Journal of Community Genetics (2020) 11:313–320
https://doi.org/10.1007/s12687-019-00451-6

ORIGINAL ARTICLE

Prenatal detection of congenital anomalies and related factors in Argentina

Maria Paz Bidondo [1,2] · Boris Groisman [1,3] · Santiago Duarte [1,2] · Agostina Tardivo [1] · Rosa Liascovich [1,3] · Pablo Barbero [1]

Received: 21 August 2019 / Accepted: 26 December 2019 / Published online: 3 January 2020

Abstract

Congenital anomalies (CAs) are a leading cause of neonatal death. Many CAs can be diagnosed prenatally. To estimate the prenatal detection rate (PDR) of CA in hospitals participating in the RENAC (National Network of Congenital Anomalies of Argentina) and to analyze the PDR according to different factors. Sources were reports of RENAC from the 2013–2016 period. Congenital anomalies included were those detectable by ultrasound or by a prenatal karyotype. PDR was calculated by region, health subsector, clinical presentation, maternal age, sex, and twining. Using multiple logistic regression analysis, we evaluated predictors of prenatal detection. In total, 9976 cases were defined as prenatal detectable; 5021 were detected (PDR = 50.3%). Multiple presentation increased the chances of prenatal detection (Adj. OR = 1.6; 95%CI 1.4–1.9). Prenatal detection was lower in the public subsector (Adj. OR = 0.8; 95%CI 0.7–0.9) and in the northern regions of the country. PDR was higher than 75% in isolated cases of urinary malformation, anencephaly, and gastroschisis. Prenatal detection increased the chance of birth in higher complexity–level hospitals (Adj. OR = 2.5; 95%CI 2.3–2.8). PDR was within the range previously reported. Heterogeneity between regions and health subsector suggests the need for training to achieve equity in detection.

Keywords Congenital anomalies · Birth defect · Public health surveillance · Prenatal ultrasound · Prenatal detection rate

Introduction

Obstetric ultrasound and prenatal karyotype allow prenatal diagnosis of a wide subset of major congenital anomalies (CAs). Prenatal diagnosis facilitates timely referral of women to a health provider with the adequate level of complexity. Additionally, it enables early planning of medical or surgical treatment, thus reducing the risk of early neonatal death. Prenatal detection of CA is a factor on the reduction of perinatal mortality rates, due to the impact of early interventions. Some of these interventions may even be intrauterine (Gagnon et al. 2009; Aremu et al. 2013; González et al. 2005; Wiafe et al. 2011). Finally, in countries where elective termination of pregnancy for fetal anomaly is legal, prenatal diagnosis of fetal CA allows women to make the informed and autonomous decision to terminate or to continue with the pregnancy.

In 2017, infant mortality rate (IMR) in Argentina was 9.3 per 1000 live births and early neonatal mortality rate was 4.6 per 1000 live births. CAs were responsible for 28% of all infant deaths during this period; it was 1864 infant deaths in 2017 (DEIS 2017). In this context, prenatal detection of CA detection could be considered a key component of strategies aimed to reduce IMR.

Several studies evaluated the effectiveness of obstetric ultrasound to detect CA, showing wide heterogeneity in prenatal detection rates (PDR) (González et al. 2005; Wiafe et al. 2011; Wiesel et al. 2005; Vélez et al. 2004; Bidondo et al. 2015a). This is explained in part by the fact that CAs are not a homogeneous group and therefore, detection rates may differ for each CA subtype. In general, PDR is greater in the case of

✉ Maria Paz Bidondo
mariapazbidondo@gmail.com

[1] National Network of Congenital Anomalies of Argentina (RENAC), National Center of Medical Genetics (CNGM), National Administration of Laboratories and Health Institutes (ANLIS), National Ministry of Health and Social Development, Av. Las Heras 2670, C1425ASP Buenos Aires, Argentina

[2] Department of Cellular Biology, Histology, Embryology and Genetics, Medicine College, University of Buenos Aires (UBA), Buenos Aires, Argentina

[3] National Scientific and Technical Research Council- (CONICET), Buenos Aires, Argentina

CA of larger size or greater severity, or if the fetus has more than one CA. The operator's skills and the equipment are also relevant factors in the diagnostic accuracy of CA prenatal detection (Strizek et al. 2015; Carvalho et al. 2002; Sarkola et al. 2015). The present study was performed with data from the National Network of Congenital Anomalies of Argentina (in Spanish: Red Nacional de Anomalías Congénitas de Argentina-RENAC), a hospital-based surveillance system of major CA established in Argentina in 2009 (Groisman et al. 2013). RENAC includes the main maternity hospitals of the 24 jurisdictions of the country, covering approximately 300,000 births per year, which represents 43% of births. Since 2013, prenatal detection has been included in RENAC reports.

The objectives of the present study are as follows: (1) to estimate PDR of CA in newborns in the 2013–2016 period; (2) to analyze predictors of PDR.

Material and methods

This is a cross-sectional study. Data sources were RENAC reports from the period 2013–2016. Cases from a total of 186 maternity hospitals were included, spanning Argentina's 24 jurisdictions. The 24 jurisdictions of Argentina are grouped into 5 geographical regions: Center, Cuyo (center-west), Northeast, Northwest, and Patagonia (south). Around 65% of the population lives in the Center region (WHO 2017). The healthcare system in Argentina is divided into public and nonpublic sectors. The nonpublic is divided by social security and private insurance. The public sector is funded through taxes and is available free of charge to the entire population. It serves approximately 46% of the population, mainly the lower income population (Bidondo et al. 2015b). Only hospitals of the public subsector were classified in levels of complexity (from lower to higher: II, IIIA, IIIB) by a national decree of the National Ministry of Health (Resolution 641/2012). The nonpublic hospitals included in the study were not classified by the National Ministry of Health. A total of 148 hospitals in this study were from the public sector; the remaining 38 were maternities of the nonpublic sector. And 50 over 148 public (34%) had the high level of complexity with adequate resources for early care of newborns with CA.

The case definition included all live births and stillbirths weighting 500 g or more, with major morphological CA, whether externally or internally located, identified from birth until hospital discharge, and detected by either physical examination, complementary tests, surgical interventions, or autopsy. Since elective termination of pregnancy for fetal anomaly (ETOPFA) is illegal in Argentina, RENAC does not include reports of terminations. RENAC reports include a verbatim description of the CA observed on the affected newborn, along with a core set of variables (Groisman et al. 2013). For each case, descriptions of the postnatally reported CA were reviewed along with the prenatal findings. A code from chapter 17 (codes Q00.0 to Q99.9) of the International Classification of Diseases, 10th Revision (ICD-10) with the adaptation of the Royal College of Pediatrics and Child Health, was assigned to each CA. For other findings detected prenatally, codes from other ICD-10 chapters were also used (P01.2: oligohydramnios; P01.3: polyhydramnios; P05.9: intrauterine growth retardation, P83.2: hydrops). A subset of CAs were selected as prenatally detectable (in function of severity, local diagnostic capacity, and inclusion in previously published studies): anencephaly, encephalocele, spina bifida, microcephaly, hydrocephalus, holoprosencephaly, hydranencephaly, critical congenital heart disease, diaphragmatic hernia, gastroschisis, omphalocele, renal agenesis, renal cysts, hydronephrosis, bladder/cloacal exstrophy, megabladder, ambiguous genitalia, limb reduction defects; sirenomelia; conjoined twins. Some syndromic conditions were also considered prenatally detectable: bone dysplasias with neonatal manifestation (i.e., thanatophoric dysplasia, achondroplasia, osteogenesis imperfecta types II–III, short rib polydactyly, campomelic, among others); Down, Turner, Edwards, and Patau syndromes.

Clinical presentation was also analyzed into the following categories (Rasmussen et al. 2003): isolated (the case presented a single anomaly or a primary anomaly which generated secondary anomalies–sequence); syndromic (the case presented two or more CAs with an identified cause, whether genetic or environmental); or multiple (the case presented two or more CAs which have a known association or not, but without an identified cause).

PDR was calculated as the quotient between the number of cases that were prenatally detected (numerator) and the total number of cases (denominator). PDR for specific anomalies included only isolated cases.

We compared cases with and without prenatal diagnosis using multiple logistic regression. The crude and adjusted odds ratios (Adj. OR) with 95% confidence intervals were calculated. The statistical software used was Stata 13.0. In the first model, the PDR was considered the dependent variable, and the following variables were considered predictors: sex (female, male, indeterminate); twinning (yes/no); clinical presentation (isolated, multiple, syndromic); health subsector (public/nonpublic); geographic region of residence (Center, Cuyo, Northeast, Northwest, and Patagonia); maternal age (in years). In the second model, prenatal detection was considered an independent variable and the association with the following dependent variables was evaluated: level of complexity of birthing hospital (high versus low; considering high level IIIB and low levels IIIA and II; this information only available for public hospitals); perinatal survival (perinatal death versus perinatal survival). Both analyses were performed for total and isolated cases and syndromes when the number of cases was at least 200.

Results

In the period 2013–2016, 19,070 cases with CA were reported to RENAC over 1,261,534 births. In total, 9976 cases had at least one CA defined as detectable prenatally (9593 live births and 383 stillbirths). Prenatal detection was achieved in 5021 cases (PDR = 50.3%). The Center region, nonpublic sector, and multiple clinical presentation had the highest PDR (Table 1).

Regarding selected isolated CA, the highest PDR values were observed in megacystis, cystic kidney disease, hydronephrosis, anencephaly, and gastroschisis. Ambiguous genitalia and reduction limb defects had the lowest values (Table 2). Down syndrome had a low PDR (Table 3).

Multiple clinical presentation increased the chance of prenatal diagnosis (Adj. OR = 1.6; 95%CI 1.4–1.9). Three regions of maternal residence, i.e., Northeast (Adj. OR = 0.5; 95%CI 0.4–0.7), Cuyo (Adj. OR = 0.7; 95%CI 0.6–0.9), and Northwest (Adj. OR = 0.7; 95%CI 0.6–0.9), were significantly associated with lower prenatal detection. Also, the public subsector was significantly associated with lower PDR (Adj. OR = 0.8; 95%CI 0.7–0.9) (Table 4). When adjusting for specific isolated CA with more than 200 cases, geographic region and health subsector modified the chance of prenatal detection (Tables 4 and 5). The chance of prenatal diagnosis of Down syndrome increased more than twice in the nonpublic sector (Adj. OR = 2.2; 95%CI 1.6–2.9). And for Down syndrome, Northeast (Adj. OR = 0.5; 95%CI 0.3–0.8) and Northwest (Adj. OR = 0.6; 95%CI 0.4–0.9) regions were significantly associated with lower prenatal detection (Table 5).

Prenatal detection was found to be a predictor for birth in a high complexity hospital and for perinatal survival, after adjusting by geographical regions (Adj. OR = 2.5; 95%CI 2.3–2.8). In turn, the lack of prenatal detection was associated with a 60% increase of chance of perinatal death adjusted by the institution's complexity level and geographical region (Adj. OR = 0.4; 95%CI 0.3–0.4). However, prenatal detection of selected isolated CA increased the chance of birth in a higher level of care institution in cases with gastroschisis (Adj. OR = 5.3; 95%CI 3.6–7.7); spina bifida (Adj. OR = 5.2; 95%CI 3.4–8.0); critical congenital heart defects (Adj. OR = 3.2; 95%CI 2.2–4.5); diaphragmatic hernia (Adj. OR = 2.7; 95%CI 1.5–4.7); and hydrocephalus (Adj. OR = 2.3; 95%CI 1.4–3.8). Regarding cases with critical congenital heart defects, the chance of perinatal death increased with the lack of prenatal diagnosis (Adj. OR = 0.6; 95%CI 0.4–0.9) and lower complexity of the institution at birth (Adj. OR = 0.5; 95%CI 0.3–0.7). The perinatal lethality of cases with

Table 1 Prenatal detection rates (PDR) of prenatally detectable cases with congenital anomalies (CAs), by geographical region, healthcare subsector, clinical presentation, and maternal age, National Network of Congenital Anomalies of Argentina (RENAC), years 2013–2016

Covariables		Cases with CA	Cases detected prenatally	PDR (%)
Geographical region*	Northeast	1165	431	37.0
	Cuyo	835	366	43.8
	Northwest	1727	750	43.4
	Patagonia	605	316	52.2
	Center	5644	3158	56.0
Healthcare subsector	Public	9078	4506	49.6
	Nonpublic	898	515	57.3
Clinical presentation	Syndrome	966	427	44.2
	Isolated	6890	3382	49.1
	Multiple	2120	1212	57.2
Maternal age	< 20 years old	2171	1107	51.0
	20–34 years old	6191	3150	50.9
	≥ 35 years old	1614	764	47.3
Sex	Male	5278	2220	42.1
	Female	4418	2644	59.8
	Indeterminate	280	152	54.3
Twinning	Singleton pregnancy	9613	4823	50.2
	Twins	354	194	54.8
	Nonspecified	9	4	44.4

*Jurisdictions grouped into geographical regions: Center: Ciudad de Buenos Aires, Buenos Aires, Córdoba, Entre Ríos, Santa Fe; Cuyo: La Rioja, Mendoza, San Juan y San Luis; Northeast: Corrientes, Chaco, Formosa, Misiones; Northwest: Catamarca, Jujuy, Salta, Santiago del Estero, Tucumán; Patagonia: Chubut, La Pampa, Neuquén, Rio Negro, Santa Cruz, Tierra del Fuego

Table 2 Prenatal detection rate (PDR) of selected isolated congenital anomalies, National Network of Congenital Anomalies of Argentina (RENAC), years 2013–2016

Isolated congenital anomalies (ICD-10 code)*	Cases	Cases detected prenatally	PDR (%)
Anencephaly (Q00)	244	188	77.0
Encephalocele (Q01)	72	47	65.3
Microcephaly (Q02)	102	28	27.5
Hydrocephalus (Q03)	454	337	74.2
Holoprosencephaly (Q04.1–04.2)	133	100	75.2
Spina bifida (Q05)	544	350	64.3
Critical congenital heart defects**	999	344	34.4
Oral cleft (Q35-Q37)	1281	321	25.1
Cleft palate with cleft lip (Q37)	710	216	30.4
Ambiguous genitalia (Q56.4)	49	8	16.3
Renal agenesis (uni-bilateral); Potter's sequence (Q60.0–Q60.2 and Q60.6)	154	117	76.0
Cystic kidney disease (Q61)	289	247	85.5
Congenital hydronephrosis (Q62.0)	245	190	77.6
Megacystis (Q64.79)	17	17	100.0
Limb reduction defects (Q71.0–Q73.8)	363	68	18.7
Diaphragmatic hernia (Q79.0–Q79.01)	314	215	68.5
Congenital abdominal wall defects (Q79.2–Q79.5)	1049	780	74.4
Omphalocele (Q79.2)	112	68	60.7
Gastroschisis (Q79.3)	883	673	76.2

**ICD-10* International Classification of Diseases, version 10, with the RCPCH adaptation

**Q20.0, Q20.3, Q20.4, Q21.3, Q21.82, Q22.00, Q22.40, Q22.5, Q23.4, Q25.1-Q25.19, Q25.2, and Q26.2

diaphragmatic hernia increased if birth occurred at low complexity institutions, independent of prenatal detection (Adj. OR = 0.5; 95%CI 0.3–0.9).

Discussion

This study is the first description of PDR of CA in Argentina, and its correlation with several variables, using a large hospital-based sample from all jurisdictions of the country. The overall PDR was 50.3%. This rate is within the range previously reported in other settings: 34.9–62.0% (Rydberg and Tunón 2017; Postoev et al. 2015; Rossi and Prefumo 2013; CAROBB 2012; Campaña et al. 2010). Birth in an institution belonging to the nonpublic sector was shown to be a predictor for a higher chance of prenatal detection. The health sector can be considered a proxy of socioeconomic status; women of higher socioeconomic status are frequently treated in nonpublic institutions, which have more human and physical resources. This could explain access to more and earlier prenatal visits and higher rates of detection. Regarding the overall rate of prenatal ultrasound detection, the study by Campaña et al. (2010), which employed data from 13 hospitals in Argentina, showed no difference between public and nonpublic sectors. However, prenatal detection was made at earlier gestational age in the nonpublic sector (Campaña et al. 2010). In countries with legal elective termination of pregnancy for fetal anomaly, early prenatal detection

Table 3 Prenatal detection of selected congenital syndromes, National Network of Congenital Anomalies of Argentina (RENAC), years 2013–2016

Selected congenital syndromes (ICD-10 code*)	Cases	Cases detected prenatally	PDR (%)
Thanatophoric dysplasia (Q77.1)	24	22	91.7
Achondroplasia (Q77.4)	18	13	72.2
Osteogenesis imperfecta (Q78.0)	26	22	84.6
Down's syndrome (Q90.0–Q90.9)	2117	344	16.2
Edward's syndrome (Q91.0–Q91.3)	153	104	68.0
Patau's syndrome (Q91.4–Q91.7)	56	33	58.9

**ICD-10* International Classification of Diseases, version 10, with the RCPCH adaptation

Table 4 Predictors of prenatal detection in total cases with CA, National Network of Congenital Anomalies of Argentina (RENAC), years 2013–2016.

Covariables		Adj. OR (95%CI)
Geographical region	Northeast	0.5 (0.4–0.7)*
	Cuyo	0.7 (0.6–0.9)*
	Northwest	0.7 (0.6–0.9)*
	Center	1.2 (0.9–1.4)
	Patagonia (reference)	1
Healthcare subsector	Public	0.8 (0.7–0.9)*
	Nonpublic (reference)	1
Clinical presentation	Isolated	1.2 (0.9–1.3)
	Multiple	1.6 (1.4–1.9)*
	Syndrome (reference)	1
Maternal age	Continuous variable	1.0 (0.9–1.1)
Sex	Male	1.0 (0.9–1.1)
	Female (reference)	1
Twinning	Twins	1.1 (0.9–1.4)
	Singleton pregnancy (reference)	1

Jurisdictions grouped into geographical regions: Center: Ciudad de Buenos Aires, Buenos Aires, Córdoba, Entre Ríos, Santa Fe; Cuyo: La Rioja, Mendoza, San Juan y San Luis; Northeast: Corrientes, Chaco, Formosa, Misiones; Northwest: Catamarca, Jujuy, Salta, Santiago del Estero, Tucumán; Patagonia: Chubut, La Pampa, Neuquén, Rio Negro, Santa Cruz, Tierra del Fuego

Ref.: *Adj. OR* adjusted odds ratio, *95%CI* 95% confidence interval

*Statistical significance

Table 5 Predictors associated with prenatal detection of selected isolated congenital anomalies (CAs) and Down syndrome, National Network of Congenital Anomalies of Argentina (RENAC), years 2013–2016

Selected isolated CA (ICD-10 code)*	Predictor		Adj. OR (95%CI)
Spina bifida (Q05)	Healthcare subsector	Nonpublic	2.2 (1.1–4.9)
Critical congenital heart defects**	Healthcare subsector	Nonpublic	2.3 (1.6–3.3)
	Geographical region	Centre	6.0 (2.3–15.4)
		Cuyo	4.2 (1.5–12.2)
		Northwest	4.3 (1.6–11.9)
Cleft palate with cleft lip (Q37)	Healthcare subsector	Nonpublic	3.0 (1.7–5.4)
	Geographical region	Northeast	0.3 (0.1–0.6)
Cystic kidney disease (Q61)	Healthcare subsector	Nonpublic	1.7 (0.4–8.1)
Congenital hydronephrosis (Q62.0)	Twining	Singleton pregnancy	0.2 (0.1–0.7)
Diaphragmatic hernia (Q79.0–Q79.01)	Geographical region	Northeast	0.2 (0.1–0.9)
		Northwest	0.2 (0.1–0.9)
Gastroschisis (Q79.3)	Geographical region	Northwest	0.5 (0.2–0.9)
Down's syndrome (Q90.0–Q90.9)	Healthcare subsector	Nonpublic	2.2 (1.6–2.9)
	Geographical region	Northeast	0.5 (0.3–0.8)
		Northwest	0.6 (0.4–0.9)

Jurisdictions grouped into geographical regions: Center: Ciudad de Buenos Aires, Buenos Aires, Córdoba, Entre Ríos, Santa Fe; Cuyo: La Rioja, Mendoza, San Juan y San Luis; Northeast: Corrientes, Chaco, Formosa, Misiones; Northwest: Catamarca, Jujuy, Salta, Santiago del Estero, Tucumán; Patagonia: Chubut, La Pampa, Neuquén, Rio Negro, Santa Cruz, Tierra del Fuego

Ref.: *Adj. OR* adjusted odds ratio, *95%CI* 95% confidence interval

**ICD-10* International Classification of Diseases, version 10, with the RCPCH adaptation

**Q20.0, Q20.3, Q20.4, Q21.3, Q21.82, Q22.00, Q22.40, Q22.5, Q23.4, Q25.1-Q25.19, Q25.2, and Q26.2

of CA allows women to do an informed decision on termination of pregnancy. In Argentina, abortion is forbidden with some exceptions, such as in cases in which the woman's life or health is threatened, or in cases of rape. A fetus with a severe CA (such as anencephaly) has been considered a cause of psychological health impact to women. However, the access to legal termination in these cases is still heterogeneous in Argentina. Women with a higher socioeconomic level have more access to prenatal diagnosis followed by termination of pregnancy performed in the nonpublic sector (Barbero et al. 2018). In Argentina and other countries where the termination of pregnancy is not legal, women perform it clandestinely and unsafe termination of pregnancy is a major contributor to maternal morbidity and mortality.

European surveillance programs showed the influence on PDR of different legislations regarding mandatory fetal screening of CA. Countries without mandatory prenatal screening had the lowest rates (Postoev et al. 2015; Stoll et al. 2001; Garne et al. 2005). Likewise, in the Swedish experience, the routine use of a checklist to investigate CA prenatally increased prenatal detection (Rydberg and Tunón 2017). In Argentina, there is no legislation regarding prenatal ultrasounds. The National Ministry of Health and Social development published a "Guide for the practice of preconception care and prenatal control" (Decree 648/2003), which recommends a minimum of 5 prenatal visits and 3 prenatal ultrasounds for low-risk pregnancies (DINAMIA 2013). However, a report of the Perinatal Information System shows that 6.9% of pregnancies (95%CI 6.8–7.1) had no prenatal visits and that 33.5% (95%CI 33.3–33.8) had insufficient prenatal visits. In the Northeast region, these figures reach 8.1% (95%CI 7.7–8.5) and 38.0% (95%CI 37.3–38.8), respectively (SIP-G 2013). The results of our study may be partially explained by regional differences. The heterogeneity between regions and health sectors shows the importance of training for improving detection rates. Staboulidou et al. (2010) showed an increase of 40%, in detection of fetal malformations when physicians received systematic training with ultrasound simulation.

Maternal age is a known risk factor for trisomies. Rydberg and Tunón (2017) published that the detection of CA was significantly higher as maternal age increased, maybe due to the effect on the operator's knowledge of the risk factor. However, in our sample, maternal age was not associated with higher detection. The slightly higher PDR was shown in the group of mothers with less than 20-year-olds. This may be due the high PDR of gastroschisis, which is more frequent in this age group.

As observed in several publications (Rossi and Prefumo 2013; Stoll et al. 2001; Garne et al. 2005) when considering CAs as a whole, cases with multiple presentation had the highest chance of detection; and when considering isolated cases, the detection rate of urinary CA was higher. This is due in part to the fact that the detection of urinary CA (i.e., unilateral renal agenesis) is usually performed prenatally, and then, the prenatal finding is sought postnatally. However, postnatal diagnosis when there is no prenatal detection is less frequent, because when isolated, these anomalies do not have a major impact on health. This effect has already been published by other surveillance programs (Postoev et al. 2015; EUROCAT 2018). Prenatal detection of urinary CA impacts on infant morbimortality and in reproductive outcomes. In cases with extrauterine lethality (i.e., bilateral renal agenesis), the intervention may be labor induction or elective termination of pregnancy (Garne et al. 2005; Policiano et al. 2015).

The PDR of isolated microcephaly was low, whereas detection of other brain CAs such as anencephaly, hydranencephaly, hydrocephalus, and holoprosencephaly was higher than 70%. The low PDR of microcephaly is relevant in the context of the congenital syndrome associated with ZIKV in which prenatal microcephaly is one of the features. In other studies, the low detection of microcephaly has been attributed to incorrect measurement of gestational age, the cutoff point, and the low detection in the first and second trimesters (De Catte et al. 2012; Gelber et al. 2017; ISUOG 2018; Chibueze et al. 2017; Miquel-Verges et al. 2015).

Low PDR of isolated oral cleft prevents referral of pregnant women to maternities with oral cleft treatment teams. In Argentina, there is an oral clefts care network comprised by 61 treatment teams. Thirty-three of these teams are located in maternity hospitals where RENAC works (Cassinelli et al. 2018).

Critical congenital heart defects with isolated presentation had a PDR lower than 35%, and it was predicted by health sector and region of maternal residence. Prenatal planning of optimal postnatal care is particularly useful for newborns with critical congenital heart defects, because they may not survive the neonatal period without early interventions. Patients with risk factors for congenital heart defects or abnormal results in screening examination should be referred for second trimester fetal echocardiography (Bishop et al. 2017). After birth, pulse oximetry screening in the maternity wards can improve diagnosis. Pulse oximetry showed high diagnosis specificity and accuracy for critical congenital heart defects (Du et al. 2017). However, prenatal detection of congenital heart defects is related to the experience and skill of the operator (Sarkola et al. 2015). A prospective multicenter study which evaluated the accuracy of the four-chamber view in Italy, showed a higher sensitivity of the four-chamber scan when applied by a trained team of operators in a controlled and supervised setting, both before and after 24 weeks of gestation (Oggè et al. 2006). In Argentina, The National Program of Congenital Heart Defects (DINAMIA 2008 National Health Resolution 107/2008) supports diagnosis and timely treatment in the public sector. Increased prenatal detection may facilitate early referral, leading to better outcomes. Down syndrome showed a strikingly low PDR. In the public sector, first trimester screening is not usually available and is restricted mainly to the Center and

Patagonia regions. The public sector and the most socioeconomically disadvantaged regions in our country (Northwest and Northeast) presented the lowest detection rate of Down syndrome.

We observed an association between a PDR and the complexity level of the hospital of birth, which is consistent with previous reports (Bidondo et al. 2015a). Prenatal detection of CA increases referral of pregnant women with fetal anomalies, favoring delivery at the most adequate level of care. This association was observed in the group of CA as a whole, and in specific isolated anomalies (hydrocephaly, spina bifida, critical congenital heart defects, diaphragmatic hernia, and gastroschisis). Referral to a high level of care hospital is an intervention that reduces neonatal deaths (Bidondo et al. 2015a; DINAMIA 2014). In the case of critical congenital heart defects, prenatal detection increased 3 times the chance of birth in a hospital with adequate level of care, and nondetection decreased 40% the chance of early neonatal survival. This is consistent with a recent national study in Denmark, which found that mortality among live born children with a major congenital heart defect has been decreasing after the introduction of prenatal screening (Lytzen et al. 2019).

This study had some limitations. It was not possible to evaluate the following factors: experience of the operator; number of ultrasounds performed per pregnancy; and the type and timing of the ultrasound performed (i.e., ultrasound scan of the first trimester, second-trimester ultrasound first level, detailed second-trimester ultrasound, Doppler ultrasound, fetal echocardiography, ultrasound followed by fetal resonance). The different methodologies of prenatal cytogenetic studies and the use of prenatal screening methods were not evaluated in this specific study either; these studies are still restricted to a limited population in Argentina.

In terms of health policy, the results of this study show heterogeneity between regions and health subsector, suggesting the need for training in order to achieve equity in detection.

Acknowledgments The authors thank the RENAC working group.

Funding information RENAC was supported by the National Center for Genetic Medicine (CNGM, ANLIS C, Malbrán), National Ministry of Health (NMH) of Argentina, Grants Abraam Sonis 2016–2017, the National Agency for Science and Technology, National Ministry of Science and Technology of Argentina.

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

Compliance with ethical standards

Ethical statement 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 is not no possibility of individual identification are not subject to evaluation by an Ethics Committee."

References

Aremu AA, Ajadi T, Atanda OO et al (2013) Prenatal diagnosis of congenital anomalies-preliminary report from a new specialized ultrasound unit. IJARS 2(4):17–21 http://www.ijars.net/article_abstract.asp?issn=0973-709x&year=2013&month=December &volume=2&issue=4&page=17-21&id=1996

Barbero P, Liascovich R, Tellechea A et al (2018) Inequity in prenatal diagnosis and termination of pregnancy due to fetal anomaly in Argentina. Arch Argent Pediatr 116(6):e810–e815 Available at: https://www.sap.org.ar/docs/publicaciones/archivosarg/2018/v116n6a32.pdf Accessed: 10 December, 2019

Bidondo MP, Groisman B, Gili JA et al (2015a) Study on the prevalence and neonatal lethality in patients with selected congenital anomalies as per the data of the National Registry of Congenital Anomalies of Argentina. Arch Argent Pediatr 113(4):295–302. https://doi.org/10.5546/aap.2015.295

Bidondo MP, Groisman B, Barbero P, Liascovich R (2015b) 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

Bishop KC, Kuller JA, Boyd BK et al (2017) Ultrasound examination of the fetal heart. Obstet Gynecol Surv. 72(1):54–61. https://doi.org/10.1097/OGX.0000000000000394

Campaña H, Ermini M, Aiello HA et al (2010) Prenatal sonographic detection of birth defect in 18 hospital of South America. J Ultrasound Med. 29(2):203–212. https://doi.org/10.7863/jum.2010.29.2.203

CAROBB. Third report of the Congenital Anomaly register for Oxforshire. Bershire and Buckinghamshire. Oxford (UK): Oxford University. National Perinatal Epidemiology Unit. 2012. Birth 2005–2010: 1–23. Available at: http://www.binocar.org/content/CAROBB%20Report%202012.pdf. Accessed March 2019

Carvalho JS, Mavrides E, Shinebourne EA et al (2002) Improving the effectiveness of routine prenatal screening for major congenital heart defects. Heart. 88(4):387–391

Cassinelli A, Pauselli N, Piola A et al (2018) National Health Care Network for children with oral clefts: organization, functioning, and preliminary outcomes. Arch Argent Pediatr. 116(1):e26–e33. https://doi.org/10.5546/aap.2018.eng.e26

Chibueze EC, Parsons AJQ, Lopes KD et al (2017) Diagnostic accuracy of ultrasound scanning for prenatal microcephaly in the context of Zika virus infection: a systematic review and meta-analysis. Sci Rep. 7(1):2310. https://doi.org/10.1038/s41598-017-01991-y

De Catte L, De Keersmaeker B, Claus F (2012) Prenatal neurologic anomalies: sonographic diagnosis and treatment. Paediatr Drugs 14(3):143–155. https://doi.org/10.2165/11597030-000000000-00000

DEIS (Dirección de Estadísticas e Información de Salud -Vital Statistics. Basic Information of the year 2017). 2017. Available at: http://www.deis.msal.gov.ar/index.php/anuario-2017/. Accessed March 2019

DINAMIA (National Maternity and Children´s Head-office of National health Ministry of argentina) 2008: National Health Resolution 107/2008. National Program of Congenital Heart Disease. https://www.argentina.gob.ar/salud/cardiopatiascongenitas. Accessed March 2018

DINAMIA (National Maternity and Children's Head-office of the National Health Ministry of Argentina). Recommendations for the Practice of Preconception, prenatal and puerperal control. 2013: 1–163. Available at: http://www.msal.gob.ar/images/stories/bes/

graficos/0000000158cnt-g02.control-prenatal.pdf. Accessed April 2018

DINAMIA (National Maternity and Children's Head-office of the National Health Ministry of Argentina) 3rd Revision: Infant Mortality according to criteria of reducibility. 2014: 1–55. Available at:http://www.msal.gob.ar/images/stories/bes/graficos/0000000193cnt-s03-criterios-reducibilidad.pdf. Accessed March 2018

Du C, Liu D, Liu G et al (2017) A meta-analysis about the screening role of pulse oximetry for congenital heart disease. Biomed Res Int. 2123918. https://doi.org/10.1155/2017/2123918

EUROCAT (European surveillance of congenital anomalies). Prenatal diagnosis of 18 selected congenital anomaly subgroups for registries with complete data from 2012 to 2016 Available at: http://www.eurocat-network.eu/prenatalscreeninganddiagnosis/prenataldetection(pd)rates [Accessed: March, 2018]

Gagnon A, the GENETICS COMMITTEE (2009) Evaluation of prenatally diagnosed structural congenital anomalies. J Obstet Gynaecol Can. 31(9):875–881. https://doi.org/10.1016/S1701-2163(16)34307-9

Garne E, Loane M, Dolk H et al (2005) Prenatal diagnosis of severe structural congenital malformations in Europe. Ultrasound Obstet Gynecol. 25(1):6–11. https://doi.org/10.1002/uog.1784

Gelber SE, Grünebaum A, Chervenak FA (2017) Prenatal screening for microcephaly: an update after three decades. J Perinat Med. 45(2):167–170. https://doi.org/10.1515/jpm-2016-0220

González G, Dezerega P, Vásquez M (2005) Contribution of routine ultrasound in the period 22 to 26 weeks to the diagnosis of congenital anomalies: experience of 2 years, in 1162 ultrasound scans. Rev. Chil Obstet Ginecol 70:289–295. https://doi.org/10.4067/S0717-75262005000500003

Groisman B, Bidondo MP, Barbero P et al (2013) RENAC: National Registry of Congenital Anomalies of Argentina. Arch Argent Pediatr 111:484–494. https://doi.org/10.5546/aap.2013.484

ISUOG Provisional guide in ultrasound for infection by the ZIKA virus during pregnancy: information for health professionals. Available at: https://www.isuog.org/uploads/assets/uploaded/9c6208f2-8afa-4e25-8df631ea6bfbf57b.pdf. Accessed March 2018

Lytzen R, Vejlstrup N, Bjerre J et al (2019) Mortality and morbidity of major congenital heart disease related to general prenatal screening for malformations. Int J Cardiol. https://doi.org/10.1016/j.ijcard.2019.05.017

Miquel-Verges F, Mosley BS, Block AS et al (2015 Mar) A spectrum project: preterm birth and small-for-gestational age among infants with birth defects. J Perinatol. 35(3):198–203. https://doi.org/10.1038/jp.2014.180

National Ministry of Health: Resolution 641/2012. Available at: https://www.argentina.gob.ar/normativa/nacional/resoluci%C3%B3n-641-2012-197943/texto. Accessed 10 Dec 2019

Oggè G, Gaglioti P, Maccanti S et al (2006) Prenatal screening for congenital heart disease with four-chamber and outflow-tract views: a multicenter study. Ultrasound Obstet Gynecol. 28(6):779–784

Policiano C, Djokovic D, Carvalho R et al (2015) Ultrasound antenatal detection of urinary tract anomalies in the last decade: outcome and prognosis. J Matern Fetal Neonatal Med 28(8):959–963. https://doi.org/10.3109/14767058.2014.939065

Postoev VA, Grjibovski AM, Nieboer E et al (2015) Changes in detection of birth defects and perinatal mortality after introduction of prenatal ultrasound screening in the Kola Peninsula (North-West Russia): combination of two birth registries. BMC Pregnancy Childbirth. 15:308. https://doi.org/10.1186/s12884-015-0747-1

Rasmussen SA, Olney RS, Holmes LB et al (2003) Guidelines for case classification for the National Birth Defects Prevention Study. Birth Defects Res A Clin Mol Teratol. 67(3):193–201. https://doi.org/10.1002/bdra.10012

Rossi AC, Prefumo F (2013 Dec) Accuracy of ultrasonography at 11-14 weeks of gestation for detection of fetal structural anomalies. Obstet Gynecol. 122(6):1160–1167. https://doi.org/10.1097/AOG.0000000000000015

Rydberg C, Tunón K (2017 Feb) Detection of fetal abnormalities by second-trimester ultrasound screening in a non-selected population. Acta Obstet Gynecol Scand 96(2):176–182. https://doi.org/10.1111/aogs.13037

Sarkola T, Ojala TH, Ulander VM et al (2015) Screening for congenital heart defects by transabdominal ultrasound - role of early gestational screening and importance of operator training. Acta Obstet Gynecol Scand. 94(3):231–235. https://doi.org/10.1111/aogs.12572

SIP-G (Perinatal information system-management). The first national report of epidemiological survey based on SIP-G system. Ministry of Health of the Nation, 2013: 1–125. Available at: http://iris.paho.org/xmlui/handle/123456789/3463. Accessed May 2018

Staboulidou I, Wüstemann M, Vaske B et al (2010) Quality assured ultrasound simulator training for the detection of fetal malformations. Acta Obstet Gynecol Scand. 89(3):350–354. https://doi.org/10.3109/00016340903280941

Stoll C, Tenconi R, Clementi M (2001) detection of congenital anomalies by fetal ultrasonographic examination across Europe. Community Genet. 4(4):225–232

Strizek B, Cos Sanchez T, Khalifé J et al (2015) Impact of operator experience on the variability of fetal lung volume estimation by 3D-ultrasound (VOCAL) and magnetic resonance imaging in fetuses with congenital diaphragmatic hernia. J Matern Fetal Neonatal Med. 28(7):858–864. https://doi.org/10.3109/14767058.2014.935760

Vélez JE, Herrera LE, Arango F, Lopez G (2004) Congenital malformations: correlation, ecographic and clinical diagnosis. Rev Colomb Obstet Ginecol 55:201–208 Available at: http://www.scielo.org.co/pdf/rcog/v55n3/v55n3a04.pdf. Accessed March 2019

WHO (World Health Organization) Argentinian report 2017. Available at: https://administracionsalud.com.ar/organizacion-mundial-de-la-salud-informe-argentina-2017/ Accessed March 2018

Wiafe Y, Odoi A, Dassah E (2011) The role of obstetric ultrasound in reducing maternal and perinatal mortality. Ultrasound Imaging Med Appl:207–234. https://doi.org/10.5772/22847

Wiesel A, Queisser-Luft A, Clementi M et al (2005) EUROSCAN Study Group. Prenatal detection of congenital renal malformations by fetal ultrasonographic examination: an analysis of 709.030 births in 12 European countries. Eur J Med Genet. 48(2):131–144. https://doi.org/10.1016/j.ejmg.2005.02.003