Tabriz University of Medical Sciences

Perinatal Infections

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Introduction

✓Infections during pregnancy are one of the major causes of fetal and neonatal morbidity and mortality.

Mother to baby transmission of infection can occur:

✓in utero (congenital)

✓ at and around the time of delivery (perinatal)

✓subsequently (postnatal) as illustrated by transmission of organisms by breastfeeding.

Introduction (cont.)

Maternal infections spread to the embryo and fetus by:

- Ascending infection from the upper vagina via the uterine cervix to the amniotic fluid
- Hematogenous spread as a result of maternal viremia, bacteremia or parasitemia.

Introduction (cont.)

Prevention

✓Systematic Screening

✓Education

✓Immunization: Poliomyelitis Mumps, Hepatitis B, Rubella, Measles, Varicella zoster (not yet confirmed), Tetanus

عفونتهای ویروسی

- ✓واریسلا زوستر
- ✓روبلا
- ✓سیتومگالوویروس
- ✓هرپس زوستر

عفونتهای تک یاخته ای

- ✓توکسوپلاسموز

تغییرات ایمونولوژیک در حاملگی

- ✓عفونتهای ادراری

Varicela-Zoster virus (VZV)

✓Varicella (Chickenpox), is a highly contagious disease of childhood caused by Varicella Zoster Virus.

✓average incubation period: 14 to 16 days (range 10-20 days)

✓Following primary infection, **lesions** develop in three or more successive waves for 3 to 7 days.

✓Lesions progress through macular, papular, vesicular, and pustular stages. Eventually scabs form, which usually heal without scarring unless secondary bacterial infection occurs.

Varicela-Zoster virus (cont.)

Clinical manifestation of congenital varicella infection following chickenpox in pregnancy	
Stage of maternal infection	Sequelae
First and second trimester	Congenital varicella syndrome
Second and third trimester	Zoster in infancy or childhood
Perinatal	Disseminated neonatal varicella

Congenital Varicella Syndrome

Congenital varicella syndrome can occur among infants born to mothers infected during the first half of pregnancy and may be manifested by:

- ✓Low birth weight
- ✓Limb hypoplasia
- ✓Microcephaly
- ✓Cortical atrophy
- ✓Chorioretinitis
- ✓Cerebral ventriculomegaly
- ✓Cataracts and other eye anomalies

Neonatal Varicella

✓The onset of varicella in pregnant women in the period from 5 days before birth to 2 days after birth can result in severe neonatal varicella in 17-30% of the newborn infants.

✓The risk of death among neonates has been estimated to be 31% among those whose mothers had rash onset 0-4 days before delivery.

✓The interval between the mother's rash and the infant's rash is usually 12-13 days, but may be as brief as 2 days, suggesting transplacental infection.

Diagnosis

Maternal Varicella:

- PCR
- Direct Fluorescent Assay
- Seroconversion or a significant increase in serum varicella IgG antibody
- IgM tests.

Diagnosis

Infant Varicella:

- History of maternal symptomatic varicella infection during pregnancy.
- Presence of cicatricial skin lesions
- Demonstration of specific IgM antibody after birth.
- Persisting IgG antibodies after 7 months of age, in the absence of postnatal varicella.

Treatment

✓Oral acyclovir treatment should be used if varicella infection occurs during pregnancy due to the risk of severe outcomes and should be initiated within 24 hours of rash onset.

✓varicella pneumonia or other signs of dissemination: hospitalization and early treatment with intravenous acyclovir

✓Newborn infants with severe or rapidly progressing varicella should be treated with intravenous acyclovir at a dose of 1500 mg/m2 in three divided daily doses.

Prevention

- ✓Maternal vaccination
- ✓Maternal exposure

Infant exposure: Passive immunization of the neonate with ZIG is recommended if the mother develops infection from 5 days before to 2 days after birth.

تماس خانم باردار با فرد مبتلا به آبله مرغان یا ابتلای مادر به آبله مرغان

- سابقه عدم ابتلا یا عدم اطلاع از ابتلا قبلی
  - آزمایش سرولوژی IgG با جواب ۲-۱ روزه در طی ۷-۵ روز بعد از تماس
    - IgG مثبت
      - بدون خطر
    - حد مرزی یا عدم انجام آزمایش در عرض ۷-۵ روز
      - مادر بدون علامت
      - مادر علامت دار
    - IgG منفی
      - فرد حساس است
        - تزریق VARZIG در طی ۵ روز بعد از تماس با دوز ۴۰۰ میلی گرم/ kg
          - بروز علائم بیماری
          - عدم بروز علائم
            - ادامه مراقبت ها و بررسی سلامت جنین
- سابقه ابتلای قبلی
  - بدون خطر
- وجود بثورات
  - تجویز داروی آسیکلووير ۷۲-۲۴ ساعت بعد از بروز با نظر متخصص عفونی

مادر بدون علامت

تکرار آزمایش ۴-۳ هفته بعد از تماس

IgG منفی

ادامه مراقبت روتین بارداری

IgG مثبت (۴ برابر میزان طبیعی) یا بروز علامت در مادر

مادر علامت دار

بروز علائم بیماری

تجویز داروی آسیکلووِیر ۷۲-۲۴ ساعت بعد از بروز با نظر متخصص عفونی

ابتلا در هفته ۲۰ بارداری یا بعد از آن

ادامه مراقبت روتین بارداری

ابتلا قبل از هفته ۲۰ بارداری

آمنیوسنتز و انجام PCR

در صورت بروز علائم ۵ روز قبل از زایمان یا ۲ روز پس از زایمان

به نوزاد IVIG یا VAZIGتزریق با مشاوره متخصص نوزادان

ایزولاسیون و ادامه درمان نوزاد طبق نظر متخصص نوزادان

عدم پذیرش مادر برای انجام PCR

سونوگرافی در هفته ۲۰-۱۸ بارداری

منفی

ادامه مراقبت روتین بارداری

مثبت

مشاوره با مادر باردار و همسر وی

غیرطبیعی

طبیعی

تکرار سونوگرافی در هفته ۲۴-۲۲ بارداری

مشاوره با مادر باردار و همسر وی

ادامه مراقبت ها

غیرطبیعی

طبیعی

Rubella

Rubella

✓Rubella virus is the first virus documented to be a teratogen, causing severe congenital anomalies.

✓It is a contagious disease transmitted via the respiratory system secretions from the nose or throat.

✓Viremia occurs 5-7 days after the contact period during which the virus may be transmitted from the mother to the fetus by hematogenous transplacental spread.

Diagnosis: Maternal

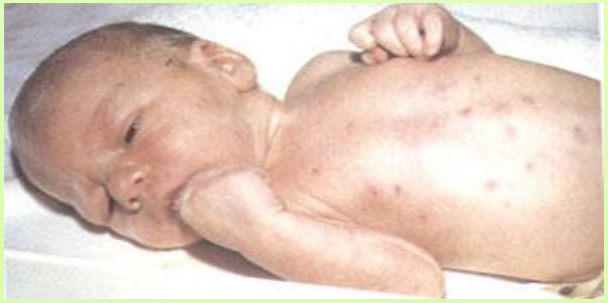
✓Clinical features

✓Laboratory: Acute rubella infection can be confirmed by the presence of serum rubella IgM, a significant rise in IgG antibody titer in acute and convalescent serum specimens, positive rubella virus culture, or detection of the rubella virus by RT-PCR and ELISA.

Diagnosis: Neonatal

Congenital Rubella Syndrome (CRS) is characterized by:

Cardiac defects	Cataracts	Hearing impairment
Developmental delay	Hepatosplenomegaly	skin lesions
Pneumonitis	Myocarditis	Disturbances of bone growth
Microcephaly	IUGR	Thrombocytopenic purpura



Rubella (cont.)

CONGENITAL DEFECTS ACCORDING TO THE TIME OF INFECTION		
Gestational period	Congenital anomaly	Risk (%)
First trimester	Ocular , Cardiovascular, CNS, Hearing Impairment, IUGR	38- 100
Second trimester	Hearing impairment, retinopathy, microcephaly, mental retardation	4- 60
Third trimester	IUGR	0-18

Prevention of Rubella

✓A single dose of rubella-containing vaccine (e.g: MMR vaccine), is 95% effective.

✓Susceptible women should be aware of the risk of contact during pregnancy with children or adults with rubella-like or any flu like illness.

✓Screening for rubella susceptibility is recommended for all women of childbearing age at their first preconception Encounter.

✓All susceptible non pregnant women of childbearing age should be offered vaccination.

✓Pregnant women who remain seronegative to rubella should receive rubella vaccine post partum.

اخذ شرح حال و سابقه مشاوره با متخصص عفونی در صورت وجود راش و تب

بررسی نتیجه IgG قبل از بارداری

مثبت

ایمنی مادر

عدم نیاز به اقدام بعدی

منفی

عدم ایمنی

آزمایش سرولوژی (حداکثر تا یک هفته پس از تماس

IgM مثبت یا افزایش ۴ برابر در سطح IgG

عفونت سرخجه و پرخطر از نظر سرخجه مادرزادی در ۳ ماهه اول

-آگاهی خانواده از نظر خطرات احتمالی
– توصیه به ختم بارداری با توجه به نظر پزشک قانونی زیر هفته ۱۶ بارداری

IgM منفی و عدم تغییر در سطح IgG

رد شدن بیماری

عدم دسترسی

سابقه مطمئن واکسیناسیون

ایمنی احتمالی

انجام تست سرولوژی در صورت بروز راش

IgM منفی و عدم تغییر در سطح IgG

رد شدن بیماری

IgM منفی و افزایش شاخص در سطح IgG

عفونت مجدد و با خطر در CRSناچیز برای سه ماهه اول

IgM مثبت

عفونت سرخجه و پرخطر از نظر سرخجه مادرزادی در سه ماهه اول

عدم اطمینان از واکسیناسیون قبلی

مشاوره عفونی برای تشخیص سرخجه

Cytomegalovirus

Human CMV is a DNA virus of the herpes virus group.

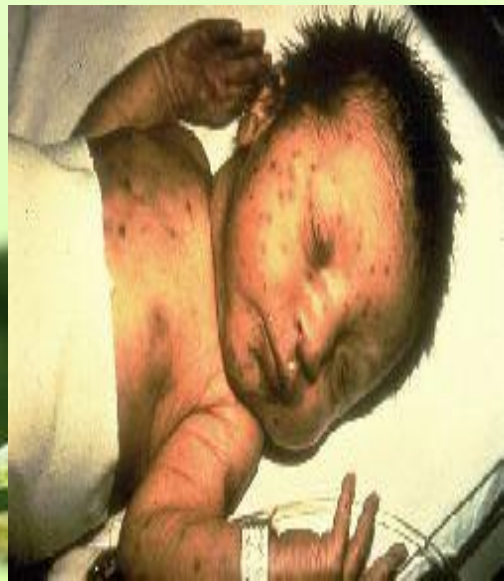
- Prenatal infection is by transplacental route.
- Perinatal infection may occur intrapartum by exposure to CMV in the genital tract.
- Postnatally, the infant can become infected with CMV by contact with infected body fluids such as human milk or saliva or by receipt of blood transfusions.
- Of the many possible CMV transmission routes, the most common are via breast milk, exposure to young children, or through sexual contact.
- Transmission is especially frequent in day care settings.

Clinical Features

Pregnant Women: CMV infection may be asymptomatic or may cause mild hepatitis, atypical lymphocytosis and non-specific symptoms during the self-limited primary infection.

Infants: Clinical symptoms in the infant can be non-specific and may include:

- Intrauterine growth retardation
- Hepatosplenomegaly
- Chorioretinitis
- Periventricular calcifications
- Microcephaly
- Jaundice
- Petechiae or Purpura
- Sensorineural hearing loss
- Encephalitis



Laboratory Diagnosis

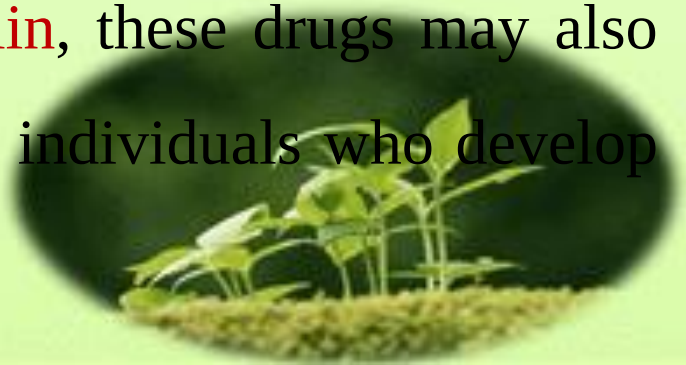
Maternal and Prenatal Diagnosis: Maternal serum IgM , PCR.

Newborn Diagnosis:

- A monoclonal antibody is used to detect early CMV antigen to identify the virus in urine or saliva before 3 weeks of age.
- PCR detection of CMV DNA in urine or saliva has been shown to reliably diagnose
- congenital CMV.

Treatment

- Patients with proven symptomatic congenital CMV infection: intravenous ganciclovir at a dose of 6 mg/kg every 12 hours for a total of 42 days.
- The most significant toxicity is neutropenia.
- For immuno compromised individuals who develop CMV retinitis: Ganciclovir, IV and PO, and foscarnet IV.
- Combined with anti-CMV immune globulin, these drugs may also be helpful in treating immuno compromised individuals who develop pneumonitis.



Prevention

➢vaccines against CMV are not yet available.

• Careful hand washing with soap and running water for 15 to 20 seconds after

✓exposure to a child's bodily fluids and diaper changes

✓handling dirty laundry

✓touching the child's toys and other objects

✓bathing the child

Prevention (cont.)

- **Wearing protective gloves**

✓during diaper changes

✓when handling the child's dirty laundry

- **Avoiding intimate contact with the child such as**

✓kissing on the mouth or cheek

✓sleeping together

✓sharing towels and washcloths

✓sharing or tasting foods or drinks with the same utensils (spoons, forks glasses)

Prevention (cont.)

- For pregnant women working in a day care center:

✓Avoid working with children younger than 2 ½ years of age.

✓Mothers who have CMV infection should not stop breastfeeding.

Genital Herpes Simplex Virus (HSV)

The two types of HSV have different disease characteristics:

HSV-2: The majority of cases of genital herpes are caused by HSV-2 and nearly all are sexually acquired. Recurrent lesions are common.

HSV-1: The majority of persons with HSV-1 antibody have oral HSV infection (cold sores around the mouth) acquired during childhood, which might also be asymptomatic.

Burden of disease

- Primary HSV infection in the first trimester is associated with an increased risk of early miscarriage.
- The vast majority of neonatal herpes cases occur as a result of contact with HSV in the maternal birth canal during delivery.
- Much less commonly, neonatal herpes results from transplacental or ascending infection, or from postnatal acquisition of HSV-1 from close contact with persons with oral herpes.

Diagnosis

Clinical: Neonatal herpes can be classified as:

1) Disseminated disease: involving multiple organs including lung, liver, adrenal glands, skin, eye, and/or brain

2) Central nervous system (CNS) disease, with or without skin involvement

3) Skin, eyes, and/or mouth (SEM) disease

LABORATORY

Indirect Serologic Tests: Serologic test for HSV-1 and HSV-2, including IgM tests, have limited value in the diagnosis of neonatal herpes.

Direct Viral Tests: Viral isolation using culture, Direct immunofluorescent , PCR assays for HSV DNA are more sensitive than viral culture and are the preferred method for detecting HSV in the cerebrospinal fluid (CSF).

Treatment

Maternal genital herpes

➢Antiviral therapy is recommended for women with a symptomatic first episode of genital herpes during pregnancy.

Neonatal herpes

➢Infants with known or suspected neonatal herpes is systemic: Acyclovir 20 mg/kg body weight IV every 8 hours for 21 days for disseminated and CNS disease, or for 14 days for disease limited to skin, eye, and mucous membranes.

Prevention

Maternal counseling: Women should be aware of:

• potential for recurrent episodes

• asymptomatic viral shedding

• sexual transmission when lesions are present

• risk of receptive oral sex with a partner with oral herpes or intercourse during the third trimester with men who have genital herpes.

Neonatal prevention: Maternal antenatal management is the best prevention for vertical transmission.

Type of delivery

- C- section is not routinely recommended in women with recurrent genital herpes, as the risk of vertical transmission is small.
- C- section should be considered only if active genital lesions that cannot be covered are present at the onset of labor.
- C- section does not completely eliminate the risk for HSV transmission to the infant.

Toxoplasmosis

➢*Toxoplasma gondii* is an intracellular protozoan parasite that infects up to a third of the world's population.

➢Infection is acquired primarily by ingestion or handling of undercooked or raw meat containing tissue cysts or by ingestion of food or water contaminated with oocysts excreted in the faeces of infected cats.

➢Primary infection is usually asymptomatic or has mild, non-specific, symptoms. Some individuals develop cervical lymphadenopathy or ocular disease.

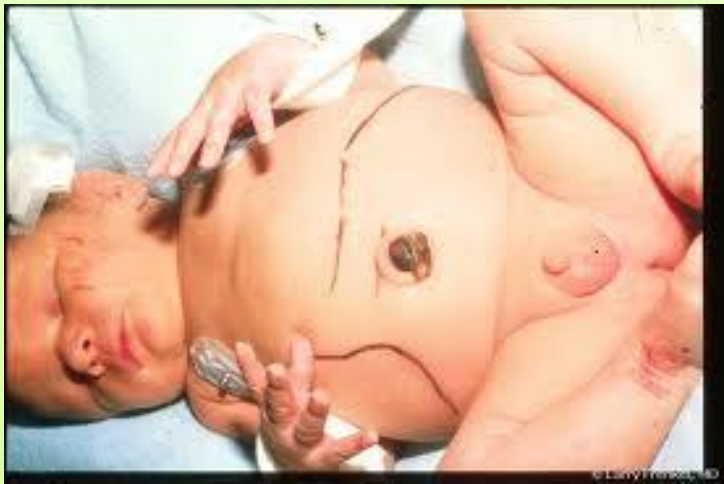
Infection acquired during			
Outcome in offspring	First trimester	Second trimester	Third trimester
Congenital toxoplasmosis	9·0%	27·0%	59·0%
Subclinical (at birth)	22·2%	74·4%	89·8%
Clinically apparent	77·8%	15·6%	10·2%
Perinatal death or stillbirth	5·0%	2·0%	0%

Diagnosis

Clinical features of Congenital Toxoplasmosis

Neonatal clinical manifestations of congenital toxoplasmosis vary widely and include:

- Hydrocephalus
- Microcephaly
- Diffuse intracranial calcifications
- Chorioretinitis
- Blindness
- Epilepsy
- Psychomotor or mental retardation
- Petechiae due to thrombocytopenia
- Anemia



Diagnosis (cont.)

- Laboratory

Direct detection: PCR

Indirect detection/serology: IgG and IgM

Treatment

- Spiramycin (for the first and early second trimester)

- Pyrimethamine/ sulfadiazine (for late second and third trimester) for women with suspected or confirmed acute *T gondii infection.*

Treatment (cont.)

- In case of a positive PCR result or very highly probable infection of the fetus (i.e., acquisition of maternal infection in late second or third trimesters): Pyrimethamine/ sulfadiazine, which may be alternated with Spiramycin.
- Folinic acid is added to pyrimethamine treatment to reduce bone-marrow suppression.
- Careful monitoring for haematotoxicity is mandatory.

Prevention

➢There is no effective vaccine against human *T gondii infection*.

Recommendations are:

- Avoid consumption of undercooked meat.
- Wash hands thoroughly after handling raw meat.
- Wash all uncooked vegetables thoroughly.
- Wear gloves when gardening or working in soil.

Prevention (cont.)

Recommendations are (CONT.):

• If possible, keep cats indoors throughout pregnancy and do not feed cats uncooked meat.

• Avoid untreated (unfiltered) water.

پروتکل عفونت ادراری

نوع اقدام		شرح اقدام
اخذ شرح حال و سابقه		تب و لرز، سوزش و تکرر ادرار، احساس دفع ادرار، دردهای کولیکی
معاینه		علائم شوک، کنترل علائم حیاتی (تب)، معاینه شکم و پهلوها (تندرنس پهلوها)، انقباضات رحمی، سمع قلب و ریه
اندیکاسیون بستری		شوک، تنگی نفس و تاکی پنه، تب، انقباض های رحمی، پیلونفریت، سنگ های ادراری
پاراکلینیک	آزمایشگاه	CBC, BUN, Cr، کشت خون، کامل و کشت ادرار و بر اساس هر پروتکل
	تصویربرداری	سونوگرافی
	سایر تست های تشخیصی	با توجه به هر پروتکل

پروتکل عفونت ادراری (ادامه)

درمان دارویی	نوع دارو با ذکر دارو	سرم کریستالوئید، استامینوفن، مسکن، اریترومایسین، آموکسی سیلین، آمپی سیلین، سفالوسپورینها، نیتروفورانتوئین به مدت ۱۰-۳ روز، آنتی بیوتیک وریدی سفازولین یا سفتریاکسون، آمپی سیلین و جنتامایسین
	اندیکاسیون	علائم شوک، پیلونفریت، سنگ های ادراری، یورتریت کلامیدیایی، سیستیت، باکتریوری آسیمپتوماتیک
درمان جراحی	اندیکاسیون	
	نوع عمل	
درمان غیردارویی و آموزش ها		توصیه به مصرف دارو تا ۱۰ روز
اندیکاسیون ختم بارداری		
مدت بستری		بسته به شرایط بیمار و نظر پزشک
اندیکاسیون ترخیص		۲۴ ساعت پس از قطع تب
دستورات Follow up		انجام U/C, U/A در فواصل مناسب
سایر اقدامات		مشاوره با متخصص داخلی، اورولوژی

عفونت ادراری (ادامه)

ارزیابی علائم اورژانس شامل: ✓علایم شوک سپتیک ✓تب و لرز ✓تنگی نفس ✓تاکی پنه ✓انقباضات زودرس رحمی	علائم شوک سپتیک	-مشاوره با متخصص داخلی و درمان آنتی بیوتیکی مطابق نتیجه مشاوره
	تنگی نفس / تاکی پنه	مشاوره اورژانس با متخصص داخلی و درمان مطابق نتیجه مشاوره
	انقباضات زودرس رحمی	-مراجعه به الگوریتم زایمان زودرس -درمان پیلونفریت مطابق همین الگوریتم

عفونت ادراری (ادامه)

✓اخذ شرح حال ✓کنترل علائم حیاتی ✓معاینه شکم و پهلوها ✓انجام آزمایش U/C, U/A, B/C, CBC, BUN, Cr	تب و لرز و تندرنس پهلوها	پیلونفریت	– تزریق کریستالوئیدهای وریدی برای برقراری حجم ادرار حداقل ۳۰ CC/h -شروع درمان آنتی بیوتیک وریدی -تجویز استامینوفن برای کاهش تب
	درد کولیکی / درد پهلوها /هماچوری	سنگ های ادراری	– تجویز مسکن و هیدریشن – مشاوره اورولوژی و اقدام با توجه به نتیجه مشاوره
	سوزش و تکرر ادرار / حس دفع ادرار / پیوری در U/A ولی U/C منفی	یورتریت کلامیدیایی	درمان با اریترومایسین به مدت ۷ روز
	سوزش ادرار، کشت مثبت ادرار بدون درد پهلوها	سیستیت	درمان دارویی
	علائم ادراری منفی / کشت ادرار مثبت	باکتریوری آسمپتوماتیک	درمان دارویی

Thanks a lot for your attention