPLE) supplements for the treatment of dengue fever with thrombocytopenia and its drawback. International Journal of Pharmaceutical Research. 2020 Jul;12(3).
79. Mandal S, Bhumika K, Kumar M, Hak J, Vishvakarma P, Sharma UK. A Novel Approach on Micro Sponges Drug Delivery System: Method of Preparations, Application, and its Future Prospective. Indian J of Pharmaceutical Education and Research. 2024;58(1):45-63.
80. Pal N, Mandal S, Shiva K, Kumar B. Pharmacognostical, Phytochemical and Pharmacological Evaluation of Mallotus philippensis. Journal of Drug Delivery and Therapeutics. 2022 Sep 20;12(5):175-81.
81. Porter, T. Flint, Cynthia Gyamfi-Bannerman, and Tracy Manuck. 2018. "Fisiopatología de La Preeclampsia y La Eclampsia." *Obstetrics and Gynecology*.
82. Ramírez-Vélez, Robinson, Ana Cecilia Aguilar de Plata, Mildrey Mosquera Escudero, Isabella Echeverry, José Guillermo Ortega, Blanca Salazar, Juan José Rey, Claudia Hormiga, and Patricio López-Jaramillo. 2011. "Influence of Regular Aerobic Exercise on Endothelium-Dependent Vasodilation and Cardiorespiratory Fitness in Pregnant Women." *The Journal of Obstetrics and Gynaecology Research*. https://doi.org/10.1111/j.1447-0756.2011.01582.x.
83. Ramírez-Vélez, Robinson, Juanita Bustamante, Analia Czerniczyniec, Ana C. Aguilar De Plata, and Silvia Lores-Arnaiz. 2013. "Effect of Exercise Training on Enos Expression, NO Production and Oxygen Metabolism in Human Placenta." *PLoS ONE*. https://doi.org/10.1371/journal.pone.0080225.

84. Regitz-Zagrosek, Vera, Jolien W. Roos-Hesselink, Johann Bauersachs, Carina Blomström-Lundqvist, Renata Cífková, Michele De Bonis, Bernard Iung, et al. 2018. "2018 ESC Guidelines for the Management of Cardiovascular Diseases during Pregnancy." *European Heart Journal*. https://doi.org/10.1093/eurheartj/ehy340.
85. Roberge, Stephanie, Emmanuel Bujold, and Kypros H. Nicolaides. 2018. "Meta-Analysis on the Effect of Aspirin Use for Prevention of Preeclampsia on Placental Abruption and Antepartum Hemorrhage." *American Journal of Obstetrics and Gynecology*. https://doi.org/10.1016/j.ajog.2017.12.238.
86. Rossen, Lauren M., Katherine A. Ahrens, and Amy M. Branum. 2018. "Trends in Risk of Pregnancy Loss Among US Women, 1990–2011." *Paediatric and Perinatal Epidemiology*. https://doi.org/10.1111/ppe.12417.
87. Schaefer, Viola, Denise Hilfiker-Kleiner, and Corinna Keil. 2023. "Hypertension in Pregnancy." *Cardiovascular Medicine*. https://doi.org/10.4414/cvm.2023.02272.
88. Selvaratnam, R. J., M. A. Davey, B. W. Mol, and E. M. Wallace. 2020. "Increasing Obstetric Intervention for Fetal Growth Restriction Is Shifting Birthweight Centiles: A Retrospective Cohort Study." *BJOG: An International Journal of Obstetrics and Gynaecology*. https://doi.org/10.1111/1471-0528.16215.
89. Shen, Minxue, Hongzhuan Tan, Shujin Zhou, Graeme N. Smith, Mark C. Walker, and Shi Wu Wen. 2017. "Trajectory of Blood Pressure Change during Pregnancy and the Role of Pre-Gravid Blood Pressure: A Functional Data Analysis Approach." *Scientific Reports*. https://doi.org/10.1038/s41598-017-06606-0.
90. Songthamwat, Srisuda, Chatchanawadee Na Nan, and Metha Songthamwat. 2018. "Effectiveness of Nifedipine in Threatened Preterm Labor: A Randomized Trial." *International Journal of Women's Health*. https://doi.org/10.2147/IJWH.S159062.
91. Spencer, Lucy, Nigel Simpson, and Elizabeth Bonney. 2022. "The Management of Preterm Labour." *Obstetrics, Gynaecology and Reproductive Medicine*. https://doi.org/10.1016/j.ogrm.2022.08.002.
92. Tesfalul, Martha, Jeffrey Sperling, Cinthia Blat, Nisha Parikh, Juan Gonzalez Velez, Marya Zlatnik, and Mary E. Norton. 2020. "119: Adverse Perinatal Outcomes Associated with Elevated Blood Pressure and Stage 1 Hypertension." *American Journal of Obstetrics and Gynecology*. https://doi.org/10.1016/j.ajog.2019.11.135.
93. Tikkanen, Minna. 2011. "Placental Abruption: Epidemiology, Risk Factors and Consequences." *Acta Obstetricia et Gynecologica Scandinavica*. https://doi.org/10.1111/j.1600-0412.2010.01030.x.
94. Valenzuela, Ignacio, Mari Kinoshita, Johannes van der Merwe, Karel Maršál, and Jan Deprest. 2022. "Prenatal Interventions for Fetal Growth Restriction in Animal Models: A Systematic Review." *Placenta*. https://doi.org/10.1016/j.placenta.2022.06.007.
95. Volkova, Natalia I., Ilya Yu Davidenko, and Yuliya S. Degtyareva. 2021. "Gestational Diabetes Mellitus." *Akusherstvo i Ginekologiya (Russian Federation)*. https://doi.org/10.54393/df.v2i2.18.
96. Wang, Chanmin, Rui Gao, Lihua Huang, Pian Hu, Liqing Zhu, and Wei Qing Chen. 2022. "Effect of Prenatal Nutritional Intervention on Foetal Growth Restriction: A Real-World Study in Shenzhen, China." *Journal of Maternal-Fetal and Neonatal Medicine*. https://doi.org/10.1080/14767058.2020.1786512.
97. Wasim, Tayyiba, Natasha Bushra, Saher Riaz, and Hafiza Iqra Iqbal. 2020. "Fetomaternal Outcome in Patients with Placenta Previa." *Pakistan Journal of Medical Sciences*. https://doi.org/10.12669/pjms.36.5.1647.
98. Wastnedge, Elizabeth A.N., Rebecca M. Reynolds, Sara R. van Boeckel, Sarah J. Stock, Fiona C. Denison, Jacqueline A. Maybin, and Hilary O.D. Critchley. 2021. "Pregnancy and COVID-19." *Physiological Reviews*. https://doi.org/10.1152/physrev.00024.2020.
99. White, Erin, Jim Pivarnik, and Karin Pfeiffer. 2014. "Resistance Training during Pregnancy and Perinatal Outcomes." *Journal of Physical Activity and Health*. https://doi.org/10.1123/jpah.2012-0350.
100. White, Helen, Victoria Hodgetts Morton, Sarah J. Stock, and Tina Lavender. 2019. "Preterm Labour Decision-Making and Experiences of Care for Women and Clinicians (QUIDS Qualitative): A Qualitative Exploration." *Sexual and Reproductive Healthcare*. https://doi.org/10.1016/j.srhc.2019.06.005.
101. World Health Organization (WHO). 1992. "World Health Organization Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death, Ninth Revision." *Geneva, Switzerland*.
102. Yang, Juseok, Jina Lee, and Dong Hyung Lee. 2022. "Placental Abruption with Subamniotic Hemorrhage: A Case Report." *Clinical and Experimental Obstetrics and Gynecology*. https://doi.org/10.31083/j.ceog4912274.
103. Yeni, Cut M., Rismawati, and Hasanuddin. 2020. "Threatened Preterm Labor: Which Are Become Preterm Labor?" *Indonesian Journal of Obstetrics and Gynecology*. https://doi.org/10.32771/inajog.v8i4.1299.
104. Zhang, Lizi, Shilei Bi, Lili Du, Jingjin Gong, Jingsi Chen, Wen Sun, Xinyang Shen, et al. 2020. "Effect of Previous Placenta Previa on Outcome of next Pregnancy: A 10-Year Retrospective Cohort Study." *BMC Pregnancy and Childbirth*. https://doi.org/10.1186/s12884-020-02890-3.
105. Zur, Rebecca L., John C. Kingdom, W. Tony Parks, and Sebastian R. Hobson. 2020. "The Placental Basis of Fetal Growth Restriction." *Obstetrics and Gynecology Clinics of North America*. https://doi.org/10.1016/j.ogc.2019.10.008.