ORIGINAL ARTICLE

CrossMark

Birth defects surveillance: experiences in Argentina and Colombia

Boris Groisman[1] · Rosa Liascovich[1] · María Paz Bidondo[1] · Pablo Barbero[1] · Santiago Duarte[1] ·
Ana Laura Tellechea[1] · Jorge Holguín[2] · Catherine Rodríguez[3] · Paula Hurtado-Villa[4] · Natalia Caicedo[4] ·
Gabriela Botta[5] · Ignacio Zarante[5]

Abstract

Birth defects (BDs) are structural or functional anomalies, sporadic or hereditary, of prenatal origin. Public health surveillance is defined as the ongoing systematic collection, analysis, and interpretation of outcome-specific data for use in the planning, implementation, and evaluation of public health practice. BD surveillance systems may have different characteristics according to design, coverage, type of surveillance, case ascertainment, case definition, BD description, maximum age of diagnosis, pregnancy outcomes, coding systems, and the location of the coding process (central or local). The aim of this article is to describe and compare methodology, applications, and results of birth defect surveillance systems in two South-American countries: Colombia and Argentina. In both countries, the surveillance systems developed activities in relation to the Zika virus emergency. For most BDs, a statistically significant higher prevalence is observed in Argentina-RENAC than in Colombian registries. This may be due to methodological reasons or real differences in prevalence. The strengths, weaknesses, and the future perspectives of the Argentine and Colombian systems are presented. When developing a surveillance system, the objectives, the available resources, and previous experiences in similar contexts must be taken into account. In that sense, the experience of Argentina and Colombia can be useful for others when developing a birth defect surveillance system.

Keywords Birth defects · Argentina · Colombia · Registries · Surveillance

Introduction

Birth defects (BDs) are structural or functional anomalies, sporadic or hereditary, of prenatal origin. BDs comprise a variety of conditions including physical malformations, sensory deficiencies, chromosomal abnormalities, metabolic errors, and neurodevelopmental abnormalities. Its overall prevalence is 1 to 3% in live births. However, due to the late diagnosis of some diseases (i.e. blindness, deafness, mental retardation, among others), it amounts to 8% by 5 years of age. BDs cause great impact on morbidity since they involve serious and frequently chronic disorders. Around the world, every year, about 5 million babies are born with a BD and almost 3 million children under 5 die from these diseases. These figures vary according to regions of the world and, in some cases, between different ethnic or geographical groups within countries or regions (Christianson et al. 2006). They affect all social sectors, but families with lower socio-economic status are more negatively affected by the birth of a child with a disabling condition. The impact is also high for the health system facing the costs of extended treatments intended predominantly for palliative or rehabilitation purposes. BDs are responsible for a high proportion of years of potential life lost, infant hospital admissions, and medical costs (Sever et al. 1993).

Public health surveillance is defined as the ongoing systematic collection, analysis, and interpretation of outcome-specific data for use in the planning, implementation, and evaluation of public health practice (Thacker and Berkelman

✉ Boris Groisman
  bgroisman@gmail.com

1   National Network of Congenital Anomalies of Argentina (RENAC), National Center of Medical Genetics, National Administration of Laboratories and Health Institutes, National Ministry of Health, Av. Las Heras 2670, 3rd floor, 1425 City of Buenos Aires, Argentina

2   Secretaria de Salud Pública Municipal de Cali, Pontificia Universidad Javeriana Cali, Cali, Colombia

3   Congenital Malformations Surveillance Programme of Bogotá, Secretaria de Salud de Bogotá, Bogotá, Colombia

4   Congenital Birth Defects Surveillance Programme of Cali, Pontificia Universidad Javeriana Cali, Cali, Colombia

5   Pontificia Universidad Javeriana Bogotá, Cali, Colombia

1988). The ultimate goal of surveillance programs is prevention. BD surveillance systems were started after the thalidomide tragedy occurred between 1957 and 1961, to monitor the frequency of birth defects, detect geographic clusters, and research on risk factors. They were established in the 1960s in the Czech Republic, Finland, England and Wales, Sweden and Alberta, Canada, Atlanta, USA, Norway, and Latin America. For many years, the Latin American Collaborative Study of Congenital Malformations (ECLAMC) was the only source of data on BDs available in the Latin American region. It was created in 1967 as a voluntary non-governmental network of hospitals with a case-control design (Castilla and Orioli 2004). In the 1960s, most infant deaths in the region were attributable to infections and malnutrition, so BDs were not a public health priority. In order to share data between countries, two international consortiums for birth defects monitoring were created: in 1974, the International Clearinghouse for Birth Defects Monitoring Systems, ICBDMS (Botto et al. 2006)—now International Clearinghouse for Birth Defects Surveillance and Research—and the European Congenital Anomalies and Twins (EUROCAT) consortium in 1979.

The main purpose of the BD surveillance programs is to describe the prevalence in a given population and observe changes in their trends. Epidemiological surveillance of BD provides the basis for the information needed to investigate causes or risk factors such as drugs, nutritional factors, environmental exposures, maternal diseases, and genetic factors related to BD. This is especially important because the etiology is unknown for most of them. Additionally, the data generated by these systems have been progressively used for other purposes, such as health service planning for those conditions, identification and referral of children to health care services, and evaluation of programs for the prevention. These systems lead to systematic newborn screening of birth defects by physical examination, thus allowing greater awareness of the health problem. They have the big potential for early detection of affected infants, allowing referral to health services. As other epidemiological surveillance systems, the surveillance of BDs also aims at the primary prevention (Luquetti and Koifman 2011).

BD surveillance systems may have different characteristics according to design, coverage, type of surveillance, case ascertainment, case definition, BDs description, maximum age of diagnosis, pregnancy outcomes, coding systems, and the location of the coding process (central or local). Although the definition of BDs includes both structural and functional anomalies, BD surveillance programs often monitor major structural birth defects and some genetic abnormalities. Some programs include all BD (even minor anomalies), but others include only major anomalies. The standardization of collection methods, coding, and analysis, with standard operating procedures and training of the professionals involved, is essential for obtaining good-quality data (WHO/CDC/

ICBDSR 2014). In addition to the multiple and different objectives of the programs, the heterogeneity of the available data resources determine the methods of data collection. There is no single or more adequate model for a surveillance system (Castilla and Peters 1992).

The aim of this article is to describe and compare methodology, applications, and results of birth defect surveillance systems in the South-American countries Colombia and Argentina.

Methods

We compared Argentina and Colombia regarding basic demographic, health system, and mortality characteristics as well as congenital defect monitoring systems in both countries.

The prevalence per 10,000 individuals was calculated for 48 specific BDs selected based on their clinical significance, their impact on morbidity and mortality. The prevalence was calculated as per Poisson's distribution, with a 95% confidence interval. We compared the prevalence of the Argentine and the Colombian's surveillance programs: for each specific BD, a "Z" value was obtained using the National Network of Congenital Anomalies of Argentina (RENAC) as a reference (expected value) and the Bogotá (Z_1) and Cali (Z_2) as comparator values (observed value) [$Z = $ (observed value-expected value)/root (*expected* value)]. The statistical significance was established using Bonferroni's correction for multiple comparisons, in $Z = \pm 3.89$, corresponding to a *p* value of 0.0005. The Stata statistical software was used.

Results

Argentina's health care system is divided in three sub-systems: public, social security, and private insurance. The public system covers around 46% of the population and is funded through taxes and is available free of charge to the entire population. It covers the lower-income population that lacks other health coverage. The social security setting is funded by mandatory contributions from employers and registered workers, covering about 44% of the population (workers, employees, and retirees). The private insurance setting (for-profit) is funded by specific payments from the insured and covers 10% of the population, mainly the higher-income fraction. The three systems are independently managed with little interaction between them, which results in overlapping, inefficiency, and high health expenditure (about 6.61% of the Gross Domestic Product) (Bidondo et al. 2015a).

Demographic, health system, and mortality characteristics of Argentina are presented in Table 1. The infant mortality rate (IMR) decreased from 33.2/1000 live births in 1980 to 9.7/1000 live births in 2016. Neonatal deaths (< 28 days)

Table 1 Demographics, health systems, and infant mortality of Argentina and Colombia

Characteristics	Argentina	Colombia
Area	2,780,400 km^2	2,129,748 km^2
Politic organization	Federal Republic, 24 jurisdictions	Republic, 32 department + capital district
Population	44,494,502 (year 2018). 91% living in urban areas)	48,203,405 (76.4% living in urban areas)
Health insurance/health sectors	Universal coverage	Universal coverage
	Public sector (50%); non public- social security (45%); private insurance (5%)	Contributory regime (44.5%); Subsidized scheme (48.1%); Special sectors (5%)
% Hospital births	99.6%	99.0%
Number of live births (source)	728,035 (DEIS, 2017)	647,679 (DANE 2017)
Infant mortality rate (source)	9.7 × 1.000 (DEIS, 2017)	10.17 × 1.000 (DANE 2017)
Neonatal mortality rate (source)	6.5 × 1.000 (DEIS, 2017)	8.5 × 1.000 (WHO, 2015)
ETOPFA	Illegal (unless the life or health of the mother is at risk, or in case of rape)	Only legal if the malformation of the fetus will cause a non- viable extrauterine life or because of severe disability
% of infant mortality due to BD (source)	27% (DEIS, 2017)	25% (DANE)

represent two thirds of infant mortality. Proportional infant mortality due to BD was approximately 10% in 1980, rising from 17.9 to 23.6% between 1998 and 2009 and reaching 27% in 2016 (DEIS 2017). There was a reduction in IMR; however, the proportional infant mortality attributable to birth defects increased. Among 7093 infant deaths that occurred in 2016, 2175 were due to BD. By 2016 birth defects are a leading cause of infant deaths. Therefore, although infant mortality attributable to birth defects has decreased, this happened at a lower rate than other causes of infant death. That is the reason why the proportional mortality attributable to birth defects has increased.

The increase in the contribution of BDs to IMR and the lack of official information about birth prevalence were two reasons for the creation of the National Network of Congenital Anomalies of Argentina (in Spanish "Red Nacional de Anomalías Congénitas", RENAC). Also, in the 2000s, media reports alleged high prevalence of BD in some regions due to exposure to pesticides in agricultural activity. This assumption mobilized health policy makers, and BDs were introduced in the health agenda. There was also a need to improve care of affected newborns and to monitor BDs prevalence due to social concern about pesticides. Therefore, RENAC was created in 2009.

Characteristics of RENAC design are summarized in Table 2. RENAC started in four hospitals, and progressively included maternity centers of the 24 jurisdictions of Argentina. In 2016, there were 160 participating institutions, 144 from the public sector and 36 from nonpublic sector (social security, and private insurance), covering 60% of births of the public sector and 40% of all country. RENAC is a hospital-based surveillance program; reporting neonatologists collect information about the affected cases and send the data to the coordination through a web-based forum. Cases include all newborns and stillborns with major BD. The website allows interaction among members, data sending, solving operational issues, and quality assurance of data. The coordination team may suggest diagnosis, detection of associated birth defects, and referral to genetic services. Forum interaction increases social cohesion among participants who feel themselves members of the same team.

RENAC holds an annual meeting, which is essential for face-to-face interaction of members. There is also an annual blended learning course for the reporting neonatologists (Groisman et al. 2013a, b). Since 2012, the RENAC has become an active member of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR). According to the objective of detection and referral of children to health care services RENAC, since 2015, RENAC created a network for care of oral clefts, talipes, and developmental dysplasia of the hip (Groisman et al. 2016a; Cassinelli et al. 2018).

Colombia's health care system is composed primarily by the General System of Social Security in Health (GSSSH). It contains two insurance schemes: there is the contributory regime, which is funded by its affiliates, such as companies, formal and independent workers with income equal to or above a minimum wage, pensioners, and their families. There is also the subsidized system, which covers all the people without payment capability; it is funded by the national government, the territorial entities, and by the contributory regime cross-subsidy. The Colombian system includes also a special regime that is directed to military forces, national police, the Magisterial, the Colombian Petroleum Company (ECOPETROL), and public universities.

Becoming a member of the GSSSH is mandatory to all the population and is done through the public or private health-promoting entities, which offer the Mandatory Health Plan

Table 2 Characteristics of birth defects surveillance systems in Argentina and Colombia

Element	Argentina (RENAC)	Colombia
Coverage	Hospital-based. National	Hospital-based. Subnational Bogotá (BCMSP) and Cali (CCMSP)
Year of implementation	RENAC: 2009	BCMSP:2001
		CCMSP: 2010
		SIVIGILA: 2011
Surveillance (passive, hybrid, or active)	Hybrid: data collection by champions responsible in each institution	Hybrid: active (case-control study, follow-up program), and passive (SIVIGILA)
Case ascertainment	Single source: reports from RENAC champions in maternity hospitals	Multiple sources: SIVIGILA, case-control study, follow-up program
Case definition	Major birth defects	Major and minor birth defects
Pregnancy outcomes: livebirths (LB) o stillbirths (SB)	LB and SB($\geq$ 500 g); ETOPFA excluded.	LB and SB($\geq$ 500 g) ETOPFA included through 215 form of SIVIGILA
Time of follow up—period (age)	Until hospital discharge	Up to 1 year old
Description of congenital anomalies	Verbatim	Verbatim
Coding system	ICD 10, RCPCH adaptation	ICD 10 and ECLAMC coding system
Coding process	Central level	Central level for case-control and local level for SIVIGILA
Data on maternal risk factors	No	Yes
Data on healthy controls	No. Only for special studies	Yes
Periodical dissemination	Yes, annually	Yes BCMSP: monthly, quarterly, semiannual and annual. CCMSP: semiannual and annual
Training activities	Face-to-face training courses (formal courses and annual meetings). Virtual training courses	Text guides, meetings, face-to-face, and training courses

ICD International Classification for Diseases, 10 Edition, *RCPCH* Royal College of Pediatrics and Child Health, *LB* live birth, *SB* stillbirth, *ETOPFA* elective termination of pregnancy for fetal anomaly

(MHP). The health-promoting entities provide the health services included within the MHP through Benefit Plan Administrator Entities. There is also a private sector predominantly used by the upper classes. In this case, they hire private insurances (prepaid medicine) or go to a private practice.

In terms of infant mortality rate (IMR), it has decreased from 20.40/1000 live births in 2005 to 17.23/1000 live births in 2014. In 2000, neonatal deaths per 1000 live births due to BD were 2.3, rising in 2010 to 2.8, and decreasing again to 2.3 in 2015. There has been a reduction in IMR during the last years, and the proportional infant mortality attributable to BD increased or remained the same. From the total deaths in children under 5 years of age in the year 2015, 24.8% were due to BD (DANE 2017).

Bogotá and Cali are two main cities of Colombia that have their own BD hybrid surveillance systems, with both passive and active case ascertainment. There are three coordinated sources for BD surveillance: SIVIGILA, case-control study, and a follow-up program. These last two were developed entirely by researchers at the Pontifical Javerian University (Pontificia Universidad Javeriana) in agreement with District

Health Secretary (Secretaría Distrital de Salud - SDS) of each city (Zarante et al. 2016). These systems are active members of ECLAMC and the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR).

The Bogotá Congenital Malformations Surveillance Program (BCMSP) and Cali Congenital Malformations Surveillance Program (CCMSP) have a case-control design in 7 and 3 hospitals, respectively. Cases include all newborns and stillborns with BD weighing more than 500 g. For each case, the control is the next newborn with the same sex without BD. Physicians trained in systematic physical examination to diagnose BD report major and minor structural BD through an ECLAMC form (SGSS. Sistema General de Seguridad Social en Salud, Colombia 2013).

Besides the case-control design in selected hospitals, BCMSP and CCMSP cover 100% of the city's births using a special form, which is the result of the collaboration with the District Health Secretary through the Public Health Surveillance System (SIVIGILA). This passive system includes completion of a notification form with basic data and description of the BD.

Table 3 Prevalence of selected birth defects, RENAC (year 2016), BCMSP (years 2001–2016), and CCMSP (years 2010–2016)

Selected birth defects	RENAC		BCMSP			CCMSP		
	n	Prevalence per 10,000 (CI 95%)	n	Prevalence × 10,000 (CI 95%)	Z1	n	Prevalence × 10,000 (CI 95%)	Z2
Anencephaly (Q00)	57	1. 87 (1. 41–2. 42)	31	0.71 (0.49–1.02)	− 4.65	9	1.89 (0.86–3.60)	0.09
Encephalocele (Q01)	39	1. 28 (0. 91–1. 75)	13	0.3 (0.16–0.52)	− 4.78	2	0.41 (0.04–1.54)	− 4.19
Spina bifida (Q05)	175	5. 73 (4. 91–6. 64)	25	0.58 (0.37–0.85)	− 11.89	13	2.73 (1.45–4.68)	− 6.93
Hydrocephalus (Q03)	212	7. 01 (6. 10–8. 01)	145	3.3 (2.83–3.94)	− 7.53	14	2.94 (1.60–4.94)	− 8.40
Holoprosencephaly (04.1–04.2)	67	2. 19 (1. 70–2. 79)	26	0.6 (0.39–0.88)	− 5.94	5	1.05 (0.33–2.47)	− 4.27
Microcephaly (Q02)	77	2. 52 (1. 99–3. 15)	141	3.25 (2.74–3.84)	2.57	17	3.57 (2.07–5.72)	3.64
Microphthalmia + anophthalmia (Q11.1; Q11.2)	43	1. 41 (1. 02–1. 90)	19	0.43 (0.26–0.69)	− 4.51	3	0.63 (0.12–1.86)	− 3.63
Anotia + microtia (Q16; Q17.1)	122	3. 9 (3.3–4.8)	173	3.9 (3.42–4.64)	3.60	19	3.99 (2.39–6.23)	3.62
Coarctation fo the Aorta (Q25.1–Q25.19)	67	2. 19 (1. 70–2. 79)	63	1.45 (1.12–1.86)	− 2.75	5	1.05 (0.33–2.47)	− 4.27
Hypoplastic left heart (Q23.4)	51	1. 67 (1. 24–2. 20)	105	2.42 (1.98–2.94)	3.24	6	1.26 (0.45–2.76)	− 1.76
Tetralogy. Pentalogy of Fallot (Q21.3. Q21.82)	50	1. 64 (1. 21–2. 16)	35	0.8 (0.56–1.13)	− 3.58	8	1.68 (0.72–3.32)	0.18
Transposition of Great vessels (Q20.3)	65	2. 13 (1. 64–2. 71)	53	1.22 (0.92–1.60)	− 3.42	5	1.05 (0.33–2.47)	− 4.09
Persistent truncus arteriosus (Q20.0)	7	0. 23 (0. 09–0. 47)	9	0.2 (0.09–0.40)	− 0.24	1	0.21 (0.00–1.20)	− 0.22
Tricuspid atresia/stenosis (Q22.4)	2	0. 07 (0. 01–0. 24)	26	0.6 (0.39–0.88)	11.56	3	0.63 (0.12–1.86)	12.18
Ebstein's anomaly (Q22.5)	18	0. 59 (0. 35–0. 93)	12	0.27 (0.14–0.49)	− 2.25	1	0.21 (0.00–1.20)	− 2.73
Interrupted aortic arch (Q25.2)	14	0. 46 (0. 25–0. 77)	6	0.13 (0.05–0.3)	− 2.61	3	0.63 (0.12–1.86)	1.40
Pulmonary atresia (Q22.0)	12	0. 39 (0. 20–0. 69)	30	0.69 (0.47–0.99)	2.65	7	1.47 (0.58–3.04)	9.49
Total anomaly of the pulmonary venous return (Q26.20; Q26.21; Q26.22)	6	0. 20 (0. 07–0. 43)	27	0.62 (0.41–0.91)	5.33	0	NR	− 2.45
Double outlet of the right ventricle (Q20.1)	26	0. 85 (0. 56–1. 25)	8	0.18 (0.08–0.37)	− 3.99	2	0.41 (0.04–1.54)	− 2.59
Cleft palate (Q35)	99	3. 24 (2. 63–3. 95)	186	4.2 (3.70–4.96)	3.24	24	5.03 (3.22–7.50)	5.51
Cleft lip (Q36; excludes Q36.1. medial cleft)	59	1. 96 (1. 50–2. 53)	124	2.86 (2.38–3.42)	3.71	9	1.89 (0.86–3.60)	− 0.17
Cleft lip and palate (Q37)	341	11. 16 (10. 01–12. 41)	163	3.76 (3.21–4.39)	− 12.24	15	3.15 (1.76–5.20)	− 13.26
Pierre-Robin sequence (Q87.08)	19	0. 62 (0. 37–0. 97)	13	0.3 (0.16–0.52)	− 2.25	1	0.21 (0.00–1.20)	− 2.89
Esophageal atresia (Q39.0–Q39.11)	100	3. 27 (2. 66–3. 98)	128	2.95 (2.47–3.52)	− 0.97	10	2.09 (1.00–3.87)	− 3.59
Intestinal atresia (Q41.1–Q41.9)	46	1. 51 (1. 10–2. 01)	28	0.64 (0.43–0.94)	− 3.87	0	NR	− 6.78
Duodenal atresia (Q41.0)	53	1. 74 (1. 30–2. 27)	31	0.71 (0.49–1.02)	− 4.27	0	NR	− 7.28
Anorectal malformation (Q42.0–Q42.3)	140	4. 58 (3. 86–5. 41)	142	3.28 (2.76–3.87)	− 3.36	7	1.47 (0.58–3.04)	− 8.04
Diaphragmatic hernia (Q79.0–Q79.01)	105	3. 44 (2. 81–4. 16)	88	2.03 (1.63–2.51)	− 4.19	9	1.89 (0.86–3.60)	− 4.62
Choanal atresia (Q30.0)	6	0. 20 (0. 07–0. 43)	22	0.50 (0.32–0.77)	3.89	2	0.41 (0.04–1.54)	2.78
Cryptorchidism (Q53.2)	37	1. 21 (0. 85–1. 67)	188	4.34 (3.75–5.01)	15.73	44	9.23 (6.70–12.40)	40.27
Ambiguous genitalia (Q56.4)	42	1. 38 (0. 99–1. 86)	56	1.29 (0.98–1.68)	− 0.38	13	2.73 (1.45–4.68)	6.37
Hypospadias (Q54.1-Q54.3)	46	2. 65 (2. 11–3. 30)	165	3.81 (3.25–4.44)	10.39	47	9.86 (7.24–13.12)	37.63
Epispadias (Q64.0)	7	0. 23 (0. 09–0. 47)	8	0.18 (0.08–0.37)	− 0.51	1	0.21 (0.00–1.20)	− 0.22
Renal agenesis (Q60.1)	19	0. 62 (0. 37–0. 97)	33	0.76 (0.52–1.07)	0.98	5	1.05 (0.33–2.47)	2.99
Renal cysts (Q61.1–Q61.90)	103	3. 37 (2. 75–4. 09)	78	1.08 (1.42–2.25)	− 4.72	11	2.31 (1.15–4.14)	− 3.20
Preaxial polydactyly (Q69.00; Q69.1; Q69.20)	46	1. 51 (1. 10–2. 01)	158	3.65 (3.10–4.27)	9.66	11	2.31 (1.15–4.14)	3.61
Post-axial polydactyly (Q69.02; Q69.22)	148	4. 85 (4. 10–5. 69)	419	9.68 (8.78–10.66)	12.14	77	16.15 (12.74–20.19)	28.39
Syndactyly (Q70.0-Q70.30; Q70.4-Q70.90)	69	2. 26 (1. 76–2. 86)	139	3.21 (2.70–3.79)	3.50	14	2.94 (1.60–4.94)	2.49
Transverse limb deficiency (Q71.2–Q71.30)	42	1. 38 (0. 99–1. 86)	13	0.30 (0.16–0.52)	− 5.06	11	2.31 (1.15–4.14)	4.40
Preaxial limb deficiency (Q71.31, Q72.5)	19	0. 62 (0. 37–0. 97)	75	1.73 (1.36–2.17)	7.78	10	2.09 (1.00–3.87)	10.34
Post-axial limb deficiency (Q71.5, Q72.6)	10	0. 33 (0. 16–0. 60)	24	0.55 (0.35–0.83)	2.19	7	1.47 (0.58–3.04)	11.02
Intercalary limb defciency (Q71.1. Q73.1)	0	0. 00	4	0.09 (0.02–0.24)	–	8	1.68 (0.72–3.32)	–
Talipes equinovarus (Q66.0)	180	5. 89 (5. 06–6. 82)	701	16.1 (15.02–17.44)	23.46	99	20.77 (16.87–25.28)	33.87
Talipes calcaneovalgus (Q66.4)	16	0. 52 (0. 30–0. 85)	95	0.67 (0.45–0.96)	12.76	20	4.19 (2.65–6.49)	28.04

Table 3 (continued)

Selected birth defects	RENAC		BCMSP			CCMSP		
	n	Prevalence per 10,000 (CI 95%)	*n*	Prevalence × 10,000 (CI 95%)	Z1	*n*	Prevalence × 10,000 (CI 95%)	Z2
Omphalocele (Q79.2)	66	2. 16 (1. 67–2. 75)	67	1.54 (1.20–1.97)	− 2.30	5	1.05 (0.33–2.47)	− 4.18
Gastroschisis (Q79.3)	239	7. 82 (6. 86–8. 88)	121	2.79 (2.32–3.34)	− 9.94	7	1.47 (0.58–3.04)	− 12.56
Prune belly (Q79.4)	8	0. 26 (0. 11–0. 52)	7	0.16 (0.06–0.34)	− 1.08	1	0.21 (0.00–1.20)	− 0.56
Down's syndrome	548	17.94 (16.47–19.51)	499	11.53 (10.54–12.59)	− 8.36	74	15.52 (12.18–19.49)	− 3.15

The third component of the Colombian systems is the follow-up program. After analyzing the information collected by the physicians, both programs carry out the follow-up through phone calls and classification of the patients with disability risk; and if necessary, the patients are evaluated by a clinical geneticist.

The prevalence of specific BD between the registries was compared. We observed statistically significant differences in frequencies for most BD (Table 3).

Discussion

Argentina and Colombia are among the few countries in the Latin America region with BD surveillance programs. RENAC and BCMSP-CCMSP share a common purpose, to monitor prevalence of structural BD in live births and stillbirths to offer an adequate follow up, prevent and detect future cases, and perform research studies.

Among the similarities between Argentina and Colombia, both underwent epidemiological transition. This has changed the pattern of causes of infant deaths, increasing the relative importance of BD over infectious and nutritional causes. Faced with the challenge, both countries have developed systems for BD surveillance. When comparing Colombia and Argentina, the latter has lower infant mortality and a higher proportional mortality due to BD, which is consistent with the fact that countries with lower infant mortality rate have a higher relative contribution of BD (Christianson and Modell 2006).

The surveillance strategies have been different between the two countries. Regarding methodology, there is always a trade-off between coverage and detail of the information collected. The greater the coverage, the lower the detail of information collected for the system to be feasible. Argentina has a national surveillance system, which collects information about a core set of variables of the affected cases, without information from controls or risk factors. RENAC does not have full coverage, but it is national in scope because it includes the 24 provinces of the country, with hospitals in all the main cities.

In contrast, Colombia's systems have full coverage in two cities, but not nationwide. In addition, the Colombian systems have some hospitals where there is ongoing collection of information on healthy controls and risk factors. In RENAC, case-control studies have been developed for special investigations, which, unlike surveillance, are not continuous but limited in time (Tellechea et al. 2018).

The systems of both countries have in common some good practices for BD surveillance. For example, they use a verbatim description of cases with BD. Health professionals report the cases using their own words, giving a greater level of detail than what would be obtained through checklists. They can also send photographs which are a good complement of descriptions. The two countries use the ICD 10 as a coding system, which allows them to speak a "common language" with other programs at ministries or share data for international projects.

In both countries, the surveillance systems developed activities in relation to the Zika virus emergency. Although it is the astute clinician who usually detects BD epidemics (Rasmussen et al. 2016), surveillance systems of Argentina and Colombia have established the microcephaly baseline, documented the increase in frequency, and have developed case-control studies (Hurtado-Villa et al. 2017). Nowadays, RENAC coordinates the follow-up of newborns with microcephaly and other brain anomalies jointly with the National Institute for Viral Human Diseases (Instituto Nacional de Enfermedades Virales Humanas, Dr. Maiztegui), which performs laboratory tests. The notification of these cases departs from the routine, as they are reported to the coordination immediately. The report of each case triggers the collection and delivery of blood and urine samples to the reference laboratory, and the direct communication with the mother of the affected baby for a questionnaire on risk factors. In Colombia, the Zika epidemic was reported by the National Institute of Health of Colombia (Instituto Nacional de Salud, INS) in epidemiological week 40 in 2015, and a peak of cases was reported at week 4 in 2016. After this, INS started a strategy to monitor infected persons with emphasis on risk groups, including pregnant women, and intensified surveillance of BD

was implemented, using SIVIGILA and INS guidelines. The microcephaly peak in Colombia was reported in July 2016 (8 months after the reported start of the Zika virus epidemic).

For most of the selected BD with a statistically significant higher prevalence, the frequency in RENAC is higher than in Colombian registries. This may be due to methodological reasons or real differences in prevalence. Among the methodological reasons, RENAC includes only hospitals reporting actively through champions. Champions are professionals committed to the program. In contrast, the Cali and Bogotá systems have a passive component through SIVIGILA, and passive systems usually report lower prevalence (Mai et al. 2015).

However, for few BDs, a higher prevalence is observed in the Bogota and Cali systems. For example, the prevalence of microcephaly is higher in these registries, although not statistically significant. This may be due to the Zika virus epidemic in Colombia, with the increased risk associated with the infection. Argentina had limited outbreaks of Zika virus and the increase in the prevalence of microcephaly has been lower, mainly due to awareness bias (Tellechea et al. 2018). Talipes is another BD more frequent in Colombia: this may be related to the inclusion of positional cases. In RENAC, the prevalence of hypospadias is lower, probably related to underreporting of isolated, mild cases. The prevalence of cryptorchidism is also lower in Argentina, probably related to the case definition, since RENAC only includes cases of bilateral cryptorchidism in term births.

In Argentina, ETOPFA are illegal and excluded from the program; in Colombia, ETOPFA are included through the SIVIGILA form (passive ascertainment). Despite being legal in Colombia, the surveillance programs have a low number of reported ETOPFA.

Regarding the strengths of RENAC, the system is national and has a relatively high coverage, which reduces referral bias because it is hospital based; it works under the National Ministry of Health and has a full-time coordination with expertise in genetics and epidemiology. Reports are sent to the central coordination by champions, motivated neonatologists working with the program. Communication takes place through a web forum that facilitates the improvement of the quality data, as well as an initial counseling to the family. Dissemination of information is a main activity of the system, adapting the message to different stakeholders. Weaknesses are it does not collect risk factors routinely. The lack of controls restricts the possibility of performing analytical studies of research for risk factors; the period of data collection is until discharge from maternity, which results in underreporting of BDs that can be detected later, such as congenital heart disease; pregnancy terminations are not included. The future perspectives of RENAC are to extend the network of referral of affected newborns, to expand diagnosis with genomic tests to improve counseling and care of some patients with BDs,

and to strengthen partnerships with other areas of the National Ministry of Health, like communicable diseases area.

RENAC reviewed the public health situation in Argentina with regard to birth defects (Bidondo et al. 2015a), analyzed the characteristics of the surveillance system (Groisman et al. 2013a, b) and its expanded objectives (Groisman et al. 2016a). Additionally, RENAC presented the prevalence of selected BDs and their potential impact on health services (Bidondo et al. 2014), neonatal lethality by BDs (Bidondo et al. 2015b), and effectiveness of neural tube defect prevention by food fortification with folic acid (Sargiotto et al. 2015; Bidondo et al. 2015c). Finally, RENAC investigated temporal and geographic clusters (Groisman et al. 2017; Groisman et al. 2016b), and some specific BDs (López et al. 2015; Martín et al. 2014; Bidondo et al. 2016; Groisman et al. 2016c).

The strengths of BCMSP and CCMSP are that they have total coverage of births in both cities, Bogotá y Cali. They have hybrid case ascertainment: the active part is the identification of cases through physicians trained in systematic physical examination. Cases are reviewed, and then confirmed by a Medical Geneticist. Medical records are also reviewed systematically for ascertainment of major and minor BD, as well congenital hypothyroidism, congenital rubella, congenital syphilis, and orphan diseases using the ECLAMC methodology (case/control). The passive case ascertainment consists in the detection cases using vital records from the Public Health Surveillance System (SIVIGILA), promoted by the District Health Secretary, working in all health institutions in both cities. The programs report the frequency, distribution, and prevalence of BD, as well as the pre-conceptional, prenatal, obstetric, family, and sociocultural risk factors associated with the BDs, in order to develop prevention actions in the population. Among weaknesses, approximately 15% of the cases are missed in the case-control design. This is because although there is a doctor from the program that goes every day to the hospitals to examine newborns, some mothers are already discharged by then. However, the missed cases, especially those with major malformations, are detected through data sent by the SIVIGILA (the passive surveillance system). Perspectives of the system are to work closely with other programs for prevention, rehabilitation, and to integrate the whole country in a program.

The Colombian programs have reviewed the descriptive epidemiology of congenital heart defects (Tassinari et al. 2018), hypospadias (Fernández et al. 2017; Baltaxe and Zarante 2006), and BD in general (Zarante et al. 2010). The Bogotá program described the sonographic detection of congenital heart defects has been described in the city of Bogotá (García et al. 2014). Regarding etiological research, the Colombian programs have studied risk factors for urological BD (Calderón and Zarante 2006), microtia (Garcia-Reyes et al., 2006); craniofacial malformations (Zarante et al.

2009), hypospadias (Fernández et al. 2016), and anomalies of surgical interest (Correa et al. 2014). With regard to the protective factors, they have studied the prenatal use of vitamins and the prevention of genitourinary anomalies (Fernández et al. 2012).

Finally, the systems from Argentina and Colombia, along with PAHO, CDC, and the Costa-Rican surveillance system, joined to promote the organization of surveillance programs in other Latin American countries. This was done through two blended training programs, one in Costa Rica in 2015 and the other in Colombia in 2016.

A major limitation of hospital-based surveillance systems is the referral bias, that is, the selective delivery of affected pregnancies in hospitals participating in the program. In addition, it is important to take into account that this reference bias may vary over time, either because the reference guidelines are modified or because the hospitals are added or removed from the program. This aggravates the challenges posed by the longitudinal use of these data for follow-up. Additionally, since newborns are discharged from maternity hospitals a few days after delivery, hospital-based programs usually record only BDs that are evident during the hospital stay, unless they also include those who are re-admitted for a surgical intervention or other procedures. Newborns diagnosed after childbirth in a hospital participating in the program are not included in surveillance, unless the childbirth has also occurred in a participating hospital of the program.

Conclusions

As the epidemiological transition progresses, BD becomes more important in public health. It is essential to know the frequency of BD and their impact on health, in order to carry out preventive actions. Therefore, surveillance systems should be developed in order to measure BD. When developing a surveillance system, the objectives, the available resources, and previous experiences in similar contexts must be taken into account. In that sense, the experience of Argentina and Colombia can be useful for others when developing a birth defect surveillance system.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

Baltaxe E, Zarante I (2006) Prevalence of congenital heart disease in 44, 985 newborns in Colombia. Arch Cardiol Mex 76(3):263–268 Spanish

Bidondo MP, Groisman B, Gili J, Liascovich R, Barbero P (2014) Grupo de Trabajo RENAC. Prevalencia de anomalías congénitas en Argentina y su potencial impacto en los servicios de salud. Rev Argent Salud Pública 5(21):38–44

Bidondo MP, Groisman B, Barbero P, Liascovich R (2015a) Public health approach to birth defects: the argentine experience. J Community Genet 6(2):147–156. https://doi.org/10.1007/s12687-014-0209-x

Bidondo MP, Groisman B, Gili JA, Liascovich R, Barbero P (2015b) Estudio de prevalencia y letalidad neonatal en pacientes con anomalías congénitas seleccionadas con datos del Registro Nacional de Anomalías Congénitas de Argentina. Arch Argent Pediatr Ago 113(4):295–302

Bidondo MP, Liascovich R, Barbero P, Groisman B (2015c) Prevalencia de defectos del tubo neural y estimación de casos evitados posfortificación en Argentina. Arch Argent Pediatr 113(6):498–501

Bidondo MP, Groisman B, Tardivo A, Tomasoni F, Tejeiro V, Camacho I, Vilas M, Liascovich R, Barbero P (2016) Diprosopus: Systematic review and report of two cases. Birth Defects Res A Clin Mol Teratol 106:993–1007. https://doi.org/10.1002/bdra.23549.

Botto LD, Robert-Gnansia E, Siffel C, Harris J, Borman B, Mastroiacovo P (2006) Fostering international collaboration in birth defects research and prevention: a perspective from the international clearinghouse for Birth defects surveillance and research. Am J Public Health 96(5):774–780

Calderón J, Zarante I (2006) Congenital urological anomalies: epidemiological description and associated risk factors in Colombia 2001–2004. Arch Esp Urol 59(1):7–14 Spanish

Cassinelli A, Pauselli N, Piola A, Martinelli C, Alves de Azevedo JL, Bidondo MP, Groisman B, Barbero P, Liascovich R, Sala A (2018) National health care network for children with oral clefts: organization, functioning, and preliminary outcomes. Arch Argent Pediatr 116(1):e26–e33

Castilla EE, Orioli IM (2004) ECLAMC: the Latin-American collaborative study of congenital malformations. Community Genet 7(2–3): 76–94

Castilla EE, Peters PW (1992) Public health impact of birth defects monitoring systems: national and international efforts. Birth Defects Orig Artic Ser 28(3):27–36

Christianson A, Modell B (2006) Medical genetics in developing countries. Annu Rev Genomics Hum Genet 5:219–265

Christianson, A., Howson C, Modell C (2006). March of dimes global report of birth defects: the hidden toll of dying and disabled children. Available from : https://www.marchofdimes.org/global-report-on-birth-defects-the-hidden-toll-of-dying-and-disabled-children-full-report.pdf Accessed June 20, 2018

Correa C, Mallarino C, Peña R, Rincón LC, Gracia G, Zarante I (2014) Congenital malformations of pediatric surgical interest: prevalence, risk factors, and prenatal diagnosis between 2005 and 2012 in the capital city of a developing country. Bogotá, Colombia. J Pediatr Surg 49(7):1099–1103. https://doi.org/10.1016/j.jpedsurg.2014.03.001

DANE, 2017 (National Administrative Statistics Department in Colombia) Available at: http://www.dane.gov.co/ Accessed on: June 20, 2018

DEIS, Dirección de Estadísticas e Información en Salud (2017) Deaths of children under 5 years old by age group according to selected causes - year 2016. Available at: http://www.deis.msal.gov.ar/wp-content/uploads/2016/09/2016-Tabla35.html Accessed June 20, 2018

Fernández N, Henao-Mejía J, Monterrey P, Pérez J, Zarante I (2012) Association between maternal prenatal vitamin use and congenital abnormalities of the genitourinary tract in a developing country. J Pediatr Urol 8(2):121–126. https://doi.org/10.1016/j.jpurol.2011.07.005

Fernández N, Lorenzo A, Bägli D, Zarante I (2016) Altitude as a risk factor for the development of hypospadias. Geographical cluster distribution analysis in South America. J Pediatr Urol 12(5):307.e1–307.e5. https://doi.org/10.1016/j.jpurol.2016.03.015

Fernández N, Pérez J, Monterrey P, Poletta FA, Bägli DJ, Lorenzo AJ, Zarante I (2017) ECLAMC study: prevalence patterns of hypospadias in South America: multi-national analysis over a 24-year period. Int Braz J Urol 43(2):325–334. https://doi.org/10.1590/S1677-5538.IBJU.2016.0002

García MA, Imbachí L, Hurtado PM, Gracia G, Zarante I (2014) Ultrasound detection of congenital anomalies in 76,155 births in the cities of Bogotá and Cali, 2011-2012. Biomedica 34(3):379–386. https://doi.org/10.1590/S0120-41572014000300008 Spanish

Groisman B, Bidondo MP, Barbero P, Gili J, Liascovich R, Grupo de Trabajo RENAC (2013a) Registro Nacional de Anomalías Congénitas de Argentina. Arch Argent Pediatr 111(6):484–494

Groisman B, Bidondo MP, Gili J, Barbero P, Liascovich R (2013b) Strategies to achieve sustainability and quality in Birth defects registries: the experience of the National Registry of Congenital Anomalies of Argentina. J Registry Manag 40(1):29–31

Groisman B, Bidondo MP, Barbero P, Liascovich R (2016a) La Red Nacional de Anomalías Congénitas (RENAC): objetivos ampliados de la vigilancia. Arch Argent Pediatr 114(4):295–297

Groisman B, Liascovich R, Gili J, Barbero P, Bidondo MP, the RENAC Task Force (2016b) Sirenomelia in Argentina: prevalence, geographic clusters and temporal trends analysis. Birth Defects Research (Part A) 106:604–611

Groisman B, Bidondo MP, Liascovich R, Barbero P (2016c) Microcefalia en Argentina según datos de la Red Nacional de Anomalías Congénitas. Rev Argent Salud Pública 7(26):39–42

Groisman B, Gili J, Gimenez L, Poletta F, Bidondo MP, Barbero P, Liascovich R, López-Camelo J (2017) Geographic clusters of congenital anomalies in Argentina. J Community Genet 8(1):1–7

Hurtado-Villa P, Puerto AK, Victoria S, Gracia G, Guasmayán L, Arce P, Álvarez G, Blandón E, Rengifo N, Holguín JA, Durán A, Zarante I (2017) Raised frequency of microcephaly related to Zika virus infection in two birth defects surveillance systems in Bogotá and Cali, Colombia. Pediatr Infect Dis J 36(10):1017–1019

López B, Polo C, Martín MC, Mercado G, Groisman B, Bidondo MP, Liascovich R, Barbero P (2015) Secuencia Moebius. Análisis retrospectivo de 30 pacientes. Med Inf XXII(2):76–82

Luquetti DV, Koifman RJ (2011) Surveillance of birth defects: Brazil and the US. Cien Saude Colet 16(Suppl 1):777–785

Mai CT, Isenburg J, Langlois PH, Alverson CJ, Gilboa SM, Rickard R, Canfield MA, Anjohrin SB, Lupo PJ, Jackson DR, Stallings EB, Scheuerle AE, Kirby RS, for the National Birth Defects Prevention Network (2015) Population-based Birth defects data in the United States, 2008 to 2012: presentation of state-specific data and descriptive brief on variability of prevalence. Birth defects research part a, clinical and molecular. Teratology 103(11):972–993. https://doi.org/10.1002/bdra.23461.

Martín MC, Cristiano E, Villanueva M, Bonora MC, Berguio N, Tocci A, Groisman B, Bidondo MP, Liascovich R, Barbero P (2014) Esophageal atresia and prenatal exposure to mycophenolate. Reprod Toxicol 50:117–121

Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR (2016) Zika virus and Birth defects—reviewing the evidence for causality. N Engl J Med 374(20):1981–1987. https://doi.org/10.1056/NEJMsr1604338

Sargiotto C, Bidondo MP, Liascovich R, Barbero P, Groisman B (2015) Descriptive study on neural tube defects in Argentina. Birth Defects Res A Clin Mol Teratol 103(6):509–516

Sever L, Lynberg MC, Edmonds LD (1993) The impact of congenital malformations on public health. Teratology 48(6):547–549

SGSS. Sistema General de Seguridad Social en Salud, Colombia (2013) Guía de práctica clínica Detección de anomalías congénitas en el recién nacido. Para uso de profesionales de salud. - Guía No. 03

Tassinari S, Martínez-Vernaza S, Erazo-Morera N, Pinzón-Arciniegas MC, Gracia G, Zarante I (2018) Epidemiology of congenital heart diseases in Bogotá, Colombia, from 2001 to 2014: improved surveillance or increased prevalence? Biomedica 38:148–155. https://doi.org/10.7705/biomedica.v38i0.3381

Tellechea AL, Luppo V, Morales MA, Groisman B, Baricalla A, Fabbri C, Sinchi A, Alonso A, Gonzalez C, Ledesma B, Masi P, Silva M, Israilev A, Rocha M, Quaglia M, Bidondo MP, Liascovich R, Barbero P, RENAC Task Force1 (2018) Surveillance of microcephaly and selected brain anomalies in Argentina: relationship with Zika virus and other congenital infections. Birth Defects Res 110:1016–1026. https://doi.org/10.1002/bdr2.1347

Thacker SB, Berkelman RL (1988) Public health surveillance in the United States. Epidemiol Rev 10:164–190

WHO/CDC/ICBDSR (2014) Birth defects surveillance: a manual for programme managers. World Health Organization, Geneva

Zarante I, López MA, Caro A, García-Reyes JC, Ospina JC (2009) Impact and risk factors of craniofacial malformations in a Colombian population. Int J Pediatr Otorhinolaryngol 73(10):1434–1437. https://doi.org/10.1016/j.ijporl.2009.07.012

Zarante I, Franco L, López C, Fernández N (2010) Frequencies of congenital malformations: assessment and prognosis of 52,744 births in three cities of Colombia. Biomedica 30(1):65–71 Spanish

Zarante M, Sarmiento K, Mallarino C, Gracia G (2016) Description of Bogotá birth defects surveillance and follow-up program. J Registry Manag 43:116–121