
بسم الله الرحمن الرحيم

Risk of Venous Thromboembolism during Pregnancy and the Puerperium

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RISK ASSESSMENT

- VTE increases with gestational age
- maximum just after delivery.
- Caesarean section is a significant risk
- vaginal deliveries are also at risk.
- postpartum is five-fold higher to antepartum

RISK ASSESSMENT

- Assessment of risk
- In early pregnancy or prepregnancy.
- Repeated if admitted to hospital
- Immediately postpartum
- Repeated again intrapartum

RISK ASSESSMENT

- Pre-existing
- Obstetric risk factors
- New onset/transient
- Potentially reversible
- May resolve

And therefore what is important is an ongoing individual risk assessment

HIGH RISK

Any previous VTE except a single event related to major surgery

Requires antenatal prophylaxis with LMWH

Refer to trust-nominated thrombosis in pregnancy expert/team

low-risk thrombophilia

Heterozygous for factor V Leiden prothrombin G20210A mutations

High-risk thrombophilia

Antithrombin deficiency

protein C or S deficiency

compound or homozygous for low-risk thrombophilias

1 SCORE

- Family history of unprovoked or estrogen-related VTE in first-degree relative
- Known low-risk thrombophilia (no VTE)
- Age (> 35 years)
- Obesity BMI> 30
- Parity ≥ 3
- Smoker
- Gross varicose veins

Symptomatic or
above knee
or associated with
phlebitis/oedema/skin changes

1 SCORE

- Pre-eclampsia in current pregnancy
- ART/IVF (antenatal only)
- Multiple pregnancy
- Elective caesarean section
- Mid-cavity or rotational operative delivery
- Prolonged labour (> 24 hours)
- PPH (> 1 litre or transfusion
- Preterm birth < 37+0 weeks in current pregnancy
- Stillbirth in current pregnancy

2 SCORE

- Obesity
- BMI ≥ 30 = 1; BMI ≥ 40 = 2
- Caesarean section in labour

3 SCORE

- Previous VTE provoked by major surgery
- Known high-risk thrombophilia
- Medical comorbidities e.g. cancer, heart failure; active systemic lupus erythematosus, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease; current intravenous drug use
- Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, postpartum sterilisation

4 SCORE

- Previous VTE (except a single event related to major surgery)
- APS
- Hyperemesis
- (first trimester only) OHSS

MANAGEMENT

- If total score ≥ 4 antenatally, consider thromboprophylaxis from the first trimester.
- If total score 3 antenatally, consider thromboprophylaxis from 28 weeks.
- If total score ≥ 2 postnatally, consider thromboprophylaxis for at least 10 days.
- If prolonged admission (≥ 3 days) or readmission to hospital within the puerperium consider thromboprophylaxis.

- pretnatally Fewer than three risk
- Mobilisation and
- avoidance of dehydration factors

Postnatal assessment and management

- Any previous VTE‘
- Anyone requiring antenatal LMWH
- High-risk thrombophilia
- Low-risk thrombophilia + FHx

HIGH RISK

At least 6 weeks’ postnatal prophylactic LMWH

Postnatal assessment

INTERMEDIATE RISK

At least 10 days' postnatal prophylactic LMWH

Antenatal and postnatal prophylactic dose of LMWH

- Weight < 50 kg = 20 mg enoxaparin/2500 units
- Weight 50–90 kg = 40 mg enoxaparin/5000 units
- Weight 91–130 kg = 60 mg enoxaparin/7500 units
- Weight 131–170 kg = 80 mg enoxaparin/10 000
- Weight > 170 kg = 0.6 mg/kg/day enoxaparin/ 75 u/kg/day

Minidose prophylactic UFH, *5000 units SC Q12 h*

- Prophylactic UFH, 5000 to 10,000 units SC Q 12h
- UFH, 5000 to 7500 units SC Q 12h in first trimester
- UFH, 7500 to 10,000 units SC Q 12h in the second trimester
- UFH, 10,000 units SC Q 12h in the third trimester, unless the aPTT is elevated

Contraindications/cautions to LMWH use

- Bleeding disorder (e.g. haemophilia, von Willebrand's or acquired coagulopathy)
- Active antenatal or postpartum bleeding (e.g. placenta praevia)
- (platelet count < 75 × 109/l)
- Acute stroke in previous 4 weeks (haemorrhagic or ischaemic)
- Severe renal disease ([GFR] < 30 ml/minute/1.73m2)
- Severe liver disease (prothrombin time above normal range or known varices)
- Uncontrolled hypertension (blood pressure > 200 mmHg systolic or > 120 mmHg diastolic)

The risk of VTE should be discussed with women at risk and the reasons for individual recommendations explained

what is the magnitude of risk

- Previous VTE or thrombophilia Heritable in 20– 50% of pregnancy-related VTE
- Obesity 60% of PE
- Age: 35 and over had a 70% increase in risk
- Immobility and long-distance travel

The NICE and the RCOG : all long-distance (more than four hours) travel (not exclusively by air) and antepartum immobilisation (defined as strict bed rest 1 week or more prior to delivery

Admission to hospital

18-fold increased risk of first VTE

Remains increased after discharge

Being six-fold higher in the 28 days after discharge

women with previous VTE
risk of recurrence in
pregnancy and
postpartum
2–11%.

Heritable thrombophilia &previous VTE

previous VTE with antithrombin deficiency

(who will often be on long-term oral anticoagulation)

higher dose LMWH (either 50%, 75% or full treatment dose)

RISK ASSESSMENT

- Women in whom the original VTE was unprovoked/idiopathic or related to estrogen (estrogen containing contraception/pregnancy) or related to a transient risk factor other than major surgery or who have other risk factors
- **should be offered thromboprophylaxis with LMWH throughout the antenatal period**

RISK ASSESSMENT

- In women in whom the original VTE was provoked by major surgery from which they have recovered and who have no other risk factors

  Thromboprophylaxis with LMWH can be withheld antenatally until 28 week

- They require close surveillance for the development of other risk factors

Women with previous VTE should not be screened for thrombophilia in pregnancy unless the result will influence recommendations regarding thromboprophylaxis

Detection of antithrombin deficiency or APS will alter the dose of thromboprophylaxis offered in pregnancy

When should thromboprophylaxis be started?

previous VTE should begin as early in pregnancy as practical.

with four other risk factors, should be considered for antenatal prophylaxis throughout pregnancy.

with three other risk factors, can start antenatal prophylaxis at 28 weeks of gestation

What are the first trimester risk factors for VTE and how should they be managed?

- admitted with hyperemesis: should be
- discontinue thromboprophylaxis when the hyperemesis resolves.

- OHSS : should be considered for thromboprophylaxis in the first trimester.

- IVF : pregnancy and three other risk factors should be considered for thromboprophylaxis starting in the first trimester

At present it is unclear

- whether women undergoing surgical management of miscarriage and surgical termination of pregnancy are at increased risk of VTE

When should thromboprophylaxis be interrupted for delivery?

- LMWH
- vaginal bleeding or once labour begins.
- Regional techniques should be avoided until at least 12 hours after LMWH.
- LMWH should not be given for 4 hours after use of SA or after the epidural catheter has been removed

Therapeutic LMWH

- Regional techniques should be avoided if possible for at least 24 hours.

High risk for haemorrhage

- May be managed with anti-embolism stockings (AES), foot impulse devices or intermittent pneumatic compression devices

Asymptomatic thrombophilia

- family history of VTE and an identified thrombophilia
- **For 6 weeks' postnatal thromboprophylaxis**
- **LMWH for 10 days**

Those having an caesarean section +any additional risk factors

Which agents should be used for thromboprophylaxis?

- Doses of LWHs should be reduced in renal impairment.
- Doses based on most recent weight
- monitor the platelet if the woman has had prior exposure to (UFH).
- Anti-Xa levels is not required when LMWH is used for thromboprophylaxis.
- safe in breastfeeding

- Prolonged UFH use may result in osteoporosis and fractures, but this risk is very low with LMWH
- Increased risk of bleeding is more controversial
- Less than 2% with prophylactic doses
- Heparin-induced thrombocytopenia (HIT) is lower with LMWH

Anti-Xa levels

- provide only a rough guide of the concentration of heparin present and provide little or no evidence on the efficacy in relation to prevention of thrombosis

Unfractionated heparin

- At very high risk of thrombosis
- Used peripartum in preference to LMWH
- Where increased risk of haemorrhage
- Regional anaesthetic techniques may be required
- Platelet count every 2–3 days from days 4–14 or until heparin is stopped

UFH

- Shorter half-life than LMWH
- More complete reversal of its activity by protamine sulfate

Regional analgesia

UFH less than (4 hours)
LMWH (12 hours)
less concern regarding neuraxial haematomas with UFH

Low-dose aspirin

- Aspirin is not recommended for thromboprophylaxis in obstetric patients
- NICE guideline
- 300 mg or more of aspirin daily reduced the risk of postoperative DVT in patients undergoing a variety of surgical procedures.
- Any benefit of aspirin in VTE prevention appears uncertain and significantly less than that of LMWH

Warfarin

- Use in pregnancy is restricted
- Where heparin is considered unsuitable
- Mechanical heart valves.
- Women receiving long-term anticoagulation with warfarin can be converted from LMWH to warfarin postpartum when the risk of haemorrhage is reduced, usually 5–7 days after delivery.
- Warfarin is safe in breastfeeding

Warfarin

- Crosses the placenta
- Congenital abnormalities
- Warfarin embryopathy
- 5% of fetuses exposed between 6 and 12 weeks
- Dose-dependent greater than 5 mg/ day

Warfarin

- Conversion from LMWH back to warfarin should be delayed for at least 5–7 days after delivery to minimise the risk of haemorrhage during the period of overlap of LMWH and warfarin treatment

Anti-embolism stockings

- With a calf pressure of 14–15 mmHg is recommended in pregnancy and the puerperium
- Hospitalised and have a contraindication to LMWH.
- Hospitalised post-caesarean section (combined with LMWH) and considered to be at particularly high risk of VTE (e.g. previous VTE, more than four risk factors antenatally or more than two risk factors postnatally) and women travelling long distance for more than 4 hours.

Anti-embolism stockings

- More DVTs in pregnant women are iliofemoral
- Nonpregnant population where calf vein DVTs.
- Studies of AES in pregnancy have only concerned full-length stockings.
- Full-length stockings becoming bloodstained. full-length AES are advocated for pregnant women but knee-length AES should be considered if full-length AES are ill-fitting or compliance is poor.

THE END

اقدامات توصیه شده، بعد از ارزیابي عوامل خطر در مقطع بارداري

نتیجه ارزیابی	اقدام
مجموع امتیاز= ٤ یا بیشتر	تجویز داروی ضد انعقاد با دوز پروفیلاکسی از ابتدای بارداری توجه: در موارد سابقه VTE یا ابتلا به ترومبوفیلی ارثی یا اکتسابی با توجه به اینکه مقدار تجویز دارو ممکن است بیشتر باشد باید با متخصص هماتولوژی یا داخلی نیز مشاوره شود
مجموع امتیاز= ۳	تجویز داروی ضد انعقاد با دوز پروفیلاکسی از هفته ۲۸ بارداری

نکات مهم

در مورد برخي عوامل خطر حتي اگر به تنهايي وجود داشته باشند به شرح زير اقدام شود:

- زناني كه به علت استفراغ شديد بارداری بستری مي شوند بايد دارو به صورت پروفيلاكسي برای آنان تجويز و پس از بهبودی، دارو قطع شود.
- زنان مبتلا به سندرم هيپراستيمولیشن تخمدان بايد تا پايان سه ماهه اول، دارو به صورت پروفيلاكسي برای آنان تجويز شود.
- در صورت انجام عمل جراحي در بارداری، تجويز دارو به صورت پرفيلاكسي حداقل تا زمان ترخيص يا تحرک كامل بيمار بايد اين است كه فرد Mobilityادامه يابد منظو ر ا ز تحرک كامل يا در
- زمان بيداری، بيش از 50 درصد اوقات در حال حركت بوده و در بستر نباشد.

- در دوران شیردهي بلامانع است.
- ASA UFH LMWH

- fondaparinux,dabigartan. ترجیحا جایگزین شود
- محدود به واکنشهای آلرژیک شدید به هپارین HIT

اقدامات توصيه شده، بعد از ارزيابي عوامل خطر در مقطع پس از زايمان طبيعي يا سزارين

- مجموع امتياز3 يا
- بيشتر
- تجويز داروی ضد انعقاد با دوز پروفيلاكسي تا 10 روز پس از زايمان
- مجموع امتياز= 2
- تجويز داروی ضد انعقاد با دوز پروفيلاكسي حداقل تا ترخيص يا زمان تحرک كامل بيمار

INTERMEDIATE RISK

- Hospital admission
- Single previous VTE related to major surgery
- High-risk thrombophilia + no VTE prc prs antith3
- Medical comorbidities e.g. cancer, heart failure, active SLE, IBD or inflammatory polyarthro-pathy, nephrotic syndrome, type I DM with nephropathy, sickle cell disease, current IVDU
- Any surgical procedure e.g. appendicectomy

Pre exist

- Previous VTE provoked by major surgery
- Known high-risk thrombophilia
- Medical comorbidities e.g. cancer, heart failure; active systemic lupus erythematosus, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease; current intravenous drug user

Transient risk factors:

- OHSS (first trimester only)
- long-distance travel Immobility
- hyperemesis; Dehydration
- current systemic infection
- Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, postpartum sterilisation

Caesarean section in labour

- BMI ≥ 40 kg/m2
- Readmission or prolonged admission (≥ 3 days) in the puerperium
- Medical comorbidities e.g. cancer, heart failure, active SLE, IBD or inflammatory polyarthropathy; nephrotic syndrome, type I DM with nephropathy, sickle cell disease, current IV

- Postnatal assessment
- Fewer than two risk factors
- LOWER RISK
- Early mobilisation and avoidance of dehydration

Women with B-lactamas allergy(ACOG 2018)

- There are no well studied alternative regimens for women allergic to B- lactam antibiotic s, it may be reasonable to administer erythromycin alone.

Women with Penicillin allergy:

- If the patient history suggest **a low risk for anaphylaxis** (isolated maculopapular rash without urticarial or pruritus) we suggest:

- Cephazolin 1 gr IV every 8 h for 48 h
  - Plus
- A single oral dose of azithromycin 1 gr upon admission.

  - followed by
- cephalexin 500 mg orally 4 times daily
- Erythromycin 333 mg every 8 h for 5 days.

- If the patient history suggest **a high risk for anaphylaxis** (anaphylaxis , angioedema, respiratory distress, urticaria, particularly if these symptoms occurred within 30 min of drug administration) we suggest:

- Clindamycin 900 mg every 8 h for 48 h
  - Plus
- Gentamicin 5 mg/kg every 24 h for 2 days
  - Plus
- A single dose of azithromycin 1 gr upon admission

  - Then:
- Oral clindamycin 300 mg every 8 h for 5 days
- and Erythromycin 333 mg every 8 h for 5 days.

Antibiotic therapy
In
intraamniotic infection

The American College of Obstetricians and Gynecologists(2018) makes the following recommendations:

- the diagnosis of suspected intraamniotic infection is made when :
- the maternal temperature is greater than or equal to 39.0°C without a clear source
- or when the maternal temperature is 38.0–38.9°C on two occations (30 min apart) and one additional clinical risk factor is present including:

- Leukocytosis
- Purulent cervical drainage
- Fetal tachycardia

- **Confirmed IAI is based on:**

- Positive AF Test result (gram stain, glucose level, culture result)
- Or placental pathology

Antibiotic therapy in intra amniotic infection

- **intra partum regimen:**

- Ampicillin 2 gr IV Q 6 h
- Plus
- Gentamicin 5 mg/kg once daily

Alternative regimen :

- **Regimen 1:**

- Ampicillin 2 gr Q 6 h
  - Plus
- Gentamicin 1/5 mg/kg Q 8h for patient with NL renal function (or 2mg/kg stat then 1/5 mg/kg Q 8h)

- **Regimen 2 :**
- Ampicillin – sulbactam 3 gr Q 6 h

- **Regimen 3 :**
- Ticarcillin – clavulanate 3/1 gr Q 4 h

- **Regimen 4 :**
- Cefoxitin 2 gr Q 8h

- **Regimen 5 :**
- Cefotetan 2 gr Q 12 h

- **Regimen 6:**
- Piperacillin – tazobactam 3/375 gr Q6h or Q8h

- **Regimen 7:**
- Ertapenem 1 gr Q 24 h

Table 1. Recommended Antibiotic Regimens for Treatment of Intraamniotic Infection

Primary Regimen	
Recommended Antibiotics	**Dosage**
• Ampicillin *and* • Gentamicin	2 g IV every 6 hours 2 mg/kg IV load followed by 1.5 mg/kg every 8 hours *or* 5 mg/kg IV every 24 hours
Recommended Antibiotics (Mild Penicillin Allergy)	**Dosage**
• Cefazolin *and* • Gentamicin	2 g IV every 8 hours 2 mg/kg IV load followed by 1.5 mg/kg every 8 hours *or* 5 mg/kg IV every 24 hours
Recommended Antibiotics (Severe Penicillin Allergy)	**Dosage**
• Clindamycin *or* • Vancomycin* *and* • Gentamicin	900 mg IV every 8 hours 1 g IV every 12 hours 2 mg/kg IV load followed by 1.5 mg/kg every 8 hours *or* 5 mg/kg IV every 24 hours
Postcesarean delivery: One additional dose of the chosen regimen is indicated. Add clindamycin 900 mg IV or metronidazole 500 mg IV for at least one additional dose. *Postvaginal delivery*: No additional doses required; but if given, clindamycin is not indicated.	
Alternative Regimens	
• Ampicillin–sulbactam	3 g IV every 6 hrs
• Piperacillin–tazobactam	3.375 g IV every 6 hrs or 4.5 g IV every 8 hrs
• Cefotetan	2 g IV every 12 hrs
• Cefoxitin	2 g IV every 8 hrs
• Ertapenem	1 g IV every 24 hrs
Postcesarean delivery: One additional dose of the chosen regimen is indicated. Additional clindamycin is not required. *Postvaginal delivery*: No additional doses required, but if given, clindamycin is not indicated.	

Abbreviation: IV, intravenous.

*Vancomycin should be used if the woman is colonized with group B streptococci resistant to either clindamycin or erythromycin (unless clindamycin-inducible resistance testing is available and is negative) or if the woman is colonized with group B streptococci and antibiotic sensitivities are not available.

Recommended antibiotic regimen for treatment of IAI (ACOG)

Antibiotic	Dosage
Ampicillin & Gentamicin	2 gr IV Q6 h 2 mg/kg stat then 1/5 mg/kg q 8h Or 5 mg/kg Q 24h
Mild penicillin allergy	
Cefazolin & Gentamicin	2 gr IV Q8 h 2 mg/kg stat then 1/5 mg/kg q 8h Or 5 mg/kg Q 24h
Sever penicillin allergy	
Clindamycin or Vancomycin & Gentamicin	900 mg IV Q 8h 1 gr IV Q12h 2 mg/kg stat then 1/5 mg/kg q 8h Or 5 mg/kg Q 24h

Drug regimen in Cesarean delivery in IAI:

- Anaerobic ?

- Ampicillin 2 gr Q 6h
  - Plus
- Gentamicin 5 mg/kg once daily
  - Plus
- Either clindamycin 900 mg or metronidazole 500 mg
  - Also
- Azithromycin 500mg IV as a part of routine prophylaxis for c/s

Postpartum treatment in IAI:

- Continue the administration of antibiotics after delivery in all patient until they are afebrile and asymptomatic for at least 24 hours
- There is no evidence that oral antibiotics are beneficial after discontinuation of parenteral therapy

Postpartum treatment in IAI (ACOG)

- **After vaginal delivery:**
- They may not require postpartum antibiotics.

- **After cesarean delivery :**
- At least one additional dose of antimicrobial agent is recommended.

- Presence of the other maternal risk factors such as bacteremia or persistent fever in postpartum period may be used to guide continuation of antibiotic therapy both in vaginal and cesarean deliveries.

توضیحات

* علائم کوریوآمنیونیت:

پارگی کیسه آب به همراه تب (۳۸ درجه سانتی گراد و بیشتر) و حداقل یکی از علائم زیر، کوریوآمنیونیت محسوب می شود:

ضربان قلب جنین بیش از ۱۶۰ بار در دقیقه، تندرنس رحمی، نبض مادر بیش از ۱۰۰ بار در دقیقه، ترشحات بدبو و تعداد گلبول های سفید بیش از ۱۵۰۰۰ یا افزایش آن.

** درمان کوریوآمنیونیت:

در موارد ختم بارداری به طریق زایمان واژینال: تزریق آمپی سیلین ۲ گرم وریدی هر ۶ ساعت و جنتامایسین ۱/۵ mg/kg هر ۸ ساعت (با عملکرد طبیعی کلیوی)

در موارد ختم بارداری به طریق سزارین: کلیندامایسین ۹۰۰ میلی گرم هر ۶ ساعت یا مترونیدازول ۵۰۰ میلی گرم هر ۸ ساعت، به رژیم آمپی سیلین ۲ گرم وریدی هر ۶ ساعت و جنتامایسین ۱/۵ mg/kg هر ۸ ساعت (با عملکرد طبیعی کلیوی) اضافه می شود.

درمان آنتی بیوتیکی حداقل تا ۲۴ ساعت پس از قطع تب و بهبود علایم بالینی ادامه یابد.

در صورت حساسیت مادر به پنی سیلین، از وانکومایسین استفاده شود.

*** درمان آنتی بیوتیکی در زمان ختم بارداری:

زیر هفته ۳۷ بارداری تجویز ۲ گرم آمپی سیلین هر ۶ ساعت (۴۸ ساعت اول وریدی و ۵ روز بعد خوراکی)

از هفته ۳۷ بارداری به بعد تجویز ۲ گرم آمپی سیلین هر ۶ ساعت تا زمان زایمان در صورتی که بیش از ۱۸ ساعت از پارگی کیسه آب گذشته باشد.

**** درمان آنتی بیوتیکی در دوره انتظار:

در ۴۸ ساعت اول تزریق ۲ گرم آمپی سیلین وریدی هر ۶ ساعت تا دو روز و سپس آموکسی سیلین ۵۰۰ میلی گرم خوراکی هر ۸ ساعت و اریترومایسین به میزان ۴۰۰ میلی گرم هر ۶ ساعت تا پایان هفته اول.

نکته ۱: NST در هفته های ۲۵ تا ۲۸ بارداری قابل تفسیر نیست.

نکته ۲: در صورت نیاز به تجویز کورتیکواستروئید مطابق راهنمای صفحه ۲۰۵

نکته ۳: در صورت القا زایمانی مادر، اگر بیش از ۱۲ ساعت در فاز نهفته باقی ماند ختم بارداری به روش سزارین انجام شود.

تجویز سولفات منیزیوم جهت حفاظت عصبی نوزاد

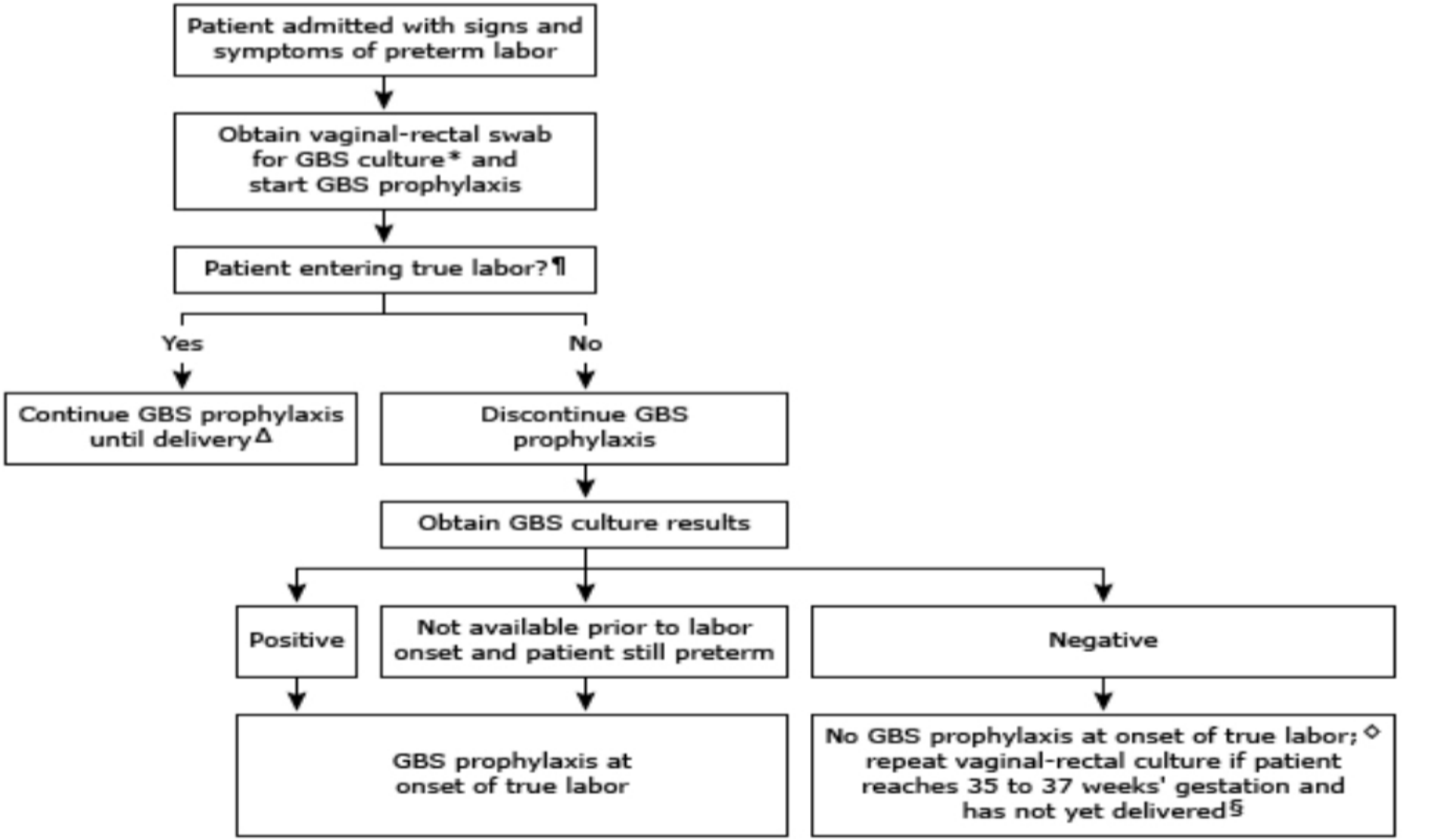
جهت حفاظت عصبی نوزادان در هفته ۳۲-۲۳ بارداری در صورت که وقت کافی وجود دارد، تزریق ۶ گرم سولفات منیزیوم اولیه و بعد هر ساعت ۲ گرم حداقل تا ۱۲ ساعت تجویز شود.

Antibiotic therapy in preterm labor

Antibiotic therapy in preterm labor

- There is no evidence – based role for antibiotic therapy in prevention of prematurity in patient with acute preterm labor.

GBS management:



Antibiotic therapy
in
Urinary tract infection
in
pregnancy

Asymptomatic bacteriuria

- Initialy asymptomatic women is defined as two consecutive voided urine specimen with ≥ 10^5 cfu/ml or a single catheterized urine specimen with one bacterial species isolated in a count ≥ 10^2

- In clinaical only one voided urine speciemen is typicall obtained and diagnosis is made with ≥ 10^5 cfu/ml with out obtaining a confirmatory repeat culture and for group B Streptococcus ≥ 10^4 cfu/ml.

- **Duration of treatment:**
- Short courses are preffered and usually is effective in eradicating asymptomatic bacteriuria

- **Follow up:**
- Repeat culture is recommended a week after completion of therapy

- If repeat culture has no growth , there is no indication for further testing in absence of symptoms

- If repeat culture yielded the same species **as the first culture** , we give either the same antimicrobial for a longer course (seven days vs three day) or a different antimicrobial for a typical duration.

- **For recurrent bacteriuria** 100 mg nitrofurantoin or cephalexin 250 mg orally at bed time for 21 days has been success (lucas 1994)

- For women with persistent or frequent bacteriuria recurrences , **suppressive therapy** for the reminder of pregnancy can be give routinely use 100mg nitrofurantoin at bedtime(Boggess,1996)

ACUTE CYSTITIS

- Acute cystitis should be suspected in pregnant women who complain about dysuria.
- Although urinary frequency and urgency are typical findings of acute cystitis, Systemic symptoms, such as fevers and chills, are absent in simple cystitis.
- it is reasonable to use a quantitative count $\geq 10^3$ cfu/mL in a symptomatic pregnant woman as an indicator of symptomatic UTI.

Antimicrobial treatment

- Antibiotic treatment of acute cystitis and asymptomatic bacteriuria in pregnant women is often **empiric**

- and then tailored to the susceptibility pattern of the isolated organism once urine cultures return.

Antimicrobial treatment

- Potential options for empiric and directed therapy include **beta-lactams , nitrofurantoin, and fosfomycin**

- For women are thought to be at risk for or have documented infection with extended spectrum beta lactamas – producing Enterobacteriaceae , **nitrofurantoin and fosfomycin** are potential oral options.

Antibiotics for asymptomatic bacteriuria and cystitis in pregnancy

Antibiotic	Dose	Duration	
Nitrofurantoin SR Nitrofurantoin	100 mg orally Q12 h 100 mg orally Q6h	5-7 days	Avoid use during first trimester and at the term and G6PD deficiency
Amoxicillin *	500mg orally Q8h or 875 mg Q12h	5-7 days	
Amoxicillin – clavulante	500mg orally Q8h or 875 mg Q12h	5-7 days	
Cephalexin *	500 mg orally Q6h	5-7 days	
Cefpodoxime	100 mg orally Q12h	5-7 days	
Fosfomycin	3 gr orally as single dose		
Trimethoprim-sulfamethoxazole	800/160 mg Q12h	Three days	Avoid use during first trimester and at the term

Duration of treatment

- As with asymptomatic bacteriuria, short courses of antibiotics are preferred, to minimize the antimicrobial exposure to the fetus.

- We treat acute cystitis with a three to seven day course of antibiotics as long as there are no symptoms suggestive of pyelonephritis

- **Follow-up** :
- As with asymptomatic bacteriuria, a follow-up culture should be obtained as a test of cure. We typically perform this a week after completion of therapy

Management of recurrent cystitis

- In women who have **three or more episodes** of recurrent cystitis during pregnancy, antimicrobial prophylaxis for the duration of pregnancy is a reasonable strategy to prevent additional episodes.

- Prophylaxis can be post coital if the cystitis is thought to be sexually related (which it commonly is) or continuous.

- In the setting of other conditions that potentially increase the risk of urinary complications during episodes of cystitis (eg, **diabetes or sickle cell trait**), prophylaxis following the first episode of cystitis during pregnancy is also reasonable.

Choice of antimicrobial for prophylaxis

- Ideally, daily or post coital prophylaxis with low-dose nitrofurantoin (50 to 100 mg orally post coitaly or at bedtime) or cephalexin (250 to 500 mg orally post coitaly or at bedtime) can be used

Acute pyelonephritis

- The typical symptoms of acute pyelonephritis in the pregnant woman include:
- fever (>38°C or 100.4°F)
- flank pain
- nausea, vomiting,
- and/or costovertebral angle tenderness.
- Symptoms of cystitis (eg, dysuria) are not always present.
- Pyuria is a typical finding.
- Most cases of pyelonephritis occur during the second and third trimesters.

Empiric antibiotics :

- Third generation cephalosporins , **such as ceftriaxone or beta-lactams** are the preferred antibiotics for initial empiric therapy of pyelonephritis

- The choice between them should be guided by local microbiology and susceptibility data as well as expected patient tolerance.

Prenatal regimen for empiric treatment of pyelonephritis

Antibiotic	Dose
Mild to moderate pyelonephritis	
cefteriaxon	1 gr Q 24 h
cefepime	1 gr Q 12 h
aztreonam	1 gr Q 8 h
Ampicillin + Gentamicin	1-2 gr Q 6 h + 1/5 mg/kg Q 8 h
Sever pyelonephritis with an impaired immune system and/or incomplete urinary drainage	
Piperacillin – tazobactam	3.375 gr Q 6h
Meropenem	1 gr Q 8h
Ertapenem	1 gr Q 24 h
Doripenem	500 mg Q 8h

Empiric antibiotics :

- **Fluoroquinolones and aminoglycosides**, which are often used for pyelonephritis in nonpregnant individuals, **should be avoided in pregnancy if possible.**

- For women with a history of infections with extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae (or other risk factors), **carbapenem** is an appropriate choice for empiric therapy.

- Some animal studies have shown adverse fetal effects with imipenem-cilastatin, so **meropenem, ertapenem, or doripenem are the preferred carbapenems for use during pregnancy**

- pregnant women generally have definite improvement within 24 to 48 hours of appropriate antibiotic therapy.

- Once afebrile for 48 hours, pregnant patients can be switched to oral therapy guided by culture susceptibility results and discharged to complete **10 to 14 days of treatment** .

- **Oral options are mainly limited to beta-lactams or, if in the second trimester, trimethoprim sulfamethoxazole.**

- **Nitrofurantoin and fosfomycin are not appropriate for treatment of pyelonephritis due to inadequate tissue levels**

- **If symptoms and fever persist beyond the first 24 to 48 hours of treatment:**

- A repeat urine culture and renal ultrasound should be performed to rule out persistent infection and urinary tract pathology.

- For women who do not use antimicrobial prophylaxis for the duration of pregnancy following an episode of pyelonephritis , we generally check **monthly** urine cultures to evaluate for recurrent bacteriuria and treat as indicated because of the risk of recurrent pyelonephritis.

Preventing recurrence :

- After an initial episode of pyelonephritis, low-dose antimicrobial preventive therapy with an agent to which the original organism is susceptible for the remainder of the pregnancy is a reasonable strategy

- If preventive therapy is utilized, reasonable options included:

- Nitrofurantoin (50 to 100 mg orally at bedtime) or cephalexin (250 to 500 mg orally at bedtime)

- bacteriuria can occur during preventive therapy, so we usually perform at least one later culture, such as at the start of the third trimester, to ensure preventive therapy is working.

- If a follow-up culture is positive (≥10^5colony-forming units/mL), then a course of antimicrobial therapy based on susceptibility data should be administered.

- In addition, the preventive regimen should be reassessed and adjusted if needed.

عفونت ادراری در بارداری- ادامه

راهنمای دارویی عفونت ادراری

سیستیت: پس از آنکه نمونه جهت کشت ادرار گرفته شد، درمان با یک آنتی‌بیوتیک مناسب مانند آموکسی‌سیلین ۵۰۰ میلی گرم سه بار در روز، آمپی‌سیلین ۵۰۰ میلی گرم سه بار در روز، سفالوسپورین ها و یا نیتروفورانتوئین ۱۰۰ میلی گرم دو بار در روز به مدت ۱۰ ـ ۳ روز تجویز می‌شود. یک تا دو هفته پس از درمان بیمار، کشت ادرار مجدداً گرفته می‌شود. اگر جواب کشت مجدداً مثبت باشد یا عفونت ادراری عود کند، آنتی‌بیوتیک مناسب با جواب کشت برای مدت سه هفته تجویز شود. در صورت عود مجدد، پس از درمان عفونت، به عنوان پروفیلاکسی، نیتروفورانتوئین ۱۰۰ میلی‌گرم و یا آموکسی‌سیلین ۲۵۰ میلی‌گرم یا سفالکسین ۲۵۰ میلی‌گرم یک دوز در هنگام خواب در تمام مدت بارداری تجویز شود.

نکته: در صورت عود مجدد جهت بررسی سنگ، سونوگرافی کلیه و مجاری ادراری انجام شود.

پیلونفریت: درمان آنتی‌بیوتیکی وریدی شامل سفازولین یا سفتریاکسون ۱ گرم ۲ بار در روز و یا آمپی‌سیلین به علاوه جنتامایسین است. درمان خوراکی یا قطع تب شروع و حداقل ۱۰ روز و حداکثر ۳ هفته ادامه دارد. ۱ تا ۲ هفته بعد مجدداً کشت ادرار انجام می‌شود. در صورت مثبت شدن مجدد کشت، درمان آنتی‌بیوتیکی مناسب با جواب کشت برای مدت ۵ هفته تجویز می‌شود. درمان پروفیلاکسی در تمام مدت بارداری نیز مانند درمان سیستیت انجام می‌شود.

باکتریوری آسیمپتوماتیک: درمان سه روزه یا تک دوز و پیگیری آن همانند سیستیت است. در صورت عدم قبول درمان پروفیلاکسی از طرف بیمار، هر دو هفته باید U/A, U/C انجام شود.

Antibiotic in labor &delivery
(ACOG 2018)

Is antibiotic prophylaxis appropriate for patients undergoing cesarean delivery?

- Cesarean delivery is a risk factor for postpartum infection
- Antibiotic prophylaxis is recommended for **all cesarean deliveries** unless the patient is already receiving an antibiotic regimen with equivalent broad spectrum coverage (eg, chorioamnionitis)
- Such prophylaxis should be administered **within 60 min before** the start of cesarean delivery
- If this is not possible (eg, need for emergent delivery) , prophylaxis should be administered **as soon as possible** after the incision is made.

Timing and choice of antibiotic regimen

- For c/s prophylaxis , a single dose of first generation cephalosporin , is the first line antibiotic of choice , unless significant drug allergic are present.
- A 1 gr intravenous dose of cefazolin as prophylaxis before c/s for women weighting 80 kg or less
- Increasing the dose to 2 gr for patient weighting 80 kg or more is recommended
- Administering 3 gr in patient weighting 120 kg or more (?)
- **For ease of administering , some institutions dispense a 2 gr cefazolin dose for all adult patient undergoing c/s.**

Surgical weight adjusted antibiotic prophylaxis regimen

weight	antibiotic	Intravenous regimen
Normal BMI (weight≤ 80 kg)	Cefazolin or Clindamycin + Gentamicin	1 gr 900 mg + 5 mg/kg
Obese (BMI ≥ 30) or Weight ≥ 80 kg)	Cefazolin or Clindamycin + Gentamicin	2gr 900 mg + 5 mg/kg

- The addition of 500mg azithromycin infused over 1 hour , to a standard antibiotic prophylaxis regimen may be considered for women undergoing **a nonelective c/s.**

- For most antibiotics including cefazolin , prophylaxis should be administered within 1 hour before the skin incision

- **These patients should receive an additional dose of the same antibiotic given for prophylaxis:**

1. Pateint with lengthy surgical procedure (eg, greater than two half-lives of antibiotic , which is 4 hour for cephazolin and measured from the initiation of preoperative dose, not from the onset of surgery)

2. Who experience excessive blood loss (eg , greater than 1500 ml)

Antibiotic prophylaxis appropriate for patient with PROM:

- ACOG and SOGC recommend the use of prophylactic antibiotic for PROM (less than 34 w) and delivery is not imminent with options including a regimen of amoxicillin and erythromycin for a total 7 days.
- A 2-day course of therapy with a combination of intravenous ampicillin and erythromycin followed by a 5 –day course of oral amoxicillin and erythromycin is recommended to prolong pregnancy and decreased short term neonatal complications
- Azithromycin has been substituted in situation for which erythromycin is not available .

Recommendations for the use of antibiotics in women preterm labor?

- **For patient with preterm labor with intact membranes:**

- Do not use antibiotics to prolong pregnancy

- Use intrapartum antibiotics to prevent GBS infection until GBS test result are available unless the patient has had a negative test result within 5 weeks.

- If the GBS test result is positive at the time of admission but true labor dose not ansue . The GBS prophylaxis should be discontinued and restarted at the onset of true labor.

Is antibiotic prophylaxis appropriate for patient undergoing repair of third or fourth degree laceration?

- A single dose of second generation cephalosporin (cefotetan or cefoxitin) or clindamycin if the patient was penicillin allergic , was protective against perineal wound complications.(Duggal et all ,2008)

Is antibiotic prophylaxis appropriate for patient undergoing cervical cerclage?

i. Evidence is insufficient to recommend antibiotic prophylaxis for history , US or examination – indicated cervical cerclage

ii. Similarly ,consistent data are lacking regarding the use of antibiotic prophylaxis for abdominal cerclage.

Is antibiotic prophylaxis appropriate for patient undergoing other obstetric procedure(ie, manual removal of the placenta , intrauterine balloon catheters or dilatation and curettage)?

- Anti microbial prophylaxis is recommended for women undergoing uterine evacuation for induced abortion or early pregnancy loss. (ACOG ,2009)

- ACOG advises Doxycycline 100mg orally one hour before uterine evacuation (suction D&C , D&E , surgical abortion) and 200 mg orally after procedure for prevention of surgical site infection.(ACOG bulletin 2009)

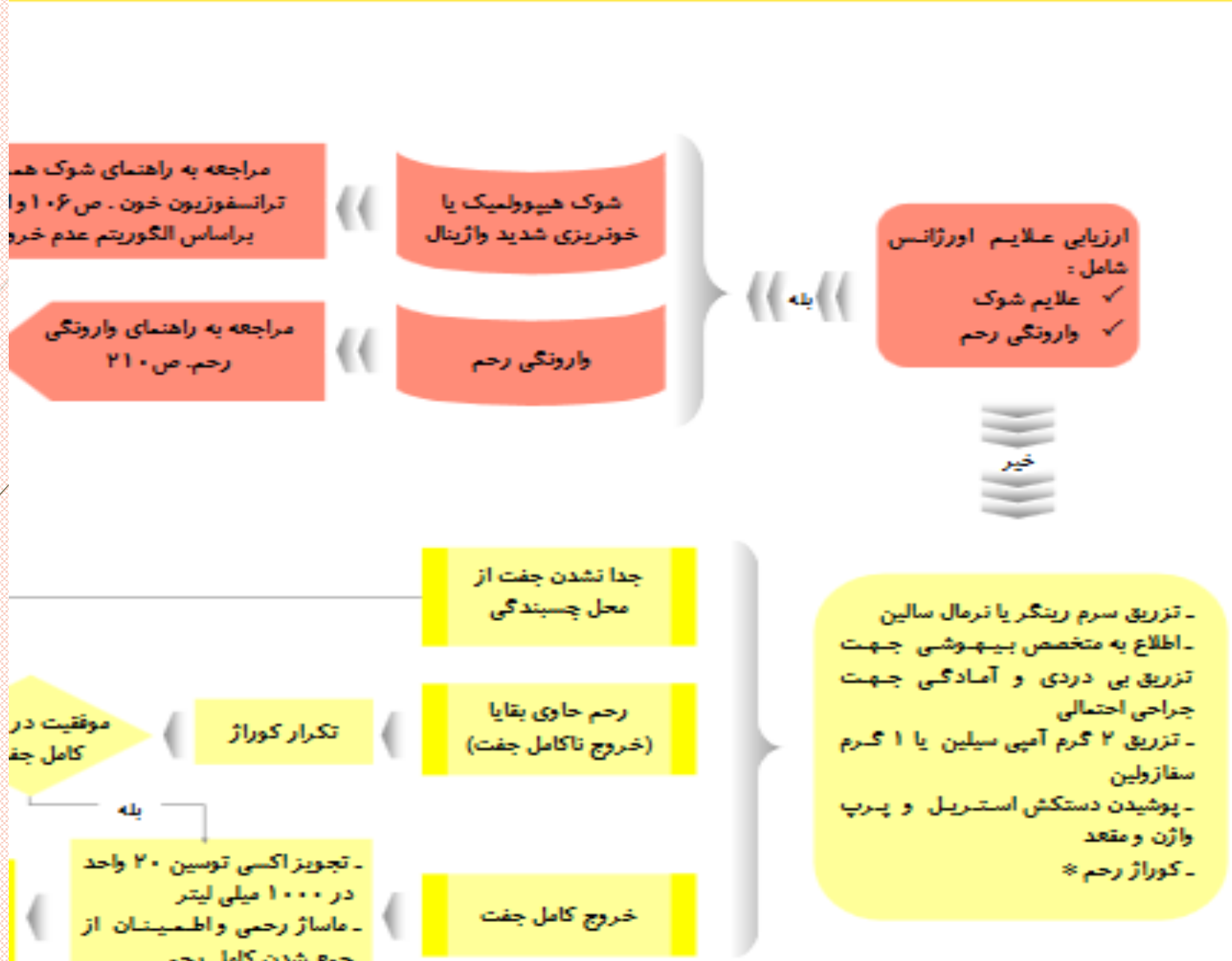
Is antibiotic prophylaxis appropriate for patient undergoing other obstetric procedure(ie, manual removal of the placenta , intrauterine balloon catheters or dilatation and curettage)?

- There are no data to recommend for or against prophylactic antibiotics for postpartum dilatation and curettage or placement of indwelling intra uterine balloon catheter in the clinical situation of retained placenta or postpartum hemorrhage.

- In the cases of manual extraction of placenta after vaginal delivery , WHO recommended to administer prophylactic antibiotics , although there are no data to support or refuse this practice(Chongsomchai et al , 2014)

- We administer a single dose of broad spectrum antibiotic (eg, ampicillin or a first –generation cephalosporin , or Clindamycin if allergic to penicillin).

عدم خروج کامل جفت




Thank you