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FEDERATION OF OBSTETRIC AND GYNAECOLOGICAL SOCIETIES OF INDIA

Sampoorna
Swastha Janm Abhiyan

TOG CONCLAVE
PRETERM LABOUR

Pre-term Labour

PRACTICE ALGORITHMS

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Dear Seniors and Colleagues,

Preterm labour is the leading cause of neonatal morbidity and mortality worldwide as it complicates 5% to 10% of pregnancies. However, it is challenging to identifying women at high risk of preterm delivery, as scoring systems based on socioeconomic status, obstetric or medical history, and antenatal events in the current pregnancy have shown only a suboptimal correlation with subsequent preterm birth. The strongest risk factor for preterm labour is a prior history of preterm delivery, making reliable prediction difficult in a first pregnancy. Studies indicate that the risk of preterm delivery increases to 15% after one previous preterm birth and 41% after two.

To improve risk assessment, diagnostic tools such as fetal fibronectin testing and cervical ultrasound can help identify high-risk women, with cervical length measurement serving as a predictive marker for preterm delivery.

The management of preterm labour involves determining the underlying cause, optimizing delivery conditions, and carefully weighing the benefits and risks of delaying delivery to extend gestational age. Clinicians must assess each case individually, considering factors such as fetal well-being, intrauterine infection, and membrane status. While fetal compromise or infection may necessitate immediate delivery, an early gestational age with uncomplicated preterm labour and intact membranes may allow for delay.

Pharmacological interventions, including antibiotics, corticosteroids, and tocolytics, play a key role in management. However, the primary objective is not merely prolonging pregnancy but improving neonatal outcomes by reducing morbidity and mortality. Clinical decisions should always be based on a thorough risk-benefit analysis tailored to patient's unique circumstances.

Best wishes!

Dr Sunita Tandulwadkar

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PRETERM LABOUR:
CLINICAL PRACTICE MANAGEMENT UPDATE

BACKGROUND AND SCOPE

- Preterm birth (PTB) affects approximately 15 million infants annually, accounting for 11% of global births.[1]
- The incidence of preterm labour (PTL) in India is reported to be 23.3%, with preterm delivery occurring in 10%–69% of cases.[2]
- In 2020, India recorded an estimated 3.02 million PTBs, representing over 20% of the global burden.[3]
- Preterm delivery accounts for approximately 40%–75% of neonatal deaths and is a leading cause of perinatal morbidity and mortality.[2]

PRETERM LABOUR MANAGEMENT IN INDIA: KEY CHALLENGES

Preterm labour in India presents distinct challenges compared to global contexts, primarily due to demographic variations, healthcare infrastructure differences, and specific clinical presentations.[4] India has the highest number of preterm PTB globally, with key contributing factors such as maternal age, nutritional status, and socioeconomic disparities.[5] The healthcare system in India is characterized by stark contrasts between urban and rural settings, affecting access to quality antenatal care and skilled healthcare providers.[6,7]

The management of PTL involves a multifaceted pharmacologic strategy that utilizes therapeutic approaches aimed to sustain pregnancy, enhance fetal lung maturity, and reduce uterine contractions (tocolysis).[8] Corticosteroids are anti-inflammatory and immunosuppressant agents, which can promote fetal lung maturity and improve outcomes of PTB such as reducing respiratory distress syndrome, intraventricular hemorrhage (IVH), and improving the stability of neonates.[8] Tocolytics effectively increase the average latency period, delay delivery by >48 hours, and improve perinatal outcomes.[9] Magnesium sulfate is used in PTL for fetal neuroprotection in surviving infants.[8]

Given these treatment approaches, global guidelines may not be directly applicable; instead, tailored interventions that consider local risk factors and healthcare capabilities are essential for improving maternal and neonatal outcomes in India.[2, 10]

Therefore, these practice points provide evidence-based, standardized approaches to prevention, diagnosis, treatment, and management of PTL to reduce variability in clinical practice and improve patient outcomes (enhance patient health, safety, and overall outcomes). These practice points summarize the best available research and translate it into actionable steps for healthcare providers.

DEFINITION OF DIAGNOSED, THREATENED, AND ESTABLISHED PRETERM LABOUR

Definition of preterm birth

- PTB is the delivery of a live infant before 37 completed weeks of gestation.[11]

The causes of PTB include: [12]

- Preterm labour: Spontaneous labour with intact fetal membranes before 37 weeks of gestation.
- Premature rupture of membranes in preterm gestation: Spontaneous rupture of the fetal membranes before 37 weeks of gestation.
- Iatrogenic preterm deliveries: These occur due to an unfavorable intrauterine environment for the fetus or the mother as a result of various medical and surgical complications. Common conditions include severe preeclampsia, chronic hypertension, diabetes, placenta previa, or placental abruption.

Criteria for preterm labour

Regular uterine contraction after 20 weeks or before 37 weeks of gestation, four or more in 20 minutes, and accompanied by one or more of the following:[12,13]

- Progressive change in the cervix
  - » Cervical dilatation of 2 cms or more and/or
  - » Cervical effacement of 80% or more

Symptoms of preterm labour

- A woman presents before 37 weeks of pregnancy with symptoms suggestive of PTL, such as abdominal pain, pelvic pressure or discharge, but has not undergone any clinical assessment, including a speculum or digital vaginal examination.[14]

Suspected/threatened preterm labour

- Criteria: Uterine contractions without cervical dilatation.[15]

Diagnosed preterm labour

- Criteria: Uterine contractions with cervical changes. Cervical dilatation more than 2 cms.[15]

Established preterm labour

- A woman is considered to be in established PTL if she has progressive cervical dilatation from 4 cms with regular contractions.[14,15]

Categories of preterm birth

PTB is categorized based on the gestational age of the baby at birth.[11]

- Extremely preterm: Born before 28 weeks of pregnancy
- Very preterm: Born between 28 and 32 weeks of pregnancy
- Moderate preterm: Born between 32 to 34 weeks
- Late preterm: Born between 34 to 37 weeks

RISK FACTORS FOR PRETERM BIRTH

- The identification of risk factors (Table 1) for predicting PTB is advantageous because it may provide insights into a better understanding of the mechanisms leading to PTB.[13]

Table 1. Risk factors for preterm birth (PTB)[13]

Modifiable risk factors for PTB	
• Cigarette smoking • Illicit drug use • Anemia • Bacteriuria/urinary tract infection • Gingival disease • Strenuous work/work environment	• Lower genital tract infections (including bacterial vaginosis, *Neisseria gonorrhoeae, Chlamydia trachomatis, Group B Streptococcus, Ureaplasma urealyticum, and Trichomonas vaginalis*)
Non-modifiable risk factors for PTB	
• Prior PTB • Age <18 years or >40 years • Poor nutrition • Low prepregnancy weight • Low socioeconomic status • Sub optimal prenatal care	• Cervical injury or anomaly • Uterine anomaly • Excessive uterine activity • Premature cervical dilatation (<2 cm) or effacement (> 80%) • Overdistended uterus (twins, polyhydramnios) • Vaginal bleeding • Assisted reproductive technology pregnancies

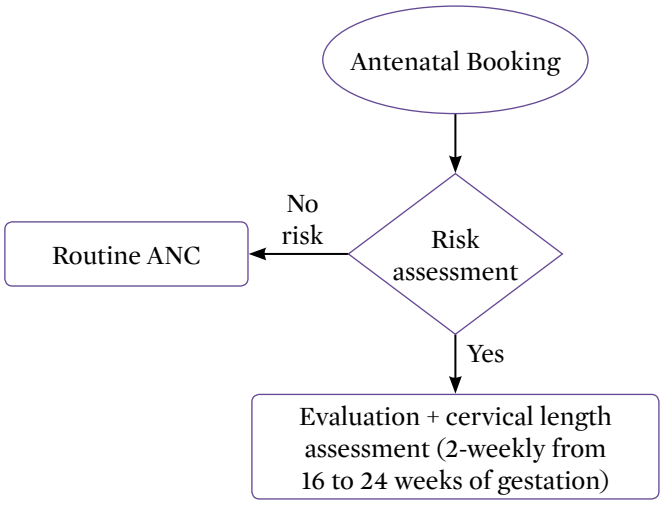
SCREENING AND PREVENTION OF PRETERM LABOUR

- Risk assessment for PTB in the antenatal period is elaborated in Table 2[13]

Table 2. Risk assessment for preterm birth (PTB) in the antenatal period

Category	Assessment method	Key findings	Clinical relevance
Physical assessment	Speculum and digital examination	Cervical integrity, prior cervical injury	Helps assess the risk of cervical insufficiency or previous trauma
	Screening for asymptomatic bacteriuria, STDs, and BV	Presence of infection	Infections are associated with an increased risk of PTL
History	Prior preterm deliveries	A strong predictor of recurrent PTB	Women with prior PTB are high-risk and require closer monitoring
Cervical length	Transvaginal ultrasound (TVUS)	Cervical length ≤25 mm at 16-24 weeks	Short cervix is a major risk factor for spontaneous PTB
Laboratory tests			
	Vaginal pH/wet smear/ whiff test	Identification of bacterial vaginosis (BV)	BV is associated with an increased risk of PTB
	Complete urine culture	Presence of a significant amount of bacteria in the urine (colony count exceeding 100,000 colony forming units [CFU] per milliliter of urine from a midstream sample).[16]	Asymptomatic bacteriuria and urinary tract infections (UTI) are associated with an increased risk of spontaneous preterm labour (sPTL), and UTI symptoms may mimic those of sPTL.[17]
	Vaginal swab test (presence of fetal fibronectin (fFN)[18]	Elevated levels of fFN	A positive fFN indicates the risk of delivery

Prevention of preterm birth: Initial and further risk assessment[19]



Risk assessment

1. Smoking
2. Maternal age <20 years old
3. Screen for UTI symptoms
4. Screen for genital tract infection symptoms
5. History for preterm birth
6. History of cervical surgery
7. BMI<18.5 kg/m^2

Further risk assessment

1. History of mid trimester loss or SPTB (16 and <37 weeks)
2. Previous PPROM
3. Previous cervical surgery
4. Previous cervical cerclage
5. Known uterine anomaly

ANC: Antenatal care; UTI: Urinary tract infection; BMI: Body mass index;
SPTB: spontaneous preterm birth; PPROM: Preterm premature rupture of membranes

Prevention strategies for preterm labour[13]

Cervical Cerclage

- Indicated for women with previous spontaneous PTB, singleton gestation, and cervical length <25 mm.
- No evidence for cerclage in women without short cervix or for emergency procedures.
- Post-operative cervical cerclage patients can be administered tocolytics.[20]

Progesterone Supplementation

- Indicated in women with history of PTB or short cervix.
- Not effective in: Preterm premature rupture of membranes (PPROM) or multiple pregnancies (twins/triplets).
- Vaginal progesterone for cervical shortening (<24 weeks)

Etiology or comorbid conditions requiring treatment

- Medical condition of mother and fetus
- Malaria, human immunodeficiency virus (HIV), Infection, idiopathic contractions, multiple pregnancies, cervical dysfunction, antepartum hemorrhage, malnutrition, hypertension, diabetes, and intra uterine growth retardation.

UTILITY OF PRETERM LABOUR PREVENTION STRATEGIES[13, 21]

Table 3. Preterm labour prevention strategies

Strategies that have limited or no proven efficacy
• Bed rest • Pelvic rest (avoidance of intercourse) • Intensive education and prenatal care • Screening and treatment of asymptomatic lower genital tract infections • Treatment of gingival disease • Empirical broad-spectrum antibiotic therapy
Strategies that may have some benefit
• Prevention and early diagnosis of sexually transmitted and genitourinary infections • Treatment of symptomatic lower genital tract infection • Cessation of smoking and illicit substance use • Prevention of multiple pregnancies • Elective (prophylactic) cervical cerclage, if indicated • Folic acid supplementation • Vitamin D supplementation

REFERRAL FOR CERVICAL LENGTH SCREENING

- Women with a singleton pregnancy who can be offered a referral for a single cervical length between 16–24 weeks' gestation are:[22]
  - » Women with a history of mid-trimester loss or PTB between 16–34 weeks gestation.
  - » Women with a history of preterm pre-labour rupture of membranes in a previous pregnancy.
  - » Women with a previous large loop excision of the transformation zone (LLETZ) of >10 mm depth.

Who to offer cervical length screening?[15]

- Low-risk population - Suggested (as a part of Universal Screening)
- High-risk population - Recommended

When to offer screening for short cervical length[23]

- Recommended timeframe: 16–24 weeks.
- However, in high-risk populations it can be performed during the first trimester anomaly scan.

Universal cut–off for cervical length[24]

- Transvaginal route: Recommended
- Cervical length: ≤ 25 mm

Outcome of screening short cervical length[25]

- If an ultrasound shows a cervical length of <25 mm, the woman should be offered vaginal progesterone, cervical cerclage, and tocolytics after a discussion about the risks and benefits.

Other screening tests for the risk of preterm labour[26,27]

- Litmus paper test/nitrazine paper test.
- Fetal fibronectin (fFN) levels, if facility available.

Fetal fibronectin levels

- Negative predictive value is excellent.
- Negative test implies negligible risk of PTB in the next 7 days.
- Positive predictive values are equally good and levels >200 should be used as a cut-off for antenatal corticosteroids and in utero transfer.

TOCOLYTICS IN THE MANAGEMENT OF PRETERM LABOUR

Inhibiting uterine contractions is the primary focus of PTL treatment, achieved with tocolytic drugs.[13]

- Acute tocolysis involves the short-term use of tocolytics to suppress uterine contractions, aiming to delay PTB for approximately 48 hours.[10]
- Maintenance tocolysis is often prescribed to prolong pregnancy after an acute episode of PTL, to maintain uterine quiescence, and to reduce the risk of recurrent PTL.[10]

The Federation of Obstetric and Gynecological Societies of India (FOGSI) recommends tocolytics to:[9,10,13]

- Allow time for antenatal corticosteroid and magnesium sulfate administration.
- Reduce neonatal complications, including intraventricular hemorrhage and respiratory distress syndrome.
- Facilitate patient transfer to specialized centers, if needed.

MAINTENANCE TOCOLYTIC THERAPY[9,10]

- Maintenance tocolysis extends beyond 48 hours to prolong pregnancy and reduce neonatal morbidity and mortality.
- Preterm contractions persist in 20%–30% of women after acute tocolysis, with recurrence in up to 60% following arrested labour.[10]
- Despite limited evidence, maintenance tocolysis is extensively used in India.[10]
- Despite recommendations, maintenance tocolysis remains common:
  - » Germany: 80.8% of obstetric units practice maintenance tocolysis.
  - » Austria: 40.8% of initial tocolysis cycles exceed 48 hours, with many requiring multiple cycles.
  - » France: 50% of cases involve maintenance tocolysis.
- This ongoing use, despite established guidelines, highlights a clear disconnect between clinical practice and recommendations.
- Continuing tocolysis until an optimal gestational age supports:
  - Reduced risk of late-PTBs
  - Enhanced neonatal outcomes
  - Lower projected healthcare costs

While tocolysis can effectively prolong pregnancy, its continuation supports better outcomes, highlighting the importance of balance between guideline adherence and clinical decision-making.[9,10]

A retrospective study by Rebarber et al in the US analyzed 4,253 stable singleton pregnancies that electively discontinued tocolysis between 33.0 to 36.9 weeks of gestation.[28] Key finding of the study:

- Spontaneous PTL within one week after stopping tocolysis was experienced by 58.1% of women.

Clinical implications of the study finding:

- Earlier discontinuation was associated with higher rates of late-PTB, low birth weight, prolonged NICU stays, and increased healthcare costs.
- Maintenance tocolysis beyond 33 weeks demonstrated greater pregnancy prolongation and improved neonatal outcomes. Optimizing patient management to support prolonged pregnancy could significantly reduce PTB rates and newborn care costs.

Tocolytics in India

Globally, various tocolytics are used, but in India, the Central Drugs Standard Control Organization (CDSCO) has approved:[13, 29]

- Isoxsuprine (the first β-adrenergic agonist used in India, widely used for six decades)
- Ritodrine (betamimetic drug)
- Atosiban (oxytocin receptor antagonist)

ISOXSUPRINE IN THE MANAGEMENT OF PRETERM LABOUR

- Isoxsuprine is a CDSCO-approved tocolytic that has been used in India for over six decades.[9,10]

Mechanism of action of isoxsuprine[10]

- β-adrenergic receptor stimulation in the myometrium, leading to smooth muscle relaxation.
- α-adrenergic receptor inhibition in arteries.
- Direct spasmolytic action similar to papaverine.

Clinical use of isoxsuprine in preterm labour[10]

- Most frequently used tocolytic agent in India.
- Isoxsuprine is recommended by FOGSI for maintenance tocolysis, as it effectively prolongs pregnancy, delays delivery by >48 hours, and improves perinatal outcomes when used in appropriate dosages.
- Recent evidence demonstrated optimal isoxsuprine therapy yields superior maternal and fetal outcomes:
  - » Initial IV infusion: 40 mg isoxsuprine in 500 mL 5% dextrose/Ringer lactate solution, starting at 0.04 mg/min (8 drops/min) and increasing every 15 min until uterine quiescence is achieved (continued for 12 hours).
  - » Intramuscular therapy: Following uterine quiescence, intramuscular injections of 10 mg every 4 hours for 24 hours are given.
  - » Maintenance therapy: 40 mg sustained-release capsules twice daily, continued based on patient response or up to 37 weeks of gestation.
- In cases of PROM, isoxsuprine is administered via IV, followed by IM and oral routes, depending on gestational age.[9,10]

Clinical evidence for the use of isoxsuprine in patients at risk of preterm labour

Evidence 1

A systematic review was conducted to evaluate the efficacy of isoxsuprine (administered acutely (intravenous administration) and as maintenance therapy (oral or intramuscular administration), to reduce the risk of both PTB and abortion. Two double-blind studies were included in the first analysis that determined the effect of isoxsuprine vs. placebo. The second analysis reviewed data from 25 publications containing individual and general patient data. A positive outcome (at term delivery, pregnancy ongoing, patient discharged, at home, ≥8th month, or a delay of pregnancy was >1 week) was evaluated.[30]

Analysis of two double-blind studies:

- A positive outcome was observed with isoxsuprine in 92% of cases compared to placebo (44.4%, p<0.001). This beneficial effect was maintained with isoxsuprine; for those with a risk of abortion (92.5% in the isoxsuprine-treated group showed positive outcomes vs. 46.4% in the placebo group, p<0.001). Further, for those with a risk of premature delivery (89.5% in the isoxsuprine-treated group showed positive outcomes vs. 29.4% in the placebo group, p<0.001).

Secondary analysis of individual patient data (11 studies):

- Isoxsuprine was effective in prolonging pregnancy in 54.5% of women at risk of abortion and in 82.3% of women at risk of premature delivery.

Combination of individual and general data (25 studies):

- Isoxsuprine was beneficial in 77.3% of women at risk of abortion and in 89% at risk of premature delivery.

Evidence 2

In a multi-centric, retrospective study by Jaju et al. conducted across five centers in India (2014–2016), the management of PTL was evaluated with 285 patients enrolled. Findings showed that isoxsuprine was the most used tocolytic agent (60.1%), followed by nifedipine (23.8%). Prolongation of delivery beyond 48 hours was significantly higher in the isoxsuprine group compared to the nifedipine group. Patients treated with isoxsuprine demonstrated longer latency period (36.77±28.09 vs. 1.44±1.33 days), higher birth weight (2.25±1.34 vs. 1.07±0.34 kg) and better Apgar scores (7.56±2.36 vs. 4.87±2.10), especially in extreme to very PTL cases (<32 weeks). Similar trends in latency period and Apgar score were observed for both drugs in late PTL cases (>32 weeks). Therefore, isoxsuprine was more effective in prolonging pregnancy beyond 48 hours and improving maternal and perinatal outcomes, including latency period, Apgar score, birth weight, and reduces NICU admissions.[2]

Evidence 3

In a prospective study by Jaju et al, 50 patients with PTL at 24–37 weeks were treated with 40 mg IV isoxsuprine until uterine quiescence, followed by 10 mg IM every 4 hours for 24 hours, and 40 mg sustained-release capsules twice daily until delivery or 37 weeks. Findings showed a 100% efficacy in achieving tocolysis within 24- and 48-hours post-administration of isoxsuprine (IV/IM). The mean latency period of 58.5 (18.5) days was reported when isoxsuprine was continued at 40 mg twice daily until 37 weeks, and 90% of patients completed 37 weeks of gestation. No congenital anomalies or fetal infections were reported. Mean fetal birth weight was 2.7 (0.3) kg, and mean Apgar scores were 7.5 (0.6) at 1 minute and 9.2 (0.4) at 5 minutes. Common side effects were tachycardia and vomiting, both resolved with dose adjustment.

Further more, the number of infants requiring NICU admission (2%) were lower. Overall, isoxsuprine was found to be an effective and well-tolerated agent when used as maintenance tocolysis until 37 weeks.[10, 31]

Expert consensus for maintenance Isoxsuprine therapy[10]

- The experts opined that isoxsuprine as maintenance tocolysis has been associated with improved perinatal outcomes, including lesser incidence of NICU admission, improved birth weight outcomes, and extended latency periods.
- The experts emphasized that maintenance therapy is important, as there is a possibility of spontaneous recurrence of PTL after the cessation of active labour therapy.
- Maintenance therapy is beneficial for patients with cervical cerclage, as well as those experiencing threatened or active PTL.
- Isoxsuprine as maintenance therapy can be administered in a dosage of 40 mg once daily at bedtime to minimize side effects or in divided doses of 30-40 mg to effectively manage potential side effects.

Expert consensus for Isoxsuprine in Threatened and Active PTL[9]

- IV isoxsuprine should be administered for threatened and active PTL. Isoxsuprine 40 mg IV infusion diluted in 500 mL 5% w/v dextrose, with a drop rate set at eight drops per minute (0.04 mg/min). The drop rate should be elevated by eight drops per minute every 15 minutes until uterine quiescence is achieved, and infusion should be continued for 12 hours.
- The experts opined that after increasing the drip rate, waiting for 15 minutes to monitor blood pressure and pulse rate is suggested, and then further the drip rate can be increased. This gradual dose titration helps prevent any potential side effects.

ATOSIBAN IN THE MANAGEMENT OF PTL

Atosiban[15]

- Give 6.5 mg (0.9 mg of 7.5 mg/mL of solution from vial) IV over 1 minute via a 1 mL syringe

- Prepare infusion in 0.9% sodium chloride
- Withdraw 10 mg from hundred ml back and discard at 10 mg of 7.5 MT/ml concentrated (from two vials) to the back and mix well*
- Resulting sodium content solution contains 750 mcg/mL

- Set form to run infusion at 24 mL/hour for 3 hours i.e set volume to be infused 272 ml when pump alarms at end of 72 ml
- When pump alarms at end, DO NOT discard remain solution

- Decrease rate to 8 mL/hour

* for subsequent bags withdraw 5 ml from 50 ml 0.9% sodium chloride back and discard

- Add 5 mL of 7.5 mg/mL concentration (i.e. 1 vial) to the back and run at 8 mL per hour for 50 mL
- Discontinue if labour establishes
- Review after 24 hours. In most cases, discontinuation is reasonable
- Total duration of treatment should not exceed 48 hours

Monitor <120 mmHg - Watch for hypotension and tachycardia

OFF-LABEL DRUGS FOR MANAGING PRETERM LABOUR IN INDIA[9,10]

Common off-label drugs

- Nifedipine
- Indomethacin
- Nitric oxide donors

Approval status

- These agents are used in Western countries but have not been approved by the Central Drug Standard Control Organization (CDSCO) for use in India.

Nifedipine and magnesium sulfate

- The concomitant administration of nifedipine and magnesium sulfate was not recommended as this can lead to neuromuscular blockade and fatal respiratory arrest, due to action of both molecules on blockage of calcium channels.
- Nifedipine usage: Nifedipine is not licensed for preterm labour management in India.

Neuroprotective agent

Magnesium sulphate[14, 32, 33]

- Confers neuroprotection to the neonate and is used for this benefit.
- Offer intravenous magnesium sulphate for neuroprotection of the baby to women between 24+0 and 31+6 weeks of pregnancy who are:
  - » In established preterm labour or
  - » Having a planned PTB within 24 hours.
- It is generally well tolerated but requires monitoring for toxic effects, including respiratory depression and cardiac arrest at supertherapeutic levels.
- Common side effects: Maternal side effects include flushing, nausea, headache, drowsiness, and blurred vision. Magnesium sulfate can cross the placenta, potentially causing respiratory and motor depression in neonates.
- Effectiveness: While magnesium sulfate was used as a tocolytic agent in the past, currently it is no longer used as tocolytic.

Dosage regime[15]

- A loading dose of 4 g (8 ml of 50% magnesium sulphate), diluted with 12 ml of saline 0.9% (total 20 ml), is given IV over 5–10 minutes using a 20 ml syringe.
- A maintenance dose of 10 g (20 ml magnesium sulphate), diluted with 30 ml of saline 0.9% (total 50 ml) is set up to deliver 1 gram per hour (5 ml/hr) using a syringe driver, until delivery.
- If delivery is imminent, it is appropriate to give only the loading dose.
- For a planned lower segment cesarean section delivery, administer magnesium sulphate prior to 24 hours of delivery.

ROLE OF PROPHYLACTIC CERVICAL CERCLAGE

- Consider prophylactic cervical cerclage for women in whom a transvaginal ultrasound scan has been carried out between 16–24 weeks of pregnancy that reveals a cervical length of less than 25 mm and who have either:[14]
  - » Had PTL or PPROM (history indicated cervical insufficiency or ultrasound indicated).
  - » A history of cervical trauma.

Progesterone

- Indications: Short cervix on transvaginal ultrasound.[21]
- For asymptomatic women with singleton pregnancy without prior spontaneous PTB and with transvaginal sonography (TVS) – cervical length (CL) measurement of ≤25 mm before 24 weeks, administration of natural vaginal progesterone is recommended.[34]

Maternal antenatal corticosteroids

- For women between 23+0 and 23+6 weeks of pregnancy who are in suspected or established PTL, are having a planned PTB or have PPROM discuss with the woman (and her family members or care givers as appropriate) the use of maternal corticosteroids in the context of her individual circumstances.[14]
- Consider maternal antenatal corticosteroids 24–26 weeks of pregnancy who are in suspected or established, or having a planned PTB or have PPROM.[14]
- Offer maternal antenatal corticosteroids 26+0 and 33+6 weeks of pregnancy who are in suspected or established PTL, are having a planned PTB or have PPROM.[14]

Choice of corticosteroids[35]

- Dexamethasone or betamethasone either can be used.
- Dosages: Dexamethasone/Betamethasone 12 mg IM, two doses, 24 hours apart should be administered.[35]
- Do not routinely offer repeat courses of maternal corticosteroids, but take into account:
  - » The interval since the end of the last course
  - » Gestational age
  - » The likelihood of birth within 7 days.

ANTIBIOTICS IN PRETERM LABOUR/PPROM

Should antibiotics be given?

Table 4. Antibiotic use in preterm labour/PPROM

Recommendation	Evidence quality	Strength	Notes
Erythromycin should be given 10 days following the diagnosis of PPROM, or until the woman is in established labour (whichever is sooner)	1+	A	A Cochrane review demonstrated benefits when antibiotics were administered; it reduced chorioamnionitis, prolonged latency, and improved neonatal outcomes.[36]

- The ideal agent is penicillin if the patient is allergic to erythromycin
- Co-amoxiclav is not recommended owing to its association with NEC

WHEN DO WE PLAN DELIVERY?

When is the appropriate time to deliver the baby?

Table 5. Appropriate time for delivery of the baby

Recommendation	Evidence quality	Strength	Notes
Women in whom pregnancy is complicated by PPROM and who have no contraindications to continuing the pregnancy should be offered expectant management care as this is associated with better outcomes compared with early birth.[37]	1+	A	A Cochrane review found clear benefits from expectant management, rather than early delivery, following PPROM.[37]
Early delivery may be preferable when PPROM occurs beyond 34+0 weeks of gestation in women known to be colonized with group B streptococcus[15]	4	D	RCOG Green-top Guideline No. 36.

RCOG: Royal College of Obstetricians and Gynecologists; PPROM: Preterm premature rupture of the membranes.

WHICH IS THE PREFERRED ROUTE OF DELIVERY?

Discuss the general benefits and risks of cesarean section and vaginal birth with women in suspected, diagnosed or established PTL and women with P-PROM (and their family members or care givers as appropriate).[15]

WHAT ARE THE OPTIONS IF THERE IS A MALPRESENTATION?

Consider cesarean section for women presenting in suspected, diagnosed or established PTL between 26+0 and 36+6 weeks of pregnancy with breech presentation.[15]

HOW DO WE MONITOR THE FETUS IN LABOUR?

Discuss with the woman[15]

- Counsel the patient and close relatives with regards to monitoring of the fetus.
- Continuous fetal heart rate monitoring should ideally be performed.

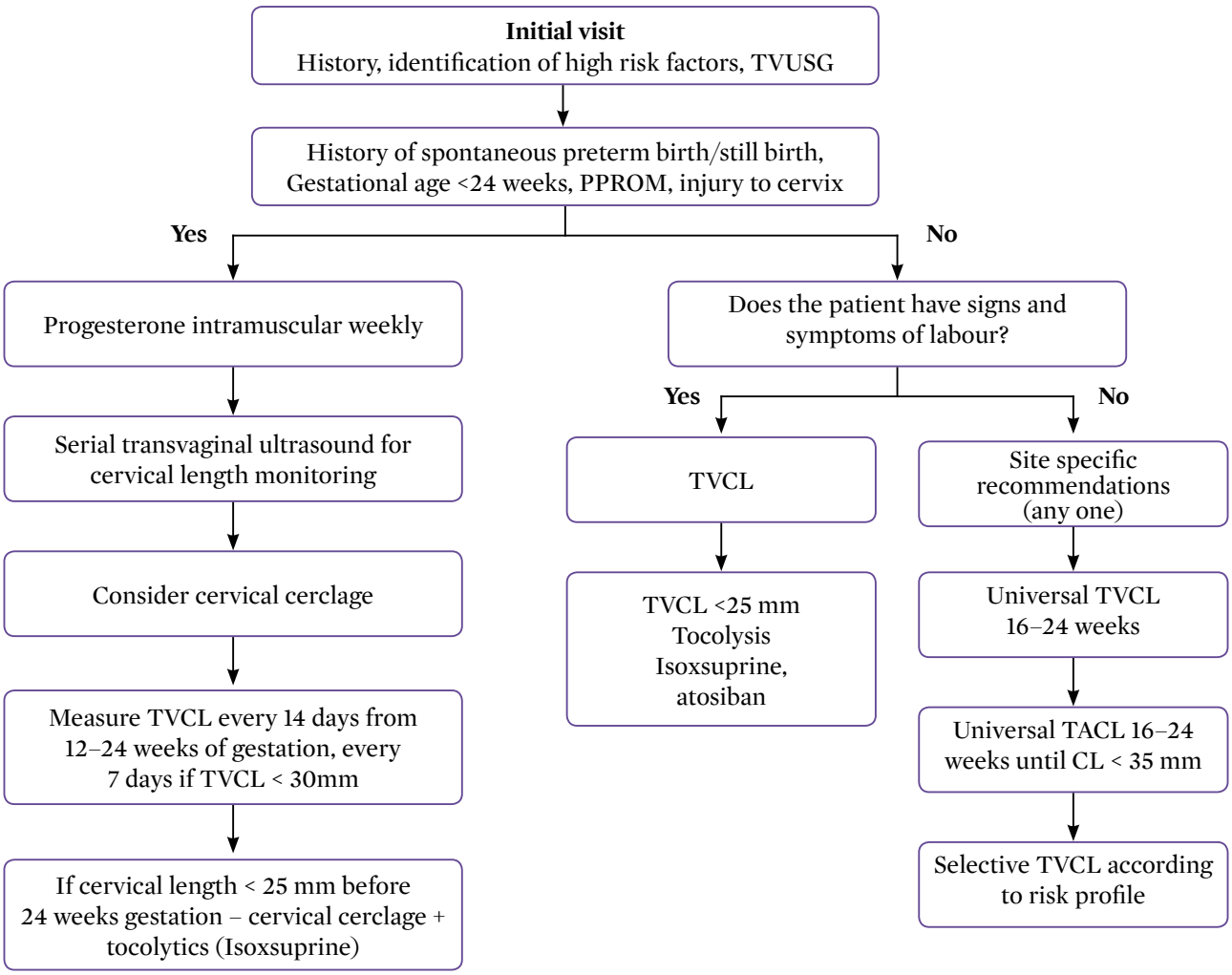
Delivery considerations[15]

- Aim for atraumatic delivery
- Avoid Ventouse
- Obstetric forceps, if indicated
- Neonatologist present
- Early transfer to NICU after stabilization
- Delayed cord clamping is recommended except in compromised conditions of fetus and the mother

CLINICAL PRACTICE ALGORITHM FOR THE MANAGEMENT OF PRETERM LABOUR[9,10,15]

Acute tocolysis refers to the short-term use of medications to inhibit uterine contractions and delay PTL, typically for 48 hours. The primary goal is to allow time for corticosteroid administration to enhance fetal lung maturity and facilitate in-utero transfer to a higher-level care facility if needed.

Maintenance tocolysis involves the prolonged use of tocolytic agents after initial acute tocolysis to prevent recurrent preterm contractions and delay delivery.



TVCL: Transvaginal cervical length; TACL: Transabdominal cervical length; CL: Cervical length; PPROM: Preterm premature rupture of the membranes; TVUSG: Transvaginal ultrasound

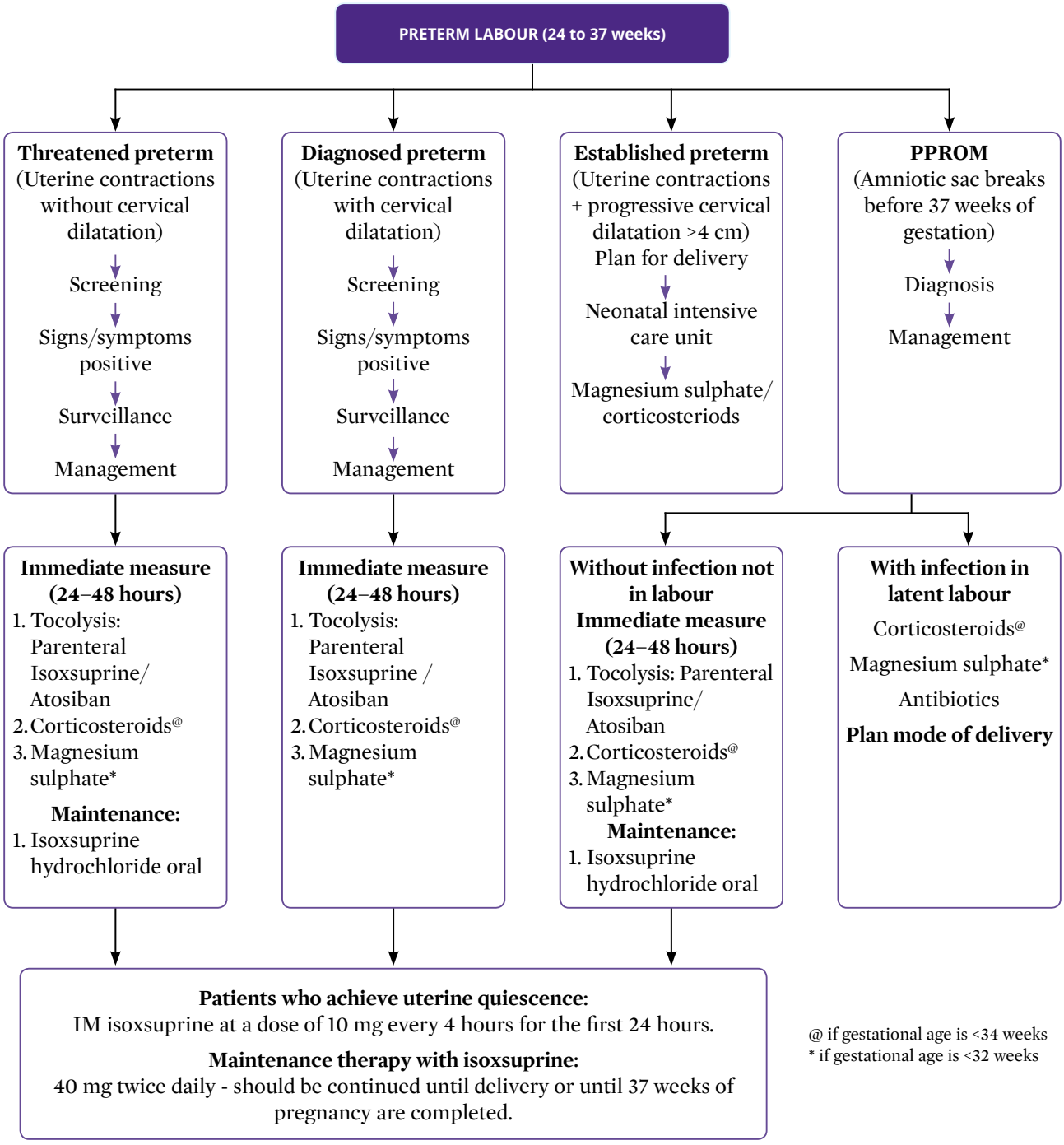


Table 6. Isoxsuprine dosage for acute and maintenance tocolysis

Phase	Route	Dosage	Duration
Acute tocolysis	IV	40 mg infusion until uterine quiescence	Until stable
	IM	10 mg every 4 hours	First 24 hours
Maintenance therapy	Oral (SR capsules/ tablets)	In divided dosage 60 to 80 mg daily	Until 37 weeks

PPROM: Preterm premature rupture of the membranes; SR: Sustained release; IV: Intravenous; IM: Intramuscular

CONCLUSION

1. Need for Indian Guidelines

- Preterm labour management in India faces unique challenges due to demographic variations, socioeconomic disparities, and healthcare infrastructure limitations. While global guidelines provide a framework, they may not always align with the realities of the Indian healthcare system.
- India has for the highest number of PTB globally, with risk factors such as maternal malnutrition, infections, and limited access to antenatal care playing a significant role.
- There is a pressing need for India-specific guidelines that address local risk factors, resource constraints, and cultural practices. Tailored interventions, such as the use of maintenance tocolytics such as isoxsuprine, are essential to improve obstetric outcomes.

2. Different Tocolytics in India

- In India, the management of PTL relies on a limited range of tocolytics due to regulatory approvals and cost considerations.
- The CDSCO has approved only isoxsuprine and atosiban for PTL management.
- Off-label drugs like nifedipine and indomethacin, commonly used in Western countries, are not approved for this indication in India, limiting their use despite their global acceptance.

3. Isoxsuprine and Atosiban: Approved Tocolytics in India

- Isoxsuprine is the most widely used tocolytic in India, with over six decades of clinical use. It is approved for both acute and maintenance tocolysis and has demonstrated efficacy in prolonging pregnancy, improving neonatal outcomes, and reducing NICU admissions.
  - » **Acute tocolysis**: IV infusion (40 mg) until uterine quiescence, followed by IM injections (10 mg every 4 hours) for 24 hours.
  - » **Maintenance therapy**: Oral sustained-release capsules (40 mg twice daily) until 37 weeks of gestation.
- **Atosiban**, an oxytocin receptor antagonist, is also approved but is less commonly used due to its higher cost and limited availability in resource-constrained settings.

4. Nifedipine

Nifedipine, a calcium channel blocker, is not approved by the CDSCO for PTL management in India. Despite its usage, the safety and efficacy remain unvalidated.

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