children exposed to Zika virus during pregnancy

Lavínia Schuler- Faccini

SIAT (TIS) Porto Alegre – Brazil

No conflicts of inte

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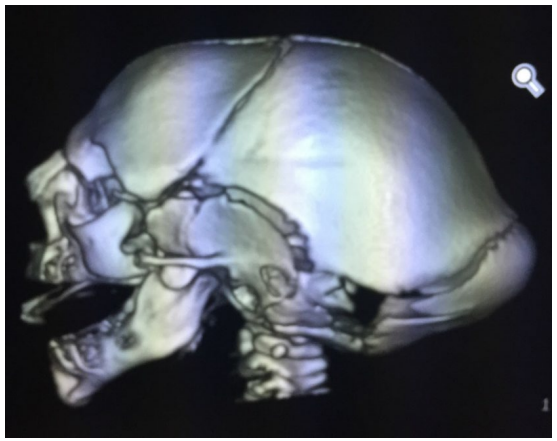
Background



Microcephaly outbreak – Northeast Brazil

2015

Congenital Zika Syndrome described

- Brain Disruption Sequence
- Arthrogryposis
- Neurological – cerebral paralysis, epilepsy, feeding difficulties
- Sensorial: ocular, auditive

2016

2016

Zika vírus is a teratogen for humans

Questions 2016 – 2023 ...

What is the whole spectrum of CZS?

What are the risks for the embryo / fetus exposed?

What is the development in the long range?

Mortality? Morbidity?

What happen to those exposed children born without microcephaly?

Challenges for clinical and epidemiological studies

Variable results

Difficulties and reliability of serologic and molecular testing to confirm the exposure

Maternal symptoms: mild, non-specific, asymptomatic

Who was actually exposed or non-exposed?

Cohorts

Risk of adverse outcomes in offspring with RT-PCR confirmed prenatal Zika virus exposure: an individual participant data meta-analysis of 13 cohorts in the Zika Brazilian Cohorts Consortium

Ricardo Arraes de Alencar Ximenes,[a,b,ak,*] Demócrito de Barros Miranda-Filho,[b,ak] Elizabeth B. Brickley,[c] Thalia Velho Barreto de Araújo,[d] Ulisses Ramos Montarroyos,[b] Marília Rosa Abtibol-Bernardino,[e,f] Marisa M. Mussi-Pinhata,[g] Geraldo Duarte,[h] Conrado Milani Coutinho,[h] Silvia Fabiana Biason de Moura Negrini,[g] Maria das Graças Costa Alecrim,[e,f] Lucíola de Fátima Albuquerque de Almeida Peixoto,[e,f] Maria Elisabeth Lopes Moreira,[i] Andrea Zin,[j] José Paulo Pereira Júnior,[k] Karin Nielsen-Saines,[l] Celina Maria Turchi Martelli,[m] Laura Cunha Rodrigues,[c] Wayner Vieira de Souza,[m] Liana O. Ventura,[n,o] Consuelo Silva de Oliveira,[p] Haroldo de Matos,[q] Emilene Monteiro Furtado Serra,[p] Luna Thais Souza Gomes,[p] Maurício L. Nogueira,[r] Cassia Estofolete,[r] Denise Cristina Vaz-Oliani,[s] Saulo Duarte Passos,[t] Antonio Moron,[u] Maria Manoela Duarte Rodrigues,[v] Stéphanno Gomes Pereira Sarmento,[w] Marília Dalva Turchi,[x] Luiza Emylce Pela Rosado,[y] Ana Laura de Sene Amâncio Zara,[x] Maria Bárbara Franco Gomes,[y] Lavínia Schuler-Faccini,[z] Juliana Herrero-Silva,[aa] Melania M. Amorim,[ab] Adriana Oliveira Melo,[ab] Antônio José Ledo Alves da Cunha,[ac] Arnaldo Prata-Barbosa,[ad] Joffre Amim, Jr.,[ae] Jorge Rezende-Filho,[ae] Juan Ignacio Calcagno,[af] Luiz Carlos Júnior Alcântara,[ag] Breno Lima de Almeida,[ag] Cristina Barroso Hofer,[ah] Elizabeth S. Machado,[ah] Isadora Cristina de Siqueira,[ag] Flor Ernestina Martinez-Espinosa,[e,f,ai,al] and Patrícia Brasil,[aj,al] on behalf of the Zika Brazilian Cohorts Consortium (ZBC-Consortium)[am]

The Lancet Regional Health - Americas
2023;17: 100395
Published Online 28 November 2022
https://doi.org/10.1016/j.lana.2022.100395

1548 pregnant women

Individual Participant Data Meta-Anaysis

Risk of adverse outcomes in offspring with RT-PCR confirmed prenatal Zika virus exposure: an individual participant data meta-analysis of 13 cohorts in the Zika Brazilian Cohorts Consortium

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Miscarriage: 0.9 % (IC95% 0.2 – 2.-)

Stillbirth: 0.3 % (IC95% 0.0 – 1.4)

Preterm: 10.5 %. (IC95% 8.8 – 12)

Low Birth Weight: 7.7 % (IC95% 5.6 – 10.1)

Small for Gestational Age: 16.2 % (IC95% 5.2 – 31.3)

Risk of adverse outcomes in offspring with RT-PCR confirmed prenatal Zika virus exposure: an individual participant data meta-analysis of 13 cohorts in the Zika Brazilian Cohorts Consortium

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% (IC95%)

Microcephaly at birth: 2.6 % (1.1–4.5) anytime: 4.0 % (2.0 –6.6)

Severe Microcephaly: at birth 0.3% (0.0–1.1) anytime 1.3% (0.5-2.4)

Neuroimaging Abnormalities: 7.9% (2.8 –14.7)

Functional Neurological Abnormalities: 18.7% (2.6 – 41.5)

Ophtalmic abnormalities: 4.0 % (0.2 – 10.7)

Overall risk: microcephaly, neuroimaging, neurological, or ophtalmic

24.7% (95CI 0.10 – 63.6)

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	Microcephaly at birth or first evaluation		
	n/N (%)	OR (95% CI)[b]	p-value
Timing of infection in pregnancy[a]			
First trimester	18/169 (10.6%)	7.52 (2.75–20.6)	<0.001
Second trimester	7/364 (1.9%)	1.23 (0.42–3.57)	0.706
Third trimester	7/441 (1.5%)	1.0	
Missing trimester	5/85	–	–

What about other cohort / consortia?

OVERALL PREVALENCE OF MICROCEPHALY <7%

OVERALL RISK: 15 - 29%

IMAGING ABNORMALITIES: Calcifications / Ventriculomegaly

NEUROIMAGING ABNORMALITIES IN CHILDREN WITHOUT MICROCEPHALY

EPILPEPSY

OPHTALMOLOGICAL : Colombia (11.85) , US (2%)

Honein MA, Dawson AL, Petersen EE, et al. Birth defects among fetuses and infants of US women with evidence of possible zika virus infection during pregnancy. *JAMA*. 2017;317(1):59–68.

Rice ME, Galang RR, Roth NM, et al. Vital Signs: zika-associated birth defects and neurodevelopmental abnormalities possibly associated with congenital zika virus infection — U.S. territories and freely associated states, 2018. *Morb Mortal Wkly Rep*. 2018;67(31):858–867.

Zika virus–associated birth defects and evaluation of all U.S. infants with congenital Zika virus exposure — U.S. Zika Pregnancy Registry, 2016. *Morb Mortal Wkly Rep*. 2017;66(13):373.

Hoen B, Schaub B, Funk AL, et al. Pregnancy outcomes after ZIKV infection in French territories in the Americas. *N Engl J Med*. 2018;378(11):985–994.

Pomar L, Vouga M, Lambert V, et al. Maternal-fetal transmission and adverse perinatal outcomes in pregnant women infected with Zika virus: prospective cohort study in French Guiana. *BMJ*. 2018;363:k4431.

Calle-Giraldo JP, Rojas CA, Hurtado IC, et al. Outcomes of congenital Zika virus infection during an outbreak in Valle del Cauca, Colombia. *Pediatr Infect Dis J*. 2019;38(7):735–740.

LONG-TERM DEVELOPMENT OF NORMOCEPHALIC CHILDREN

Original Article

Journal of Child Neurology
1-5
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DOI: 10.1177/0883073819892128
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Neurodevelopment of Nonmicrocephalic Children, After 18 Months of Life, Exposed Prenatally to Zika Virus

Laís Rodrigues Gerzson[1], Carla Skilhan de Almeida[2], Juliana Herrero da Silva[3], Michelle Mirttes Albuquerque Feitosa[4], Lucia Nunes de Oliveira[5], and Lavínia Schuler-Faccini[6] [AQ1]

viruses

MDPI

Article

Neurodevelopment in Children Exposed to Zika Virus: What Are the Consequences for Children Who Do Not Present with Microcephaly at Birth?

Paula Fabiana Sobral da Silva [1,2,*], Sophie Helena Eickmann [3], Ricardo Arraes de Alencar Ximenes [1], Celina Maria Turchi Martelli [4], Elizabeth B. Brickley [5], Marília C. Lima [3], Ulisses R. Montarroyos [1], Maria Durce Costa Gomes de Carvalho [1,2], Laura Cunha Rodrigues [5], Thalia Velho Barreto de Araújo [6], Liana O. Ventura [7], Danielle Maria da Silva Oliveira [1], Regina Coeli Ferreira Ramos [8], Demócrito de Barros Miranda-Filho [1] and on behalf of the Microcephaly Epidemic Research Group (MERG) [†]

viruses

MDPI

Article

Does Intra-Uterine Exposure to the Zika Virus Increase Risks of Cognitive Delay at Preschool Ages? Findings from a Zika-Exposed Cohort from Grenada, West Indies

Michelle Fernandes [1,2,3,4,*,†], Roberta Evans [4,†], Mira Cheng [5], Barbara Landon [4], Trevor Noël [4], Calum Macpherson [4], Nikita Cudjoe [4], Kemi S. Burgen [4], Randall Waechter [4,6], A. Desiree LaBeaud [4,5,‡] and Karen Blackmon [7,‡]

- After 48 months of age, no significant diferences were observed between normocephalic children exposed and non-exposed
- Abnormal image or neuroclinical examination is a predictor of developmental delay

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Julia do Amaral Gomes
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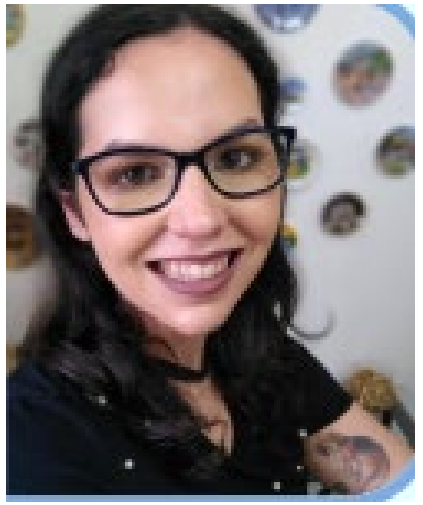

Thayne Woycinck Kowalski
tkowalski@hcpa.edu.br

TERATOGENESIS IS A MULTFACTORIAL EVENT

MECHANISMS

viruses

MDP

Article

Association between Genetic Variants in *NOS2* and *TNF* Genes with Congenital Zika Syndrome and Severe Microcephaly

Julia A. Gomes [1,2,3,4,*], Eduarda Sgarioni [1], Juliano A. Boquett [1,3], Ana Cláudia P. Terças-Trettel [5], Juliana H. da Silva [6], Bethânia F. R. Ribeiro [7], Marcial F. Galera [8], Thalita M. de Oliveira [9], Maria Denise F. Carvalho de Andrade [10], Isabella F. Carvalho [11], Lavínia Schüler-Faccini [1,2,3] and Fernanda S. L. Vianna [1,2,3,4,12,*]

frontiers in Cellular and Infection Microbiology

BRIEF RESEARCH REPORT
published: 07 July 2021
doi: 10.3389/fcimb.2021.641413

Functional Polymorphisms in the p53 Pathway Genes on the Genetic Susceptibility to Zika Virus Teratogenesis

Julia A. Gomes [1,2,3,4], Eduarda Sgarioni [1], Igor A. Vieira [1,4], Lucas R. Fraga [2,3,4,5], Patrícia Ashton-Prolla [1,4], Ana Cláudia P. Terças-Tretell [6], Juliana H. da Silva [7], Bethânia FR Ribeiro [8], Marcial F. Galera [9], Thalita M. de Oliveira [10], Maria Denise F. Carvalho de Andrade [11], Isabella F. Carvalho [12], Lavínia Schuler-Faccini [1,2,3] and Fernanda S. L. Vianna [1,2,3,4*]*

EPIGENETICS
2023, VOL. 18, NO. 1, 2145061
https://doi.org/10.1080/15592294.2022.2145061

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BRIEF REPORT

OPEN ACCESS Check for updates

Contribution of miR-124 rs531564 polymorphism to the occurrence of congenital Zika syndrome

Julia A Gomes[b,c,d], Igor Araujo Vieira[d,m], Eduarda Sgarioni[d], Ana Cláudia P Terças-Tretell[e], Juliana H da Silva[f,g], Bethânia FR Ribeiro[h], Marcial F Galera[i], Thalita M de Oliveira[j], Maria Denise F Carvalho de Andrade[k], Isabella F Carvalho[l], Lavínia Schüler-Faccini[a,b,c], and Fernanda SL Vianna [a,b,c,d]

- TP53 rs1042522 associated with lissencephaly and a more potent p53-induced apoptosis

CG genotype of rs531564 (MIR-124) more frequent in CZS children

Journal of Molecular Neuroscience
https://doi.org/10.1007/s12031-023-02126-x

RESEARCH

Downregulation of Microcephaly-Causing Genes as a Mechanism for ZIKV Teratogenesis: A Meta-analysis of RNA-Seq Studies

Julia A. Gomes[1,2] · Eduarda Sgarioni[2,3] · Thayne W. Kowalski[1,2,3,4,5] · Giovanna C. Giudicelli[2,3,5] · Mariana Recamonde-Mendoza[5,6] · Lucas R. Fraga[1,2,7] · Lavínia Schüler-Faccini[1,3] · Fernanda S. L. Vianna[1,2,3]

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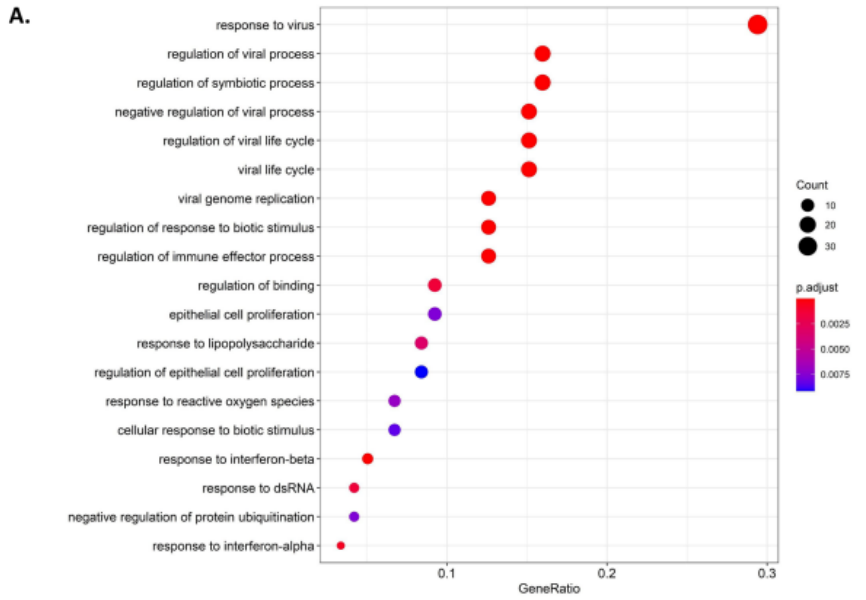
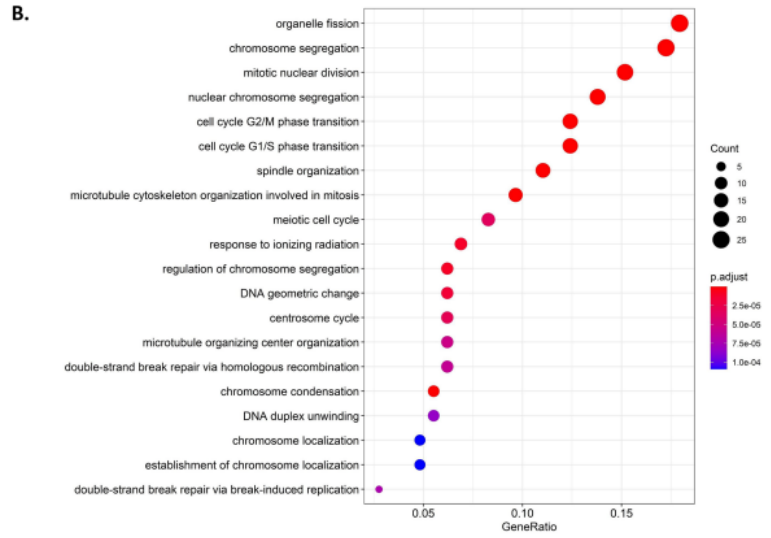
- 125 upregulated genes in neural cells, mainly **interferon-stimulated genes**: *IFI6*, *ISG15*, and *OAS2:* antiviral response.
- 167 **downregulated genes** involved with cellular division: classic microcephaly-causing genes: *CENPJ*, *ASPM*, *CENPE*, and *CEP152*
- possible mechanism of **ZIKV impairment on brain development and CZS.**



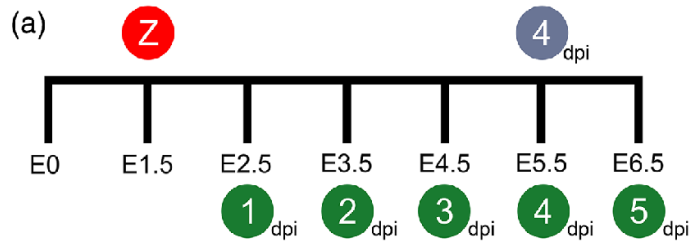


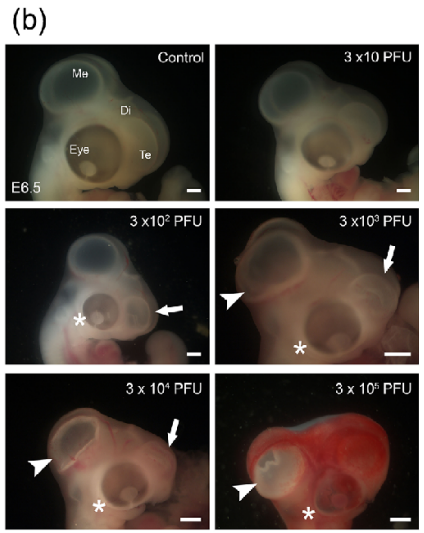
RESEARCH ARTICLE

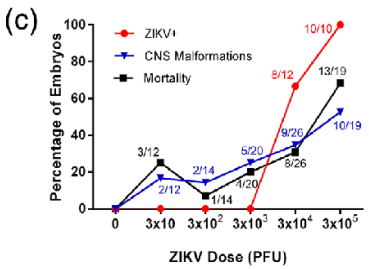
Birth Defects Research | Teratology Society | WILEY

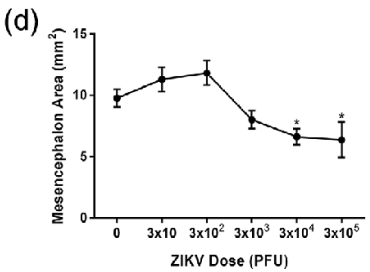
Zika virus-induced brain malformations in chicken embryos

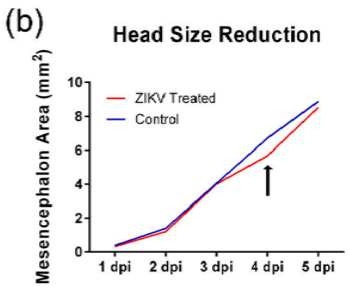
Gabriela Elis Wachholz[1,2,3] | Ana Paula Muterle Varela[4] |
Thais Fumaco Teixeira[5] | Sophia Martins Simon de Matos[3] |
Paula Rigon da Luz Soster[6] | Fernanda Sales Luiz Vianna[1,2,3] |
Diogo Onofre Gomes de Souza[7] | Paulo Michel Roehe[5] |
Lavínia Schuler-Faccini[1,2] | Lucas Rosa Fraga[2,3,6]

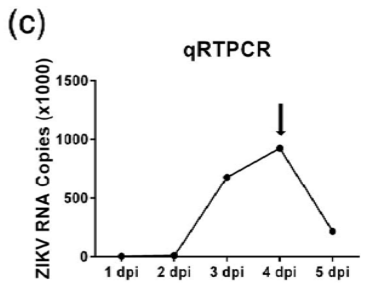


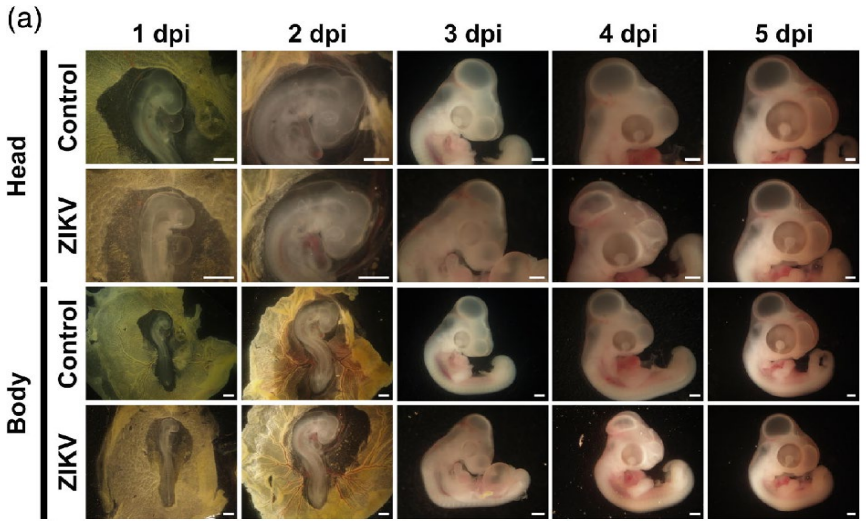












Question 2023

ZIKV is now “endemic”

How is the epidemiological situation?

Was ZIKV gone away?

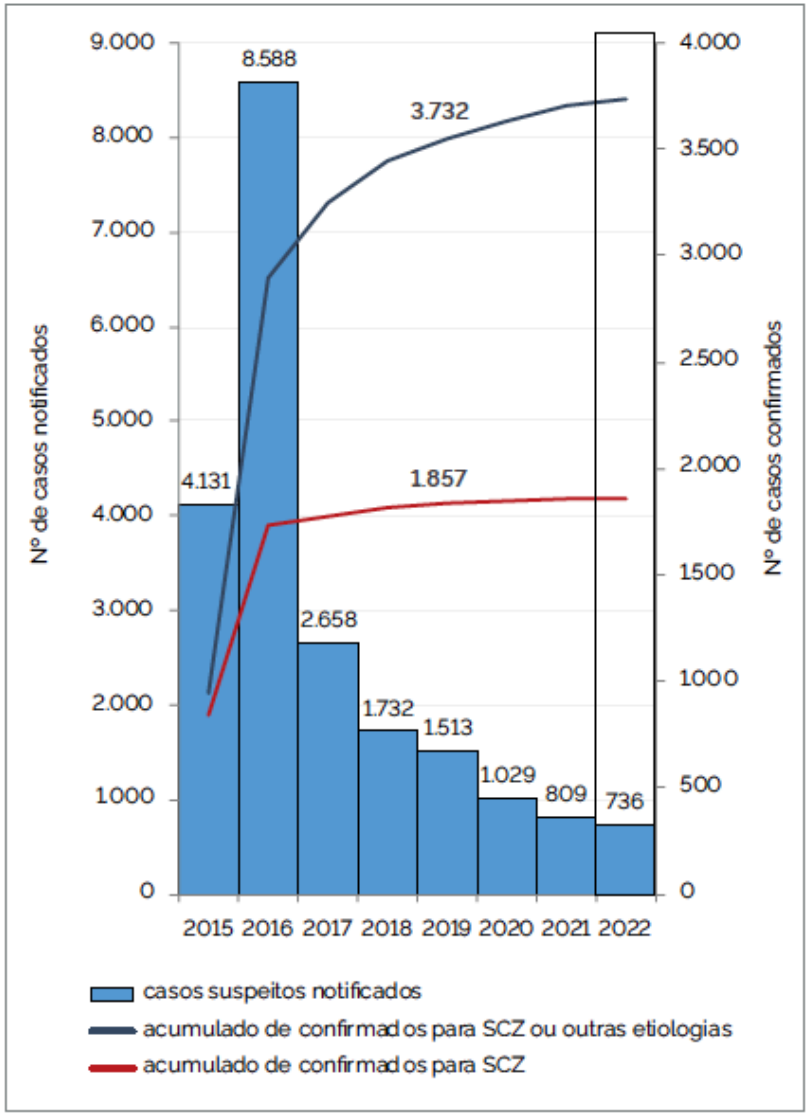
BRAZIL

2023:

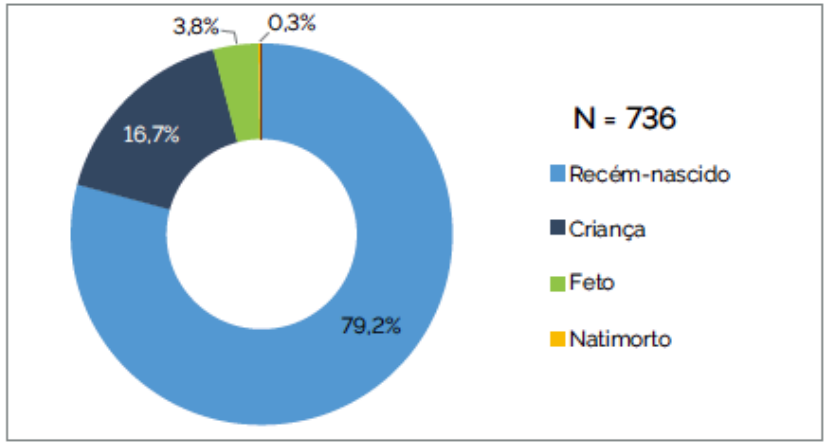
556 suspected SCZ

(an increase compared to 2022)

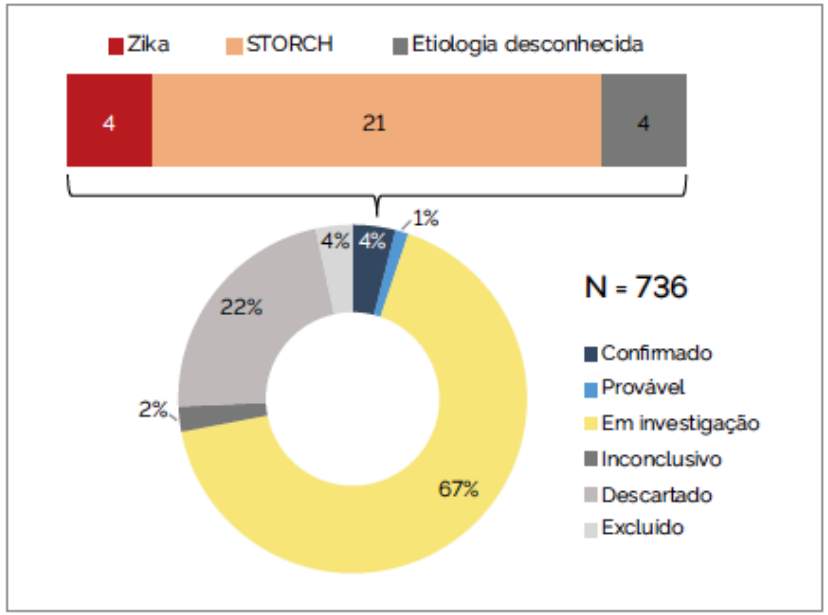
A) por ano de notificação: 2015-2022



B) por tipo de notificação: 2022



C) por classificação final e etiologia: 2022



Go raibh maith agat
Obrigada

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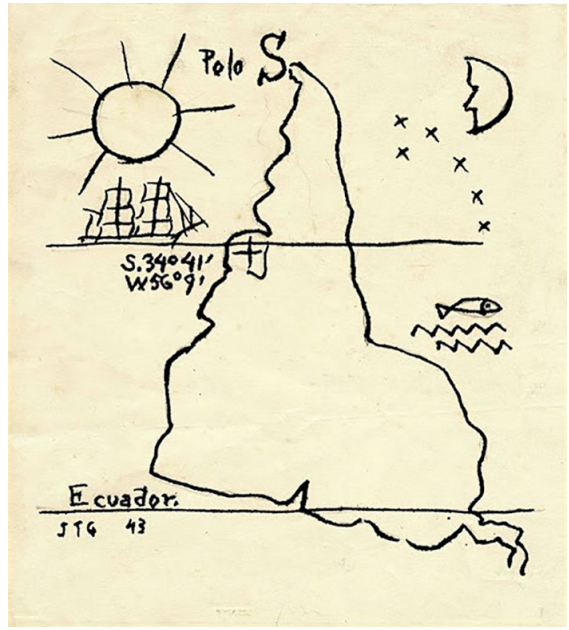

Joaquin Torres Garcia: "America Invertida", 1943

Sistema Nacional de Informação sobre Agentes Teratogênicos
30 anos