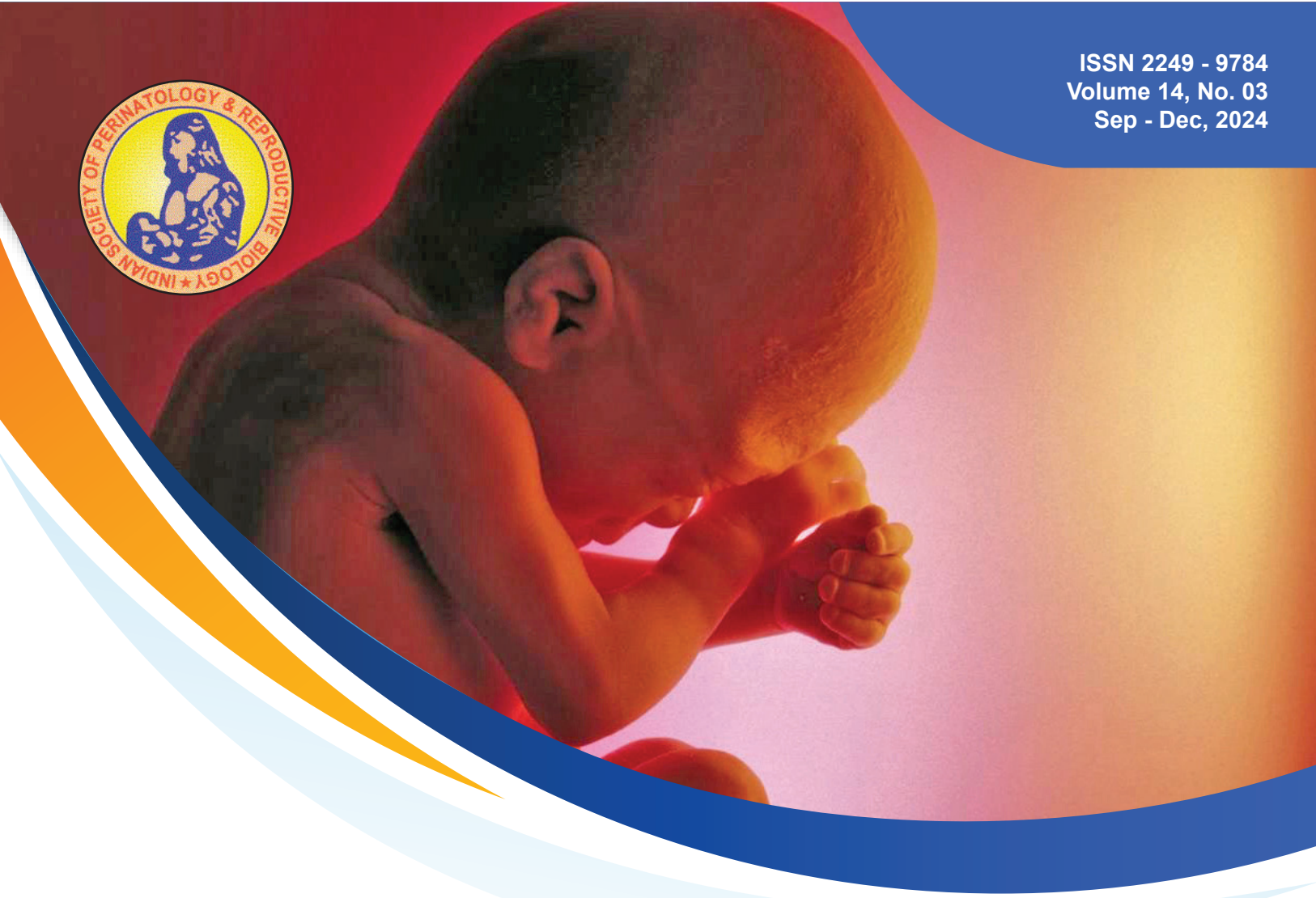
ISSN 2249 - 9784
Volume 14, No. 03
Sep - Dec, 2024



IJOPARB

Indian Journal of Perinatology and Reproductive Biology

Official Journal of Indian Society of Perinatology and Reproductive Biology

IJOPARB

Indian Journal of Perinatology and Reproductive Biology

Vol. 14 | No. 03 | September – December, 2024 | ISSN 2249-9784

www.ijoparb.co.in

Official Journal of
INDIAN SOCIETY OF PERINATOLOGY AND REPRODUCTIVE BIOLOGY (ISOPARB)

Indian Society of Perinatology and Reproductive Biology

Estd. 1978

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ISSN 2249-9784 RNI No. WB ENG/2010/39056

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Contents

Review Article

Fluid Management in Pregnancy and Caesarean Section

Prof (Dr) Ramprasad Dey[1], Prof (Dr) Bibek Mohan Rakshit[1]

Introduction

Fluid management is one of the cornerstones of patient care, particularly during pregnancy & Caesarean Section. Management of the volume state is vital for maintaining adequate cardiac output, blood pressure and oxygen delivery, with maintenance of tissue bed and organ perfusion. In any critical illness this is vital, but in pregnancy particularly so as to preserve uteroplacental flow and placental perfusion. Unlike many other tissue beds, the uteroplacental circulation autoregulates poorly, leaving it reliant on maternal cardiac output, blood pressure and metabolic homeostasis in order to function correctly and avoid fetal compromise. In addition, the pregnant woman undergoes a number of physiological adaptations in pregnancy that impact upon fluid management, including an increase in the circulating volume and a reduction in systemic vascular resistance.

Fluid resuscitation is a key component of patient care, especially in scenarios such as caesarean section, haemorrhage and sepsis[1]. However, injudicious or aggressive fluid therapy and volume overload have been associated with harm in a number of settings including precipitation of pulmonary edema in pregnant women. The complicated obstetric patient may have a number of additional factors that make fluid management more challenging. Amongst other problems, cardiac, pulmonary or renal disease (pre-existing or acquired during pregnancy), sepsis, haemorrhage and hypertensive disorders of pregnancy all pose management dilemmas regarding the administration and optimization of fluid therapy.

Physiological changes in pregnancy that impact fluid management: Normal pregnancy is associated with a number of physiological changes that may impact on fluid management. Pathophysiological changes in the pregnant population need to interpreted in light of the expected physiological alterations. Accurate assessment may be extremely challenging in the setting of acute deterioration superimposed upon complex or chronic maternal illness. In pregnancy, cardiovascular system increases cardiac output, heart rate, circulating volume but decrease systemic vascular resistance[2]. In renal function increase glomerular filtration rate but decrease creatinine. In haematology here is dilutional anaemia.

Which fluid in Pregnancy? Whilst evidence is scarce, in the critically ill pregnant patient, isotonic crystalloids represent a safe initial choice in a wide variety of maternal conditions[3]. Other synthetic colloids and starches have some significant risks associated with anaphylaxis, excess kidney injury and increased mortality and should be avoided in critical ill pregnant women. Cochrane review did not find a difference between crystalloids and colloids in preventing hypotension during caesarean section, rather less adverse effect in crystalloids. Fluid therapy in obstetric haemorrhage, generally isotonic crystalloids are used as first-line fluid resuscitation until appropriate blood and blood products become available.

Pre & Per operative fluid management: Hypotension is the most significant adverse effect in women

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undergoing spinal anaesthesia for caesarean delivery, affecting on average 70% of pregnant women. The administration of intravenous fluids (i.e., crystalloids and colloids) prior to and/or during anaesthesia represents one of the most common strategies to prevent maternal hypotension. Among the intravenous fluids, crystalloid solutions are the most frequently used, with normal saline (NS) and Ringer's lactate (RL) as the most common choices[4]. Colloids are frequently used nowadays for several reasons. Preloading with crystalloids alone have shown poor effectiveness in decreasing hypotension. While crystalloids co-loading is considered superior, variable effectiveness were reported. Systematic reviews and meta-analyses indicate that preloading or co-loading with colloids—specifically hydroxyethyl starches (HES)—is superior to crystalloids alone, with volumes larger than 500 mL offering no significant additional benefits. Current practice advocate combining colloids and crystalloids solutions rather than colloids along.

Post operative fluid management & Care

1. Shift to Post operative care unit (PACU) at least 6 hrs if not 12 hrs
2. IV fluids – 100ml per hour, Ringer lactate/ Normal saline for 6-12 hours
3. Analgesic – inj paracetamol 1000mg 1v infusion 6 hourly (Diclofenac suppository 100mg 12 hrly or 75mg 12 hrly im, better to be avoided)
4. inj ondansetron 4mg & ing pantoprazole 40 mg
5. Start oral fluid by 6 -12 hrs

Complications of Fluid Therapy

Fluid therapy may be harmful if the incorrect fluids are given, if fluids are given in inadequate amounts, or if too much fluid is administered[4]. Correct timing of fluid resuscitation is also vital to maximize benefit and minimize harm.

Inappropriate fluid type: Colloids may be associated with anaphylaxis, whilst starches have been associated with excess renal Failure and mortality in ICU populations and should be avoided[5,6]. The tissue accumulation of hydroxyethyl starches is widespread and rapid, and may be harmful. Although starches have been used safely to prevent hypotension during caesarean section, any effects on the fetus from prolonged exposure in utero are unknown. Excess crystalloid fluid administration in women with postpartum haemorrhage may result in worsening anaemia, shock and coagulopathy. Use of hypotonic (or less commonly hypertonic) fluids may lead to severe dysnatremias and other electrolyte abnormalities, with resultant potentially catastrophic neurological complications[2]. Excessive administration of chloride-rich fluids may lead to a normal anion gap metabolic acidosis.

Inadequate fluid volume: Fluid resuscitation is an integral part of the treatment of a variety of complex and critical illnesses. In particular, sepsis, trauma and haemorrhage require early, balanced and focused fluid resuscitation in the early stages. There is still debate about optimal strategies in the non-pregnant population, and little to no evidence in the maternity group, but lack of fluid resuscitation is associated with poorer outcomes.

Excessive fluid volume: Normal pregnancy is marked by an increase in the maternal circulating volume. Both pre-existing and superimposed conditions such as cardiac disease and renal dysfunction may exacerbate this, and hypertensive disorders of pregnancy may be associated with significant edema and varying degrees of volume state disturbance[5,6]. Pre-eclamptic women are also at considerably increased risk of developing pulmonary edema, which has been associated with increased maternal mortality.

Specific Scenarios

The hypertensive disorders of pregnancy are a unique group of disorders that are, along with obstetric haemorrhage & sepsis leading causes of maternal morbidity & mortality.

Hypertensive disorders of pregnancy: The multisystem nature of these disorders can make fluid therapy challenging, and there have been conflicting findings and views over time about the circulation and volume state in these women, as well as how best to manage them. Injudicious fluid management has been implicated as a contributor to maternal death. Intravascular volume state is contracted in pre-eclampsia and severe pre-eclampsia is associated with maternal cardiovascular changes, including altered maternal left ventricular (LV) morphology. Left ventricular systolic function may be impaired, but often the development of LV hypertrophy and reduced LV relaxation occurs, resulting in primarily diastolic

dysfunction[7]. This, combined with capillary leak, abnormal lung permeability and severe hypertension contributes to the increased risk of pulmonary edema.

Practice points regarding fluid management in hypertensive disorders of pregnancy[6,7]: Multisystem disorder with multiple organ systems affected. Preservation of uteroplacental flow is vital in the antepartum period. Intravenous fluid may worsen hypertension (and its sequelae). Maternal circulatory dynamics are altered. There may be significant maternal cardiac effects. These women are very prone to volume overload and pulmonary edema. Renal failure may be prominent, exacerbating volume overload and hypertension. Minimizing intravenous fluid volumes is recommended.

Obstetric haemorrhage: Obstetric haemorrhage is one the leading causes of maternal mortality worldwide. Management should focus on stopping the bleeding, replacing circulating volume, and avoiding/ameliorating the consequences of massive haemorrhage, including coagulopathy, acidosis, hypothermia and end organ dysfunction. There are a variety of guidelines discussing fluid management and blood product administration in obstetric haemorrhage. A recent international consensus statement (incorporating FIGO) suggests initial restrictive resuscitation with crystalloid solutions, using 1–2 ml per ml of blood loss. Continuous resuscitation with crystalloid solutions at the expense of blood product replacement should be avoided as worsening oxygen delivery and dilutional coagulopathy will result. The ideal blood component ratio and fluid regime in massive obstetric haemorrhage is still under investigation and requires further research,

Fluid and Blood & Blood Products Mangement

- Infuse till blood & blood products available
- Infuse up to 3.5 L of warmed Clear fluids
  - 2 L of isotonic crystalloid (Hartman's solution)
  - 1.5 L of isotonic colloid (succinylated Gelatine)
- Blood transfusion ASAP (Best of cross matched)
  - If immediately needed- Group O Rh D Negative K negative PRBC
  - Switch to group specific PRBC as soon as possible
- FFP:
  - If PT/ APTT prolonged & haemorrhage continuing – 12-15 ml / kg of FFP (eg: 1000 ml need for 70 kg that means 4 units 250 ml each)
  - If haemorrhage continues after transfusion of 4 units PRBC & coagulation tests are unavailable – transfuse 4 units of FFP
- Platelet Concentrates:
  - If platelet count <75×10^9/ L & haemorrhage continues- transfuse 1 pool of platelets (5 Donors) RDP or SDP
- Cryoprecipitate:
  - If fibrinogen< 2 g/ L & haemorrhage continues - transfuse 2 pools of cryoprecipitate (10 units)

Sepsis: Initial fluid resuscitation in sepsis is vital to restore circulating volume and prevent sepsis induced end organ dysfunction. secondary to hypoperfusion 7. However, in different healthcare settings and different patient populations the expected benefit has not always been observed. Generally pregnant women can be managed in a similar fashion to non-pregnant women, although caution needs to be applied to avoid iatrogenic fluid overload in the setting of pre-existing volume expansion.

Practice points regarding fluid management in sepsis: An initial fluid bolus should be administered promptly to restore circulating volume and cardiac output/blood pressure. An isotonic crystalloid is recommended as first line. Initial bolus should be approximately 20 ml/kg up to a suggested maximum of 2 L. Depending on the situation and environment, a second bolus may be indicated but strong consideration should be given to early vasopressor support. Excessive fluid administration and ongoing positive fluid balances may be harmful.

Recommendations for best clinical practice5,6

1. Hypotension following spinal or combined spinal epidural anaesthesia at caesarean section causes both maternal and fetal/neonatal adverse effects.
2. Hypotension is frequent and, therefore, vasopressors should be used routinely and preferably prophylactically.
3. α-agonist drugs are the most appropriate agents to treat or prevent hypotension following spinal anaesthesia. Although those with a small amount

of b-agonist activity may have the best profile (noradrenaline (norepinephrine), metaraminol), phenylephrine is currently recommended due to the amount of supporting data.

4. Left lateral uterine displacement and intravenous (i.v.) colloid pre-loading or crystalloid coloading, should be used in addition to vasopressors.
5. The aim should be to maintain systolic arterial pressure (SAP) at ≥ 90% of an accurate baseline obtained before spinal anaesthesia, and avoid a decrease to < 80% baseline.
6. Maternal heart rates can be used as a surrogate for cardiac output if the latter is not being monitored; both tachycardia and bradycardia should be avoided.
7. Women with pre-eclampsia develop less hypotension after spinal anaesthesia than healthy women. Abrupt decreases in blood pressure are undesirable because of the potential for decreased uteroplacental blood flow.
8. Women with cardiac disease should be assessed on an individual basis; some conditions are best managed with phenylephrine (an arterial constrictor without positive inotropic effect), whereas others respond best to ephedrine (producing positive inotropic and chronotropic effect).

Conclusion

Fluid therapy is a critical aspect in pregnancy and perioperative care in Caesarean section. This review articles provides recommendations from various guidelines for fluid therapy to ensure optimal patient outcomes in pregnancy and delivery. It is essential to individualize fluid therapy based on patient's clinical status, laboratory values, and urine output.

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Original Article: Obstetrics

Placenta Accreta Spectrum: Trends in Diagnosis and its Outcome with Limited Resources

Meena Samant[1], Ritu Singh[1], Pooja Shinde[1,2], Jayoti Malhotra,[1] Poonam Lal,[1] Zarin Rahman[1]

ABSTRACT

Introduction: Placenta accreta spectrum (PAS) is a nightmare for every obstetrician as there is torrential bleeding during delivery. It is due to disorder of placentation caused by damage to the interface of inner and middle layer (endometrial–myometrial) of the uterus.

Objective: There are many centres in India, in which advanced services like Magnetic resonance imaging (MRI), uterine artery embolization (UAE) for diagnosis and management are not accessible. So, we have conducted this study in the resource limited setting to see the risk factors associated, trends in its diagnosis and its outcome.

Method: The cross-sectional study was conducted from January to December 2020 in limited resource private hospital located in eastern India. A predesigned and pretested questionnaire was used to record history, which included women demographic details, risk factors, ultrasound findings, intra- and post-operative events were recorded. Also, whether PAS was diagnosed pre operative on USG or intraoperatively. The outcome measure was patient morbidity or mortality. We have used part of Severe maternal morbidity (SMM) list of US Centers for Disease control and prevention, list of surgical morbidity given by Matsuzaki et al.

Result: Of the 4125 total deliveries, 17 patients had PAS, i.e., the prevalence was 0.41%. Placenta previa was present in 15 (88.23%) of patients. There are 15 (88.23%) patients with previous caesarean section and 9 (52.94%) with previous history of dilatation and evacuation (D&E). USG was not conclusive in any of the case. Caesarean hysterectomy had been done in 13 (76.47%) patients, in other 4 patients there was focal placenta accreta which was left in situ and haemostatic suture taken. 88.23% women need transfusion. 35.29% had bladder injuries.88.23% women needed ICU care

Conclusion: There is high incidence of PAS in previous caesarean with placenta previa and ultrasound is not conclusive in its diagnosis. So, high index of suspicion and proper arrangement is necessary in every placenta previa with previous caesarean section. Conservative approach is feasible with focal excision, haemostatic sutures but when it is a major degree, early recourse to hysterectomy is essential.

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Introduction

Placenta accreta spectrum (PAS) is a nightmare for every obstetrician as there is torrential bleeding during delivery. It is due to disorder of placentation caused by damage to the interface of inner and middle layer (endometrial–myometrial) of the uterus[1] either due to previous Caesarean scar, previous dilatation and evacuation, ART procedure. That leads to abnormal decidualization and abnormal anchoring of villus and trophoblast, deeply invading the myometrium. So, there will be no plane of cleavage for placenta separation.

PAS encompasses whole spectrum of disorder, abnormal adherent placenta (placenta accreta) and abnormally invasive placenta (including placenta increta and placenta percreta). In the placenta accreta, placenta is attached directly to the middle layer of the uterine wall (myometrium) without invading it, so there is no obvious plane of cleavage. In Placenta increta, invasion is into the myometrium and in percreta into surrounding pelvic tissues, vessels and organs. FIGO defines theses as Grades 1,2 and 3, respectively[2].

PAS incidence has shown its elevation as 1 in 2510 before 1994, 1 in 533 in 2002, 4 in 1000 in 2003 to 272 women in 2016[3,4]. A recent study in 2021 also reported that in PAS there is increase in maternal morbidity and maternal mortality by 18-fold and 30% respectively[5].

Now a days, there are many advanced techniques that have come for diagnosis and management of PAS like Magnetic resonance imaging (MRI), uterine artery embolization (UAE). But there are many centres in India, in which these services are not accessible. So, we have conducted this study in the resource limited setting to see the risk factors associated, trends in its diagnosis and its outcome.

Material and Method

The cross-sectional study was conducted from January to December 2020 in limited resource private hospital located in eastern India. After ethical clearance, a predesigned and pretested questionnaire was used to record history, which included women demographic details, whether women were admitted in an emergency or from an outpatient department, and what were there presenting complaints. Other than that, risk factors present for PAS or not, that is previous history of Dilatation & evacuation (D&E), number of previous Lower segment caesarean section (LSCS), previous uterine surgery, placenta previa, history of Invitro fertilization (IVF).

Other than history ultrasound findings, intra- and post-operative events were recorded. Also, whether PAS was diagnosed pre operative on USG or intraoperatively. MRI or UAE were not available for the management at the time of study. Placenta was not left in situ for delayed hysterectomy as it was not part of our protocol.

The outcome measure was patient morbidity or mortality. We have used Severe maternal morbidity (SMM) list of US Centers for Disease control and prevention [CDC 2019] for maternal morbidity[6]. The list has 21 components, of which we included blood transfusion, hysterectomy, shock, Disseminated intravascular coagulation (DIC). In surgical morbidities given by Matsuzaki et al we have included Urinary track injury, Intensive care unit (ICU) Admission[7]. We have also taken length of stay in the hospital, postoperative hospital stay.

Inclusion Criteria- Diagnosed case of PAS either intraoperatively or postoperatively at any weeks of gestation.

Exclusion Criteria- Women who have not given consent, Obstetrics Hysterectomies for cause other than PAS

Statistical analysis was done using Jamovi 2.3.28 solid version software. Qualitative variables were expressed as number and percentage whereas quantity variable was expressed as mean and standard deviation.

Result

Of the 4125 total deliveries, 17 patients had PAS, i.e., the prevalence was 0.41%. Almost half of the patient (52.94 %) admitted for vaginal bleeding. (Table 1) In patients who were admitted with no complaints, one was for oligohydramnios, other was Rhesus (Rh) Negative with severe anaemia for blood transfusion and other five was at term gestation for safe confinement.

Table 1: Demographic characteristics, Presenting complaints

Parameter	Cases (N=17) N %
Age (years) (mean ± SD)	32.4±5.48
Occupation	
Housewife Employed	15(88.23%) 2(11.76%)
Education	
Illiterate Matriculation and below Higher Secondary Graduation	2 (11.76%) 7 (41.17%) 4 (23.52%) 4 (23.52%)
Religion	
Hindu Muslim	13 (76.47%) 4 (23.52%)
Gravidity % (n)	
1 2 3 4 or more	1(5.9%) 2(11.76%) 8 (47.05%) 6 (35.29%)
Period of gestation at admission	
14-28 Weeks 28 +1 -34 weeks 34+1 - 37 weeks >37 weeks Postpartum Post-abortal	0 (0%) 8 (47.05%) 7 (41.17%) 2 (11.76%) 0 (0 %) 0 (0 %)
Admission From	
Outpatient department (OPD) Casualty	4 (23.52%) 13 (76.47%)
Booked /Un booked	
Booked Unbooked Referred	9 (52.94%) 7 (41.17%) 1 (5.89%)
Presenting complaints	
Vaginal bleeding Leaking Per vaginum No Complaint/ Safe	9 (52.94%) 1 (5.89%) 7 (41.17%)

Talking about risk factors, out of total 17, 15 (88.23%) were previous caesarean section in which 7 were previous 2 caesarean. 9 (52.94%) had history of previous dilation and curettage. (Table 2) Placenta previa was present in all patients except 2, of which one was a diamniotic dichorionic twin and others had anterior placenta. IVF twin was present in 2 (11.76%). Only one had pre-op ultrasound diagnosis of PAS, rest all diagnosed intraoperatively during caesarean section. MRI was not done in any of the patients, as it is not accessible to the patients.

Table 2: Risk factor and Diagnosis of PAS

Risk Factor	
Previous Dilatation and curettage Previous Cesarean section/hysterotomies Previous Uterine surgery Placenta Previa Invitro fertilization - twin	9 (52.94%) 15 (88.23%) 0 (0%) 15 (88.23%) 2 (11.76%)
PAS (diagnosed before surgery)	
Yes No	1 (5.89%) 16 (0.94%)

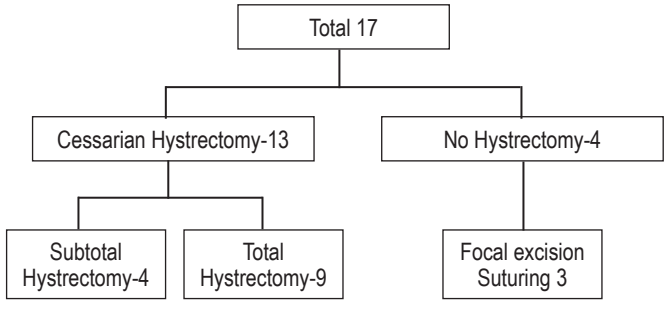
As these cases where not diagnosed preoperative, we have used Pfannenstiel incision in abdominal incision and Lower segment uterine incision in all uterine incisions. There were 10 emergency caesarean section.

Talking about outcome measures, we don't have any mortality. Morbidity factors have been listed in (Table 3) (figure 1). In hospital stay, patients mostly get admitted for duration between 4–14 days. The one patient that stayed for > 28 days that is 37 days is mainly preoperative admitted at 28 weeks then emergency LSCS was done for bleeding at 32+ 5 days had bladder injury. Bladder injury had increased hospital stays, but PAS itself is a risk factor for antepartum haemorrhage that increases duration of hospital stays. There was no patient of DIC in our study.

Table 3: Maternal morbidities

Parameter (N=17)	Yes	No
Blood transfusion	15 (88.23%)	2 (11.76%)
Shock	10 (58.82%)	7 (41.17%)
Cesarean Hysterectomy	13 (76.47%)	4 (23.52%)
Urinary track injury - Bladder	6 (35.29%)	11 (64.70%)
Intensive care unit Admission	15 (88.23%)	2 (11.76%)
Disseminated intravascular coagulation	0 (0)	17 (100%)
Duration of Surgery	Number of patients	
< 1 hour	2	
1-2 hours	10	
> 2 hours	5	

Figure 1: Outcome of PAS patients in term of hysterectomy



Disscusion

Placenta accreta spectrum prevalence was 0.41%, similar to other studies that reported 0.01–1.1%[2], 0.12% (range 0.036 –0.36)[8].

Risk Factors

Foremost risk factor in PAS is placenta previa with previous caesarean section[9]. In our study placenta previa was present in 15 (88.23%) of patients, which is similar to the studies which showed 86%[8] and also 90 % of PAS patient[10].

There are 15 (88.23%) patients with previous caesarean section and 9 (52.94%) with previous history of dilatation and evacuation (D&E). Other study also found 98.7% of patient of PAS have caesarean section and D&E as risk factor[8]. There is also documentation that, the risk of PAS increases with increase in number of prior caesarean deliveries, from 3% in previous one caesarean delivery to 11% in second and 40 % in previous 3 caesarean deliveries[9].

This is because of the uterine insult due to caesarean section, this is also true for insult due to myomectomy, dilation and evacuation operation for abortion. Disorder of endometrial scarring like Asherman's syndrome, prior endometrial ablation, invitro fertilization also counts in risk factors. There is also data that multifetal pregnancy is also a risk factor for PAS[11,12,13].

Diagnosis

According to recent study by Brett D et al., there are many flaws in the diagnosis of PAS, and they are not diagnosed till delivery[14]. If diagnosis is not made before hand, delivery can occur in hospital which doesn't have facilities that leads to poor consequences[15].

There are many biomarkers understudy[16], but they are not ready to use. MRI is a better alternative but it can't be used routinely because of its high price and restricted accessibility of competent person to diagnose PAS by MRI[14]. As a result, we have to consider risk factor assessment and ultrasound as a standard for PAS diagnosis. Despite that, if ultrasound is normal also it doesn't rule out PAS[17].

USG findings are also mostly subjective, and sensitivity is based on the competency of the radiologist. In our study, USG was not conclusive in any of the case. In other eastern Indian studies also USG was able to diagnose only 57% of women only[8]. In the literature, estimate of missed diagnosis is up to 50 %[18,19] In our study, only one patient was diagnosed as PAS, was also overdiagnosis in which placenta has come out completely.

Morbidity

According to evaluation by Leonard SA 2020, PAS leads to more endangering morbidity than situations that are contemplated for not continuing the pregnancy like chronic kidney disease, heart disease, pulmonary hypertension[20].

Talking about Hysterectomy, In our study, caesarean hysterectomy had been done in 13 (76.47%) patients, in other 4 patients there was focal placenta accreta which was left in situ and haemostatic suture taken. In a study by Crocetto et al. it showed that PAS is a primary cause of caesarean hysterectomy[21]. In United States also, caesarean hysterectomy has existed for a long period as standard treatment for PAS[22]. In a retrospective study by Kong et al. caesarean hysterectomy due to PAS has increased, 45 % to 73.3% from 2011 to 2014[23]. There is study[8] which showed that in focal placenta accreta, haemostatic sutures and balloon tamponade had prevented hysterectomy in 12 of their patients.

In Blood transfusion- According to study, in PAS, 50 % of delivery need transfusion[24]. In our study 88.23% women need transfusion, this can be explained by the fact that almost all Indian women are anaemic in pregnancy.

For ICU Admission- PAS patients commonly go to intensive care unit (ICU)[15,24]. In our study also 88.23% women needed ICU care.

In Urinary track injury- According to studies 5-30% of women suffers urinary track injury intraoperatively[15,30]. This is consistent with our study with 35.29% injuries.

Conclusion

There is high incidence of PAS in previous caesarean with placenta previa and ultrasound is not conclusive in its diagnosis. So, high index of suspicion and proper arrangement is necessary in every placenta previa with previous caesarean section. Conservative approach is feasible with focal excision, haemostatic sutures but when it is a major degree, early recourse to hysterectomy is essential. With the advanced techniques (UAE) we could have saved the uterus and further decreased the maternal morbidity

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Original Article: Obstetrics

Perinatal Depression Using the EPDS in Tertiary Maternity Centers in India

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ABSTRACT

Background: Perinatal depression (PND), a prevalent mood disorder among pregnant women and new mothers, exerts profound effects on mothers and impacts the development of their children. It significantly contributes to maternal and infant morbidity worldwide. Investigating the risk factors and prevalence of PND is essential for implementing effective interventions that can mitigate its adverse effects on maternal health.

Objectives: The primary objective of this study included reporting the incidence of depression among antenatal and postnatal women receiving obstetric care at a tertiary maternity hospital. Secondary objectives included identifying associated risk factors and outlining potential management strategies for PND.

Methods: A hospital-based cross-sectional design was used for the study. The total sample consisted of 174 women, including 95 in the antenatal period and 79 in the postnatal period, undergoing obstetric care at Cloudnine Hospitals, Bangalore, India. They were evaluated for PND using the Edinburgh Postpartum Depression Scale (EPDS). Descriptive statistics were employed to analyze the data.

Results: The median scores for depression on EPDS were 9 and 10 for the antenatal and postnatal groups, respectively, with a prevalence rate of 22%. Statistical analysis revealed no significant differences in depression incidence between the two groups ($p<0.55$). However, maternal age and previous mental health concerns emerged as significant risk factors for PND.

Conclusion: Despite previous indications of variance in depression incidence between antenatal and postnatal women, our findings show no significant differences between these two groups. Healthcare providers must prioritize the identification and management of PND to enhance outcomes for both mothers and children.

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1. Introduction

Pregnancy represents a notably vulnerable period in a woman's life. Alongside health concerns, such as gestational diabetes, hypertension, and anemia, mental health issues also present significant challenges.[1] Perinatal depression (PND) is a nonpsychotic depressive episode ranging from mild to severe that occurs during pregnancy and persists for up to 1 year after childbirth.[2] A systematic literature review revealed a mean global PND rate of 26.3%.[2] Globally, it is a significant contributor to maternal and infant morbidity,[3] necessitating careful monitoring of the mother due to the increased risk of suicidal behavior associated with it.[4] Suicidal ideation is a common aspect of screening for PND. Recent evidence suggests antenatal and postnatal depression have distinct causes and symptoms.[4] A systematic review identified personal mental illness history, stressful life events, poor social support, maternity blues, childcare stress, chronic health conditions, gestational diabetes mellitus, and sleep disturbances as key factors correlated with PND.[2]

The Diagnostic and Statistical Manual of Mental Disorders defines postpartum depression (PPD) as the occurrence of a major depressive episode between birth and 4 weeks after birth, often characterized by symptoms such as panic, irritability, and excessive crying. Such episodes may, however, commence or persist throughout the first year after delivery.[5] In India, approximately 22% of women experience PPD.[6,7] A systematic review found higher PPD prevalence in developing regions (19.99%) than in developed regions (14.85%).[8] If left untreated, PPD can lead to long-term adverse effects for both mother and infant.[9] A systematic review found antenatal depression prevalence in Indian women ranging from 3.8% to 65%.[10] A study from South India linked depression to low education, socioeconomic status, family conflicts, unplanned pregnancies, preference for male children, multiparity, and poor obstetric history.[11] Child developmental challenges, low infant birth weight, premature delivery, and birth complications also pose significant risks for depression.[3]

Women with antenatal depression face a higher risk of PPD. A study of 333 participants found that over 50% with antepartum depression later developed PPD.[12] Maternal depression during pregnancy is associated with preterm delivery and low birth weight babies.[13] It can lead to developmental delays, cognitive functioning deficits, and behavioral problems in the offspring.[3,14] Notably, family members generally had positive attitudes toward PPD, but stigma and misconceptions persisted. Culturally sensitive education is needed to address prejudices, with nurses playing a key role in awareness efforts.[15] Therefore, screening in antenatal care can predict mental distress, enhance treatment efficiency, and promote a healthier postpartum period.[16] PPD interventions include pharmacological, psychosocial, psychological, educational, and somatic therapies. Given the variety of options and extensive comparative research, evaluating their effectiveness and acceptability is crucial for clinicians and patients.[17]

The current study aimed to investigate the incidence of depression in postnatal and antenatal women. The study intended to identify potential differences in the prevalence and severity of depression symptoms between the two groups and to explore possible risk factors contributing to the development of depression during these periods. This research is crucial for early detection and providing intervention for managing PPD in order to enhance maternal and infant outcomes. Understanding these disparities can guide the development of tailored screening and intervention initiatives to support women's mental health throughout the perinatal period, thus improving overall care for pregnant and postpartum women.

2. Materials and Methods

2.1. Study design

This is a cross-sectional observational study conducted at Cloudnine Hospitals, Bangalore, India.

2.2. Study population

This study recruited 174 women receiving perinatal care at Cloudnine Hospitals, Bangalore, including 95 in the antenatal (third trimester) and 79 in the postnatal (up to 10 days postpartum) periods. Participants were aged 18–35 years, conceived either naturally or through *in vitro* fertilization, and delivered either vaginally or via lower-segment cesarean section. Exclusion criteria included unwilling participants and those from other hospitals.

2.3. Data collection

A structured questionnaire was utilized for data collection. Depression levels in these women were assessed using the Edinburgh Postpartum Depression Scale (EPDS); the EPDS scale, Stanford,[18] was used to examine the intensity of depressive symptoms. The EPDS, a leading screening tool for PPD, consists of ten multiple-choice questions scored from 0 to 3, with a total score range of 0–30; scores >12 indicate PND. Antenatal assessments included gestational age, family type, recovery, and medical history, while postnatal assessments covered delivery mode, breastfeeding, pregnancy experience, NICU admission, infant health, and maternal conditions. Data on pregnancy type, order, education, socioeconomic status, occupation, religion, marital/family conflict, mental preparedness, and past mental health were collected for both periods.

2.4. Procedure

Participants who provided informed consent and met the inclusion criteria were included in the study. Data were collected by requesting the participants to visit the Cloudnine Hospital in Bangalore and to fill out structured questionnaires. The study protocol was approved by the ethical committee, and informed consent was obtained from all patients before inclusion.

2.5. Data Analysis

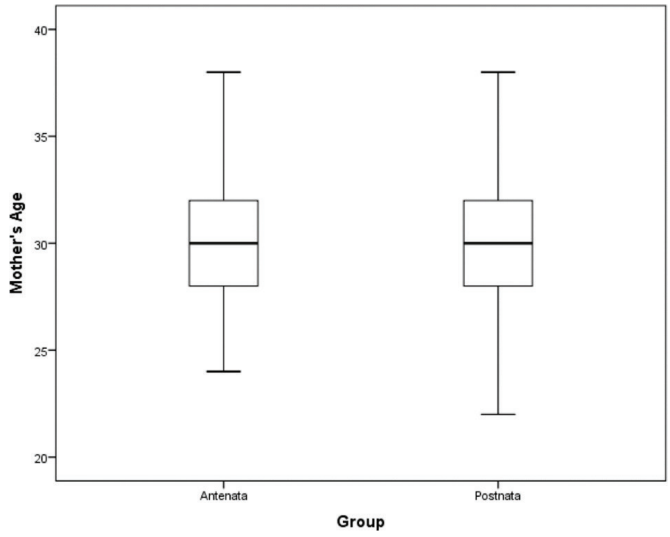
The collected data were entered into Microsoft Excel, a spreadsheet software, and analyzed using R software (version 4.0.2). Categorical variables are presented as counts and percentages and continuous variables as means with standard deviations. The Mann–Whitney U test was used to compare the medians of two groups, and a p value of <0.05 was considered statistically significant.

3. Results

3.1. Population Characteristics

A total of 174 patients were included in this study, which included 95 women in the antenatal period and 79 in the postnatal period. The mean ages of the mothers in the antenatal and postnatal groups were 29.4±2.99 and 30.4±3.04 years, respectively (Figure 1). The differences in mothers' ages between the two groups were not statistically significant. Supplementary Figure 1 represents the different demographic characteristics of the study population.

Figure 1: Box plot showing mean age (years) ± standard deviation of mothers in the antenatal and postnatal groups.



3.1.1. Antenatal Group

Data from the antenatal group revealed that 22% of the participants could be diagnosed as having major depressive disorder as per their scores on the EPDS questionnaire (Figure 2 [a]). The average age of mothers in this group was 30 years, with babies having an average gestational age of 27 weeks. Among them, 62 (77%) women reported a normal conception, and the average duration of marriage was 5 years, with 46 experiencing their first or second pregnancies. Furthermore, 43 women recovered at home after delivery, and 51 reported no delivery complications. At the time of data collection, 57 women were not engaged in paid employment. A majority of the women were identified as Hindu (44 women). Moreover, most reported no current marital conflicts (51 women) or family conflicts (54 women). A significant majority (62 women) felt mentally prepared for pregnancy and delivery, although a small portion (seven women) reported previous mental health concerns.

3.1.2. Postnatal period

In the postnatal group, 16% (13 women) of women met the criteria for major depressive disorder based on the EPDS scores (Figure 2[b]). The mean maternal age was 31 years, with all pregnancies full-term (38–40 weeks). At data collection, babies averaged 17 days postpartum, all 81 mothers had initiated

breastfeeding, and no NICU admissions were reported. Most women were moderately educated, with 64 unemployed. Marital (63) and family (60) conflicts were minimal; 62 women were mentally prepared for pregnancy and delivery, and only three had prior mental health concerns.

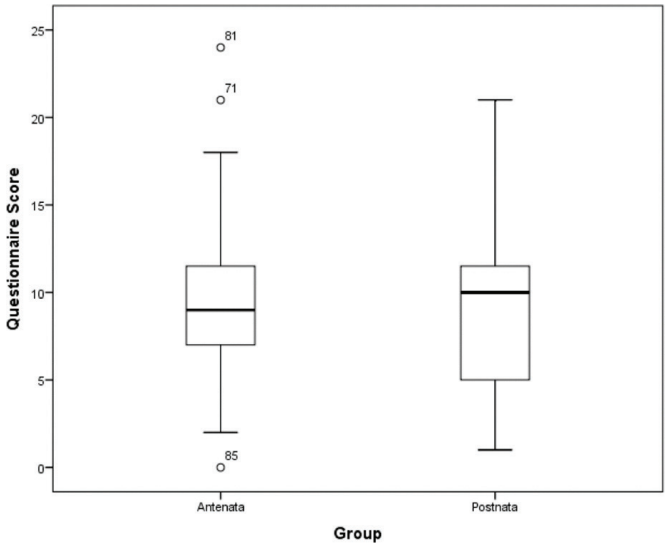
Figure 2: Percentage of women with major depressive syndrome. (A) Percentage of women with PPD in the antenatal period. (B) Percentage of women with PPD in the postnatal period.

PPD: Postpartum depression.

3.2. EPDS Scores

The median EPDS score was 9/30 for antenatal women and 10/30 for postnatal women (≥12 indicates potential antenatal depression). Depression score distributions were similar, ranging from 0 to 24 antenatally and from 1 to 21 postnatally (Figure 3), with no significant difference. The prevalence of PND was 22%.

Figure 3: Box plot showing the median Edinburgh Postnatal Depression Scale (EPDS) scores of the antenatal and postnatal groups.



Maternal age and prior mental health issues were significant predictors of antenatal depression. Depression was slightly higher postnatally (22.8%) than antenatally (21.8%). Younger mothers (29±2.99 years) had a higher risk of antenatal depression (n=39, p=0.035), as did those with prior mental health concerns (n=14, p=0.028). No significant links were found with socioeconomic status, marital status, conception type, family/marital conflicts, or mental readiness.

3.3. Association between the incidence of PPD and different factors

In an attempt to identify the risk factors linked with PPD, statistical analysis of the various key factors revealed the following:

3.3.1. Maternal Age: The age of the mother did not show a statistically significant association with the occurrence of PPD; however, in the antenatal period, a higher incidence rate of depression was seen in younger mothers than in older mothers (p=0.035).

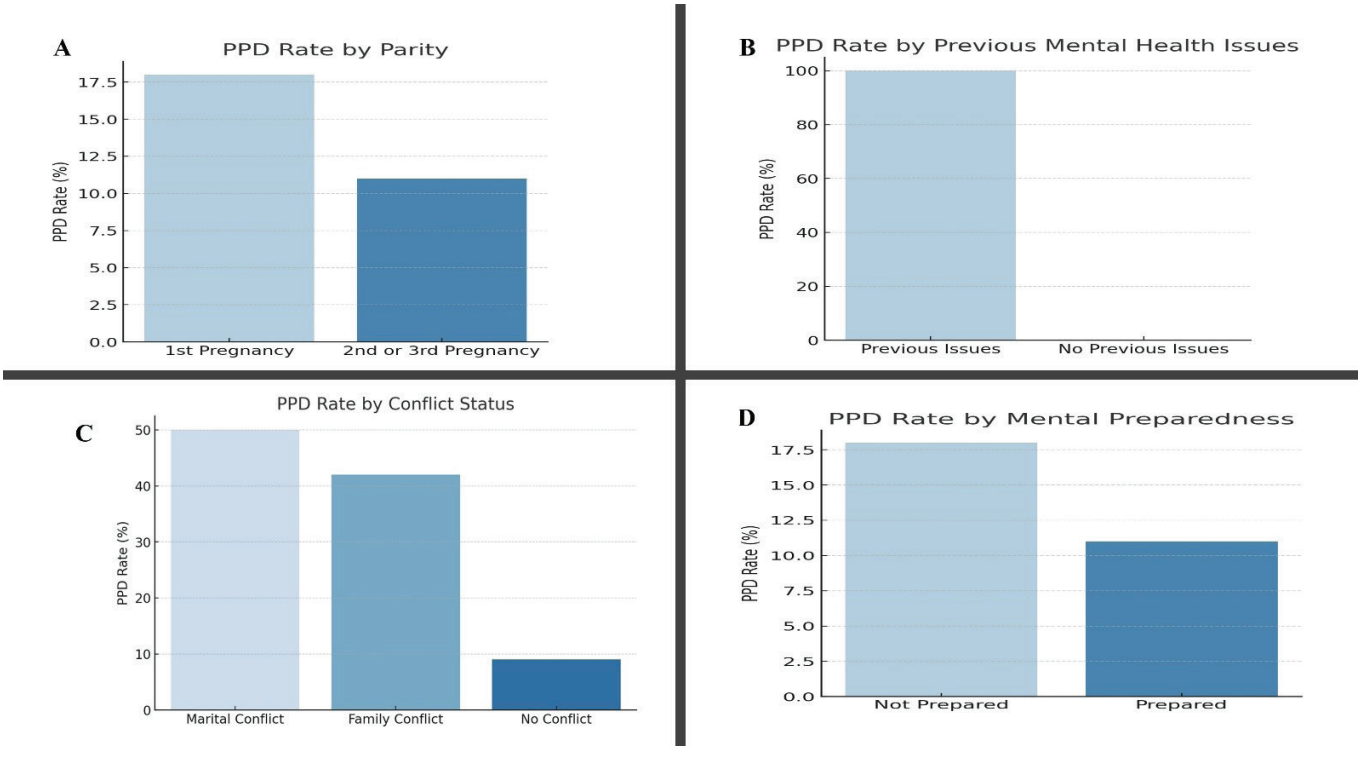
3.3.2. Religion: No significant association (p<0.197) was seen between the incidence of PPD in women belonging to different religions (Supplementary Figure 2[A]).

3.3.2. Education Level: There was no significant association (p<0.550) between the mothers' educational backgrounds and the occurrence of PPD. Women diagnosed with PPD belonged to various educational backgrounds, ranging from those who had received moderate levels of education to those who had pursued higher education (Supplementary Figure 2[B]).

3.3.3. Socioeconomic Status: No significant association (p<0.090) was seen between socioeconomic status and PPD. Women diagnosed with PPD hailed from diverse socioeconomic backgrounds, including middle and higher socioeconomic classes.

3.3.4. Birth Order: PPD incidence was higher in first-time mothers (18%) than in those with subsequent pregnancies (11%), though not statistically significant (p<0.540) (Figure 4[A]). This suggests greater susceptibility during first pregnancies due to physical, emotional, and lifestyle adjustments. Further research is needed to account for confounding factors like age, socioeconomic status, and mental health history.

Figure 4: Associations between the incidence of PPD and various factors, such as (A) parity; (B) previous mental health issues; (C) conflict status; and (D) mental preparedness for pregnancy and delivery.



3.3.5. Previous Mental Health Issues: A significantly positive association (p=0.028) was observed between a history of mental health issues and PPD. All the women who reported prior mental health concerns were diagnosed with PPD, highlighting a strong link between past mental health issues and the risk of PPD (Figure 4[B]).

3.3.6. Marital/Family Conflict: Marital and family conflicts demonstrated a moderately positive, though statistically nonsignificant (p<0.140) association with the incidence of PPD. Women experiencing such conflicts had a higher incidence of PPD than those without such conflicts (Figure 4[C]).

3.3.7. Mental Preparedness: The level of mental preparedness for pregnancy and delivery was moderately positively associated with PPD; however, this was statistically nonsignificant (p<0.32). Women who were not mentally prepared experienced a higher rate of PPD than those who were prepared, suggesting that mental preparation might potentially lower the risk (Figure 4[D]).

4.0. Discussion

This study explored depression in postnatal and antenatal women. The prevalence of depression was 22% in both groups, with no significant difference. Research highlights the need to clarify phenotypic heterogeneity in maternal depression for personalized pharmacological treatments. Variability may arise from symptom patterns, onset timing, chronicity, recurrence, and hormonal or genetic factors.[3] In this study, among the various risk factors examined, maternal age and previous mental health concerns were identified as statistically significant predictors of depression during both periods. The findings indicate a slightly higher prevalence of postnatal depression (22.8%) compared with antenatal depression (21.1%) among women experiencing PND; however, this difference was not statistically significant. Conversely, in a prospective cohort study, the heritability of depressive symptoms was found to be 16.2% for prenatal depression and 25.7% for postnatal depression.[19]

A comparable prevalence rate of PND (20.6%) was observed in a study conducted over 3 months on 170 randomly selected pregnant women in Mumbai, India. However, this study also found that the occurrence of PND was associated with the education level and socioeconomic status of these women.[11] In an observational study of 123 participants in Mumbai, India, the prevalence of PPD was 4.87% based on EPDS screening on postpartum days 3 and 14. In

contrast, a study conducted in Palestine involving 380 mothers (18–44 years) reported a higher PPD prevalence of 33.9%, with significant predictors including a stressful pregnancy, low social support, and husbands with lower education levels.[5]

The postpartum period is vital for both mother and infant, with maternal care essential for their physical, emotional, and psychological well-being.[20] In the current study, maternal age, religion, education, socioeconomic status, and breastfeeding showed no significant links to PPD. Prior mental health issues had a strong association, while marital/family conflicts and mental preparedness showed moderate links. Primigravid women had a significantly higher PPD incidence. A recent review from India has also shown similar risk factors for PPD, encompassing a history of psychiatric illness, stress, marital conflicts, pregnancy complications, and financial difficulties. Pregnant women with a history of depression should be evaluated to reduce the risk of PPD occurrence/recurrence.[21] Further, other reported risk factors for PPD in India include domestic violence, lack of spousal support, and the birth of a female baby.[22]

A recent study by Froeliger *et al.* (2024) that used multivariate analysis to investigate factors associated with PPD indicates that a history of psychiatric illness is associated with higher risks of developing PPD.[23] Furthermore, a longitudinal study of 615 women identified prior depression and stress as key risk factors for PPD from pregnancy to 5 years postpartum.[17] A hospital-based study in urban Pune found that 26.3% of 240 postnatal mothers had EPDS scores ≥13, indicating depression. PPD was significantly linked to social support, attention shift to the baby, and partner support, but not to sociodemographic factors.[6]

Maternal age emerged as a notable factor contributing to the onset of antenatal depression in our investigation. This aligns with the findings from a study in South India, which included 314 pregnant women undergoing prenatal checkups. The results indicated that 21.98% of the women suffered from possible depression, with a mean EPDS score of 10.61±7.48. Younger women faced a higher risk of depression than older ones. Maternal age and health issues during pregnancy were also significantly linked to antenatal depression.[24] However, a recent study by Froeliger *et al.* (2024) indicated that women <25 years of age or those of advanced age were at a higher risk of developing PPD.[23]

This study highlights key factors influencing PND. While maternal age and education exhibited no significant links to PPD, previous mental health issues and marital conflicts were strong predictors. Further research is needed to explore these interactions. Targeted interventions addressing modifiable risks may help reduce PPD and improve maternal well-being. Although this study provides valuable insights into PND in India, it has several limitations. The cross-sectional design of the study limits causal inferences about PND, highlighting the need for longitudinal studies to track risk progression. The sample, drawn from a specific healthcare setting, may restrict generalizability to broader populations in India. Reliance on self-reported measures introduces response bias. Incorporating clinical interviews could enhance validity.

Future research should include diverse, representative samples and explore protective factors and targeted interventions to reduce PND. Understanding its long-term impact on child development and maternal mental health can inform comprehensive care models for better maternal support.

5.0. Conclusion

This study highlights the prevalence of depression during the perinatal period, revealing no significant difference in the incidence of depression between antenatal and postnatal women. Considering this study was carried out incidentally during the COVID-19 pandemic, this is a significant finding. Maternal age and previous mental health concerns emerged as significant predictors of depression during both periods, emphasizing the importance of early identification and support for at-risk individuals. Understanding these risk factors can guide the development of tailored interventions to enhance maternal mental health and improve overall outcomes during pregnancy and the postpartum period. Given its widespread occurrence, depression warrants prioritization within national mental health initiatives. More robust research is imperative to gain a thorough understanding of the factors contributing to PND in India.

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Original Article : Obstetrics

The Impact of Anti-thyroid Peroxidase Antibodies on Maternal Outcome in Pregnancy with Subclinical Hypothyroidism

Kavleen Kaur Bindra[1], Shuchi Gupta[2]

ABSTRACT

Numerous studies worldwide have found inconsistent associations between subclinical hypothyroidism (SCH) in pregnancy and adverse obstetrical outcomes including miscarriage, fetal death, preterm delivery, gestational diabetes (GDM), hypertensive disorders of pregnancy (HDP), placental abruption. This study aimed to further evaluate and discuss on the outcomes of pregnancy with Anti-TPO antibodies in patients with proven subclinical hypothyroidism and whether supplementation with levothyroxine potentially reduces the adverse outcomes.

Patients with deranged TSH levels, normal free T4 levels, with either positive or negative Anti- TPO antibodies were recruited in this study and followed till delivery/ miscarriage. It was found that the median S. TSH values in 1st trimester in Anti-TPO positive women was 5.91μIU/ml while, in Anti- TPO negative women it was 4.87 μIU/ml. Out of 150 Anti- TPO positive pregnant women, 51 (34%) developed GDM and 8 (5.3%) developed HDP while out of 150 Anti- TPO negative pregnant women, 39 (26%) developed GDM and only 1 (0.7%) developed HDP. Amongst Anti- TPO positive mothers, 7 (4.7%) had missed abortion in first trimester, 13 (8.7%) had RPL and 14 (9.3%) had threatened abortion, while none of these complications were observed in the Anti- TPO negative mothers.

Thus, timely diagnosis and adequate supplementation can reduce the associated maternal and fetal morbidity and improve the pregnancy outcomes even in women with thyroid autoimmunity.

Introduction

Thyroid hormones T4 and T3 affect almost every metabolic process of the body. Pregnancy is considered to be a physiologically altered state of metabolism as the body tries to cater to the needs of the growing fetus. The requirement of iodine increases in pregnancy, as demand for synthesis of excess thyroid hormones is there during pregnancy. This is because of fetal dependency on maternal thyroid hormones till 12 weeks of gestation as fetal thyroid tissue is not matured enough to produce adequate amount of hormones for the growing fetus. Hence, the gland becomes over stimulated and hyperactive to secrete more T4 and T3 to meet the increased

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demand. Human Chorionic Gonadotropin (hcg) is known to have a Thyroid stimulating hormone (TSH) simulating effect and hence attributes to raise the thyroid hormone synthesis to meet the increased demand via its thyrotrophic effect.[1] Therefore, dietary iodine deficiency or intake of excess goitrogens in diet can be the major cause of overt and subclinical hypothyroidism in pregnancy.

Overt hypothyroidism is an increase in serum TSH (more than 10 mIU/L) as a result of decrease thyroxine and negative feedback, while subclinical hypothyroidism is serum TSH level in the range of 4-10 mIU/L with normal thyroxine (T4) levels.

Apart from this, autoimmune basis of overt and sub clinical hypothyroidism is also equally important in pregnant women. Data shows presence of antibodies like anti thyroperoxidase antibody (anti TPO antibody) and anti-thyroglobulin antibody (anti Tg antibody) in pregnancy is associated with increased prevalence of overt and sub clinical hypothyroidism and aggravation of the symptoms associated with it.[1]

On a worldwide scale, numerous studies with variable methodological quality have found inconsistent associations between subclinical hypothyroidism (SCH) in pregnancy and adverse obstetrical outcomes including miscarriage, fetal death, preterm delivery, gestational diabetes (GDM), hypertensive disorders of pregnancy (HDP) and placental abruption.[2] This study aims to further evaluate and discuss on the outcomes of pregnancy with positive Anti-TPO antibodies in patients with proven subclinical hypothyroidism and whether supplementation with levothyroxine potentially reduces the adverse outcomes.

Material and Methods

Study Area: Department of Obstetrics and Gynecology, The Fatima Hospital, Lucknow.

Ethical Approval: The research method was approved by Institutional Ethical Committee vide no. IEC/FH/22/0002 dated 15/07/2022

Study Population: Pregnant women attending OPD of The Fatima Hospital in the first trimester. Their thyroid function tests were done. Patients with deranged TSH levels, normal free T4 levels, with either positive or negative Anti- TPO antibodies after obtaining consent form were recruited in this study. Patients were followed up till delivery.

Study Design: Prospective observational study (Case control study)

Inclusion Criteria:

1. Mothers with a singleton pregnancy without any known previous thyroid disorder
2. Women with deranged thyroid function tests upto 13 weeks of gestation (1st trimester)

Exclusion Criteria:

1. Mothers with pregnancy in congenitally malformed uterus, fibroid uterus, known cervical incompetence
2. Previous history of any thyroid abnormalities
3. H/o any autoimmune diseases
4. Chronic hypertensive and diabetic patients
5. Subjects not willing to participate in the study
6. Subjects not coming for regular follow-up

Methodology For Data Collection: Total 300 pregnant women satisfying the above criteria were chosen for the above-mentioned study after taking written and informed consent. All the pregnant women selected experienced regular menstrual cycles and precisely recorded the dates of their last menstrual periods. If menstrual history and examination findings were not correlating, then ultrasonography was done to find the exact gestation period.

A proper detailed obstetric history including demographic characteristics and systemic examination was done. Women were evaluated for risk factors for adverse perinatal outcome and any associated underlying disorders.

Depending on the levels of TSH, free T4 and Anti-TPO antibodies, patients were supplemented with levothyroxine therapy and followed up with regular ante-natal check-ups and required biochemical and radiological tests. Tests were repeated at an interval of 4-6 weeks. Patients were followed up throughout the course of pregnancy for various associated maternal complications like HDP, GDM and pre-term labour. While conducting the study, the patient was informed of her condition and the risks associated, to enforce the drug compliance.

Regular follow up was done and confidentiality of the subjects maintained. Data for the study was recorded on Performa and shall be disclosed only to the ethics committee or appropriate authorities.

ATA Guidelines (2017) recommended establishing population-based trimester-specific reference ranges for serum thyroid-stimulating hormone (TSH) levels. In our study, we used the following criteria to supplement the patients with levothyroxine irrespective of their antibody status.

TRIMESTER	UPPER LIMIT OF TSH RANGE
1st trimester	2.5 mIU/L
2nd trimester	3 mIU/L
3rd trimester	3 mIU/L

The cut-off for Anti- TPO antibodies were:

>34 IU/L – POSITIVE

< 34 IU/ L- NEGATIVE

Results and Discussion

1) AGE GROUP

The age of the hypothyroid women studies varied from 20- 40 years. In the Anti- TPO positive group, 14 (9.3%) women were in age group 20-24 years, 62 (41.3%) in age group of 25- 29 years, 46 (30.7%) in age group of 30-34 years and 28 (18.7%) in age group of 35-40 years. In the Anti- TPO negative group, 15 (10%) women were in age group of 20- 24 years, 80 (53.3%) in age group of 25-29 years, 47 (31.3%) in age group of 30-34 years and 8 (5.3%) in age group of 35- 40 years.

2) PARITY

In women with Anti- TPO positive, 69 (46%) were primigravida and 81 (54%) were multigravida. In women with Anti- TPO negative, 89 (59.3%) were primigravida and 61 (40.7%) were multigravida.

3) 1ST TRIMESTER TSH VALUES

The median S. TSH values in 1st trimester in Anti-TPO positive women was 5.91μIU/ml while, in Anti- TPO negative women the median S. TSH was 4.87 μIU/ml. In a study done by Bhattacharyya et al[3], the mean serum TSH level was significantly ($p < 0.0001$) higher (2.31 vs. 1.73 μIU/ml) among TPO-Ab positive than negative mothers.

4) ASSOCIATED MEDICAL DISORDERS

Out of 150 Anti- TPO positive pregnant women, 51 (34%) developed GDM, 8 (5.3%) developed HDP and 13 (8.7%) developed IHCP.

Out of 150 Anti- TPO negative pregnant women, 39 (26%) developed GDM, 1 (0.7%) developed HDP and 19 (12.7%) developed IHCP.

There is documented evidence that shows thyroid hormones are required for the decidual angiogenesis, trophoblastic invasion and the placental hormones secretion. Therefore, improper placentation is associated with higher prevalence of pre- eclampsia and other hypertensive disorders in patients with thyroid dysfunction.[4] Similar results were reported in studies done by Saki F et al[5] in 2014 and Sitoris et al[6] in 2020.

5) MATERNAL COMPLICATIONS

Out of 150 Anti- TPO positive women, 7 (4.7%) had missed abortion in first trimester while out of 150 Anti- TPO negative women, none had this complication.

In the Anti- TPO positive group, 14 (9.3%) had threatened abortion. Pregnancy was continued on levothyroxine; dose adjusted every trimester. 13 (8.7%) had RPL.

9 (6%) Anti- TPO positive women developed PPROM while 3 (2%) Anti- TPO negative developed PPROM.

In Anti- TPO positive group, 19 (12.7%) had preterm labour. In Anti- TPO negative group only 1(0.7%) had this complication. The p value is <0.005 for the maternal which is statistically significant. The t value is 2.77.

Various studies done previously have found similar results. In the meta-analysis done by Shakila T et al[7] in, results showed that there was a tripling in the odds of miscarriage with the presence of thyroid autoantibodies. Raghunath et al[3] found similar results in their prospective study done. Also, Pradhan et al[8] reported higher incidence of threatened and spontaneous abortions in their study. James E Haddow et al[9] in their prospective study found that, women with elevated levels of thyroperoxidase, thyroglobulin antibodies, or both in the first trimester have a higher

rate of preterm delivery before 37 weeks of gestation than antibody negative women (7.5% compared with 6.4%, odds ratio [OR] 1.18; 95% confidence interval [CI] 0.95-1.46). Yan Han et al[10] in their prospective birth cohort study done in 2018 in iodine sufficient area of China, found that TPO-Ab positivity in the second trimester was associated with a 1.863-fold higher risk of premature birth (OR = 1.863, 95% CI 1.009, 3.441), after adjustment for potential confounding factors.

Summary

This study was done with an aim to determine the prevalence of subclinical hypothyroidism in pregnancy with positive Anti-TPO antibodies and study the course of pregnancy. Pregnancy course was evaluated in terms of any association with miscarriage, HDP, GDM, pre-term labour. This was a prospective observational study done over a period of 2 years on pregnant women attending our OPD. First trimester booking is the ideal time to screen for hypothyroidism, this was done by measuring FT4, TSH and subsequently Anti- TPO. The patients were supplemented with levothyroxine depending on the S. TSH levels and thereafter, measured at 6 weeks interval for necessary dose adjustments. ATA guidelines were followed for the trimester specific S.TSH values. All the mothers were followed till delivery/ miscarriage in both anti-TPO negative and positive and the adverse outcome was recorded.

It was found that the median S. TSH values in 1st trimester in Anti-TPO positive women is 5.91μIU/ml while, in Anti- TPO negative women the median S. TSH is 4.87 μIU/ml. Out of 150 Anti- TPO positive pregnant women, 51 (34%) developed GDM and 8 (5.3%) developed HDP while out of 150 Anti- TPO negative pregnant women, 39 (26%) developed GDM and only 1 (0.7%) developed HDP. In our study, out of 150 Anti- TPO positive mothers, 7 (4.7%) had missed abortion in first trimester, 13 (8.7%) had RPL and 14 (9.3%) had threatened abortion, while none of these complications were observed in the Anti-TPO negative mothers. Amongst 150 Anti- TPO positive women, 19 (12.7%) had preterm labour and 9 (6%) developed PPROM while amongst Anti- TPO negative women only 1 (0.7%) had preterm labour while 3 (2%) developed PPROM.

Conclusion

Thyroid autoimmunity is an important etiology for the development of hypothyroidism in pregnancy and is associated with adverse maternal and fetal outcome. First trimester is the ideal time for screening for hypothyroidism however, every woman should be screened for it whenever she first visits a doctor, irrespective of her gestational age. Anti- TPO screening must be offered to women with a history of recurrent miscarriages and preterm labour to start levothyroxine supplementation at an earlier gestational age. Similarly, woman with other pregnancy associated disorders like hypertensive disorders of pregnancy and gestational diabetes mellitus must also be screened for this.

Woman who are at a high risk or have been identified to have positive titers for antibodies must be educated about their adverse effects and encouraged to ask relevant questions so as to improve the medication adherence.

Timely diagnosis and adequate supplementation can reduce the associated maternal and fetal morbidity and improve the pregnancy outcomes even in women with thyroid autoimmunity

Acknowledgement: The funding for the above study was provided by The Fatima Hospital, Lucknow.

Conflict of Interest: There is no conflict of interest in the study.

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Table 1: Tabular representation of age of enrolled women

ANTI TPO	Positive		Negative	
Age (years)	Number	%	Number	%
20-24	14	9.3%	15	10.0%
25-29	62	41.3%	80	53.3%
30-34	46	30.7%	47	31.3%
35-40	28	18.7%	8	5.3%
Total	150	100.0%	150	100.0%

Table 2: Statistical analysis of age of women in each group

Statistics	Age	
	Positive	Negative
Number	150	150
Mean	29.92	28.58
Median	29	28
SD	4.13	3.61

Table 3: Tabular representation of parity of enrolled women

ANTI TPO	Positive		Negative	
Parity	Number	%	Number	%
Primigravida	69	46.0%	89	59.3%
Multigravida	81	54.0%	61	40.7%
Total	150	100.0%	150	100.0%

Table 4: Tabular representation of TSH values of enrolled women

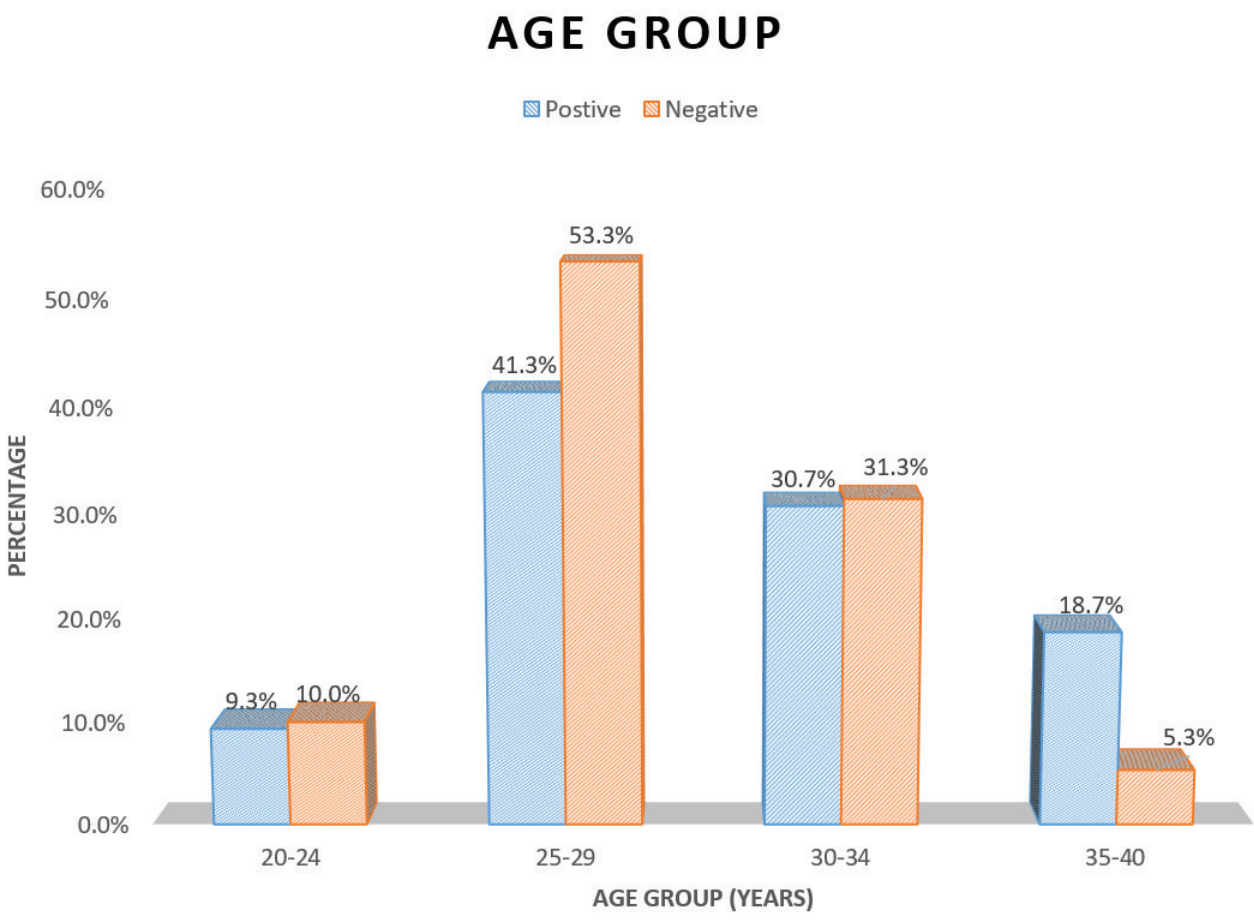
Statistics	1st Trimester TSH	
	Positive	Negative
Number	150	150
Mean	5.91	5.13
Median	5.71	4.87
SD	1.53	1.27

Table 5: Tabular representation of associated medical disorders

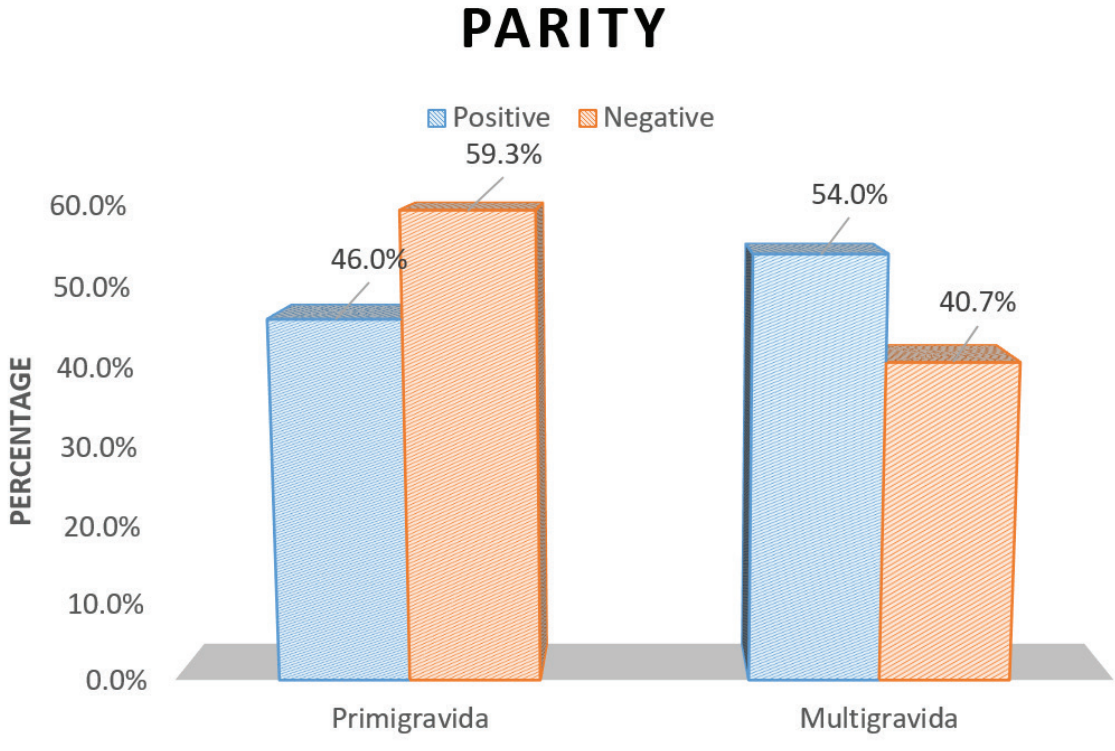
ANTI TPO	Positive		Negative	
Medical Disorder	Number	%	Number	%
GDM	51	34.0%	39	26.0%
HDP	8	5.3%	1	0.7%
IHCP	13	8.7%	19	12.7%

Table 6: Tabular representation of associated medical disorders

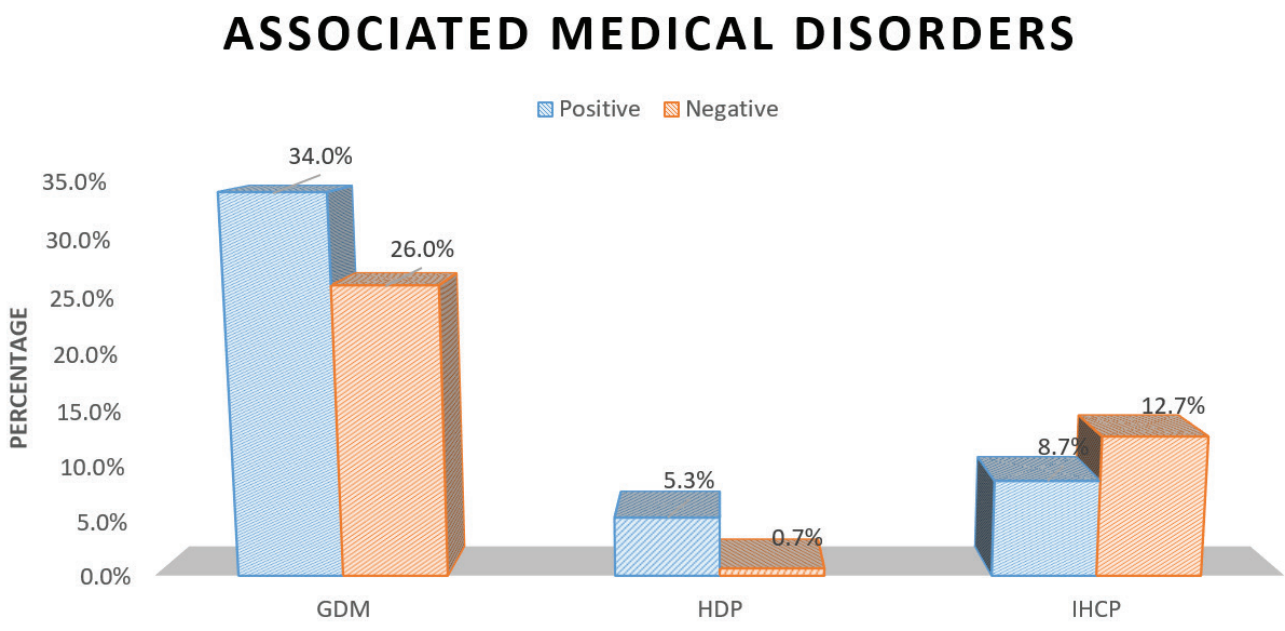
ANTI TPO	Positive		Negative	
Complications	Number	%	Number	%
Missed Abortion	7	4.7%	0	0.0%
Threatened Abortion	14	9.3%	0	0.0%
RPL	13	8.7%	0	0.0%
PPROM	9	6.0%	3	2.0%
PTL	19	12.7%	1	0.7%



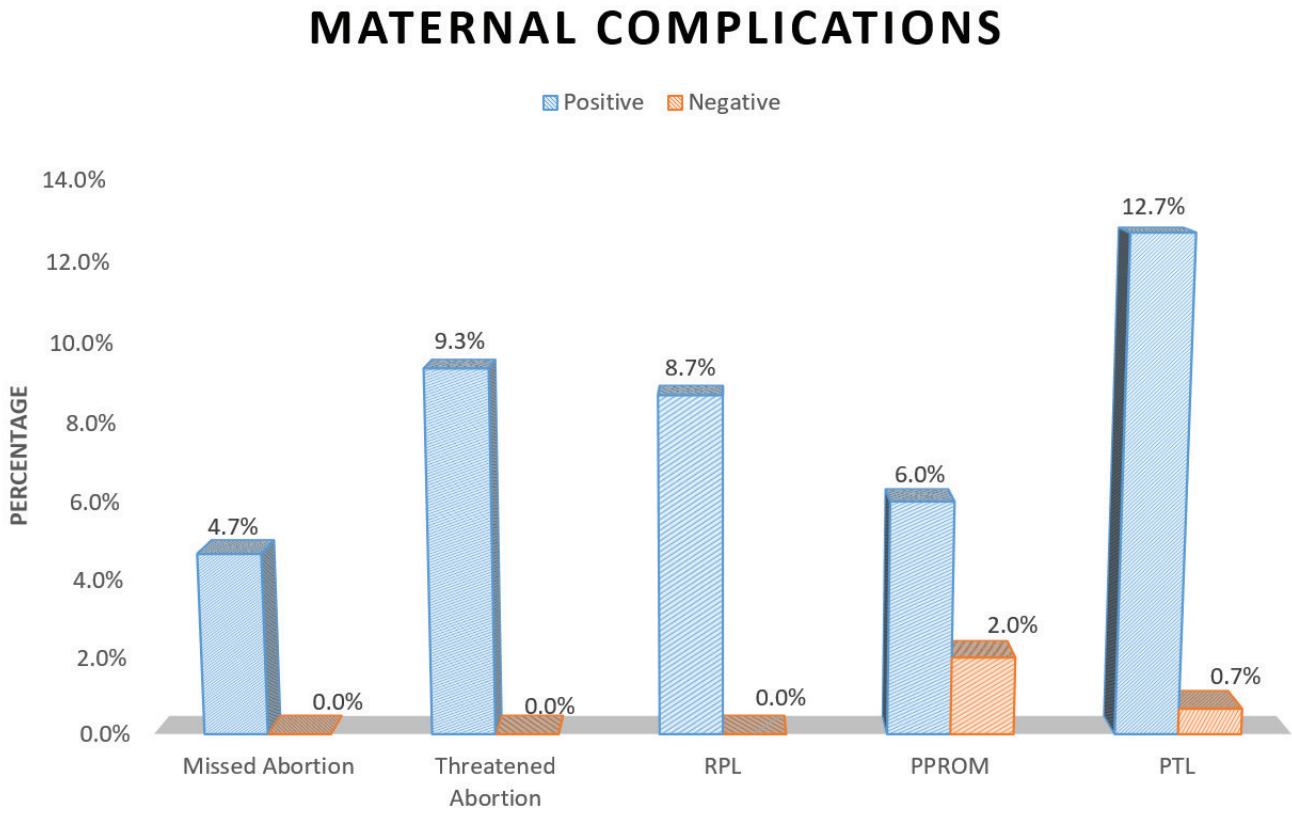
Graph 1: Graphical representation of age of enrolled women



Graph 2: Graphical representation of parity of enrolled women



Graph 3: Graphical representation of associated medical disorders in enrolled women



Graph 4: Graphical representation of maternal complications in enrolled women

List of abbreviations:
hcg- Human chorionic gonadotropin
TSH- Thyroid stimulating hormone
Anti-TPO- Anti-thyroid peroxidase antibody
Anti- Tg - Anti-thyroglobulin antibody
SCH - Subclinical hypothyroidism
TAI - Thyroid autoimmunity
GDM - Gestational diabetes mellitus
HDP - Hypertensive disorders of pregnancy
IHCP - Intrahepatic cholestasis of pregnancy
PTL - Preterm labour
PPROM - Preterm prelabour rupture of membranes
RPL - Recurrent pregnancy loss
ATA - American Thyroid association
LT4 - Levothyroxine

Case Report

Heterotopic Pregnancy — A Diagnostic Challenge

Shireen Islam[1], Ramprasad Dey[2], Nilanjana Chaudhury[3]

ABSTRACT

Introduction: Heterotopic Pregnancy is simultaneous presence of single or multiple intrauterine pregnancy along with ectopically located pregnancy, most commonly tubal ectopic. The prevalence in naturally conceived pregnancy is rare, approx. 1 in 30,000 cases. With ART incidence increased to 1 in 100 cases.

The Case: A 23 year primigravida with gestational age of 12 week presented with pain at right iliac fossa and bleeding per vagina for 2 days. On examination, her vitals was stable with mild pallor. Per abdominal examination revealed mc Burney's point tenderness with mild per vaginal bleeding. Patient was scheduled for emergency laparotomy. Intra-operatively it was diagnosed as a case of ruptured tubal ectopic pregnancy with viable intrauterine pregnancy.

Conclusion: Intrauterine pregnancy doesn't rule out the coexistence of another pregnancy on ectopic site. So careful examination is utmost needed during first trimester especially in symptomatic mother.

Introduction

Heterotopic Pregnancy is simultaneous presence of single or multiple intrauterine pregnancy along with ectopically located pregnancy, most commonly tubal ectopic. The prevalence in naturally conceived pregnancy is rare, approx. 1 in 30,000 cases. But with increased number of assisted reproductive technique, incidence of heterotopic pregnancy increased up to 1 in 100 to 1 in 3900 cases. Other risk factors are previous history of ectopic pregnancy, chronic pelvic inflammatory disease, any surgery at adnexal region, failure of contraceptive method such as tubal ligation, intrauterine devices. According to recent data, clomiphene citrate is related to higher risk.

Case Presentation

A 23 year primigravida with gestational age of 12 week presented with pain at right iliac fossa and bleeding per vagina for 2 days. She has been suffering from this type of symptoms on and off for 2 month. She had a history of subfertility which has been treated with ovulation induction with letrozole.

On examination, her vitals was stable with mild pallor. Per abdominal examination revealed mc Burney's point tenderness with mild per vaginal bleeding.

Investigations

Her serial ultrasonography report shows:

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Early scan at 6 week	Single live fetus with corpus luteal cyst on right ovary
Scan at 8 week	Single live fetus with sub chorionic hemorrhage of 1.3* 1.0 cm
Scan at 9 week	Single live fetus, large sub chorionic collection of 6.4685.43 cm. Enlarged appendix with thick irregular echogenic walls and surrounding fluid. Luteal cyst on right ovary
Scan at 10 week (at presentation)	Single live fetus, Sub chorionic hemorrhage of 3.8*2.9 cm. Hypoechoic lesion with ill-defined margin seen in right adnexa 4.9*3.8 cm. ? Hemorrhagic corpus luteal cyst. Mild fluid collection in pouch of Douglas and hepato-renal pouch of Morrison. Right iliac fossa- mild inflammatory changes noted and appendix not visualized separately.
Repeat scan for diagnosis	Single live fetus, Sub chorionic hemorrhage of 6.2*6.9 cm. Right ovary bulky with no vascularity. Suggestive of ovarian torsion. No sign of appendicitis or appendicular abscess.

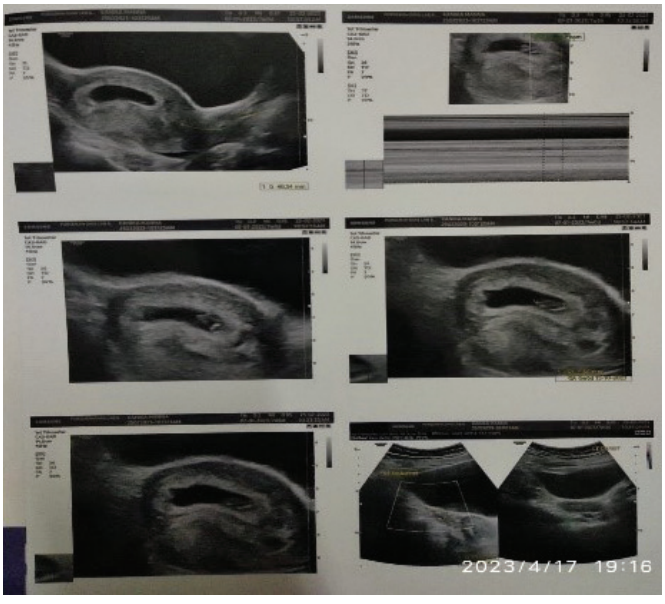

Fig 1: Intrauterine G-sac with adnexal pathology.

Blood investigation: Hemoglobin at presentation was 9.8 but decrease to 6.5

Management: Patient was initially diagnosed as a case of appendicitis or appendicular abscess and decided to manage conservatively. But after USG report of ovarian torsion and falling hemoglobin level the patient was scheduled for emergency laparotomy. Intra-operatively it was diagnosed as a case of ruptured tubal ectopic pregnancy with viable intrauterine pregnancy. Histopathology report of the tubal specimen confirmed the presence of trophoblastic tissue.

Follow up: The patient followed up with serial ultrasonography up to 37 weeks when she has undergone emergency cesarean section with indication of fetal distress and delivered a 2750 gram live baby.

Discussion

Diagnosing and managing heterotopic pregnancy is challenging. The most frequent symptoms includes abdominal pain, adnexal sol with uterine enlargement and vaginal bleeding. Abdominal and pelvic ultrasound very often fail to detect ectopic pregnancy in presence of intrauterine pregnancy because heterotopic pregnancy still considered as a rare case. Therefore, presence of intrauterine pregnancy is not a very reliable indicator to rule out the possibility of ectopic pregnancy.

In terms of management, medical management with systemic methotrexate injection is contraindicated to preserve the intrauterine pregnancy. Surgical method remains the primary treatment approach, although, local KCl injection can be used in certain cases.

Conclusion

Intrauterine pregnancy doesn't rule out the coexistence of another pregnancy on ectopic site. So careful examination is utmost needed during first trimester especially in symptomatic mother.

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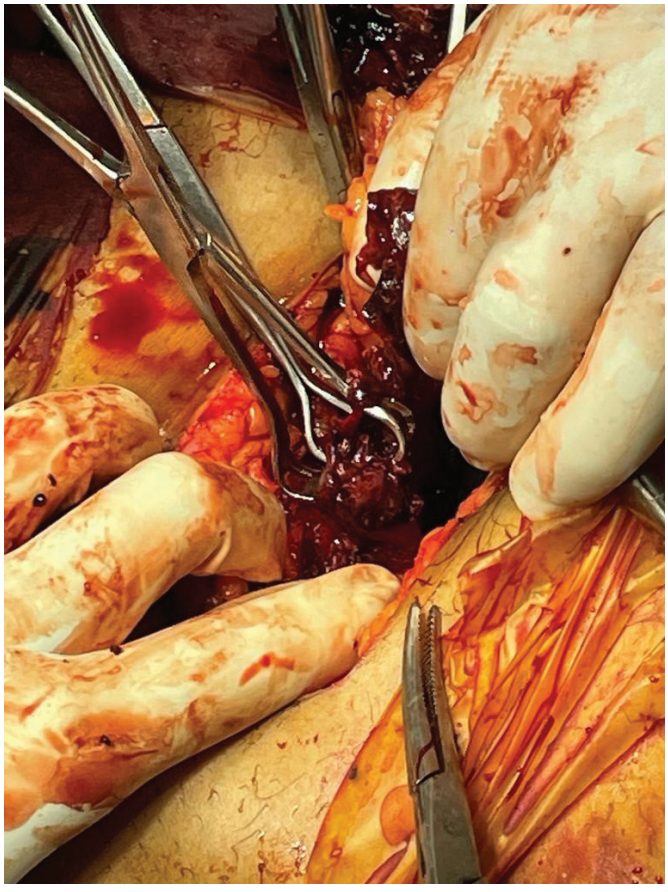

Fig 2: Ruptured ectopic intraoperative view.

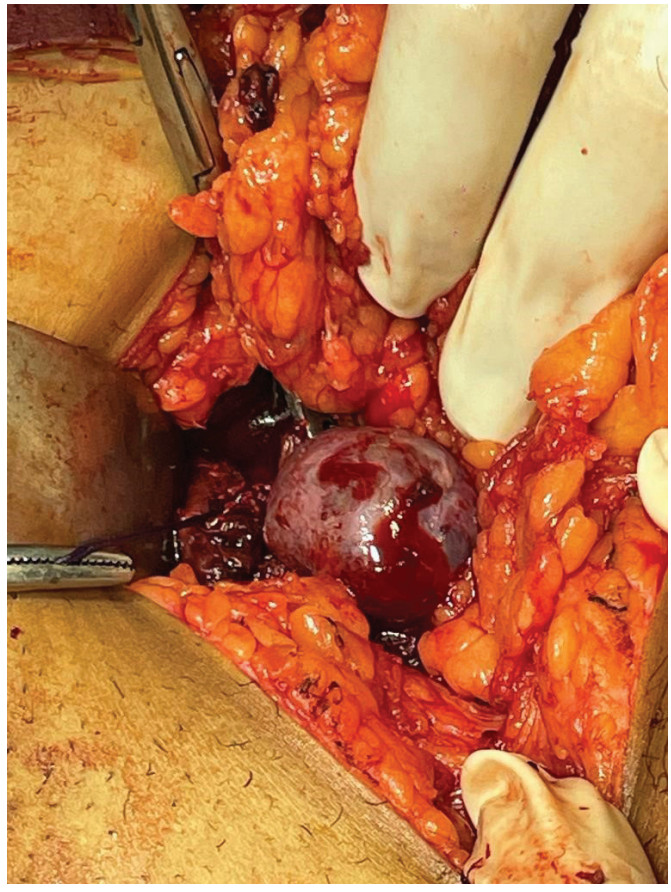

Fig 3: Enlarged gravid uterus with adnexal pathology.

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(4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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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.

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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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Main text

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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Brief communications should be no more than 400 words, excluding the first-page information, synopsis, keywords, author contributions, acknowledgments, conflicts of interest, references, figure legends, and tables and figures. There should be no more than 4 references and no more than 1table or 1figure.

Power calculations, statistics, and reporting of numbers.

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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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