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ORIGINAL ARTICLE

Birth prevalence of congenital anomalies in Argentina, according to socioeconomic level

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Abstract

Birth prevalence of congenital anomalies (CA) in Argentina is estimated around 1.7%. CA are the second leading cause of infant mortality. Poverty and other adverse socioeconomic conditions have been associated with birth defects. To describe the prevalence at birth of CA, according to the two proxy variables of socioeconomic level: the health subsector of the hospital where the cases were born (PUB-public versus PRI-private or social security) and its geographical location. The design of the study was ecological using the data of the National Network of Congenital Anomalies of Argentina (RENAC); from October 2010 to December 2018. CA birth prevalence was estimated using the Poisson regression. We used a logistic regression model to analyze the association birth prevalence to health subsector and geographical region. A total of 2,202,994 births were examined in the study period, with a global CA prevalence of 1.69% (95% CI 1.68–1.71). The highest prevalence was observed in PUB hospitals when comparing to PRI hospitals at the country level and in all regions. There were differences in the prevalence of selected congenital anomalies with a statistically significant association to PUB (observed in anencephaly, encephalocele, hydrocephalus, microcephaly, holoprosencephaly, microtia/anotia, cleft lip and palate, postaxial polydactyly, talipes equinovarus, talipes calcaneovalgus, and gastroschisis). The prevalence of critical heart defects and chromosomal anomalies was significantly higher in PRI hospitals. Although this is an ecological study with no information on socioeconomic status at individual level, we found an association between CA frequency and selected CA with the PUB subsector. Vulnerable populations affected with CA require a greater effort from policy makers and health care providers to allocate more resources and design strategies to access to health.

Keywords Birth defects · Argentina · Socioeconomic status

Introduction

Congenital anomalies are structural or functional alterations, of prenatal origin, that are present at birth, although they may be detected later in life. Congenital anomalies are caused by genetic factors, maternal diseases, infections, exposure to medications during pregnancy, and environmental pollutants, among others etiology (Stevenson et al. 1993).

Poverty and other adverse socioeconomic conditions have been associated with congenital anomalies (Mage et al. 2019; Baldacci et al. 2018; Yu et al. 2014; Vrijheid et al. 2000). In Argentina, two studies identified a significant association between low socioeconomic status and increased risk of cleft lip with or without cleft palate and ventricular septal defect (Pawluk et al. 2014; Pawluk et al. 2018).

Low socioeconomic status is associated with extreme maternal ages, malnutrition, and higher exposure to teratogenic agents, among other factors. On the other hand, low socioeconomic status is associated with health providers with lower capacity for prenatal diagnosis and therefore with lower access to termination of pregnancy due to fetal anomalies (Adegbosin et al. 2019).

In Argentina, infant mortality (IM) was 8.9 per 1000 births in 2018, ranging from 12.9 to 6.0 among provinces.

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Congenital anomalies are currently the 2nd leading cause of IM and represent approximately 28% of total infant deaths (Dirección de Estadísticas e Información de Salud (DEIS) 2018). The healthcare system is divided into three settings: public, social security, and private insurance. The public system is funded through taxes and is available free of charge to the entire population, being used mainly by those of lower income, who lack other health coverage. The social security setting is comprised of labor union-based coverage, funded by mandatory contributions from employers and registered workers. The private insurance setting (for profit) is funded by out of the pocket payments from the insured and serves the higher income population (Arce 2012). In 2012, 38% of the population had exclusive public coverage, 57% was covered by social works, and 5% was covered by private medicine companies (Tobar et al. 2012).

Argentina is divided into 23 provinces plus the capital city, Buenos Aires (CABA). The provinces are grouped into five regions: central (the most populous), west (Cuyo), northwest, northeast, and south (Patagonia). Around 65% of the population is concentrated in the central region provinces, particularly in the province of Buenos Aires, with 38.95% of the country´s population.

The aim of this study was to describe the prevalence at birth of congenital anomalies, according to two proxy variables of socioeconomic level: the health subsector of the birthing hospital: PUB (public) versus PRI (private/social security) and its geographical location.

Materials and methods

The design of the study was ecological. We investigated the relationship between the prevalence of congenital anomalies at birth and socioeconomic level in Argentina. Two proxy variables of the socioeconomic level were considered: the health subsector (PUB versus PRI) and the geographic region of birthing hospitals. Geographic regions and their provinces are Center (CABA, Buenos Aires, Córdoba, Entre Ríos, and Santa Fe), Northwest (Catamarca, Jujuy, Salta, Santiago del Estero, and Tucumán), Northeast (Corrientes, Chaco, Formosa, and Misiones), West (Cuyo: La Rioja, Mendoza, San Juan, and San Luis), and South (Patagonia: Chubut, La Pampa, Neuquén, Río Negro, Santa Cruz, and Tierra del Fuego).

The source of data was the National Network of Congenital Anomalies of Argentina (RENAC) and the national surveillance system for congenital anomalies (Groisman et al. 2016). RENAC is a hospital-based system which includes approximately 200 hospitals in the 24 jurisdictions of the country, with coverage of around 52% of births in the PUB subsector and 7% in the PRI subsector.

The calculation of prevalence was based on the number of cases with congenital anomalies detected in each participating hospital (numerator) and the total number of births in the same hospitals (denominator). The case definition includes all newborns and stillbirths weighing 500 g or more, with major structural anomalies, external or internal, identified from delivery to hospital discharge, and detected by physical examination or complementary studies, surgeries, or autopsies. Cases with minor or functional congenital anomalies are excluded. The detection and description of the anomalies are carried out by the local staff of the hospitals. The clinical review (coding and classification of cases) is made by two geneticists of the coordination (MPB and PB). Coding is done using the International Classification of Diseases, Tenth Revision (ICD-10), adapted by the Royal College of Pediatrics and Child Health. The clinical classification of cases includes three mutually exclusive categories: isolated anomalies, multiple anomalies (without a defined etiology), and syndromes (Rasmussen et al. 2003). RENAC does not include routine information on risk factors or socioeconomic status of families.

For the present study, 206 hospitals were selected: 161 were from the public subsector and reported to the data in the period between October 2010 and December 2018 (PUB hospitals); 45 were private/social security hospitals, which reported data between January 2013 and December 2018 (PRI hospitals).

Ten groups of cases with congenital anomalies were defined: cases born in PRI hospitals and cases born in PUB hospitals, combined with the five regions. In these ten groups, the prevalence of congenital anomalies was calculated for the total cases, for 6 categories of congenital anomalies grouped, and for 36 specific anomalies selected according to their impact on morbidity and mortality.

The prevalence was calculated according to the Poisson distribution, with a 95% confidence interval. In these groups, we also calculated the percentages of mothers with advanced age (≥ 35 years), young mothers (≤19 years), multiparous mothers (≥4 children), preterm (≤37 weeks), low weight (≤2500 g), the prenatal detection rate, and the percentage of cases that died before hospital discharge.

The chi-square statistic was used to compare the prevalence of grouped anomalies and selected specific anomalies, with a significance level of 0.05%.

The prevalence rate ratio (PRR) was used to compare the prevalence of congenital anomalies and grouped anomalies between regions and between health subsector, using a Poisson regression model. The Center region was used as the reference region. The adjusted risk (adPRR) was calculated using a Poisson Regression model analysis, considering a cluster of hospitals in the regression model to account for intraclass correlation. The Poisson regression models included geographical region and health subsector

as independent variables, and the interaction between the two.

Equiplot graphs were used to show the differences in prevalence among the groups for specifically selected anomalies (International Center for Health Equity, n.d.).

We used the Statistical software Stata version 13.

Results

From a total of 2,202,994 births examined in the hospitals that reported to RENAC in Argentina, 37,325 newborns with major congenital anomalies (cases) were detected in the study period, resulting in a global prevalence of 1.69% (95% CI 1.68–1.71). According to the health subsector, 206,868 (9.4%) births corresponded to PRI hospitals and 1,996,126 (90.6%) births to PUB hospitals (Table 1).

The distribution of cases according to their clinical presentation and other associated variables are presented in Table 2. Statistically significant differences were observed in clinical presentation, with a higher proportion of syndromic cases in PRI hospitals and a higher proportion of isolated and multiple cases in PUB hospitals, both at the national and regional levels. Advanced maternal age (≥35 years), preterm cases, and prenatal diagnosis were significantly more frequent in PRI hospitals, while young maternal age (≤19), multiparity, and neonatal deaths were significantly more frequent in PUB hospitals nationwide and in all regions.

At the national level, the prevalence of neural tube defects, oral clefts, abdominal wall defects, and limb defects was significantly higher in PUB hospitals, whereas the prevalence of critical heart defects and chromosomal anomalies were significantly higher in PRI hospitals (Table 3).

The prevalence of neural tube defects and oral clefts were higher in PUB hospitals than in PRI hospitals, in the Centro and Northwest regions. The same was observed for abdominal wall defects in the Central region and for limb defects in the Central, West, and South regions. On the contrary, the prevalence of critical congenital heart defects was significantly higher in PRI hospitals than in PUB hospitals in the Central region, and the same was observed for chromosomal anomalies in the Central and West regions (Table 3).

The prevalence at country level of anencephaly, encephalocele, hydrocephalus, holoprosencephaly, microcephaly, anotia-microtia, cleft lip and palate, postaxial polydactyly, talipes equinovarus, talipes calcaneus valgus, and gastroschisis were significantly higher in PUB hospitals, whereas the prevalence of coarctation of the aorta, hypoplastic left heart, tetralogy of Fallot, transposition of the great vessels, hypospadias, Down syndrome, and Edwards syndrome was significantly higher in PRI hospitals (Table 4 and Fig. 1). We did not find evidence of interaction between geographical region and health subsector.

Discussion

This is the first study comparing the prevalence of congenital anomalies between the PUB and PRI hospitals at the national and regional level in Argentina. The study showed prevalence was different according to the health subsystem and the region of the hospital of birth.

A previous publication of our group found a higher prevalence of congenital anomalies in newborns from lower socioeconomic subgroup of Buenos Aires City, born in public hospitals, located in the south of the city (Bronberg et al. 2020).

In the present study, a higher prevalence of congenital anomalies was observed in PUB hospitals regardless of region of birth. This is consistent with previous observations of a higher prevalence of congenital anomalies in populations of lower socioeconomic status (Hoyt et al. 2020; Yu et al. 2014; Canfield et al. 2006). There is an association between socioeconomic status and access to health. Lower income countries tend to have worse health outcomes than higher or middle-income countries, and within each country, people with lower socioeconomic status have worse health outcome (Wagstaff 2002).

Health inequalities are associated with multiple determinants: 1—different access to the health, housing, work, education, provision of services, among others; 2—the organization of the health system, its financing and coverage, which define the availability, accessibility, and quality of both preventive and curative services and benefits; and 3—risk factors at the individual level associated with cultural and family practices, commonly called "lifestyles."

In PUB hospitals, a higher proportion of early maternal age and multiparous women were observed. Multiparity age and young maternal age are considered important risk factors in maternal-fetus-neonatal health and are associated with higher fetus-neonatal morbidity and mortality (Susacasa 2014).

A higher proportion of syndromic cases was observed in PRI hospitals, whereas PUB hospitals had more cases with multiple anomalies with no defined pattern. This could be explained by PRI hospitals having more resources (i.e., access to medical geneticists and cytogenetics laboratory) to achieve the etiological diagnosis than PUB hospitals.

Neural tube defects, as a global category, were significantly more prevalent in PUB hospitals in all regions except Patagonia. The same was observed at the country level for anencephaly, encephalocele (both with statistical significance), and spina bifida (without statistical significance). In PRI hospitals, prenatal detection was higher than in PUB hospitals. Since elective terminations are not included in RENAC, the lower prevalence in PRI hospitals may be explained by higher prenatal detection and subsequent elective termination, in addition to a better nutritional status and more adequate periconceptional intake of folic acid in the population with a higher socioeconomic level. In a recent study (Bidondo et al.

Table 1 Newborns examined, coverage, and cases with congenital anomalies, according to geographic region and health subsector (public: PUB, or private/social security: PRI), RENAC 2010–2018

Region	Total newborns *N**		Newborns examined *N* (% coverage)		Cases with congenital anomalies *N*		Prevalence by region (CI 95%)		Prevalence by subsector (CI 95%)		
	PRI	PUB	PRI	PUB	PRI	PUB	Total	PRR ^{REGION}	PRI	PUB	PRR ^{PUB}
Center	1,871,786	2,238,134	164,640 (8.8)	1,119,645 (50.0)	2657	19,563	1.73 (1.71–1.75)	Reference	1.61 (1.55–1.68)	1.75 (1.72–1.77)	1.08 ** (1.04–1.13)
Northwest	291,903	549,874	6091 (2.1)	354,361 (64.4)	48	5232	1.46 (1.43–1.50)	0.84 ** (0.82–0.87)	0.79 (0.58–1.05)	1.48 (1.44–1.52)	1.88 ** (1.42–2.56)
Northeast	250,989	476,074	522 (0.2)	247,093 (51.9)	7	4031	1.63 (1.58–1.68)	0.94 ** (0.91–0.97)	1.34 (0.54–2.76)	1.63 (1.58–1.68)	1.22 (0.59–3.05)
Cuyo	262,177	294,747	16,153 (6.2)	177,643 (60.3)	234	3682	2.02 (1.96–2.08)	1.17 ** (1.13–1.21)	1.45 (1.27–1.65)	2.07 (2.01–2.14)	1.44 ** (1.26–1.65)
Patagonia	184,526	236,905	19,462 (10.5)	97,384 (41.1)	263	1608	1.60 (1.53–1.68)	0.92 ** (0.88–0.97)	1.35 (1.19–1.52)	1.65 (1.57–1.73)	1.23 ** (1.07–1.40)
Total	2,861,863	3,795,675	206,868 (7.2)	1,996,126 (52.6)	3209	34,116	1.69 (1.68–1.71)	---	1.55 (1.50–1.61)	1.71 (1.69–1.73)	1.10 ** (1.06–1.15)

* For the year 2018, the total number of births in 2017 is used as the denominator, the latest available

PRR^{REGION} prevalence rate ratio of being born between regions, the Central region is taken as the reference region (CTRO)

PRR^{PUB} prevalence rate ratio of being born in PUB hospital

PRI private/social security; *PUB* public

** Statistically significant

Table 2 Cases according to clinical presentation, maternal age, parity, gestational age, prenatal detection, survival to discharge, geographic region and health subsector (public: PUB, or private/social Security: PRI) RENAC 2010–2018

Region	Health subsector	Clinical presentation			Maternal age ≥ 35 years *N* (%)	Maternal age ≤ 19 years *N* (%)	Multiparity (≥4) *N* (%)	Preterm (≤37s) *N* (%)	Prenatal diagnosis *N* (%)	Dead at discharge *N* (%)
		Syndromes *N* (%)	Isolated *N* (%)	Multiple *N* (%)						
Center	**PRI**	495 (19.4)	1769 (69.3)	289 (11.3)	1080 (40.7)	68 (2.6)	248 (9.3)	1114 (41.9)	1229 (46.3)	344 (13.0)
	PUB	2781 (15.1)	13.130 (71.2)	2781 (13.7) *	3616 (18.5) **	3713 (19.0) **	3778 (19.3) **	7776 (39.7) **	5723 (29.3) **	2967 (15.2) **
Northwest	**PRI**	14 (31.8)	24 (54.5)	6 (13.6)	19 (39.6)	2 (4.2)	6 (12.5)	27 (56.3)	12 (25.0)	9 (18.8)
	PUB	882 (17.4)	3283 (64.6)	914 (18.0) *	914 (17.5) **	1129 (21.6) **	775 (14.8)	2250 (43.0)	1331 (25.4)	1132 (21.6)
Northeast	**PRI**	4 (57.1)	3 (42.9)	0 (0.0)	2 (28.6)	0 (0.0)	1 (14.3)	1 (14.3)	1 (14.3)	1 (14.3)
	PUB	552 (14.3)	2712 (70.5)	584 (15.2) *	656 (16.3)	1030 (25.6)	728 (18.1)	1604 (39.8)	814 (20.2)	728 (18.1)
Cuyo	**PRI**	56 (24.7)	140 (61.7)	31 (13.7)	72 (30.8)	35 (15.0)	32 (13.7)	108 (46.2)	114 (48.7)	42 (18.0)
	PUB	447 (13.3)	2526 (75.1)	389 (11.6) *	640 (17.4) **	732 (19.9)	704 (19.1) **	1273 (34.6) **	644 (17.5) **	397 (10.8) **
Patagonia	**PRI**	88 (31.5)	168 (60.2)	23 (8.2)	78 (29.7)	28 (10.6)	22 (8.4)	123 (46.8)	112 (42.6)	42 (16.0)
	PUB	266 (17.4)	1050 (68.8)	211 (13.8) *	292 (18.2) **	266 (16.5) **	265 (16.5) **	603 (37.5) **	483 (30.0) **	246 (15.3)
Total	**PRI**	622 (20.2)	2104 (68.4)	349 (11.4)	1251 (39.0)	133 (4.2)	309 (9.6)	1373 (42.8)	1468 (45.8)	438 (13.7)
	PUB	4963 (15.4)	22703 (70.3)	4633 (14.3) *	6118 (17.9) **	6914 (20.3) **	6253 (18.3) **	13506 (39.6) **	8995 (26.4) **	5470 (16.0) **

*p statistically significant (<0.05) calculated with chi^2 for clinical presentation between subsectors

**Statistically significant p (<0.05) calculated with chi^2 for each variable between public and private subsectors

Table 3 Prevalence of the main categories of congenital anomalies according to geographic region and health subsector (public: PUB, or private/social security: PRI), RENAC 2010–2018

Region	Health subsector	Categories of congenital anomalies *N* and prevalence × 10.000 (CI 95%)					
		Neural tube defects	Critical congenital heart defects	Oral clefts	Chromosomal anomalies	Abdominal wall defects	Limb defects
Center	PRI	103 6.26 (5.11–7.59)	307 18.6 (16.6–20.9)	173 10.5 (9.0–12.2)	431 26.2 (23.8–28.8)	102 6.2 (5.06–7.52)	152 9.23 (7.82–10.8)
	PUB	1093 9.76 (9.19–10.4)	1337 11.9 (11.3–12.6)	1678 15.0 (14.3–15.7)	2125 19.0 (18.2–19.8)	1426 12.7 (12.1–13.4)	1401 12.5 (11.9–13.2)
	TOTAL	1196 9.31 (8.79–9.86)	1644 12.8 (12.2–13.4)	1851 14.4 (13.8–15.1)	2556 19.9 (19.1–20.7)	1528 11.9 (11.3–12.5)	1553 12.1 (11.5–12.7)
	PRR ^{PUB}	1.56 * (1.28–1.92)	0.64 * (0.57–0.73)	1.43 * (1.22–1.67)	0.73 * (0.65–0.81)	2.06 * (1.68–2.54)	1.36 * (1.14–1.61)
Northwest	PRI	2 3.28 (0.40–11.9)	0	5 8.21 (2.67–19.2)	11 18.1 (9.02–32.3)	3 4.93 (1.02–14.4)	5 8.21 (2.67–19.2)
	PUB	343 9.68 (8.68–10.8)	354 10.0 (8.98–11.1)	668 18.9 (17.5–20.3)	700 19.8 (18.3–21.3)	368 10.4 (9.35–11.5)	456 12.9 (11.7–14.1)
	TOTAL	345 9.6 (8.59–10.6)	354 9.8 (8.82–10.9)	673 18.7 (17.3–20.1)	711 19.7 (18.3–21.2)	371 10.3 (9.3–11.4)	461 12.8 (11.7–14.0)
	PRR ^{PUB}	2.95 (0.81–24.4)	–	2.30 (0.98–7.11)	1.09 (0.61–2.20)	2.11 (0.72–10.3)	1.57 (0.67–4.86)
	PRR ^{REGION}	1.03 (0.91–1.16)	0.77 * (0.68–0.86)	1.30 * (1.19–1.42)	0.99 (0.91–1.08)	0.87 * (0.77–0.97)	1.06 (0.95–1.18)
Northeast	PRI	0	1 19.2 (0.49–107)	1 19.2 (0.49–107)	3 57.5 (11.9–168)	0	0
	PUB	290 11.7 (10.4–13.2)	194 7.85 (6.79–9.04)	380 15.4 (13.9–17.0)	437 17.7 (16.1–19.4)	312 12.6 (11.3–14.1)	514 20.8 (19.0–22.7)
	TOTAL	290 11.7 (10.4–13.1)	195 7.88 (6.81–9.06)	381 15.4 (13.9–17.0)	440 17.8 (16.1–19.5)	312 12.6 (11.2–14.1)	514 20.8 (19.0–22.6)
	PRR ^{PUB}	–	0.41 (0.07–16.3)	0.80 (0.14–31.8)	0.31 (0.10–1.49)	–	–
	PRR ^{REGION}	1.26 * (1.10–1.43)	0.61 * (0.53–0.72)	1.07 (0.95–1.19)	0.89 * (0.81–0.99)	1.06 (0.94–1.20)	1.72 * (1.55–1.90)
Cuyo	PRI	12 7.43 (3.84–13.0)	15 9.29 (5.20–15.3)	28 17.3 (11.5–25.1)	48 29.7 (21.9–39.4)	9 5.57 (2.55–10.6)	14 8.67 (4.74–14.5)
	PUB	134 7.54 (6.32–8.93)	202 11.4 (9.86–13.1)	270 15.2 (13.4–17.1)	347 19.5 (17.5–21.7)	122 6.87 (5.70–8.20)	261 14.7 (13.0–16.6)
	TOTAL	146 7.53 (6.36–8.86)	217 11.2 (9.76–12.8)	298 15.4 (13.7–17.2)	395 20.4 (18.4–22.5)	131 6.76 (5.65–8.02)	275 14.2 (12.6–16.0)
	PRR ^{PUB}	1.02 (0.56–2.02)	1.22 (0.73–2.23)	0.88 (0.59–1.34)	0.66 * (0.48–0.91)	1.23 (0.63–2.76)	1.70 (0.99–3.15)
	PRR ^{REGION}	0.81 * (0.68–0.96)	0.88 (0.76–1.01)	1.07 (0.94–1.21)	1.02 (0.92–1.14)	0.57 * (0.47–0.68)	1.17 (1.03–1.34)
Patagonia	PRI	17 8.74 (5.09–14.0)	20 10.3 (6.28–15.9)	27 13.9 (9.14–20.2)	47 24.1 (17.7–32.1)	13 6.68 (3.56–11.4)	12 6.17 (3.19–10.8)

Table 3 (continued)

Region	Health subsector	Categories of congenital anomalies *N* and prevalence × 10.000 (CI 95%)					
		Neural tube defects	Critical congenital heart defects	Oral clefts	Chromosomal anomalies	Abdominal wall defects	Limb defects
	PUB	80 8.22 (6.51–10.2)	110 11.3 (9.28–13.6)	175 18.0 (15.4–20.8)	236 24.2 (21.2–27.5)	86 8.83 (7.06–10.9)	109 11.2 (9.19–13.5)
	TOTAL	97 8.30 (6.73–10.1)	130 11.1 (9.30–13.2)	202 17.3 (15.0–19.8)	283 24.2 (21.5–27.2)	99 8.5 (6.89–10.3)	121 10.4 (8.59–12.4)
	PRR ^{PUB}	0.94 (0.55–1.69)	1.10 (0.68–1.87)	1.30 (0.86–2.02)	1.00 (0.73–1.40)	1.32 (0.73–2.58)	1.82 * (1.00–3.62)
	PRR ^{REGION}	0.89 (0.72–1.10)	0.87 (0.72–1.04)	1.20 * (1.04–1.39)	1.22 * (1.08–1.38)	0.71 * (0.58–0.88)	0.86 (0.71–1.03)
Total	PRI	134 6.48 (5.43–7.67)	343 16.6 (14.9–18.4)	234 11.3 (9.91–12.9)	540 26.1 (24.0–28.4)	127 6.14 (5.12–7.30)	183 8.85 (7.61–10.2)
	PUB	1940 9.72 (9.29–10.2)	2197 11.0 (10.6–11.5)	3171 15.9 (15.3–16.5)	3845 19.3 (18.7–19.9)	2314 11.6 (11.1–12.1)	2741 13.7 (13.2–14.3)
	TOTAL	2074 9.41 (9.01–9.83)	2540 11.5 (11.1–12.0)	3405 15.5 (14.9–16.0)	4385 19.9 (19.3–20.5)	2441 11.1 (10.7–11.5)	2924 13.3 (12.8–13.8)
	PRR ^{PUB}	1.51 * (1.26–1.79)	0.66 * (0.59–0.75)	1.41 * (1.23–1.61)	0.74 * (0.67–0.81)	1.89 * (1.58–2.27)	1.55 * (1.33–1.81)

PRR ^{PUB} prevalence rate ratio of being born in PUB hospital

PRR ^{REGION} prevalence rate ratio of being born between regions, the Central region is taken as the reference region (CTRO)

* Statistically significant

2020), we showed a lower percentage of prenatal detection in the public sector and the Northwest and Northeast regions.

Despite mandatory fortification of wheat flour with folic acid in Argentina, there could be worse nutrition and probably lower vitamin supplementation in the population of the public subsector. The National Nutrition and Health Survey showed that the deficient intake of folates is higher in households with unsatisfied basic needs (Encuesta nacional de nutrición y salud (ENNyS) 2007). In a study conducted on the basis of 314 pregnant women who attended a public maternity hospital in the City of Buenos Aires between 2000 and 2002 for prenatal care before the 16th week of gestation, serum folate levels were lower (Perego et al. 2005). In this study, most neural tube defect cases were isolated, which are usually preventable by folic acid intake. The study by Bronberg et al. 2011 showed a higher prevalence of neural tube defects in the Northwest and Northeast hospitals. Another study assessed mortality due to anencephaly after folic acid fortification of wheat flour, showing that the most impoverished regions presented the lowest reductions in prevalence: Northeast (35%) and Northwest (49%), when comparing to the rest of the country, which had a reduction of 60% (Bronberg et al. 2011).

The prevalence of gastroschisis was also higher in PUB hospitals. There is evidence that gastroschisis is associated with low maternal age (<20 years) (Goldbaum et al. 1990; Castilla et al. 2008; Baer et al. 2015) and with recurrent genitourinary infections in young women (Feldkamp et al. 2019). In our study, the percentage of women with maternal age less than 20 years was higher in PUB hospitals in all regions and in the country as a whole.

As it was observed for anencephaly, the lower prevalence of holoprosencephaly and hydrocephalus in PRI hospitals may be explained by higher prenatal ultrasound detection and subsequent termination of affected pregnancies in a population with higher socioeconomic level. These specific congenital anomalies have high rates of prenatal detection in Argentina: anencephaly 77.0%, holoprosencephaly 75.2%, and encephalocele 65.3% (Bidondo et al. 2020).

A higher prevalence of hydrocephalus and microcephaly in PUB hospitals could be due to a higher risk of congenital infections in the population of lower socioeconomic status (Hotez 2008; Cannon et al. 2010; Torgerson and Mastroiacovo 2013).

Oral clefts are also more prevalent in PUB hospitals, mainly cleft lip and palate. Oral clefts in Argentina have previously been associated with low socioeconomic status,

Table 4 Prevalence of the 36 specific anomalies selected according to health subsector and adjusted risk by the hospital (ad PRR) of being born in PUB hospital (public: PUB, or private/social security: PRI), RENAC 2010–2018

Specifically selected anomalies (ICD-10)	*N* and prevalence × 10.000 (CI 95%)		ad PRR ^{PUB} (IC95%)	Specific selected anomalies (ICD-10)	*N* and prevalence × 10.000 (CI 95%)		ad PRR ^{PUB} (IC95%)
	PRI	PUB			PRI	PUB	
Anencephaly (Q00)	21 1.02 (0.63–1.55)	565 2.83 (2.60–3.07)	2.80 * (1.71–4.58)	**Transverse limb reduction defect (Q71.2–Q71.30)**	27 1.31 (0.86–1.90)	345 1.73 (1.56–1.92)	1.32 (0.88–2.01)
Encephalocele (Q01)	11 0.53 (0.27–0.95)	264 1.32 (1.17–1.49)	2.50 * (1.10–5.65)	**Equinovarus Talipes (Q66.0)**	71 3.43 (2.68–4.33)	1389 6.96 (6.60–7.33)	2.04 * (1.30–3.19)
Spina bifida (Q05)	104 5.03 (4.11–6.09)	1118 5.60 (5.28–5.94)	1.12 (0.57–2.18)	**Calcaneovalgus Talipes (Q66.4)**	6 0.29 (0.11–0.63)	188 0.94 (0.81–1.09)	3.26* (1.17–9.09)
Hydrocephaly (Q03)	98 4.74 (3.85–5.77)	1512 7.58 (7.20–7.97)	1.61 * (1.14–2.27)	**Esophageal atresia (Q39.0–Q39.11)**	62 3.00 (2.30–3.84)	672 3.37 (3.12–3.63)	1.13 (0.83–1.54)
Holoprosencephaly (Q04.1-04.2)	14 0.68 (0.37–1.14)	495 2.48 (2.27–2.71)	3.68 * (2.06–6.56)	**Intestinal atresia (Q41.1–Q41.9)**	26 1.26 (0.82–1.84)	338 1.69 (1.52–1.88)	1.35 (0.91–2.09)
Microcephaly (Q02)	25 1.21 (0.78–1.78)	499 2.50 (2.29–2.73)	2.08 * (1.36–3.16)	**Duodenal atresia (Q41.0)**	44 2.13 (1.55–2.86)	337 1.69 (1.51–1.88)	0.80 (0.55–1.15)
Microphthalmia / anophthalmia (Q11.1-11.2)	24 1.16 (0.74–1.73)	271 1.36 (1.20–1.53)	1.18 (0.78–1.77)	**Anorectal malformation (Q42.0–Q42.3)**	84 4.06 (3.24–5.03)	976 4.89 (4.59–5.21)	1.21 (0.92–1.60)
Anotia + microtia (Q16; Q17.1)	37 1.79 (1.26–2.47)	596 2.99 (2.75–3.24)	1.61 * (1.02–2.56)	**Diaphragmatic hernia (Q79.0–Q79.01)**	73 3.53 (2.77–4.44)	747 3.74 (3.48–4.02)	1.06 (0.51–2.24)
Cleft Palate (Q35)	63 3.05 (2.34–3.90)	426 2.13 (1.94–2.35)	1.03 (0.79–1.36)	**Gastroschisis (Q79.3)**	76 3.67 (2.90–4.60)	1657 8.30 (7.91–8.71)	2.27 * (1.50–3.44)
Cleft Lip (Q36; exclude Q36.1, medial)	32 1.55 (1.06–2.18)	412 2.01 (1.87–2.27)	1.34 (0.93–1.92)	**Omphalocele (Q79.2)**	38 1.84 (1.30–2.52)	432 2.16 (1.97–2.38)	1.18 (0.79–1.77)
Cleft lip and palate (Q37)	138 6.67 (5.60–7.88)	2099 10.5 (10.1–11.0)	1.58 * (1.24–2.03)	**Bilateral Cryptorchidism (Q53.2)**	26 1.26 (0.82–1.84)	220 1.10 (0.96–1.26)	0.88 (0.47–1.64)
Coarctation of the Aorta (Q25.1-Q25.19)	57 2.76 (2.09–3.57)	360 1.80 (1.62–2.00)	0.66 * (0.47–0.92)	**Ambiguous genitalia (Q56.4)**	24 1.16 (0.74–1.73)	319 1.60 (1.43–1.78)	1.38 (0.97–1.96)
Hypoplasic left heart (Q23.4)	60 2.90 (2.21–3.73)	342 1.71 (1.54–1.91)	0.59 * (0.45–0.79)	**Hypospadias (Q54.1–Q54.3)**	86 4.16 (3.33–5.13)	496 2.49 (2.27–2.71)	0.60 * (0.40–0.91)
Tetralogy of Fallot (Q21.3-Q21.87)	66 3.19 (2.47–4.06)	369 1.85 (1.67–2.05)	0.58 * (0.40–0.83)	**Bilateral renal agenesis (Q60.1)**	10 0.83 (0.23–0.89)	174 0.87 (0.74–1.01)	1.81 (0.87–3.79)
Transposition of the great vessels (Q20.3)	63 3.05 (2.34–3.40)	365 1.83 (1.65–2.03)	0.60 * (0.38–0.95)	**Renal cysts (Q61.1–Q61.90)**	65 3.14 (2.43–4.01)	818 4.10 (3.82–4.39)	1.31 (0.90–1.90)
Double inlet left ventricle (Q20.4)	21 1.02 (0.63–1.55)	240 1.20 (1.06–1.36)	1.19 (0.72–1.95)	**Down syndrome (Q90.0–90.9)**	422 20.4 (18.5–22.4)	3391 17.0 (16.4–17.6)	0.83 * (0.71–0.98)
Preaxial polydactyly (Q69.00; Q69.1; Q69.20)	22 1.06 (0.67–1.61)	300 1.50 (1.34–1.68)	1.42 (0.88–2.30)	**Edwards syndrome (Q91.0)**	53 2.56 (1.92–3.35)	227 1.14 (0.99–1.30)	0.45 * (0.28–0.70)
Postaxial polydactyly (Q69.02; Q69.22)	52 2.51 (1.88–3.30)	1056 5.29 (4.98–5.62)	2.11 * (1.23–3.61)	**Patau syndrome (Q91.4)**	18 0.87 (0.21–1.38)	88 0.44 (0.35–0.54)	0.51 * (0.29–0.89)

PRR prevalence rate ratio of being born in PUB hospital

* Statistically significant

probably due to poor prenatal care, low educational level, lifestyle factors, acute maternal illnesses, and native ancestry (Pawluk et al. 2018). Our study shows the highest prevalence of oral clefts in the PUB hospitals of the Northwest,

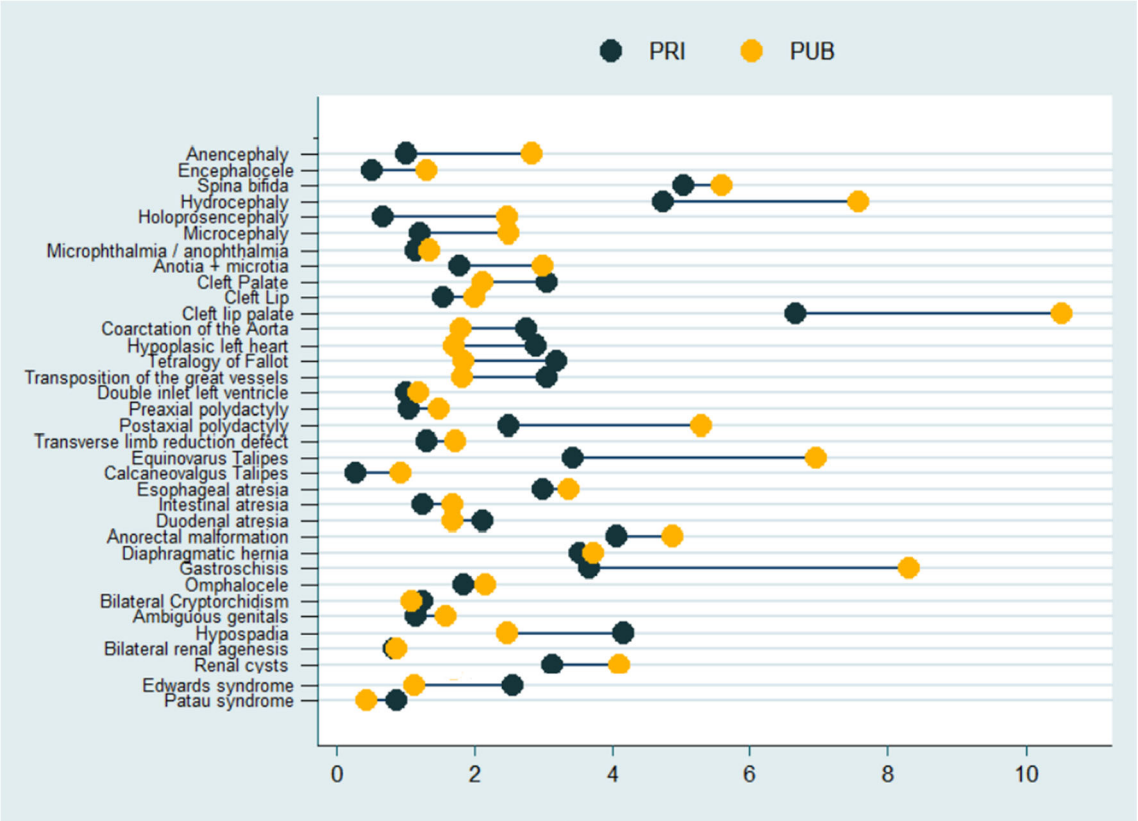

Fig. 1 Equiplot graph of the prevalence of selected congenital anomalies, according to health subsector of the birthing hospitals. RENAC

which is consistent with previous studies that detected a high-frequency cluster in the same region (Poletta et al. 2007; Groisman et al. 2016). A previous study by ECLAMC (Rittler et al. 2001) found an association between consanguinity and cleft lip, with or without bilateral cleft palate. Recent studies have also shown an association between parental consanguinity and non-syndromic oral clefts (Silva et al. 2019; Saeed et al. 2019). In a study carried out with data from the ECLAMC with hospitals from different countries in South America, consanguinity was strongly associated with poverty (Bronberg et al. 2016).

The higher prevalence of anotia-microtia in PUB hospitals may be explained by a higher proportion of native ancestors, an association found by Luquetti et al. (2011) in a global study. Hispanic ethnicity has also been reported as associated with anotia-microtia of isolated presentation in case-control studies with data from the National Birth Defects Prevention Study in the USA (Hoyt et al. 2014). Additionally, in a case-control study (Ryan et al. 2019) comprised of 669 cases of anotia-microtia and 11,797 controls, an association was shown with factors related to low socioeconomic level such as maternal multiparity and mothers from low-income households. It would be important to carry out case-control studies in our country for cases of anotia-microtia of isolated presentation to analyze these potentially associated factors.

Critical congenital heart defects and chromosomal abnormalities had a higher prevalence in PRI hospitals. The higher prevalence of critical congenital heart defects may be due to a higher detection capacity in these centers. The percentage of prenatal detection of critical congenital heart defects was 64.6% in PRI hospitals, higher than the 50% reported in an international study in which 12 countries from Europe, Asia, North, and South America participated (Bakker et al. 2019). Prenatal detection of critical congenital heart defects in PUB hospitals was notably lower, 31.8%. A previous study of our group showed a low prevalence of prenatal detection of critical congenital heart defects of isolated presentation in Argentina (Bidondo et al. 2020).

The higher prevalence of chromosomal abnormalities (Down, Edwards, and Patau Syndromes) in PRI hospitals is probably related to the higher proportion of mothers of advanced age in these hospitals (39%), in relation to PUB hospitals (17.9%). In a previous study, we showed that in the City of Buenos Aires the prevalence of chromosomal abnormalities had a different pattern (Bronberg et al. 2020). Although advanced maternal age (≥35 years) is much higher in the City of Buenos Aires in PRI hospitals, in this study, the frequency of Down syndrome was not significantly different from that of PUB hospitals (Bronberg et al. 2020). This finding was interpreted as a higher access to prenatal diagnosis and

subsequent termination of affected pregnancies in the population with higher socioeconomic level.

Khoshnood et al. (2006) suggested that inequity in access to prenatal diagnosis and subsequent termination of pregnancy, due to socioeconomic differences, has created disparities in the prevalence of Down syndrome. In a previous study (Bidondo et al. 2020), we showed a 16.2% prenatal detection rate for Down syndrome in Argentina.

One of the limitations of this study is that geographic region and hospital subsector were used as proxy measures of socioeconomic status. Since this is an ecological study, there is no information on the socioeconomic status at the individual level. Therefore, the correlations found are observed at the aggregate level and may not be extrapolated to individuals. Another limitation is that the proportion of births evaluated by the registry did not include the total number of births in the country and that the coverage of RENAC is considerably lower in the private subsector; therefore, it may not be representative of that health subsector.

Conclusions and recommendations

There are different programs in Argentina for the primary prevention of congenital anomalies (i.e., fortification of wheat flour with folic acid mandated by law, immunization for congenital rubella) and secondary-tertiary prevention (national program of ongenital heart defects, neonatal screening of congenital errors of the metabolism, early detection of congenital hearing loss, programs for care and referral of newborns with oral clefts and talipes).

However, the results of our study suggest that the vulnerable populations of the public subsector still require a greater effort from policy makers and health care providers to allocate more resources and design strategies that lead to better equity in access to health.

Finally, our study shows the usefulness of a congenital anomalies surveillance system as a source of information to identify groups at risk and guide prevention actions.

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration

Ethics approval and consent to participate In the present study, the data of the RENAC public health surveillance system was used. The data are anonymized. Therefore, the study is within the specific answers in Resolution 1480/2011 of the Ministry of National Health in Argentina (Guide for Research with Human Beings), which states that "the sources of health systems, official health programs, or public health surveillance in which no possibility of individual identification are not subject to evaluation by an Ethics Committee."

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