

Sangita Ghosh, Soumik Chaudhuri[†]**INTRODUCTION**

Varicella, or chicken pox, confers lasting immunity and second attacks are uncommon, especially in immunocompetent individuals. Women who reach their child-bearing age without developing immunity to varicella have a small but finite risk of developing chicken pox during pregnancy (0.05–0.07%).^[1] Incidence of varicella in pregnancy is calculated to be 2–3/1000 pregnancies.^[1] For the mother, the risk of severe illness is greatest after mid pregnancy when she is relatively immunocompromised. For the fetus, the risk of congenital infection is greatest when maternal infection occurs in the first or second trimester.

MATERNAL COMPLICATIONS DUE TO VARICELLA INFECTION

Although varicella infection is much less common in adults than in children, in persons >15 years of age and children under 1 year of age, it tends to be more severe with a higher rate of complications like pneumonia, hepatitis and encephalitis, and is associated with higher mortality. Pregnant women who contract varicella in the last trimester are at a higher risk of severe pneumonia and death. Pneumonia can occur

in up to 10–20% of pregnant women with chicken pox, and the severity of these complications seems to increase in later gestation leading to a mortality rate of 14%, whereas in the general population, varicella pneumonia has a mortality rate of 10–11%.^[2–4] Risk factors for the development of varicella pneumonitis in pregnancy include third trimester infection, cigarette smoking, chronic obstructive lung disease, history of taking systemic steroid in the preceding 3 months or immunosuppression or more than 100 skin lesions or hemorrhagic lesions.^[2,5]

HOW TO PREVENT MATERNAL VARICELLA?

Pregnant women who have never had varicella infection in the past and/or have not received varicella vaccine, or in whom varicella antibody serology (immunoglobulin gamma) is negative, are considered non-immune. A previous history of chicken pox infection is 97–99% predictive of the presence of serum varicella antibodies.^[2]

Varicella zoster immunoglobulin (VZIG), which is a disease-specific immunoglobulin prepared by pooling plasma of donors with high levels of varicella zoster antibody, is recommended as post-exposure prophylaxis for non-immune pregnant women. It has been shown to lower varicella infection rates if administered within 72–96 h after exposure.^[1] Protection is estimated to extend through 3 weeks, which corresponds with the half-life of the immunoglobulin. VZIG has no therapeutic benefit once chicken pox has already developed. Aciclovir, as preventive therapy, has been suggested by some authors and is best given on the seventh day post-exposure, but the prophylactic role of this drug in chicken pox is yet to be established.^[3]

Varicella vaccine (Varivax) contains live attenuated virus derived from the Oka strain. It is not recommended for pregnant women or for those expected to be pregnant in the next 1 month. However, termination of pregnancy

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should not be recommended in case of inadvertent vaccination during pregnancy.^[6] Varicella vaccination pre-pregnancy (at least 1 month prior conception) or post-partum can be considered for women who are found to be seronegative for VZV IgG before pregnancy or in the post-partum period [Table 1].

HOW TO MANAGE MATERNAL VARICELLA INFECTION?

Women with significant varicella infection should be treated with oral aciclovir 800 mg five times a day for 7 days starting within 24–72 hours of onset of rash.^[3] Aciclovir is a pregnancy category B drug, and, before 20 weeks of gestation, should be used when potential benefits outweigh risk.^[7] In case of progression to varicella pneumonitis, if the severity of infection warrants, intravenous aciclovir (10–15 mg/kg, every 8 hours for 5–10 days) can be considered.^[4] Fetal ultrasound scan 5 weeks after the primary infection and appropriate follow-up is recommended to all pregnant women who develop varicella during the first or second trimester to screen for fetal abnormalities. They should be advised to avoid contact with other pregnant women and neonates during the period of communicability, which starts 1–2 days prior to the eruption, until the lesions have all crusted, which usually starts 5 days after the onset of rash. Symptomatic treatment and hygiene is advised to prevent secondary bacterial infection of the lesions.

FETAL COMPLICATIONS OF MATERNAL VARICELLA

Fetal effects of varicella can manifest as either “Fetal or congenital varicella syndrome” (embryopathy) or neonatal varicella (no embryopathy, but chicken pox infection within the first 10–12 days of life). The implications of primary maternal varicella on her baby vary with the gestational age at infection.

MATERNAL VARICELLA IN THE FIRST AND SECOND TRIMESTERS

“Fetal varicella syndrome” develops in <2% of the babies born to mothers infected with varicella between 7 and 28 weeks of pregnancy, through transplacental infection, and it has a mortality rate of 30% in the first month of life.^[6] It does not occur at the time of initial fetal infection but results from a subsequent herpes zoster reactivation *in utero* and only occurs in a minority of the infected fetuses.^[3] Clinically, the newborn presents with low birth weight (LBW), cutaneous scars in a dermatomal distribution, papular lesions resembling connective tissue nevi, ocular abnormalities like cataract, microphthalmia and chorioretinitis, bone and muscle hypoplasia, neurological abnormalities like mental retardation, seizures, hydrocephalus, cortical atrophy and microcephaly, Horner’s syndrome, nystagmus and dysfunction of bladder and bowel sphincters.^[6]

Table 1: CDC guidelines for varicella vaccine and varicella zoster immunoglobulin

Varicella vaccination (live Oka strain)	Varicella zoster immunoglobulin
<ol style="list-style-type: none"> Children 1 to under 13 years age <ul style="list-style-type: none"> 1st dose (0.5 mL) of varicella vaccine at 12–15 months of age 2nd dose at 4–6 years of age Children aged 13 years or older and adults <ul style="list-style-type: none"> Two doses of varicella vaccine, 4–8 weeks apart. <p>Formulation: Live attenuated varicella virus prepared from Oka/Merck strain. Each vial of 0.5 mL contains 1350–2000 plaque-forming units</p> <p>Availability: It is readily available commercially in regular pharmacies. The available brands in India are Varivax (VHB GenBioTech), Varilrix (GSK), Okavax (Aventis Pasteur), indexed in the CIMS INDIA directory</p> <p>Cost: 1 vial containing 0.5 mL of vaccine costs about 1500 INR in India</p> <p>Administered as subcutaneous injection in the deltoid region. It should ideally be given with other live vaccines MMR, at separate sites</p> <p>Contraindicated in pregnancy</p>	<p>VZIG is given as post-exposure prophylaxis with a dose of 125 IU/10 kg up to a maximum dose of 625 IU and minimum of 125 IU, in:</p> <ol style="list-style-type: none"> Immunocompromised patients Non-immune pregnant women Neonates whose mother had varicella between 5 days antepartum to 2 days post-partum Premature infants born at <28 weeks, weighing ≤1000 gm at birth and exposed during the neonatal period, irrespective of maternal immunity Premature infants born at ≥28 weeks of gestation, who were exposed during the neonatal period and whose mothers are non-immune <p>Formulation: Varicella zoster immunoglobulin, a disease-specific immunoglobulin prepared by pooling plasma of donors with high levels of varicella zoster antibody. Each vial of 5 mL contains 125 IU of immunoglobulin</p> <p>Availability: Commercially limited availability (in major cities in India). The only brand indexed in CIMS INDIA directory is Vartiect-CP (Paviour Pharma)</p> <p>Cost: 5 mL vial (25 IU/mL) costs 6815 INR</p> <p>Administered as single-dose intramuscular injection in the upper outer quadrant of the buttock or anterolateral thigh. If a second exposure occurs after 3 weeks, a further dose is required</p> <p>Safe in pregnancy</p>

MATERNAL VARICELLA IN THE THIRD TRIMESTER

When maternal infection occurs in the last 3 weeks to >5 days before delivery, there is a significant risk (23%) of neonatal varicella despite high titers of passively acquired maternal antibody.^[3] The route of infection can be transplacental, ascending vaginal or can result from direct contact with lesions during or after delivery. Transplacentally transmitted infection manifests in the first 10–12 days of life, whereas chicken pox after that time is most likely acquired by post-natal infection.^[5]

If the onset of varicella in the mother is 5 days before delivery to 2 days after delivery, an estimated 20–50%



Figure 1: “Neonatal varicella” in a 6-day-old child whose mother had chicken pox 3 days before delivery

of the newborns contract “neonatal varicella,” and 30% of them develop “severe or fulminant neonatal varicella” with disseminated cutaneous lesions and visceral involvement [Figure 1]. This period correlates with the development of maternal IgG; hence, the neonate does not get enough time to acquire passively transferred maternal antibody and there is also a relative immaturity of the neonatal immune system.^[8] In that case, the neonate should be given prophylactic VZIG immediately after birth. With the use of VZIG, the mortality rate has declined from 31% to 7% among neonates with severe varicella infection.^[9,10] Aciclovir therapy should be administered promptly within 24 hours of the onset of rash as it reduces the duration and severity of chicken pox at a dosage of 10–15 mg/kg every 8 h intravenously for 5–7 days.^[8,11] Date of delivery may be post-poned allowing maternal antibodies to pass the placental barrier. No controlled study has yet established the effectiveness of aciclovir or valacyclovir for post-exposure prophylaxis to neonates or pregnant women^[3] [Tables 2 and 3].

CONCLUSION

Chicken pox during pregnancy can have gestational age-specific adverse outcomes both in the mother and in the fetus. Varicella vaccine is contraindicated in pregnancy. Non-immune exposed expectant mothers can be offered VZIG as prophylaxis before infection occurs. Once infection occurs, oral or intravenous

Table 2: Consequences of varicella infection during pregnancy according to gestational age

Gestational age	Effect on mother/fetus/neonate
1. Varicella between 5 days antepartum to 2 days post-partum	– Neonatal varicella. (Risk 20–50%, mortality 20–23%) ^[8] – Severe form of neonatal varicella. (Risk 17–30%, mortality 31%) ^[8]
2. Varicella ≥5 days before delivery (last 3 weeks of pregnancy)	– Neonatal varicella 0–4 days after birth. (Risk 23%; mortality 0–3%) ^[9]
3. Varicella at 3 rd trimester of pregnancy	– Maternal pneumonia (risk 10–20%; mortality 14%) ^[2] – Infantile shingles in the first few years of life due to activation of virus after a primary infection <i>in utero</i> ^[2]
4. Varicella before 13 weeks of gestation	– Fetal varicella syndrome (Risk 0.4%) ^[8]
5. Varicella between 13 weeks and 20 weeks	– Fetal varicella syndrome (Risk 2%); – mortality is 30% in the 1 st month of life ^[6,8]
6. Severe varicella at any stage of pregnancy	– Intrauterine death ^[9]

Table 3: Management of maternal and neonatal varicella

Maternal varicella	Fetal/neonatal varicella
Varicella before 20 weeks of pregnancy – Aciclovir therapy should be used when benefit outweighs risk (in severe varicella or varicella pneumonia) ^[7]	Congenital varicella syndrome – No treatment is effective. Has a very high mortality rate (30%) ^[8]
Varicella after 20 weeks of pregnancy – Oral aciclovir 800 mg five times a day for 5–7 days ^[7] OR Intravenous aciclovir 10–15 mg/kg every 8 hours for 5–10 days if the severity of the infection warrants ^[7]	Neonatal varicella – Neonatal varicella should be promptly treated with intravenous acyclovir 10–15 mg/kg every 8 hours for 5–7 days ^[9]

aciclovir can be advised depending on the severity of infection. Neonatal varicella infection should be treated promptly with intravenous aciclovir.

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