International Clearinghouse for Birth Defects
Surveillance and Research

50th Annual Meeting of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR)

September 1 – 4, 2024
Prague, Czech Republic

Organized by the ICBDSR and the Czech Society of Medical Genetics and Genomics

Annual Meeting Planning Committee (in alphabetical order)

ICBDSR website: www.icbdsr.org

The ICBDSR Executive Committee and ICBD Staff thank the **Czech Society of Medical Genetics and Genomics** for their cooperation and support and **all ICBDSR members** who work in birth defects surveillance and research, to achieve our common goal of improving primary prevention and care of birth defects.

International Clearinghouse for Birth Defects
Surveillance and Research

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The ICBDSR is a Promoting Organization of

www.worldbirthdefectsday.org

PROGRAM

	Sunday, September 1st, 2024 **Meeting Rooms Lucida & Tahoma**
11:00-13:00	**Executive Committee Meeting** *(Executive Committee members and ICBD staff only)*
14:00-15:30	**Pre-Annual Meeting Workshop "Enhancing Birth Defect Surveillance: Interactive Case Studies for Quality Improvement"** *Lorenzo D. Botto, Marcia Feldkamp, Cara Mai and Ashley Smoots*
15:30-16:00	*Coffee break*
16:00-18:00	**Pre-Annual Meeting Workshop on CA**
16:00-18:30	**Registrations** ICBDSR Annual Meeting
19:30	***Welcome Reception*** *at Hermitage Hotel Prague, offered by ICBDSR*

	Monday, September 2nd, 2024 **Meeting Room Verdana**
9:00-9:15	**Welcome** *Prof. Ondrej Seda, Chief Medical Genetics Representative, First Faculty of Medicine, Charles University in Prague* *Antonin Sipek Jr, Czech Society of Medical Genetics and Genomics, Czech Republic*
9:15-9:30	**ICBDSR Executive Committee Talk** *Anke Rissmann, ICBDSR Chair* *Lorenzo D. Botto, ICBD Director (Annual Report and other updates)* *Presentation of Distinguished Service Award*
9:30-10:00	**The History of the ICBDSR** *Pierpaolo Mastroiacovo, ICBD and Simonetta Zezza, Past General Manager ICBDSR*
10:00-10:20	**Keynote Lecture –** Power of Prevention: CDC's Story to Unravel a B Vitamin's Role in Neural Tube Defect Prevention and Strategies to Improve Birth Outcomes *Cara Mai, Division of Birth Defects and Infant Disorders. National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention*
10:20-11:00	**J. David Erickson Lecture- A Review of human embryology to improve our understanding of gastroschisis pathogenesis** *Marcia Feldkamp, University of Utah School of Medicine*
11:00-11:15	*Coffee break*
11:15-12:30	**Session I – Oral Presentations** **Moderators:** *Cara Mai* and *Karen Sarmiento*
11:15-11:30	Integrated surveillance strategy to support the prevention of neural tube defects through food fortification with folic acid: the experience of Costa Rica *Adriana Benavides-Lara*
11:30-11:45	Birth defects surveillance in resource-limited settings: Challenges faced in Sri Lanka *Kapila Jayaratne*
11:45-12:00	DELFOS: Research Program for the diagnosis, training, logistics, education, organization and monitoring of patients with congenital heart disease in Colombia *Ignacio Zarante*
12:00-12:15	Perceptions experiences, and meanings attached to external visible birth defects by parents of children with birth defects, healthcare workers, and community health extension workers in Uganda *Joyce Namale-Matovu*
12:15-12:30	An audit of capacity in community genetic services in South Africa: A sector in crisis *Helen L. Malherbe*

12:45-13:45	*Buffet lunch*
13:45-15:30	**Session II – Oral Presentations** **Moderators:** *Emma Kalk* and *Ignacio Zarante*
13:45-14:00	Congenital Anomalies in limb body wall complex in 53 cases from the Alberta Congenital Anomalies Surveillance System, 1997-2019 *Mary Ann Thomas*
14:00-14:15	Moving towards triple surveillance: tracking congenital heart disease outcomes through the lifespan *Lorenzo D. Botto*
14:15-14:30	Epidemiological characterization of arthrogryposis multiplex congenita in Bogotá and Cali: Insights from a case-control study on risk factors *Karen Sarmiento*
14:30-14:45	Improving the congenital anomalies surveillance system in Emilia-Romagna region: does secondary health data integration matter? *Marco Manfrini*
14:45-15:00	Trends in total and live birth prevalence of orofacial clefts and the effect of prenatal detection on pregnancy outcome in the northern Netherlands *Dieuwke C. Broekstra*
15:00-15:15	Post-fortification Changes among Spina Bifida Cases by Subtypes and Lesion Level *Cara Mai*
15:15-15:30	Evaluation of the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) data linkage with the Maternity Services Dataset (MSDS) for pregnancies in 2020 and 2021 in England *Gabriella Melis*
15:30-15:45	*Coffee break*
15:45-16:15	**Poster session** – *Conference Foyer*
16:15-17:45	**Session III – Oral Presentations** **Moderators:** *Adriana Benavides-Lara* and *Dieuwke C. Broekstra*
16:15-16:30	DELFOS - use of an automated chatbot for the surveillance of patients with congenital heart disease in Bogotá, Colombia *Nicolás Niederbacher*
16:30-16:45	Application of Bayesian Hierarchical Models in the Spatial Analysis of Congenital Heart Diseases in Rio Grande do Sul *Márcia H. Barbian*
16:45-17:00	Does Folic Acid Food Fortification Increase the Risk of COVID-19 Infection and Mortality? A Public Health Intervention with Unintended Consequences? *Wendy N. Nembhard*
17:00-17:15	Hypertrophic Cardiomyopathy in Children: one condition for multifaceted diseases. The importance of multisystemic and multidisciplinary approach in children *Anwar Baban*
17:15-17:30	Prevalence of adverse birth outcomes and external birth defects among women living with HIV in Malawi *George Bello*
17:30-17:45	MALFOVAR (Malformation and variable anatomy registry) case series 2007-2024: Congenital Tumors *Tidhar Steiner*
19:30	*Dinner at Hermitage Hotel Prague (included in the registration fee of delegates staying at the hotel)*

	Tuesday, September 3rd, 2024 **Meeting Room Verdana**
8:30-11:00	**Session on collaborative projects – Round table** EUROCAT Updates *Florence Rouget, President EUROCAT Association, Brittany, France* NBDPN Updates *Wendy N. Nembhard, Vice Chair of NBDPN, University of Arkansas for Medical Sciences, USA* sSCAN *Emma Kalk, School of Public Health, SA* Impact of COVID pandemic on birth surveillance as a whole *Anke Rissmann, Saxony-Anhalt, Germany* Why Foster Birth Defect Research? *Anke Rissmann, Saxony-Anhalt, Germany* Rethinking the Annual Report through the lens of triple surveillance *Lorenzo D. Botto ICBD Director, Utah, USA* World Birth Defects Day (WBDD) *Cara Mai, Division of Birth Defects and Infant Disorders, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention*
11:00-11:20	*Coffee break*
11:20-12:45	***ICBDSR Business Meeting*** *(ICBDSR members only)*
12:45-13:45	*Buffet lunch*
14:00-18:00	*Prague guided bus tour - personal payment, optional*
19:45	*Social dinner - personal payment, optional*

	Wednesday, September 4th, 2024 **Workshop: Shaping the Future by Reflecting on the Past: 50 Years of Congenital Anomalies Research** **Joint Workshop with Czech Society of Medical Genetics and Genomics** **Moderators:** ***Milan Macek Jr*** and ***Antonin Sipek Jr*** **Meeting Room Verdana**
9:00-9:10	**Welcome - Prof. *Milan Macek Jr*, President of the Czech society of Medical Genetics and Genomics**
9:10-9:45	**Rare diseases in the Czech Republic** *Milan Macek Jr*
9:45-10:10	**Surveillance of congenital anomalies in the Czech Republic: Six decades of experience** *Antonin Sipek Jr*
10:10-10:40	**60 years of the Hungarian Congenital Abnormality Registry: Review of the function, challenges, value, and current role** *Csaba Siffel*
10:40-11:10	*Coffee break*
11:10-11:40	**From Karyotypes to Genomes: The Evolution of Cytogenetics** *Jana Drabova*
11:40-12:00	**A personal historical reflection on ICBDSR activities** *R. Brian Lowry, MD* *Retired Medical Program Director, Alberta Congenital Anomalies Surveillance System (ACASS)* *Professor Emeritus, Department of Medical Genetics, University of Calgary, Canada* *(Pre-recorded)*
12:00-12:40	**History of Metabolic Medicine in the Czech Republic** *Jiri Zeman*
12:45	Group photo
12:50-13:50	*Buffet lunch*
13:50-14:20	**Review of maternal, environmental, and genetic risk factors associated with gastroschisis** *Marcia Feldkamp*
14:20-15:00	**Current State and Prospects of Czech Obstetrics** *Pavel Calda*
15:00-15:30	*Coffee break*
15:30-16:15	**Molecular genetics and developmental biology uncover the teratogenic mechanisms: thalidomide** *Frantisek Liska*
16:15	**Closing**

Posters

(Alphabetical order by corresponding author's last name)

The posters will be shown on Monday 2nd September
Conference Foyer

Molecular characterization of newborns with alpha thalassemia identified through newborn screening - *Maria Melanie Liberty B. Alcausin*

Congenital upper and lower airway anomalies: data from the IMER Registry - *Elisa Ballardini*

Population-based prevalence and trend of birth defects in Costa Rica from 2000 to 2019 – *Adriana Benavides-Lara*

Association between Covid-19 infection during pregnancy and congenital limb defects: results of a study in Southern Brazil - *Simone Karam*

Trends and causes of infant mortality in Chile, 2012-2021 - *Allisson Müller*

Birth prevalence of omphalocele and gastroschisis in Chile: Data from the National Registry of Congenital Anomalies - *Allisson Müller*

Impact of maternal race and ethnicity on cardiovascular disease risk in women with infants affected by congenital heart defects in Arkansas, 1997-2011 - *Wendy N. Nembhard*

Changes in mortality associated with Neural Tube Defect in Chile, 2012-2021 - *Rosa Pardo*

Congenital hip dysplasia: A case-control study for risk factor analysis in newborns, Bogotá, Colombia (1982-2022) - *Karen Sarmiento*

Epidemiological description and risk factors of congenital genitourinary tract anomalies in Colombia (1982-2022), an ECLAMC case-control study - *Karen Sarmiento*

Adolescent pregnancy and birth defects: A case control study in Bogotá and Cali, between 2001 and 2020 - *Karen Sarmiento*

Perinatal characteristics and factors associated to the presentation of single ventricle in Bogotá and Cali, Colombia - *Karen Sarmiento*

High prevalence of gastroschisis in Roraima, Brazil: The impact of maternal demographics - *Lavinia Schuler-Faccini* presented by *Simone Karam*

VACTERL Association; The hidden iceberg. Case series and article review in Malta - *Mohamed Shoukry*

Tatton Brown Rahman Syndrome with congenital abdominal wall defect. A Rare Case Report - *Mohamed Shoukry*

Incidence and sex ratio in children born with tetralogy of Fallot in the Czech Republic - *Antonin Sipek Sr*

ICBDSR / MALFOVAR Museum network accreditation system - *Tidhar Steiner*

Can be viewed at: www.icbdsrtraining.org

Sunday, September 1st, 2024

Pre-Annual Meeting Workshop

Meeting Rooms Lucida & Tahoma

"Enhancing Birth Defect Surveillance: Interactive Case Studies for Quality Improvement"

WHO/CDC/ICBDSR Birth Defects Surveillance Toolkit

Program

Overview. High quality birth defect surveillance blends clinical knowledge and data science, along with a passion for quality improvement: we can always do better, ensure fewer errors, be more efficient.

In this workshop, catered to both novices and seasoned professionals, participants will work in small groups to refine their skills in recognizing, diagnosing, and understanding birth defects of clinical and public health importance. Participants will also gain insight into a broader context by exploring fundamental concepts such as sequences, syndromes, and associations; delving into common syndromes; and examining major risk factors.

Carefully crafted clinical and epidemiologic case studies will be used to facilitate practical learning and discussion. Participants will hone their skills in utilizing checklists for high-quality reporting, interpreting key findings in visual and textual formats, and using a smartphone app tailored to support their practice. A pre-and-post workshop assessment (anonymously conducted) will enable participants to gauge their progress.

	Topic / Focus
14:30	Registration Pre-test (anonymous)
15:00	Introduction and organization - distribution and review of tools, introductions, small groups
15:15-16:15	Case study: focus on data quality - elements of data quality - building informative tables step by step
16:15-16:30	Coffee break (working break)
16:30-17:30	Case study: from clinical exam to surveillance data. Three case studies to choose from, of varying complexity but similarly structured: - approaches to diagnosing, describing, coding, and classifying selected congenital anomalies - use of QRH and checklists - examples of sequences, associations, syndromes - review of associated risk factors (e.g., diabetes, smoking, folate insufficiency)
17:30-17:45	Post-test (anonymous)
17:45-18:00	Wrap-up and evaluation

Monday, September 2nd, 2024

Speaker Presentations

Meeting Room Verdana

The History of the ICBDSR
Pierpaolo Mastroiacovo, ICBD and Simonetta Zezza, Past General Manager ICBDSR

Keynote Lecture – Power of Prevention: CDC's Story to Unravel a B Vitamin's Role in Neural Tube Defect Prevention and Strategies to Improve Birth Outcomes
Cara Mai, Division of Birth Defects and Infant Disorders. National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention

J. David Erickson Lecture- A Review of Human Embryology to Improve Our Understanding of Gastroschisis Pathogenesis
Marcia Feldkamp, University of Utah School of Medicine

The History of the International Clearinghouse for Birth Defects Surveillance and Research

P Mastroiacovo[1], S Zezza[2]
[1] *Past Director of the International Center for Birth Defects (ICBD), Rome, Italy*
[2]*Past General Manager of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR), Rome, Italy*

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It would be impossible to comprehensively describe 50 years of history of an organization like the International Clearinghouse for Birth Defects Surveillance and Research (Clearinghouse – ICH -, in short), in a half-hour talk, so we imposed ourselves to present **only ten relevant items** to tell you the history of our organization:

1. **The beginning** the Clearinghouse was founded in Helsinki on June 7, 1974 at a meeting organized by Gabriel Stickle, Vice-President of March of Dimes (USA). The founders were 11 Directors of surveillance systems from the US and Europe. The twelfth founder was Sylvia Hay, the first ICH coordinator.
2. **Exchange of information and data:** through Quarterly Reports and Annual Reports, then by the "Online Platform for Sharing Data". Since 2015, a Monthly Newsletter is distributed by email to a wide audience of health professionals.
3. **Expanded surveillance**: not only birth defects, but also surveillance of Multiple Congenital Anomalies (MCA), Limb Reduction Defects (LRD) by type, newborns with birth defects exposed to medications during first trimester of pregnancy (Maternal Drug Exposure – MADRE), and Prenatal Diagnosis of Down Syndrome
4. **Valproic Acid and Spina Bifida**: ICH was instrumental in giving the first evidence of the teratogenicity of valproic acid. The whole story started with an observation of Dr. Elisabeth Robert at the 9th Annual Meeting in London, 1982, will be narrated.
5. **Three volunteers at work**: A trio of volunteers was active from 1984 to 1988 in the Clearinghouse: Lisbeth Knudsen as Coordinator, Bengt Källén as leader and Pierpaolo Mastroiacovo.
6. **International Center on Birth Defects (ICBD):** it was established with the purpose to coordinate the Clearinghouse activities, and promote researches on birth defects. It was based in Bergen (Norway) from 1989 to 1991, then Rome (Italy) from 1992 to 2018, and now at the University of Utah in Salt Lake City, USA.
7. **Training Courses/Workshops:** since 2014 several training courses and workshops some online were organized in Africa, Central and South America, and Europe, in cooperation with other organizations. An online self-paced course on surveillance and prevention of birth defects is also available on the platform www.icbdsrtraining.org
8. **Collaborative scientific papers**: a graph with the number of collaborative papers proposed and made by two or more ICH Members by year is shown
9. **World Birth Defects Day (WBDD)**: WBDD, observed on March 3 each year, unites people and organizations working in the field of birth defects. ICH made the first proposal to establish a WBDD at the 41st Annual Meeting in Helsinki (September 2014). www.worldbirthdefectday.org
10. **Champions of ICH:** a proposal to elect three "Unforgettable Champions" and two "Champions of Tireless Presence" in the Clearinghouse.

    Few final considerations from the General Manager's Point of View (POV) show the meaning and importance of a so high-level international collaboration experience.

Power of Prevention: CDC's Story to Unravel a B Vitamin's Role in NTD Prevention and Strategies to Improve Birth Outcomes

C Mai

Health Scientist Infant Outcomes Monitoring
Research and Prevention Branch
Division of Birth Defects and Infant Disorders
National Center on Birth Defects and Developmental Disabilities
Centers for Disease Control and Prevention

CDC named its folic acid prevention portfolio as one of the ten great public health achievements in the United States in the first decade of the 21st century (https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6019a5.htm). The backbone of this work and its continued prevention efforts have been decades in the making.

In 1992, CDC recommended intake of folic acid, a synthetic form of vitamin B9, for neural tube defects (NTD) prevention (https://www.cdc.gov/mmwr/preview/mmwrhtml/00019479.htm). CDC was involved in the foundational research to form the basis of this recommendation and provided the scientific evidence to the Institute of Medicine (IOM) that recommended folic acid intake for the prevention of NTDs. In 1998, the U.S. Food and Drug Administration (FDA) mandated folic acid fortification of enriched cereal grains products in the United States. As part of this process, monitoring occurs on the effectiveness and safety of this national program. Population-level biomarker and intake estimates allow for a better understanding of vitamin B9 sources and changes to blood folate concentrations within this population. In addition, population-based birth defects surveillance systems have been instrumental in examining changes in NTD prevalence before and after fortification periods.

Understanding the impact of an intervention that affects the entire population is critical. Fortification of enriched staple grains is an established successful public health modality to reduce disparities and increase health equity. Intermittent and limited access to fresh food stocks leads to increases in micronutrient deficiencies. Low dose continuous folic acid fortification of shelf and heat stable products prevents folate deficiency anemia common in areas and communities without access to fresh produce or stable food stuffs. In the US, folate deficiency anemia was nearly eliminated after mandatory folic acid fortification.

Continued work in folic acid fortification and education is critical for sustained NTD prevention. This includes expanding fortification efforts to communities who do not commonly consume currently fortified products, such as Hispanics who consume corn masa products. Additionally, educating people capable of becoming pregnant and their health care providers on the importance of folic acid for NTD prevention remains pertinent, given the proliferation of folic acid misinformation spread via social media.

Globally, over 70 countries have implemented mandatory folic acid fortification. However, a large portion of the estimated preventable NTDs worldwide remains. Opportunities and progress, including the 2023 World Health Assembly resolution to accelerate fortification efforts, can aid in NTD prevention efforts. Staying abreast of and being able to address emerging issues are vital to ensure new generations of people capable of becoming pregnant benefit from a known prevention intervention.

A Review of Human Embryology to Improve Our Understanding of Gastroschisis Pathogenesis

M Feldkamp

Emeritus Research Professor
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University of Utah School of Medicine
Salt Lake City, UT, United States

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Over the past several decades different hypotheses have been proposed to explain the pathogenesis of gastroschisis. These hypotheses led researchers to evaluate risk factors for gastroschisis that might support a specific pathogenesis. In addition, these different hypotheses have led to confusion for scientists, clinicians, and families. This presentation aims to briefly describe relevant aspects of normal human development and embryogenesis and review the contemporary hypothesis related to the occurrence of gastroschisis.

A description of gastroschisis, though not then called such, was first published in 1733 by James Calder who detailed the findings in two infants with intestines outside the abdomen. John Hunter, a Scottish surgeon, collected a series of fetal specimens from the 1700's that are now in London's Hunterian Museum. From this collection of embryos, Dr. Spitz photographed and published a short article in 2008 about a 97-day-old fetus that, for over 200 years, went unrecognized as a case of gastroschisis. In 1878, William Fear, a surgeon from Kent, published a case report in the BMJ. It was in 1894 that Cesare Taruffi (Bologna) coined the term and defined human gastroschisis as – gastro, meaning belly, and schisis, meaning separation. These early case reports are quite similar in their description of the clinical findings observed in these infants with gastroschisis.

Normal human embryology provides basic knowledge to help us understand the pathogenesis of gastroschisis. Based on this knowledge and observations of fetuses/infants dating back centuries, a gastroschisis defect almost certainly results from a separation of the amnio-ectodermal junction at the pars flaccida during the normal physiologic hernia. Human evidence does not support that gastroschisis is due to vasoconstriction, vascular event, or a full-thickness defect of the abdominal wall. However, to further improve our understanding and to develop prevention strategies, we need help from developmental and cell biologists to detail cellular movement at the amino-ectodermal junction and how the normal cellular structure might be disrupted. This information will be critical for those studying risk factors that might interfere with normal development at the amnio-ectodermal junction and result in its separation.

Monday, September 2nd, 2024

Session I – Oral Presentations

Moderators:
Cara Mai and ***Karen Sarmiento***

Integrated surveillance strategy to support the prevention of neural tube defects through food fortification with folic acid: the experience of Costa Rica
Adriana Benavides-Lara

Birth defects surveillance in resource-limited settings: Challenges faced in Sri Lanka
Kapila Jayaratne

DELFOS: Research program for the diagnosis, training, logistics, education, organization and monitoring of patients with congenital heart disease in Colombia
Ignacio Zarante

Perceptions experiences, and meanings attached to external visible birth defects by parents of children with birth defects, healthcare workers, and community health extension workers in Uganda
Joyce Namale-Matovu

An audit of capacity in community genetic services in South Africa: A sector in crisis
Helen L. Malherbe

Integrated surveillance strategy to support the prevention of neural tube defects through food fortification with folic acid: the experience of Costa Rica

A Benavides-Lara[1], O Fernández-Sánchez[1], MP Barboza-Arguello[1], T Alfaro-Calvo[1], H Martínez[2]
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Birth Defects Program on which the work is based: CREC, Costa Rica

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Background and Objectives: Neural tube defects (NTDs) are a major preventable public health burden, especially in developing countries. We covered two objectives: (1) to describe how Costa Rica implemented integrated surveillance of folate deficiency, NTDs-prevalence, NTDs-associated infant mortality rate (NTDs-IMR), and folic acid food fortification (FAFF), to support with evidence prevention policies for NTDs; (2) to disseminate updated data from monitoring programs.

Methods: We performed a cross-sectional analysis, using the databases of national surveillance systems for NTDs outcomes to compare NTDs-prevalence and NTDs-IMR observed in the pre-fortification (1987-1998) and post-fortification (2010-2020) periods. Using data from national nutrition surveys (1996 and 2008-2009), we compared the percentage of women of childbearing age (WCA) with serum folate deficiency (serum folate <6ng/mL). In addition, using data from the FAFF monitoring program (2010-2020) means of folic acid (FA) concentration (mg/kg) and FA daily intake (µg/day) were calculated for each fortified food (corn and wheat flour, rice and milk), as well as its contribution to FA Estimated Average Requirement (EAR).

Results: After FAFF Costa Rica showed a decrease of 84% in FA deficiency in WCA, 53% in NTDs-prevalence (from 11.82/10,000 to 5.52/10,000 live-births), and 76% in NTDs-IMR (from 77.01/100,000 to 18.66/100,000 live-births). The reduction in these indicators increased as more foods were fortified. All fortified foods provided an average contribution of 119% of the EAR of FA in the population, and consumption didn´t exceed the upper limit for FA (UL: 1000 µg/day).

Discussion and Conclusions: In Costa Rica, the strategy of fortifying several foods with FA has been successful insofar as it is complementary (several foods) and universal (all options in the market for the same food). It has come to resolve the heterogeneity of the population's consumption habits and has given responsibility for population health to various food producers, creating awareness in the food industry of the shared responsibility to contribute to the health of the population. To reduce NTD risk, an integrated surveillance strategy is essential to base prevention strategies on evidence and to demonstrate their impact, and improve interventions over time. Costa Rica shows how this type of surveillance is feasible to be implemented in developing countries.

Birth defects surveillance in resource-limited settings: Challenges faced in Sri Lanka

K Jayaratne[1], CD Silva[1]
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Birth Defects Program on which the work is based: NA

Background and Objectives: Sri Lanka, being a low-and-middle-income country, reports a low infant mortality rate (8.1 per 1000 live births). Nearly 35 - 40% of stillbirths and infant deaths are incriminated to birth defects. A paper-based national birth defects surveillance program was piloted and launched in 2017. In 2019, it was upgraded to a web-based National Birth Defects Registry (NBDR).

Methods: Under the NBDR, all specialized hospitals (with an Obstetrician/Pediatrician) notify and abstract all cases of birth defects identified within the institution and enter data into the NBDR. The inclusion criteria include conception up to the age of completed 2 years. When a baby with a birth defect is identified, a Birth Defects Case Abstraction Format is filled under the guidance of a specialist clinician of the unit and completed format is sent to head of hospital. A designated medical officer enters data into web-system. ICD-10 coding with RCPCH extensions are used to classify cases.

Results: Both government and private sector hospitals (n=131) throughout country are enrolled in NBDR. Number of cases reported to NBDR in the years 2019, 2020, 2021 and 2022 up to mid-August are 56, 353, 846 and 814 (total=2069) respectively. Majority of cases (n=1075, 52%) were identified at birth, 979 (47%) during first year and 2 (<1%) 2nd year of age. Only a few cases (n=13, 0.63%) were diagnosed antenatally. Most (n=1026, 49.6%) cases were males and a few cases (n=46, 2.2) had ambiguous sex. Anomalies of circulatory system were the majority (n=464, 22%) followed by anomalies of musculoskeletal system (n=208, 10%). Congenital malformations of nervous system accounted for 7% (n=137) and Cleft lip and palate was found in 6% (n=123). A significant number of cases (n=660, 31.9%) were reported from mothers 31-40 years old.

Discussion and Conclusions: A web-based simple common format to capture cases is feasible and effective for counting and gathering essential information on birth defects at hospital level even in resource-limited settings provided strong governance mechanisms are in place. Systematic training of data originators and close monitoring yield meaningful outcomes. Capacity, attitudes and logistic issues limit capturing of data.

DELFOS: Research program for the diagnosis, training, logistics, education, organization and monitoring of patients with congenital heart disease in Colombia

I Zarante[1], N Niederbacher[1], JM Montealegre[1], P Pineda[1], J Lores[2], C Castro[3], JC Briceño[3], J Navarro[4], M Ronderos[5], AM Guaca[6]
[1]Institute of Human Genetics, Pontificia Universidad Javeriana, Bogotá D.C., Colombia, [2]Department of Basic Sciences, Faculty of Health Sciences, Pontificia Universidad Javeriana, Cali, Colombia, [3] Biomedical Engineering Department, Universidad de los Andes, Bogotá D.C., Colombia, [4]Industrial Engineering Department, Pontificia Universidad Javeriana, Bogotá D.C., Colombia, [5]Cardiology Institute, Fundación Cardioinfantil, Bogotá D.C., Colombia, [6]Secretaría de Salud de Bogotá, Bogotá D.C., Colombia

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Birth Defects Program on which the work is based: Congenital Malformations Surveillance Programme (CMSP). Bogotá, Colombia.

Background and Objectives: Congenital heart defects (CHDs) are structural or functional defects of the cardiovascular system that are present at birth, which according to EUROCAT, represent 28% of all birth defects. Furthermore, they are the main cause of child mortality during the first year of life. In Colombia, according to the National Institute of Health in 2022, CHDs represent the most frequently notified birth defect, with a prevalence rate of 45.7 cases per 10.000 live births. The most prevalent are atrial septal defects, followed by ventricular septal defects and patent ductus arteriosus. Some previously identified risk factors for CHD in a case control study from Bogotá were maternal age above 45 years, pregestational diabetes, and low educational level. Taking into account the relevance of CHDs in the context of child mortality, the Research Program for the Diagnosis, Training, Logistics, Education, Organization and Monitoring of Patients with Congenital Heart Disease (DELFOS) was established.

Methods: Five projects were developed inside the research program, involving data from reported CHDs in Bogotá and Cali, Colombia: 1. Development of a control panel for the surveillance of congenital heart diseases. 2. Prenatal diagnosis training and efficiency evaluation of prenatal diagnosis of congenital heart disease. 3. Screening using machine learning to detect congenital heart disease. 4. Cost-effectiveness evaluation. Conventional screening versus machine learning.
5. Evaluation of the ability to perform cardiac surgery in patients with congenital heart disease in Colombia. These projects had the objective to solve different problems related to the appropriate attention of patients with CHD in Colombia. To date, data collection of the first two projects has already started completely and preliminary results have been analyzed. Data collection of the other projects is still in progress.

Results: Project 1: We have been able to collect information and follow 639 patients since the project started its implementation phase. Furthermore, healthcare affiliation status was registered, demonstrating a similar distribution between the public and private systems. Additionally, we did not identify disease clusters related to the patients' and their families' living place. On average, cases traveled a mean of 106 km (Bogotá) and 130 km (Cali) from their place of living to the healthcare institution where they were being treated.
Project 2: In this project, we identified that approximately 36% of obstetric ultrasounds were practiced outside of the guidelines established by law. Moreover, prenatal diagnosis of CHD was made in 40% of cases. Finally, 20% of patients with complex CHD were diagnosed by using prenatal ultrasound.

Discussion and Conclusions: Taking into account the impact of CHDs on perinatal and neonatal health, the timely diagnosis and treatment of this group of disorders is a clear priority for healthcare promotion. By using the data of our research, we did not identify a tendency towards specific health affiliation or living place, denoting that the correct treatment and surveillance of these pathologies is not a problem of a specific demographic group. Parental income levels were not taken into account in this analysis, which is a limitation

of our results.

Prenatal diagnosis is fundamental to diminish adverse outcomes in children with CHD. Data on inaccuracy of CHD diagnosis by obstetric ultrasound prompts the development of tailored courses for ultrasound technicians and OB/GYN related staff. Collaboration of private and public entities with state support is needed to improve the health management of CHD patients.

Perceptions experiences, and meanings attached to external visible birth defects by parents of children with birth defects, healthcare workers, and community health extension workers in Uganda.

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Birth Defects Program on which the work is based: NA

Background and Objectives: Each year, an estimated 8 million babies (6% of worldwide births) are born with birth defects (BDs), and the prevalence varies from region to region. In Uganda, the overall prevalence of BD was 66.2/10,000 births (95% CI 60.5–72.5), the most prevalent being hypospadias in 2017. Since 2015, Makerere University–Johns Hopkins University (MU-JHU) Research Collaboration, in Kampala, Uganda, has operated a BD surveillance system. The objective is to determine BD prevalence and identify any associations between maternal use of antiretroviral therapy (ART) and common medicines in early pregnancy with the incidence of birth defects. As part of this project, a qualitative sub-study was conducted to explore parents', healthcare workers', and community health extension workers' (CHEWs') perceptions, experiences, and meanings attached to visible major external BDs, as a first step for investigators to gaining a deeper understanding that parents, health workers and wider community had about BDs.

Methods: Between October 2022 and May 2023, we conducted a qualitative sub-study involving thirty in-depth interviews (IDIs) with parents whose children were born with a BD, ten key informant interviews (KIIs) with health workers caring for such children at health facilities, and four focus group discussions (FGDs) with CHEWs from communities. Participants were purposively selected and were provided with BD pictures for visual reference during the interviews. We obtained informed consent and interviewed them until no new information emerged from any additional interviews. The data were collected either in Luganda or English, and the audio recordings from the KIIs, IDIs and FGDs were transcribed and then translated into English for thematic analysis. We developed a codebook from the initial analysis of transcripts and uploaded the data into ATLAS.ti version 9.1.3.0 software for detailed coding. We held iterative meetings with the research team to refine and enhance the analysis.

Results: Parents and CHEWs held various views and understandings of the causes and meanings attached to major external BD. Their understanding and awareness of the causes was low and included use of family planning methods; physical harm, stress, or illnesses; taking multiple medicines/herbs during pregnancy; effects of earthquakes/bombs; COVID-19 vaccines; witchcraft; God's plan; and self-administration of drugs. Parents reported being psychologically shocked and experiencing pain, stress, financial constraints, and strained relationships. Participants reported considering BD uncommon/seasonal, or a curse. CHEWs and health workers struggled to provide the necessary counseling support and health education services. Participants suggested the need for specialized support services for affected families, including social, financial, and emotional support. Pregnancy scans and avoidance of herbs and unprescribed medicines were recommended as BD prevention strategies by participants.

Discussion and Conclusions: In this sub-qualitative study, three conclusions can be drawn. One, parents, healthcare workers, and the wider community need to be sensitized and made aware of BD causes and prevention. Two, having a child with BD presents challenges for parents/families, health care workers and the community alike. This underscores the need to equip health workers and CHEWs with specialized skills to effectively communicate, counsel, and provide necessary care/support for affected families and the community at large. Three, the majority of parents, health workers and CHEWs would benefit from specialized follow-up services, early healthcare access for BD and medical care for children born with BD.

An audit of capacity in community genetic services in South Africa: A sector in crisis

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Birth Defects Program on which the work is based: NA

Background and Objectives: Community genetic services in South Africa (SA) were established through cytogenetic laboratories in the 1950's which rapidly grew with the establishment of academic chairs of Human Genetics, in Cape Town and Johannesburg 1972-1974. In state healthcare, services are mainly a partnership between provincial Departments of Health and academic institutions. Despite early investment, services have been in decline for the last 20 years, following reallocation of resources to other healthcare priorities, most notably HIV/AIDS. Capacity recommendations indicate that for the current SA population, there should be 31 medical geneticists and 106 genetic counsellors practising. Previous reports indicate that genetic units are operating with inadequate capacity due to the lack of posts allocated for these healthcare professionals (HCP) and the loss of others to retirement, emigration, and other factors.
The aim of this study was to undertake a capacity audit of these two HCP categories in 2024.

Methods: This desktop study was undertaken in May-June 2024. A list of all qualified and registered medical geneticists and genetic counsellors was generated from the register of the Health Professions Council of South Africa. Emails were sent out to the clinical heads of the three academic genetic units in Cape Town, Stellenbosch, and Johannesburg requesting a summary of medical geneticists and genetic counsellors practising/currently in-training and estimated completion date. All HCP servicing the state and private healthcare services were contacted countrywide to confirm their year of registration and where they are currently practicing. Medical laboratory scientists were excluded from this study. Descriptive statistics were used to evaluate and compare the data received with recommended numbers of the two HCP categories for the current population, and the future expected capacity based on HCP in-training. Loss of capacity was recorded, including retirement, emigration, career change etc.

Results: SA recommends 1 medical geneticist to 2 million and 1 genetic counsellor to 580 000 of the population or 31 medical geneticists and 106 genetic counsellors.
Currently 12 medical geneticists are practising (39% capacity). Of these, 6 (50%) work in state/private, 4 (33%) practise privately, 2 (17%) practise in state - collectively across Gauteng (GP) (n=7), Western Cape (WC) (n=4), Northern Cape (n=1) provinces. Of 29 previously qualified and not practising: 14 (48%) emigrated, 8 (28%) retired, 4 (14%) passed away, 2 work in academia, 1 no longer practises. 29 genetic counsellors are currently practising (27% capacity). Of these, 18 (62%) practise privately, 7 (24%) state/private, 4 (14%) practise in state - collectively across GP (n=13), WC (n=12), KwaZulu Natal (n=3) and Free State (n=1) provinces. Of an additional 26 qualified genetic counsellors, 16 (62%) emigrated, 6 (23%) work in academia, 3 retired,1 passed away. Most emigrations have occurred in the past 5 years (9/16;56%).

Discussion and Conclusions: This 2024 capacity audit indicated significant understaffing of both HCP categories. This is supported by 2030 Human Resources for Health Strategy which indicated only 0.01 medical geneticists per 10 000 population versus the required 0.21 per 10 000 in 2019.

A significant proportion of qualified medical geneticists and genetic counsellors are being lost to emigration, often immediately following completion of studies (6 genetic counsellors moved to the UK since 2020), due to the lack of posts in SA. Many remaining are forced to practice privately or stop practicing altogether. A

moratorium on creating new state posts for these HCP has been in place for many years, despite the growing burden of congenital disorders (CD) in the country.

The genetic basis of most CDs means that those impacted will require medical genetic services at some point in their healthcare journey. Addressing this lack of capacity is now imperative to ensure the care and management of those affected.

Session II – Oral Presentations

Moderators:
Emma Kalk and ***Ignacio Zarante***

Congenital anomalies in limb body wall complex in 53 cases from the Alberta Congenital Anomalies Surveillance System, 1997-2019
Mary Ann Thomas

Moving towards triple surveillance: tracking congenital heart disease outcomes through the lifespan
Lorenzo D. Botto

Epidemiological characterization of arthrogryposis multiplex congenita in Bogotá and Cali: Insights from a case-control study on risk factors
Karen Sarmiento

Improving the congenital anomalies surveillance system in Emilia-Romagna region: does secondary health data integration matter?
Marco Manfrini

Trends in total and live birth prevalence of orofacial clefts and the effect of prenatal detection on pregnancy outcome in the northern Netherlands
Dieuwke C. Broekstra

Post-fortification Changes among Spina Bifida Cases by Subtypes and Lesion Level
Cara Mai

Evaluation of the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) data linkage with the Maternity Services Dataset (MSDS) for pregnancies in 2020 and 2021 in England
Gabriella Melis

Congenital anomalies in limb body wall complex in 53 cases from the Alberta Congenital Anomalies Surveillance System, 1997-2019

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Birth Defects Program on which the work is based: Alberta Congenital Anomalies Surveillance System (ACASS)

Background and Objectives: Limb Body Wall Complex (LBWC) is a well described human malformation condition that remains largely unexplained. It has been proposed as a recurrent constellations of embryonic malformations (RCEM) condition with shared features with other RCEM conditions, including overlapping anomalies and an increased twin rate. LBWC has anomalies that co-occur in the same individual more frequently than expected. Van Allen's diagnostic criteria (1987) are frequently used and include at least two: exencephaly or encephalocele with facial clefts, thoracoschisis and/or abdominoschisis, and limb defects. This study reviews the congenital anomalies, additional characteristics, and overlap with other RCEM conditions.

Methods: Cases with LBWC, born between January 1, 1997 and December 31, 2019, were abstracted from the provincial and population-based Alberta Congenital Anomalies Surveillance System (ACASS). Cases with a known teratogen or genetic condition were excluded. Multiple data sources were reviewed, including reports from specialty clinics, diagnostic imaging, and pathology, to support a diagnosis of LBWC and identify associated congenital anomalies. ACASS ascertains livebirths, stillbirths and termination of pregnancies (ToPs) less than 20 weeks gestation.

Results: There were 53 cases with LBWC born during the 23 year study period giving a frequency of 1 in 20,282. Pregnancy outcomes included 3 (6%) live births, 2 (4%) stillbirths and 48 (90%) ToPs. The majority were identified in early pregnancy with early termination. The average gestational age at delivery was 19 weeks.
Forty-nine (92%) had an abdominal wall defect, most consistent with abdominoschisis; 24 (45%) had a thoracoschisis; 50 (94%) had limb anomalies including limb reduction, clubfoot or other types; 26 (49%) had a neural tube defect, including spina bifida, encephalocele and/or acrania +/- exencephaly; 39 (74%) had scoliosis, most were described as severe and 13 (25%) had an orofacial cleft.
Five (9%) were twins, which exceeds the Alberta twin pregnancy rate of 3.3%. Minimally, 20/53 cases (38%) had a single umbilical artery. Nine (17%) had an overlapping phenotype with a second RCEM condition.

Discussion and Conclusions: This study identified 53 cases with LBWC and contributes population- based data regarding associated congenital anomalies and other characteristics. There was overlapping phenotype with other RCEM conditions including Pentology of Cantrell (POC), VACTERL or OEIS. There were features that were more unique in LBWC, including a short umbilical cord and a high rate of abnormal adherence of fetal anomalies or the cord to membranes. The high rate of a single umbilical artery raises the possibility of a related etiological mechanism.
Additional findings from this study included a high number, twenty-two cases (42%), with limited or no autopsies, and with phenotyping being derived from prenatal imaging. This highlights the limited postnatal phenotyping in this condition due to the early prenatal ultrasound identification of life limiting anomalies and early termination, and makes studying this condition challenging.

Moving towards triple surveillance: Tracking congenital heart disease outcomes through the lifespan

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Birth Defects Program on which the work is based: NA

Background and Objectives: People with congenital heart disease (CHD) are increasingly living longer, yet their comorbid conditions over the lifespan are not well known. In this multi-site population-based study we assessed comorbid conditions in adults with CHD at five sites in the United States using multiple linked data sources, including birth defect registries.

Methods: This retrospective cross-sectional study included 18,672 adults aged 19 to 64 years living in one of five US geographic areas and who had a healthcare encounter between 2011 and 2013 associated with > 1 CHD-related diagnosis code. Data were derived from linked clinical and administrative sources, reflecting inpatient, emergency department (ED), and outpatient encounters.

Results: Most adults with CHD experienced at least one (89%) and usually multiple (76%) comorbidities. Non-cardiac comorbidities typically exceeded cardiac comorbidities. The presence and number of comorbidities were higher in males and with increasing age. Individuals of Black and multiracial background experienced higher rates of many comorbidities, both cardiac and non-cardiac, compared to individuals of White racial background. This was true at all ages and regardless of CHD type. The most frequent non-cardiac comorbidities typically treatable or preventable, including endocrine/metabolic conditions (e.g., diabetes, hyperlipidemia, hypothyroidism), hypertension, and neuropsychiatric conditions (e.g., anxiety, depression).

Discussion and Conclusions: Birth defect surveillance programs can contribute to population-based surveillance of outcomes through the lifespan, provided they actively share information and link with other clinical and administrative data sources. In this example focusing on CHD in adults, comorbidity and multimorbidity were common, increased with age, included preventable conditions, and occurred unequally in different racial and ethnic groups. Management guidelines that explicitly address such comorbid and multimorbid conditions, with specific attention to existing health disparities, may help reduce premature mortality in the large and increasing population of adults with CHD.

Epidemiological characterization of arthrogryposis multiplex congenita in Bogotá and Cali: Insights from a case-control study on risk factors

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Birth Defects Program on which the work is based: ECLAMC, Colombia

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Background and Objectives: Arthrogryposis Multiplex Congenita (AMC) presents with joint contractures in tho or more body areas, causing limited fetal mobility during pregnancy and restricted joint movement at birth, accompanied by muscle weakness and fibrosis. There exist two primary types: amyoplasia and distal arthrogryposis (DA). AMC prevalence ranges from 1 per 3,000-5,000 live births (LB), with musculoskeletal birth defects, including AMC, accounting for 24.4% of all birth defects in Colombia. This study aims to conduct an epidemiological characterization of AMC prevalence and identify associated risk factors using data from the Program for the Prevention and Surveillance of Birth Defects and Rare Diseases of Bogotá and Cali (PREVERDEC) spanning from January 2002 to March 2020

Methods: A population-based case-control study utilized PREVERDEC data, employing the ECLAMC method for documenting major and minor birth defects in newborns weighing over 500g via standardized physical examinations. Each case of AMC reported between January 2002 and March 2020, with a birth weight exceeding 500g, was included and classified as amyoplasia or DA based on clinical presentation. Maternal interviews post-birth provided comprehensive prenatal, pregnancy, and newborn-related data. However, detailed clinical aspects and additional laboratory/genetics tests were unavailable for analysis. Cases were further categorized into isolated, complex isolated, polymalformed, and syndromic based on associated conditions

Results: From 555,255 registered births, 29 cases of AMC and 126 controls were identified, with 86.21% of cases classified as LB. Amyoplasia accounted for 51.72% of cases. Further classification revealed isolated cases (31.03%), complex isolated cases (10.34%), and polymalformed cases (55.17%), with one syndromic case identified. Prevalence of AMC was 0.52 cases per 10,000 LB. For risk factor analysis, variables associated with AMC presentation included: low birth weight <2,500g (OR: 23.26; 95% CI 8.50 - 63.67), low gestational age <37 weeks (OR: 6.42; 95% CI 2.62 - 15.74) and polyhydramnios on ultrasound (OR: 55.55; 95% CI: 6.93 - 445.59), whilst variables that decreased association with AMC in newborn were: paternal age >35 years (OR: 0.21; 95% CI 0.05 - 0.93), male newborns (OR: 0.32; 95% CI: 0.14 - 0.73) and gestational folic acid use (OR: 0.30; 95% CI: 0.13 - 0.73).

Discussions and Conclusions: Prevalence of AMC observed in our study was lower than that reported by national registries in high-income countries. Furthermore, AMC is frequently associated with additional limb involvement, such as clubfoot or subluxated/dislocated hips. Preterm birth and AMC share a complex relationship, as it is challenging to determine whether they are the cause or consequence or associated with other BD. Prenatal ultrasound findings of polyhydramnios are attributed to decreased fetal swallowing, possibly linked to concomitant BD associated with AMC rather than AMC itself. This study provides essential insights into the prevalence and risk factors of AMC in Bogotá and Cali, Colombia, which is crucial for a low-middle income country. Identifying these factors is vital for reducing morbidity in vulnerable populations. Strengthening BD surveillance systems is paramount for early detection, accurate diagnosis, and effective treatment of AMC, ultimately improving healthcare outcomes

Improving the congenital anomalies surveillance system in Emilia-Romagna region: does secondary health data integration matter?

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Birth Defects Program on which the work is based: IMER registry

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Background and Objectives: The surveillance of major congenital anomalies (MCA) relies on data from population-based registries. IMER, the Emilia-Romagna region (Italy) MCA registry is characterized by a complex data capture and integration process. The aim is to maximize surveillance and transmission of quality data to EUROCAT (https://eu-rd-platform.jrc.ec.europa.eu/eurocat_en) the European network of population-based registries for the epidemiological surveillance of congenital anomalies. Case ascertainment via healthcare professionals provides high quality data but suffers from lack of human resources so cases can be lost. Healthcare databases collect data not always following EUROCAT definitions. Hence multi-source ascertainment using EUROCAT coding and classification enables better data capture both in terms of quality and quantity. The linkage strategy plays a crucial role in this process.

Methods: The IMER Registry is a population-based registry which covers the entire Emilia-Romagna Italian region an area of 22.453km2 with a population of 4,455,188 inhabitants – 1st January 2024 – and approximately 30,000 births occur each year. IMER uses multisource ascertainment, including hospital discharge records (HDR) from 2009, through a validated algorithm to recognize CA not communicated to the registry by clinicians. Cases are notified also from the rare disease registry. Live birth, stillbirth and TOPFA (termination of pregnancy for fetal anomalies) are included. The registry follows EUROCAT coding guidelines and CA definitions. Drug exposure was integrated in the collected data by linkage with regional prescription reimbursement data flow. The linkage process has been optimized to obtain the best match by deterministic approach, linking collected data by healthcare professionals using REDCap software to HDR thus improving efficacy.

Results: Our data source integration strategy allowed us to build a surveillance ecosystem able to report to the regional health authority and to the EUROCAT network robust and comprehensive data. In the period 2016-2021, we collected 4693 cases, the greatest part (44.83%) come from the reports made by birth center representatives while the congenital anomalies recorded through the analysis of the HDR contributes 33.35% . HDR cases recorded more than seven days after birth (6.35%). Cases derived from general birth registry constitute 3.07% of total cases. Data relating to TOPFA represent 17.22% of total cases are reported only by clinicians. The cases obtained from the rare disease registry represent 1.53%. 20% of cases due to poor-quality unique identifier were not linked.

Discussion and Conclusions: The amount of work carried out by the clinician directly involved in the data collection and curation process, is the foundation of our registry but the integration of other data sources has increased both the number of cases and malformations registered. The strength of this system is it allows clinicians to focus their activity on diagnosis and care, leaving collection of sociodemographic and exposure data to the registry. To maintain a high quality of the collection and integration processes, accurate revision of the final dataset must be carried out. The major weakness is the high number of cases that cannot be linked

and cases with vague descriptions, difficult to code. This will be the main aim of future work.

Trends in total and live birth prevalence of orofacial clefts and the effect of prenatal detection on pregnancy outcome in the northern Netherlands

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Birth Defects Program on which the work is based: EurocatNNL

Background and Objectives: Clinicians in the northern Netherlands have noted a decrease in orofacial clefts (OFCs), which could potentially be explained by a decrease in live birth (LB) prevalence of OFCs because of changes in prenatal screening. This study was aimed to investigate trends in the total and LB prevalence of OFCs and the effect of prenatal screening on the LB prevalence of OFCs in the Northern Netherlands (NNL) over a period of 21 years.

Methods: We categorized OFCs into two main types, cleft lip with or without palate (CL±P) and cleft palate (CP). These types were divided into three subgroups regarding anomaly type: isolated clefts, clefts associated with genetic/syndromic anomalies, and clefts associated with other congenital anomalies. We assessed the prevalence of OFCs by determining the ratio of total and live births with OFCs to all births in the NNL from 2001 to 2021. We analyzed trends in prevalence and temporal patterns in prenatal detection and termination of pregnancy by calculating the annual percentage change (APC) using Joinpoint regression.

Results: During the study, 361,109 children were born in the NNL, with 359,519 born alive. We included 760 fetuses/neonates with OFCs, resulting in a total prevalence of 2.10/1000 births and a LB prevalence of 1.9/1000 births. The total prevalence of CL±P decreased from 1.65/1000 births in 2001 to 1.17/1000 births in 2021 (APC=-0.82 [95%CI: -2.18, 0.55]), with the LB prevalence decreasing from 1.57/1000 births in 2001 to 0.93/1000 births in 2021 (APC=-1.65 [95%CI -3.03,-0.25]). The prenatal detection rate of CL±P exhibited substantial growth between 2001 and 2007 (APC=34.38 [95%CI 24.27, 52.26]), followed by a more gradual increase until 2021 (APC=3.57 [95%CI 0.59, 6.08]). The percentage of terminated pregnancies rose between 2001 and 2021 from 3.8% to 12.7% (APC=52.29 [95%CI 53.16, 61.53]), with most abortions occurring in the subgroups genetic/syndromic and other congenital anomaly clefts.

Discussion and Conclusions: Between 2001 and 2021, the LB prevalence of CL±P decreased, while the total prevalence showed a less strong decrease. This decline in LB prevalence could be related to better prenatal detection and, consequently, a rise in pregnancy terminations after an unfavorable prognosis.

Post-fortification changes among Spina Bifida cases by subtypes and lesion level

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Birth Defects Program on which the work is based: Six population-based birth defects programs in the US [Arizona, California (covering 8 counties), metropolitan Atlanta (Georgia), Oklahoma, South Carolina, and Utah]

Background and Objectives: Mandatory folic acid fortification has been shown to reduce the prevalence and severity (lesion level) of spina bifida (SB) in the United States. However, limited data exist on the impact of fortification on SB subtypes and case classification. This project seeks to examine post-fortification changes among isolated/non-isolated SB cases by lesion level and subtypes.

Methods: Six active population-based birth defects programs [Arizona, California (covering 8 counties), metropolitan Atlanta (Georgia), Oklahoma, South Carolina, and Utah] provided SB cases for birth years 1992–1996 (pre-fortification) and 1999–2016 (post-fortification period). Cases were classified as isolated or non-isolated, and assigned a subtype (spinal rachischisis, myelomeningocele/meningomyelocele, meningocele) and lesion level (upper for cervical and thoracic; lower for lumbar and sacral). Statistical analyses were performed using SAS

Results: Overall, 76.8% of SB cases were isolated and 23.2% were non-isolated (n=2,594; pre-fortification n=572, post-fortification n=2022). The proportion of isolated/non-isolated cases across the two periods did not change overall (p=0.91) or by sex (males p=0.34, females p=0.24). The proportion of isolated upper lesion level cases decreased from 75.4% pre-fortification to 60.6% post-fortification and increased for non-isolated cases (24.7% to 39.4%) (p=0.005); no differences for lower lesion level cases (p=0.55). When examining SB subtypes, the proportion of rachischisis cases did not differ between isolated/non-isolated overall (p=0.35) nor among lower lesion level cases (p=0.44) but shifted for upper lesion level cases (non-isolated 25.0% to 57.1%; isolated 75.0% to 42.9%, p=0.05). Similarly, the proportion of myelomeningocele cases changed significantly for upper lesion cases only (p=0.01). Finally, isolated meningocele cases decreased ~25% post-fortification, regardless of lesion level.

Discussion and Conclusions: Folic acid fortification impacts phenotypic characteristics among infants with SB. Specifically, differences were seen in upper lesion level cases by SB case classification and subtypes. Further exploring demographic and clinical characteristics can elucidate what might drive the observed differences.

Evaluation of the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) data linkage with the Maternity Services Dataset (MSDS) for pregnancies in 2020 and 2021 in England

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Birth Defects Program on which the work is based: National Congenital Anomaly and Rare Disease Registration Service, National Disease Registration Service, NHS England, England

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Background and Objectives: There is increasing need for data linkage across electronic health records (EHR) for monitoring population health measures and outcomes. This work looks at the effect of linkage between the NCARDRS Congenital Anomaly and Rare disease Analysis (CARA) data and MSDS. NCARDRS collects and quality assures population-level data on congenital anomalies and rare diseases in England. MSDS is a database collecting data on the health status of pregnant people and their babies, from the time of the first booking appointment up to the point of discharge from maternity services. MSDS collects multiple fields that are either also collected by NCARDRS, or that would provide further information on causes, risks and treatment of congenital anomalies. The aim of this project is to identify fields in the CARA data that could be sourced directly from MSDS, and compare values to determine accuracy. We also aim to evaluate the degree to which completeness of each field in CARA could be improved using MSDS.

Methods: Deterministic linkage between the two databases was run based on national identifiers (NHS number) of the mother and baby, and expected delivery date (EDD) for births in 2020 and 2021 in England. The linkage and analyses were carried out in a secure Data Access Environment (DAE). Data quality in terms of field completeness across the datasets and type of coding systems used to categorise the data was assessed and an evaluation of differences with the fields already held in NCARDRS was carried out. CARA fields were mapped to the equivalent entries in MSDS. Data completeness was assessed for both databases. A first check of data quality was run once linkage had been established, based on assessing congruency. Where the values were present only in one of the two databases, we assumed their correctness. In cases where we have found conflicting values, NCARDRS aims to liaise with the MSDS team, as well as with national health Trusts, to assess validity and agree on correct values.

Results: Mother NHS number and birth date are fully completed in MSDS, whilst presenting a few null values in CARA. In MSDS, EDD is also fully complete, whilst in CARA this is null for 17% of the pregnancies. Other key fields of great relevance to NCARDRS such as gestational length at birth and NHS number (baby) present considerably higher completion in MSDS than in CARA. Some key fields such as number of births per labour and delivery present around 10% of null values in MSDS against 29% in CARA. Other fields in MSDS, such as number of fetuses at dating ultrasound scan, in its raw form, is null for 78% of pregnancy events in MSDS, whilst it is null only for 22% of the pregnancies in CARA. Maternal and baby ethnicity are well completed in MSDS, with a proportion of missing and null data around 12% against over 40% in CARA for maternal ethnicity; CARA does not collect ethnicity for the baby, suggesting linkage with MSDS would also benefit CARA's completion for sociodemographic fields.

Discussion and Conclusions: EHR linkage is becoming central to enhance data quality across related datasets, benefitting analytical applications for the assessment of the effect of wider factors such as sociodemographic characteristics on the distribution of health conditions in the population. The linkage between high quality data on congenital anomaly from NCARDRS and complementary socio-demographic information from MSDS will drive further understanding of social determinants of congenital anomalies in babies, informing possible interventions on modifiable risk factors. MSDS is one of the available options to enhance data quality in CARA,

however other databases should also be explored. For instance, the Hospital Episode Statistics (HES) database also collects high-quality data on sociodemographic characteristics of pregnant people and babies. Future research is needed to explore the contribution of further dataset linkages.

Session III – Oral Presentations

Moderators:
Adriana Benavides-Lara and ***Dieuwke C. Broekstra***

DELFOS - use of an automated chatbot for the surveillance of patients with congenital heart disease in Bogotá, Colombia
Nicolás Niederbacher

Application of Bayesian Hierarchical Models in the spatial analysis of congenital heart diseases in Rio Grande do Sul
Márcia H. Barbian

Does folic acid food fortification increase the risk of COVID-19 infection and mortality? A public health intervention with unintended consequences?
Wendy N. Nembhard

Hypertrophic Cardiomyopathy in children: one condition for multifaceted diseases. The importance of multisystemic and multidisciplinary approach in children
Anwar Baban

Prevalence of adverse birth outcomes and external birth defects among women living with HIV in Malawi
George Bello

MALFOVAR (Malformation and variable anatomy registry) case series 2007-2024: Congenital tumors
Tidhar Steiner

DELFOS - use of an automated chatbot for the surveillance of patients with congenital heart disease in Bogotá, Colombia

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Birth Defects Program on which the work is based: Congenital Malformations Surveillance Programme (CMSP). Bogotá, Colombia.

Background and Objectives: Patients with congenital heart defects (CHDs) encounter healthcare access barriers, stemming from social disparities. Studies link higher CHD mortality to factors like adolescent maternal age, low educational level , and affiliation to public health insurance. Regarding access to cardiac surgery, barriers include caregiver education, gender bias, and financial constraints. In a study performed in Latin America, barrier perception was positively associated with educational level, household monthly outcome and psychological well-being. Therefore, strategies that aim to reduce healthcare access barriers are essential for timely intervention and prevention of sequelae. This project aimed to develop a chat-bot facilitating caregiver access to healthcare appointments and exams through direct assistance from the Bogota Secretary of Health.

Methods: The chatbot algorithm was designed by a team composed of pediatric cardiologists, geneticists, and social service physicians who were enrolled into project 1 of DELFOS, a program made for the diagnosis, training, logistics, education, organization and monitoring of patients with congenital heart disease in Colombia. The design of this tool took into account the patients' and its relatives' accessibility, feasibility, and the possibility of implementing it long-term. After identifying cases of CHD, the patient's relative is contacted through the chatbot via WhatsApp to identify possible attention barriers that the patient might be having .Chat-bot answers are registered, allowing a broad knowledge of the healthcare follow-up which the patient is receiving.

Results: Since the start of the implementation phase, the chatbot enrolled 171 patients into surveillance. The percentage of people who answered after being contacted was 50%, most of which reported that the patient's health condition was good. After reviewing the attention barriers related to the patient's healthcare, most of them were related to delayed appointment or consultation by specialists (pediatric cardiologists, pediatric cardiac surgeons), delayed appointment of cardiac surgery, and failure to deliver medication needed by the patient. Interventions were made by our team to diminish these barriers, which were proven to be effective and bettered the attention of patients with CHD.

Discussion and Conclusions: Patients with congenital heart defects (CHDs) globally face healthcare access barriers, exacerbated by social determinants of health. Studies indicate a higher mortality risk among CHD patients born to adolescent or low-educated mothers, or those covered by public health insurance. Preoperative obstacles, such as caregiver education, gender discrimination, and financial constraints, hinder access to cardiac surgery. Research in Latin America reveals that barrier perception correlates positively with educational level, household income, and psychological well-being. Notably, among eight countries surveyed, Colombia ranks second lowest in caregiver barrier perception. This project introduces a chat-bot developed with the Bogota Secretary of Health, designed to assist caregivers in navigating healthcare systems, thus facilitating timely access to appointments and examinations, and preventing CHD sequelae.

Application of Bayesian Hierarchical Models in the spatial analysis of congenital heart diseases in Rio Grande do Sul

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Birth Defects Program on which the work is based: NA

Background and Objectives: Congenital heart defects (CHDs) are the most common group of birth defects in humans. They have been associated with high mortality, morbidity, and burden in the health system. CHDs represent the leading cause of death among newborns with malformations in Brazil. The objective of this study is to model the geographical distribution of congenital heart defects cases in the state of Rio Grande do Sul from 2010 to 2021.

Methods: We utilized data on Congenital Heart Diseases (CHDs) from Rio Grande do Sul state, located in the southern region of Brazil, recorded between 2010 and 2021. This data was sourced from a robust Brazilian tool for population-based information systems known as The Live Birth Information System (Sinasc). The analysis considers the number of live births, categorized by the presence or absence of congenital heart diseases, aggregated by maternal residence municipality in the estimation of relative risk. We applied the Bayesian hierarchical model BYM proposed by Besag-York-Mollié (1991), with a modification proposed by Simpson (2015). For the computation of the posterior distribution, the integrated nested Laplace approximation (INLA) was implemented using the R-INLA package. The algorithms for database manipulation and model estimation were developed in the R language, utilizing R version 4.2.2 and RStudio.

Results: Given the covariates considered in the model, only the natural logarithm of per capita income exhibited a statistically significant positive association. Consequently, it is anticipated that municipalities with higher per capita incomes will have a greater incidence of congenital heart diseases. The mode of the spatial dependency parameter is 0.92, signaling a high degree of spatial dependency. It is observed that a considerable portion of municipalities in the southwest region, along with some in the northwest, southeast, and northeast regions, exhibited significantly lower relative risks. Conversely, municipalities with significantly higher risks are situated in the metropolitan area (Porto Alegre, Cachoeirinha, Gravataí, and Alvorada), the eastern central region (comprising Vera Cruz and Santa Cruz), and the municipality of Bento Gonçalves.

Discussion and Conclusions: It was observed that municipalities with higher per capita income tend to exhibit a greater incidence of congenital heart disease cases. The study identified specific regions in Rio Grande do Sul with significantly higher relative risks, and these municipalities are those that possess greater healthcare infrastructure and higher income. Conversely, municipalities with lower relative risks are those with lower income and infrastructure. We would like to emphasize that the limitation encountered is the presence of underreporting in the records of congenital heart diseases, which impacts the obtained results. Therefore, the findings of this study can assist healthcare managers in formulating more effective action plans to combat underreporting.

Does folic acid food fortification increase the risk of COVID-19 infection and mortality? A public health intervention with unintended consequences?

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Birth Defects Program on which the work is based: NBDPS

Background and Objectives: Is it possible that a global public health intervention, folic acid food fortification, shown to reduce the risk of neural tube defects may have inadvertently exacerbated the COVID-19 pandemic? Some researchers postulated that SARS- CoV-2 "hijacks" folate, a vitamin and cofactor in the one-carbon metabolism pathway, for viral replication in humans. Other studies demonstrate that folic acid supplementation plays a protective role against SARS-CoV-2 infection but may increase the risk of post-infection mortality. Give the significant implications of these findings, the objective of the study was to further evaluate these observations by assessing the association between country-specific folic acid intake levels and COVID-19 incidence and mortality rates.

Methods: Our ecologic study used folic acid fortification legislation status, and potential folic acid intake from fortification (mg/day) of wheat, maize, and rice for each country (n=196) as of December 2019 from the Global Fortification Data Exchange. COVID-19 incidence and mortality data were obtained, December 2019–April 2023 from the World Health Organization (WHO). Countries were categorized into 6 WHO-regions and were classified into 3 income groups (low, middle, and high income) using World Bank categories. Rate ratios (RR) and 95% CI were calculated from negative binomial regression analyses to estimate the association between folic acid fortification/potential intake and COVID-19 incidence and mortality rates per 100,000 stratified by region and income. Propensity score weighting balanced population size, sex and age distribution, and income between countries with and without folic acid fortification, for adjusted comparison of COVID-19 incidence and mortality.

Results: We found a statistically significant association between mandatory folic acid fortification policies and COVID-19 incidence among countries in Africa and Europe. In Africa and Europe, countries with mandatory fortification with folic acid had a 70% lower COVID-19 incidence than those without folic acid fortification policies (RR=0.3; 95% CI: 0.1, 0.6 and RR=0.3; 95% CI: 0.1, 0.6 respectively). There was no statistically significant association between mandatory folic acid fortification policies or potential intake and COVID-19 mortality in countries by income category or WHO region. For high-income countries, those that had mandatory folic acid fortification policies had a 30% lower COVID-19 incidence than those that did not fortify with folic acid (RR=0.7; 95% CI: 0.5, 1.0). In the adjusted analysis, we still found a significant difference in COVID-19 incidence between the fortification countries and non-fortification countries, but no statistically significant results for mortality.

Discussion and Conclusions: Folic acid fortification was associated with lower incidence of COVID-19 even after adjusting for income, region, sex, and age distributions but does not appear to be associated with mortality. Folic acid fortification and supplementation may have additional population health benefits beyond reduction of structural central nervous system defects. Additional studies using individual level data are needed to further investigate this possible association since ecologic fallacy is a potential weakness of the current study.

Hypertrophic Cardiomyopathy in children: one condition for multifaceted diseases. The importance of multisystemic and multidisciplinary approach in children

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Birth Defects Program on which the work is based: NA

Background and Objectives: Hypertrophic cardiomyopathy (HCM) is a rare heart disorder in children characterized by unexplained left ventricular hypertrophy (LVH) which may present with a high degree of clinical variability, ranging from asymptomatic to refractory heart failure, major arrhythmias and sudden cardiac death. HCM is common among adults, but it is rare in children (0.24–0.47/100.000). In the latter group, the underlying etiology is highly heterogeneous: metabolic, RASopathies, rare syndromes, neuromuscular, malformative, hormonal, due to hypertension and obesity, or isolated monogenic diseases. Long-term outcome is generally poor, especially for early onset cases. As far as we know, current studies are limited to small cohorts with "unidirectional" etiologic investigations. We aim to characterize the etiology in relation to outcome and potential major adverse cardiac events in a cohort of 210 pediatric HCM to establish a genotype-phenotype correlation that can help in clinical diagnosis and prognosis.

Methods: We performed a systematic collection of data for patients admitted to our hospital from 2009 till 2024. The database includes: gender, ethnicity, BMI, age at diagnosis, date of last visit, etiology, genotyping (SNP-array, NGS - Next generation sequencing, variant segregation), extracardiac morbidity, family history of HCM, maximum LV value, NYHA/Ross classification, arrhythmias, Cardiac magnetic resonance (CMR) and myectomy.

Results: The study brings light into the importance of multisystemic evaluation in a large cohort of children with HCM. Metabolic conditions represented a reasonable proportion of patients. RASopathies reached one fifth of the cohort. Sarcomeric variants were majorly in MYH7 and less MYBPC3 and often inherited from an affected relative. Rarer conditions were observed including variants in LAMP2, PRKAG2, and DES. Patients without positive molecular or biochemical diagnosis were more prone to present subtle or frank endocrinologic or anatomical changes that are discussed within this presentation.

Discussion and Conclusions: To the best of our knowledge this is the first HCM cohort in children discussing not only molecular but also prognosis in a cohort of patients with biochemical, endocrinological and anatomical changes leading to HCM in a child.

Prevalence of adverse birth outcomes and external birth defects among women living with HIV in Malawi

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Birth Defects Program on which the work is based: NA

Background and Objectives: Routine surveillance for birth outcomes is essential to monitor safety of antiretroviral therapy (ART) during pregnancy among women living with HIV (WLHIV). We examined the prevalence of adverse birth outcomes and major external birth defects (BDs) by maternal HIV and ART status in Malawi.

Methods: Adverse birth outcomes (prematurity, low birthweight) and BDs were recorded for all live and stillbirths delivered at four Malawian hospitals from December 2016 to July 2020 and July 2021 to September 2022. BDs were confirmed by experts at the Centers for Disease Control and Prevention. Maternal characteristics were collected from interviews and health records. Pooled prevalence and crude prevalence ratios (cPRs) were calculated using maximum likelihood estimates for adverse outcomes and BDs.

Results: Of 213,314 deliveries, 209,361 (98.1%) informative births (newborns well-formed enough to ascertain whether there is a birth defect) were enrolled in the surveillance study. The prevalence of prematurity and low birthweight, respectively, was significantly higher for the following populations: ART naïve WLHIV (30.7%, 18.3%), WLHIV on ART (22.6%, 14.7%) and women with unknown HIV status (27.2%, 19.2%) than HIV-negative women (20.3%, 12.4%). The most prevalent BDs (excluding syndromes- birth defect(s) with a recognizable pattern of multiple malformation that is known or presumed to have a specific cause) were talipes equinovarus (18.9 per 10,000 births, 95% CI: 17.1, 20.8), hypospadias (16.2, 95% CI: 13.9, 18.8 and neural tube defects (NTDs) (6.5, 95% CI: 5.5, 7.6); higher prevalence of these conditions among WLHIV on ART than HIV-negative women. There was slightly higher likelihood of WLHIV on ART delivering a baby with an NTD than HIV-negative women (cPR: 1.6, 95% CI: 1.01, 2.62).

Discussion and Conclusions: Higher prevalence of adverse birth outcomes and BDs was observed among HIV-positive women. Further analyses are needed to understand the impact of a COVID-related data collection pause between 2020 and 2021, and to explore risk factors of HIV and ART status by ART regimen and timing for adverse outcomes and BDs among WLHIV in Malawi.

MALFOVAR (Malformation and variable anatomy registry) case series 2007-2024 : Congenital tumors.

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Birth Defects Program on which the work is based: MALFOVAR

Background and Objectives: To search for congenital tumors in MALFOVAR registry in order to summarise types and burdens of congenital tumors. Tumors are considered congenital when detected during pregnancy or in the first 3 months of life.

Methods: MALFOVAR is a multicentric multimodality registry situated in Budapest Hungary which is dedicated to the detection of congenital malformations. The multicenter registry includes Semmelweis University, Heim Pal National Children Hospital, National Institute of Neuroscience (OMIII) and MIND clinic. We searched the MALFOVAR registry for congenital tumors in the period between the years 2007-2024. All together 613 cases were searched for congenital tumors.

Results: We found a total of 30 cases which had congenital tumors. Concerning localisation, most tumors were localised in the face and neck and thorax. Some tumors had extended to multiple areas. Some tumors were detected as a systemic disease or as a multiorgan manifestation as in tuberous sclerosis.
Concerning histology type:
Two cases of aggressive malignant tumors were detected which had caused death of the newborns within the first month of life: melanoma and sarcoma. Further six cases of lymphatic cystic tumors were found. In the thorax we detected nine cases: 3 CPAM, 3 sequestration , two cystic structures and one case of neuroblastoma (diagnosis was altered after delivery initially assessed as CPAM).
Other cases were detected of:
Rhabdomyoma, tuberous sclerosis (4)
mesemnchymal tumor (1)
Arachnoid cyst (1)
Hand AVM (1)
Thymus hyperplasia (1)
Nasal Glial heterotopy (1)

Discussion and Conclusions: Congenital tumors are extremely rare and come from diverse types of histology. In very rare instances malignant tumors can be found (such as melanoma and sarcoma) and result in devastating effect on the newborn and parents. Early detection and recognition of benign tumors is of importance in order to plan treatment of tumor after delivery by operation or embolisation.

Multimodality harmonization (US and MRI) is of superior value in the detection and assessment of fetal tumors and specifically gives an added value in assessment of aggressivity of disease and detection of multiple localisation of disease. It is important to recognise congenital tumors as an unique entity in oncology since these tumors are usually not affected by epigenetics (environmental factors) but may be manifested due to inherited disease or denovo inutrauterine genetic changes.

Tuesday, September 3rd, 2024

Session On Collaborative Projects

Round Table

EUROCAT Updates
Florence Rouget, President EUROCAT Association, Brittany, France

NBDPN Updates
Wendy N. Nembhard, Vice Chair of NBDPN, University of Arkansas for Medical Sciences, USA

sSCAN
Emma Kalk, School of Public Health, SA

Impact of COVID pandemic on birth surveillance as a whole
Anke Rissmann, Saxony-Anhalt, Germany

Why Foster Birth Defect Research?
Anke Rissmann, Saxony-Anhalt, Germany

Rethinking the Annual Report through the lens of triple surveillance
Lorenzo D. Botto, ICBD Director, Utah, USA

World Birth Defects Day (WBDD)
Cara Mai, Division of Birth Defects and Infant Disorders, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention

World Birth Defects Day: United globally to raise awareness about birth defects and improve care and treatment

Cara Mai

Health Scientist
Infant Outcomes Monitoring, Research and Prevention Branch
Division of Birth Defects and Infant Disorders
National Center on Birth Defects and Developmental Disabilities
Centers for Disease Control and Prevention

March 3 is **World Birth Defects Day (WBDD)!** ICBDSR, as the coordinating and founding partner of this health observance day, works to unite people and organizations to raise awareness about birth defects and improve care and treatment. Engagement and planning coordination occur through the WBDD Partners Work Group, which plans for upcoming WBDD activities and events.

WBDD 2024 engagement included a Live Chat on X and Threads in English and Spanish, global and regional webinars, "8 Seconds for Birth Defects" challenge, and social media activities. Fresh ideas and activities are always welcome. As we plan for WBDD 2025, we invite existing and new partners to indicate their interest at https://www.worldbirthdefectsday.org/partner-form.

For more information about WBDD, please visit the website at https://www.worldbirthdefectsday.org.

Wednesday, September 4th, 2024

Workshop: Shaping the Future by Reflecting on the Past: 50 Years of Congenital Anomalies Research

Joint Workshop with Czech Society of Medical Genetics and Genomics

Moderators:
Milan Macek Jr **and** ***Antonin Sipek Jr***

Medical genetics and rare diseases
Milan Macek Jr

Surveillance of congenital anomalies in the Czech Republic: Six decades of experience
Antonin Sipek Jr

60 years of the Hungarian Congenital Abnormality Registry: Review of the function, challenges, value, and current role
Csaba Siffel

From karyotypes to genomes: The evolution of cytogenetics
Jana Drabova

History of metabolic medicine in the Czech Republic
Jiri Zeman

Review of maternal, environmental, and genetic risk factors associated with gastroschisis
Marcia Feldkamp

Current state and prospects of Czech obstetrics
Pavel Calda

Molecular genetics and developmental biology uncover the teratogenic mechanisms: thalidomide
Frantisek Liska

Surveillance of congenital anomalies in the Czech Republic: Six decades of experience

Antonín Šípek Jr

Institute of Biology and Medical Genetics
First Faculty of Medicine
General Faculty Hospital
Prague, Czech Republic

The surveillance of congenital anomalies in the former Czechoslovakia was initiated by the late Dr. Jiří Kučera at the end of the 1950s. In 1961, he successfully established a nationwide registration program. After a short period of unofficial registration, the process was officially set up in 1964 as one of the first official country-wide surveillance programs for congenital anomalies in the world. The Czechoslovak registry became one of the founding members of the ICBDMS clearinghouse in 1974. The registry is managed by the State Institute of Health Information and Statistics, a government-based and funded organization. The registration process is mandated by national law.

Over 60 years of evolution, the number of registered anomalies has increased, as has the possible age of the child at the time of registration. Since 2016, the registry has transitioned from traditional paper registration forms to electronic submissions. All cases of congenital anomalies, according to the ICD-10 classification, can be included. Additionally, we now have the capability to register all genetic disorders, inherited metabolic disorders, and rare diseases using appropriate OMIM, SSIEM, or ORPHA codes.

The outcomes of this registration have numerous applications, including public health implications, prenatal diagnostic strategies, and research purposes.

60 years of the Hungarian Congenital Abnormality Registry: Review of the function, challenges, value, and current role

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[*]*Previous Head of the Hungarian Congenital Abnormality Registry*

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Birth Defects Program on which the work is based: Hungarian Congenital Abnormality Registry

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Background and Objectives: Following the thalidomide tragedy, in 1962 the Ministry of Health in Hungary ordered the mandatory notification of patients ("cases") with different congenital abnormalities diagnosed from birth (including live births and stillbirths) until the end of the first year of age by medical doctors. The evaluation of cases required epidemiological expertise, thus the registry continued as the Hungarian Congenital Abnormality Registry (HCAR) in the National Institute of Public Health from 1970 based on international recommendations. The author provides a brief overview of the expanded function of the HCAR in the past 60 years, the challenges the Registry faced, and the value and current role of the Registry.

Methods: Based on key published papers, the author 1) describes the system that has been developed over the 60 years of HCAR's operation, including the key activities as well as the changes made to keep the surveillance system running; and summarizes 2) the challenges that have been encountered over the years, 3) the value (benefits and usefulness), and 4) the current role of the Registry.

Results: The primary objective of the HCAR is to identify patterns and assess the prevalence and temporal/spatial trends of congenital anomalies in Hungary. From the 1990s information on prenatal diagnosis, and recently, data on rare diseases have been collected. The HCAR contributed to other activities, such as the post marketing surveillance of drug teratogenicity.
Over the past six decades, the HCAR has faced organizational and financial challenges. It was able to adapt to the operational and legal changes, including switching from paper-based to electronic data collection, decreasing budgets, and amendments in mandatory reporting laws.
The HCAR has been an invaluable resource for surveillance, and the data collected have provided the basis for national and international research collaborations, and supported the implementation of prevention strategies.
Currently, operated by a small staff, the HCAR collects data on both congenital anomalies and rare diseases in fetuses and throughout life.

Discussion and Conclusions: Due to the centralized health system in Hungary, the HCAR enjoyed optimal conditions: all deliveries took place in inpatient clinics, congenital anomalies had mandatory notification, and autopsy was mandatory in infant death. Despite the many challenges the HCAR faced over the years, it proved to be a valuable resource for various surveillance, research, and prevention activities. It was also one the founding members of the International Clearinghouse for Birth Defects Monitoring System. Unfortunately, the support and operational budget of the HCAR was substantially decreased in recent years. However, the hope is that the expanded data content on congenital anomalies and rare diseases in fetuses and throughout life will help refocus attention and recognize the public health importance of the Registry again.

From karyotypes to genomes: The evolution of cytogenetics

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This lecture explores the historical development of cytogenetics, from its early days of karyotype analysis to the modern era. We will journey through significant milestones, including the development of karyotyping, the identification of chromosomal abnormalities, and the introduction of molecular cytogenetics techniques such as fluorescence in situ hybridization (FISH) and comparative genomic hybridization (CGH). We will remember key milestones and breakthroughs that have shaped the field and let to state-of-the-art techniques. The lecture will then transition to the modern era, highlighting how the integration of cytogenetics with genomic technologies such as microarrays, next-generation sequencing (NGS) and optical genome mapping (OGM) has revolutionized the field. Additionally, we will discuss how these historical insights inform current trends and future prospects in the field, particularly in clinical diagnostics and genetic research.

History of metabolic medicine in the Czech Republic

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When the emperor Rudolf II invited in the end of the 16th century to Prague many famous alchemists including John Dee and Edward Kelly and accommodated them at the Charles square, nobody anticipated, that they will evolve new biochemical methods, which will be later used in the diagnostics of inherited metabolic disorders (IMD). In 1969, Josef Hyanek started in Charles square the regional screening for phenylketonuria (PKU) and then together with B. Blehova started the national screening for PKU in the former Czechoslovakia. With increasing knowledge in the field of biochemical medicine, the biochemical laboratory in Charles square was gradually enlarged and transferred to the Department of Paediatrics. Hyanek´s successor, Milan Elleder, established new enzymatic and molecular laboratories, which were except research also responsible for the diagnostics of IMD in the whole Czech Republic with 10.5 million of inhabitants. During the last 25 years, their PhD students and postDocs including S. Kmoch, V. Kozich, M. Hrebicek, T. Honzik and others participated within the huge international cooperation on the discoveries of > 25 genes and new diseases.

Review of maternal, environmental, and genetic risk factors associated with gastroschisis

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Gastroschisis is unique among birth defects because of its increasing prevalence over the past several decades and that the risk is greatest among younger women. Over the past several decades, numerous maternal and environmental risk factors have been found to be associated with increasing the risk of gastroschisis. I will present a review of the literature focused on maternal, environmental, and genetic risk factors. It is based on published literature found through PubMed, initially in October 2022 and recently updated in June 2024. A total of 406 papers were evaluated. Papers were excluded because 1) gastroschisis was combined with other abdominal defects (i.e., abdominal wall defects, limb body wall complex, or gastroschisis and omphalocele), 2) the study did not include a control or comparison group, 3) the paper only presented prevalence data, or 4) the paper was a review article only. Young maternal age and cigarette smoking continue to be the strongest and most consistent risk factors for gastroschisis.

Questions that remain with the existing or new risk factors under study: (1) are we measuring what we think we are measuring? (2) does the risk factor vary by maternal age? (3) what role does maternal genetics play in responding to environmental exposures? and (4) what role does the maternal immune system play in responding to environmental risk factors? In addition to these questions, the challenge is understanding the underlying pathogenesis (if the amnio-ectodermal junction separates, how and why?). To move forward we will need to understand normal development of the umbilical ring at the cellular level and use an appropriate animal model and cell cultures to determine how and why the separation occurs.

Current state and prospects of Czech obstetrics

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The Czech Republic has witnessed a decline in birth rates from 110,000 per year to 90,000 per year, despite a population of approximately 11 million. Despite this, the country remains one of the safest places in the world to give birth, with key statistics showing a Perinatal Mortality Rate (PMR) of 4-5 per thousand, a Stillbirth Rate (SBR) of 3-4 per thousand, and an Early Neonatal Mortality Rate (ENMR) of 1 per thousand. This success is largely attributed to the centralization of care into 12 perinatology centers.

The prenatal care model employed is based on the "Inverted Pyramid of Prenatal Care" as proposed by Kypros Nicolaides in 2011. Key fetal and maternal assessments are conducted at the end of the first trimester to determine individual risks of pregnancy complications such as preeclampsia, growth restrictions, chromosomal abnormalities, preterm birth, fetal demise, gestational diabetes, and thyroid disorders. Important initial assessments include the correct gestational age based on ultrasound-determined crown-rump length, determining pregnancy frequency and chorionicity, early detection of major congenital anomalies, and exclusion of risks like preeclampsia and a spectrum of placental pathologies (PAS).

Non-Invasive Prenatal Testing (NIPT) is considered the best screening method for Trisomy 21, although microdeletion syndromes and rare diseases associated with psychomotor retardation can only be diagnosed through chorionic villus sampling or amniocentesis. The risks of these diagnostic methods are minimal, at 0.2% and 0.1%, respectively, in experienced hands.

A significant challenge for many developed countries, including the Czech Republic, is the declining birth rate, which will necessitate a reorganization of the entire prenatal care system.

Molecular genetics and developmental biology uncover the teratogenic mechanisms: thalidomide

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The thalidomide disaster in 1950s and 1960s demonstrated that at that time our understanding of the teratogenic processes was very limited. One of the main reasons of the calamity was the fact that in preclinical toxicity testing in rodents, no teratogenic potential was discovered. It was concluded later that rodents were resistant to its teratogenic effects. Interestingly, we showed that thalidomide is teratogenic in the rats heterozygous for a recessive limb malformation mutation Lx in 1989. We could not explain the molecular mechanism, since the discovery of the molecular target of thalidomide (cereblon) had to wait until 2010. In the meantime (2009) we were able to ascertain that the Lx rats carry a hypomorphic allele with downregulated expression of Plzf (Zbtb16). Subsequently, in 2021, PLZF was shown to be a substrate of cereblon, explaining the frequent limb malformations after thalidomide administration, 68 year after thalidomide introduction.

Posters

(Alphabetical order by corresponding author's last name)

The posters will be shown on Monday 2nd September
Conference Foyer

Molecular characterization of newborns with alpha thalassemia identified through newborn screening - *Maria Melanie Liberty B. Alcausin*

Congenital upper and lower airway anomalies: data from the IMER Registry - *Elisa Ballardini*

Population-based prevalence and trend of birth defects in Costa Rica from 2000 to 2019 - *Adriana Benavides-Lara*

Association between Covid-19 infection during pregnancy and congenital limb defects: results of a study in Southern Brazil - *Simone Karam*

Trends and causes of infant mortality in Chile, 2012-2021 - *Allisson Müller*

Birth prevalence of omphalocele and gastroschisis in Chile: Data from the National Registry of Congenital Anomalies - *Allisson Müller*

Impact of maternal race and ethnicity on cardiovascular disease risk in women with infants affected by congenital heart defects in Arkansas, 1997-2011 - *Wendy N. Nembhard*

Changes in mortality associated with Neural Tube Defect in Chile, 2012-2021 - *Rosa Pardo*

Congenital hip dysplasia: A case-control study for risk factor analysis in newborns, Bogotá, Colombia (1982-2022) - *Karen Sarmiento*

Epidemiological description and risk factors of congenital genitourinary tract anomalies in Colombia (1982-2022), an ECLAMC case-control study - *Karen Sarmiento*

Adolescent pregnancy and birth defects: A case control study in Bogotá and Cali, between 2001 and 2020 - *Karen Sarmiento*

Perinatal characteristics and factors associated to the presentation of single ventricle in Bogotá and Cali, Colombia - *Karen Sarmiento*

High prevalence of gastroschisis in Roraima, Brazil: The impact of maternal demographics - *Lavinia Schuler-Faccini* presented by *Simone Karam*

VACTERL Association; The hidden iceberg. Case series and article review in Malta - *Mohamed Shoukry*

Tatton Brown Rahman Syndrome with congenital abdominal wall defect. A Rare Case Report - *Mohamed Shoukry*

Incidence and sex ratio in children born with tetralogy of Fallot in the Czech Republic - *Antonin Sipek Sr*

ICBDSR / MALFOVAR Museum network accreditation system - *Tidhar Steiner*

Can be viewed at: www.icbdsrtraining.org

Molecular characterization of newborns with alpha thalassemia identified through newborn screening

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Birth Defects Program on which the work is based: NA

Background and Objectives: The thalassemias are the most common single genetic disorder known when considered as a group, and thus constitute an important global health problem. The Philippines is located in an important geographic region called the thalassemia belt which spans from the shores of the Mediterranean to southeastern Asia, however, there is paucity of data as to the prevalence and the common mutations of alpha thalassemia in the Filipino population. Newborn screening in the Philippines for alpha thalassemia started in December 2014 as part of expansion of the newborn screening program. Objective: To determine the molecular characteristics of newborns identified to have alpha thalassemia through newborn screening.

Methods: A retrospective, descriptive study was done to determine the prevalence of alpha-thalassemia and the common mutations among Filipino newborns with elevated Bart's hemoglobin on NBS from December 2014 to December 2023. De-identified data were gathered from the confirmatory center at the Institute of Human Genetics with supplemental data from the Newborn Screening Reference Center, both at the National Institutes of Health of the University of the Philippines Manila. Genotypic and allelic frequencies, as well as point prevalence were determined.

Results: Among the 7,117,133 newborns screened through the national NBS from December 2014 to December 2023, 2,892 were confirmed with alpha thalassemia disease giving a prevalence of one in 2460 (1:2460). Almost all (99.3 percent) have deletional hemoglobin alpha gene mutations namely SEA, FIL, 3.7 and 4.2. Among the few non-deletional mutations, Hb Constant Spring is the most common.

Discussion and Conclusions: The expansion of the national NBS program in the Philippines allowed for determination of prevalence of HbH or alpha thalassemia disease in the Filipino population to be one in 2460 live births. Almost all mutations are deletional namely SEA, FIL, 3.7 and 4.2. The high prevalence of deletional alpha thalassemia disease can impact on the prevalence of non-immune hydrops fetalis. The result of this study can help in the crafting of national policies to address this condition to include increasing awareness, strengthening genetic education and genetic counseling programs that can help decrease the disease prevalence.

Congenital upper and lower airway anomalies: data from the IMER Registry.

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Birth Defects Program on which the work is based: IMER registry

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Background and Objectives: Congenital Anomalies (CA) of the Respiratory System are rare malformations involving upper and lower airway.
The estimated prevalence of upper airway (UA) anomalies is 0.2-1 per 10 000 (Varela 2021), mainly choanal atresia/stenosis. Most cases occur in association with chromosomal conditions, other malformation or sequences (as CHARGE syndrome) (Benjamin 2024). Choanal atresia is usually diagnosed postnatally due to respiratory distress, and rarely antenatally (Sgayer 2024).
Lower airway (LA) anomalies regard mainly lungs. Estimated prevalence is 3.5 per 10 000 (Doktor 2022): CPAM (congenital pulmonary airway malformation) is the most common (30–40%), followed by bronchopulmonary sequestration (BPS), bronchogenic cysts (BC), congenital lobar emphysema (CLE). The antenatal diagnosis reaches 85.7%. Prenatal diagnosis and monitoring of appearance of complication is fundamental for planning birth, as EXIT (ex utero intrapartum treatment) treatment can be recommended (Leblanc et al 2017).

Methods: Data are extracted from IMER registry, a population-based CAs database covering the first year of life, and the entire Emilia Romagna Region, an area of 22,510 km2 in the Northern Italy. About 4,5 million inhabitants live in this area, and approximately 30,000 births occur each year. IMER uses multisource ascertainment, including hospital discharge records (HDR), through a validated algorithm to recognize CA not communicated by clinicians. Live birth, stillbirth and TOPFA (termination of pregnancy for fetal anomalies) are included. The registry follows EUROCAT coding guidelines; CA are grouped in isolated cases (can have more than one CA, belonging to the same system), chromosomic cases (karyotype defect), syndromic cases (known origin as sequences, drugs effects or genetic syndromes) and multiple cases (CAs involving more than one organ system). Aim of this work is to present epidemiology of CAs of the respiratory system (ICD10 code Q30-Q34, years 2013-2022).

Results: In the last 10 years (2013-2022), the overall prevalence of respiratory system CAs in the IMER registry is 4.72 (4.01 – 5.52) per 10 000 (158 cases/ 334 661 live births), stable and comparable to the same value reported in the EUROCAT website 4.07 (3.92 - 4.23) per 10 000 live births (https://eu-rd-platform.jrc.ec.europa.eu/eurocat_en consulted on the 26th of April 2024). Isolated cases are 63% (99/158) and live births are 87% (140/158). Prenatal diagnosis was reported in 55% of cases (86/158) with no significant differences between groups of CA. Clinicians sent 64% of cases, while 35% have been obtained from HDR.
Of UA CAs (50), choanal atresia/stenosis represents 54% of cases (27/50): only 37% (10/27) are isolated, and prenatal diagnosis occurred in 33% (9/27).
Apart from 2 cases of tracheal atresia, LA CAs involve lungs (106/108): live births are 93% (100/108) and prenatal diagnosis was reported in 62% (67/108). CPAM represent 25% of cases (27/106), followed by BPS, 20% (21/106).

Discussion and Conclusions: CAs of the respiratory systems are rare, as confirmed by this study, with a stable prevalence. Knowing their epidemiology is not easy but relevant: clinicians need to be aware of these CAs as the prenatal diagnosis is not always possible, but they often require special care at birth. Upper CA are more

often associated to other anomalies or conditions and prenatal diagnosis is unusual. Lower anomalies are mainly isolated, but prenatal diagnosis occurs more often. These data suggest the creation of a dedicated network between clinicians to better organize prenatal and postnatal management of these patients.

Population-based prevalence and trend of birth defects in Costa Rica from 2000 to 2019

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Birth Defects Program on which the work is based: CREC, Costa Rica

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Background and Objectives: In Costa Rica birth defects (BDs) are the second leading cause of infant mortality. The Costa Rican Birth Defects Registry Center (CREC) was created in 1985 to carry BDs surveillance. In the last two decades, several changes related to the coverage and specificity of the BDs registry, demographic changes, and public health events may have affected the prevalence of BDs in the country. The most important changes occurred in 2008 with the increase in the age of the mandatory report to the first year of life, and the inclusion of the National Children's Hospital (NCH), the only national reference hospital in pediatrics, to the CREC network. We aim to describe the epidemiological behavior of the main groups of BDs in the period 2000-2019, in the context of important context changes.

Methods: We performed a descriptive analysis of BDs prevalence and trends during 2000-2019 , based on data from the CREC, a hospital-based surveillance system, with a population scope. Case definition includes all live or dead newborns, weighing >500 g, and older than 20 weeks of gestational age, with any structural congenital anomalies –major or minor-. Costa Rican law does not allow the elective termination of pregnancy due to fetal anomalies, and coverage of dead births or stillbirths is less than 5%, so this analysis was carried out in live births.
We used Joinpoint regression to identify any calendar year where a significant change in trend occurred; the annual percent change (APC) and the average annual percent change (AAPC) were determined. Using Poisson regression, marginal means, and prevalence ratios (PR) by sub-period (2000-2009 as referent, and 2010-2019) were estimated and compared using Wald's chi-square tests (alpha ≤0.05).

Results: During 2000-2019 BDs´ prevalence was 2.3% live births; 73% presented with major BDs. Males had a significantly higher prevalence (sex ratio 1.13 boys/girls); 98% of cases were reported by public hospitals. Trend showed an AAPC of +3.7 ($p<0.05$) with two joinpoints, 2005 and 2013. A significant APC (+11.3) was observed during 2005-2013, within the context of improvements in the surveillance system, such as the increase in the reporting age, and the incorporation of other data sources in addition to maternity hospitals. Most of the BDs groups presented a significant upward trend, the highest AAPC were observed for the respiratory system (+11.7), congenital heart defects (+9.5), and nervous system (+8.5). Specific BDs with a greater increase in prevalence were in descending order: microcephaly, urinary obstructive defects, other brain defects, lower respiratory tract defects, severe congenital heart disease, upper respiratory tract defects and non-severe congenital heart disease.

Discussion and Conclusions: The prevalence of BDs in Costa Rica during 2000-2019 coincides with the prevalence of major BDs worldwide. The BDs present a clear upward trend in the last two decades; this increase has been greater in the groups of internal/not evident BDs, that require more specialized test for their diagnosis, such as CHDs and chromosomic anomalies. This trend was probably due to the increase in the age of registration, combination of passive and active surveillance strategies, and the incorporation of specialized diagnostic and treatment centers into the network, complementing the information provided by maternity wards. There are still pending challenges in our country, such as advancing in prenatal detection, rise the coverage of stillbirths, including other data sources such as medical and forensic pathology services, and schools that provide special attention to children with disabilities due to birth defects.

Association between Covid-19 infection during pregnancy and congenital limb defects: results of a study in Southern Brazil.

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Birth Defects Program on which the work is based: NA

Background and Objectives: The complex process of limb formation, combined with high exposure to the uterine wall, are contributing factors to development of congenital limb anomalies. These can be classified as reduction anomalies, congenital clubfoot, polydactylies, and arthrogryposes. Prevalence varies according to type of anomaly, reaching up to 8-9/10,000 live births for foot anomalies and polydactylies. However, in addition to genetic and inherent factors, it is essential to highlight external factors that may be related to this type of malformation. Teratogens are agents that lead to alterations in embryonic development. In this context, viral infections can play an important role. Regarding SARS-CoV-2, however, no data have been found associating infection during pregnancy with congenital anomalies. This study aimed at assessing the association of SARS-CoV-2 infection during pregnancy with limb malformations, as well as to outline the profile of newborns with this type of anomaly.

Methods: This study is nested in the Pilot-Project based on National Birth Registration System: Surveillance and Care for Congenital Anomalies in Rio Grande do Sul state- Brazil, conducted since 2021 in south of Brazil. It follows eight anomalies groups selected based on its prevalence, reliability of diagnosis, impact on health and possibility of prevention and care in the public health system in Brazil. A questionnaire administered to mothers include questions related to newborn, mother, pregnancy, delivery; mother's exposure to infectious diseases, legal / illegal drugs, COVID vaccination and infection. We analyzed the risk for congenital anomalies according to COVID-19 during pregnancy. Analyses were performed in the software Stata. We described the sample by means of absolute and relative frequencies, ran bivariate analyses through Fisher exact test and conducted crude and adjusted analysis using logistic regression. The significance level was set at 5% for two-tailed tests.

Results: Three hundred and eight newborns were identified but we obtained information about gestational infection from 303 mothers. Seventy one children were born with limb anomalies, 56% of the them were male, 35% were low birth weight, 36% were premature, 18% of these mothers had eleven years of schooling, 65% attended seven or more prenatal consultations, 36% discovered the anomaly after birth, 23% had a family history of congenital anomaly. Among women exposed to COVID-19, prevalence of newborns with limb congenital anomalies was 50% while those women not exposed it was 26,5%. Prevalence was 89% higher in women exposed to COVID-19. When we analyze limb defects, excluding those associated to other malformations, the association measures become even stronger. Adjusting for potential confounders, odds ratio also increased. It may also be worth mentioning that there was no difference in type of limb anomaly, when comparing polydactyly versus other types, in relation to covid association

Discussion and Conclusions: An association was observed between maternal infection by Sars-Cov-2 during pregnancy and limb defects. This finding differs from other four studies found in literature. Those studies did not find a significant relationship between referred viral infection and the development of limb defects.

Satnarine, Dias and Calvert did not find a significant ratio of members congenital anomalies with COVID-19 during pregnancy. Fernandez discussed the risk of digital/limb ischemia, thromboembolic events and placental changes.

Our study has some limitations. There may have been under-diagnosis as some women may have had covid without knowing it because they had not been tested. Besides, we did not have a group without anomalies to know what would be the measure of effect for presenting limb anomalies versus not presenting any anomalies. Further studies are needed to elucidate the relationship between this viral infection and limb congenital anomalies.

Trends and causes of infant mortality in Chile, 2012-2021

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Birth Defects Program on which the work is based: Registro Nacional de Anomalías Congénitas de Chile, RENACH

Background and Objectives: Chile has undergone significant changes in its demographic and epidemiological profile, transitioning towards chronic non-communicable diseases as the main causes of mortality. This study evaluates the trends and causes of infant mortality from 2012 to 2021, with interest in the group of congenital anomalies and its effects on different age groups.

Methods: Data from the Department of Health Statistics and Information (DEIS) were reviewed over a ten-year period from 2012 to 2021, analyzing infant, neonatal, and perinatal mortality. Rates were calculated per 1,000 for general mortality and per 100,000 live births for mortality due to specific conditions. Categorization of deaths was based on the International Classification of Diseases, Tenth Revision (ICD-10), to evaluate the main causes of mortality.

Results: Over the study period, infant mortality in Chile showed a consistent downward trend until 2021, decreasing from 7.4 per 1,000 live births in 2012 to 5.8 in 2021.
The main contributors to infant mortality were conditions originating in the perinatal period (42%), particularly those related to gestational duration and fetal growth, and congenital malformations, deformations and chromosomal abnormalities (38%). Within the latter category, congenital malformations of the circulatory system were the leading cause of death, followed by chromosomal abnormalities and congenital malformations of the nervous system. Deaths due to circulatory system malformations occurred more frequently in the late neonatal and post neonatal periods, while mortality from chromosomal abnormalities and malformations of the nervous system was more frequent in the perinatal period

Discussion and Conclusions: Despite the reduction in mortality rates in our country, congenital anomalies, particularly congenital heart defects and chromosomal abnormalities, have consistently contributed to infant mortality in Chile. Evaluating the factors that influence these rates, is crucial for improvements to future public policies planning.
Because congenital malformations, deformations and chromosomal abnormalities are a leading cause of infant mortality in Chile, they require specific attention in public health policies. It is essential to maintain continuous surveillance and analyses of these trends to improve strategies aimed at reducing infant mortality.

Birth prevalence of omphalocele and gastroschisis in Chile: Data from the National Registry of Congenital Anomalies

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Birth Defects Program on which the work is based: Registro Nacional de Anomalías Congénitas de Chile, RENACH

Background and Objectives: Omphalocele and gastroschisis are neonatal anterior abdominal wall defects with different prevalence and associated factors. Omphalocele, often associated with other anomalies, has a global prevalence of approximately 2-3 per 10,000 births, whereas, gastroschisis, usually isolated and associated with environmental factors and younger maternal age, has a reported global prevalence of 0.5-10 per 10,000 births and has been increasing worldwide in recent decades. Since 2016, the Ministry of Health has implemented a mandatory Chilean National Registry of Congenital Anomalies (RENACH) that collects information on all live-born newborns with one or more structural congenital anomalies. RENACH is a valuable source of information to plan public health strategies. This study aims to describe the prevalence and characteristics of both abdominal wall defects using RENACH data.

Methods: Newborn with omphalocele or gastroschisis were identified within the RENACH database (2017-2020). Maternal demographics, case demographics, gestational age at birth, and data on associated anomalies were analyzed.

Results: Among 440,574 live births, 76 omphalocele and 163 gastroschisis cases were identified. The prevalence was 1.7 per 10,000 live births for omphalocele (male-to-female ratio, 1.0) and 3.7 per 10,000 for gastroschisis (male-to-female ratio, 0.8). Of the omphalocele cases, 24 out of 66 (31%) had associated anomalies, compared to 10 out of 163 (6%) for gastroschisis. The average maternal age was 31 years for omphalocele (52/76) and 23 years for gastroschisis (117/163). Regarding gestational age, 47% (74/76) of omphalocele cases had a gestational age < 37 weeks, compared to 81% (153/163) of those with gastroschisis.

Discussion and Conclusions: The prevalence of omphalocele and gastroschisis in Chilean live births between 2017 and 2020 is consistent with international data. Compared to omphalocele cases, neonates with gastroschisis are more likely to have an isolated defect, be born earlier, and have younger mothers. Future studies should evaluate the prevalence and associated factors of these abdominal wall defects in all births, including stillbirths and elective terminations due to fetal anomalies, to inform health policy, reduce morbidity and mortality, and optimize care for affected children and families.

Impact of maternal race and ethnicity on cardiovascular disease risk in women with infants affected by congenital heart defects in Arkansas, 1997-2011

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Birth Defects Program on which the work is based: NBDPS

Background and Objectives: A recent study suggested a possible association between maternal history of congenital heart defects (CHDs) in offspring and increased risk of developing cardiovascular diseases (CVDs) later in adulthood; however, it is unknown if this risk varies by maternal race/ethnicity. A retrospective cohort study was conducted to determine if maternal race and ethnicity modifies the association between having a CHD-affected pregnancy and the risk of developing CVD later in adulthood.

Methods: The Arkansas Center of the National Birth Defects Prevention Study (1997-2011) identified 1,423 women who delivered an infant with at least one of selected CHDs, 1,020 women who delivered a live-born infant without structural birth defects, and 1,426 women who delivered an infant with structural birth defects other than CHDs. After linking it to the Arkansas All-Payers Claims Database (2000-22), CVD was identified using ICD-9 and 10 Clinical Modification codes and was categorized as ischemic, cerebrovascular, essential hypertension, other heart diseases, other CVDs, and any CVDs. Women were followed from the estimated date of delivery of their offspring (in years) until the date of the first CVD event (defined as diagnosis or hospitalization as noted in the medical record), death, or the end of the study (Jan 1, 2023), whichever occurred first. Hazard ratios (HR) with corresponding 95% confidence intervals (CIs) were calculated from the Cox Proportional Hazard regression analyses.

Results: Compared to NH-Black women with live-born infants with no structural birth defects, NH-Black women with a CHD-affected pregnancy had a two-fold increased risk of developing any type of CVD (HR=2.1; 95% CI: 1.2, 3.6) a 1.90 times risk for developing hypertension (HR=1.9; 95% CI: 1.1, 3.4), after adjusting for potential confounders. Similarly, NH-Black women with a CHD-affected pregnancy had greater risk of developing any CVD (aHR=1.8, 95% CI: 1.1, 3.1) and hypertension (aHR=1.7; 95% CI: 1.1, 3.1) in comparison to women who delivered a child with a non-CHD birth defect.

Discussion and Conclusions: NH-Black women with a history of a CHD-affected pregnancy have an increased risk of developing CVD and hypertension later in life. CHD-affected pregnancies may be early signs of cardiometabolic dysregulation and CVD in later life. Additional studies are needed to further investigate this possible association.

Changes in mortality associated with Neural Tube Defect in Chile, 2012-2021

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Birth Defects Program on which the work is based: NA

Background and Objectives: Infant mortality in Chile showed a consistent downward trend until 2021, decreasing from of 7.4 per 1,000 live births in 2012 to 5.8 for 2021.
Chile has undergone significant changes in its demographic and epidemiological profile, transitioning towards chronic non-communicable diseases as the main causes of mortality. The second leading cause of infant mortality is the category of congenital malformations, deformations, and chromosomal abnormalities. Within this category, malformations of the circulatory system, were the leading cause of death, followed by chromosomal abnormalities and congenital malformations of the nervous system, with neural tube defects (NTDs) being the main cause. The aim of this study is to describe the mortality associated with NTDs from the fetal period to under 5 years old of age in Chile, from 2012 to 2021.

Methods: Data from the Department of Health Statistics and Information (DEIS) were used, analyzing mortality among children under five years old, including infant, neonatal, perinatal, and fetal mortality. Rates were calculated per 100,000 live births; fetal mortality was included when necessary. Cases were categorized by type of NTD, sex, place of residence of the mother, and maternal age.

Results: During the study period, 619 deaths were attributed to NTDs, 552(89.2%) cases were due to anencephaly, 45 (7,3%) to encephalocele (A), and 22 (3,6%) to spina bifida (SB). The accumulated mortality rate associated with NTDs was 27.7 per 100,000 births (24.7 per 100,000 births for A, 2.0 for encephalocele and 1.0 for SB). The rate of mortality associated to NTDs decreased since 2018, from 35.7 per 100,000 (2012 -2017) to 16.3 per 100,00 (2018-2021), p-value <0.0001. This reduction was primarily due to the decreased rate of A from 32.4 to 10.8 per 100,000, p<0.0001. The highest rate of mortality occurred in fetuses (1277.9 per 100,000 fetal deaths), followed by perinatal deaths (24.5 per 100,000 fetal deaths plus live births) and deaths under 5 years old (21.6 per 100,000 livebirths), with neonatal deaths being the most frequent (20.4 per 100,000 live births) within the under-5 years group. The lowest mortality rates were observed in post-neonatal (0.9 per 100,000 livebirths).

Discussion and Conclusions:
Understanding the mortality rate associated to NTDs, and the period in which the deaths occur aids in monitoring this group and inferring the needs of the health system to prevent them.
This study showed a statistically significant reduction in the mortality rate due to NTDs since 2018, which may be associated with the early termination of pregnancy involving embryos or fetuses with anencephaly. This change aligns with the enactment of the law for voluntary interruption of pregnancy due to fetal anomalies incompatible with life in September 2017.
As expected, most mortality cases due to NTDs occur in the perinatal period, while less occurs in cases of Spina bifida. In conclusion, despite the decrease in mortality rates since 2018, further studies are required to thoroughly investigate perinatal mortality. Such research could identify underlying causes and support the development of targeted interventions to continue reducing mortality rates from NTDs.

Congenital hip dysplasia: A case-control study for risk factor analysis in newborns, Bogotá, Colombia (1982-2022)

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Birth Defects Program on which the work is based: ECLAMC, Colombia

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Background and Objectives: Congenital Hip Dysplasia (CHD) refers to a spectrum of congenital hip defects characterized by abnormal development of the femoral head and acetabulum, resulting in articular instability that may progress to subluxations or luxations of the femoral head. The prevalence of CHD in the US is estimated to be 76.1 per 1,000 births, no specific reports have been described in Colombia. Additionally, CHD has been associated with various risk factors, including fetal breech position, congenital foot defects, swaddling, and female sex. If left untreated, CHD can lead to diverse outcomes, ranging from gait abnormalities to avascular necrosis of the femoral head or hip replacement. Our objective was to perform an epidemiological characterization of CHD regarding its associated risk factors in Bogotá, Colombia, between 1982 and 2022.

Methods: A retrospective case-control study was performed using the data of newborns with birth defects (BD) from the Program for The Prevention and Surveillance of Birth Defects and Rare Diseases (PREVERDEC). Cases were defined as LB with CHD with a birth weight ≥500g, while controls were infants without any BD. Cases were classified based on articular instability (subluxation or luxation), associated BD: isolated case if just CHD was registered, complex isolated if another major BD of the musculoskeletal system was evident, polymalformed if major BDt from another system was found, and syndromic case if a genetic pattern was established, such as Down syndrome. For risk factor analysis we obtained adjusted odd ratios through a logistic regression model. All statistical analysis was performed using IBM SPSS statistics for Mac.

Results: A total of 257 cases of CHD were registered. Considering cases classification, 216 (84%) presented hip subluxation, whilst 34 (13.2%) had hip luxation. Furthermore, 204 cases (79.4%) were classified as isolated cases, 37 polymalformed, 14 complex isolated and 2 syndromic cases. Clubfoot was the most relevant associated malformation in 9 cases, followed by 5 cases with hypospadias. Risk factors for CHD included female new born sex (aOR: 3.05; 95% CI 2.12 - 4.39), podalic presentation (aOR: 11.76; 95% CI 6.35 - 21.75), primiparous mother (aOR: 1.55; 95% CI 1.10 - 2.20) and maternal unemployment (aOR: 1.59; 95% CI 1.09 - 2.30)

Discussions and Conclusions: CHD has been reported alongside other major BD, predominantly musculoskeletal as observed in our study. Our investigation identified female newborn sex as a risk factor of CHD, attributable to increased ligamentous laxity resulting from elevated circulating relaxin, relaxin receptors, and estrogens in female fetuses. Additionally, podalic presentation emerged as a substantial risk factor for CHD, as it can lead to mechanical constraint to the hip, malpositioning and limited movement of the lower limb in utero. Furthermore, primiparous pregnant mothers were identified as a significant risk factor, as the first newborn is exposed to restrictive mechanical forces due to a lack of elasticity in the uterine tissue. Given the resource constraints of low-middle-income countries, investigating risk factors for BD, including CHD, is crucial for preventing and

reducing morbidity by addressing public health initiatives that provide timely diagnosis and prevention in at-risk populations

Epidemiological description and risk factors of congenital genitourinary tract anomalies in Colombia (1982-2022), an ECLAMC case-control study

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Background and Objectives: Congenital genitourinary tract anomalies (GUTAs) result from anomalies in the morphogenesis of the kidney, urinary tract, or genitalia. They present isolated, alongside other birth defects (BD) or within syndromes. According to EUROCAT, in 2022 the prevalence of kidney/urinary tract BD and genital defects was 36.95 and 19.03 per 10,000 births respectively. In Colombia, GUTAs prevalence has been estimated at 10.37 per 10,000 livebirths (LB). These BD are the most common causes of chronic kidney disease in children, predisposing them to hypertension, cardiovascular disease, sexual and fertility complications. Risk factors encompass antibiotic usage, family history of GUTAs and lack of prenatal vitamin intake. This study aims to determine the prevalence of GUTAs and associated risk factors in Colombia from 1982 to 2022

Methods: A retrospective case-control study was carried out, utilizing a 9:1 ratio. Data from the Latin Collaborative Study of Congenital Malformations (ECLAMC) from 1982 to 2022 in Colombia was used. Cases were defined as all LB and stillbirths (SB) with a birth weight over 500g who had a GUTA diagnosed postnatal or prenatal. Cases were classified as: isolated (if only one GUTA was present), polymalformed (if additional BD from another system was found) and syndromic. Controls were defined as the subsequent LB without BDs born in the same hospital. Sociodemographic variables underwent descriptive analysis, while frequencies and percentages characterized categorical variables. The association of risk factors was assessed through logistic regression models, yielding odds ratios (OR) with 95% confidence intervals (CI). All statistical analyses were conducted using Microsoft Excel.

Results: 18,504 births were recorded, of which 8,927 were controls and 912 GUTAs cases. Of these, 884 were LB, 27 SB and 1 case not specified, resulting in a prevalence of 8.41 per 10,000 LB. The most prevalent GUTA was cryptorchidism. Only 309 cases (33.8% were diagnosed prenatally, in 35 cases was not specified time of diagnosis (3.8%), while 568 cases (62.2%) were diagnosed postnatally. Among cases 711 (77.9%) were males, 148 (16.2%) females and 49 (5.3%) indetermined at birth. 603 (66.1%) cases were isolated, 207 (22.7%) cases polymalformed and 102 (11.1%) syndromic. Risk factors included male sex (OR 3.75; 95% CI 3.12 - 4.5). Parental exposures such as: maternal medication use (OR 1.26; 95% CI 1.05 - 1.52) and maternal and paternal age over 35 years (OR 1.14; 95% CI 0.91 - 1.42 and OR 1.22; 95% CI 1.04 - 1.43 respectively) were identified as risk factors. Additionally, low birth weight (OR 2.15; 95% CI 1.85 - 2.51), preterm delivery (OR 1.87; 95% CI 1.52 - 2.32).

Discussions and Conclusions: The prevalence of GUTA in our study was lower than global and national statistics. Previous reports indicated that hypospadias was the most frequent diagnosis, contrasting with our findings. GUTA cases showed lower weight and gestational age than the controls, consistent with literature. In a study conducted in our population from 2001 to 2004, consanguinity and alcohol consumption during pregnancy were identified as risk factors of GUTA. Other factors such as chronic diseases in the mother should be further investigated. GUTAs are common in prenatal ultrasound, with a prevalence of 3 per 1,000 births according to Scott JE in 1993. However, our study had low prenatal

diagnosis, possibly due to the low sensitivity of prenatal US in Colombia and incidental findings during check-ups. Strengthening prenatal diagnosis is crucial for improving pregnancy and newborn care, impacting prognosis and treatment.

Adolescent pregnancy and birth defects: A case control study in Bogotá and Cali, between 2001 and 2020

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Background and Objectives: Adolescent pregnancy constitutes a formidable public health challenge, given an estimated 21 million pregnancies occurring among individuals aged 15-19, resulting in 12 million annual births. This demographic carries an increased risk of obstetric and fetal complications, notably congenital anomalies (CA). This study aims to conduct an epidemiological characterization of birth defects (BD) among newborns in the teenage population and to analyze associated risk factors contributing to their occurrence

Methods: Using data from the Program for the Prevention and Surveillance of Birth Defects and Rare Diseases of Bogotá and Cali spanning from January 2001 to February 2020, a population-based retrospective case-control study was conducted; newborns with BD born to teenage mothers were identified as cases. Controls comprised newborns from teenage mothers without BD. Demographic variables underwent a student t-test with a 95% confidence interval. Risk factor analysis employed multiple linear regression

Results: Of the 1,764 registered cases, the maternal age interval was 8-19 years. The most prevalent major BD were the urinary tract system anomalies (10.74%), while minor BD were ear-face-neck anomalies (18.34%). Multiple linear regression revealed associations between psychoactive substance uses during pregnancy, low levels of maternal-paternal education, and the occurrence of BD, also shows a protective association between highest paternal age and occurrence of BD in their offspring.

Discussions and Conclusions: This study underscores the critical public health implications of adolescent pregnancy, emphasizing the need for a comprehensive, nuanced approach. Beyond the affectation to the well-being of teenage mothers, the associated risks extend to their offspring, establishing modifiable factors influencing CA development. Effective public policies should prioritize preventing adolescent pregnancy while addressing the identified risk factors associated with congenital anomalies.

Perinatal characteristics and factors associated to the presentation of single ventricle in Bogotá and Cali, Colombia

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Background and Objectives: Single ventricle (SV) is a congenital heart defect (CHD) that comprehends multiple anatomical malformations, some of these are tricuspid atresia (TA), Ebstein anomaly (EA), double outlet right ventricle (DORV), double outlet left ventricle (DOLV) and atrioventricular canal defect (AVCD). Worldwide, SV is seen in about 8% of all patients born with CHD. In Colombia, the prevalence rate of SV is 0.5 per 10,000 live births, significantly less than the global incidence, however this can be explained by the lack of systematic notification. There are some environmental and genetic factors associated with SV, some of which are increasing parental age, low socioeconomic status, use of certain medications and the presence of some diseases. This study aims to determine the prevalence and risk factors of SV cases in Bogotá and Cali, Colombia between 2002 and 2023, using the registries from The Latin American Collaborative Study of Congenital Malformations approach (ECLAMC).

Methods: A retrospective case-control study design was performed, analyzing data from birth defect reports provided by the Latin-American Collaborative Study of Congenital Malformations (ECLAMC). Cases included live births or stillbirths with SV weighing more than 500g, while controls consisted of infants without birth defects, matched in terms of birth date and hospital. A case-to-control ratio of 1:4 was utilized. Prevalence was calculated as a rate per 10,000 live births, considering a 95% confidence interval using Poisson distribution, and risk factors were assessed through odds ratios obtained by a logistic regression model using IBM SPSS Statistics ©. Birth weights were classified according to Intergrowth data into low, adequate and high birth weight for gestational age. The study received a waiver for ethical approval from the local Ethics Committee of Pontificia Universidad Javeriana (FM-CIE-8324-14).

Results: 108 cases were identified between 2002 and 2023, amongst which 105 were live births and 3 were stillbirths. With 476,600 births, a prevalence rate of 2.1 cases (95% CI 1.8-2.67) per 10,000 live births was estimated. Among the cases, 52.78% were male newborns. When categorized based on gestational age, 16.2% had a low birth weight, 78.38% an expected birth weight, and 5.41% a high birth weight. Regarding prenatal care, cases had a mean of 6.37 (SD 3.14) prenatal visits, with a mean of 3.83 (SD 2.37) obstetric ultrasounds. Regarding diagnosis and postnatal evaluation, 78.64% were diagnosed prenatally, 19.42% were diagnosed at the time of birth, and 1.94% were diagnosed within the first week of life. Odds ratios analysis demonstrated a statistically significant correlation between SV and birth weight below 2,500 grams (OR: 1.92, CI: 1.174-3.152), and preterm birth (OR: 2.01, CI: 1.133-3.57). Low maternal educational level was found to be a protective factor (OR 0.098 CI: 0.06-0.16).

Discussions and Conclusions: The prevalence rate of SV in this study (2.1 of 10.000 LB) was significantly superior to a previous estimated rate in Bogota from 2001-2014 (0.5 of 10,000 LB). In other matters, SV diagnosis is focused on US and genetic characterization, with a rate of detection of 30% or 60% in developed countries, while in this study a higher rate of prenatal diagnosis was observed. However, this can be explained by the mean number of prenatal visits and obstetric ultrasounds, underscoring the importance of routine prenatal control avoiding late diagnosis as much as possible. In conclusion, a higher prevalence

rate was observed in this study, and some associated factors such as low birth weight and preterm birth were observed. Moreover, a high rate of prenatal diagnosis was observed.

High prevalence of gastroschisis in Roraima, Brazil: The impact of maternal demographics

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Birth Defects Program on which the work is based: NA

Background and Objectives: Over the past decades, the global incidence of gastroschisis has been steadily increasing, with wide regional differences. The precise causes of gastroschisis are not fully understood, although younger maternal age is one of the most recognized risk factors. Recently a rumour of a high number of children with gastroschisis in Roraima state raised an alert. Roraima, in the North of Brazil (Amazonian region), with 650,000 inhabitants (65% in the capital, Boa Vista), is one of the poorest states in the country, with only one children´s hospital equipped with a neonatal intensive care unit and surgery. In recent years, Roraima became the main route for Venezuelan refugees and migrants. Roraima is also one of the states with a higher indigenous population (Yanomami) with demarcated land in Brazil. Our objective was to determine the prevalence of gastroschisis among live births in the state of Roraima and the associated risk factors.

Methods: From 2021 to 2023 we tried to actively identify all births with gastroschisis in Roraima. Sources included surgery records and ICU admissions in the state reference children´s hospital, public maternity, and the state death registry. Two meetings (one in person and one virtual) were held with local health authorities, including those for indigenous health. A standardized questionnaire developed by the Pilot Project for Active Surveillance of Congenital Anomalies (Projeto Piloto) was applied personally to the mothers. The GDDB app was used in its surveillance mode, so the core team could check the images confirming the anomaly. Mean and 95CI were calculated for the prevalence per 10,000 and compared to those notified in the Brazilian System for Live Births (Sinasc). This project was approved by the Brazilian Ethics Committee and registered at Plataforma Brazil (CAAE 67379223.7.1001.5327). It was supported by the Brazilian Ministry of Health (DAENT-SVSA-MS-Brazil)

Results: In 2021, we identified 8 cases of gastroschisis among 12,729 live births (LB), (6.3/10,000, IC95% 7-13); in 2022, 10/11,916 LB (8.3/10,000, IC95% 5-14); and in 2023, 12/11,806 LB (10.2/10,000, IC95% 6-19). In comparison, the overall prevalence in Brazil was reported at 3.2/10,000 LB in 2021 by the Sinasc. There was a difference between the gastroschisis cases actively searched by our project compared to those notified in the Sinasc database (3 in 2021 and 8 in 2022). Of the 30 cases in our study, 15 mothers (50%) were under 20 years old. Maternal age under 20 for all LB in Roraima was 21% in the same period and 14% in Brazil. Fourteen (46%) were Brazilian, 14 (46%) Venezuelan and only 2 (8%) indigenous. The proportion of Venezuelan mothers for all LB in Roraima in the Sinasc was 18.3% in 2021; 19.6% in 2022, and 23.0% in 2023.

Discussion and Conclusions: Although the numbers are small, the prevalence of gastroschisis at birth in the 3 years of active surveillance in RR was higher than registered in the literature and the ICBDSR Gastroschisis Project (Feldkamp et al., 2024). Moreover, we probably couldn't ascertain all cases. Stillbirths were not included. We based our search on reference hospitals and death notifications. Cases referred to other states or centers may not be included. Of particular concern is the indigenous population in reserves (15% of the total population) where data from births and congenital anomalies is almost non-existent. Young maternal age, as expected, was the leading risk factor, and pregnancies among adolescents in the north are 1.5 higher than the average for the country. The high percentage of mothers of Venezuelan origin is impressive and

probably reflects the presence of other risk factors related to the challenging conditions for refugees, like poorer nutrition and difficult access to health support.

VACTERL association; The hidden iceberg. Case series and article review in Malta

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Background and Objectives: VACTERL association is a rare condition. Its prevalence reported 1 in 20,000 births. According to Solomon, et al. the mostly used classification and accepted by researchers and clinicians. It's characterised by the presence of one the following criteria: (i) 3 or more major component features of VACTERL association or (ii) 2 major component features together with an affected 1st degree relative or (iii) 2 major component features together with another anomaly. No evidence of genetic or phenotypic predistortion has been reported.

Methods: This case series reports retrospectively; clinical presentations, perinatal management and outcomes of patients diagnosed with VACTERL association in tertiary referral centre serving country with small population. We discussed related anomalies, health burdens and reviewed recent updated research studies.

Results: All patients presented in this case series are boys. Three presented with triad of VACTERL component features, one had a tetrad, and one had a pentad. The most common VACTERL component in the reported cases, was cardiac, renal and vertebral anomalies. The vast majority of the patients had one of these anomalies, whilst the least prevalent was limb anomalies since only one of the patients exhibited this. Imperforate anus was the most common form of anal anomaly, seen in two patients. None noted antenatally and all have been screened for all features postnatally.

Discussion and Conclusions: This review discusses the following endpoints, VACTEL criteria, clinical presentation, perinatal management and outcomes. we reviewed relevant articles from North America and Europe research centres. With high index of suspicion, we would recommend screening for all different component features of VACTERL association once there is clinical evidence of congenital anomaly to avoid potential morbidity and mortality. Take home message from this report that charring results and opinions between research centers has a tremendous impact on health professionals and decision making.

Tatton Brown Rahman Syndrome with congenital abdominal wall defect. A rare case report

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Background and Objectives: Tatton Brown Rahman Syndrome (TBRS) is a syndrome initially identified in 2014 and is caused by mutation in the DNMT3A gene. TBRS is a congenital anomaly that manifests with skeletal overgrowth, macrocephaly, and characteristic facial features.
None of the documented cases reported association with congenital abdominal wall defect so far.

Methods: A retrospective review of case notes of a patient was referred to pediatric surgery in view of uncomplicated hernia via centrally located abdominal wall defect which presented since birth. After full investigations performed, she underwent the surgical repair of cardiac defects, medical optimisation and systems clinical review, the patient was scheduled for an elective repair of the congenital abdominal wall defect. The hernia was corrected surgically without using a mesh, and the postoperative period was uneventful. Regular follow-up revealed no residual defects.

Results: A comprehensive article review revealed that TBRS is a congenital anomaly syndrome characterised with skeletal and abnormal facial features. The syndrome is diagnosed based on the presence of these two major clinical features, as well as a constitutive variant of the DNMT3A gene. No gender predominance was reported in literature review. Since TBRS is usually caused by a de novo pathogenic variant - most probands represent simplex cases; the first case in the family.
Other common clinical features which may be seen in 20 - 80% of individuals with TBRS, include joint hypermobility, obesity, hypotonia, kyphoscoliosis, and afebrile seizures.
TBRS is one of several overgrowth disorders associated with intellectual disability, with other examples including Sotos syndrome and Weaver syndrome.

Discussion and Conclusions: This case is unique because it describes the first documented case of a congenital hernia of the umbilical cord associated with TBRS, a rare congenital anomaly. Despite several similar overgrowth disorders associated with intellectual disabilities, TBRS is caused by a constitutive variant of the DNMT3A gene. In conclusion, this case report highlights the importance of identifying and managing associated congenital anomalies in TBRS, particularly when they are rare and have not been reported previously.

Incidence and sex ratio in children born with tetralogy of Fallot in the Czech Republic

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Background and Objectives: The co-occurrence of birth defects among infants with Congenital diaphragmatic hernia (CDH) in China remains underexplored. This study aims to elucidate the complex patterns of co-occurring defects in this population.

Methods: This study utilized data from the National Registry of Congenital Anomalies, part of the National Registry of Reproductive Health managed by the Institute of Health Information and Statistics of the Czech Republic. Registration is population-wide, mandatory by national law, and does not require informed consent. All cases diagnosed with Q213 (ICD-10 classification) were included. The analysis focused on annual incidence rates and sex ratios, calculated using Fisher's exact test.

Results: From 1994 to 2020, over 2.8 million children were born in the Czech Republic, with more than 65,000 congenital heart defect cases. Among them, 849 cases were Tetralogy of Fallot, comprising 476 boys and 373 girls. The incidence rate was 2.78 per 10,000 live births overall, 3.75 for boys, and 1.77 for girls. Boys accounted for 69.1% of cases, while girls accounted for 30.9%.

Discussion and Conclusions: Congenital heart defects are among the most common birth defects. Our analysis showed an increasing incidence of Tetralogy of Fallot since 1994, peaking between 2000 and 2006, after which the frequency declined. Additionally, boys were significantly more affected than girls. The reason for this discrepancy in sex ratio remains unexplained and warrants further investigation.

Supported by Ministry of Health, Czech Republic – conceptual development of research organization (Thomayer University Hospital - TUH, 00064190)

ICBDSR / MALFOVAR Museum network accreditation system :

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Birth Defects Program on which the work is based: MALFOVAR

Background and Objectives: The goal of the ICBDSR/MALFOVAR museum network establishment is to create better exposure, accessibility to knowledge and information (statistics, imaging, genetics) and its dissemination to the professional community and individuals who are interested to contribute to the field of understanding and prevention of congenital malformation.
Since occurrence and presentation of malformations may vary in different regions according to geography, ethnography and exposure to harmful conditions, therefore the goal of ICBDSR /MALFOVAR museum network is to represent local malformation information and tendencies compared other regions and global tendencies.
The statistical analysis may be represented in following levels:

1. Local levels (country level)
2. Region levels (Geography , ethnography, Teratogen exposure, facility)
3. Global World level. (ICBDSR , WHO)

Methods: The museum will contain information within two dimensions: The first is the Exhibition hall Museum which will have real specimens and facilities that can present movies posters and lectures. The second dimension is the digital museum which will be available on the web.
In Summary the goal of the museum is to act as a visual simulation and data source that can contribute to the understanding of morphological changes and mechanisms of dysgenesis of the Human body development.

Results: Accreditations System/ Process for accreditation: Museum accreditation organization and committee:
1.The Museum network accreditation committee members are as following: 5 members of them one chair+ four delegates, each from every continent. The committee will access the application if the applicant museum had fulfilled the perquisites for the accreditation.
2.ICBDSR voting accreditation voting acceptance in accordance to committee recommendations during the Annual meeting.
3.Final approval of accreditation. An official certificate will be given to the museum which will be hanged in the facility.
A list of ICBDSR / MALFOVAR accredited museums list will be listed on ICBDSR internet site. The Process of application for accreditation of ICBDSR /MALFOVAR Museum will be according to list of perquisites for accreditation.

Discussion and Conclusions: Final steps of approval by the ICBDSR:
Application certificates will be reviewed by the ICBDSR museum network committee.
The digital and exhibition museum will be surveyed and approved by the ICBDSR museum network committee. In the next stage a post survey final approval meeting will occur.
The ICBDSR museum network committee will adjourn for the vote on the final approval.
Voting on approval by the ICBDSR Annual Business Meeting in accordance to recommendation by .The ICBDSR museum network committee. Reassessment of the museum accreditation by the ICBDSR should take place every 10 years to assess that museum was upgraded and is UpToDate.

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Printed and supported by

Pontificia Universidad Javeriana

Human Genetics Institute of the Pontificia Universidad Javeriana

Secretary of Health of Bogotá

Program for the Prevention and Surveillance of Rare Diseases and Congenital Defects (PREVERDEC)