**Prenatal infection**

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**4th class**

**Objectives:**

**1. Identify the different infectious agents that cause a range of morbidity and mortality.**

**2. Demonstrate the maternal and fetal diagnostic tests to confirm the in –utero infection.**

**3.Dsescribe the classification of prenatal infection including those causing congenital abnormalities, or associated with pregnancy loss and preterm pregnancy ,and serious neonatal consequences.**

**4. Describe the clinical features, complications of perinatal infections.**

**5.Determine the management protocol of prenatal infection .**

**6. Discuss the prevention protocol through vaccination.**

**In 1971 Andres Nahmias propsed Acronym (TORCH) and in 1975 Harold fuerst added syphilis to the acronym.**

* **S-- syphilis**
* **T-- toxoplasmosis**
* **O--other diseases, as Trich. vaginalis, E. coli and H. influenza.**
* **R --rubella**
* **C --cytomegalovirus**
* **H ---5 Herpes, HIV, Hepatitis B, humans’ parvo virus and Human papilloma virus.**
* **Latest addition is zika virus**

**1.Infections causing congenital abnormalities:**

**1. Rubella:** Is toga virus spread by the droplets transmission, incubation period 2-3 weeks.Is characterized by a febrile rash but may be asymptomatic in the mother in 20-50% of cases.

**Clinical features:**

**Transient :** Intrauterine growth restriction,Thrombocytopenic purpura (25% - 'blueberry skin'), Haemolytic anaemia, Hepatosplenomegaly, Jaundice (common), Radiolucent bone disease (20%), Meningoencephalitis (25%) +/- neurological sequelae.

 **Developmental**: Sensorineural deafness 80% ,General learning disability (55%), Insulin-dependent diabetes (20%,) 'Late-onset' disease at 3-12 months with rash, diarrhoea, pneumonitis and high mortality.

**Permanent:** **Congenital heart disease** (commonly patent ductus arteriosus or pulmon ary artery stenosis). **Eye defects** ( cataracts, congenital glaucoma, pigmentary retinopathyand called 'salt and pepper'), severe myopia, microphthalmia, Microcephaly.

**-Intrauterine infection is called congenital rubella syndrome** : cataract, microphthalmia, sensorinural deafness, encephalitis,and endocrine problems. In which the risk reduces with gestation.

-Infection in weeks 8-10 of pregnancy result in damage in up to 90% of surviving infants. The risk reduced to 10-20% in 11-16 weeks, and it is rare over 18 weeks.

**Diagnosis:**

**1.**Isolation of the rubella virus in culture .

**2.**Demonstration of rubella-specific IgM antibodies.

**3.** Demonstration of rubella-specific IgG antibodies that persist at a higher concentration or longer duration which indicates previous infection or immunization.

**4.**Detection of rubella virus RNA by reverse- transcriptase polymerase chain reaction in nasopharyngeal swabs, urine, CSF, and blood at birth .

**5.** Avidity testing of IgG: avidity is the Strength with which IgG binds to antigenic epitropes expressed by a specific protein. Gradually matures over months. IgG produced in first few months following primary infection Low avidity (Bind weakly to Ag).

Therefore, **LOW IgG avidity** is a marker of RECENT PRIMARY infection.

 **High avidity** excludes primary infection in preceding 3 months.

**Management:**

**1.**-Vaccination of children remains the cornerstone of the preventive strategy for this fetal disease, is live attenuated vaccine and should be avoided in pregnancy.

2.**If infection is confirmed in the first trimester,** termination of pregnancy should be offered as the sequelae of congenital infection are devastating.

3.**Later in pregnancy** , fetal blood sampling to measure levels of Rubella –specific IgM may be performed and Rubella –specific RNA identified using RT-PCR.

**2.Syphilis:**-is a sexually acquired infection caused by spirochaete Treponema pallidum.

Infant usually infected in utero by transplacental passage of Treponema pallidum from infected mother at any time.

Infection may also occur from contact with an infectious lesion during passage through the birth canal.

Infection can be transmitted to fetus at any stage of disease.

Rate of infection 60% - 100% during second stage, then slowly decreases with increasing duration of the disease.

Women, untreated early syphilis: 40% of pregnancies result in spontaneous abortion, stillbirth, or perinatal death.

**Clinical Manifestations** Damage to fetus depends on the stage of development at which infection has taken place and time elapsed before treatment.

 **Early infection, untreated**: miscarriage, stillbirth, neonatal death, IUGR, premature delivery.

 **Survivors :** Early congenital syphilis : clinical manifestations within first 2 years of life .Late congenital syphilis : clinical manifestations after 2years.

**EARLY CONGENITAL SYPHILIS** : Hepatosplenomegaly, Jaundice – due to hepatitis ,Generalized lymphadenopathy , Coombs – hemolytic anemia, thromobocytopenia, ,Hydrops fetalis, rhinitis (highly infectious) , “snuffles”, mucous patches , Chorioretinitis,

**LATE CONGENITAL SYPHILIS**: from chronic inflammation of bone, teeth, and CNS. Interstitial keratitis (inflammatory) ,Nerve deafness , Hutchinson’s triad (teeth, intersitial keratitis, 8 th nerve deafness) ,Hydrocephalus , Mental retardation ,Frontal bossing ,Saddle nose ,Protruding mandible , Gumma: Thin atrophic scar.

**Diagnosis :**

 1.Examination of placenta/umbilical cord for pathology.

2. Dark field microscopy of suspicious lesions/body fluid.

3.Clinical findings suggestive of syphilis: Non immune hydrops/ jaundice/hepatosplenomegaly/ rhinitis/ skin rash.

 4.Quantitative Non-treponemal test: VDRL, RPR Quantitative results correlate with disease activity, therefore helpful in screening. Titers rise when disease is active, fall when treatment is adequate. These tests become non- reactive within a few months of adequate treatment.

5.Treponemal tests: the fluorescent treponemal antibody absorbed (FTA-ABS) test,, the T pallidum hemagglutination assay, and enzyme immunoassays that detect Treponemal antibodies, microhemagglutination assay for T pallidum, the T pallidum particle agglutination,

6.Infant Testing Reactive serology in neonate could be due to IgG passively transferred to newborn through placenta, and does not indicate active infection.

If infant’s titer higher than mother’s congenital infection , If decreasing titer in infant passive transfer of antibodies, should disappear by 3-4 months of age. Persistently reactive VDRL, with rising titer this is **Active Infection**

**Treatment** :

**1. Aqueous crystalline Penicillin G** 100,000-150,000U/kg/day (given q8- q12hrs) IV for 10 days OR **Procaine Penicillin G** 50,000 U/kg/day IM for 10days. If >1 day of therapy missed, entire course should be restarted.

**3.Toxoplasmosis:**

**-** Toxoplasma gondii is a unicellular protozoon found in cat faces , soil, or uncooked meat.

-**Infection** occur from ingestion of the parasite from uncooked meat or unwashed hand, and transplacentally to the fetus.

**Clinical features:**

The initial infection may be relatively asymptomatic or may be a glandular fever like illness, (mild malais , lethargy, lyphadenopathy).

Infection during the first trimester of pregnancy is more likely to cause sever fetal damage (85%), and 10% risk of fetal infection transmission.

In third trimester 85% of infection are transmitted but the risk of fetal damage is 10 %.

**Congenital toxoplasmosis** is marked by the classic triad of chorioretinitis, intracranial calcification and hydrocephalus.

**1.If infection occurs in the first trimester ---**spontaneous miscarriage is common.

**2.**The risk of fetal infection rises throughout gestation, with 65% of fetuses affected in the third trimester, transplacental passage is more common when maternal infection occurs in the later half of pregnancy but fetal injury is less sever.

**3.**Majority of infants are born without any obvious problem.., but may develop sequelae several years later.

**Diagnosis:**

**Serology** by the sabin-feldman dye test , Enzyme-linked immunosorbant assay (ELISA) are available for measurement of IgG, IgM antibodies, serial testing for rising titers is necessary.

**Ultrasound** detection of fetal abnormalities.

**Amniocentesis** and PCR analysis for the identification of T.gondii.

**Treatment:**

1. Spiramycin can be used in pregnancy 2-3 g per day for 3 weeks , reduces the incidence of transplacental infection.
2. If fetal abnormalities detected by ultrasound due to toxoplasmosis, the termination of pregnancy can be offered.
3. **Cytomegalovirus (CMV):**

CMV is a doubles stranded DNA herpes virus.

The most common congenital viral infection.

CMV infection requires intimate contact through saliva,urine, and/ or other body fluids. Possible routes of transmission include 1. sexual contact, 2. organ transplantation, 3.transplacental transmission, 4. transmission via breastmilk,and 5.blood transfusion(rare)

Primary,reactivation,or recurrent CMV infection can occur in pregnancy and can lead to congenital CMV infection.

 Approximately 85 percent of newborns with congenital CMV infection can be asymptomatic at birth. 15 percent will develop progressive hearing loss and visual impairment as they age.

Transplacental infection can result in : intrauterine growth restriction, Sensorineural hearing loss, Intracranial calcifications, Petichiae ,Jaudice , microcephaly, hydrocephalus , hepatosplenomegaly, Delayed psychomotor development, Thrombocytopenia and/ Chorioretinitis.

**Vertical transmission** of CMV can occur at any stage of pregnancy. Severe sequelae are more common with infection in the 1st trimester. The overall risk of infection is greatest in the 3rd trimester. The risk of transmission to the fetus in primary infection is 30%-40%

**Diagnosis :**

1.Virus culture from urine/saliva .

2.CMV-DNA PCR in urine, blood, saliva and CSF.

 3.CMV IgM antibodies in blood before 3 weeks of age.

 4.IgG Avidity testing

**Treatment** : **Ganciclovir** 5mg/kg IV every 12 hours for 14 days OR **Valganciclovir** 900mg PO daily for 3- 6 months OR **CMV-specific hyperimmune globulin** (200 units/kg of body weight) ,**Foscarnet, Cidofovir** for refractory CMV/ Ganciclovir resistance.

**5.Varicella:**

Neonatal Varicella Infants whose mothers demonstrate varicella in the period from 5 days prior to delivery to 2 days afterward are at high risk for severe varicella.

The infant acquires the infection transplacentally .The infant's rash usually occurs toward the end of the 1st week to the early part of the 2nd week of life .maternal immunoglobulin G (IgG) is able to cross the placenta if delivery occurs after 30 wk of gestation.

-**Transmitted** by respiratory droplets, direct contact with the vesicle fluid, IP is 10-21 weeks , the disease is infectious 48 hours before rash appears and untile the vesicle crust over.

-**The primary infection** is characterized by fever , malaise , pruritic rash, becomes maculopapular , vesicular finally crust.

-**Maternal infection <20 weeks** ma y result in fetal varicella syndrome skin scarring , eye defects, (microphthalmia, chorioretinites, cataract), microcephaly.

-**Maternal infection >20 weeks** and up to 36 weeks---dosent appear to be associated with adverse fetal effect effects.

**Congenital varicella syndrome**: Include: cicatricial skin lesions, ocular defects, limb abnormalities, CNS abnormalities, IUGR, and fetal demise or early death. The syndrome most commonly occurs with maternal VZV infection between weeks 7 and 20 of gestation

 **Zoster:** is uncommon in young infants but may occur as a consequence of in utero fetal infection with VZV. usually self-limiting, with only symptomatic therapy indicated in otherwise healthy children.

 **Postnatal varicella**:mild disease likely due to the presence of maternal antibodies against the virus.Rarely, severe disseminated disease occurs in newborns exposed shortly after birth following an acute maternal infection.

 **DIAGNOSIS** :

**1**.clinical findings and maternal history.

2.culture of vesicular fluid.

3. VZV antibody titer by the fluorescent antibody to membrane antigen assay or by ELISA.

4. Antigen detected from cells at the base of a vesicle By immunofluorescent antibody or PCR detection.

 **Treatment:**

**1.Newborn will have protective antibodies** :

Likelihood of severe disease is low ,do not separate baby from mother, Continue breast feeding ,No VZIG, Acyclovir if baby develops rash.

**2.Newborn will not have protective antibodies** **and Likelihood of severe disease is high** ,Separate baby from mother, If baby devps rash stay with mother, VZIG within 72 hours ,Acyclovir,

**3.Newborn will not have protective antibodies ¬ But, likelihood of severe disease is low** : Separate baby from mother ,f baby devps rash stay with mother, No VZIG ,Acyclovir if baby develops rash.

**Congenital infection associated with pregnancy loss and preterm pregnancy:**

1. **Parvovirus:**
* Parvovirus B19 (erythema infectiousum, fifth disease).
* Single stranded DNA virus , spreed by droplet infection.
* Common in women who works with young children like teachers.
* No evidence that it is teratogenic.
* Cause unexpected stillbirth, late misscarge, main concern of fetal infection is development of fetal hydrops secondary to fetal anemia or cardiac dysfunction due to myocardities.
* Diagnosed by detection of parvovirus specific IgM from maternal and fetal blood.

**2..Listeria:**

* **Listeria monocytogenes** is an aerobic and facultatively anaerobic motile G+ve bacilli.
* **Pregnant women with listeriosis** commonly suffer from a flue like illness with fever and general malaise , may be asymptomatic.
* **Transmission** : ascending rout through cervix or transplacentally.
* results in miscarriage , preterm delivery, neonate may have RDS, fever, sepsis, neurological symptoms.
* **Treatment during pregnancy** by Ampcillin 2 gm l 6 hours.

**3.Malaria:**

* Caused by parasite plasmodium , falciparum, vivax , ovale, and malaria.
* May cause miscarriage, preterm labour, FGR and congenital malaria
* **Diagnosis by** blood film
* **Treatment** : quinine sulphate, fansidar and combination of chloroquine .
* **Infections acquired around the time of delivery with serious neonatal consequences:**

**1.Herpes:**

* Is a double stranded DNA virus.
* Two viral types HSV-1 cause orolabial infection and HSV-2 cause genital herpes.
* **Genital herpes** presents as ulcerative lesions on vulva , vagina, cervix.may give a history of recurrence
* **Neonatal herpes** mostely by HSV 1 or 2 ,manifests itself in three forms: skin, eyes, and mouth herpes (SEM) .
* **Diagnosis :** is confirmed by the direct detection of HSV ,a swab for viral culture .
* **Factors increase transmission are:** type of infection, duration of rupture membrane , primary infection during 3rd trimester especially 6 weeks before delivery.
* **Management :**
1. **Primary infection** ---caesarean delivery to all pregnant women with primary episode genital herpes at the time of delivery, or within 6 weeks of expected date of delivery..
* **To reduce exposure of the fetus to HSV in genital secretions**.
* **If patient opts for vaginal delivery** –avoid rupture membrane +invasive procedures, give IV acyclovir intrapartum to mother and then to the neonate.
1. **Recurrent infection during antenatal period or at the time of delivery-**C/Sis not indicated. mode of delivery individualized according to the clinical circumstances, and patient preferences because the risk of neonatal herpes is very small 1-3%.
* **If HSV lesion were detected at the onset of labour + patients opts for C/S daily acyclovir from the 36 weeks until delivery , likely reduce active herpes lesion at term.**
* **If recurrent genital herpes + confirmed membrane rupture at term advise to have delivery expedited by appropriate means, and avoid invasive procedures during delivery.**

 **2.Group B streptococcus:**

* common bacteria which are often found in the vagina, rectum or urinary bladder of women**.**
* If a woman has these bacteria without having any symptoms, she is said to be **colonized (positive).**
* -40 – 70% of colonized mothers pass the bacteria onto their babies during the birthing process.
* **Risks for neonatal infection:** Preterm labour, prelabour rupture of membranes, maternal pyrexia, and growth restricted fetuses or birth asphyxia.
* **Treatmen:** Expectant mothers who tested positive for GBS bacteria will be treated with antibiotics when they go into labour or if their membranes rupture (water breaks) early.

**3.Chlamydia infection:**

* Is intracellular organism, commonest bacterial, STD.
* May cause neonatal eye infection (ophthalmia neonatorum) and pneumonia.
* **Diagnosis: 1.**Endocervical, rectal and first pass urine, organism can be detected  **2.**ELISA **3.**DNA detection or direct immunoflouresence.
* **Treatment:**  Doxycycline 100 mg twice daily for 2 weeks avoided in second and third trimester.

**4.Gonorrhea:**

* **Is sexually transmitted** bacterial infection causing pelvic inflammatory disease.
* may cause **neonatal eye infection**, it may lead to blindness-local & systemic antibiotic should be given.
* **Diagnosis:** microscopy and culture, DNA detection tests.
* **Treatment:** ceftriaxone 250 mg single dose, azithromycin 1 gm, Ophthalmia neonatarum is treated with topical and systemic antibiotics acc. to sensitivity.
* **Perineatal infection causing long term disease:**
1. **HIV:**
* is a virus that causes AIDS (Acquired Immunodeficiency Syndrome)**.**
* **A baby can become infected with HIV in the womb**, during delivery or while [breastfeeding](http://americanpregnancy.org/first-year-of-life/breastfeeding-overview/), if the mother does not receive treatment.
* **Zidovudine (also known as ZDV, AZT and Retrovir®) was the first drug licensed to treat HIV**.
* **Now it is used in combination with other anti-HIV drugs** and is often used to prevent perinatal transmission of HIV. ZDV should be given to HIV-infected women beginning in the second trimester and continuing throughout pregnancy, labor and delivery. Side effects include nausea, [vomiting](http://americanpregnancy.org/pregnancy-concerns/vomiting-during-pregnancy/) and low red or white blood cell counts.
* **If no preventative steps are taken,** the risk of HIV transmission during childbirth is estimated to be 10-20%, even greater if the baby is exposed to HIV-infected blood or fluids. should avoid performing  [episiotomies](http://americanpregnancy.org/labor-and-birth/episiotomy/).
* [**Cesarean sections**](http://americanpregnancy.org/labor-and-birth/cesarean-procedure/)**performed before labor and/or the rupture of membranes** may significantly reduce the risk of perinatal transmission of HIV.
* About 15% of newborns born to HIV-positive women will become infected if they breastfeed for 24 months or longer.

**2.Hepatites B.**

HBV infection during late pregnancy or near the time of delivery, howeverA ,may result in up to 90% transmission rate in the absence of any prophylaxis and is most common in women who have both HBsAg and HBeAg detected in blood, indicating high plasma HBV DNA level.

Risk of vertical transmission mother HBsAG +VE BUT HBeAg –VE: 5-20% HBsAg +ve and HBeAg +ve: 70-90% • No contraindication for breast feeding • Hepatitis B vaccine : 90% active immunity HBIG: additional 5- 10% immunity • 90% of infected infants become chronic case.

NEONATE BORN TO MOTHER WITH HEPATITIS B (prenatal testing of all pregnant womens for HBsAG is recommanded At birth : Hepatitis B vaccine with HBIG(200 IU IM) (Perferably within 12 hrs but not after 48 to 72 hrs) FOLLOWUP: complete HBV immunization as per schedule 3 dose schedule Infants<2kg: do not count birth dose and give 3 more dose Infants>2kg:give total 3 doses FOLLOW UP TESTING DONE AT 9 TO 18 MONTHS OF AGE FOR ANTI-HBs and HbsAg.

**THE END**