**Symposium Title:** Congenital infections and Intellectual and Developmental Disabilities: Child and Family Consequences of Congenital Zika Syndrome

**Chair:** Anne C. Wheeler

**Discussant:** Audrey Thurm, NIH/NICHD

**Overview:** In early 2016, Brazil declared a National Public Health Emergency and the World Health Organization (WHO) declared a Public Health Emergency of International Concern (PHEIC) due to an epidemic of birth defects resulting from Zika infection in pregnant women. “Congenital Zika syndrome” (CZS) reflects the spectrum of symptoms observed in children who were exposed to the Zika virus in utero. Although Zika no longer meets the WHO definition of PHEIC, nearly 4000 infants worldwide have been affected. Severe microcephaly was the first and most significant clinical finding of CZS. However, it is now clear that CZS differs from other congenital infections, with five distinct features: “(1) severe microcephaly with partially collapsed skull; (2) thin cerebral cortices with subcortical calcifications; (3) macular scarring and focal pigmented retinal mottling; (4) congenital contractures; and (5) marked early hypertonia and symptoms of extrapyramidal involvement.” Based on the severity of these clinical features on the developing child, the extent of impairment in these children will be lifelong and profound. Understanding the profiles of developmental and behavioral trajectories in the children and the impact of the diagnosis on families is important for identifying appropriate supports and interventions to improve quality of life. The three presentations in this symposium will highlight some of the work being done to understand the profiles of strengths and weaknesses in children and families affected by CZS. The first presentation will describe findings on the developmental and medical profiles of 160 toddlers with CZS in Recife, Brazil. The second presentation will provide an overview of the physical and emotional impact of CZS on the mothers of these same children. The third presentation will focus on reports of family outcomes and the impact CZS has had on their lives.

**Paper Title:** Developmental Profiles of Toddlers with Congenital Zika Syndrome

**Authors:** Anne Wheeler, Danielle Toth, Camila Ventura, Liana Ventura, Lucélia Lima Nobrega, Raine Costa Borba Firmino, Claudia Marques da Silva, Don Bailey

**Introduction:** Previous reports of developmental profiles in small samples of infants and toddlers with CZS have been conducted using primarily parent report of milestone attainment. These studies relied on the Ages and Stages Questionnaire to assess the overall extent of delays and emerging strengths and weaknesses in developmental profiles. These reports suggest nearly all affected children are functioning well below developmental expectations, with most demonstrating skills in the 3-6-month age range. Communication and gross motor skills have been reported to be relative strengths while problem-solving and fine motor skills were relative weaknesses. Although these studies provide an important glimpse into the development of these children, they are limited by the small sample size and reliance on parent report. This presentation will provide a more comprehensive examination of developmental profiles of children with CZS using direct assessment tools, parent report, and medical record reviews.

**Methods:** As part of a 5-year longitudinal study of the consequences of CZS, 155 toddlers and their primary caregivers participated in an initial assessment at the Altino Ventura Foundation (FAV) in Recife, Brazil. The children were assessed by trained data collectors using the Brazilian Bayley Scales of Infant and Toddler Development (BSID), and caregivers completed several measures to assess problem-solving, communication, and functional skill attainment. Medical records were also reviewed to identify co-occurring conditions. All children were between 19 – 37 months of age at the time of the assessment.
Results: Results from the BSID support previous findings suggesting general developmental functioning in the 2-4 month range across all areas of development; however, variability in functioning was seen across the sample and across developmental domains. While the majority of children were found to have profound developmental delays, a small sub-set (n =10) were meeting milestones at a delayed, but still progressive pace. Receptive communication was a noted strength for the sample as a whole on the BSID and caregivers report most children have mastered communicating their needs and wants effectively. Fine motor skills appear to be the most profoundly impacted area of development, with co-morbid visual impairments, seizures, and contractures resulting in limited use of their hands.

Discussion: CZS will have lifelong consequences for affected children and their families. Understanding the developmental and behavioral trajectories of affected infants will help in identifying appropriate individual and family supports to improve quality of life. Our data suggests that at around 30 months of age nearly all toddlers have severe to profound developmental delay; however, variability in profiles suggest some potential avenues for intervention. Planned longitudinal research to identify variables associated with better or worse outcomes will be discussed.


Paper 2 of 3

Paper Title: Caregiving Stress and Mental Health Effects among Parents of Children with Congenital Zika Syndrome

Authors: Danielle Toth1, Anne Wheeler1, Don Bailey1, Camila Ventura2, Liana Ventura2, Lucélia Lima Nobrega2, Raine Costa Borba Firmino2, Claudia Marques da Silva2

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Introduction: Families who have a child with CZS face not only the immediate challenges that come with caring for a child with severe cognitive, motor, and communication impairments, but also the uncertainty around the long-term prognosis of CZS. While parent reported stress and health outcomes in caregivers have been explored for several disabilities, there are limited findings on the impact of CZS on parenting stress and health concerns experienced by primary caregivers. This presentation explored the relationship between parent reported experiences and the extent to which they may be predictive of parenting stress among families with a child with CZS.

Methods: 174 families who visited the multidisciplinary rehabilitation center at the Altino Ventura Foundation (FAV) consented to completing a semi-structured interview consisting of a series of standardized assessment scales, including the Parenting Stress Index Short Form (PSI-4-SF) and the Self-Reporting Questionnaire (SRQ). The PSI-4-SF is a 36-item questionnaire that measures stress based on parent characteristics, parent perceptions of their child’s characteristics, and child/parent interaction.\(^5\) The SRQ is an instrument designed by the World Health Organization (WHO) as a screening tool for psychiatric disturbances, developed primarily for use in developing countries.\(^6\)

Results: PSI-4-SF scores revealed clinically significant levels of parental distress and total stress among 35.6% and 10.9% of the sample, respectively. Only 1.7% of parents had clinically significant scores in the Parent-Child Dysfunction Interaction subscale. Among highly endorsed symptoms, a significant difference in group means emerged of total stress scores between parents who did and did not report the following: sleeping badly ($Z=4.1237$, $P<0.0001$), feeling nervous, tense, or worried ($Z=-2.6384$, $P<0.0083$), and feeling tired all the time ($Z=-6.1313$, $P<0.0001$). Total SRQ scores were a significant predictor of total parenting stress ($R^2 = 0.3587$, $F = 96.19$, $P<.0001$).

Discussion: These findings provide a deeper understanding of the rates and types of parenting stress experienced by primary caregivers of children with CZS and underscore the importance of mental health screening and interventions. Further research should explore factors such as sleep quality, anxiety, and depression experienced among parents. Higher rates of parental distress as compared to the difficult child and parent-child dysfunctional Interaction subscale scores indicate causes of parenting stress independent of the parenting experience that contribute to total stress. This symposium will further explore additional health outcomes related to parenting stress and the mediating effects of other variables on parenting stress and health among parents of children with CZS.

Paper 3 of 3

Paper Title: Family Outcomes of Congenital Zika Syndrome in Brazil

Authors: Don Bailey\(^{1}\), Anne Wheeler\(^{1}\), Danielle Toth\(^{1}\), Amanda Wylie\(^{1}\), Melissa Raspa\(^{1}\), Camila Ventura\(^{2}\), Liana Ventura\(^{2}\)

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Introduction: Families of children with intellectual and developmental disabilities often face a lifetime of challenges in supporting their children and adapting to unique caregiving responsibilities, and will certainly be true for families of children affected by congenital Zika syndrome (CZS). Unfortunately, much attention has been paid to the severity of disability in CZS, with relatively little attention to family consequences.\(^1\) This presentation is the first analysis of outcomes reported by a large sample of mothers of children with CZS in Brazil.

Methods: 166 mothers of children with CZS in northeastern Brazil completed the Family Outcomes Survey-Revised (FOS-R). The FOS-R is a self-report instrument designed to measure the extent to which parents have attained outcomes in five domains: (1) understanding their child’s strengths, abilities, and special needs; (2) knowing rights and advocating for their child; (3) helping their child develop and learn; (4) having support systems; and (5) accessing the community. Studies in the U.S., Japan, and Singapore have demonstrated that the FOS-R has good psychometric properties. The instrument was translated into Brazilian Portuguese and mothers completed the scale when their child was between 18 and 34 months of age.

Results: A majority of families reported that they were able to help their child develop and learn (72.3%) and that they understood their child’s strengths, needs, and abilities (56.7%). Families were less like to be able access community services (43.4%), know their rights and advocate for their children (40.4%), or have support systems (39.8%). Attainment of all outcome domains was positively correlated with perceived helpfulness of services, but only outcome 1 (understanding child’s strengths needs and abilities) was associated with quantity or amount of services. Outcomes were generally lower than those reported by families of children disabilities in the U.S., but comparable to those reported by families in Singapore and Japan.
Discussion: CZS has unique implications for families, including severity of impact, a likely lifetime of caregiving and economic burden; uncertainty about the future, lack of specialized professional knowledge, and lack of informal supports.¹ This study, the first to report data on family outcomes of CZS, shows that families in this sample understand their child’s disability and feel relatively confident in their ability to help their child develop and learn, but are more challenged in accessing community services and informal support systems. Perceived helpfulness of services was more strongly correlated with family outcomes than the actual amount of services, reinforcing the importance of a family-centered approach. These data provide a baseline for understanding family outcomes, which will continue to be tracked over the 5-year course of this longitudinal study.

References/Citations: