OBSTETRICS & GYNECOLOGY

# Clinical Approach to Infections in PREGNANCY

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JAYPEE

# Contents

CHAPTER 4

# 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.

### Queries

- 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 parvovirus 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.[1] 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.[2] 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.[3]

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.[4]

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.[5]

Parvovirus B19 has an affinity for hematopoietic system cells, including erythroid progenitor cells, and to a lesser degree, leukocyte and megakaryocyte cell lines.[6] 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.[6] Chronic bone marrow suppression after parvovirus B19 infection leading to chronic severe anemia has been described in immunodeficient patients (example HIV infection).[6]

Rarely parvovirus B19 infection can lead to acute myocarditis, heart failure,[7] 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)**.[9] 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.[11] 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.[12]

## 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[13]

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

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

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

## 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.[10] Testing for fetal parvovirus B19 is indicated when ultrasonography reveals fetal hydrops and may be done prior to an intrauterine transfusion.

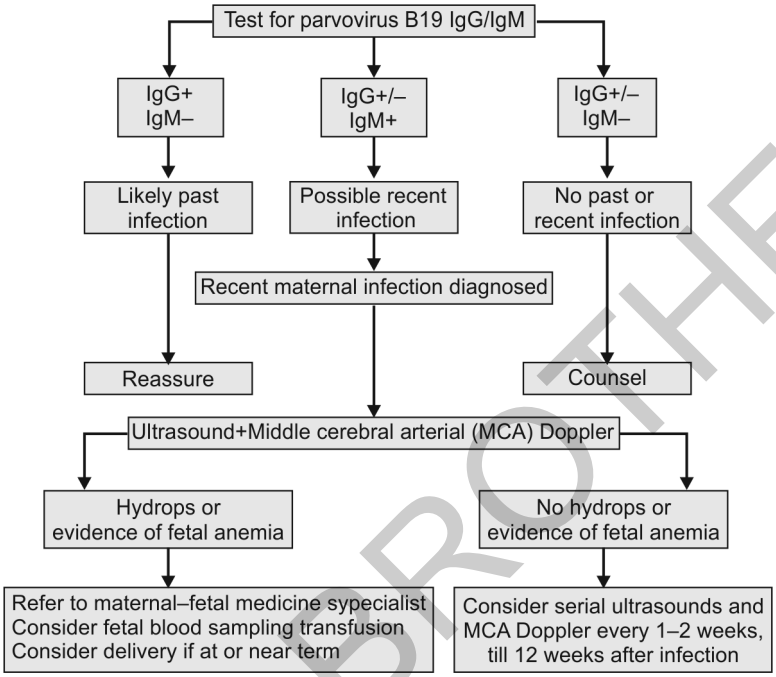
Serology testing for parvovirus B19 IgM in fetal blood cannot be depended to make the diagnosis of fetal infection, because the fetus does not begin to make its own IgM until 22 weeks' gestation.[10]

## 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[11]

## 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. **Parvovirus B19 infection 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 will be:**
   a. IgG positive , IgM positive
   b. IgM positive, IgG negative
   c. IgG negative, IgM negative
   d. IgG positive, IgM negative
4. **Causes of fetal hydrops in parvovirus B19 infection is:**
   a. Severe fetal anemia
   b. High output cardiac failure
   c. Fetal viral myocarditis
   d. 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
6. **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
9. **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 infection
    b. Syphilis infection
    c. Parvovirus infection
    d. Rubella infection

## ANSWERS

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

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