# Clinical Approach to Infections in PREGNANCY

Madhuri Chandra Vineet Mishra



# Contents

1.	Overview: Impact of Viral Infections on Mother and Fetus  K Aparna Sharma, Alka Kriplani  Case Scenario 1; Objectives 2; Predominantly Fetal/  Neonatal Affection 2; Both Maternal and Neonatal  Affection 7; Predominantly Maternal Affection 9	1
2.	Screening for Infections in Pregnancy: Current Guidelines Suchitra N Pandit, Swati Bhargava Classification of Infections in Pregnancy 13; Antenatal Screening for Infections 14; Screening and Referral Algorithm for Hepatitis B Viral Infection in Pregnant Women 17; Recommendations for Screening for Human Immunodeficiency Virus Infection 19; Recommendations for Screening for Urinary Tract Infections 20	13
3.	Rubella Ashwini Bhalerao Gandhi, Shilpy Lakhtakia Case Scenario 23; Pathophysiology 23; Clinical Manifestations 24; Vertical Transmission Rates and Risk of Congenital Rubella Syndrome 24; Congenital Rubella Syndrome 25; Diagnosis of Rubella Infection 25; Management of Rubella Infection in Pregnancy 27; Treatment 28; Vaccination Schedule 29	23
4.	Parvovirus B19 Alka Pandey, Chitra Sinha Case Scenario 33; Objective 33; Pathophysiology 34; Clinical Presentation 34; Management 35	33
5.	Cytomegalovirus  Uday Thanawala, Anand Nanavati  Case Scenario 40; Pathophysiology 41;  Clinical Presentation 41; Care Pathway 47	40
6.	Enterovirus: Coxsackie Virus  Charu Mittal  Epidemiology 51; Clinical Presentation 52;  Effects of Coxsackie Virus Infection during Pregnancy 53;  Management 54	51
7.	Varicella (Chickenpox) Chanchal Singh, Mala Arora Case Histories 57; Fetal Varicella Syndrome 59	57

8.	Viral Hepatitis A and E  Gorakh Gopalkrishna Mandrupkar  Case Scenario 64; Viral Hepatitis in Pregnancy 64;  Hepatitis A in Pregnancy 64; Hepatitis E in Pregnancy 66	64
9.	Viral Hepatitis B and C Girija Wagh, Meenal Khanderparkar Case Scenario 71; Hepatitis B and C in Pregnancy 71; Hepatitis B in Pregnancy 73; Hepatitis C 75	71
10.	Mumps and Measles  Dilip Kumar Dutta, Indranil Dutta  Mumps 79; Pathophysiology 79; Complications to Mother and Fetus 80; Measles 80; Pathophysiology 81; Complications in Pregnancy 81	79
11.	Influenza Roza Olyai, S Sampathkumari Case Scenario 85; Etiopathogenesis 86; Pregnancy and Influenza 86; Clinical Manifestations 86; Management 88; WHO Recommendations for Treatment 89; Decision for Delivery 91; Postnatal Management 91	85
12.	Genital Herpes Vineet Mishra, Priyankur Roy Case Scenario 94; Etiopathogenesis 95; Clinical Manifestations 97; Management 98; Treatment 98	94
13.	Human Immunodeficiency Virus: Preventing Vertical Transmission Shreya Goenka, Sarita Agrawal Case Scenario 103; Objectives 103	103
14.	Preventing HIV Transmission: Pre-exposure Prophylaxis and Postexposure Prophylaxis  Madhuri Chandra  Case Scenario 118; Pathophysiology 119; Occupational Exposure and Postexposure Prophylaxis 120	118
15.	Vector-borne Viral Infections: Dengue, Chikungunya and Zika Ashis Kumar Mukhopadhay, Priyankur Roy Vector-borne Viral Infections 128; Dengue Virus 128; Chikungunya Virus 131; Zika Virus 133	128

16.	Tuberculosis Sadhana Gupta, Hema J Shobhane Case Scenario 138; Clinical Manifestations 139; Treatment of Tuberculosis in Pregnancy 141; First-line Drugs 142; Second-Line Management 143	138
17.	Syphilis and Other Bacterial Sexually Transmitted Infections Ragini Agrawal, Monika Gupta Case Scenario 146; Defense Mechanism of Genital Tract in Pregnancy 147; Syphilis 147; Clinical Manifestations 149; Chlamydia Trachomatis 152; Gonorrhea 153; Trichomoniasis 156	146
18.	Bacterial Vaginosis Saswati Sanyal Choudhury Case Scenario 160; Pathophysiology 161; Clinical Features 161	160
19.	Malaria  Deepti Gupta, Madhuri Chandra  Case Scenario 166; Malaria Transmission in India 166;  Pathophysiology 167; Clinical Presentation 169;  Investigations 170; Treatment Guidelines 170; Prevention 173	<b>166</b>
20.	<b>Toxoplasmosis</b> Parikshit Tank Illustrative Case History 176; Questions and Controversies 177; Objectives 177; Pathophysiology 178; Clinical Manifestations 179; Diagnosis 180; Management Rationale for Termination of Pregnancy 182	176
21.	Listeriosis  Deepti Gupta, Durga Shankar Dash  Case Scenario 187; Incidence 187; Pathophysiology 188;  Clinical Presentation 188; Management 189; Treatment 190	187
22.	Gastrointestinal Infections and Infestations Kirtan Vyas, Shirish N Daftary Case Discussion 195; Common Parasitic Infestations 196; Helminthic (Worm) Infections 197	195
23.	Urinary Tract Infections  Madhuri Chandra  Case Scenarios 202; Objectives 202; Definitions 202;  Classification 203; Etiopathogenesis 204;  Clinical Presentation, 204	202

<i>2</i> 4.	Offrasound imaging: Fetal Manifestations of Viral Exposure		
	and Infections	210	
	PK Shah, Lovely Jethwani		
	Diagnosis 210; Role of Ultrasound in the Management of		
	Congenital Infections 211; Ultrasound Findings in Congenital		
	Viral Infections 211; Specific Ultrasound Findings 219;		
	Interventional Ultrasound in Congenital Viral Infections 223;		
	Doppler Ultrasound in Congenital Infections 224;		
	3D Ultrasound in Congenital Infections 225;		
	Anomalies Detected in Relation to Congenital Infection 225;		
	Disadvantages of 3D Ultrasound 226		
25	Vaccination for Women Contemplating Pregnancy	231	
20.	Laxmi Shrikhande, Rujuta Fuke	201	
	Measles, Mumps and Rubella (German Measles) 231;		
	Varicella (Chicken Pox) 232; Influenza Vaccine 232;		
	Diphtheria, Tetanus, Pertussis Vaccine 233; Pneumococcal		
	Vaccine 234; Hepatitis A 234; Hepatitis B 234;		
	Meningococcal Vaccine 235		
	Meningococcai vaccine 255		
<b>26.</b>	Antibiotic Use in Pregnancy	<b>238</b>	
	Jaideep Malhotra, Pallavi Gupta		
	Pregnancy and Antibiotics 238; Infections and Pregnancy 239		
27.	Managing the Pregnant Woman with Systemic Inflammatory		
	Response Syndrome, Sepsis and Septic Shock		
	Alpesh Gandhi, Munjal Pandya		
	Case History 247; Objectives 247; Pathophysiology 248;		
	Specific conditions 252; Complications 254;		
	Management 254		
	Index	<b>261</b>	

# Parvovirus B19

■ Alka Pandey, Chitra Sinha

#### **CASE SCENARIO**

A pregnant nursery school teacher has been recently exposed to parvovirus B19 infection. She consulted the obstetrician and was very worried about her pregnancy and the baby. She had lots of queries.

#### **Oueries**

- · Whether I will become infected?
- If yes then what will be the effect on my pregnancy?
- Is this infection going to harm my baby?
- · Can it be treated?

#### **OBJECTIVE**

- To know the prevalence of parvovirus B19 in pregnant women.
- Study the effect of paryovirus B19 infection on mother and fetus.
- Diagnosis and management of pregnant women exposed to/with symptoms of parvovirus B19.

#### INTRODUCTION

Parvovirus B19 is a single-stranded DNA virus that causes exanthema erythema infectiosum, also called Fifth disease or slapped cheek, a common childhood illness. Parvovirus B19 renamed erythrovirus affects only humans, it is a widespread infection that may affects 1–5% of pregnant women, usually with normal pregnancy outcome. The prevalence of infection is higher during epidemics between 3% and 20% with seroconversion rate of 3–34%. Parvovirus infection in pregnancy can cause fetal anemia, nonimmune fetal hydrops and fetal death. It is an important cause of intrauterine fetal demise in the second and third trimesters of pregnancy. There is no specific treatment or prophylaxis available against B19 infection, but counseling of nonimmune mothers, ultrasound monitoring of mothers with confirmed infections and intervention to correct fetal anemia is likely to decrease fetal mortality. Once infected, the immunity is lifelong.

#### **PATHOPHYSIOLOGY**

Parvovirus spreads by respiratory secretions or from hand to mouth contact.<sup>1</sup> Rarely it may be transmitted via blood and blood product transfusion and transplacental transfer to the fetus. As the main mode of transmission is respiratory, epidemics of parvovirus B19 infection can occur, usually in spring and mainly affect children aged 4–11 years. Incubation period is 4–20 days. Fever and prodromal symptoms may develop in the last few days of the incubation period, but many women remain asymptomatic. A rash develops approximately two weeks after exposure. The woman is infectious from 4 to 10 days prior to appearance of rash, once rash and arthralgia begin, the person is usually no longer infectious.

Infection with parvovirus B19 usually gives lifelong immunity. Approximately 50–75% of women of reproductive age are shown to be immune to parvovirus B19.<sup>2</sup> The risk of acquiring parvovirus in pregnancy is about 1 in 400. Nursery school teachers have a 3-fold higher risk of acute infection than other pregnant women, and other school teachers have a 1.6-fold increased risk.<sup>3</sup>

Parvovirus B19 virus has a predilection for infecting rapidly dividing cell lines, such as bone marrow erythroid progenitor cells, which are found in bone marrow, fetal liver, umbilical cord, and peripheral blood. Transplacental transmission leads to fetal anemia, nonimmune hydrops and fetal death.

#### **CLINICAL PRESENTATION**

# **Symptoms and Signs**

The clinical picture associated with B19 infection varies from an asymptomatic infection in healthy individuals to influenza-like illness often with a rash, and acute arthropathy in 30–60% people, which lasts for more than 2 months in at least 20% people. Its symmetrical involvement tends to occur in peripheral joints. B19 has been reported to cause a wide variety of hematologic disorders such as neutropenia, thrombocytopenia, pancytopenia, and hemophagocytic syndrome.<sup>4</sup>

About 50% pregnant women infected with parvovirus B19 virus show no symptoms or signs. Adults with parvovirus B19 infection usually do not have the characteristic "slapped cheek" or "gloves and socks" lace-like rash on trunk and limbs. The onset of the rash usually coincides with the appearance of parvovirus B19 antibodies (IgM), suggesting that this symptom is immune-mediated.

Arthropathy is common in adults and affects up to 50% of pregnant women with parvovirus infection, affecting the hands, wrists, ankles, and knees.<sup>5</sup>

Parvovirus B19 has an affinity for hematopoietic system cells, including erythroid progenitor cells, and to a lesser degree, leukocyte and megakaryocyte cell lines. Infection can result in transient aplastic crisis and pure red cell anemia. Aplastic anemia, is more common with underlying hematologic disorders like sickle cell disease. Chronic bone marrow suppression after parvovirus B19 infection leading to chronic severe anemia has been described in immunodeficient patients (example HIV infection).

Rarely parvovirus B19 infection can lead to acute myocarditis, heart failure, vasculitis, encephalitis, nephritis, pruritus, chronic bone marrow failure and chronic fatigue syndrome.

#### **Fetal Manifestations**

Pregnancy does not appear to affect the course of the infection, but infection may affect the pregnancy. The transmission rate of maternal parvovirus B19 infection to the fetus is 17-33%.8 Most fetuses infected with parvovirus B19 have spontaneous resolution with no adverse outcomes (Table 4.1). There is no evidence that parvovirus B19 infection increases the risk of congenital anomalies. Parvovirus B19 is associated with fetal anemia and nonimmune hydrops fetalis. The virus infects erythroid precursor cells and combined with the shorter half life of fetal red blood cells, leads to severe fetal anemia, hypoxia, and high output cardiac failure, fetal viral myocarditis and chronic hepatitis that are associated with fetal hydrops. The P antigen expressed on fetal cardiac myocytes enables the parvovirus B19 to infect myocardial cells and produce myocarditis that aggravates the cardiac failure. 10 Impaired hepatic function is caused by direct damage to hepatocytes and indirect damage due to hemosiderin deposits.<sup>11</sup> If a fetus develops hydrops, ultrasound signs include ascites, skin edema, pleural and pericardial effusions and polyhydramnios. The fetus may recover completely or intrauterine death could occur. Most intrauterine fetal deaths (IUFDs) occur 4-6 weeks after maternal illness. Hydrops is unlikely to occur if it has not done so by 8 weeks after maternal infection.

*Long-term neonatal outcome*: Severe anemia and fetal hydrops associated with parvovirus B19 fetal infection, may cause long-term neurological sequelae in neonate. Parvovirus B19 myocarditis can lead to severe dilated cardiomyopathy and may even require heart transplantation.<sup>12</sup>

#### MANAGEMENT

Systematic screening for parvovirus immunity in low-risk pregnancies is not currently recommended.  $^{13}$ 

If a pregnant woman is exposed to, or develops signs or symptoms of parvovirus B19 infection, serological testing for both parvovirus B19- specific IgG and IgM must be done. Parvovirus B19 IgM usually appears within 2–3 days of acute infection (10–12 days after exposure) and may persist up to 6 months. Parvovirus B19 IgG appears a few days after IgM appears and usually remains present for life **(Table 4.2)**.

■ **Table 4.1:** Effects of parvovirus B19 infection on fetus<sup>13</sup>

Term of gestation	Fetal consequences
<20 weeks	Spontaneous abortion 13% Fetal hydrops 4.7%
>20 weeks	Spontaneous abortion <2% Fetal hydrops 2.3%

IgG	IgM	Interpretation
Positive	Negative	Previous exposure and immunity. Will not develop infection in pregnancy
Negative	Negative	Susceptible to parvovirus If exposed, repeat IgG and IgM, 2–4 weeks from suspected exposure: If IgM and IgG positive – acute infection
Negative	Positive	Acute infection or false positive Collect 2nd sera 1–2 weeks later for IgG, IgM
Positive	Positive	Acute infection, monitor for potential fetal infection

■ **Table 4.2:** Serologic evaluation of pregnant woman exposed to parvovirus B19

### **Diagnosis of Fetal Infection**

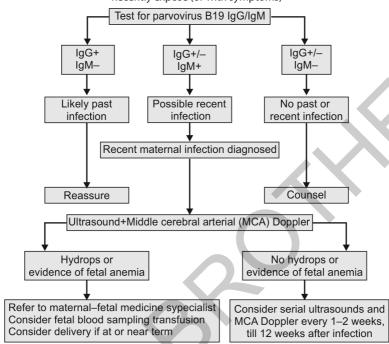
The most reliable way to diagnose acute fetal infection is to detect in amniotic fluid or fetal serum viral DNA by polymerase chain reaction (PCR) or viral particles by electron microscopy, however invasive diagnosis of this condition is not required for all suspected or confirmed maternal infections. <sup>10</sup> Testing for fetal parvovirus B19 is indicated when ultrasonography reveals fetal hydrops and may be done prior to an intrauterine transfusion.

Serology testing for parvovirus B19 IgM in fetal blood cannot be depended to make the diagnosis of fetal infection, because the fetus does not begin to make its own IgM until 22 weeks' gestation.<sup>10</sup>

# Management of Fetal Hydrops and Anemia

Pregnant women with acute parvovirus B19 infection should be monitored by serial ultrasonography for features of fetal anemia (Flow chart 4.1). USG findings of fetal ascites, skin edema, pleural and pericardial effusions, placental edema, cardiomegaly, impaired growth and hydrops fetalis suggest fetal infection. In addition, color Doppler in presence of fetal anemia show altered flows in fetal middle cerebral artery. USG is recommended every 1–2 weekly till 12 weeks after exposure. If there are no signs of fetal involvement till then, adverse fetal outcome is unlikely.

If ultrasonography shows signs of fetal anemia or hydrops, the mother should be referred to center with expertize of intrauterine transfusion. Fetus with anemia, should have cordocentesis, for fetal hematocrit, reticulocyte count and intrauterine transfusion if required. If the fetus is at or near term, delivery should be considered. Intrauterine transfusion has increased fetal survival rate to 80% and most infants with parvovirus infection treated by intrauterine transfusions have normal neonatal outcomes.



**Flow chart 4.1:** Management of a pregnant woman exposed to parvorirus B19 infection: Recently expose (or with symptoms)

Source: Society of Obstetricians and Gynaecologists of Canada (SOGC)
Clinical Practice Guideline no 316, December 2014<sup>11</sup>

# KEY POINTS

- Routine screening of pregnant women for parvovirus B19 is not recommended.
- Serology testing of women with symptoms of parvovirus B19 or those with confirmed exposure is advised. May also be recommended for those with diagnosed fetal hydrops or intrauterine fetal death.
- If parvovirus B19 IgG positive and IgM is negative, the woman is immune and should be reassured that she will not develop infection.
- Pregnant women with parvovirus B19 IgM positivity (acute infection), should be
  counseled regarding risks of fetal transmission, fetal loss, and hydrops. They should
  undergo serial ultrasonography and Doppler for peak systolic velocity of middle
  cerebral artery, every 1–2 weeks to monitor fetus for signs of fetal anemia and hydrops
  fetalis
- If hydrops or evidence of fetal anemia develops, referral should be made to a specialist capable of intrauterine fetal blood sampling and fetal transfusion.

# MULTIPLE CHOICE QUESTIONS

1	Darwovirus	B19 infectio	n ic most	commonly	caroad by
١.	Parvovirus	D 19 Intectio	n is most	commonly	spread by:

- a. Respiratory secretions b. Hand to mouth transmission
- c. Blood transfusion d. Transplacental transfer
- 2. PV B19 outbreaks occur in:

a. Spring b. Summer c. Autumn d. Winter

- 3. On serological examination if the patient is immune to parvovirus B19, the result
  - a. IgG positive , IgM positiveb. IgM positive, IgG negativec. IgG negative, IgM negatived. IgG positive, IgM negative
- 4. Causes of fetal hydrops in parvovirus B19 infection is:
  - a. Severe fetal anemiab. High output cardiac failurec. Fetal viral myocarditisd. Impaired hepatic failure
  - e. All of the above
- 5. Diagnosis of fetal infection is most commonly done by:
  - a. Amniotic fluid viral DNA by PCR
  - b. Serum viral DNA by PCR
  - c. Viral particles by electron microscopy
  - d. Viral culture
- In parvovirus B19 infection, what is the most appropriate test to screen for fetal anemia:
  - a. Biophysical profile b. Umbilical artery Doppler
  - c. Middle cerebral artery Doppler d. Neonatal CBP
- 7. Causes of nonimmune fetal hydrops include all except:
  - a. CMV infection b. Parvovirus infection
  - c. Rh incompatibility d. Trisomy 21
- 8. Viral infections in pregnancy associated with fetal hydrops are all except:

a. CMV b. Parvovirus c. Coxsackie virus d. HIV 1 and 2

. The most common cause of nonimmune hydrops is:

- a. Viral infections b. Chromosomal abnormalities
- c. Fetal cardiac abnormality d. Thalassemia
- 10. This infection suppresses fetal erythropoiesis causing anemia and fetal death in 9% of infected fetuses:
  - a. Toxoplasmosis infectionb. Syphilis infectionc. Parvovirus infectiond. Rubella infection

#### **ANSWERS**

- 1. a 2. a 3. d 4. e 5. a 6. c 7. c 8. c
- 9. c 10. c

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# **Clinical Approach to Infections in Pregnancy**

#### **Salient Features**

- Authored by very experienced senior practitioners in obstetrics (maternal health), and members of the professional body, The Federation of Obstetric and Gynaecological Societies of India (FOGSI).
- · Wherever possible, the authors have included Indian statistical data on infections in pregnancy.
- All chapters start with a short illustrative case history, with questions or controversies arising from it. With the objectives
  clearly defined, the clinical approach includes differential diagnosis, investigations and treatment.
- The precise evidence-based management guidelines are illustrated with figures, tables, algorithms and flow charts, making the chapters a comprehensive and handy reference tool.
- The management of the specific infections is practical based, with references to the standard guidelines, Cochrane reviews, ACOG, SAFOG, NICE and SOGC, for management protocols.
- Key points and multiple choice questions are included at the end of each chapter for quick revision and evaluation of comprehension.
- Useful for the postgraduate students, practicing obstetricians and gynecologists, and the physicians involved in maternal health.

**Madhuri Chandra** MD (OBG) DNB (OBG) FICOG CMCL-FAIMER Fellow is currently working as Professor and Head, Department of Obstetrics and Gynecology, Mahavir Institute of Medical Sciences, Bhopal, Madhya Pradesh, India. She is a Former Professor, Department of Obstetrics and Gynecology, Gandhi Medical College, and associated with Sultania Zanana Hospital, Bhopal, and has extensive clinical experience in maternal health, having worked at one of the largest maternity hospitals in Madhya Pradesh with over 13,000 deliveries a year. With keen interest in high-risk pregnancy and labor, social obstetrics, and adolescent health, she has served



as a trainer for maternal health, medical disorders in pregnancy, infant and young child feeding, prevention of parent-to-child transmission (PPTCT) of HIV infection, and adolescent health. For adolescent sexual and reproductive health, she has trained with SIDA, and certified by GFMER. She has a Diploma in Advanced Gynec–Endoscopy from Clermont-Ferrand, France. She has been the Chairperson, HIV and AIDS Committee (2014–2016), FOGSI; and, is currently the President, AMPOGS Research and Public Welfare Society. As undergraduate and postgraduate teacher, she has supervised research projects and theses on obstetrics and gynecology topics. She is an invited faculty at many international, national and state conferences, CMEs and workshops. She is on the board of reviewers of many journals in obstetrics and gynecology, and has also served as a reviewer for Maternal Infections Module of Global Health Training Centre and GFMER. She has authored chapters in various books and published research papers on issues of maternal health and medical education.

Vineet Mishra MD PhD is Professor and Head, Department of Obstetrics and Gynecology, Institute of Kidney Diseases and Research Centre (IKDRC), Institute of Transplant Sciences, BJ Medical College, Ahmedabad, Gujarat, India. He is currently the Vice President of FOGSI, and has served as the Chairperson of Urogynec Committee, FOGSI (2011–2013). He is a Founder Member, Gynaecological Endocrine Society of India (GESI), Member of National Academy of Dialysis and Transplantation, Indian Red Cross Society, Indian Society of Hypertension, NASI, International Society for Research on Civilization Diseases and Environment (SIRMCE),



and has been the Organizing Chairperson of the International Urogynecology Conferences, in 2013, 2015 and 2016. He was awarded the PhD, for his work on oxidative stress in female reproductive lifespan at BJ Medical College under Dr SP Nagpal. His research led to the publication of more than 50 peer-reviewed papers and book chapters. He has also supervised more than 20 theses. He is an honorary Assistant Editor of Asian Journal of Dialysis and Transplantation. He is the recipient of the 'Young Investigator Award' in 1987. He adds to his innovation Prosthesis of Urogynec Indian sling 'Freedom–VM'. He is the principal innovator of vitrification. He has delivered many guest lectures in various international and national conferences, organized and conducted over 100 live endoscopy, and urogynec workshops. His philosophy is "Mother's womb is the cradle that holds the future of humanity. Let us protect it, strengthen it, and nurture it".

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