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Prospective Study of Pregnancy and Newborn Outcomes in Mothers with West Nile Illness during Pregnancy

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Abstract

Background—A previous case report of West Nile virus (WNV) illness during pregnancy suggested that WNV could be a cause of congenital defects. We performed a prospective, longitudinal cohort study of pregnant women with WNV illness to increase our knowledge of the effects of WNV illness during pregnancy.

Methods—Participants were enrolled in 2005 to 2008 from pregnant women with serologically confirmed WNV illness reported to the Centers for Disease Control and Prevention. Comparison was made to WNV-uninfected women, matched on maternal age and enrollment month. Pregnancy and newborn data were collected; cord blood WNV serology was obtained. Pediatric exams and the Bayley Scales of Infant and Toddler Development-Third Edition (Bayley-III) were performed.

Results—Twenty-eight WNV-infected mothers and 25 WNV-uninfected mothers participated. Maternal demographics were similar except for a higher rate of planned pregnancies, education, and household income in the WNV-uninfected mothers. There were no differences in pregnancy and delivery characteristics except that infected mothers had a higher incidence of febrile illnesses and used more medications. Birth weight, length, head circumference, and rate of congenital malformations were similar in babies born to WNV-infected and -uninfected mothers. Follow-up physical exams were generally normal. The Bayley-III assessments, available for 17 children born to mothers with WNV illness, showed performance at or above age level across domains.

Conclusion—The risk for adverse pregnancy and newborn outcomes in women experiencing WNV illness in pregnancy appears to be low, but future studies with larger numbers are needed to rule out a small risk.

Keywords

infant development; perinatal infection; pregnancy; West Nile virus

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Introduction

In 2002, 3 years after West Nile virus (WNV) was first detected in the Western hemisphere (Nash et al., 1999), the first case of maternal infection with vertical transmission during human pregnancy was reported (CDC MMWR, 2002a). The mother developed WNV encephalitis at 27 weeks of gestation, recovered from her acute illness, but subsequently delivered a full-term infant with chorioretinitis, cystic destruction of cerebral tissue, and laboratory evidence of WNV infection.

The finding of neurologic abnormalities in the newborn of the infected mother reported in 2002 led to concern that WNV infection might be teratogenic, particularly to the central nervous system. Subsequently, O'Leary et al. (2006) described the outcomes of 72 newborns of mothers infected by WNV who were reported to the Centers for Disease Control and Prevention (CDC) between 2003 and 2004. Three infants had WNV infection that could have been congenitally acquired but postnatal infection through mosquito bite or breast milk could not be ruled out. One of these three infants had lissencephaly, but this was not thought to be attributable to the WNV infection based on the timing of the mother's infection.

To increase the knowledge regarding the effects of WNV illness during pregnancy on infant outcomes, we performed a prospective, longitudinal, cohort study of pregnant women with WNV illness. We specifically assessed pregnancy and newborn outcomes, particularly to determine the risk of congenital malformations (primary outcome). Given the report of chorioretinitis and cystic destruction of cerebral tissue in an infected newborn, we hypothesized that we would see a higher rate of congenital malformations, particularly of the central nervous system, in infants born to WNV-infected mothers.

Material and Methods

This study enrolled pregnant women with serologically confirmed WNV illness reported to the CDC from 2005 through 2008. When WNV illness in a pregnant woman was reported to the CDC, the mother was invited to participate in the study.

We also prospectively recruited uninfected pregnant women from hospitals where study participants with WNV illness delivered, and from local area hospitals, such as Tulane Hospital and Clinic and Medical Center of Louisiana, New Orleans. The study was approved by the Tulane University Biomedical Institutional Review Board.

Women with WNV infection during pregnancy who were invited to participate had laboratory criteria for diagnosis included the following: (1) fourfold or greater change in virus-specific serum antibody titer; or (2) isolation of virus from tissue, blood, cerebrospinal fluid, or other body fluid; or (3) virus-specific immunoglobulin M (IgM) antibodies demonstrated in cerebrospinal fluid by antibody-capture enzyme-linked immunosorbent assay (ELISA), or (4) virus-specific IgM antibodies demonstrated in serum by antibody-capture ELISA and confirmed by demonstration of virus-specific serum immunoglobulin G (IgG) antibodies in the same or a later specimen by another serologic assay (e.g., neutralization or hemagglutination inhibition).

WNV-uninfected mothers were pregnant women who had no symptoms consistent with encephalitis or meningitis at any time during pregnancy, no other exposure that was believed to be teratogenic, and no preexisting diabetes. Cord blood from potential uninfected participants was tested for WNV IgG to confirm uninfected status; participants whose specimens indicated past WNV infection were removed from the study. Uninfected participants were matched to the infected participants by month of gestation and age group (less than 25, 25–35, and greater than 35 years of age) at enrollment.

LABORATORY TESTING

Cord blood from infants born to WNV-infected mothers were tested at Tulane University School of Public Health and Tropical Medicine for the presence of WNV IgM antibodies using the West Nile Virus IgM Capture DxSelect™ ELISA kit (Focus Diagnostics, Cypress, CA) according to the manufacturer's instructions. Cord blood of infants born to WNV-uninfected mothers was tested for WNV specific IgG. Confirmation of WNV diagnosis was performed with anti-WNV neutralizing antibodies by using a Plaque Reduction Neutralization Test (Lieberman et al., 2009).

OUTCOME ASSESSMENT

Information on demographics, socioeconomic status, and family history of birth defects was obtained for infected and noninfected mothers by a self-administered questionnaire at the time of enrollment. The mother's physician completed a questionnaire regarding the maternal prenatal course and intrapartum complications. Supplemental information was obtained from review of the medical record pertaining to pregnancy and delivery.

Infant outcomes were obtained from the medical record and the infant's healthcare provider's completed questionnaire regarding examination at birth and follow up visits. Study physicians did not systematically examine study newborns. A newborn was designated small-for-gestational-age if birth weight was less than the 10^{th} percentile for gestational age at birth and large-for-gestational-age if the birth weight for gestational age was greater than the 90^{th} percentile using US data from intrauterine growth curves of Olsen et al. (2010). Pediatricians were recommended to follow the interim guidelines for evaluation of babies born to mothers with WNV illness in pregnancy (MMWR, 2004). Babies were examined by their pediatrician at birth and at 6 months intervals until 2 years of age. Infants had hearing and vision screening; full ophthalmologic examination was provided to the pediatrician free of charge.

Birth defects were defined according to the CDC's Metropolitan Atlanta Congenital Defects Program guidelines (CDC, 2004). Birth defects were classified as major or minor. Major anomalies were defined as those that create significant medical problems or require specific surgical or medical management. Minor anomalies were features that may vary from those that are commonly seen in the normal population but alone do not cause increased morbidity.

DEVELOPMENTAL TESTING

The Bayley Scales of Infant and Toddler Development –Third Edition (Bayley-III) were administered to children at approximately 24 months of age by local participating psychologists, using standardized assessment procedures (Bayley, 2006). The Bayley-III provides standardized measures of child development in five domains: Cognitive (problem-solving), Language (receptive and expressive skills), Motor (fine- and gross-motor skills), Social-Emotional (social behavior and self-regulation), and Adaptive Behavior (for example, communication, self-care, and pre-academic skills). The Cognitive, Language, and Motor domains are assessed through direct testing with the child; the Social-Emotional and Adaptive Behavior domains are assessed through interviews with the parent. The standardization sample of the Bayley-III provides the reference mean for the domain composite scores (Mean = 100, standard deviation [SD] = 15).

Statistical analysis was performed by the two-sided Student's *t* test for continuous data, chi square and Fisher's Exact test for categorical data and the Mann-Whitney *U* test for nonparametric data. An alpha error probability of less than 0.05 was considered statistically significant.

Results

Of the 49 cases of WNV illness in pregnancy reported to the CDC from 2005 to 2008 (Nicole Lindsey, personal communication), 28 mothers agreed to participate in this study; data are available for 26 WNV-uninfected women who were matched for age category, and trimester of pregnancy at enrollment. One mother from Louisiana selected for the uninfected group was excluded from the study because of evidence of prior WNV infection based on the presence of WNV IgG in cord blood.

At initial enrollment, the most common symptom of women in the WNV illness group was fever, reported in 20 of 28; a diagnosis of meningitis or encephalitis was made in 11 women, 3 of whom did not report fever. Other commonly reported maternal symptoms were rash, headache, nausea, vomiting, fatigue, poor concentration, and muscle weakness. Onset of WNV illness occurred in 4, 11, and 13 women in the first, second, and third trimesters, respectively.

Self-reported maternal characteristics in the WNV-infected and -uninfected groups were generally similar except for a higher number of planned pregnancies ($p = 0.002$), level of education ($p = 0.005$), and household income ($p = 0.002$) in the uninfected group (Table 1). There were no significant differences between the groups in rates of family history of birth defects.

Pregnancy characteristics as well as pre-existing pregnancy complications were generally similar between groups (Table 2). One woman in the WNV illness group had epilepsy before pregnancy but was not on anti-seizure medication. No women in the uninfected group reported a pre-existing medical condition. The incidence of prior spontaneous abortion, preterm birth, stillbirth, fetal growth restriction, and preeclampsia were similar between the groups. In the WNV illness group, one woman had a previous child with Down syndrome.

There were no differences between the WNV-infected and -uninfected groups in frequency of prenatal care or folic acid supplementation.

MATERNAL OUTCOMES

Women in the WNV illness group had more episodes of febrile illness ($p < 0.001$) and used more medications during the pregnancy ($p = 0.001$; Table 2). No woman in either group developed gestational diabetes, oligohydramnios, polyhydramnios, or preterm premature rupture of membranes. The frequencies of other pregnancy complications such as hypertension, vaginal bleeding after 20 weeks, placental abruption, and placenta previa were not statistically different between the groups. The rates of intrapartum complications and the cesarean delivery rate were similar among both groups. One woman in the WNV illness group underwent an emergent cesarean section at 30 weeks of gestation because of placental abruption that occurred 3 weeks after the onset of WNV symptoms. A second WNV-infected mother was diagnosed with a placental abruption at 37 weeks of gestation, 19 weeks after onset of WNV symptoms. The diagnosis of placental abruption was made on the basis of vaginal bleeding. Other than the bleeding, the mother had an uneventful labor and delivered a healthy newborn by the vaginal route.

NEWBORN OUTCOMES

None of the infants born to WNV-infected mothers were born with evidence of clinical infection, and none were noted to have neurologic deficits at birth. No infants born to WNV-infected mothers tested positive for WNV IgM (Table 3). There were no stillbirths. All newborns delivered at or near term except one aforementioned infant born to a WNV-infected mother at 30 weeks gestation because of placental abruption. The newborn was born with a birth weight average for gestational age and died shortly after emergency cesarean delivery. Serologic testing of cord blood was negative for WNV IgM. Placental pathology was normal; autopsy was not performed, but there were no gross structural abnormalities noted. Neonatal death was attributed to placental abruption.

Mean birth weight, birth length, head circumference, and median APGAR scores at 1 and 5 min were similar in the maternal WNV-infected and -uninfected groups. Based on review of medical records, no baby was reported to have dysmorphic features. Hearing screen was normal at birth or at subsequent physical examinations for 26 of 27 newborns of mothers with WNV illness (excluding neonatal death) and 23 of 25 newborns in the WNV-uninfected group. Hearing testing data were not available for one child in the WNV group and two in the WNV-uninfected group.

NEWBORN FOLLOW-UP

Information from pediatric postnatal examinations was available for 22 babies of mothers with WNV illness and 8 babies born to uninfected mothers at 2 months of age; 19 and 11 children, respectively, at 6 months of age; 19 and 9, respectively, at 12 months of age. Pediatric examinations were available for 8 children of WNV-infected mothers at 18 and 24 months, but no children of WNV-uninfected mothers.

The frequency of congenital anomalies was not different between the maternal WNV-infected and -uninfected groups. One child born to a mother in the WNV-infected group had a major birth defect, pyloric stenosis, muscular hypertrophy of the pylorus causing obstruction to the duodenum. The mother of this child also had pyloric stenosis requiring surgical repair. No children in the WNV-uninfected group had major birth defects. One child in the WNV-infected group had a minor birth defect, an umbilical hernia diagnosed at 12 months of age. One child in the WNV-uninfected group had minor birth defect, a patent foramen ovale (failure of timely postnatal closure of the foramen ovale), that resolved during the first year of life. No other congenital malformations were found. Vision screening was normal in the WNV-illness and WNV-uninfected groups. Detailed ophthalmologic examination with retinal exam was performed on 22 children in the WNV-illness group and 1 child in the control group (because of mild ptosis that resolved). No visual or retinal abnormalities were noted.

DEVELOPMENTAL OUTCOMES

Seventeen children in the maternal WNV illness group completed the Bayley-III. Mean age at testing was 28.6 months (range, 18–35 months). Most of the children performed at or above age level across domains (Table 4). Two children showed mild delays: one on the Cognitive domain (standard score [SS] = 80) and one on the Language (SS = 79), Social-Emotional (SS = 60), and Adaptive (SS = 80) domains. The Bayley-III was not performed for children in the uninfected group; however, development screenings were performed during their physical examinations and no deficiencies were noted except for one child with mild fine-motor delay at 12 months of age.

Discussion

In our prospective cohort study, none of the children of mothers with WNV illness during the pregnancy were born with evidence of WNV infection, either clinically or by detection of WNV-specific IgM antibody in their cord blood. Thus, we had no evidence of transplacental transmission of WNV to any newborns among 28 mothers in our study with WNV during pregnancy. Furthermore, we did not find a greater rate of congenital malformations or developmental delay in children born of mothers who had WNV illness in pregnancy, compared with infants born to WNV-uninfected mothers. The congenital malformations seen in our study were not of the central nervous system, and were within the range of frequency of anomalies seen in the general population (Frias and Carey, 1996; CDC, 2004; Correa et al., 2007).

WNV is a neurotropic virus transmitted primarily through infected mosquitoes. Only approximately 20 to 25% of infected individuals become symptomatic (Petersen et al., 2013). Of symptomatic individuals, most develop nonneuroinvasive disease, manifested by fever, headache, fatigue, malaise, poor concentration, muscle pain, and weakness, which is eventually self-limiting (Hayes et al., 2005). The remainder develops neuroinvasive disease, including encephalitis, meningitis, or acute flaccid paralysis. In children, WNV illness is more likely to manifest as meningitis compared with older adults (Lindsey et al., 2009).

Until recently, little was known regarding WNV infection in pregnancy. In a mouse model, WNV was shown to infect placenta and possibly mouse embryos (Julander et al., 2006). The 2002 case report (CDC MMRW, 2002a; Alpert et al., 2003) demonstrated that maternal infection with WNV in the late second trimester of pregnancy could be transplacentally transmitted to the fetus and could possibly be teratogenic to the central nervous system. Subsequently, several pregnant women with WNV illness were reported without evidence of transplacental transmission (Chapa et al., 2003; Bruno et al., 2004; Skupski et al., 2006). One pregnant woman with WNV illness was reported with probable WNV transmission to her child through breast milk (CDC MMWR, 2002b), but this was likely a rare event (Hinckely et al., 2007). In the retrospective assessment of 77 pregnant women with WNV illness reported to the CDC during 2003 to 2004, four mothers had spontaneous abortions, two had elective terminations of pregnancy, and the remaining 71 mothers delivered 72 live infants. Of the 66 newborns for whom information was available, 7 had a major birth defect (aortic coarctation, cleft palate, Down syndrome, lissencephaly, microcephaly, polydactyly) (O'Leary et al., 2006). However, there was no evidence of transplacental transmission, with cord blood serologic testing negative for WNV-specific IgM.

In our study, pregnancy complications were not higher in the mothers who had WNV illness in pregnancy. Similar rates of complications were seen in the babies born to mothers with and without WNV illness. Of note, two mothers in the WNV illness group had a placental abruption and none in the WNV-uninfected group. One mother, diagnosed with WNV encephalitis at 21weeks of gestation, presented at 38 weeks of gestation with bleeding and was diagnosed with a placental abruption, but labor and delivery were unremarkable. The other had an acute placental abruption diagnosed 3 weeks after onset of WNV meningitis; emergency cesarean delivery at 30 weeks was performed, followed by neonatal death. Because the newborn's cord blood was negative for WNV-specific IgM and there were no signs of chorioamnionitis or placental pathology, it is unlikely that WNV infection was causative.

Developmental testing in the children born of mothers with WNV illness in pregnancy was generally normal; global developmental delays were not noted. This finding is in concordance with a retrospective study of developmental outcomes in children born to mothers with West Nile illness during pregnancy (Sirois et al., 2014). These data represent early childhood developmental assessments; no information is available regarding development in later childhood.

One mother initially selected for the WNV-uninfected group (from Louisiana) was excluded from our study because cord blood was positive for WNV IgG, evidence of previous WNV infection. Paisley et al. (2006) showed that after a community-wide epidemic in a Northern Colorado community, 569 asymptomatic women who presented to labor and delivery had cord blood assessment of WNV-specific antibodies; 4% (95% confidence interval, 2.4–5.7%) had WNV-specific IgG antibodies but not WNV-IgM.

Our study has several strengths. The prospective, longitudinal nature of the study design allowed us to follow women with documented WNV illness during pregnancy. Additionally, all newborns born to WNV-infected mothers had cord blood testing for congenital infection

using WNV-specific IgM. The study also has several limitations. Our original sample size calculation was based on the assumption of a 10% adverse pregnancy outcomes (including malformations) in the uninfected women; we would require 51 exposed women and 102 unexposed women to detect a relative risk of 3.00 at 80% power and $\alpha = 0.05$. However, we were only able to enroll 49 women infected WNV reported to the CDC during our study period. Of 49 women with WNV illness, only 28 women agreed to participate in this study. Therefore, our study has limited statistical power to detect possible differences in rates of adverse pregnancy outcomes. Furthermore, it is possible that more second and third trimester WNV illness mothers were enrolled if mothers with first trimester WNV illness experienced a spontaneous pregnancy loss. Also, the WNV-uninfected mothers in our study had more planned pregnancies, a higher level of education, and higher household income, suggesting the possibility of selection bias in the samples.

While various investigators may use different definitions of anomalies, we ultimately compared the two groups, and our designation of anomalies was similar for each group. We chose to list what was seen and be more inclusive. For example, we could have removed the pyloric stenosis, the child's mother had pyloric stenosis (multifactorial, polygenic inheritance) by attributing the malformation to genetic risk alone and not teratogenicity. We could have also removed Down syndrome as it is well known that it does not develop as a result of teratogenicity. However, the authors believed it important to be complete in reporting.

In summary, based on our study, the risk of congenital infection, congenital malformations, and developmental delay among infants born to women infected with WNV illness during pregnancy does not appear to be elevated, but future studies with larger numbers are needed to rule out a small risk.

Pregnant women should avoid mosquito-infested areas, especially at times of high mosquito infestation (summer and early fall) and particularly in the early morning and late evening. Pregnant women should also wear protective clothing and use insect repellent for prevention (CDC, 2015).

WNV should be considered as a cause of illness in mothers with meningitis or related symptoms throughout the year because seasonal epidemics are difficult to predict (Jamieson et al., 2006; Lindsey et al., 2010). In suspected cases of WNV illness in pregnancy, confirmation of maternal infection can be performed with WNV serology. If maternal West Nile virus illness is diagnosed, a detailed ultrasound examination of the fetus to evaluate for structural abnormalities should be considered no sooner than 2 to 4 weeks after onset of illness in the mother. Amniotic fluid, chorionic villi, or fetal serum can be tested for evidence of West Nile virus infection. However, the sensitivity, specificity, and predictive value of tests that might be used to evaluate fetal infection are not known.

It is not clear if these findings for West Nile Virus have implications for the emerging Zika virus outbreak in the Americas. Although West Nile and Zika virus are closely related flaviruses, they may have substantially different pathologic effects on the developing fetus.

For this reason, it is important to conduct investigations into any emerging vector-borne threat to understand both the short- and long-term impacts of maternal infections.

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TABLE 1

Maternal Characteristics

	West Nile virusillness *N* = 28	Uninfected women *N* = 25	*p*-Value
Maternal age (mean ± SD)	29.4 ± 6.0	31.8 ± 4.3	0.109
Pre-pregnancy BMI (mean ± SD)	25.2 ± 4.0	26.3 ± 7.0	0.480
Planned pregnancy	17	24	0.002
Ethnicity			
White	24	24	0.399
Hispanic	3	1	
Native American	1	0	
Education			
Graduate/professional	2	8	0.005
College	15	17	
High school	12	0	
Household income[a]			
>$60,000	7	16	0.002
$40,000–$60,000	4	2	
$9000–$40,000	9	3	
<$9,000	4	0	
Tobacco use	7	1	0.053
Alcohol use	5	2	0.256
Drug use	2	0	0.492
Maternal birth defects	1 (pyloric stenosis)	0	1.000
Maternal family history of birth defects[b]	1	2	0.597
Paternal family history of birth defects[c]	3	3	1.000

[a]Four in each group declined to report.

[b]One of WNV group unsure.

[c]Three of WNV group unsure.

BMI, body mass index.

TABLE 2
Pregnancy and Delivery Characteristics

	West Nile virus illness *N* = 28	Uninfected women *N* = 25	*p*-Value
Gravidity, median (range)	2 (1–6)	2 (1–4)	0.339
Parity median (range)	1 (0–4)	1 (0–2)	0.734
Pre-existing maternal illness			
Epilepsy	1	0	1.000
Pre-existing pregnancy complications			
Prior spontaneous abortion	8	8	1.000
Prior preterm birth	3	3	1.000
Prior stillbirth	2	1	1.000
Prior fetal growth restriction	1	0	1.000
Prior preeclampsia /eclampsia	1	0	1.000
Prior children with birth defects	1 (Down syndrome)	0	1.000
Current pregnancy			
Had prenatal care	28	25	1.000
Folic acid supplement[a]	24	23	1.000
Other medications used by indication[b]			
Cold/upper respiratory infection	5	2	0.426
Urinary tract infection	4	1	0.355
Hypothyroidism	1	2	0.597
Nausea and vomiting	4	3	1.000
Fever	3	0	0.238
Sleep	3	0	0.238
Mood disorders	2	1	1.000
Other	3	2	1.000
Total medications used	25	11	0.001
Pregnancy complications			
Gestational hypertension / pre-eclampsia	1	3	0.333
Febrile illness	15	0	< 0.001
Vaginal bleeding over 20 weeks	3	0	0.238
Placental abruption	2	0	0.492
Placenta previa	1	0	1.000
Maternal infection (other than WNV)			
Cold or flu	4	2	0.672
Urinary tract infection	4	0	0.113
Recurrent Herpes	1	2	0.597
Chlamydia	1	0	1.000
Intrapartum complications			

	West Nile virus illness *N* = 28	Uninfected women *N* = 25	*p*-Value
Non-reassuring fetal heart tracing	1	0	1.000
Primary cesarean delivery	5	6	0.582
Group B streptococcus colonization	3	4	0.694
Chorioamnionitis	1	0	1.000

[a] Four and two missing entries for WNV and uninfected groups, respectively.

[b] Medication use in WNV group: acetaminophen, bupropion, hydroxyzine, diphenhydramine, zolpidem, morphine, pantoprazole, azithromycin, methylprednisolone, ondansetron, levothyroxine, nitrofurantoin, oseltamivir; medication use in control group: bupropion, levothyroxine, enoxaparin, ondansetron, promethazine, acyclovir.

WNV, West Nile virus.

TABLE 3

Newborn Characteristics

	West Nile virus illness *N* = 28	Uninfected women *N* = 25	*p*-Value
Presence of umbilical cord blood WNV antibody[a]			
IgM negative	28	-	
IgG negative	-	25	
Gestational age at birth, weeks (mean ± SD)	38.6 ± 1.9	38.6 ± 1.1	0.924
Preterm birth	1	0	1.000
Live birth	28	25	1.000
Neonatal death	1	0	1.000
APGAR[b] median (range)			
1 min	8 (3 – 9)	9 (4–9)	0.377
5 min	9 (8 –10)	9 (7–9)	0.472
Birth weight,[b] gm (mean ± SD)	3384 ± 374	3501 (± 515)	0.365
Birth length, cm (mean ± SD)	50.5 ± 3.1	50.1 ± 2.4	0.620
Birth head circumference, cm (mean ± SD)	34.3 ± 1.2	34.4 ± 2.0	0.982
Small for gestational age[b]	0	0	1.000
Respiratory distress	2	2	1.000
Signs of infection at birth[c]	0	1	0.481
Hearing test passed[d]	26	23	1.000
Birth defects-major[e]	1 (pyloric stenosis)	0	0.481
Birth defects-minor	1 (umbilical hernia)	1 (patent foramen ovale)	1.000

[a] Newborns from WNV illness mothers not tested for IgG; newborns from uninfected mothers not tested for IgM.

[b] A preterm birth with neonatal death not included; two missing WNV group birth weight entries.

[c] Includes sepsis, pneumonia, seizures, skin rash, thrombocytopenia, cataracts.

[d] Two missing entries in each group; one in the WNV illness group because of neonatal death.

[e] The mother of the child with pyloric stenosis also had hypertrophic pyloric stenosis.

IgG, immunoglobulin G; IgM, immunoglobulin M; WNV, West Nile virus.

TABLE 4

Bayley-III Developmental Assessment – Children of Mothers with West Nile Virus Illness

Domain Composite Score	*N*	Mean	SD	Range
Cognitive	17	112.4	19.6	80–145
Language	17	110.9	19.3	79–153
Motor	16	116.3	18.7	85–154
Social-Emotional	15	111.0	22.9	60–145
Adaptive Behavior	14	106.7	13.3	80–127

Not all children were tested, and not all were tested in all domains. The reference mean ± SD of the Bayley-III for Domain Composite Scores is 100 ± 15.