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# INTRODUCTION

- Pediatric patients infected with Zika are at risk of sequels not only in the form of microcephaly but also birth defects including inner ear problems and communication delay.
- The American Academy of Audiology warns that infants contracting the virus through infected mothers might have absent or poorly functioning hearing at birth, or develop hearing loss at a later time (3).

<u>https://www.audiology.org/news/zika-virus-disease-outbreak-and-infant-hearing-loss</u>



## LEARNING OBJECTIVES

- Understand possible etiologies of hearing loss and communication disorders in infants infected with Zika virus
- Learn about experiences in Puerto Rico in regard to management of infants with hearing loss related to Zika virus infection
- Review recommendations related to hearing screening and management for infants and children infected with Zika virus



- A Brazilian retrospective study of hearing assessments in 70 infants aged 0-10 months with microcephaly and lab evidence of Zika virus infection found that:
  - 5 infants (7.1%) had sensorineural hearing loss
  - The laboratory confirmation was of ZIKA virus was establish by having a positive virus-specific IgM.
- Conclusion: Congenital Zika virus infection should be considered a risk factor for hearing loss



 Sensorineural hearing loss diagnosis was performed using Auditory Brainstem Evoked Potentials (ABR).

 Researchers on the Leal team also observed that sensorineural hearing loss occurred predominantly in infants whose mothers had a rash illness during pregnancy.



- Satterfield-Nash and collegues (2017) reported on results of their ZODIAC project after following 19 patient's between 19 and 24 months of age that were born from ZIKA infected mothers.
- They found a high incidence of visual and auditory abnormalities among these children.
- 13 to 19 of the children had impaired responses to auditory stimuli. No gender effects were obtained.
- Also neurological and motor disorders were reported as well.



## POSSIBLE ETHIOLOGIES

- Some evidence points to calcifications in the brains of the infants, while other points to insufficient neurons or to eighth nerve damage.
- On another Brazilian study, conducted by Fauci, all Zika-infected babies followed developed a type of hearing loss associated to nerve damage. The babies were born between November and May of 2016.



 The Leal study as well as a study conducted by Mittal, Liu and Fiffer (2018) revealed a prevalence of auditory disorders between 6 to 9 % in infants with congenital ZIKA virus.



# ZIKA AND ASSOCIATED EFFECTS IN THE INNER FAR OF ADULTS

- Dr. Viviane Bonaventura, a Brazilian ENT reported that some of her patients who had contracted ZIKA were still exhibiting inner ear related symptoms months after the other symptoms were extinguish.
- The patients were exhibiting sensorineural hearing loss, tinnitus and imbalance.
- Other symptoms reported were memory and attention problems. Their theory is that these areas of the brain where targeted by the virus because they have pluripotent progenitor cells.



## POSSIBLE ETIOLOGIES

 Tang et al. revealed that the Zika virus tends to target developing brain cells, such as progenitor cells in the fetus.

 Garcez et al showed that Zika virus targets human brain cells, reducing viability and growth as neurospheres and brain organoids.



By December 30, 2017, 40,630 cases of Zika were reported by the Puerto Rico Department of Health. Until then 4,134 pregnant women were infected (1). Three hundred and forty four babies were born to mothers infected by ZIKA according to statistics from three hospitals in Puerto Rico; the Pediatric University Hospital, San Juan Municipal Hospital and UPR Hospital in Carolina (2).



 Although our results are preliminary we already have four cases diagnosed with hearing loss. Three of those cases were normocephalic infants and one microcephalic. All cases reported were infants borned from mothers with comfirmed ZIKA infection during pregnancy.

#### **CASE I**

- HISTORY
- Normocephalic infant who did not passed hearing screening in the left ear. Has a negative familial history for hearing loss. The health history is otherwise unremarkable. Eventually diagnosed with a **unilateral** sensorineural hearing loss in the left ear and normal hearing on the right. However it was observed that even when his physiological thresholds in the right ear were at 30 dB nHL which is consistent with normal hearing the ABR waves waves I, III and V were resolved but delayed at 80 dB nHL resulting on prolonged inter-latencies I-V and III-V which supports the need of Auditory Processing Follow-up. Normal middle ear function was registered by the tympanometry.



#### CASE 2

- HISTORY
- Normocephalic Patient referred to audio-physiological battery due to maternal Zika infection and for failing neonatal hearing screening on both ears. Product of natural birth without complications. Negative familial history for hearing loss.

#### CLINICAL IMPRESSION:

 Audiological physiological battery results were consistent with a bilateral sensorineural hearing loss; moderately-severe to severe from 1 to 4 K in the right ear and mild to severe on the left ear from 500 Hz to 4 K. Adequate middle ear function but cochlear dysfunction at the outer hair cell level on both ears. No cochlear michophonic reversal registered consistent with negative results for Auditory Neuropathy.



#### CASE 3

- HISTORY
- **Microcephalic** patient referred to audio-physiological battery due to maternal Zika infection and for failing neonatal hearing screening on the right ear. Product of natural birth without complications. Negative familial history for hearing loss.
- Audiological physiological battery results were consistent with an apparent mild unilateral sensorineural hearing loss in the right ear but normal peripheral hearing on left ear. Adequate middle ear function bilaterally. Cochlear dysfunction at the outer hair cell level on the right ear but normal cochlear function on left.



#### • CASE 4

- HISTORY
- Normocephalic infant who did not passed hearing screening in the right ear. Has a negative familial history for hearing loss. Health history otherwise unremarkable.
- Audiological physiological battery results were consistent with normal peripheral hearing sensitivity in the left ear. Adequate middle ear and cochlear function at the outer hair cell level on left ear were also registered. Right ear ABR results were consistent with a **unilateral** sensorineural hearing loss of a projected mild degree which is consistent with the right cochlear dysfunction at the outer hair cell level in the intermediate frequencies registered by the emissions in lieu of normal middle ear function.



## **RECOMMENDED ACTIONS**

- The PR Department of Health has addressed this need by implementing a protocol following CDC guidelines (Administrative Order 388 of May 4, 2018) The Protocol comprises periodic developmental reevaluations during the first three years of age, beginning at one month of age, re-assessing them at 6 and 18 months and then at 3 years (15, 16).
- This agrees with one of WHO's long term objectives which states that appropriate research and development efforts should be intensified for Zika virus vaccines, diagnosis and intervention (18).



# PROJECTIONS

- Additional studies should be performed to understand the incidence and prevalence of hearing loss in pediatric patients with congenital ZIKA virus. Therefore it is our team's goal to conduct such research in Puerto Rico.
- We understand that the focus should be broader than just establish incidence and prevalence of peripheral hearing deficits but also protocols to rule-out communication and auditory processing disorders should be included. In order to achieve that it is important to follow-up not only the infants that are diagnosed with hearing loss but all ZIKA infected babies.
- We are working at the present time in the development of a protocol that will cover all of the above areas in our ZIKA-CHIPS project.



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# QUESTIONS ???





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