Congenital and Neonatal Varicella

Background

Varicella in pregnancy may cause spontaneous abortion or premature delivery. If the infection occurs in the first 20 weeks of gestation, the fetus may be affected. The literature suggests the risk of embryopathy is approximately 0.4% when maternal infection occurs before 13 weeks and 2% when it occurs between 13 and 20 weeks gestation. Fetuses exposed to varicella also have between 0.8 and 1.7% risk of developing herpes zoster in the first two years of life. When maternal varicella occurs in the four weeks before delivery, fetal infection rate is high and infants may develop varicella after birth. Postnatal exposure may also cause neonatal varicella, which has been considered to carry a high mortality, although no information on its effects had been collected in Australia prior to this study.

Objectives

- To estimate the incidence and severity of congenital and neonatal varicella in Australia
- To estimate the potential benefits of vaccinating non-immune women prior to pregnancy

Case definition

Congenital varicella (including varicella embryopathy)

Any stillborn, newborn infant or child up to the age of 2 years who, in the opinion of the notifying paediatrician, has definite or suspected congenital varicella, ***with or without defects****, based on history, clinical and laboratory findings.*

Neonatal varicella

Any infant with clinical or laboratory-confirmed varicella, with onset in the first month of life, and ***without*** *features of varicella embryopathy. The infection may result from peripartum maternal infection or postnatal exposure.*

Results - 1997

In 1997 there were three confirmed cases of congenital varicella and 13 confirmed cases of neonatal infection. Cases came from New South Wales (6), Queensland (5), Western Australia (3) and Victoria (2). Maternal ages ranged from 21 to 34 years and seven cases were first children.

Congenital varicella

In Western Australia, one pregnancy was terminated at 21 weeks because of hydrocephalus following maternal varicella at 11 weeks gestation. Skin scars were found at autopsy. Another mother had varicella at 16 weeks gestation in her second pregnancy. The child was severely affected with neurological damage (encephalopathy, bulbar palsy, neurogenic bladder), colonic atresia and skin scars, but had no eye defects. Varicella virus was isolated from the infant, who also developed shingles at six weeks of age. In NSW, a mother had varicella at eight weeks gestation. The infant was severely affected with limb, skeletal, heart and nervous system defects, but had normal eyes. The child died at 12 days of age and at autopsy varicella virus was found in the brain by polymerase chain reaction.

Neonatal varicella

Details of the 13 neonatal cases are shown in Table 12. Five mothers had varicella before delivery, six had varicella after delivery and one had a varicella contact at term, but had no illness. In one infant, the source of infection was unknown. Use of zoster immune globulin (ZIG) in 10 children was associated with mild illness. Two of these children also received acyclovir. One infant who did not receive ZIG and whose mother had contact with varicella at term, but no illness, was the only case with a moderately severe illness. He was treated with acyclovir.

Table 12 **Neonatal varicella in Australia, 1997**

Time of mother's varicella contact	Gender	Rash onset (days of age)	Disease severity*	Age baby given ZIG	Time mother given ZIG	Acyclovir for baby
Before delivery	M	7	+	at birth		
	F	7	+	day 1	at infection	
	F	at birth	+	at birth		
	F	13	+	–	at contact	
	F	1	+	day 2		
At term	M	21	++	–		Yes
After delivery	F	25	+	day 1		Yes
	F	7	+	day 2		
	F	21	+	day 5		
	F	14	+	day 3		
	M	20	+	day 11		Yes
	M	18	+	day 2		
No known source of infection	NA	21	+	–		

*Severity of disease: + mild ++ moderate ZIG zoster immune globulin NA not available

Overview 1995-1997

Over this three year period, 75 notifications were received and 71 (95%) questionnaires were returned. From these, 51 confirmed cases of congenital and neonatal varicella infection, including one termination, were identified. The annual incidence, shown in Table 13, is expressed per 100,000 live births and excludes the termination of pregnancy. Of the 50 incident cases, 20 were males, 26 females and the sex of four remains unknown. Maternal ages ranged from 18 to 39 years. No cases were reported from Tasmania.

Table 13 **Annual incidence of congenital and neonatal varicella, 1995-1997**

	Congenital varicella	Incidence* (95% CI)	Neonatal varicella	Incidence* (95% CI)
1995	3	1.2 (0.3-3.7)	15	5.9 (3.4- 9.9)
1996	1	0.4 (0.02-2.6)	16	6.3 (3.7-10.5)
1997	2[#]	0.8 (0.3-1.8)	13	5.2 (2.9- 9.1)
Total	**6**	**0.8 (0.3-1.8)**	**44**	**5.8 (4.3- 7.8)**

* national incidence per 100,000 live births per annum
[#] the termination of pregnancy was excluded

Congenital varicella

The incidence of congenital varicella did not vary over the study period (Table 13). Clinical severity of cases varied (Table 14). Severe malformations were seen both following maternal infection in the first 13 weeks as well as later in the pregnancy. Timing of maternal infection ranged from eight to 26 weeks gestation. There were too few cases to determine whether the risk of congenital malformation was significantly lower after maternal infection in the first 13 weeks than between 13 and 20 weeks gestation, as has been shown in larger series. In the literature, there are few reported cases of congenital varicella following maternal infection after 20 weeks' gestation. It is therefore interesting that the infant exposed to maternal infection at 26 weeks gestation was severely affected.

Conversely, two infants whose mothers had varicella at 13 and 18 weeks were born without defects. They developed zoster at five and four months of age respectively, with complete recovery. One child with defects, whose mother was infected at 12 weeks gestation, also developed herpes zoster at the age of 10 weeks.

Table 14 **Clinical features of congenital varicella, 1995-1997**

Timing of maternal varicella in pregnancy (weeks)	Year of birth	Clinical features in the infant
8	1997	Severe limb, skeletal, heart and central and peripheral nervous system defects, eyes no abnormality detected. Died aged 10 days.
11	1997	Skin scars, hydrocephalus.
12	1996	Skin scars, severe eye damage (blind), zoster at 10 weeks.
13	1995	No defects, disseminated zoster at 5 months – recovered.
16	1997	Skin scars, neurological & gastrointestinal defects, eyes no abnormality detected.
18	1995	No defects, zoster at 4 months - recovered.
26	1995	Skin scars, eye damage (chorioretinitis).

Neonatal varicella

All 44 infants with neonatal varicella recovered without reported sequelae. Of these cases, only two were severely affected. One followed maternal infection on day 14 postpartum and one followed intrapartum infection. Neither was given ZIG. The use of ZIG in infants at exposure seemed to modify the illness, however, ZIG did not prevent infection of the mother or transmission to the fetus in all cases.

The illness in infants whose mothers were infected within a week before or a week after delivery was more severe in the six who did not receive ZIG than in the 17 who did. However, the illness in these children was no more severe than in those infants whose mothers were infected outside the two-week period around delivery.

Conclusion

There has been a small but consistent annual incidence of congenital and neonatal varicella which has not previously been documented in Australia. The severely affected child with congenital varicella, whose mother had varicella at 26 weeks gestation, is important because there are few reported cases with defects whose mothers were infected so late in pregnancy. Infected cases with no defects at birth may be overlooked and may not have been reported. This study suggests that all affected pregnancies should be carefully monitored and infants screened for systemic complications. It also suggests that zoster immune globulin should be given to all exposed neonates.

Investigators

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