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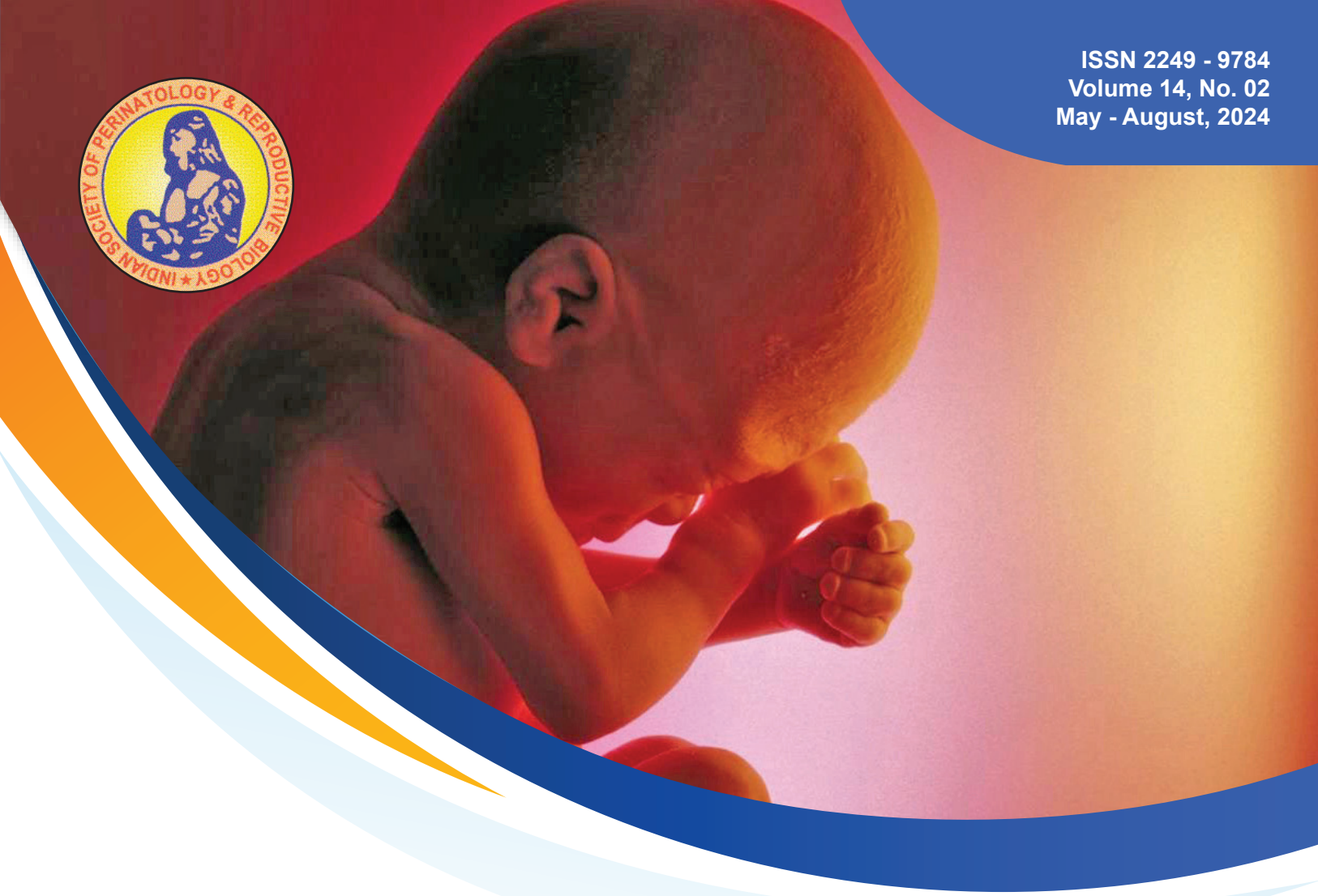

# IJOPARB

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Editor's Choice

# Intrahepatic Cholestasis of Pregnancy

**Ramprasad Dey[1], Shipra Agarwal[2]**

## Introduction:

Intrahepatic cholestasis of pregnancy is a complication in 0.2–2% of pregnancies[1] causing pruritis and increased serum bile acids, liver transaminases, and, occasionally, bilirubin. It is a multifactorial condition. The onset of symptoms is most common in the third trimester, but can be earlier in pregnancy.

It is characterized by pruritus in the absence of a primary skin condition, with abnormal maternal bile acid concentrations. Intrahepatic cholestasis of pregnancy causes minimal risk to the mother except for itching[2]. It has been associated with increased risks of fetus due to prematurity, birth asphyxia, meconium-stained liquor, fetal distress, and unexplained stillbirths[3,4].

Intrahepatic cholestasis has been diagnosed in women based on self-reported itching with an elevation of any of a wide range of liver function tests beyond pregnancy-specific limits.

Serum bile acids may be the only specific laboratory marker for intrahepatic cholestasis in pregnancy. Serum bile acid levels are slightly higher in healthy pregnant women compared to non-pregnant women[5].

There is now increasing evidence that most liver function tests do not reflect the risk of fetal demise and only increased maternal total serum bile acid concentration is associated with an increased risk of stillbirth[6].

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## Etiopathogenesis of Intrahepatic Cholestasis of Pregnancy:

Throughout pregnancy, the female body undergoes a multitude of physiological and anatomical transformations to optimize conditions for fetal development. Every system and organ adjusts its functions to support a healthy gestation. Notably, the liver dynamically modifies its metabolism to accommodate the growing fetus. For instance, changes in glucose metabolism occur due to altered insulin sensitivity and increased gluconeogenesis. Hormonal shifts and rising insulin resistance also influence maternal lipid metabolism. Additionally, the liver's role in bile transportation is affected, leading to a gradual elevation in total bile acid (TBA) levels in the bloodstream. While most pregnancies experience a moderate rise within normal ranges, some may encounter excessive increases, indicating intrahepatic cholestasis of pregnancy (ICP).

The exact etiology of ICP remains incompletely understood, with focus primarily on genetic, hormonal, and environmental factors. Genetic elements, particularly mutations affecting the hepatobiliary transport protein-multidrug resistance protein 3 (MDR3), crucial for phospholipid biliary secretion, are implicated in ICP's pathogenesis. MDR3 mutations are detected in around 16% of ICP cases, correlating with disease severity and total bile acid (TBA) levels exceeding 40 μmol/L. However, MDR3 mutations may also manifest in conditions like hereditary low phospholipid-associated cholelithiasis (LPA) and drug-induced cholestasis. Additionally, the multidrug resistance-related protein 2 (MRP2) is implicated in ICP

development. Mutations in other genes such as BSEP, FIC1, and FXR are also associated with ICP[7,8,9,10,11,12].

The role of sex hormones in the development of intrahepatic cholestasis of pregnancy (ICP) is supported by the occurrence of ICP in multiple pregnancies and among individuals using oral contraceptives. Levels of estrogen, progesterone, and their metabolites rise during pregnancy, peaking in the third trimester and declining postpartum, aligning with the course of ICP. However, the precise mechanism by which sex hormones contribute to ICP remains unclear. Higher levels of 17-β-D-estradiol and progesterone sulfates have been observed in pregnant women with ICP as compared to healthy women[13,14].

With respect to the environmental factors, attention is drawn to dietary factors, excess erucic acid from rapeseed oil, selenium deficiency, or the impact of pesticides[15].

## Clinical Characteristic of Intrahepatic Cholestasis of Pregnancy:

The primary and most prominent symptom of intrahepatic cholestasis of pregnancy (ICP) is pruritus, typically manifesting in the second or third trimester, often after 30 weeks of pregnancy. This itching is commonly experienced on the palms and soles, although it can affect any part of the body. The pruritus tends to intensify at night, potentially causing insomnia, irritability, and even depression. Occasionally, ICP may present with rare symptoms such as abdominal pain, nausea, and vomiting. In approximately 10–15% of cases, mild jaundice may develop within four weeks of the onset of pruritus. Some ICP patients may also experience fatty stools due to absorption issues, particularly lipid malabsorption. This can lead to deficiencies in fat-soluble vitamins, notably vitamin K, potentially resulting in prolonged prothrombin times and consequent perinatal hemorrhages or bleeding into the fetal central nervous system (CNS). Typically, symptoms resolve spontaneously within 2–3 weeks following delivery. However, ICP poses significant risks to the fetus, including an increased likelihood of premature delivery (20–60%), intrauterine asphyxia (up to 44%), meconium staining of the amniotic fluid, and fetal bradycardia. The risk of adverse fetal effects escalates with maternal blood total bile acid (TBA) levels. Moreover, the risk of stillbirth is elevated in women with ICP, particularly when serum bile acid concentrations exceed 100 μmol/L[16,17].

## Diagnosis of Intrahepatic Cholestasis of Pregnancy:

New onset pruritus in pregnant women, if associated with rash, is unlikely to be ICP. If the itchy skin looks abnormal (other than excoriations) then another cause should be considered. Liver function tests and bile acids are not required routinely. Clinicians should be aware however, that skin conditions (e.g. eczema) and ICP can co- exist. If the itchy skin looks normal, or there is only skin trauma due to scratching, the diagnosis may include gestational pruritus, or ICP and measurement of bile acid concentrations and liver function tests should be undertaken. Currently, the primary biochemical indicator utilized in diagnosing intrahepatic cholestasis of pregnancy (ICP) is the total bile acid (TBA) level, which may serve as the initial or sole laboratory-detected sign. In healthy pregnant women, TBA levels are marginally higher than in non-pregnant counterparts but remain clinically insignificant. The diagnostic threshold for ICP is set at a total bile acid concentration exceeding 19 micromoles/L. If the itchy skin appears normal or shows only minor damage from scratching, the diagnosis may include gestational pruritus or intrahepatic cholestasis of pregnancy (ICP) (refer to Table 1). It is recommended to conduct measurements of bile acid concentrations and liver function tests. A bile acid concentration of 19 micromoles/L or higher during pregnancy supports a diagnosis of ICP. Bile acid measurements should be taken at a convenient time when clinically indicated, and fasting is not necessary. However, a retrospective study by Kondrackiene et al.[17] suggests that TBA levels alone lack sufficient sensitivity and specificity for diagnosing ICP. The authors propose that concentrations of specific bile acids such as cholic acid (CA), chenodeoxycholic acid (CDCA), and their ratio (CA/CDCA) serve as better markers. Notably, analyzing total bile acids without considering the bile acid ratio decreases the accuracy of positive results by over 2%[18].

**Table 1: Terminology for pregnant women with itching of normal skin**

| Diagnosis | Clinical Features |
|---|---|
| Gestational Pruritus | Itching and peak bile acid concentrations <19 micromol/L[a] |
| Mild ICP | Itching and raised peak bile acid concentrations 13-39 micromol/L |
| Moderate ICP | Itching and raised peak bile acid concentrations 40-99 micromol/L |
| Severe ICP | Itching and raised peak bile acid concentrations ≥100 micromol/L |

The elevation in total fatty acids is typically accompanied by an increase in the activity of aminotransferases, notably alanine aminotransferase (ALT) which may rise up to approximately 2–15-fold, occasionally exceeding 1000 IU/L. Nevertheless, determining the reference range for ALT in pregnant women remains a subject of debate. There is a proposal to lower the upper limit of the reference range to enhance the accurate identification of pregnant women with hepatic disorders, including intrahepatic cholestasis of pregnancy. Although ICP patients may exhibit elevated alkaline phosphatase activity (AP), its diagnostic value is limited due to placental and bone production of AP. Also, there is typically no increase in gamma-glutamyltransferase activity in ICP. Dyslipidemia may manifest with elevated total cholesterol, low-density lipoprotein cholesterol, and apolipoprotein levels. However, all maternal serum parameters assessed in liver function tests typically return to normal shortly after delivery.

Previously, the Royal College of Obstetricians and Gynaecologists (RCOG) advocated for routine laboratory and imaging investigations to rule out other potential causes for the clinical presentation of intrahepatic cholestasis of pregnancy (ICP), such as viral and autoimmune tests along with liver ultrasound. However, recent studies suggest that the probability of identifying a viral, autoimmune, or structural cause for the itching and liver abnormalities that were not suspected based on other clinical indicators is exceedingly low and no new diagnoses were discovered following these investigations. Consequently, their routine utilization is no longer recommended. The UK National Screening Committee advises against routine screening for hepatitis C during pregnancy due to a lack of evidence demonstrating benefits. Screening should only be considered in pregnant women with an unusual or unclear presentation of ICP. This may encompass women exhibiting significantly elevated transaminases, early-onset ICP in the first or second trimester, a rapidly deteriorating biochemical profile, any signs of liver failure or evidence of acute infection, or if symptoms persist after childbirth[19,20].

## Fetomaternal monitoring in ICP :

- **MATERNAL MONITORING :**

  For all women experiencing itching and initial elevated bile acid levels, a second bile acid measurement should be conducted approximately one week later before making any diagnostic or care decisions. This precaution is crucial because many women with bile acid levels exceeding 100 micromol/L or falling within the 40–100 micromol/L range often show subsequent concentrations that are significantly lower[21].

  Subsequent biochemical assessments for women and pregnant individuals will be tailored individually, based on the potential impact of results on further care decisions:

  - Women with mild intrahepatic cholestasis of pregnancy (ICP) and peak bile acids between 19 and 39 micromol/L may consider weekly testing as they approach 38 weeks of gestation to assist in determining the optimal timing for delivery.
  - Those with moderate ICP and peak bile acids ranging from 40 to 99 micromol/L, particularly as they approach 35 weeks of gestation, should consider weekly testing. This approach helps manage the timing of birth should levels reach or exceed 100 micromol/L.
  - In cases of severe ICP with peak bile acids of 100 micromol/L or higher, routine testing may not significantly influence decision-making and thus may not be routinely necessary.

- **FETAL MONITORING :**

  In intrahepatic cholestasis of pregnancy (ICP), evidence indicates that cardiotocography (CTG) monitoring or biophysical profiles do not reliably predict stillbirth. Several studies have documented fetal demise despite intensive surveillance and previously normal ultrasound

scans, including fetal Doppler measurements and CTG monitoring[22,23,24,25].

ICP is not typically associated with fetal growth restriction, as there is no significant difference in birthweight centiles compared to babies born to women without ICP. Therefore, strategies for antenatal monitoring aimed at detecting placental insufficiency are unlikely to provide substantial benefits in cases of isolated ICP.

It is recommended that all pregnant individuals monitor both the quality and quantity of fetal movements regularly. Any reduction or change in fetal movements should be promptly reported to their local maternity unit, aligning with national guidelines.

## Management of Intrahepatic Cholestasis of Pregnancy:

- **DRUG TREATMENT IN ICP :** Drug treatment for intrahepatic cholestasis of pregnancy mainly reduces maternal itching, which can vary in intensity and isn't necessarily linked to bile acid levels. However, there's no evidence suggesting that standard medical treatments effectively lower maternal bile acid levels or improve perinatal outcomes[26]. (Level 1 evidence)
  - Topical emollients : It may relieve some of the discomfort associated with itching and has no known harmful effects
  - Antihistamines : The effectiveness of the treatment is uncertain in women and pregnant people with ICP, and relief may be more related to its sedative action than a direct effect. Eg. Chlorphenamine
  - Ursodeoxycholic acid : The drug works by displacing hydrophobic bile acids, thereby protecting hepatocytic membranes. Ursodeoxycholic acid (UDCA) has been demonstrated to enhance the transplacental removal of bile acids from the fetus. It is typically administered orally at a dosage of 300 mg 2–3 times daily (or 10–16 mg/kg/day)[27]. It is effective in reducing alanine transaminases levels but the clinical implications of this are uncertain, as al-anine transaminase levels have no association with stillbirth[28].
  - Vitamin K : It is recommended only if there appears to be reduced absorption of dietary fats (e.g. presence of steatorrhoea) and/or evidence of abnormal prothrombin time if coagulation studies are performed. It is prescribed as a water soluble formulation such as menadiol sodium phosphate at a dose of 10 mg daily[29].
- **TIMING AND MODE OF DELIVERY :**

  The risk of stillbirth is 0.13% in women whose peak bile acids are less than 40 micromol/L, which is comparable to the background population risk. Despite this low risk throughout pregnancy, the benefits of delivering by 40 weeks may outweigh continuing the pregnancy further.

  For women with peak bile acids between 40 and 99 micromol/L, the risk of stillbirth is 0.28%, similar to the overall background population risk, but it appears to increase around 38-39 weeks of gestation. Therefore, it is reasonable to consider planned delivery around this time for these women, especially if other conditions like gestational diabetes or pre-eclampsia are present.

  In women with peak bile acids of 100 micromol/L or more, the risk of stillbirth rises to 3.44%, which is higher than the background population rate. This risk appears to increase starting from 35-36 weeks of gestation and hence, it is reasonable to plan delivery around this time[30].

| BILE ACIDS LEVEL | RECOMMENDATION |
|---|---|
| 19– 39 micromol/L | Consider options of planned birth by 40 weeks' gestation or ongoing antenatal care according to national guidance in women with mild ICP |
| 40– 99 micromol/L | Consider planned birth at 38– 39 weeks' gestation in women with moderate ICP |
| 100 micromol/L or more | Consider planned birth at 35– 36 weeks' gestation in women with severe ICP |

Pregnant women with ICP do not have increased rates of assisted or operative birth compared with women without ICP. Mode of birth should therefore be based on usual obstetric or medical indications[31].

- **MONITORING IN LABOUR :**

  When considering intrapartum care, it is important to assess any pre-existing obstetric or medical conditions that could influence fetal

monitoring decisions during labor. For women with mild intrahepatic cholestasis of pregnancy (ICP) (peak bile acids 19-39 micromol/L) and no other risk factors, intrapartum care can align with national guidelines[32].

In cases of moderate ICP (peak bile acids 40-99 micromol/L), decisions should be individualized. The uncertainty regarding the benefits of continuous electronic fetal monitoring should be discussed, taking into account the presence of additional risk factors.

For women with severe ICP (peak bile acids 100 micromol/L or higher), given evidence indicating heightened risks of adverse perinatal outcomes, continuous electronic fetal monitoring should be recommended.

- **CONTRACEPTION AND FUTURE PREGNANCIES :**

The 2016 UK Medical Eligibility Criteria (UKMEC) for Contraceptive Use indicate that copper-bearing intrauterine devices, levonorgestrel-releasing intrauterine systems, progestogen-only implants, progestogen-only injectables, and progestogen-only pills are suitable for use without restriction in women with a history of intrahepatic cholestasis of pregnancy (ICP) (UKMEC category 1).

Combined hormonal contraception can be considered in women with ICP (UKMEC 2), provided they do not have a history of cholestasis related to contraception. Previously, concerns existed that women with a history of ICP might have an increased risk of cholestasis with estrogen-containing hormonal contraception, but this risk is unlikely for most women. The 2016 UKMEC advises that for women who have had ICP, the benefits of using these estrogen-containing methods outweigh this theoretical risk (UKMEC category 2), allowing them to choose this method if desired[33].

Women and individuals of reproductive age with history of intrahepatic cholestasis of pregnancy (ICP) in previous pregnancy have a higher likelihood of developing ICP again in subsequent pregnancies compared to the general population. However, the exact extent of this increased risk remains uncertain.

**Differential diagnosis & management of Pruritus in pregnancy**

| Pruritic Dermatoses of pregnancy | Areas affected | Risk factors | Recurrence risk | Management | Pregnancy outcome |
|---|---|---|---|---|---|
| Intrahepatic cholestasis of pregnancy | scalp, anus, vulva, abdominal skin | Indian- Asian origin, Pakistani- Asian origin, previous obstetric cholestasis | 60-70 % in future pregnancies | • Ursodeoxycholic acid<br>• Topical emollients<br>• Sedating anti-histamines | Increased risk of stillbirth,<br>Increased risk of PPH,<br>Increased risk of fetal distress,<br>Increased risk of premature birth |
| Atopic Eruption of Pregnancy | Face, neck, chest, extensor surfaces of limbs and trunk | Family history of atopy | Limited data | • Topical emollients<br>• Topical anti-pruritics<br>• Topical steroids<br>• Antihistamines | No adverse effects on mother of fetus |
| Polymorphic eruption of pregnancy | Abdominal striae with peri-umbilical sparing, can progress to trunks and extremities, sparing palms, soles and face | Nulliparity, multiple pregnancy, any cause of overdistension of skin | Rarely recurs | • Topical steroids (first line)<br>• Topical emollients<br>• Antihistamines<br>• Oral steroids | No adverse effects on mother of fetus |
| Pemphigoid Gestationis | Appears around umbilicus, can progress to trunks and extremities, palms, soles sparing mucosa | Recognised correlation with HLA-DR3, HLA-DR4,<br><br>Other autoimmune conditions | May recur in subsequent pregnancies with earlier onset and increasing severity<br>May recur with oral contraception/ menstruation | • Topical/ oral steroids<br>• Antihistamines<br>• Antibiotics<br>• Immunophoresis<br>• immunosuppressants | IUGR,<br>Preterm labour,<br>Self limiting skin lesions in neonates |

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Review Article

# Environmental Toxins and Reproductive Health

**Meena Samant[1], Neha Singh[2], Hannah Elza Kurian[3]**

## Introduction

Human fertility rates are declining globally. It has been below the population replacement rate in many countries for decades.[1] One in six people globally will experience involuntary infertility at some point in their lives.[1]

A recent study report lists about 350,000 different synthetic chemicals on the market today.[2] Roughly 70% of these chemicals have not been adequately assessed for toxicity.[2] Even when testing is conducted, the reliability of standard tests in predicting effects on human reproduction remains a subject of debate.

Beyond the commonly discussed impacts of environmental toxins on respiratory or cardiovascular systems, one of the most critical and yet underexplored aspects is the effect on reproductive health. Modern life exposes individuals to a range of pollutants—whether through air, water, or even food. Over time, exposure to these toxins disrupts the body's natural hormonal processes, with lasting repercussions for fertility, pregnancy outcomes, and the health of future generations. Understanding how these environmental toxins, particularly endocrine-disrupting chemicals (EDCs), affect reproductive systems at the cellular level is essential for both medical practice and public health policies.

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This review explores the connection between environmental pollutants and reproductive health, diving into the cellular mechanisms of endocrine disruption and highlighting the pressing need for policy intervention to reduce exposure risks.

## Environmental Pollutants and Human Exposure

Environmental pollution, once viewed as a peripheral concern, is now recognized as a major driver of various health conditions. The World Health Organization (WHO) attributes nearly 24% of global disease burden to environmental factors, with children bearing a disproportionate load. Among the most concerning pollutants are airborne chemicals, heavy metals, pesticides, and synthetic compounds that mimic or interfere with hormonal function.

Many of these chemicals are endocrine disrupting chemicals (EDCs) (i.e., chemicals or mixtures of chemicals that affect any stage of human development).[3] EDCs are part of environmental chemical contaminants that are present in all the populations studied, and it has been said that "babies are born pre-polluted".[4]

Everyday items such as plastics, industrial chemicals, cosmetics, and pesticides contain EDCs like bisphenol A (BPA), phthalates, and polychlorinated biphenyls (PCBs). While exposure levels are often low, the cumulative effect over time can result in significant health problems.

EDCs are especially harmful because they mimic or block hormonal signals, often disrupting the endocrine system's delicate balance. These chemicals

also interfere with metabolic pathways, often contributing to obesity, diabetes, and cardiovascular conditions.

The impact of these pollutants, however, becomes particularly severe when exposure occurs during critical developmental windows, such as prenatal or early childhood periods. During these stages, exposure to toxins can result in long-term or even transgenerational health issues, affecting not only those directly exposed but also their offspring. We will discuss these in detail in the following text.

## Cellular Mechanisms of Endocrine Disruption

EDCs are distributed widely, contaminating our air, water, soil, and food. EDCs work by mimicking or blocking the action of natural hormones. EDCs like BPA and phthalates, bind to hormone receptors, often causing hormonal signals to go awry. Some EDCs act as agonists, mimicking natural hormones like estrogen or testosterone and overstimulating hormonal pathways. Others act as antagonists, blocking the action of hormones, resulting in decreased signalling. A third group interferes with the synthesis, transport, or metabolism of hormones, disrupting hormonal balance without directly binding to hormone receptors.[5]

The damage caused by these disruptions can be profound, especially when exposure occurs during critical periods of reproductive development. Prenatal exposure to EDCs, for example, has been shown to increase the risk of developing reproductive abnormalities, such as cryptorchidism in males or polycystic ovary syndrome (PCOS) in females.

## Impact on Reproductive Health

The reproductive system is particularly sensitive to disruptions caused by environmental toxins. As the body's reproductive processes are regulated by hormones, any interference with the hormonal balance can have serious repercussions for fertility, pregnancy outcomes, and the health of future generations.

Infertility is perhaps the most obvious impact of EDC exposure. Both male and female fertility can be compromised by the hormonal disruptions caused by environmental toxins. In males, exposure to phthalates and other EDCs has been linked to reduced sperm counts, abnormal sperm morphology, and decreased sperm motility. In females, toxins like BPA can interfere with ovulation, leading to fewer viable eggs and an increased risk of infertility.[5]

Endometriosis: Studies suggest that EDCs such as dioxins and PCBs may contribute to the development of endometriosis by disrupting the body's hormonal balance. These chemicals trigger inflammatory responses and interfere with the normal functioning of the uterine lining, leading to endometriosis.[5]

Additionally, there is increasing evidence that exposure to EDCs can raise the risk of hormone-sensitive cancers, such as breast, ovarian, and prostate cancer. These cancers are driven by hormonal imbalances, and the chronic exposure to chemicals that mimic estrogen or androgen can lead to uncontrolled cell growth and tumor development. For example, BPA has been shown to increase the risk of breast cancer by promoting abnormal cell growth in breast tissue.

## Long-Term Health Implications and Transgenerational Effects

Recent research has shown that exposure to certain chemicals, particularly during pregnancy, can cause epigenetic changes that alter gene expression. These changes can increase the risk of reproductive disorders and other health problems not only in the person exposed but also in their descendants.[6]

For example, prenatal exposure to phthalates has been linked to reduced sperm quality in male offspring, a condition that can persist into adulthood. Similarly, exposure to BPA during pregnancy has been shown to affect fetal development, leading to abnormal hormone levels and an increased risk of reproductive health issues later in life. The possibility of transgenerational effects raises serious concerns about the long-term impact of environmental pollution, particularly as these chemicals continue to accumulate in the environment.

Beyond reproductive health, the long-term consequences of EDC exposure extend to metabolic disorders, cardiovascular disease, and neurodevelopmental issues. EDCs are now recognized as a major contributing factor for diabetes, with many chemicals interfering with insulin signaling and glucose metabolism. Persistent exposure to pollutants

like BPA and PCBs has been linked to increased rates of obesity, insulin resistance, and type 2 diabetes.[7]

The brain and nervous system are also vulnerable to the long-term effects of EDCs. Prenatal and early childhood exposure to chemicals like BPA, dioxins, and heavy metals has been associated with neurodevelopmental disorders, including attention-deficit/hyperactivity disorder (ADHD), autism, and reduced cognitive function.

## Prevention and Policy Implications

Given the growing body of evidence linking environmental toxins to reproductive and long-term health problems, it is crucial that both policymakers and healthcare professionals take action to mitigate these risks. One of the most effective ways to reduce the impact of EDCs is through stricter regulation and control of industrial chemicals. Governments must prioritize the reduction of toxic emissions and ensure that industries adhere to environmental standards that limit the release of harmful pollutants into the air, water, and soil.[1]

Public awareness campaigns are equally important in educating individuals about the dangers of EDCs and how to reduce their exposure. Simple actions like avoiding plastics that contain BPA, using natural or organic personal care products, and reducing consumption of processed foods can significantly lower the levels of these chemicals in the body. Healthcare professionals also play a critical role in advising patients on how to minimize exposure to environmental toxins, particularly during pregnancy and early childhood.

In addition to public health initiatives, more research is needed to fully understand the long-term effects of EDCs on reproductive health and other systems. Future studies should focus on identifying the most harmful chemicals, understanding their mechanisms of action, and developing strategies to reverse or mitigate their effects. Policymakers must also push for international cooperation in addressing environmental pollution, as these issues are global in scope and require a coordinated response.

## Conclusion

Environmental toxins pose a growing threat to reproductive health, demanding urgent action. Healthcare professionals must recognize this impact and advocate for stronger regulations. Preventing exposure is a global public health priority requiring collaboration among governments, industries, and individuals. By enforcing stricter policies, raising public awareness, and advancing research on endocrine-disrupting chemicals, we can mitigate risks and protect future generations. Prevention is paramount; while past damage cannot be reversed, decisive action now can prevent further harm. The responsibility lies with policymakers, healthcare professionals, organizations, and the public to safeguard the well-being of current and future generations. The time to act is now.

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Original Article: Obstetrics

# Maternal and Perinatal Outcomes in Preeclampsia with Respect to Organ Involvement

**Shruti Pansare[1], Ramprasad Dey[2]**

**ABSTRACT**

**Objective:** Preeclampsia is a leading cause of maternal and perinatal morbidity and mortality, characterized by new-onset hypertension after 20 weeks of gestation. This study explores the maternal and perinatal outcomes associated with organ involvement in preeclampsia, focusing on identifying complications and their effects.

**Materials and Methods:** This prospective observational analytical study was conducted over 18 months at a tertiary care hospital in Kolkata. A total of 106 pregnant women diagnosed with preeclampsia beyond 20 weeks of gestation were included. Exclusion criteria encompassed pre-existing renal or liver disease, multifetal gestation, and other conditions potentially confounding the study.

**Results:** Renal dysfunction was observed in 6.6% of cases, characterized by proteinuria and, in severe cases, acute kidney injury. Hepatic dysfunction, including elevated liver enzymes and HELLP syndrome, occurred in 10.4% of participants, similarly lung involvement characterized by basal lung crepitations suggestive of pulmonary edema, indicative of severe fluid overload, was seen in 10.4%. Multi-organ dysfunction was documented in 1.88% of cases, significantly correlating with adverse maternal outcomes such as increased cesarean deliveries (34.9%), maternal ICU admissions, and higher perinatal complications. NICU admissions were required in 54.7% of neonates, with 41.5% exhibiting fetal growth restriction and 7.5% neonatal mortality.

**Conclusion:** Organ-specific involvement in preeclampsia plays a critical role in determining maternal and perinatal outcomes. Multi-organ dysfunction markedly increases risks, underscoring the importance of early diagnosis and targeted interventions. Vigilant monitoring and timely management strategies can significantly improve outcomes, reducing morbidity and mortality associated with this condition.

**Keywords:** Preeclampsia, maternal outcomes, perinatal outcomes, organ involvement, HELLP syndrome, hypertensive disorders in pregnancy.

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## Introduction

Pre-eclampsia accounts for majority of referrals in a tertiary care centre as it is one of the major causes of maternal and perinatal morbidity and mortality[1]. It complicates almost 10% of all pregnancies. Preeclampsia, affecting 5-8% of pregnancies worldwide, is a complex condition involving multi-system dysfunction[2–3]. Severe cases can lead to eclampsia, HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count), and other critical complications. Fetal complications which are related to preeclampsia include impaired fetal growth, neonatal respiratory distress syndrome, and stillbirth.

Despite extensive research, the relationship between specific organ involvement and maternal and fetal outcomes remains underexplored. Close surveillance, early detection, and prompt management comprise the main clinical management strategy. There are several studies focused on developing useful pre-eclampsia prediction methods[4].

Even after extensive research, there are no rational preventive or therapeutic interventions available. Currently, the only definitive treatment for pre-eclampsia is delivery of the fetus and placenta as early as possible[5]. Although the discussion is on-going, perinatal survival is thought to be increased in patients with early onset preeclampsia by expectant, non-interventional management, using antihypertensive drugs to control Hypertension, magnesium sulphate in eclampsia and corticosteroids to enhance fetal lung maturity[6].

Although there are many studies focused on the study of maternal and fetal outcome in preeclampsia, severe preeclampsia and eclampsia, there are very few studies which are determining the impact of organ involvement on the outcome of pregnancy. Moreover, there is no study comparing the outcome with respect to single versus multi-organ involvement. This is important to note because the result will help us to focus on the preventive and prophylactic screening of patients by determining the organ involvement by history taking, clinical examination and laboratory investigations which are very easily available and affordable at a tertiary care centre of a developing nation like India. Thus, enabling us to prevent morbidity and mortality in patients of preeclampsia more effectively.

## Methodology

This prospective observational analytical study was conducted over 18 months at a tertiary care hospital in Kolkata. All pregnant women beyond 20 weeks of gestation attending antenatal OPD or admitted in the hospital were clinically screened for detection of hypertensive disorders of pregnancy. Among these, preeclampsia was confirmed as per the ACOG guidelines[7] and thus 106 patients were recruited in the study after obtaining an informed consent. Exclusion criteria encompassed pre-existing renal or liver disease, multifetal gestation, and other conditions potentially confounding the study. Data collection involved clinical examinations, laboratory investigations, and fetal monitoring via ultrasonography and Doppler studies.

Patient characteristics were described as means with the standard deviation for normally distributed numerical data and as percentage for categorical variables. Differences were analyzed by Student's t- test for normally distributed data and the Mann-Whitney U-test for no normally distributed data. Chi-square and Fischer's exact tests were used for comparisons of categorical variables. In all analyses, values <0.05 were considered statistically significant.

## Results

### Demographic and Clinical Characteristics

Age Distribution: The majority (65.1%) were aged 21-30 years, with 13.2% aged ≤20 years and 21.7% aged 31-40 years. Table 1

**Table 1: Distribution of age in group**

| Age in group | Frequency | Percent |
|---|---|---|
| ≤20 | 14 | 13.2% |
| 21-30 | 69 | 65.1% |
| 31-40 | 23 | 21.7% |
| Total | 106 | 100.0% |

Gravida: Primigravida constituted 71.6% of cases. 12.3% patients were 2nd gravida and (16.0%) patients were 3rd gravida. Table 2

**Table 2: Distribution of Gravida or Parity**

| Gravida or Parity | Frequency | Percent |
|---|---|---|
| G2P1 | 13 | 12.3% |
| G3P2 | 17 | 16.0% |
| PRIMI | 76 | 71.6% |
| Total | 106 | 100.0% |

Family History: In our study, (34.9%) patients had history of hypertension in the maternal side of their family and 69 (65.1%) patients had no H/O hypertension in the family. The value of p is significant at < .00001.

### Clinical Presentations and Symptoms

Common symptoms included severe headache (29.2%), vomiting (24.5%), blurred vision (13.2%), and bilateral pitting pedal edema (64.2%).

Basal lung crepitations were observed in 10.4% of cases.

## Organ Involvement

### Renal Dysfunction:

Proteinuria was a prominent feature, with 37.7% showing 1+, 33% with 2+, and 29.2% with 3+ dipstick readings.

Severe renal involvement included oliguria and elevated serum creatinine levels, leading to acute kidney injury in critical cases.

### Hepatic Dysfunction:

Liver involvement included elevated liver enzymes in 10.4% of cases.

HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count) was observed in severe cases, contributing to maternal complications such as right upper quadrant pain and subcapsular hematomas.

### Pulmonary Involvement:

Pulmonary edema was present in 10.4% of participants. This was often associated with severe fluid overload and required intensive care.

### Multi-Organ Involvement:

It was observed that 3.77% patients had liver & kidney involvement, 1.88% patients had kidney & lung involvement, 2.83% patients had liver & lung involvement, and 1.88% patients had features suggestive of all three organ involvement. Table 3

**Table 3: Multi-organ Involvement**

| Organ Involvement | Frequency | Percent |
|---|---|---|
| Liver, Kidney | 4 | 3.77% |
| Kidney, Lung | 2 | 1.88% |
| Liver, Lung | 3 | 2.83% |
| Liver, Kidney, Lung | 2 | 1.88% |
| Total | 106 | 100.0% |

## Maternal and Perinatal Outcomes with respect to organ involvement

### Kidney involvement

In our study, out of the 7 patients with kidney involvement, 14.28% patient had PPH, 42.85% patients had FGR, 100% patients had normal vaginal delivery, and 3 patients died. The value of p is significant at .01208. Table 4

**Table 4**

| Maternal Outcome | | Frequency | Percentage |
|---|---|---|---|
| APH | | 0 | 0% |
| PPH | | 1 | 14.28% |
| FGR | | 3 | 42.85% |
| Mode of Delivery | C-Section | 0 | 0% |
| | Vaginal delivery | 7 | 100% |
| Maternal Outcome- death | | 3 | 42.85% |
| Eclampsia | | 0 | 0% |

Out of the 7 patients with kidney involvement, 14.28% patient had her baby admitted to NICU, 28.57% patients had baby with low birth weight and 14.28% patient had still birth. The value of p is .4654. Table 5

**Table 5**

| Perinatal Outcome | Frequency | Percentage |
|---|---|---|
| NICU | 1 | 14.28 |
| LBW | 2 | 28.57 |
| Still birth | 1 | 14.28 |
| Neonatal Death | 0 | 0 |

### Liver involvement

In our study, out of the total 11 patients with liver involvement, 3 (27.27%) patients had PPH, 5 (45.45%) patients had FGR, 1 (0.09%) patient underwent delivery by C-section, and 10 (90.90%) patients had normal vaginal delivery while 3 (27.27%) patients died. The value of p is significant at 0.00174. Table 6

**Table 6**

| Maternal Outcome | Frequency | Percentage |
|---|---|---|
| APH | 0 | 0% |
| PPH | 3 | 27.27% |
| FGR | 5 | 45.45% |

| Maternal Outcome | | Frequency | Percentage |
|---|---|---|---|
| Mode of Delivery | C-Section | 1 | 0.09% |
| | Vaginal delivery | 10 | 90.90% |
| Maternal Outcome-Death | | 3 | 27.27% |
| Eclampsia | | 0 | 0% |

Of all the patients with liver involvement 2 (18.18%) patients had their baby admitted to NICU, 4 (36.36%) patients had baby with low birth weight and 2 (18.18%) patients had still birth. The value of p is significant at 0.030302. Table 7

**Table 7**

| Perinatal Outcome | Frequency | Percentage |
|---|---|---|
| NICU | 2 | 18.18 |
| LBW | 4 | 36.36 |
| Still birth | 2 | 18.18 |
| Neonatal Death | 0 | 0 |

### Lung involvement

In our study, out of the 11 patients with lung involvement, 3 (27.27%) patients had PPH, 5 (45.45%) patients underwent delivery by C-sec, 6 (54.54%) patients had normal vaginal delivery, 3 (27.27%) patients died, and 1 (9.09%) patient developed eclampsia. The value of p is significant at 0.04036. Table 8

**Table 8**

| Maternal Outcome | | Frequency | Percentage |
|---|---|---|---|
| APH | | 0 | 0% |
| PPH | | 3 | 27.27% |
| FGR | | 5 | 45.45% |
| Mode of Delivery | C-Section | 5 | 45.45% |
| | Vaginal delivery | 6 | 54.54% |
| Maternal Outcome-Death | | 3 | 27.27% |
| Eclampsia | | 1 | 9.09% |

Out of 11 patients with lung involvement, 2 (18.18%) patients had their baby admitted to NICU, 1 (9.09%) patient had baby with low birth weight and 1 (9.09%) patient had still birth. The value of p is .4654. Table 9

**Table 9**

| Perinatal Outcome | Frequency | Percentage |
|---|---|---|
| NICU | 2 | 18.18 |
| LBW | 1 | 9.09 |
| Still birth | 1 | 9.09 |
| Neonatal Death | 0 | 0 |

### Multiorgan involvement

In our study, there were 2 patients who had signs, symptoms and investigations suggesting involvement of all the three organs i.e. lungs, liver and kidney. 1 patient had PPH, both the patients had FGR, both the patients had a normal vaginal delivery and but unfortunately both the patients died due to multi-organ failure following prolonged ICU admission. The value of p is <.00001. Table 10

**Table 10**

| Maternal Outcome | | Frequency | Percentage |
|---|---|---|---|
| APH | | 0 | 0% |
| PPH | | 1 | 50% |
| FGR | | 2 | 100% |
| Mode of Delivery | C-Section | 0 | 0% |
| | Vaginal delivery | 2 | 100% |
| Maternal Outcome- Death | | 2 | 100% |
| Eclampsia | | 0 | 0% |

Only 1 patient out of the 2 having multi-organ involvement had baby with low birth weight no other significant perinatal outcome was noted. Table 11

**Table 11**

| Perinatal Outcome | Frequency | Percentage |
|---|---|---|
| NICU | 0 | 0 |
| LBW | 1 | 50 |
| Still birth | 0 | 0 |
| Neonatal Death | 0 | 0 |

## Discussion

Preeclampsia is still a major problem in the field of obstetrics. There has been variation of maternal age of pregnancy from teenage to women who are 40 years or older, as compared with women between 20 and 29 years of age, with approximately two-fold increase in risk of preeclampsia, in our study we observed that majority i.e. 69 (65.1%) patients were between 21-30 years of age (p value<.00001). The mean age of patients was 26.5.

There was a significant association with family history of hypertension, as 37 (34.9%) patients had history of hypertension in the maternal side of their family and 69 (65.1%) patients had no history of hypertension in the family (p value- .0001). Thus, it can be inferred that maternal and fetal genetic factors carry strong risk for preeclampsia, with one-third attributable to maternal genetic factors[8].

Among the common symptoms and diagnostic criteria according to ACOG it was noted that 31 (29.2%) patients presented with complaint of severe headache, 14 (13.2%) patients complained of blurring of vision at the time of admission or during the hospital stay, 26 (24.5%) patients presented with vomiting, and 68 (64.2%) patients had bilateral pitting pedal edema, not relieved on rest or leg elevation. 11 (10.4%) patients were noted to have basal lung crepitation on chest auscultation. As for urine for protein 40 (37.7%) patients had urine dipstick value for protein of 1 +, 35 (33.0%) patients had a value of 2 + and 31 (29.2%) patients had a value of 3 +. The mean systolic blood pressure at the time of admission was 155, and the mean diastolic blood pressure at the time of admission was 98. The mean platelet count of patients was 1.87 lakhs/cc. In our study, 58 (54.7%) patients had to be treated with prophylactic or therapeutic injection magnesium sulphate therapy according to Pritchard regimen.

It was inferred from above findings that kidney involvement has significant adverse maternal outcome in terms of maternal morbidity and mortality (p value- 0.01208). Although it has no direct significant effect on adverse perinatal outcome (p value- 0.4654). Whereas significant maternal morbidity and mortality (p value- 0.00174) as well as perinatal morbidity (p value-0.030302) is caused due to liver involvement in pre-eclampsia patients. Lung involvement has significant effect on maternal morbidity and mortality (p value- 0.04036), although it has no significant effect on perinatal outcome (p value-0.4654).

It is noteworthy that among the two patients with all the three-organ involvement, one patient had PPH, both the patients had FGR, both the patients had a normal vaginal delivery and but unfortunately both the patients died due to multi-organ failure following prolonged ICU admission. This is a significant finding suggestive of adverse impact of multi-organ involvement on maternal morbidity and mortality (p value<0.0001). Although only one patient out of the two having multi-organ involvement had baby with low birth weight and thus no other significant perinatal outcome was noted among these patients.

## Conclusion

The findings underscore the significant impact of organ involvement in preeclampsia. Renal, hepatic, and pulmonary dysfunctions were closely associated with adverse maternal and perinatal outcomes. Multi-organ dysfunction notably increased risks of severe complications, emphasizing the importance of early detection and targeted interventions.

This study highlights the critical role of organ-specific involvement in determining outcomes in preeclampsia. Addressing dysfunctions through vigilant monitoring and timely interventions can significantly improve maternal and neonatal health outcomes, reducing the morbidity and mortality associated with this condition.

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Conflict of interest: None

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Original Article: Gynaecology

# Vaginal Removal of Fibroid Polyp – A Safe and Successful Procedure

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**ABSTRACT**

**Introduction:** Menstrual irregularity is a common symptom for attendance at gynaecology clinic particularly in the late reproductive years. A reasonable percentage of patients found to have fibroid after clinical examination and subsequently confirmed by ultrasonography investigations. Many of them undergo hysterectomy as the definitive procedure.

**Aims:** To evaluate the outcome of vaginal removal of fibroid polyp over a period of 15 years at a tertiary care semi urban private hospital.

**Methods:** Analysis of prospectively collected data of eleven cases with diagnosis of fibroid polyp was done. Two patients were excluded because of a decision for abdominal hysterectomy (one for patient preference and other additional fibroids in the uterus). In nine patients an attempt for vaginal removal of fibroid polyp under general anaesthesia was performed.

**Results:** All patients are parous and all had previous vaginal deliveries. The age range was 38 – 48 years (average – 42.7 years). Vaginal removal of fibroid was successful in eight patients. There were no immediate complications. Histological diagnosis of leiomyoma was confirmed in all cases (100%). Total abdominal hysterectomy was performed in one patient because of uncontrolled haemorrhage at the time operation. This patient required two units of blood transfusion. No subsequent hysterectomy was required in the follow up period (six months to three years).

**Conclusions:** Vaginal removal of fibroid polyp is safe, simple yet definitive procedure in well selected cases of patients with abnormal uterine bleeding. Additionally, this procedure is minimally invasive, less costly and some can be discharged after twenty-four hours.

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## Introduction

Menstrual abnormalities, either heavy periods or heavy and irregular periods are common symptoms for attendance at the gynaecology clinic particularly in the late reproductive years. Some of these patients found to have uterine fibroids after clinical examination and subsequently confirmed by ultrasonography investigations.

Fibroids affect women mainly during their reproductive years. These are diagnosed in up to 70% of white women and more than 80% of women of African origin during their lifetime 1. Many of women with fibroids remain asymptomatic throughout their life and usually diagnosed incidentally.

Fibroid polyp protruding through the external os is not very uncommon. However, moderate to large size of such polyp may pose diagnostic and therapeutic dilemma. Removal of polyps vaginally can be challenging and majority of them undergo hysterectomy as the definitive procedure.

## Aims:

To evaluate the outcome of vaginal removal of fibroid polyp over a period of 15 years at a tertiary care semi urban private hospital.

## Materials and Methods:

Analysis of prospectively collected data of eleven cases with diagnosis of moderate size fibroid polyp protruding through cervical external os was done. Two patients were excluded from this study because of a decision for abdominal hysterectomy (one for patient preference and other with several additional fibroids in the uterus). In nine patients an attempt for vaginal myomectomy under general anaesthesia were performed (Fig 1). In all cases, preoperative discussion was done with the patients and their relatives. Possibility of hysterectomy during attempted vaginal removal were explained. Appropriate informed consent was taken. Two units of packed red blood cell were kept as reserve. Anaesthetist and other operation theatre staff were informed about the possibility of conversion to hysterectomy. All cases were performed under spinal anaesthesia. The case which needed hysterectomy was converted to general anaesthesia. Initially examination under anaesthesia was performed.

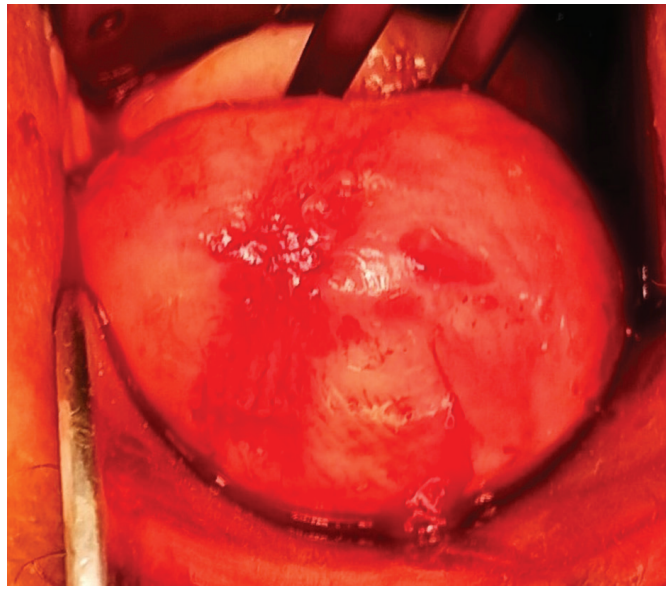

Fig 1. Examination under anaesthesia of one of the cases

In first three cases, a knot was placed on the pedicle with number '1' vicryl and then diathermy was used. Last six cases diathermy of the pedicle was done using laparoscopic Maryland forceps and diathermized part was cut by laparoscopic scissors (Fig 2). All cases received Co-amoxiclav as antibiotics and diclofenac as analgesics.

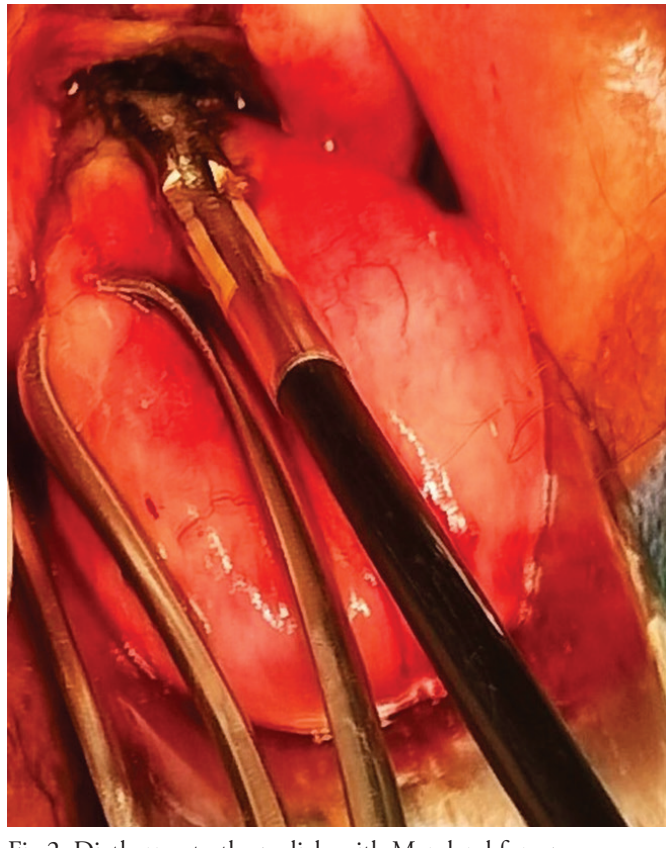

Fig 2. Diathermy to the pedicle with Maryland forceps

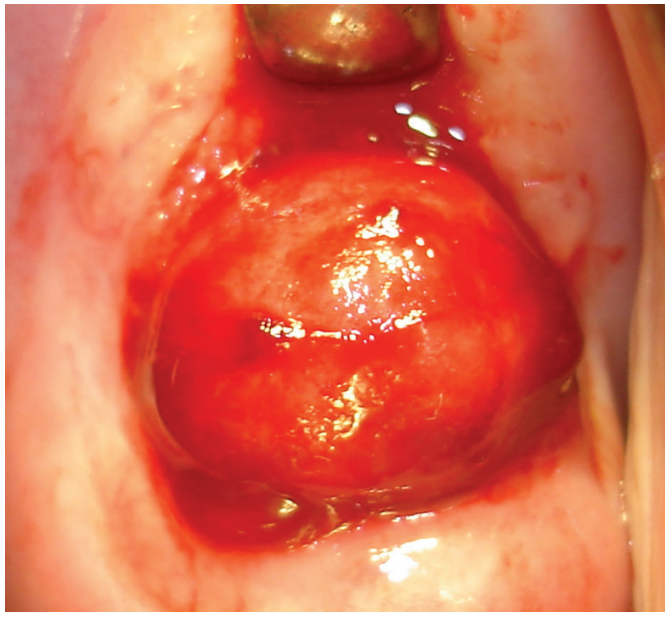

Fig 3. Examination under anaesthesia of another case

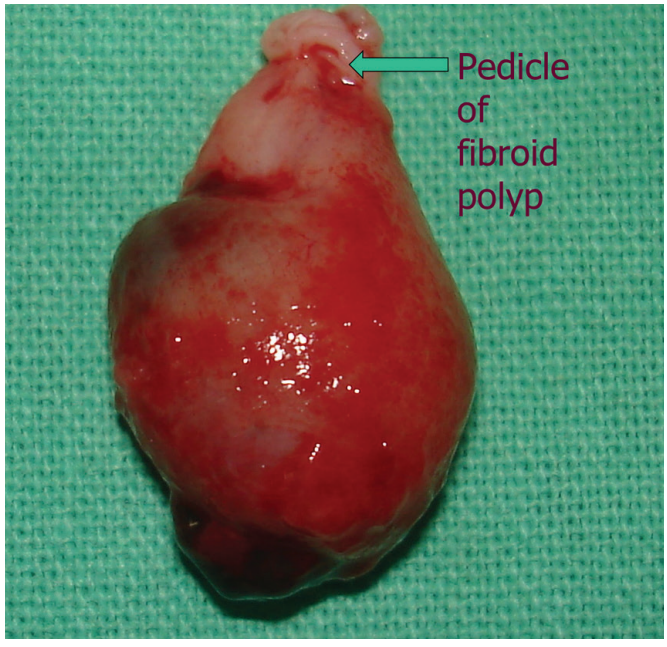


Figure 4. Specimen after removal of second case

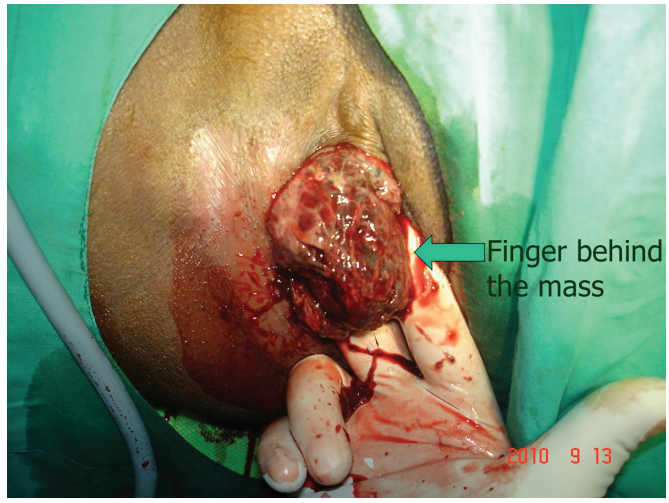


Figure 5. Fibroid polyp with degeneration

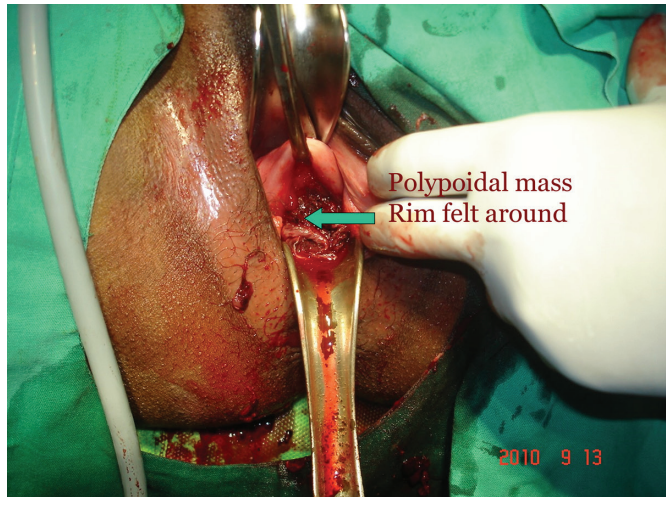


Fig 6. Rim felt around the mass (case above)

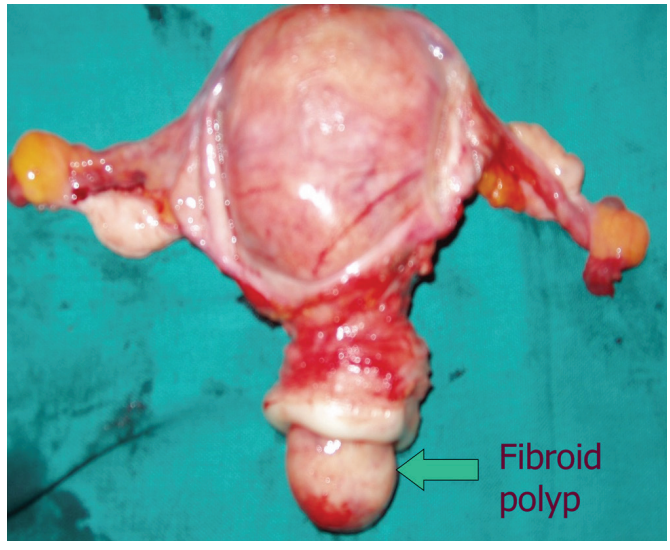


Figure 7. The hysterectomy specimen showing fibroid polyp coming out through external Os (The case in which hysterectomy done on patient's choice)

## Results:

All nine patients are parous and all had previous vaginal deliveries. The age range was 38 – 48 years (average – 42.7 years). Vaginal removal of fibroid was successful in eight patients. There were no immediate operative complications Post operative recovery was uneventful. These eight patients were discharged on first post operative day. Histological diagnosis of leiomyoma was confirmed in all cases (100%). Total abdominal hysterectomy was performed in one patient because of uncontrolled haemorrhage at the time operation. This patient required two units of packed red blood cell transfusion. No subsequent hysterectomy was required in other cases in the follow up period of six months to three years.

## Discussion:

In a retrospective observational study of larger number cases, Golan A et al observed procedure successful in 95.6% cases. However, the main difference is in their histology only 73.9% was confirmed as leiomyoma and rest were endometrial polyps 2; whereas in our study all cases are fibroid polyps.

The strength of the study is this study was performed in the same unit and performed under the supervision of a single consultant which ensured similar techniques and all cases had their follow up. The weakness of this study is small number of cases, variable time of follow up, possible subsequent surgery at other places and need for further medical treatment especially tranexamic acid for control of heavy periods.

## Conclusion:

Vaginal removal of fibroid polyp protruding through external os is safe, simple yet definitive procedure in well selected cases of patients with abnormal uterine bleeding. Additionally, this procedure is minimally invasive, less costly. Majority of the patients can be discharged after twenty-four hours.

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Case Report: Obstetrics

# PAS : In an Undiagnosed Case of Emergency Caesarean Section in Primigravida

**Ranjana Bhandari**

**ABSTRACT**

Placenta Accreta Spectrum is a state where placental tissue is abnormally invaded into uterine wall below the Nitabuch's layer. PAS (placenta accreta spectrum) has become very common these days due to raised rate of caesarean sections. In ultrasonographically prediagnosed cases, management of case can be defined but in undiagnosed cases i.e., if found during emergency caesarean section, it becomes very difficult to manage it, more so in situations where blood transfusion, skilled gynaecologists & anaesthetist, other depts doctors, SNCU etc not available.

## Introduction

PAS is the second most common cause of obstetrical haemorrhage ie. 25-30 % following uterine atony. The incidence of PAS is about 0.35 % after one CS but raised to 6.75 % after four CS[1]. PAS contributed to 30 % to maternal mortality in undiagnosed cases and the mortality increases if associated with placenta previa[2]. There are many risk factors contributing to PAS like previous uterine surgeries like caesarean, myomectomy, D&C, placenta previa, age >35 yrs, smoking, multiple pregnancies[3] etc.

## Diagnosis :

PAS is categorised by FIGO classification as placenta accreta, increta & percreta depending upon invasion of trophoblastic tissue into myometrium and beyond. It can be diagnosed with ultrasonography (gray scale = absence of hypoechoic retroplacental layer, large intraplacental lacunae, myometrial thickness < 1 mm etc. In color doppler these lacunae show turbulent blood flow. The anterior placenta may be associated with bridging vessels towards U.bladder[4]. MRI is helpful in posterior placenta previa.

## Main Body of Case Report:

This was a case of 37 yrs old, elderly primigravida, conceived after 8 yrs of marriage. She came to DHH Baripada, Mayurbhanj, Odisha at 5 PM on 12/12/24 for safe confinement at term. She had left her ultrasonography reports at home. Her blood profile was sent for investigation and USG form was given. At 9 PM she came to labour room with a severe bout of bleeding PV and labour pains. Her pulse, BP, temperature, respiratory rate was normal. Per abdomen examination showed cephalic presentation with mild contractions. FHS was 120 /min. P/V examination showed 3 cm dilated os with high up head and bleeding. Soft structure could be felt near os. She was advised a pint of blood transfusion and immediate caesarean section. LSCS was done under SA. On opening the uterus transversely, placenta was seen in lower segment. It was cut through, to deliver

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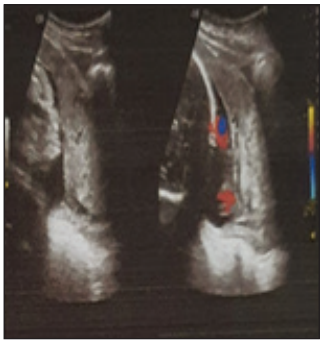
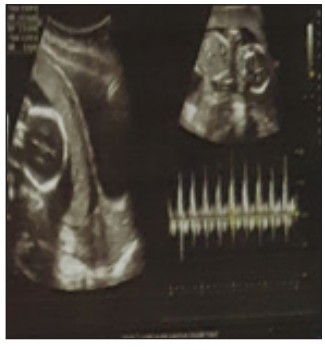
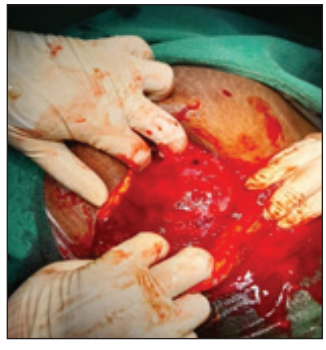
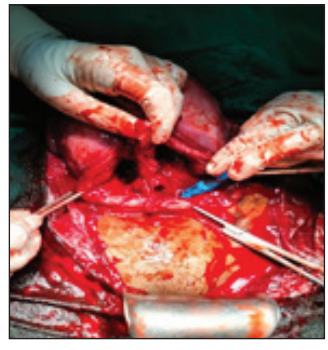
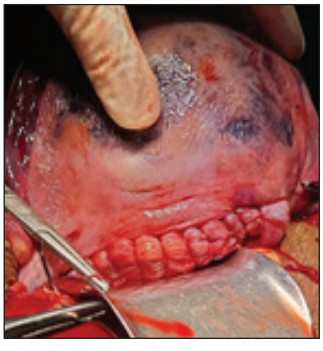
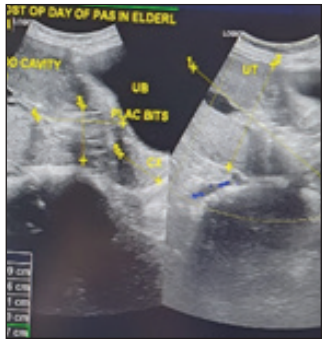
the 2780 gms baby, at 10.28 PM. Baby cried after 30 seconds of resuscitation. The upper part of placenta could be removed easily but 5x4 cm near cervical os was morbidly adherent. But it was not bleeding much. It was tied in base with chromic catgut no 1 and left in uterine cavity. Steps of devascularisation performed. Patient was given all postoperative advises along with a repeat USG scan before hospital discharge. Her postoperative period was satisfactory. Later on, her relatives got the ultrasonography report which revealed anterior low-lying placenta at 34 wks gestation. Her postoperative USG report on 5th day showed normal involuting uterus with placental tissue near internal os measuring 4x5 cm without vascularity. So patient was discharged with all warnings and follow up after 6wks.

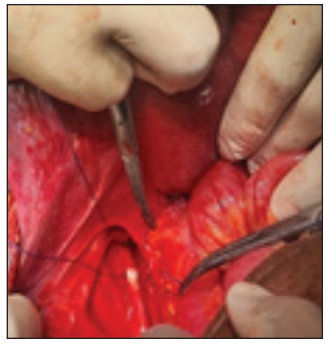
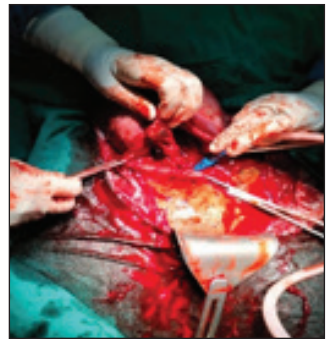
## Discussion :

PAS is emerging as one of the most serious obstetric condition causing a significant maternal and foetal morbidity and mortality, so its management has to be judicious. In prediagnosed cases of PAS, there should be comprehensive multidisciplinary team approach with frequent antenatal check-ups. Correction of co-morbidities like anaemia etc. After antenatal corticosteroid, magnesium sulphate for neuroprotection, delivery is to be done in 35-36 wks gestation at tertiary hospital with adequate blood transfusion[5] and skilled doctors of various dept. Best standard approach to PAS is caesarean hysterectomy with placenta in situ. But if patient wants future fertility or in absence of skilled doctors in the facility, conservative surgeries can be undertaken[6]. Some conservative surgeries are= leaving placenta in situ followed by inj methotrexate and follow-up scans along with beta Hcg, to find out complete resorption of placenta. Focal PAS (involving < 50% uterine surface) can be managed with removal of healthy myometrium along with placenta followed with suturing the myometrial base. Cho square stitch can be given on surface if bleeding doesn't stop. Tripple-P procedure is done in three steps. Firstly do placental localisation by TAS USG so as the deliver baby above the superior border of placenta. In the second step do devascularisation steps. Thirdly placental nonseparation with large myometrial excision and reconstruction of uterine wall. But there are some post conservative surgeries complications like uncontrolled haemorrhage leading to delayed or secondary hysterectomy, sepsis, urologic problems etc

## Conclusion:

PAS is a very high risk condition and if encountered during undiagnosed emergency caesarean section in small periphery hospital or without preparation in higher stations, the best strategy is to deliver the baby, clamp the cord then close the uterus with placenta in situ and transfer the pregnant women to the higher center for judicious management or wait for delayed hysterectomy.

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Case Report: Gynaecology

# A Rare Case of Primary Umbilical Endometriosis

**Dipika Mondal[1], Shireen Islam[2], Swarnali Das[3], Ramprasad Dey[4]**

**ABSTRACT**

Umbilical endometriosis or villar's nodule without ongoing pelvic endometriosis is uncommon. Incidence goes up to 0.5 -1.2% of all patients with endometriosis. Only 232 cases of umbilical endometriosis have been reported worldwide. The primitive location of this nodule at the umbilical level is rare. Its etiopathogenesis remains unclear.

A 39 years aged, P2+0,with previous 2 vaginal deliveries with no prior history of any surgery and not a known case of pelvic endometriosis, presented with complaining of redness and bleeding from an umbilical nodule for last two years. These symptoms were cyclical, flared up during mensuration and were not relieved by medication. O/E, a 2-3cm small multinodular reddish brown pigmented mass was seen at the umbilicus. On ultrasonography, she was diagnosed with umbilical endometriosis. MRI was done to assess the depth of invasion. Wide excision of umbilical lesion was performed. HPE showed endometrial glands and stroma, confirming the diagnosis of umbilical endometriosis. Diagnosis is challenging and relies on clinical suspicion, imaging studies, and histopathological confirmation after surgical excision.

## Introduction

Primary umbilical endometriosis (PUE) is an uncommon and often overlooked condition where endometrial tissue is found at the umbilicus, outside the usual sites such as the uterine cavity or ovaries. This rare form of endometriosis was first described 1in 1911, and fewer than 232 cases have been reported since then. PUE typically affects women of reproductive age, although cases in postmenopausal women have also been documented, often in those undergoing hormone replacement therapy.

The presentation of PUE is often marked by a well-circumscribed, painful nodule or mass at the umbilicus, which may become tender, enlarge, or even bleed in conjunction with the patient's menstrual cycle. This cyclicity of symptoms is a hallmark2 feature that can help differentiate it from other umbilical masses. However, due to the rarity of the condition and its clinical similarity to other benign umbilical lesions, such as infections, hernias, or sebaceous cysts, diagnosis is frequently delayed.

The case: A 38-year-old woman, P 2+0 with previous vaginal deliveries, presented with a complaint of a painful nodule at her umbilicus. She described the nodule as becoming more noticeable and tender with occasional mild bleeding from the mass during menstruation. The nodule was gradually enlarging over the past 8 months, but it was not associated with fever,

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discharge, or skin changes over the umbilical area. The patient did not have any significant abdominal pain, weight loss, or gastrointestinal symptoms. She had no history of any abdominal trauma or recent infections.

She experienced menses regularly in the past year. There was no significant history of pelvic pain or dysmenorrhoea. Past medical history was insignificant. No history of pelvic surgeries, gynaecological conditions, or abdominal surgeries. On examination, there was a multinodular, reddish-brown mass at the umbilicus without any visible discharge.

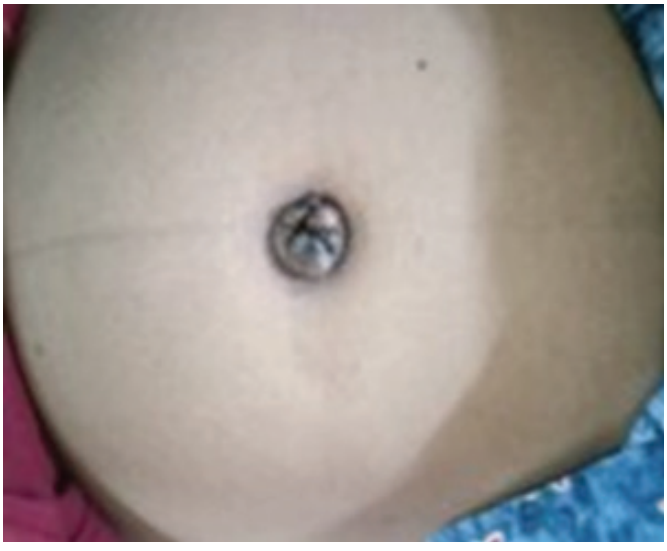

Fig: 1 [umbilical endometriosis]

On palpation, a firm, tender, irregular mass, approximately 2.5 cm in diameter was palpated at the umbilicus. The mass was mobile, non-pulsatile, and did not seem to be attached to deeper structures. No signs of abdominal hernias or other masses were noted during the abdominal examination. Gynaecological examination revealed a normal-sized uterus without palpable adnexal masses. No tenderness was noted during a bimanual pelvic examination.

Ultrasound Abdomen and Pelvis: A superficial, well-circumscribed hypoechoic lesion was identified at the umbilicus, consistent with a soft tissue mass. No abnormalities were found in the pelvic organs or in the abdominal cavity.

MRI Abdomen: Confirmed the presence of a 2.5 cm lesion at the umbilicus with characteristic features of endometrial tissue, showing well-defined borders and no evidence of malignancy. Uterus and adnexal structures within normal limits. No signs of any bladder/bowel endometriotic deposit.

Initially, medical management was done with dienogest 2mg OD for three months but no improvement with medical treatment. She was counselled regarding further treatment options of primary umbilical endometriosis. She opted for surgical treatment, wide local excision. During the surgical procedure, typical powder burnt deposits seen at the umbilicus, suggestive of endometriotic deposits. HPE showed endometrial glands and stroma in 10x and 40x power field, confirming the diagnosis of umbilical endometriosis.

A follow-up visit was scheduled 3 weeks post-surgery, during which the wound had healed completely with no signs of infection or recurrence. The patient was advised to monitor for any further symptoms or changes in the area. She was followed again 6 months postoperatively, with no recurrence of the umbilical mass or symptoms.

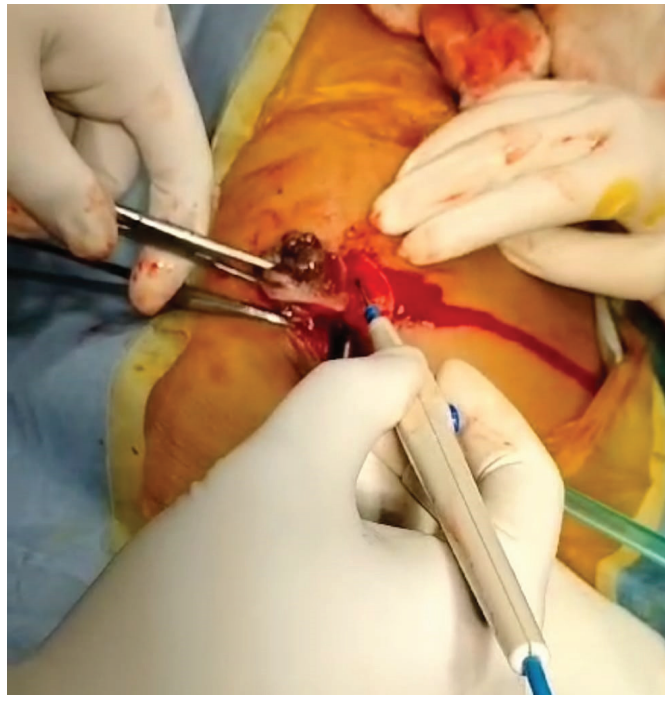

Fig: 2[excision of umbilical endometriosis]

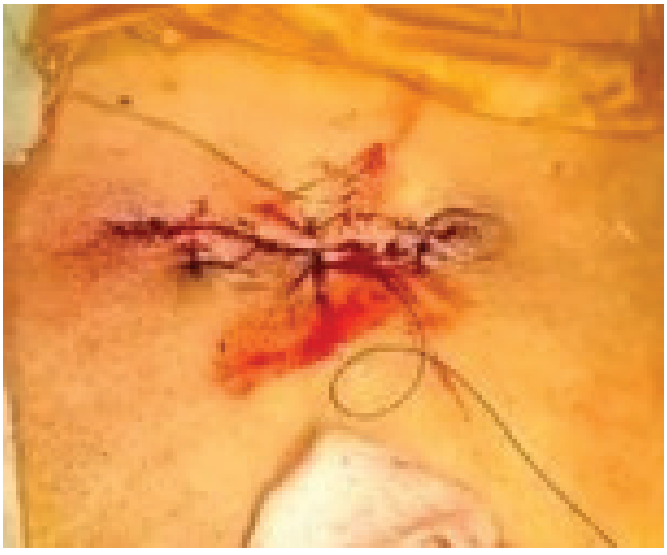

Fig: 3[skin closure after removal of lesion]

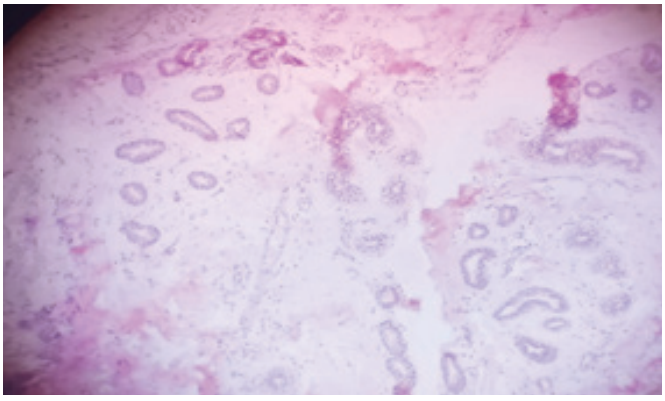

Fig: 4[endometrial gland & stroma under 10x]

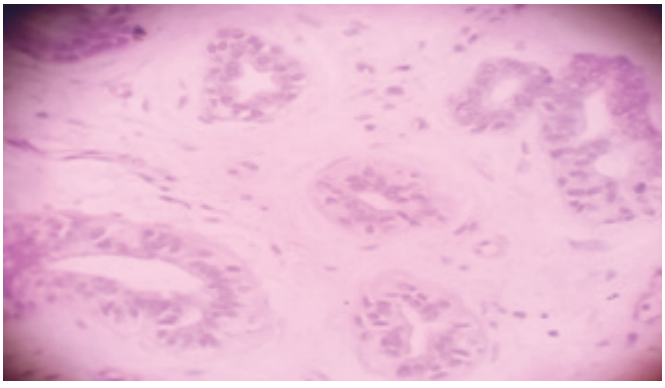

Fig 5[Endometrial gland & stroma under 40x]

## Discussion:

Primary umbilical endometriosis is a rare disease, but the secondary variety occurs naturally in patients with pelvic endometriosis. It may originate from implantation of regurgitated endometrial cells, circulated by the clockwise peritoneal circulation up to the right hemidiaphragm, and then, progressive funneling towards the umbilicus by the falciform ligament and ligamentum teres of the liver 3 but, it still remains unclear. Another hypothesis states that distant lesions are established by the hematogenous and lymphogenous spread of endometrial cells, popularly known as the Halban's theory4. In our patient, there was a gradual transformation of the normal umbilicus into several small, pigmented, firm, painful nodules which concomitantly bleeds during mensuration. In this context, this multinodular form may be an exceptional observation in some cases.

Most patients experience a good outcome following surgical excision, with complete resolution of symptoms, namely, pain and cyclic swelling at the umbilicus. The prognosis is generally excellent, with a low risk of recurrence if the lesion is completely excised with clear margins. Further follow-up is recommended based on any signs of recurrence, particularly if the lesion was large or deep.

## Conclusion:

Surgical excision is the cornerstone of treatment for primary umbilical endometriosis. A careful, well-planned surgical approach ensures complete removal of the ectopic endometrial tissue, minimizes the risk of recurrence, and offers good cosmetic results. With appropriate management, the prognosis is generally favourable, and most patients experience complete resolution of symptoms following surgery.

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Please submit a cover letter to the Editor-in-Chief mentioning the following:

- Each author's name, address, and email address.
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- The name of the author who is to deal with correspondence and proofs.

Once submitted, manuscripts undergo initial screening by the editorial staff and editors and then papers will undergo peer review.

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(3) that neither this manuscript nor one with substantially similar content by the authors has been published elsewhere or is being considered for publication elsewhere;

(4) that the manuscript has been submitted with the full knowledge and approval of the institutions or organizations given as the affiliation(s) of the author(s);

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In line with ICMJE standards, the criteria for authorship are as follows:

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(3) Final approval of the version to be published; AND

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**Clinical trials**

Submission of clinical trials must include reference to ethics approval (or explanation of why ethics approval was not received). Authors must consult the CONSORT statement and checklist and submit a CONSORT flow chart as an editable figure in Word/PowerPoi ntformat.

The clinical trial registration is preferable and information should be included at the end of the abstract of the submitted manuscript.

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Reviews based on the recent and relevant subjects of clinical interest should be considered.

**4. LAYOUT OF MANUSCRIPTS**

Manuscript text should be in English (US spelling), double-spaced, font size 12, in Arialmmes New Roman font.

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The first page of the manuscript should contain the following: (1) title; (2) full names of authors (6 maximum, although listing more authors may be considered on an individual basis if authorship requirements have been met and a request has been included in the cover letter); (3) affiliations of authors (i.e. department, section or unit of

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A structured abstract not exceeding 200 words is required for all full-length clinical articles. It should contain all and only the following headings: Objective; Methods; Results; and Conclusion.

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In full-length articles, subject matter should be organized under the following headings, with no subheadings: Introduction; Materials and methods; Results; Discussion; Acknowl edgments; Conflicts of interest; and References.

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The main text of clinical articles should not exceed 2500 words, excluding the first-page information, abstract (no more than 200 words), author contributions, acknowledgments, Conflicts of interest, references (no more than 15), figure legends, and tables and figures. Please include the word count in the cover letter and on the first page of the manuscript.

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Power calculations, statistics, and reporting of numbers.

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Where appropriate (e.g. for clinical trials), power calculations should be performed as part of the study design, and a statement providing the power of the study should be included in the Materials and Methods. Authors should state how the power calculation was determined, including what type of difference the calculation was powered to detect and on what studies the numbers are based.

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The statistical tests used and the significance level set should be listed in the methods for all studies that employed statistical analysis. Information regarding the statistical software programs used should be included in the methods: for example, "SPSS version 20 (IBM, Armonk, NY, USA)." This information should not be included in the reference list.

P values should be provided where calculated. The largest P value that should be expressed is P>0.99. The smallest P value that should be expressed is P<0.001.

For measures of effect (e.g. relative risks, risk ratios, odds ratios), authors should also report confidence intervals (e.g. 95%) so that the precision of the effect estimate can be assessed.

**5. Ethics approval and informed consent**

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**Journal article**

[1] Vellacott ID, Cooke EJ, James CE. Nausea and vomiting in early pregnancy. Int J Gynecol Obstet. 1988;27:57-59.

**Book**

[2] Speroff L, Glass BH, Kase NG. Clinical Gynecologic Endocrinology and Infertility. Baltimore: Williams and Wilkins; 1982.

**Chapter in a book**

[3] Disaia PJ, Creasman WT. Invasive Cancer of the Vulva. In: Disaia PJ, Creasman WT, eds. Clinical Gynecologic Oncology. St Louis: C.V. Mosby; 1984:214-219.

**Web reference**

[4] World Health Organization. WHO Recommended Surveillance Standards, Second Edition [WHO website). 1999. http://www.who.int/csr/resources/publications/surveillance/whocdscsrisr992.pdf.

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