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EDITORIÁL

„Veda sa nachádza v základoch každého pokroku, ktorý uľahčuje ľudský život a zmenšuje utrpenie.“

Marie Curie-Skłodowská

Základným predpokladom dynamického rozvoja vedy a výskumu v Európskom vzdelávacom a vedecko-výskumnom priestore je kvalitné vzdelávanie a medzinárodne uznávaná vedecko- výskumná činnosť. Pracovníci Fakulty verejného zdravotníctva Slovenskej zdravotníckej univerzity v Bratislave (FVZ SZU) sa aktívne zapájajú do vedecko-výskumnej činnosti doma i v zahraničí, kde úspešne využívajú svoje odborné znalosti pri riešení medzinárodných projektov. Mnohí z našich pracovníkov sú pozývaní na vedecké konferencie v zahraničí, aby predniesli výsledky svojej práce rôznych odborných disciplín, ktoré zahrnuje problematika verejného zdravotníctva.

Rozvoj verejného zdravotníctva, zvlášť v posledných desaťročiach, súvisí najmä s rozvojom epidemiológie neinfekčných ochorení. Jednou z problematík tohto multidisciplinárneho medicínskeho odboru je aj problematika riešenia výskytu vrodených vývinových chýb (VVCH) v ľudskej populácii, ktorá je jednou z príčin novorodeneckej úmrtnosti a predstavuje závažný spoločenský problém.

Pracovná skupina FVZ SZU v spolupráci s Národným ústavom zdravotníckych informácií (NCZI) zaoberajúca sa problematikou monitorovania a prevencie VVCH sa stala v roku 2004 členom medzinárodnej organizácie „International Clearinghouse for Birth Defects Surveillance and Research“ (ICBDSR) a spolupracuje s výskumnými pracoviskami z 36 krajín sveta.

Snahou pracovného tímu FVZ je naďalej rozširovať medzinárodnú spoluprácu o ďalšie európske vedecko-výskumné organizácie EUROCAT a ENTIS a vytvoriť na Slovensku „Teratologickú Informačnú Službu“, čo prispeje ku kvalitatívne vyššej úrovni výskumu a vzdelávania podľa EU požiadaviek a hlbšej integrácii nášho pracoviska do európskej výskumnej siete.

Na základe uvedených vedecko-výskumných aktivít FVZ SZU organizovala v dňoch 8-11 septembra 2019, pod záštitou rektora univerzity Prof. Petra Šimka, PhD a Ministerstva zdravotníctva SR, medzinárodnú konferenciu a míting členov ICBDSR. Na pôde univerzity sme privítali odborníkov z 26 krajín sveta, ktorých vedecké prednášky predstavujeme v tomto čísle nášho časopisu.

RNDr. Elena Szabová, CSc.

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A MULTICENTER APPROACH TO CRANIOSYNOSTOSIS PREVALENCE AND HEALTH OUTCOME IN CENTRAL GERMANY

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ICBDSR Registry on which the work is based: Malformation Monitoring Centre Saxony-Anhalt, Germany

Background and Objectives: Craniosynostosis is the premature closure of one or more sutures of the skull. Usually, these sutures are open to enable passage through birth canal. Sutures are also important for craniofacial growth in the first two years of life. European hospital data showed an increase in the prevalence. The aim of this study was to assess prevalence and time trends of craniosynostosis on a population level in Saxony-Anhalt and analyze the proportion of prenatal diagnosis in these cases.
Methods: For the time period 2000 to 2017, a retrospective multi-center patient cohort study evaluating time of diagnosis was performed via chart review. Hospitalized patients (inpatients and outpatients) diagnosed with craniosynostosis aged less than two years and who underwent surgery from January 1, 2000 to December 31, 2017 were identified at each of the three hospitals. The study included all relevant departments eligible to carry out this type of surgery within the region.
Results: Overall, 91 patients were enrolled in the study. We compared data on these patients with those of 273 controls. There were 75 males and 16 females (ratio 4.7:1). Fifty-one children had isolated craniosynostosis, consisting of 46 with a single-suture and five with a multisuturesynostosis. Twenty-nine children had other congenital malformations, and 11 were syndromic. Three cases were diagnosed prenatally, and 34 had skull deformities diagnosed immediately after birth at a mean (SD) age of 3.4 (4.7) months.The mean (SD) age at the time of first admission to a hospital in one of the three surgical centres of Saxony-Anhalt was 5.9 (5.5) months, and 65 patients were operated on at a mean age of 9.1 (6.3) months.
Discussion and Conclusions: For the first time, population-based research on the prevalence of craniosynostosis and its prenatal diagnosis has been conducted for Germany. In contrast to published European reports, we observed a prevalence of 4.8 cases of craniosynostosis/10,000 births that did not increase during the study period. 2000–2016. Although we found a low prenatal detection rate, the diagnosis and treatment in this cohort study seemed timely.

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PREVALENCE AND DESCRIPTIVE EPIDEMIOLOGY OF CONGENITAL HYDROCEPHALUS IN IOWA, 2000–2016

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Background and Objectives: Primary congenital hydrocephalus (CH) is characterized by impaired circulation and absorption of cerebrospinal fluid in the ventricular system of the brain, beginning after 20 weeks gestation. CH is a chronic illness, and those affected have disproportionally increased health care expenditures and an increased risk of mortality. There is a paucity of contemporary information on the prevalence of CH and associated factors in the United States. As such, we conducted a retrospective cohort study using data from the Iowa Registry for Congenital and Inherited Disorders (IRCID) to examine the prevalence and descriptive epidemiology of CH.
Methods: We compared IRCID surveillance data for CH cases (n=568) with birth certificate data for Iowa live births (n=663,316) delivered from 2000 through 2016. We used Poisson regression analysis to estimate prevalence per 10,000 live births, Joinpoint regression to examine changes in prevalence, and logistic regression analysis to estimate crude and adjusted prevalence ratios (cPRs and aPRs, respectively) and corresponding 95% confidence intervals (CI)s; aPRs were controlled for selected child and parental characteristics. Analyses examining all CH cases combined were stratified by CH subgroup (aqueductal stenosis, Dandy-Walker malformation, hydrancephaly, other/unspecified [e.g. communicating, noncommunicating, etc.]).
Results: Of the 568 cases, there were 377 other/unspecified, 91 with Dandy-Walker malformation, 88 with aqueductal stenosis, and 12 with hydrancephaly. These cases included 151 (26.6%) isolated, 266 (46.8%) multiple, and 151 (26.6%) confirmed or suspected syndromic phenotypes. Of the 151 syndromic cases, 132 (87.4%) were classified as having a confirmed syndrome, with trisomies being the most common syndrome (40.2%). Among all cases, CH prevalence was 8.56 per 10,000 live births (95% CI=7.89, 9.30) and remained relatively stable over the study period. For all CH cases combined, we observed positive associations for plural pregnancies (aPR=2.04; 95% CI=1.38, 3.02), maternal age at delivery ≥35 years (aPR=1.56; 95% CI=1.09, 2.22), primigravida (aPR=1.34; 95% CI=1.08, 1.66); and non-Hispanic Black paternal race/ethnicity (aPR=1.54; 95% CI=1.03; 2.30). Findings were consistent for some, but not all factors, when examined by CH subgroups.
Discussion and Conclusions: Our estimated prevalence for CH was comparable to other regions of the US. Some, but not all, of our study findings were consistent with previously reported associations with child and parental characteristics, perhaps owing to variations in case inclusion criteria, surveillance methods, and sample size. Future studies are needed to confirm prevalence patterns and associated factors among different CH phenotypes. As our findings are derived from a multi-source, population-based surveillance program, they can inform resource allocation for programs aimed at providing treatment and services to CH cases.

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CONGENITAL ANOMALIES IN KIDNEY AND URINARY TRACT IN NEWBORNS: A RETROSPECTIVE STUDY IN BOGOTÁ AND CALI, COLOMBIA, 2009-2018

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ICBDSR Registry on which the work is based: Colombia, Bogotá:CMSP Congenital Malformations Surveillance Programme and Colombia, Cali: CBDSP Congenital Birth Defects Surveillance Programme

Background and Objectives: Congenital anomalies of the kidney and urinary tract (CAKUT) are common birth defects in newborns. Previous literature reports 3-6 cases per 1,000 live births and explains 40-50% of the etiologies of chronic kidney disease in children around the world, including structural and functional kidney, collecting system, bladder, and urethral abnormalities. Some pregnancies with CAKUT can end in stillbirth or miscarriage. In newborns, CAKUTs are assoicated with impaired renal function and kidney-related disease in young adults. Generally, CAKUTs can be identified and classified at an early stage of pregnancy with ultrasonography. Owing to the poor outcomes of chronic kidney disease (CKD) in children, it is necessary to know the prevalence of CAKUTs. Our objective was evaluate the epidemiology of CAKUTs, based on data from the Congenital Malformations Surveillance Program (CMSP) in two Colombian cities.
Methods: This is a retrospective study. We obtained information from case-control databases using Latin American Collaborative Study of Congenital Malformations (ECLAMC) criteria. The study included all births and all patients with CAKUTs diagnosed between 2009 to 2018 in two hospitals in Bogotá and three hospitals in Cali. We analyzed sex, prenatal detection, and type of diagnosis among children with CAKUTs. The proportion of each subgroup of CAKUTs and associated malformations were calculated.
Results: There were 137 CAKUTs identified from over 139,300 births, with an average prevalence of 9,8 per 10,000 births. Overall, 71.7% (n=99) were males, and 27.5% (n=39) were females for a sex ratio of 2.5:1. Also, 75.4% (n=104) of cases were recognized prenatally: hydronephrosis 88% (n=103), kidney dysplasia 92% (n=13) and renal agenesis 100% (n=4). The majority, 88%, of births had isolated malformations; 6.5% had other CATKUT-associated defects.
Discussion and Conclusions: CAKUT prevalence was variable in different reports. In our study, our prevalence was 9.8 per 10,000 births, much lower than in other studies (Birth Defects Monitoring Program BDMP 70 per 10,000 births and EUROSCAN 16 per 10,000 births). We found a high proportion of CAKUTs was reported in male newborns and the majority were isolated malformations. The most frequently detected subgroup of CAKUTs was hydronephrosis, similar to other reports. Given the impact on the quality of life of complications secondary to CAKUT, it is very important that the diagnosis is timely for proper follow-up and intervention.

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MODELLED ESTIMATES FOR SELECTED CONGENITAL DISORDERS IN SOUTH AFRICA

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ICBDSR Registry on which the work is based: Not Applicable

Background and Objectives: Congenital disorders (CDs) remain an unprioritized healthcare issue in South Africa (SA). Although an estimated 1/15 live births (6.8%) are affected by CDs in SA, national surveillance is underreporting by 98%. The lack of empiric data on CDs is preventing informed policy decision-making for service planning at all levels. This underreporting perpetuates capacity and infrastructure shortages, resulting in misdiagnosis and non-diagnosis of CDs and misclassification of CD-related deaths and preventing those surviving with CDs from accessing the care they require. Modelling offers a reliable means of estimating CDs until surveillance systems are adequately developed. This study quantified the CD burden of disease at a national and provincial level using the Modell Global Database of Congenital Disorders (MGDb). In SA, child mortality rates have stagnated since 2011, and undertaking this modelling exercise for 2012 provides a baseline for comparison with future modelled data from subsequent years.

Methods: In this study, methods adapted from the MGDb and birth prevalence data from well-established surveillance systems were used with local demographic data to generate 2012 baseline birth prevalence estimates for early-onset endogenous CDs in the absence of care. The 2012 actual birth prevalence was estimated using the MGDb approach to evaluate the effect of current interventions. Access to relevant health services (including initial diagnosis and treatment) and the impact of interventions was quantified using the infant mortality rate (IMR) as a proxy. Four groups of early-onset CDs (presenting before the age of 20) with known baseline birth prevalence rates were included: single gene disorders, chromosomal disorders, malformations (non-syndromic, isolated), and additional conditions. CDs due to post-conception environmental causes, genetic risk, and late onset disorders were excluded.

Results: Total birth prevalence for baseline (no care) estimates was 30.4 per 1,000 live births. Of the 37,280 births affected, 6% were stillborn and over one-half (56%) died under age 5 from CD-related causes, with all survivors disabled. In 2012, access to care was estimated at 31% nationwide, reducing birth prevalence to 29.2 per 1,000 live births. An estimated 2,580 (7%) of affected births were avoided through pre-pregnancy/prenatal interventions. Survival increased by 14% with 3,810 more children living to age 5. Of the 18,070 survivors, 29% were effectively cured, and 12,780 (71%) survived with disability. The number of affected births per province was proportional to overall births occurring in each, for baseline and actual estimates. Estimates for access to care ranged from 93% (Western Cape) to 18% (Free State), resulting in a unique ratio of actual outcomes per province. The greatest impact of services was in Western Cape, and the least impact in Free State and KwaZulu-Natal.

Discussion and Conclusions: This study: 1) quantified the baseline scale of the burden of a subset of early-onset endogenous CDs in SA for 2012; 2) modelled estimates for access to 30% available care, demonstrating proportional changes in birth outcomes made possible by care; and 3) enabled an estimate of the effect of services. A much higher proportion of births affected by CDs is indicated than is currently documented by national CD surveillance. The MGDb approach is a tool to inform policy makers, providing conservative, interim estimates until surveillance improves and empirical data become available. While baseline estimates are strongly evidence-based, the calculations for the outcome estimates of this approach are less reliable, and the source of quality, local demographic data is essential. Further study includes analyses of modelled estimates for: (a) specific CDs; (b) specific provinces of SA; (c) costing of specific interventions; and d) repeated modelling at appropriate intervals.

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PREVALENCE AND MORTALITY AMONG INFANTS WITH CONGENITAL DIAPHRAGMATIC HERNIA: A MULTI-REGISTRY ANALYSIS

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ICBDSR Registry on which the work is based: 25 ICBDSR members registries

Nembhard, WN a kol. Prevalence and Mortality among Infants with Congenital Diaphragmatic Hernia: A Multi-Registry Analysis, s. 9-10.

Background and Objectives: Congenital diaphragmatic hernia (CDH) is a severe birth defect with a high mortality rate. The aim of this study is to examine the global prevalence and mortality trends associated with CDH.
Methods: We used data from twenty-five hospital- and population-based surveillance programs in 19 countries from members of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR) for a birth defects surveillance study between the years 1974 and 2015. Cases were infants with CDH that resulted in live births, stillbirths, or elective termination of pregnancy for fetal anomalies. In programs where data were available, we examined mortality by isolated and non-isolated case status (the latter including multiple congenital anomalies and syndromic cases combined). Prevalence and Kaplan-Meier mortality rates were calculated for all births, by each country, and by type of registry.
Results: The total prevalence of CDH between the years 1974 and 2015 was estimated to be 2.7 per 10,000 total births (95% Confidence Interval: 2.6, 2.8). Overall, the cumulative percent mortality of CDH was 37.2%, with hospital-based registries having a higher number of live births with CDH resulting in death than population-based registries (45.1% compared to 33.6%). Multiple and syndromic cases of CDH had higher one-week mortality rates (44.9%) than isolated cases (28.4%) for both hospital- and population-based registries. The highest proportion of deaths due to CDH occurred among infants aged 2 to 6 days for both registry types (36.3% for hospital-based and 12.1% for population-based).
Discussion and Conclusions: Our findings show that the global prevalence of infants with CDH remains high, with an elevated mortality rate, especially during the first week of life. A major concern is the clinical presentation of CDH and its association with other anomalies which may indicate a specific etiologic or genetic cause. Further research is needed to examine the differences between population- and hospital-based registries and the 'hidden mortality' that might be present.

Manduca, P a kol. Hospital centered surveillance at birth 2011-2018 and assessment of environmental effectors of changes in reproductive health in Gaza, Palestine, reveals long-term impact of metals weapons-remnants, s. 21-22.

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PREVALENCE OF GASTROINTESTINAL MALFORMATIONS IN 16,958,666 NEWBORNS FROM THREE SURVEILLANCE PROGRAMS SINCE 2011 TO 2015

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Background and Objectives: Gastrointestinal malformations (GM) are defined as any structural congenital anomaly of the gastrointestinal tract. GM have an impact on infant morbidity and mortality and most requiresurgical treatment. Our objective is to describe GM prevalence reported in three Surveillance Programs: National Birth Defects Prevention Network (NBDPN), National Network of Congenital Anomalies of Argentina (RENAC) and Bogota and Cali Congenital Malformations Surveillance Programme (CMSP) between 2011-2015.
Methods: We reviewed 586,786 births in the CMSP, 1,316,374 births in the RENAC and 15,348,899 in the NBDPN from 2011 to 2015. Data were obtained from each program's online databases and the prevalence per 10,000 births were calculated with their respective confidencie intervals (CIs) using the Poisson Method. We selected cases with oesophageal atresia/stenosis with or without fistula (OA), small intestine atresia/stenosis (SIA), anorectal atresia/stenosis (AA), diaphragmatic hernia (DH), omphalocele and gastroschisis.
Results: Overall, 33,443 cases of GM were reported from a total population of 16,958,666, establishing a prevalence of 19.72 per 10,000 births (95% CI: 19.51-19.93). We observed differences in GM frequencies among the surveillance programs, SIA was the most frequent GM, followed by gastroschisis in the CMSP; gastroschisis had the highest prevalence in the RENAC and NBDPN.
Discussion and Conclusions: Congenital anomalies are common, costly, and critical. In our country, GM represent the fourth leading congenital anomaly. We observed significant prevalence variation among GM in the three surveillance programs. Those differences could be explained by national coverage (NBDPN and RENAC) versus local coverage (two cities in CMSP), each surveillance strategy, and intrinsic factors to each country (nutrition, socioeconomic status, exposition). The high prevalence of gastroschisis in the RENAC program is striking. There are interesting differences in the GM prevalence between surveillance programs. This can be explained by methodological reasons or intrinsic factors in each country. It is important to carry out studies of risk factors related to these malformations to understand the differences between the countries and in this way to propose prevention strategies.

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TEMPORAL TRENDS AND SPATIAL VARIABILITY OF THE PREVALENCE OF GASTROSCHISIS IN ARKANSAS, 1998-2013

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ICBDSR Registry on which the work is based: Arkansas Reproductive Health Monitoring System

Background and Objectives: A report based on data from 14 United States (U.S.) state birth defect surveillance programs described a 30% increase in the prevalence of gastroschisis (from 3.6 per 10,000 live births in 1995−2005 to 4.9 in 2006−2012) and urged researchers to further investigate the etiology of this increase. Arkansas is an important state since it had the highest prevalence of gastroschisis in a national study based on 15 U.S. states (1995−2005). Our objective was to explore trends in prevalence and the spatial distribution of gastroschisis in Arkansas between 1998 and 2013.
Methods: Infants with gastroschisis, born 1998-2013, were obtained from the Arkansas Reproductive Health Monitoring System (ARHMS), a statewide birth defects registry that monitors live births, fetal deaths and terminations for structural birth defects. Birth record data were obtained from the Arkansas Department of Health. Data from the US Census Bureau and Arkansas Department of Environmental Quality were used for county characteristics. Maternal residence at delivery was geocoded for spatial analyses. Annual prevalence rates by county and region were calculated and Joinpoint regression analyses were used to assess temporal trends. Spatiotemporal cluster detection methods were used to identify counties with unusually high prevalence rates. Poisson regression was used to calculate crude and adjusted prevalence ratios. Covariates included individual and county level maternal race/ethnicity, age, education, poverty and county level body mass index (BMI) and agricultural characteristics.
Results: We identified 357 cases of gastroschisis among 617,404 live births. The overall prevalence of gastroschisis ranged from 3.0 per 10,000 live births in 2001 to 9.1 in 2012 (overall prevalence=5.8). We observed an annual increase of 4.7% (P=0.0001) in the prevalence of gastroschisis during the study period. A high overall prevalence (range: 15-20) was noted in 5 counties. During the study period, prevalence increased in 48 counties and decreased in 3 counties. Both Emerging Hot Spot Analysis (EHSA) and SaTScan detected one overlapping spatiotemporal cluster of gastroschisis cases in the western part of Arkansas. EHSA identified a 3-county cluster in 2013 and SaTScan identified an 18 county cluster between 2006 and 2013. Multivariable Poisson regression models for each cluster were found to be statistically significant but did not identify any individual or county factors that explained the temporal trends or spatiotemporal clusters. Hog farming emerged as a factor of interest.
Discussion and Conclusions: The prevalence of gastroschisis in Arkansas increased during the study period and varied by county and region. Spatiotemporal analysis suggests a possible cluster of gastroschisis in Western Arkansas. The etiology or factors associated with the increasing prevalence over time and spatiotemporal differences within the state remain unknown. Future studies will explore hog farming and its potential association with these clusters.

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TIME TRENDS, SPATIAL VARIATION AND RISK FACTORS FOR GASTROSCHISIS IN CANADA, 2006 TO 2017

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ICBDSR Registry on which the work is based: Canadian Congenital Anomalies Surveillance System (CCASS)

Background and Objectives: Gastroschisis is a congenital malformation characterized by a defect of the abdominal wall, exposing the viscera. Its cause is largely unknown, although there is a strong association with young maternal age. Several previous studies have shown increases in rates of gastroschisis in various countries, including Canada. We carried out a study to examine recent temporal trends and spatial variation in gastroschisis prevalence and associated maternal and infant characteristics in Canada.

Methods: The study included all hospital-based live births in Canada (excluding Quebec) between April 2006 and March 2018, with information from the Canadian Institute for Health Information (a data source for the Canadian Congenital Anomalies Surveillance System). Temporal trends by maternal age, region of residence, maternal and infant characteristics and pregnancy outcomes were quantified using prevalence rate ratios (RR) and 95% confidence intervals (CI). Multivariable Poisson regression was used to quantify the independent association between different risk factors and gastroschisis.

Results: Over the period 2006 to 2017, the proportion of mothers aged 20-24 years declined from 16.5% to 11.2%. The proportion aged <20 years halved, from 4.7% to 2.2%. Gastroschisis rates decreased from 3.78 to 2.79 per 10,000 live births (P-value for trend <0.001). While the prevalence of gastroschisis among the offspring of women aged <20, 20-24, and 30-49 years remained largely unchanged, an increasing rate was observed in the offspring of women aged 25-29 (P<0.01). The overall age-adjusted rate of gastroschisis showed a nonsignificant increase (adjusted annual average change in prevalence ratio 1.004, 95% CI 0.989, 1.020). Women in the Yukon, Northwest Territories, and Nunavut had an over 4-fold higher prevalence rate of gastroschisis compared with the rest of Canada (RR 4.27, 95% CI 3.08, 5.92). In multivariable analyses, women aged <20 years had the highest risk of having a gastroschisis-affected infant (RR 7.93, 95% CI 6.64-9.47 compared with women aged 25-29 years).

Discussion and Conclusions: Problematic substance use (RR 1.89, 95% CI 1.35-2.64), tobacco use (RR 1.74, 95% CI 1.14-2.65), rural residence (RR 1.29, 95% CI 1.12-1.48) and residence in the three territories (RR 2.15, 95% CI 1.62-3.78) were associated with a higher risk of gastroschisis. Women with diabetes mellitus had a lower risk of gastroschisis compared with women without diabetes (RR 0.36, 95% CI 0.21-0.61). Gastroschisis prevalence did not differ by infant sex, parity or plurality. The prevalence may have decreased because there are less young mothers (<25 years), and younger mothers are associated with higher rates of gastroschisis.

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RISK FACTORS CONTRIBUTING TO DEATH VERSUS SURVIVAL OF INFANTS WITH A CONGENITAL ANOMALY: A POPULATION-BASED COHORT STUDY OF WELSH LIVEBIRTHS USING DE-IDENTIFIED LINKED DATA BETWEEN 1998 AND 2017

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ICBDSR Registry on which the work is based: Congenital Anomaly Register and Information Service (CARIS), Wales, UK

Background and Objectives: Congenital anomalies are the second leading cause of infant death in the UK, accounting for over one-third of all infant deaths. To date, population-based studies of risk factors for mortality of infants with congenital anomaly have been limited. Estimates of infant mortality associated with congenital anomalies are important to inform planning of healthcare and social interventions aimed at reducing infant mortality. Congenital Anomaly Register and Information Service (CARIS) is a high-quality, population-based register established in 1998 to identify congenital anomalies in all regions of Wales and is known to have high reporting rates due to a robust surveillance system. CARIS collects data about congenital anomalies involving structural, metabolic or genetic defects, present before the end of pregnancy. The aim of this study was to investigate the nature, clinical features, and risk factors associated with the risk of infant death versus survival in infants with congenital anomalies.

Methods: A population-based cohort study was conducted using registry data from CARIS with linkage to data on livebirths and deaths from the UK Office for National Statistics. The study population included all livebirths with birthweight ≥500g, gestational age ≥22+0 weeks, and a diagnosis of a congenital anomaly between 1998 and 2017. The characteristics explored were socio-demographic, maternal, infant, and intervention factors. Univariable logistic regression was performed to obtain crude odds ratios; those with $p<0.1$ were explored in a multivariable model. Multivariable logistic regression was performed using a backward stepwise approach to obtain adjusted odds ratios, and a subsequent likelihood ratio test to examine the independent effect of each significant variable; $p<0.05$ was considered significant in the final model. The analysis was performed separately for: infants with any anomaly; those with isolated anomalies; those with multiple anomalies; and those with cardiovascular anomalies.

Results: Overall, 30,424 livebirths affected by congenital anomalies were identified, of which 20,008 (65.8%) had isolated anomalies and 10,374 (34.1%) had multiple anomalies. Cardiovascular anomalies contributed the highest infant mortality rate (IMR: 1.33 per 10,000 livebirths) among isolated anomalies. Significant increases in adjusted odds of infant mortality were found among infants born to mothers of non-White vs White ethnicity (aOR 2.25; 95% CI: 1.77-2.86); parous vs nulliparous (aOR 1.24; 1.08-1.41); active smokers during pregnancy vs non-/ex- smokers (aOR 1.20, 1.02-1.40); preterm vs term (aOR 4.38; 3.86-4.98); and female vs male infants (aOR 1.28; 1.13-1.46). Infants who required surgery in the first year of life had a lower odds of infant mortality than those who did not (aOR 0.80; 0.68-0.95). Preterm birth was a significant risk factor for all anomaly types but the effect of the other characteristics varied according to the anomaly group.

Discussion and Conclusions: Socio-demographic, maternal, infant, and intervention factors have a significant impact on infant mortality in babies with congenital anomalies by different potential mechanisms depending on the type of anomaly. For example, the excess mortality from congenital anomalies in minority ethnic groups may be due to an interplay of factors resulting in unequal access to antenatal screening and medical and surgical interventions, different attitudes toward congenital anomalies and termination of pregnancy, and consanguinity. Likely smoking-related mechanisms include placental abruption and an increased risk of sudden infant death syndrome. Prematurity increases the risk of comorbidities and related complications. Infants with an anomaly who required surgery in the first year of life had a lower risk of death compared to those who did not or whose anomalies were too severe for surgery.

Ho, P – Quigley, MA – Kurinczuk, JJ. Risk factors contributing to death versus survival of infants with a congenital anomaly: A population-based cohort study of Welsh livebirths using de-identified linked data between 1998 and 2017, s .14.

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TIMELINESS OF DATA CAPTURE AND PROCESSING IN MACDP

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ICBDSR Registry on which the work is based: Metropolitan Atlanta Congenital Defects Program (MACDP), GA, USA

Background and Objectives: National Birth Defects Prevention Network surveillance guidelines recommend data be 95% complete within two years of birth or fetal demise. Emerging risks to mothers and babies, including the Zika virus outbreak, demonstrate the need for rapid surveillance. The Metropolitan Atlanta Congenital Defects Program (MACDP) is a population-based birth defects surveillance system that collects information on birth defects that occur among residents of the central counties of Atlanta, Georgia. To ensure high data quality, MACDP employs active case finding in multiple facilities and implements comprehensive clinical and non-clinical reviews. This study aims to assess the feasibility of measuring timeliness of MACDP data.
Methods: Timeliness was initially measured by calculating days from the date of delivery to the date review processes were completed. Time to case completion was retrospectively calculated for all cases with a completion date in 2016. Data were stratified for cases that did/did not qualify for inclusion in the Birth Defects Study to Evaluate Pregnancy exposureS (BD-STEPS) case control study, as reviews are prioritized for these cases. Timeliness was also measured by calculating age at interview for BD-STEPS cases.
Results: Among 2016 cases, 97.7% were complete within two years from the delivery date. Average time from delivery to case completion was 12.5 months (range: 2.9-44.2 months). Timeliness did not differ between cases eligible for BD-STEPS (mean: 12.0 months; range: 2.9-33.0 months) and cases not eligible (mean: 12.5 months; range: 3.6-44.2 months). The average age at interview for BD-STEPS in 2016 was 8.1 months (range: 6.1-12.3 months).
Discussion and Conclusions: The difference between timeliness at age of interview and final completion for BD-STEPS cases highlights challenges in conceptualizing and measuring timeliness of birth defects surveillance data. Additional analyses are planned for 2017, stratified by defect type and number of abstractions. Data will also be stratified by prenatal vs. postnatal diagnosis. For postnatal diagnoses, days between date of diagnosis to the date review was completed will also be calculated. To more effectively respond to emerging threats to mothers and babies, MACDP is using these findings to identify additional meaningful timeliness measures for routine monitoring and improvement.

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CHALLENGES IN IMPLEMENTING PULSE OXIMETRY SCREENING FOR DETECTING CONGENITAL HEART DISEASE AS PART OF BIRTH DEFECT SCREENING IN A MIDDLE-AND LOW-INCOME COUNTRY SETTING

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ICBDSR Registry on which the work is based: Not Applicable

Background and Objectives: Kerala in India is one of the large state with 34 million population and best infant mortality rate (IMR) figures (10 per 1000 live birth based on 2017 data) is a progressive state, where various measures are taken for further reducing IMR. While considering the fixing of sustainable developmental goal targets, it was decided to focus on quality survival rather than survival. The platform included comprehensive newborn screening with components of visible birth defect screening, functional birth defect screening for congenital heart disease (CHD) using pulse oximetry (PO) and screening, and otoacoustic emissions for hearing screening. Metabolic screening for four parameters (TSH, CAH, G6PD, galactosemia)also were brought under a single umbrella. It was thought that such screening would be the most cost-effective way to improve quality survival of the newborn at this stage of development for any country. We now look back toevalute this program implemention.

Methods: Functional birth defects are a group of birth defects, which by screening during the early days of life, can improve survival of babies. CHD is among the most common functional birth defect, which is usually detected using PO. But the low specificity of PO screening as a tool for identifying CHD has already been discussed and evidence published. The effect of adding physical examination to the PO screening is also known. This presentation focuses on the problems that arose following implementation of a community-level program with 58 public sector delivery points in the state of Kerala, India, which is a low resource setting with quite good health indicators. Only 53% of the delivery points where birth defect screening was initiated were enrolled for PO screening due to resource constraints, but were able to include the delivery points with almost 70% of total deliveries per year.

Results: A protocol by American Academy of Pediatrics was used for the project and to interpret the results. It was observed that approximately 40% of cases were screened in the expected time interval of 24-48 hours. Screeners tended to complete the testing towards the end of 96 hours. Reasons observed for the delayed screening were reluctance of family members to come for screening and poor communication and very low efforts to disseminate the information among the public. A high incidence of false positives or test positives resulting in high resource utilization with regard to confirmation of diagnosis. This was due to poor adherence to the protocols for doing the screening, and improving adherence was able to bring the percentage failed from over 8% to 2.1% merely by training. It was also observed that adherence to the same screener also will improve the quality of screening. The knowledge level of the screener also produced an overall improvement in the test results.

Discussion and Conclusions: From our evaluation of this large scale public health intervention to reduced IMR, screening for CHD by PO screening was the most cost-effective tool. Screening over 80,000 newborns in the first few days of life, varying over a period of 12 to 96 hours, it was observed that beyond the use of PO screening, adherence to the screening protocol by continuous training, using the same screener, adding physical examination to identify clinical signs, such as a murmur, by using an electronic stethescope, decreasing the scope of manual error by automatic data capture, and defining a predictive score for ranking the physical examination findings will add to the value of PO screening for identifying CHD among newborns in a middle- and low-income country setting.

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A NOVEL SOFTWARE PLATFORM FOR ASSESSING PATTERNS OF MULTIPLE CONGENITAL ANOMALIES

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ICBDSR Registry on which the work is based: Texas Birth Defects Registry, USA

Background and Objectives: Clinical recognition of unique multiple congenital anomaly (MCA) patterns has been helpful for identifying and defining new syndromes, sequences, and associations. However, there are few examples where population-based data have been used to identify MCA patterns. We have developed a software platform providing large-scale assessment of combinations of congenital anomalies collected by birth defects surveillance programs.
Methods: To facilitate MCA assessment in large datasets, we developed an R-based software platform that will be made available to download for free. This platform can assess all possible 2-, 3-, 4-, and 5-way combinations for hundreds of congenital anomaly categories, outputting a metric based on the observed: expected prevalence ratio for each combination. An adjustment factor accounts for non-specific, generalized clustering of MCAs, which can lead to inflated estimates. To demonstrate proof-of-concept and feasibility, we applied our platform to data from the Texas Birth Defect Registry.
Results: When applied to data from a large congenital malformation surveillance program, our platform performed efficiently (e.g., analyzing 1.5 million 5-way combinations in less than a day). As expected, congenital anomalies that are known to be common among cases with nonsyndromicspina bifida had large adjusted observed to expected ratios, as did those known to be common among cases with trisomy 21. We estimate that computation of data from large birth defect surveillance programs will require less than a week.
Discussion and Conclusions: Our platform will allow for large-scale, systematic assessment of MCA patterns in large surveillance programs. This may help facilitate identification of new MCA patterns (e.g., associations) and/or better characterize known syndromes.

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THE UTILITY OF ROUTINE HOSPITAL ADMISSION AND MORTALITY DATA TO IDENTIFY SPINAL MUSCULAR ATROPHY TYPE 1 CASES IN ENGLAND

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Background and Objectives: Collecting data on rare diseases is challenging, as data are scarce and often fragmented. The National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) is evaluating the utility of routinely collected national data sources to support rare disease registration in England. In this study, we aimed to estimate population and birth prevalence for Spinal Muscular Atrophy Type 1 (SMA1) for England using Office for National Statistics (ONS) mortality data and national hospital admissions (HES) data.
Methods: We identified admissions in HES data with a finished consultant episode from April 01, 2008 to March 31, 2018 containing a diagnostic code of ICD-10 G12.0 Infantile spinal muscular atrophy, type I. We identified cases of SMA1 on the NCARDRS data management system. Vital status of patients was traced using the national Summary Care Record. Deaths from 2008-2016, with G12* Spinal muscular atrophy and related syndromes in the coded cause of death (COD) fields extracted from the mortality dataset. Free text COD fields were reviewed and deaths indicating either SMA1, SMA0, or SMA were identified. The resulting datasets were linked using the National Health Service (NHS) number.
Results: Using ONS mortality data and HES data, we identified 380 suspected SMA1 cases. We estimated a population prevalence of 1.9 per million (95% CI: 1.6-2.3) and a birth prevalence of 6.2 per 100,000 births (95% CI: 5.6-6.8).Of the 307 deaths in cases born in 2008-2016, 213 (69%) were ascertained from both HES and ONS mortality data; 14 (5%) from HES and 80 (26%) were from ONS mortality data only. One case was ascertained from NCARDRS only.
Discussion and Conclusions: We estimate that 1 in 16,150 babies born in England have SMA1 and that in mid-year 2016, there were 107 people living with SMA1 in England. Around one-quarter of deaths attributed to SMA1 in the mortality data had no code indicating SMA1 in the HES record in the time frame examined. These findings reinforce the need for a multi-source approach to case registration, including genetic diagnoses and subtyping. This will reduce case misclassification and improve the ascertainment usefulness of the data for healthcare planning and research.

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CONGENITAL MALFORMATIONS IN CHILDREN BORN TO MOTHERS WITH DIABETES IN THE CZECH REPUBLIC IN THE PERIOD 2000 – 2015

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ICBDSR Registry on which the work is based: National Registry of Congenital Anomalies of the Czech Republic

Background and Objectives: Diabetes mellitus (DM) in pregnancy is widely recognized as a risk factor for adverse prenatal development. The effect of DM in pregnancy on the prevalence of congenital anomalies has not been studied in our Registry. We present a retrospective epidemiological analysis of the prevalence of congenital anomalies in children born to mothers with DM compared to children born to mothers without DM.
Methods: We used data from the National Register of Reproductive Health at the Institute of Health Information and Statistics of the Czech Republic (IHIS CR) for the period 2000-2015. In our work, we divided all children born in the Czech Republic into two groups: children born to mothers with (any form of) diabetes mellitus in pregnancy and children born to mothers who did not have this disease. We also grouped children by those born with congenital anomalies (CA) and those born without CA.
Results: In the 16-year period (2000-2015), a total of 678,449 children were born in the Czech Republic, of which 52,123 children were born to mothers who were pregnant with DM. We also analyzed the representation of children born with CA in groups of mothers with DM and without DM. Prevalence of CA between the DM (3.97%) and non-DM (3.87%) groupswas very similar and the difference was not statistically significant ($p = 0.236$). Another analysis compared the prevalence of a specific CA groups among diabetic and non-diabetic mothersamong all children (with or without CA). Statistically significant differences were observed in Q20-Q28 and Q50-Q56 (higher incidence in DM mothers) and Q65-Q79 (lower incidence in DM mothers). We then analyzed the age of pregnant women. Diabetics in the whole set (regardless of CA) were on average 2 years older. This difference was statistically significant ($p <0.001$).
Discussion and Conclusions: Our results did not show an overall increased risk of birth of a child with any CA in women with DM in pregnancy. However, we observed an increased risk for two specific groups of CA: congenital heart defects and congenital malformations of the genitals. For a group of pregnant women with DM in pregnancy, we further observed a statistically significant increase in age versus women without DM.

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RECURRENT FETAL ARTHROGRYPOSIS: AN UNEXPECTED DIAGNOSIS OF FETAL ACETYLCHOLINE RECEPTOR INACTIVATION SYNDROME

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ICBDSR Registry on which the work is based: Not applicable

Background and Objectives: Arthrogryposis encompasses a heterogeneous group of conditions with varying etiologies. Fetal acetylcholine receptor (AChR) inactivation syndrome is caused by maternal AChR antibodies crossing the placenta and inhibiting fetal AChR at the neuromuscular junction resulting in decreased or lack of fetal movement, thereby causing contractures. While this condition is well established in cases of maternal myasthenia gravis, it has only been described in pregnancies of three clinically unaffected mothers. We report a case and clinical details of recurrent fetal arthrogryposis mediated by maternal AChR antibodies in a woman with no clinical signs or symptoms of myasthenia gravis.
Methods: Investigations performed on the first fetus included chromosomal microarray, a 58-gene arthrogryposis panel, myotonic dystrophy gene testing, and fetal autopsy with neuropathology. Rapid aneuploid detection was conducted on the second fetus. After the first pregnancy, the ova donor was tested with a 94-gene myopathy panel. Antibody testing for the partner who carried the pregnancies included acetylcholine receptor, MuSK, and LRP4 antibodies.
Results: The investigations performed on the first fetus were unremarkable other than a heterozygous pathogenic variant in EXOSC3 detected by the arthrogryposis panel. This mutation is known to be associated with autosomal recessive pontocerebellar hypoplasia. However, fetal autopsy did not identify posterior fossa abnormalities on neuropathology. In addition, given the recurrence of arthrogryposis with a different sperm donor, this autosomal recessive condition was not considered the likely diagnosis. Autopsy did not identify mitochondrial anomalies nor loss of anterior horn cells in the spinal cord. Interestingly, the surrogate mother was found to be AChR antibody-positive with a titer of 6.1 nmol/L and was shown to have inefficiency in neuromuscular junction function on single fiber EMG despite having no clinical features of myasthenia gravis. Accordingly, the clinical diagnosis was fetal AChR inactivation syndrome.
Discussion and Conclusions: In contrast to cases of known maternal myasthenia gravis, fetal AChR inactivation syndrome is less commonly suspected when the mother is clinically asymptomatic. This case highlights maternal AChR antibody testing as an important investigation to consider in cases of undiagnosed fetal arthrogryposis, even if the mother does not show any signs or symptoms of myasthenia gravis. As this condition is mediated by maternal antibodies, there is a very high recurrence risk, possibly as high as 100%, in future pregnancies and there exists a potential for treatment in the form of IVIG.

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HOSPITAL CENTERED SURVEILLANCE AT BIRTH 2011-2018 AND ASSESSMENT OF ENVIRONMENTAL EFFECTORS OF CHANGES IN REPRODUCTIVE HEALTH IN GAZA, PALESTINE REVEALS LONG-TERM IMPACT OF METALS WEAPONS-REMNANTS

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ICBDSR Registry on which the work is based: Not Applicable

Background and Objectives: In line with World Health Organization aims to assess health at birth and its environmental determinants, we conducted prospective longitudinal studies to obtain prevalencein 2011 and 2016-2018 of babies born preterm, with birth defects, and low birth weight at term in Gaza, Palestine and investigated the role of heavy metals in the environment in impacting these outcomes.Gaza was attacked militarily 3 times in the last 10 years with weaponry shown to discharge toxic and teratogenic heavy metals. Mothers directly exposed to these attacks had higher heavy metal load than those unexposed. The metals in contaminated mothers crossed the placenta.Investigation of changes in prevalence of adverse birth outcomes showed associations with maternal contamination with heavy metals and with metal distribution in time and over the territory. The role of confounders and genetic factors for this increased prevalence were ruled out.

Methods: Hospital based study in Shifa Maternity, Gaza included all women delivering in 2011 (n=4049), 2016 (n=6104), 2017 (n=2148), and 2018 (n=2900). EUROCAT questions were included in the questionnaire developed ad hoc by integrating 70 queries about specific local socioeconomic and physical environments (using data from the United Nations (UN) organization and local environmentalists). CD10 was used for diagnosis of major structural birth defects. The same methodology and procedures allowed for comparison of surveillance data. The load of 23 metals was determined by ICP/MS in the hair of mothers and newborns. Analysis for trend in changes in health across time was calculated using the chi-square test; logistic regression analysis identified predictor factors for negative outcomes. Comparison of metal loads with standards from outside the war area and between groups of women divided according to exposure or residence was conducted using Wilcoxon/Kruskal-Wallis tests; comparison of metal load across birth years was calculated using the median test.

Results: Prevalence of preterm birth and birth defects increased from 2011. No change in known co-factors of reproductive health justified this rise. Military attacks in 2012 and 2014 introduced a major novel risk for adverse outcomes at birth: contamination by teratogenic heavy metals weapon-remnants, which remain stable in the environment, accumulate in humans, and induce multiple epigenetic changes, was highest in women experiencing direct attacks. Delay in removal of rubble and weaponry and impaired rehabilitation of waste management increased the risks. Heavy metal load in women and babies were highest in 2016 for those living near unmanaged waste and predicted preterm birth and birth defects.Incidence of birth defects was steady in 2018, and the percentage of mothers housed in proximity to unmanaged waste was more than halved from 2017, due to partial reconstruction. The surveillance coupled with testing of heavy metal contamination show the role of these as inducers of negative birth outcomes.

Discussion and Conclusions: In Gaza, prevalence of birth defects grew steadily since Israeli withdrawlin 2005 and started attacks with weaponry containing heavy metals. Incidence of negative birth outcomes in 2011 was paralleled by higher contamination with weapons-remnant heavy metals among mothers exposed to the attacks and their babies. Two years after the 2014 attacks, contamination by heavy metals and prevalence of birth defects and preterm birth were highest for residents near unmanaged waste, which became "hot spots" of metal contamination. No changes in prevalence were observed in 2018, when residences nearest to unmanned waste had greatly decreased. Our interpretation of the data is that heavy metals remnants of weapons are a major factor for the decrease in reproductive health in Gaza and for increased perinatal death, documented by UN Relief Works Agency. High loads of mercury and

Manduca, P a kol. Hospital centered surveillance at birth 2011-2018 and assessment of environmental effectors of changes in reproductive health in Gaza, Palestine, reveals long-term impact of metals weapons-remnants, s. 21-22.

barium in newborns associated with maternal exposures and with birth defects or preterm births in 2011 and 2016. The role of other metals is also implied.

Manduca, P a kol. Hospital centered surveillance at birth 2011-2018 and assessment of environmental effectors of changes in reproductive health in Gaza, Palestine, reveals long-term impact of metals weapons-remnants, s. 21-22.

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MAJOR BIRTH DEFECTS AMONG OFFSPRING OF IOWA AGRICULTURAL HEALTH STUDY APPLICATORS

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Background and Objectives: Studies of parental pesticide exposure continue to raise concerns about its potential teratogenicity; however, findings to date are equivocal, owed in part to several study limitations. To address these limitations, we investigated major birth defects among offspring of Iowans enrolled in the United States Agricultural Health Study (AHS), a prospective study of chronic disease among pesticide applicators and their spouses.
Methods: We linked applicator and spouse data from the AHS with Iowa birth data (1972-2014) and identified 42,460 liveborn offspring, including 24,256 born from 1983-2010. Data for these 24,256 offspring were linked with surveillance data from the Iowa Registry for Congenital and Inherited Disorders. We investigated relations between paternal application of 121 pesticides shortly before or during the index pregnancy and 9 birth defect groups in offspring. Associations were estimated for defect groups with ≥5 exposed offspring compared to offspring of unexposed applicators per pesticide, adjusting for relevant covariables.
Results: We identified 400 (1.6%) of the 24,256 offspring to have a major birth defect, with heart, genitourinary, gastrointestinal, and musculoskeletal defects most frequently observed. Overall, 32 of the 121 pesticides had ≥5 exposed offspring in a case group, producing 128 estimated associations. We observed positive associations (adjusted odds ratios 1.5-3.0) for 34 pesticide-case group combinations. Eight pesticides produced positive associations in two or more case groups and included: S-Ethyl-Dipropylthiocarbamate (craniofacial, gastrointestinal); petroleum oil/distillates (craniofacial, gastrointestinal, musculoskeletal); pendimethalin (craniofacial, musculoskeletal); permethrin (craniofacial, genitourinary, heart, musculoskeletal); terbufos (craniofacial, musculoskeletal); carbofuran (craniofacial, genitourinary, musculoskeletal); carbaryl (craniofacial, musculoskeletal); and coumaphos (genitourinary, musculoskeletal).
Discussion and Conclusions: Although limited to liveborns, our findings from this large cohort suggest that paternal application of several pesticides shortly before or during early pregnancy contributed to an increased risk of major birth defects, particularly craniofacial, musculoskeletal, and genitourinary defects. Future work will investigate major birth defects among pregnancy losses and terminations.

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MATERNAL MTHFR 677 CT/TT GENOTYPE IS ASSOCIATED WITH INCREASED RISK OF CONGENITAL HEART DEFECTS IN OFFSPRING

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ICBDSR Registry on which the work is based: Not Applicable

Background and Objectives: Congenital heart defects (CHD) are among the most common congenital anomalies worldwide, occurring in approximately one in one-hundred living newborns. Heart defects at birth occur as an isolated malformation, but are also associated with other anomalies or occur as part of a syndrome. The etiology of CHD is only partly illuminated, but most CHD are thought to be of complex multifactorial origin, with one or more alleles at a number of loci interacting with environmental factors. Maternal multivitamin supplementation containing folic acid reduces the risk of neural tube defects, and evidence suggests that it may be associated with other reproductive outcomes, including CHD. Our previous results revealed in pregnant women with prenatally diagnosed CHD, an association of particular alleles of genes important in folic acid metabolism.

Methods: The purpose of our study was to establish the frequency of common single nucleotide polymorphisms in the MTHFR and MTHFD1 genes among women from West Ukraine in cases of prenatally diagnosed CHD and replication of the obtained results using a larger number of cases. Genotyping of MTHFR 677C>T (rs1801133), MTHFR 1298 A>C (rs1801131), and MTHFD1 1958G>A (rs2236225) polymorphisms was performed in 67 women with prenatally diagnosed CHD in the fetus and in 62 healthy women. The molecular- genetic analysis was performed by Polymerase Chain Reaction and Restriction Fragment Length Polymorphism analysis. Statistical analysis was conducted by chi-square tests and odds ratio (OR) estimation.

Results: We did not observe any significant differences in the MTHFD1 1958G>A (rs2236225) genotype and alleles frequencies between case and control mothers ($p>0.05$). The frequency of MTHFR 677CC genotype was significantly more often in control compared with case mothers (51% and 32%; $p=0.04$) andwas associated with a two-fold decreased risk in delivering offspring with CHD [OR=0.46 (95% CI: 0.22 - 0.96)]. The genotypes MTHFR 677CT or MTHFR 677TT were associated with two-fold increased risk in delivering offspring with CHD [OR=2.17 (95% CI: 1.04 – 4.51)]. In cases of MTHFR 1298 A>C and MTHFD1 1958G>A polymorphisms, the frequencies of alleles and genotypes were not significantly different in women with prenatally diagnosed CHD in the fetus compared to controls ($p>0.05$).

Discussion and Conclusions: Maternal MTHFR 677 CT/TT genotype seems to be highly probable risk factor for Ukrainian women to have a child with CHD, whereas the MTHFR 677CC genotype provides a credible protective effect. Studies on the relation between MTHFR 677CT polymorphism and congenital anomalies mainly focused on neural tube defects, a neural crest derivate. In our study, the maternal MTHFR 677CT and TT genotypes appeared to be genetic risk factors, in particular, for CHD in offspring. This observation supports the hypothesis that impaired folate metabolism interferes with the developing heart, possibly by affecting neural crest cells. Our results suggest a possible protective effect of periconceptional folic acid supplementation. It is extremely important that supplementation be performed in countries where food fortification with folic acid is not yet the norm.

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PATIENT´S UMBRELLA ORGANISATION ACTIVITIES IN THE FIELD OF RARE DISEASES

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Background and Objectives: Slovak alliance for rare diseases is a nongovernmental, nonprofit organization, established in December 2011.
Methods: Its main aims are to increase public awareness about rare diseases and to advocate for all rare disease patients at the national level. We support and actively create policy and decision-making process, as well as gain political influence and social recognition for rare disease patients and families. Currently, it represents 23 different rare disease patient organizations and several patients or patients groups.
Results: We are well-recognized in the European rare disease patient forum EURORDIS, actively participating in the EUROPLAN project, as well as at the national level within the working group at the Ministry of Health for rare diseases. Together we prepared the National Strategy Plan, as well as the action plan for rare diseases in Slovakia. The Slovak Alliance for Rare Diseases creates a neutral platform for interaction and discussion of all stakeholders: policymakers, professionals, health care providers, scientist, industry, and patients.
Discussion and Conclusions: With the support of national rare disease policy, we cooperate with professionals at ORPHANET or the Slovak Medical Society. For patients and patient groups, in cooperation with EURORDIS, we provide several services as Rare Connect or Rare Barometer voices. Because Slovakia, together with Malta and Greece, are the only countries that are not involved in European reference networks, we strongly support the participation of Slovak health care professionals and specialists in this unique and challenging health care environment. Another big challenge that we continue to work on is holistic care for rare diseases patients in Slovakia.

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ULTRASOUND (PRE)POSTNATAL SCREENING OF CONGENITAL UROPOIETIC DEFECTS IN SLOVAKIA

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Background and Objectives: The main purpose of neonatal sonographic screening of the urinary system is to find defects that need to be resolved in the neonatal period or early infancy. Our objective was to establish the incidence and structure of congenital malformations in Slovakia and compare the effectiveness of prenatal and postnatal screening to retrospectively determine the proportion of prenatal diagnostics in revealing congenital malformations of the urinary system in the Slovak Republic during the past decade.
Methods: In total, 38,496 newborns were enrolled in the research, representing 66.5% of the total population of 57,969 newborn children during 2017–2018. All newborns underwent postnatal sonographic screening of the uropoietic system. In cooperation with the National Center for Health Information (Slovak Republic), we obtained other statistical data (prenatal screening data, etc.).
Results: Postnatal screening: Grade 1 of the pelvicalyceal system dilatation according to Hofmann's classification occurred in 7%, grade 2 in 0.53%, grade 3 in 0.21%, and grade 4 in 0.1% of cases. One sided agenesis occurred in about 0.1% of patients. Renal cysts of various etiologies revealed in about 0.05% of children. Prenatal screening: The proportion of the prenatal diagnosis of congenital developmental defects of the urinary system increased from 13.3% in 1995 to 29.1% in recent years (an average of 24.4%). The incidence rate of congenital urinary malformations requiring nephrological and urological care and often intervention of urologist as early as in the neonatal period composes 31 out of 10,000 children. The prenatal diagnosis currently used in Slovakia finds only one-quarter of congenital developmental defects of the urinary system.
Discussion and Conclusions: The high incidence rate and low level coverage of prenatal diagnostic screening are clear arguments for the implementation of postnatal screening in all neonatal departments of the Slovak Republic.

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MATERNAL DEPRESSION AS A THREAT TO CHILDREN´S HEALTH: TREAT OR NOT TO TREAT IT?

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Background and Objectives: At present, affective disorders are among the most commonly diagnosed mental diseases. In pregnancy, they can occur as pre-delivery depression, recurrent depressive disorder, or postnatal depression. The estimated prevalence of depressive disorders in pregnancy is approximately 9-16%, with some statistics reporting up to 20%. Approximately 2-3% of pregnant women take antidepressants during pregnancy, and the number of mothers treated increases by birth to 5-7%. Treatment of depression during pregnancy and breastfeeding is a controversial issue, as antidepressants can negatively affect the developing fetus.
Methods: This review presentation provides up-to-date knowledge on the effects of maternal depression and/or antidepressant treatment on the health of the mother, fetus, and newborn.
Results: According to epidemiological studies, the effects of treated depression in pregnancy are related to premature birth, decreased body weight of the child, intrauterine growth retardation, neonatal adaptive syndrome, and persistent pulmonary hypertension. However, untreated depression can adversely affect maternal health and increase the risk of preeclampsia and eclampsia, as well as of subsequent postnatal depression, which can lead to disruption of the mother-child relationship.
Discussion and Conclusions: Based on the aforementioned facts, the basic question arises as to whether or not to treat depression during pregnancy and lactation.

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EFFECTS OF MATERNAL DEPRESSION AND/OR ANTIDEPRESSANT TREATMENT ON NEUROBEHAVIORAL DEVELOPMENT OF RAT OFFSPRING

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Background and Objectives: Depressive disorders are common among pregnant women. They represent a serious risk for mother and developing fetus and newborn. Nevertheless, pharmacotherapy during gestation and lactation raises a number of questions, which are mainly related to the safety of psychiatric drugs during this period. Antidepressants cross the placental and blood-brain barrier and are excreted into the breastmilk. Therefore, antidepressant treatment could interfere with the sensitive developmental processes in the brain and may have neurobehavioral consequences in later life. Venlafaxine as a representant of serotonin and noradrenaline reuptake inhibitors acts by blocking presynaptic transporters of serotonin and noradrenaline. The FDA has classified venlafaxine regarding to pregnancy risk as a category C, which means that there are not enough well-controlled studies examining safety to the developing fetus and child.
Methods: The aim of this work was to investigate the effects of maternal stress of the rat dams on the hippocampal excitability of the pups right after the birth. Neurobehavioral consequences of maternal stress and or venlafaxine therapy were analyzed during adolescence and in early adulthood. To do this, stressed and non-stressed Wistar rat dams were treated with either venlafaxine (10 mg/kg/day) or vehicle. Venlafaxine was administered to the dams from day 15 of gestation to day 20 post partum (PP) via cookies. On day 1 PP, all litters were culled and on day 21 PP, they were weaned from their mothers. Neurobehavioral consequences of maternal stress and/or venlafaxine therapy were analyzed during adolescence (35-40 postnatal days) and in early adulthood (75-80 postnatal days).
Results: Administration of venlafaxine during gestation and lactation did not affect selected reproductive, neurobehavioral, and hippocampal plasticity variables of rat offspring. However, maternal stress caused alteration of neuronal development of offspring manifested in depolarized resting membrane potential, suppressed depolarization-activated generation of action potentials, and increased spontaneous activity of neonatal hippocampal neurons developing in vitro. Effects of maternal stress were evident also at the behavioral level. Current work has shown that maternal stress can be associated with higher general activity of the offspring during adolescence and with anxiety-like disorders and inattentive behavior of adult offspring.
Discussion and Conclusions: Maternal stress during gestation and lactation can interfere with functional development of the brain and cause long-term behavioral changes at the level of neurobehavioral adaptations.

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SJOGREN'S SYNDROME AND PREGNANCY: MANAGEMENT OF THE DISEASE AND EFFECT ON THE FETUS

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Background and Objectives: Autoimmune diseases do not negatively affect the ability of the spontaneous conception of a woman. However, in patients with autoimmune disease, complications are likely to be expected both on the pregnancy itself and on the significant negative impact on healthy fetal development. Problems complicated by these disorders have a high clinical impact on both pregnancy and disease. The effect of autoimmune disease on pregnancy varies depending on the type of maternal disease, disease activity, severity of organ damage, antibody profile, and treatment. Sjögren's syndrome is an autoimmune disease with a high prevalence of anti-SS-A (anti-Ro) and anti-SS-B (anti-La) antibodies. Antibodies to SS-A are associated with congenital blockage of cardiac transmission (AVB).
Methods: A set of 5 patients and a review of the pregnancy outcomes in women with Sjögren's syndrome.
Results: Data on pregnancy outcomes in primary Sjögren syndrome are rare.
Discussion and Conclusions: Women with Sjögren's syndrome require prenatal counseling to explain the risks and the need for disease control before conception. High-risk pregnancy can be optimally manage by a multidisciplinary team.

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CYSTIC AND POLYCYSTIC KIDNEY IN THE FETUS: MANAGEMENT OF PREGNANCY

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Background and Objectives: Congenital cystic kidney disease may manifest during the fetal period or during the childhood and adulthood. Their impact on the body depends on the type of the disease, bilateral or unilateral renal impairment, or compensatory hypertrophy of the kidney. In the case of syndrome, it depends on the complex involvement of the organism. Diseases can be divided into a non heriditary and heriditary forms, which we will discuss in more detail. These are relatively rare anomalies. Based on heredity, we distinguish autosomal recessive and autosomal dominant polycystic kidney disease. The most common diagnostic method is prenatal ultrasonography. A characteristic picture is the cystic dilatation of the collecting ducts with often associated liver involvement. The disease may progress to renal failure.
Methods: We present case reports of prenatally diagnosed polycystic disease by ultrasonography.
Results: The aim is to clarify the importance of early diagnosis and intervention in congenital cystic kidney diseases.
Discussion and Conclusions: Pregnancy and childbirth management is individual. After birth, the condition of the child depends on the type of disability and clinical condition.

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DIAGNOSIS AND PROGNOSIS OF FETUSES WITH CMV INFECTION: PREGNANCY MANAGEMENT AND PROGNOSIS

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Background and Objectives Cytomegalovirus (CMV) is the most common cause of intrauterine viral infection. In most women the course is asymptomatic. This is the main reason for late diagnosis, often accompanied by the current neurological defect of the fetus. Congenital CMV infection can lead to abortion, stillbirth, or fetopathy with severe organ defects. To prove the presence of infection, we can use a serological examination, which is not a routine part of prenatal diagnosis today. Other diagnostic methods are amniocentesis and cordocentesis, through which we confirm the presence of viral DNA in amniotic fluid and fetal blood. Indirect signs of infection can be visualized by ultrasonography or magnetic resonance.

Methods In this work we focus on ultrasound diagnosis of fetal CMV infection. Infection is manifested by defects of the central nervous system, extracerebral abnormalities, and pathological changes in amniotic fluid or the placenta. We present a case report from our department, in which the fetus had ultrasound abnormalities suspicious of fetal CMV infection and we used amniocentesis to prove presence of infection.

Results: Fetal CMV infection was confirmed by the presence of CMV DNA in amniotic fluid.

Discussion and Conclusions: The prognosis of fetuses with congenital CMV infection depends on affected organ and degree of defect. When fetal infection is proven and we confirm ultrasound findings of the brain, abortion is recommended.

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A CASE STUDY OF THE POTENTIAL MEASURES TAKEN REGARDING EFFECTIVE MINIMIZATION OF CONGENITAL BIRTH DEFECTS IN BANGLADESH

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ICBDSR Registry on which the work is based: Not Applicable

Background and Objectives: Birth defects or congenital defects are anomalies that can be structural or functional which causes 3-6% of child illness. In South East Asia, out of 1.4 million reported births, 0.84% had birth defects. These defects are most prevalent in muskoskeletal by 27% and nervous system defects by 14%. Spina Bifida makes up 69% of neural tube defects (NTDs). Congenital defects of the nervous system were found in 52% of still born babies. In Bangladesh, no general trend of birth defects has been established. The patient's family history, family history, physical examination and follow-up are imperative in enabling detection of birth defects at prenatal stage. There is deprivation of proper healthcare due to practice of child birth and care in rural homes. Tradition, illiteracy, poverty and traveling distance primary drive of such birth defects. The lack of surveillance and prenatal screening prevent collective actions from being taken to increase awareness and intervention of birth defects.

Methods: In order to review the state birth defect intervention, data reported by various articles and hospitals were analyzed. Data from cases reported by from 2008 to 2012 by Chittagong Medical College and Hospital (CMHC) was consulted, along with data from Combined Military Hospital (CMH). Data from Bangladesh health bulletin, Dhaka Medical College Hospital and Bangabandhu Sheikh Mujib Medical University Hospital and government hospitals of various districts of Bangladesh were collected and sampled in groups and analyzed to study the pattern of congenital birth defects in Bangladesh.

Results: 13% of neonatal causes of death in Bangladesh are attributed to congenital anomalies. 18% of these were of the gastrointestinal system and 16% of the genitourinary system. In CMCH, 44.61% of surgical admissions in pediatric had birth defects. 3.97% of admissions due to birth defects died, making up 51.49% of the pediatric surgical deaths. The most common causes of deaths in these cases were due to ARM and Gastroschisis. CMH reports cases of CHD (congenital heart disease) being present in 2.5% of live births among which Down's syndrome was a common case of somatic anomaly. In reports of 1741 neonatal surgical patients, ARM was found to be the cause of 32.17% of cases, followed by Hirschsprung's disease in 19.36% cases. Pelvic Colostomy and conservative modes of treatments were the most frequent, making up 30% and 28% respectively. Of these, 10.65% cases of conservative treatment resulted in death, while 12.52% cases of surgical intervention ended in death and 8.53% in wound infection.

Discussion and Conclusions: 67% of the deaths reported by CMCH were neonatal, which were attributed to the absence of a neonatal ICU. Currently, majority of treatments for birth defects occur after birth, and are surgical in nature. As reported by CMH, early detection of developing abnormalities was successfully achieved by neonatal screening. Establishment of facilities and units offering treatment and detection of these birth defects can solve a vast majority of problems occurring due to birth defects. The lack of screening facilities and counseling prevents early awareness of the presence of these abnormalities. No government supported organizations offer neonatal and genetic screening, making the vast majority of the population unaware of the possibility of such services. The lack of consultation and concern by families for the possibility of birth defects until the symptoms are glaringly obvious lead to actions being taken too late instead of early prevention and treatment being sought out.

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POLYDACTYLY BIRTH PREVALENCE IN THE EMILIA ROMAGNA REGION: IS IT INCREASING?

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ICBDSR Registry on which the work is based: IMER (Indagine sulle Malformazioni congenite in Emilia-Romagna) Registry, Italy

Background and Objectives: There have been few reports on the prevalence of polydactyly, particularly in Italy, even if it is considered to be one of the most common congenital hand anomalies, noticed immediately at birth. It is almost always an isolated finding in healthy infants, but it could be associated with other birth defects and is a feature in about 300 syndromes. Polydactyly is heterogeneous, ranging from a broadening of a distal phalanx, to complete duplication of one or several fingers/toes. Surgical treatment is often needed, to reach a functional as well as an aesthetic goal. Epidemiologic data regarding polydactyly are important, considering its frequency, to allow monitoring of public health and distribution of resources.
Methods: The aim of this work is to describe prevalence of polydactyly, using a population-based database of all malformations diagnosed in Emilia-Romagna, Italy, (IMER Registry). IMER is since 1981 a full member of EUROCAT, a European network of population-based registries for the epidemiologic surveillance of congenital anomalies. A description of the Registry can be found at the EUROCAT website (http://www.eurocat-network.eu/membersandregistrydescriptions).
IMER registry links and integrates hospital discharge records (SDO), birth certificates with cases reported by referral clinicians to identify all structural malformations diagnosed within one year of life regarding live birth, fetal death or termination of pregnancy due to fetal malformations. Each IMER report identified with the ICD 9 BPA code 755.0 from 2008 to 2017 was considered. The overall prevalence rate and associated factors were calculated using denominator data from the Regional health authority birth database.
Results: In 2008-2017 there were 372,507 live births in Emilia Romagna, and 435 cases of polydactyly (P), for a prevalence of 11.6 per 10,000, increasing from 9.2 in the 2008 to 15.1 per 10,000 in 2017. In the same period, EUROCAT prevalence is 9.9 per 10,000, stable. Isolated cases were 85% of the P, increasing from 7 in 2008 to 13 per 10,000 in 2017, while multiples (9%), syndromic (4%) and chromosomic cases (2%) are stable. Two changes in methodology occurred: from 2009 SDO were added to IMER; in 2013 all P from SDO were considered. Cases notified directly to the registry were 50% of cases each year from 2009.Italian mothers were 46% in P and 70% in the reference population (RP); West African mothers (WA) were 21.2% of P and 2.8% in the RP. WA were increasing during the study period (2.4% to 3.7%) whilst their percentage is stable in the affected births. Prevalence of P in WA is 86 per 10,000.The male: female ratio is 1.5. No increase nor difference in median maternal age was seen
Discussion and Conclusions: This work allows us to define prevalence of polydactyly in the IMER Registry. The value of 11.6 per 10.000 and the increase in the period 2008-2017 are probably related to demographic characteristics of Emilia Romagna Region. This could also explain the difference between IMER Registry and the EUROCAT mean due to different demographic characteristics. In our study prevalence of polydactyly in West Africans is 86 per 10,000, and in the whole Region mothers from this geographic area seem increasing. Changes of the methodologies can contribute to the increase of the prevalence between 2008 and 2017, but this effect seems less important for this specific malformation. None of the other studied factors seems to be related to the increase. This study highlights the importance of monitoring citizenship in understanding prevalence change, and also the possibility to use European registries to estimate congenital anomaly prevalence in low income countries where registries are not present.

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ROLE OF IT, HEALTH INSURANCE & HOME BASED CARE IN IMPROVING QUALITY OF LIFE, PSYCHOSOCIAL FRAMEWORK & REDUCING OUT OF POCKET EXPENSES IN A FAMILY WITH A CHILD WITH BIRTH DEFECTS

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ICBDSR Registry on which the work is based: Not Applicable

Background and Objectives: India is a diverse country & has a high birth Cohort of 26 million of which 3% - 4% has birth defects (BD). The issues of availability, accessibility and affordability (AAA) of healthcare for these with BD need to be addressed. There is no medical insurance - Government &/or private as Neonates are not included in insurance policy till 3 months of birth &, BD till whole life, if not insured before pregnancy. The impact on psychosocial framework and quality of life (QOL) due to AAA of healthcare & financial implications on the affected families of children with BD was evaluated and recommendations to improve quality of services by advocating insurance coverage and use of IT to improve communication and home based care to decrease out of pocket expenses were given.

Methods: A Retrospective study involving families of 50 children with BD from neonates to 6 years of life from urban and semi urban areas of Delhi and NCR was undertaken with this background. A questionnaire was given to the parents and the extended family which included how they viewed the BD, how they could get access to specialized healthcare, gaps thereof, any support from Government or insurance sector, whether IT for communication with family meant lesser trips to hospital, whether home care where possible helped to decrease out of pocket expenses which eased the financial burden to the family and finally the impact of all these on the Quality of life (QOL) and psychosocial framework of the family

Results:

1. There were many myths associated with BD, like something wrong with mother, curse of God or bad Karma.
2. The Elderly were mostly positive and supportive.
3. Lack of timely referral due to lack of knowledge and manpower, limited specialized facilities, distance from facility & poor follow up, large out of pocket expenses led to none or incomplete management
4. IT as a tool via use of SMS and WhatsApp aided in easier communication. Follow up was not as good in Urban as in rural areas where ASHA and ANMs give personalized care.
5. Psyche of the couple became one of guilt, shame, helplessness & inadequacy from the antenatal period itself if the BD was informed to them & they avoided all cultural norms associated with pregnancy.
6. There was increased marital discord especially if defect was severe or necessitated prolonged hospital visits or therapy. Worse if one working member had to bear the financial burden
7. Very few Insurance companies provide cover for BD's

Discussion and Conclusions: Presence of BDs impacts the psychosocial framework and QOL of the affected family. The nature of the BD and its severity impact these proportionate to the short or long term disability that the BD entails, the duration and frequency of hospital visits required, ease of access to care and associated out of pocket expenses. Logistic support by the extended family, health care providers and Insurance has a role in alleviation of these stressors. Communication via IT has become important and will have definite increase in role in times to come. Based on these inputs certain recommendations were derived at i) To have a register of all BD's, ii) Free treatment for all under the Rashtriya Bal Suraksha Yojana (RBSY) & child protection. iii) Follow up by the Accredited Social Health Activist (ASHA) to help in home based care & iv) Follow up by skilled staff/ Doctors by Tele Medicine to be done to reduce cost & psychological burden.

Gambhir, A – Gambhir, S – Gambhir, A. Role of information technology, health insurance, and home-based care in improving quality of life, psychosocial framework, and reducing out-of-pocket expenses in a family with a child with birth defects, s . 34.

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GRAPH THEORY AS A STUDY MEANS OF CONGENITAL ANOMALIES ASSOCIATIONS

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ICBDSR Registry on which the work is based: Estudio Colaborativo Latino Americano de Malformaciones Congénitas (ECLAMC)

Background and Objectives: Since thalidomide and rubella tragedies, surveillance of birth defects has become an public health activity. In order to identify new teratogens, association studies between congenital anomalies have been carried out. To date, two approaches have been used to analyze this associations. The first focuses on a specific anomaly and determines the association degree with other anomalies. The second approach was based on the cases clustering considering each anomaly as a binary variable. The graph theory, offers an integrating approach, allows to analyze the complete set of anomalies and each of them in particular. A graph is constituted by nodes that represent entities and edges that represent the relationship between entities. In recent years this approach has enriched many study areas, for example, proteins interactions and diseases associations. The objective of this work is to analyze the feasibility of this approach to study anomalies complexes and associations.
Methods: We used 170,430 cases with at least one anomaly recorded in the Estudio Colaborativo Latino Americano de Malformaciones Congénitas (ECLAMC) between 1967 and 2017. We use the ECLAMC anomaly coding system, which has 207 codes. We used the volume-adjusted Chi-Squared independence test to determine the association strength between anomalies. To partition the graph we used Infomap method.
Results: The constructed graph had 98 nodes (68 major anomalies and 30 minor) and 275 edges. Its degree distribution presented a greater adjustment to an Log-Normal distribution than to a Poisson distribution. The graph partition generated 13 anomalies groups. The minor anomalies presented an Eigenvector centrality scores greater than the major anomalies (Wilcoxon p-value 0.0018).
Discussion and Conclusions: The congenital anomalies graph obtained differs from random graphs by their degree distribution. The Eigenvector score would show that the minor anomalies were associated more and with highly associated anomalies than the major anomalies, but this result could arise from underreporting of the minor anomalies. The anomalies complexes identified through graph theory would correspond to those found in the literature, such as Patau syndrome. These results would imply that it is feasible to use graph theory for the study of congenital anomalies associations.

NATIONAL REGISTRY OF CONGENITAL ANOMALIES IN CHILE

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Registry on which the work is based: RENACH, Chilean National Registry of Congenital Anomalies

Background and Objectives: Chile has a population of 17,574,003 inhabitants. In 2016 there were 231,748 live births (LB), 99.7% occurring with professional assistance, the infant mortality rate was 7.0 per 1,000 births. Congenital anomalies (CA) were the second leading cause of death in infants under 1 year, representing 42.5% of infant mortality in 2016.The Chilean Ministry of Health designed and implemented a national perinatal information system (SNIP) as a repository of maternal and perinatal data. This system includes the national registry of congenital anomalies (RENACH) which collects information of all live newborns with one or more structural congenital anomalies. The registry has two online instruments for data collection (1) Online Birth Certificate and (2) Online database ex-post to collect information after birth until the newborn is discharged from the hospital. The aim of this report is to describe the RENACH and to determine the prevalence of CA.
Methods: CA prevalence was estimated from data provided by the Statistics and Health Information Department of the Chilean Ministry of Health. This study included all cases registered during 2016 to 2018, the prevalence was calculated using the births registered in the SNIP* (*SNIP data in validation process) as denominator.
Results: In 2016 there were 231,748 LB, 152,582 of them were included in the SNIP (66%), in 2017 there were 219,186 LB, 160,708 were included in the SNIP (73%), in 2018 there were 220,950 LB, 165,908 were included in the SNIP (75%). The CA prevalence rate was 10/10,000 LB in 2016, 11/10,000 LB in 2017 and 12/10,000 LB in 2018.
Discussion and Conclusions: We believe that this registry is a good tool to evaluate the prevalence of CA in our country. We expect to achieve better ascertainment and quality of data by training and motivating those professionals responsible for reporting cases. Data on prevalence of CA, contribute to better diagnosis, prevention, treatment and redistribution of health budgets.

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PERTHES (LEGG-CALVE-PERTHES) DISEASE IN WALES

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ICBDSR Registry on which the work is based: CARIS, Congenital Anomaly and Rare Disease Register. Wales, UK

Background and Objectives: This condition affects the hips of children and is classified by Orphanet as a rare disease with an unknown prevalence. The aetiology is thought to be due to vascular interruption. As CARIS, the congenital anomaly register for Wales, has recently expanded to include a Rare Disease register, cases of Perthes disease were investigated.
Methods: Two databases were explored for cases. These were the Community Childhealth Database and the Patient Episode database in Wales (PEDW). Most cases were from PEDW as this database records coded hospital activity which can include both inpatient and outpatient episodes. The Perthes ICD10 code M91.1 was used to find cases born from the years 1998 to 2014. Deprivation scores were derived from post code and the Welsh Index of Multiple Deprivation. CARIS was searched to identify any associated congenital anomalies.
Results: In the period from 1998 to 2014, 303 cases were recorded with Perthes disease. The prevalence varied greatly with higher rates in earlier years from 1998 -2006. The mean prevalence then was 7.9 per 10,000 live births. The incidence rate varied from 0.6 (2014) and 3 (2006) per 100,000 children aged from 0-14. 2006 was the highest year with 1 case being diagnosed in 33,000. Of the 303 cases there were 113 records for analysis. There was a male to female ratio of 3:1 (86 males 27 females).Time of diagnosis was available in 111 cases and ranged from just under 2 years of age to over 14 years. The mean time of diagnosis was 5 years, 8 months. 57 cases were left sided, 36 cases were right sided, 7 cases were bilateral and 13 unknown. In unilateral cases, the left to right ratio was 1.6:1. Surgery was recorded in 35(31%) of cases. 10 (8.8%) had congenital anomalies including 3 children with cleft lip/palate anomalies. There was a linear relationship with deprivation.
Discussion and Conclusions: A prevalence rate of 7.9 per 10,000 live births in the years 1998-2006 suggests that Perthes disease is not so rare as previously thought and may give a better reflection of the frequency of the condition than quoting an incidence rate. In Wales the incidence rate is at best 3 in 100,000 (2016) of 0-14 year olds. Other countries have widely varying incidence rates. Subsequent years from 2007 record lower rates in Wales but this may reflect the nature of the condition in terms of the timing of development and diagnosis. There may also be possible changes in data sources. An increase in congenital anomaly rates in these children is in accord with the literature and points to genetic factors as a possible cause. Similarly an increase in frequency of cases is associated with deprivation. Using a prevalence rate of cases diagnosed as part of the cohort of their birth year is considered in comparison with an incidence rate within the target population.

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FAMILY OUTREACH ACTIVITIES OF THE TEXAS BIRTH DEFECTS EPIDEMIOLOGY AND SURVEILLANCE BRANCH, 2019

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ICBDSR Registry on which the work is based: Texas Department of State Health Services, USA

Background and Objectives: The Texas Birth Defects Epidemiology and Surveillance Branch (Branch) carries out three family outreach activities that are tied to Texas Birth Defects Registry (TBDR) data. One of these activities is a neural tube defect (NTD) recurrence prevention initiative. The other two activities are family/child case management by agency social workers, and surveys with mothers about the NTD recurrence prevention initiative and their affected child's health care.

Methods: For the NTD recurrence prevention initiative, the Branch mails letters to mothers of children affected with an NTD (anencephaly, spina bifida, or encephalocele, among all pregnancy outcomes). The letters remind women of their increased risk in subsequent pregnancies, and provide information about folic acid prevention opportunities. For the case management initiative, agency social workers contact mothers to identify needs and find services for families with children affected by spina bifida, encephalocele, orofacial clefts, and Down syndrome. The social workers return case management data to the Branch within 8 weeks. Finally, Texas A&M University conducts surveys by phone or internet with mothers of children living with spina bifida or encephalocele. Survey data are used to evaluate the NTD recurrence prevention initiative and health care barriers for the children.

Results: Of 459 letters sent to mothers with children affected with spina bifida and encephalocele (NTD initiative), 47 (10.2%) have been returned as undeliverable. Over 1,000 families of children with NTDs and several other birth defects have been referred to agency social workers for case management. Among the most recent cohort of 106 families, social workers successfully contacted 78 (73.6%) of the families, and 17 of 78 (21.8%) were newly referred to early childhood intervention services. The most frequent barrier for families identified was finances (17 of 78, or 21.8%). Among 177 mothers selected to be surveyed, 67 (37.9%) have completed the survey. Of these, 53 of 67 (79.1%) recalled receiving the NTD recurrence prevention mailing, and 31 of the 53 (58.5%) demonstrated accurate knowledge about folic acid prevention. Nine of 67 mothers (13.4%) indicated their child needed care during the last 12 months and did not receive it, or they had difficulty getting the care their child needed.

Discussion and Conclusions: The Texas Birth Defects Epidemiology and Surveillance Branch will continue to monitor family outreach activities and make adjustments to these projects as they proceed. For example, we will soon expand surveys to include mothers of children with critical congenital heart defects. The ultimate purpose is to determine the greatest unmet needs for these children and families. With this type of information, the next step will be to collaborate with internal and external partners to address the identified unmet needs of families and children affected with birth defects.

Canfield, MA a kol. Family Outreach Activities of the Texas Birth Defects Epidemiology and Surveillance Branch, 2019, s. 38.

FOLATE STATUS IN NON-PREGNANT WOMEN OF CHILDBEARING BY MICROBIOLOGICAL ASSAY, IN METROPOLITAN REGION, CHILE, 2018

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ICBDSR Registry on which the work is based: Not applicable

Background and Objectives: In 2000 Chile started mandatory fortification of wheat flour with 2.2 mg of folic acid (FA)/kg, this policy resulted in a reduction of 50% of the NTD´s rate. After fortification level decreased to 1.8 mg FA/kg in 2009, NTDs rate in livebirths is 7.7/10,000 births, but there are not data about folate levels, as OMS suggested to help monitor folic acid fortification programs. The objective of the study is to evaluate the folate status in non-pregnant women of childbearing by microbiological assay, in Metropolitan Region, Chile.

Methods: This is a cross-sectional observational study, that included a sample of non- pregnant women between 15 to 49 years, users of the public primary health care services in the Metropolitan Region of Chile. Blood samples, nutritional and sociodemographic data were collected in 2018. Folate was measured by microbiological folate assay in the Chilean Public Health Institute. T-Student and Chi-Square test, linear multivariate models and structural equations were used to analysis the data.

Results: A total of 500 women were included. The mean folate acid intake was 461.2 µg/day (52% came from fortified bread). The mean red blood cell folate concentration was 1072.1 nmol/L (SD 333.8; 95% CI 1042.7-1101.4), the mean serum folate concentration was 50.8 nmol/L (SD 19.1; 95% CI 49.1-52.4). Erythrocyte folate insufficiency was detected in 14% of the sample, and deficiency in 4.6%.

Discussion and Conclusions: According to red blood cell folate concentration, non-pregnant women of childbearing in Metropolitan Region in Chile, are in the optimal NTD risk category (4-<9 NTDs per 10,000 live births).

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TERATOLOGY INFORMATION SYSTEM IN VERNACULAR

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ICBDSR Registry on which the work is based: OMNI-Net Ukraine Birth Defects Program

Background and Objectives: Our experience in Ukraine indicates that the vast majority of individuals seeking information concerning teratogens have limited grasp of English. To address this gap, we created a teratology information system in Ukrainian (UTIS).
Methods: Develop UTIS under the direction of a clinical geneticist appointed by an advisory group of professionals. The priority of UTIS is the development of factsheets (F). The emphasis is on prescription drugs. Gradually, the F scope is being expanded to include other teratogenic risk factors. Each F includes a synthesis aimed at primary care physicians although redacted in a manner as comprehensible as possible to the public. The scope of F includes limited suggestions for clinical and family assessments. Contents of F represent adaptations (not passive translations) from a variety of sources, in particular, those from OTIS (Organization of Teratology Information Specialists), Reprotox (Reproductive Toxicology Center) facilitated by collaboration agreements. Revisions of F are triennially.
Results: The number of yearly visits was 3,527, 13,954, 26,252 during 2016-2018. Inquiries stemmed from Kyiv (the capital), 23,488 (38%), and 62% originated from every province of the country. Also of interest is that 65,748 visitors reviewed 136,380 F. We received 800 evaluations which ranked UTIS as excellent (30%), good (51%), satisfactory (15%), and poor or bad (4%) (http://utis.in.ua/).
Discussion and Conclusions: We conclude that UTIS is a successful implementation and a valuable component of OMNI-Net programs, in particular those concerned with prevention, reduction and amelioration of human developmental anomalies in Ukraine. We presume that the process and experience concerning UTIS may be of interest to others. Finally, UTIS provides a countrywide communication with a large number of people concerned about developmental anomalies that may be interested in additional OMNI-Net capacities.

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EUROlinkCAT -ESTABLISHING A LINKED EUROPEAN COHORT OF CHILDREN WITH CONGENITAL ANOMALIES - CONGENITAL HEART DEFECTS REQUIRING SURGERY: THE PARENT'S VOICE

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ICBDSR Registry on which the work is based: Tuscany Registry and IMER Registry, Italy

Background and Objectives: EUROlinkCAT is establishing a linked European Cohort of Children with Congenital Anomalies involving 14 countries to investigate the health and educational outcomes. One of the objectives of the project is to involve parents in addressing their research priorities and to facilitate a reciprocal relationship between families, health professionals and researchers.
Methods: Congenital heart defects requiring surgery were chosen for a focus group to address parents' experiences. Six Italian parents explored themes such as the discovery of the condition, the birth, daily life, support and information and their ideas for research questions to be answered regarding heart defects.
Results: Several parents had difficulties in gaining a clear diagnosis and in accessing appropriate care. Parents used internet but abandon it finding horror stories, conflicting information or not the needed information. Parents commented that surgery was difficult psychologically and care of the sick child created problems with siblings. Mothers have given up paid employment in order to provide home schooling and families found difficulty in gaining the support from the community to which their child was entitled.
Discussion and Conclusions: All parents expressed their interest in the project and were willing to cooperate in the future to involve families in communication no longer focused only on specialists but also on the parties directly concerned. This will improve the information requested by the families of children with congenital anomalies and establish research priorities.

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NEPHROCALCINOSIS: MANAGEMENT OF MATERNAL AND FETAL DISEASES

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Background and Objectives: Nephrocalcinosis is an overarching term involving increased calcium salt content in renal parenchyma, interstitial damage, and potential development towards renal failure. Pregnancy is many times the first diagnostic contact and the possibility of carrying out biochemical or imaging tests in young women and allows early diagnosis of this disease.
Methods: Patient management includes preconceptual counseling in nephrologic outpatient clinics, close collaboration between nephrologist and gynecologist/obstetrician throughout pregnancy, and consistent management of childbirth management with an emphasis on early recovery and renal function stabilization.
Results: Case studies focus on the specific management of pregnancy in a patient with known nephrocalcinosis and the management of pregnancy in a healthy patient with prenatally diagnosed fetal nephrocalcinosis.
Discussion and Conclusions: Conversely, even a moderate and stabilized degree of this kidney disease may pose a challenge to all participating specialists in the patient's pregnancy.

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CONGENITAL ANOMALIES IN CHILDREN BORN AFTER ASSISTED REPRODUCTION IN THE CZECH REPUBLIC: POPULATION BASED STUDY

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ICBDSR Registry on which the work is based: National Registry of Congenital Anomalies of the Czech Republic

Background and Objectives: Assisted reproduction (AR) is nowadays commonly-used method for treating various fertility problems. However, several studies have shown a higher incidence of selected types of congenital anomalies among AR-conceived children. Our goal was to study this association on a large population cohorts using data from our population based registries.
Methods: Our retrospective epidemiological study is based on the official data from the National Registry of Congenital Anomalies and National Registry of assisted Reproduction (run by the Institute of the Health Information and Statistics of the Czech Republic). The registration process is population-wide and compulsory by national law. We evaluated the incidence of congenital anomalies (ICD-10 diagnoses Q00-Q99) in AR-conceived children and compared it to the incidence of congenital anomalies in naturally-conceived children. Time period: 2013-2015.
Results: The overall incidence of congenital anomalies was slightly higher in the AR-children group however, the difference was not statistically significant. The congenital anomalies were more common in twins ($p<0.005$). The incidence of congenital anomalies in AR-twins was significantly higher than the incidence of congenital anomalies in non-AR-twins ($p<0.005$) while the difference of congenital anomalies incidence in AR and non-AR singletons was not significant.
Discussion and Conclusions: We have found that the incidence of congenital anomalies was higher especially in twins born after assisted reproduction while in singletons the difference was not significant. We will further analyze this finding during the next phases of our population study.
The study is supported by the RVO project: "Thomayerova nemocnice - TN, 00064190"

NEURAL TUBE DEFECTS (NTD) AND CHRONIC EXPOSURES TO LOW DOSES OF RADIATION

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ICBDSR Registry on which the work is based: OMNI-Net Ukraine Birth Defects Program

Background and Objectives: Following the 1986 Chornobyl disaster, we organized a network (OMNI-Net). In 2000 population-based monitoring of malformations adhering to ICBDSR and EUROCAT methodologies was started. This report concerns the Polissia (POL) and not-Polissia (notPOL) regions in the Rivne Province in Ukraine. Two characteristics of the POL soils compared to those in notPOL are: greater contamination by Chornobyl ionizing radiation (IR) concurrent with the highest index of transfer of nuclides from soil to the food chain in Ukraine. We investigated Cs-137 whole body counts (WBC) in pregnant women and the prevalence of neural tube defects (NTD), anencephaly (AN) and spina bifida (SB) in POL and notPOL.

Methods: Pregnant women under the care of the Rivne Regional Clinical Diagnostic Center were asked to undergo WBC procedures (2011-2016). The WBC reflect Bq levels from incorporated Cs-137. The prevalence of NTD (2000-2016) was established through monitoring of all pregnancy outcomes in the province, through procedures established and implemented across Europe by EUROCAT and worldwide by ICBDSR.

Results: We recorded 7,055 and 4,309 WBC of pregnant women residing in POL and notPOL, respectively. Among 633 women with WBC levels above 5,000 Bq, 624 (99%) resided in POL. The prevalence of NTD, per 10,000 live births (129,783 in POL and 132,708 in notPOL), was 23.3 and 17.1, respectively. Temporal trends of NTD prevalence were not statistically significant while NTD prevalence in POL was statistically significantly higher than in notPOL.

Discussion and Conclusions: The concurrence of higher WBC and NTD rates in POL compared to notPOL is strong and persistent. The WBC of Sr-90 and tritium known to be present in the environment remain unmeasured. The nature of this investigation precludes cause-effect conclusions. However, the persistence and strong contrasts between POL and notPOL are sufficient, in our view, to require substantive additional investigations. This view is strengthened by the fact that the NTD prevalence in POL is the highest in Europe followed by those in Cumbria and Northern England which are the most impacted UK regions by Chornobyl and are in proximity to large nuclear complexes.