- USG: Single live fetus, CRL 66 mm, GA 12 weeks 6 days, NT 1.1 mm
- cFTS: 1 in 127
- NIPS: **Low fetal fraction (2%),** no call
- Repeat NIPS: Failed
- POG 16 weeks—amniocentesis: Normal karyotype
- USG: Normal

Q1. What do you understand by this report?

This is a case of ***Low fetal fraction (<4%)/No call/ Failed NIPS***[7]

- Incidence is 1–8%
- Causes
  - Obesity
  - GA <10 weeks
  - Aneuploidy (T13, T18, Monosomy X, triploidy)
- Repeat sample may give result in 50–60% patients

Messages

- Must do invasive test in these patients as low fetal fraction is associated with aneuploidy
- Confirmation of GA by USG must before giving sample for NIPS

False positive result [7]

- Confined placental mosaicism
- Vanishing twin
- Maternal chromosomal abnormalities (mosaicism)
- Maternal malignancies

Message: Invasive testing is must in positive NIPS.

Limitations of NIPS (versus conventional screening) [7]

- Does not screen for open neural tube defects.
- Does not replace first trimester USG—accurate dating, NT, multiple pregnancy, placental abnormalities and CMF.
- Not used in higher-order pregnancies.
- No role in predicting late-pregnancy complications like pre-eclampsia.

Limitations of NIPS (versus Invasive testing)[7,8]

- Chromosomal abnormalities such as unbalanced translocations, deletions, and duplications will not be detected by NIPS. With fetal anomalies, invasive diagnostic testing and CGH array are more likely to detect chromosomal imbalances—better testing option
- NIPS cannot distinguish Down syndrome is trisomy 21, a Robertsonian translocation or mosaicism
- NIPS does not screen for single-gene mutations.

Key Points

- Pre-test and post-test counselling are an integral part of any screening test.
- Strict quality control for ultrasound examination and laboratory assays is essential for optimal performance of the screening method.
- NIPS
  - *'Super (?)'* screening test—not diagnostic, reduces invasive testing but cannot replace it
  - To be done at more than 10 weeks
  - USG mandatory before NIPS
  - No role if abnormal USG findings
  - Not to be done in low risk population—use as a contingent method but not as primary screening modality
  - Confirm with invasive testing in 'High risk' and 'No call'.

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Q5. How do you monitor neonate after delivery?

After delivery cord blood should be sent for hemogram, DCT, serum bilirubin. Then 1–2 weekly hematocrit and reticulocyte determination is performed till 3 months of age. Infants with Hb <6 g% need top up transfusions.

Q6. What is role of prophylactic anti D to prevent alloimmunization?

The most effective intervention to reduce alloimmunization is use of prophylactic anti D, however, alloimmunization cannot be completely prevented.

Routine anti D prophylaxis[4]

Antenatal:

- An antibody screen is performed at first antenatal visit, if negative again at 28 week. If still negative, 300 µg of injection anti D should be given. It neutralises fetomaternal hemorrhage of up to 30 mL and reduces risk of isoimmunization from 2% to 0.1%. For women reporting late, the prophylactic anti D can be given later but if she delivers within 3 weeks of antenatal prophylaxis, postnatal dose may be omitted as the effect of anti D persists for about 12 weeks.
- After CVS, amniocentesis, cordocentesis.
- After blunt abdominal trauma, antepartum hemorrhage and external cephalic version.

Postnatal: Injection anti D 300 µg is given within 72 hours after birth of an Rh positive infant. It can be given up to 28 days of birth. However, its efficacy gets compromised.

Postabortal: Injection anti D is given in ectopic pregnancies managed either medically or surgically, after induced abortions—medical or surgical, molar pregnancy. There is insufficient evidence regarding anti D administration after spontaneous or threatened miscarriage before 12 weeks of gestation.[5]

Q7. What are the tests available to detect fetomaternal hemorrhage?

The estimation of volume of fetomaternal hemorrhage is important to calculate the neutralising dose of anti D required (approximately 10 µg for 1 mL of fetal blood).

The methods to estimate volume of fetomaternal hemorrhage are:

- *Kleihauer-Betke test* which is based on the fact that fetal hemoglobin resists denaturation by acid as compared to adult hemoglobin.[6]
- *Flow cytometry:* It is more precise then Kleihauer-Betke test. It is utilized when large fetomaternal hemorrhage is suspected which requires accurate quantification.
- *Rosetting method:* This test is used in postpartum Rh-negative mother with Rh-positive fetus within 72 hours. Any positive rosette test needs quantification by Kleihauer-Betke test.

Case 2

A 31-year-old G2P1L1 was referred by radiologist at 30 weeks gestation in view of USG features of fetal hydrops.

Previous pregnancy: Term vaginal home delivery, had postpartum hemorrhage. No anti D given. Male baby 3 years, alive and healthy.

Examination: Uterus 30–32 weeks, cephalic, FHR 134 bpm.

Investigations: Blood group A-negative, husband's blood group A-positive, ICT-1: 128, other investigations were normal.

USG: Single live fetus 28 weeks, no malformations, placenta anterior, amniotic fluid index (AFI)-18, MCA PSV >1.5 MOM.

Diagnosis: Rh Alloimmunization.

Q1. How will you manage this pregnancy further?

The presence of hydrops indicates severe anemia in fetus with Hb deficit of >7 g% for the period of gestation. She should be referred to a fetal medicine unit. The next step is fetal blood sampling to determine fetal hemoglobin and hematocrit to quantify the severity of fetal anemia. Intrauterine transfusion is indicated if fetal Hb <9 g% or hematocrit <30%, at less than 34 weeks of gestation.

CHAPTER

3

Screening and Prediction of Preterm Labor

Karishma Bhatia, Kanika Gupta, Preeti Singh

Preterm labor is the onset of regular uterine contractions with cervical effacement or dilation anytime before 37 completed weeks of pregnancy. India, being a developing country, bears the brunt of 3.5 million preterm births every year.[1] India is the 5th country worldwide with respect to the number of preterm births.[2] Preterm birth and its complications are the leading cause of death among children under 5 years of age. Three-quarters of these deaths could be prevented if preterm labor is diagnosed early and managed appropriately.

Case 1

A 26-year-old lady G2P1L1 with 17 weeks of period of gestation came to the antenatal OPD for routine check up. On eliciting a detailed history, it was found that her previous pregnancy resulted in a preterm vaginal delivery at 35 weeks of gestation.

Obstetric history: Married for 4 years, non-consanguineous marriage.

First pregnancy spontaneous conception, 2 years back, delivered a preterm male child weighing 1.6 kg at 35 weeks of gestation vaginally.

Baby was kept in neonatal ICU for 16 days and discharged at a weight of 1.75 kg.

On examination: General condition fair, pulse: 84/min, blood pressure: 120/80 mmHg. Per abdomen—uterus corresponds to 18 weeks size. Per speculum examination—os closed, cervical length appeared <2.5 cm, no discharge or bleeding observed.

Her antenatal investigations are normal. Dual test and a level I ultrasound were done at 12 weeks which were normal.

Q1. How will you manage this patient ?

The patient has a history of previous preterm birth. She does not have any complaints at present. She should be counselled about the risk of preterm labor in the current pregnancy. A transvaginal scan should be done for early detection and prediction of preterm labor. If the scan shows cervical length >25 mm, serial measurements (every 1 to 2 weeks) should be done till 24 weeks. If the scan shows a short cervical length <25 mm, the patient should be offered prophylactic cerclage. If a patient has cervical length <25 mm and no history of previous preterm birth then she is advised vaginal progesterone.[2]

Cervical length >25 mm	Repeat weekly till 24 weeks
Short cervical length + history of preterm labor	Prophylactic cerclage
Short cervical length, No history of preterm labor	Vaginal progesterone

Q2. What are the factors predisposing to preterm labor in this case?

In this case, previous preterm birth is a predisposing factor to preterm labor. Other factors include:

Maternal:

- Short inter-conception period
- Multiple pregnancy

Q3. In which condition is conservative management contraindicated?

Conservative management is contraindicated in:

- Non reactive non stress test
- Oligohydramnios
- Absent or reversed end diastolic flow on umbilical artery Doppler
- Repetitive severe variable decelerations
- Abruption
- Fetal demise
- Chorioamnionitis
- Pregnancy >34 weeks of gestation.

Q4. Discuss the role of tocolytics in preterm labor ?

Tocolytic agents act by decreasing uterine contractions and causing uterine relaxation. They do not prevent preterm labor, but act only as a method to prolong pregnancy and delay labor for the next 48 hours, which is the time required for steroids to act (Level A evidence).[14] All the contraindications to conservative management are a contraindication to tocolytic use as well. The various tocolytics that can be used are:

a. ***Nifedipine:*** It is a calcium channel blocker and acts by blocking the cell membrane calcium channels, thus reducing intracellular calcium. It is associated with statistically and clinically better outcomes and fewer side effects and is therefore the first line agent according to RCOG.[2] It is given in a loading dose of 20 mg, followed by 3 additional doses of 20 mg each if contractions continue. Maintenance dose is 20–40 mg every 4 hourly for 48 hours. It is contraindicated in heart disease patients as it causes hypotension, tachycardia, hypoglycemia, headache, dizziness and facial flushing.

b. ***Atosiban:*** It is a modified form of oxytocin which acts as a competitive inhibitor of oxytocin receptors. It is given as an initial loading dose of 6.75 mg in 0.9 mL IV over one minute followed by a continuous infusion of 24 mL/hr for 3 hours, after which the rate of infusion is reduced to 8 mL/hr for 45 hours. It is sold by the brand name of Tosiban in India at ₹ 1500/6.75 mg, which makes it a very expensive tocolytic agent. It is used in cases where nifedipine is contraindicated.

   Side effects include headache, dizziness, hot flashes, tachycardia, hypotension, hyperglycemia, vomiting and rarely, post-partum haemorrhage.

c. β-mimetics-like ritodrine, terbutaline, isoxsuprine were used earlier but are no longer in use due to serious side effects like palpitations.

Q5. What is the role of steroids? When and how to give steroid course?

Steroids are given for fetal lung maturity. They reduce the incidence of respiratory distress syndrome, transient tachypnoea of newborn, intraventricular haemorrhage and necrotising enterocolitis. A single course of steroids is offered to women between 26 to 33+6 weeks if they are in established preterm labor or if labor is anticipated within the next 48 hours.

One should consider steroid cover at 24 to 25+6 weeks and at 34 to 35+6 weeks.[16–20]

Steroid course may be repeated (rescue dose) once when the pregnancy is less than 34 weeks and previous steroid course was given more than 14 days back and delivery is imminent within the next 7 days[21] (Level B evidence).

Both dexamethasone and betamethasone are equally efficacious. The maximum effect is seen within 2–7 days. Even a single dose confers some protective effect and thus should be given even if it seems that delivery will occur before the next dose.[16]

Betamethasone—12 mg intramuscular 24 hours apart × 2 doses.

Dexamethasone—6 mg intramuscular 12 hourly × 4 doses.

Q6. What is the role of magnesium sulphate?

Women who are more than 24 weeks but less than 32 weeks and are in preterm labor,