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Birth prevalence of Down syndrome in Argentina

Prevalencia del síndrome de Down al nacimiento en Argentina

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ABSTRACT The aim of this study was to describe the prevalence at birth of Down syndrome in Argentina. The prevalence by jurisdiction and maternal age was calculated for the 2009-2015 period and the prevalence and proportion of prenatal diagnosis was compared according to sub-sector (public and private) and complexity level of the maternity wards. The association of Down syndrome with birth weight and gestational age was analyzed. The data source was the National Network of Congenital Anomalies of Argentina [Red Nacional de Anomalías Congénitas] (RENAC). The prevalence was 17.26 per 10,000 births; by jurisdictions it varied between 10.99 and 23.71; and by maternal age between 10.32 in women <20 years of age and 158.06 in those ≥ 45 years of age. In hospitals of the private subsector there was a higher prevalence, attributable to differences in the structure of maternal age and a greater proportion of prenatal diagnosis. There was a negative correlation between birth weight and Down syndrome ($\beta = -294.7$; $p < 0.001$). No difference in the median gestational age at birth between Down syndrome newborns and newborns without major anomalies was found, but the distribution of gestational age differed. Knowledge of certain epidemiological characteristics of this health issue could contribute to the implementation of health policies.

KEY WORDS Down Syndrome; Epidemiology; Maternal Age; Argentina.

RESUMEN El objetivo de este trabajo fue describir la prevalencia al nacimiento del síndrome de Down en Argentina. Se calculó la prevalencia por jurisdicción y edad materna para el período 2009-2015 y se comparó la prevalencia y proporción del diagnóstico prenatal según subsector (público y privado) y nivel de complejidad de las maternidades. Se analizó la asociación con el peso y la edad gestacional al nacer. La fuente de datos fue la Red Nacional de Anomalías Congénitas (RENAC). La prevalencia fue de 17,26 por cada 10.000 nacimientos; por jurisdicciones varió entre 10,99 y 23,71, y por edad materna entre 10,32 en <20 años y 158,06 en ≥ 45 años. En hospitales del subsector privado hubo una mayor proporción de diagnóstico prenatal y una mayor prevalencia, esta última atribuible a diferencias en la estructura de edad materna. Se observó una correlación negativa entre el peso al nacer y este síndrome ($\beta = -294{,}7$; $p < 0{,}001$). No se evidenció diferencia en la mediana de la edad gestacional al nacer entre recién nacidos con síndrome de Down y neonatos sin anomalías mayores, pero sí en la distribución de la edad gestacional. El conocimiento de ciertas características epidemiológicas podrá contribuir a la implementación de políticas de salud.

PALABRAS CLAVES Síndrome de Down; Epidemiología; Edad Materna; Argentina.

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INTRODUCTION

Congenital anomalies are morphological or functional alterations present at birth. Their prevalence in newborns is 3% to 5%.[1] With the control of infectious and nutritional diseases, congenital anomalies have increased their importance concerning infant mortality, rising from 11% in 1980[2] to 27% in 2016, being the second cause of infant mortality in Argentina.[3] The known causes of congenital anomalies include mutations in a principal gene, chromosomal abnormalities, prenatal exposure to teratogenic factors, and the effects of predisposing genes that are shown in the presence of environmental triggering factors. Traditionally, congenital anomalies were considered to be "impossible to prevent" [own translation]. However, the preventive actions applicable at different stages of the life cycle are multiple.[2]

Down syndrome is the most prevalent genetic cause of intellectual disability. It is due to a chromosomal abnormality that, in most cases, is caused by a free trisomy of chromosome 21.[4] The prevalence of Down syndrome at birth increases with maternal age, with a risk of approximately 1/1500 at 20 years, 1/900 at 30, 1/350 at 35, 1/100 at 40, and 1/25 at 45 years.[5] During pregnancy, it is possible to estimate Down syndrome risk through a combined evaluation of maternal age, nuchal translucency, the maternal blood level of human chorionic gonadotropin, and pregnancy-associated plasma protein-A, between 11 and 14 weeks of pregnancy (first-trimester risk estimation).[6] According to the outcomes of the risk estimation, or if there are other indications, an invasive diagnostic technique is recommended to accurately determine the fetal karyotype (amniocentesis or chorionic villus sampling).

This syndrome has been associated with lower birth weight[7,8] and also with preterm birth in comparison with neonates without Down syndrome.[8] In addition, preterm birth is a cause of low birth weight.[9] Therefore, gestational age must be considered when analyzing the cause of low fetal birth weight. Furthermore, Down syndrome is associated with other congenital anomalies, the most common of which are cardiopathies. [10,11] These comorbidities are, in turn, associated with a decrease in the survival of the neonates affected.[8,12] It has been demonstrated that when children are born in designated high-risk complexity maternity wards, neonatal mortality is lower.[13] Argentine maternity wards are classified according to their complexity level as categories 2, 3A, and 3B. Category 3B represents the maternity wards with the highest complexity, with the capability of providing care for high-risk newborns, including premature infants under 1,500 grams, with less than 32 weeks of gestation, who require oxygen therapy and mechanical ventilation, parenteral nutrition, and access to all pediatric specialties (among them geneticists, general surgeons, and specialized surgeons), and they also count on support services such as diagnostic imaging, hemotherapy, and clinical and bacteriological laboratory, among others. In Argentina, infants with critical neonatal pathology and surgical pathologies (including central nervous system pathologies and cardiological pathologies) must be treated in facilities that have this complexity level.[14]

Some of the sources to estimate the prevalence of Down syndrome have been the monitoring systems of congenital anomalies, such as the Latin American Collaborative Study of Congenital Malformations (ECLAMC) [*Estudio Colaborativo Latinoamericano de Malformaciones Congénitas*],[15] the Canada Public Health Agency,[16] the International Clearinghouse for Birth Defects Surveillance and Research Committee,[17] and the European Network of Population-based Registries for the Epidemiological Surveillance of Congenital Anomalies (EUROCAT),[18] among others. In Argentina, since 2009, the National Network of Congenital Anomalies (RENAC) [*Red Nacional de Anomalías Congénitas*] monitors major congenital anomalies (among them Down syndrome) in infants born in the principal maternity wards of the national territory.[19] In a previous study, Campaña *et al.* reported a prevalence of 19.6 affected per

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10,000 births in Argentina for the years 1994-2007[20]; nevertheless, no investigations have been performed in this country examining the prevalence of Down syndrome regarding its distribution by jurisdictions or by maternal age, being this latter the main risk factor.

The aims of this study were to determine the prevalence of Down syndrome at birth at a national and jurisdictional level in Argentina according to maternal age categories, the distribution of births with Down syndrome by maternal age categories, the prevalence and proportion of neonates with Down syndrome who received a prenatal diagnosis depending on the complexity level of the maternity ward, and finally to assess the association of birth weight and gestational age at delivery of infants with Down syndrome.

POPULATION AND METHODS

The data source was RENAC, the monitoring system of congenital anomalies, which is under the National Center for Medical Genetics of the National Administration of Laboratories and Health Institutes "Dr. Carlos G. Malbrán," National Ministry of Health. This network includes the main maternity wards of all Argentine jurisdictions, covering approximately 62% of births in the public subsector and 43% of the total number of births. Newborns with major structural anomalies, external or internal, identified from birth until discharge from the hospital were reported to RENAC. The anomalies are described in an open paper without a limit on the number of anomalies per patient. All live births and stillbirths that weigh 500g or more are included. The congenital anomalies are coded by medical geneticists in the coordination department of RENAC according to the 10th revision of the International Classification of Diseases with the adaptation of the Royal College of Paediatrics and Child Health. Furthermore, each maternity ward reports the total number of births that occurred in each hospital per month.[2,19,21]

This study includes cases with Down syndrome (ICD-10: Q90) for the period November 2009 to December 2015. The prevalence[22] in newborns at the national level and by jurisdiction was estimated and calculated according to the number of cases with Down syndrome reported, divided by the total number of births that occurred in the hospitals that report to the RENAC. In order to determine if there is heterogeneity in the prevalence among jurisdictions, a meta-analysis of random effects was conducted. This method helps analyze the sample size of the different jurisdictions and compares that variability with the expected sample variability. The prevalence of the newborns affected at birth according to groups of maternal age and the distribution of births with and without Down syndrome in these groups was calculated. To do this, the total births by groups of maternal age per year for the 2009-2015 period[23] was taken from the General Office of Statistics and Health Information (DEIS) [*Dirección de Estadísticas e Información en Salud*]. The total prevalence of this disease among subsectors (maternity wards managed publicly vs. privately or through employment-based health insurance, called *obras sociales*) and according to the complexity level of the public maternity wards (category 3B vs. category 3A or 2)[24] was compared. This comparison was made through the prevalence ratio (PR); a level of significance of 95% was used according to the Poisson distribution. To make the comparison among the subsectors, a Poisson regression was made using Down syndrome prevalence as the dependent variable, the subsector as the independent variable, and maternal age as the adjustment variable. The percentage of cases with a prenatal diagnosis for the 2013-2015 period for each subsector (maternity wards in public vs. private/employment-based health insurance sectors) and the complexity level of the public maternity wards (category 3B vs. category 3A or 2) and the PR were calculated using a level of significance of 95% according to the binomial distribution.

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As a comparison group, the births reported to the RENAC that did not have major congenital anomalies (n = 1,194) were used for the analysis of weight and gestational age at birth. In order to know the relation between Down syndrome and birth weight, a multiple linear regression was made in which the dependent variable was birth weight and the independent variables were the diagnosis of Down syndrome and gestational age (adjustment variable). The Mann-Whitney U test was used to determine the difference in the distribution of the gestational age in the affected infants and those without higher congenital anomalies, with prior evaluation of the normality of this variable in both populations, which was tested with the skewness and kurtosis tests described by D'Agostino *et al*.[25] and modified by Royston.[26] The Program STATE/SE 13 was used for the statistical analysis.

RESULTS

In a total of 1,358,158 births that occurred in the hospitals involved in the study between November 2009 and December 2015, 2,344 cases with Down syndrome were observed, and 50.50% of them were of male sex. The total prevalence at birth was 17.26 per

Table 1. Prevalence of Down syndrome at birth by jurisdiction. Argentina, 2009-2015.

Jurisdiction	Newborns with Down syndrome	Total of births	Prevalence (per 10,000 LB)	95%CI
Formosa	23	20,930	10.99	6.97; 16.49
Corrientes	28	24,683	11.34	7.54; 16.4
Entre Ríos	38	30,304	12.54	8.87; 17.21
Santa Fe	127	92,340	13.75	11.47; 16.36
Santiago del Estero	54	35,488	15.22	11.43; 19.85
La Rioja	21	13,524	15.53	9.61; 23.74
Rio Negro	17	10,712	15.87	9.24; 25.41
Córdoba	115	71,234	16.14	13.33; 19.38
Chaco	80	49,385	16.20	12.85; 20.16
Buenos Aires	661	407,450	16.22	15.01; 17.51
Santa Cruz	10	6,163	16.23	7.78; 29.84
La Pampa	15	9,130	16.43	9.2; 27.1
Salta	108	65,371	16.52	13.55; 19.95
San Luis	31	16,906	18.34	12.46; 26.03
Jujuy	58	30,834	18.81	14.28; 24.32
Tucumán	161	85,172	18.90	16.1; 22.06
San Juan	69	35,634	19.36	15.07; 24.51
Mendoza	119	59,072	20.14	16.69; 24.11
CABA	374	184,382	20.28	18.28; 22.45
Chubut	29	14,270	20.32	13.61; 29.19
Misiones	113	54,904	20.58	16.96; 24.74
Neuquén	47	20,707	22.70	16.68; 30.18
Tierra del Fuego	12	5,225	22.97	11.87; 40.12
Catamarca	34	14,338	23.71	16.42; 33.14
Total	2,344	1,358,158	17.26	16.57; 17.97

Source: Own elaboration based on data from the National Network of Congenital Anomalies (RENAC) [21].
Note: Jurisdictions were organized by prevalence.
LB= Live births; CI95%= Confidence interval of 95%; CABA= Autonomous City of Buenos Aires.

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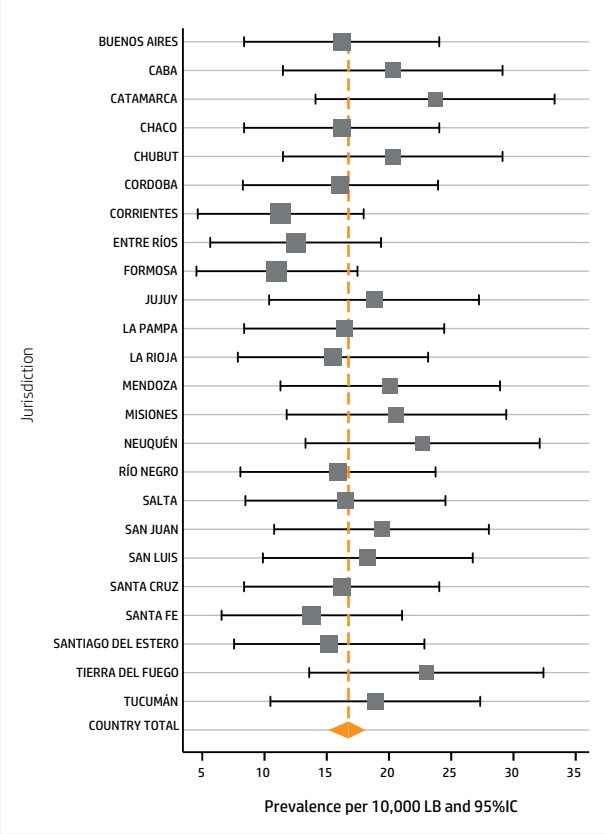

Figure 1. Meta-analysis of the birth prevalence of Down syndrome by jurisdiction and country total. Argentina, 2009-2015.

Source: Own elaboration based on data from the National Network of Congenital Anomalies (RENAC)[21].
CI 95%= Confidence interval of 95%.

10,000 births [CI95% (16.57-17.97)], and the prevalence varied between 10.99 and 23.71 by jurisdiction (table 1).

The meta-analysis did not show heterogeneity among the jurisdictional prevalence: Q of Cochrane = 16.86; degrees of freedom = 23; p = 0.8; I^2 = 0.00 (Figure 1). The prevalence of Down syndrome at birth increased as maternal age increased and it was significantly higher after 35 years old (Figure 2).

The percentage distribution of the total number of infants born with and without Down syndrome was compared according to age category, and it was observed that the higher percentage of infants born without Down syndrome occurred in women in the maternal age group of 20 to 24 years, and the higher percentage of infants born with Down syndrome occurred in women aged greater than or equal to 35 years (Figure 3). Maternity wards in the private/employment-based health insurance sector exhibited a significantly higher prevalence than public maternity wards, and within the public subsector, higher-complexity maternity wards exhibited a significantly higher prevalence (Table 2).

Prevalence was also higher in the private subsector than in the public subsector according to the Poisson regression [PR = 1.27; 95% CI (1.10; 1.47)]. However, after adjusting for maternal age, the subsector trend was not observed [PR = 0.99; 95% CI (0.79-1.25)]. The percentage of pregnancies affected by prenatal diagnosis was significantly higher in maternity wards in the private/employment-based health insurance sector, and it was also significantly higher in public maternity wards category 3B (higher-complexity) compared to public maternity wards category 3A or 2 (lower-complexity) (Table 3).

Linear regression revealed that birth weight on infants with Down syndrome,

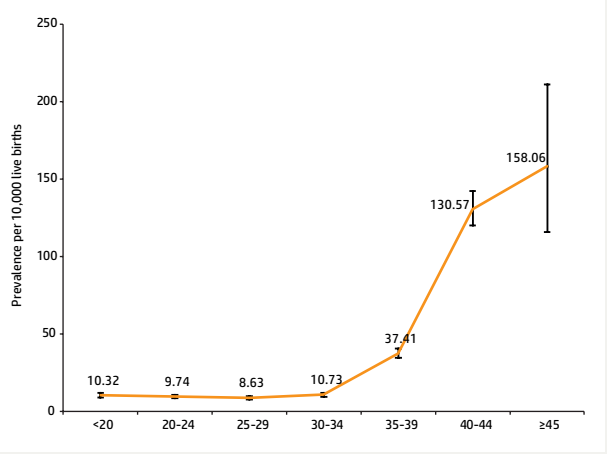

Figure 2. Prevalence of Down syndrome by maternal age. Argentina, 2009-2015.

Source: Own elaboration based on data from the National Network of Congenital Anomalies (RENAC)[21] and the General Office of Statistics and Health Information[23].

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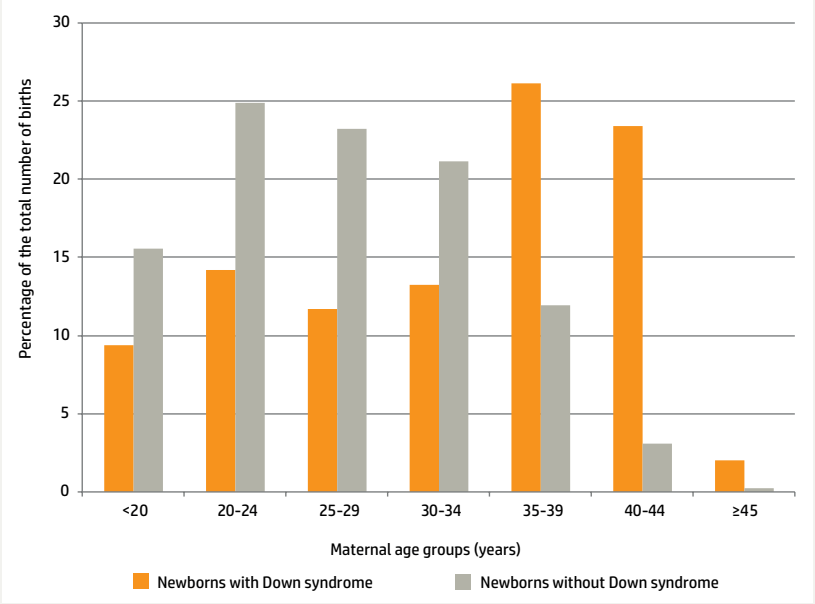

Figure 3. Percentage distribution of newborns with and without Down syndrome by maternal age groups. Argentina, 2009-2015.

Source: Own elaboration based on data from the National Network of Congenital Anomalies of Argentina (RENAC)[21] and the General Office of Statistics and Health Information (DEIS) [23].

Table 2. Prevalence and prevalence ratio of Down syndrome by subsector and complexity level of the maternity wards. Argentina, 2009-2015.

Maternity wards classification	n	Prenatal diagnosis (%)	95%CI	PR	95%IC
Private subsector/employment-based health insurance	203	21.55	18.69; 24.72	1.33*	1.27; 1.38
Public subsector[1]	2,141	16.25	15.40; 17.14	-	-
Public subsector, complexity level category 3B	1,394	17.45	16.29; 18.66	1.19*	1.14; 1.25
Public subsector, complexity level category 3A and 2[1]	747	14.62	13.38; 15.92	-	-

Source: Own elaboration based on data from the National Network of Congenital Anomalies (RENAC)[21].
[1]Value of reference: LB= Live births; 95% CI= Confidence interval of 95%; PR= Prevalence ratio; *p<0.05.

Table 3. Percentage of Down syndrome cases with prenatal diagnosis and prevalence ratio, by subsector and complexity level of the maternity wards. Argentina, 2013-2015.

Maternity wards classification	n	Prenatal diagnosis (%)	95%IC	PR	95%IC
Private subsector/employment-based health insurance	62	30.54	24.28; 37.37	2.16*	2.08; 2.24
Public subsector[1]	193	14.11	12.30; 16.06	-	-
Public subsector, complexity level category 3B	134	15.82	13.42; 18.45	1.40*	1.32; 1.46
Public subsector, complexity level category 3A and 2[1]	59	11.32	8.59; 14.15	-	-

Source: Own elaboration based on data from the National Network of Congenital Anomalies (RENAC)[21].
[1]Value of reference; 95% CI= Confidence interval of 95%; PR= Prevalence ratio; *p<0.05.

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adjusted for gestational age, was 294.78 lower than that of unaffected infants [coefficient β Down syndrome = -294.78; 95% CI (-332.02; -257.54)]; [coefficient β gestational age = 169.4; 95% CI (163.05; 175.86); $p < 0.001$; R^2 0.45]. The skewness and kurtosis tests indicated that the distribution of gestational age was not normal, both in infants born with Down syndrome ($p < 0.01$) and in infants born without major anomalies ($p < 0.01$). The median gestational age in these two groups was 39 weeks, and the Mann-Whitney U test revealed that the distribution of gestational age in both groups was not equal ($p = 0.02$).

DISCUSSION

The birth prevalence of Down syndrome, at 17.26/10,000, observed in this study, is lower than that previously reported by Campaña *et al*. for Argentina for the 1994–2007 period, which was 19.6/10,000.[20] The study was conducted by ECLAMC with data coming from a lower number of hospitals but of higher-complexity levels; in contrast, RENAC covers a higher number of maternity wards in the public sector, including hospitals with different complexity levels. The difference may be attributed to a higher referral bias in the ECLAMC study. That bias created an increase in hospital prevalence because women with a prenatal diagnosis were referred to higher-complexity hospitals to receive medical care for themselves and their newborns. Nevertheless, the prevalence in this study is similar to that reported by ECLAMC for South America in 2012, which was 17.85/10,000.[15] It covered hospitals in the public and private sectors from different countries on the continent and with different complexity levels, a fact that might make the referral bias in that study lower.

The possibility of accessing prenatal diagnosis and consequent elective termination of pregnancy for fetal anomalies must be considered in order to interpret the difference in prevalence with other countries. For example, in Canada, the Public Health Agency reported a prevalence of 14.1/10,000 for the 1998-2007 period.[16] This report does not include elective terminations of pregnancy for fetal anomalies, a medical procedure that is permitted in that country, and that justifies the lower prevalence of live births. The European Network of Population-based Registries for the Epidemiological Surveillance of Congenital Anomalies (EUROCAT) published a prevalence of Down syndrome of 10.34/10,000 in live births and stillbirths for the 2011-2015 period, which increases to 23.88/10,000 if elective terminations of pregnancy for fetal anomalies are included.[18] In 2012, a total prevalence of Down syndrome of 28.74/10,000 was registered in the state of Western Australia, including elective terminations of pregnancy (which account for 73% of Down syndrome pregnancies) and 7.33/10,000 in live births.[15] In Norway, in 2011, a prevalence of 22.55/10,000 was registered, including elective terminations of pregnancy (34.7% of Down syndrome pregnancies) and 13.9/10,000 in live births.[27]

In this study, prevalence by jurisdiction showed regional variations, but in accordance with the results of the meta-analysis, it was concluded that there was no statistically significant heterogeneity.

After analyzing the prevalence of Down syndrome by maternal age segment, it becomes evident that it remains relatively stable in age groups less than 35 years, with a visible increase starting after 40 years. These results are consistent with those previously observed in other studies.[5,28,29] After comparing the distribution of births with and without Down syndrome by maternal age, it was observed that 48.5% of children with Down syndrome were born to mothers who were less than 35 years old, which represents 85% of all births[23] and the remaining 51.5% were born to women who were 35 years or older, the age group which accounts for 15.0% of all births in the country. Unwanted pregnancy has been considered to be especially frequent among adolescents, single women, and women who are over 40 years old.[30] Although this last group represents only a

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minor proportion of the total number of pregnancies, it accounts for approximately 25% of the Down syndrome cases. Preventive measures aimed at reducing the number of unwanted pregnancies in this risk group may represent an adequate public health measure.

The health system subsector in which these patients receive medical care may be taken as an indirect indicator of socioeconomic status, as it is more frequent for women with higher socioeconomic status to receive health care in the private/employment-based health insurance sector. The prevalence of Down syndrome in the public subsector was lower than that found in the private/employment-based health insurance subsector. It was made evident that this is due to a higher maternal age in the private/employment-based health insurance subsector. This analysis is consistent with what other authors reported: maternal age is higher in women with a higher socioeconomic status.[31,32] The higher prevalence and higher percentage of prenatal diagnoses in maternity wards in category 3B (higher complexity) could be attributed to the referral of pregnant women with a pathologic prenatal diagnosis to facilities that have a higher complexity level. Moreover, prenatal diagnosis is 2.16 times higher in births in private facilities than in public facilities, which can be attributed to greater access to obstetrical care and methods of invasive prenatal diagnosis in the private sector, a fact that may reflect the existence of cultural, geographic, and economic barriers concerning these tests in Argentina. In a previous study conducted on a cohort of South American women that included Argentine women, Campaña *et al*. informed that women receiving health care in the private sector reported a higher number of consultations and prenatal ultrasounds than women in the public sector.[32] Given the morbidity and mortality profile of Down syndrome newborns, it is considered that they must be born in higher-complexity maternity wards. For that reason, it is especially important to have a prenatal diagnosis so as to plan the birth to take place in health facilities that have an adequate complexity level and to have the health care team and the family group prepared to receive the newborn.

The findings of lower birth weight are consistent with the descriptions above.[7,8] Gorlin *et al*. describe a birth weight 400 grams lower in patients with Down syndrome than in healthy infants.[33] In this study, it was made evident that the median gestational age in infants born with Down syndrome is not different from that of infants born without major anomalies, although the distribution of this variable was not equal in these two groups. That could be attributed to the fact that lower values of gestational age are registered in infants with Down syndrome, as reported by other authors.[8]

CONCLUSIONS

Down syndrome is one of the most frequent congenital anomalies in Argentina. It can be detected prenatally, and given the comorbidities associated with this syndrome, it requires the participation of an interdisciplinary team to monitor both infants and their families. In these cases, education and planned parenthood, along with an adequate periconceptional assessment, are fundamental, especially in women of advanced maternal age.

One strength of this study is the inclusion of newborns in the main maternity wards in the public sector across the 24 jurisdictions of Argentina, with high coverage of births and different complexity levels. Among the limitations of this study, it must be noted that, in relation to birth weight, there is no available data that may influence this variable, such as maternal illnesses during pregnancy. Another weakness of this study was that the prenatal diagnosis variable was reported systematically only after 2013, and earlier periods were not included.

Knowledge of certain epidemiological characteristics of this health issue could contribute to the implementation of health policies specifically designed for this patient

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group. Countries where termination of pregnancy for fetal anomalies is permitted exhibit a substantially lower prevalence of Down syndrome in live births. Access to prenatal detection and elective termination of pregnancy for fetal anomalies, along with the differences in the structure of maternal age in the population, represent the main determinants of the prevalence of newborns with Down syndrome.

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REFERENCES

1. Rimoin DL, Pyeritz RE, Korf BR. Emery & Rimoin's principles and practice of medical genetics. 6a ed. Cambridge: Academic Press; 2013.

2. Groisman B, Bidondo MP, Barbero P, Gilib JA, Liascovich R, Grupo de Trabajo RENAC. RENAC: Registro Nacional de Anomalías Congénitas de Argentina. Archivos Argentinos de Pediatría. 2013; 111(6):484-494.

3. Dirección de Estadísticas e Información en Salud. Defunciones de menores de 5 años por grupo de edad según causas seleccionadas [Internet]. Buenos Aires: DEIS; 2016 [cited 8 Apr 2018]. Available from: https://tinyurl.com/yxtk2rz9.

4. Nussbaum RL, McInnes RR, Willard HF. Thompson & Thompson genetics in medicine. 8a ed. Canada: Elsevier; 2016.

5. Snijders RJ, Sundberg K, Holzgreve W, Henry G, Nicolaides KH. Maternal age- and gestation-specific risk for trisomy 21. Ultrasound in Obstetrics & Gynecology. 1999;13:167-170.

6. Wright D, Spencer K, Kagan KK y col. First-trimester combined screening for trisomy 21 at 7–14 weeks' gestation. Ultrasound in Obstetrics & Gynecology. 2010;36:404-411.

7. Leonard S, Bower C, Petterson B, Leonard H. Survival of infants born with Down's syndrome: 1980-96. Paediatric and Perinatal Epidemiology. 2000;14:163-171.

8. Glasson EJ, Jacques A, Wong K, Bourke J, Leonard H. Improved survival in Down syndrome over the last 60 years and the impact of perinatal factors in recent decades. Journal of Pediatrics. 2016;169:214-220. doi: 10.1016/j.jpeds.2015.10.083.

SALUD COLECTIVA. 2019;15:e1863. doi: 10.18294/sc.2019.1863

9. Kliegman RM, Behrman RE, Jenson HB, Stanton BF. Nelson: Tratado de pediatría. 18va ed. Barcelona: Elsevier; 2008.

10. Cleves MA, Hobbs CA, Cleves PA, Tilford JM, Bird TM, Robbins JM. Congenital defects among liveborn infants with Down syndrome. Birth Defects Research (Part A). 2007;79:657-663. doi: 10.1002/bdra.20393.

11. Morris JK, Garne E, Wellesley D, Addor MC, Arriola L, Barisic I, Beres J, Bianchi F, Budd J, Dias CM, et al. Major congenital anomalies in babies born with Down syndrome: A EUROCAT population-based registry study. American Journal of Medical Genetics Part A. 2014;9999:1-8. doi: 10.1002/ajmg.a.36780.

12. Goldman SE, Urbano RC, Hodapp RM. Determining the amount, timing and causes of mortality among infants with Down syndrome. Journal of Intellectual Disability Research. 2011;55:85-94. doi: 10.1111/j.1365-2788.2010.01349.x.

13. Berg CJ, Druschel CM, McCarthy BJ, LaVoie M, Floyd RL. Neonatal mortality in normal birth weight babies: does the level of hospital care make a difference? American Journal of Obstetrics Gynecology. 1989;161(1):86-91. doi: 10.1016/0002-9378(89)90239-1.

14. Ministerio de Salud de la Nación Argentina. Resolución 641/2012: Directriz de organización y funcionamiento de los servicios de cuidados neonatales [Internet]. Buenos Aires: Ministerio de Justicia y Derechos Humanos de la Nación; 2012 [cited 12 Jul 2017]. Available from: https://tinyurl.com/y436j5em.

15. International Clearinghouse for Birth Defects Surveillance and Research. Annual Report 2014 [Internet]. Roma: ICBDRS; 2014 [cited 12 Jul 2017]. Available from: https://tinyurl.com/y4fus4ox.

16. Public Health Agency of Canada. Congenital anomalies in Canada 2013: A perinatal health surveillance report [Internet]. Ottawa: Public Health Agency of Canada; 2013 [cited 14 Jul 2017]. Available from: https://tinyurl.com/y5jkb9lk.

17. Leoncini E, Botto LD, Cocchi G, Annerén G, Bower C, Halliday J, Amar E, Bakker MK, Bianca S, Canessa Tapia MA, et al. How valid are the rates of Down syndrome internationally?: Findings from the International Clearinghouse for Birth Defects Surveillance and Research. American Journal of Medical Genetics Part A. 2010;152A(7):1670-1680. doi: 10.1002/ajmg.a.33493.

18. EUROCAT prevalence tables. Cases and prevalence of Down syndrome from 2011-2015 [cited 14 Jul 2017]. Available from: https://tinyurl.com/yypz69we.

19. Bidondo MP, Groisman B, Gili JA, Liascovich R, Barbero P. Estudio de prevalencia y letalidad neonatal en pacientes con anomalías congénitas seleccionadas con datos del Registro Nacional de Anomalías Congénitas de Argentina. Archivos Argentinos de Pediatría. 2015;113(4):295-302.

20. Campaña H, Pawluk MS, López Camelo JS. Prevalencia al nacimiento de 27 anomalías congénitas seleccionadas, en 7 regiones geográficas de la Argentina. Archivos Argentinos de Pediatría. 2010;108(5):409-417.

21. Groisman B, Duarte S, Gili J, Liascovich R, Camelo L, Santiago J, Grupo de Trabajo RENAC. Registro Nacional de Anomalías Congénitas de Argentina, Reporte anual RENAC 2016: Análisis epidemiológico de las anomalías congénitas en recién nacidos registradas en el año 2015 en la República Argentina. Buenos Aires: Ministerio de Salud de la Nación; 2016.

22. Mason CA, Kirby RS, Sever LE. Prevalence is the preferred measure of frequency of birth defects. Birth Defects Research Part A. 2005;73(10):690-692.

23. Dirección de Estadísticas e Información en Salud. Estadísticas vitales [Internet]. Buenos Aires: Ministerio de Salud de la Nación [cited 12 Jul 2017]. Available from: https://tinyurl.com/y2b-ftfyw.

24. Dirección Nacional de Maternidad, Infancia y Adolescencia. Mapa sanitario [Internet]. Buenos Aires: Ministerio de Salud de la Nación [cited 7 Feb 2018]. Available from: http://datos.dinami.gov.ar/produccion/cuadromando.

25. D'Agostino RB, Belanger A, D'Agostino RB Jr. A suggestion for using powerful and informative tests of normality. The American Statistician. 1990; 44(4):316-321.

26. Royston P. Comment on sg3.4 and an improved D'Agostino test. Stata Technical Bulletin. 1992;1(3):23-24.

27. International Clearinghouse for Birth Defects Surveillance and Research. Annual Report 2013 [Internet]. Roma: ICBDRS centre; 2013 [cited 19 Mar 2018]. Available from: https://tinyurl.com/y58sag3j.

28. Cuckle HS, Wald NJ, Thompson SG. Estimating a woman's risk of having a pregnancy associated with Down's syndrome using her age and serum alpha-fetoprotein level. British Journal of Obstetrics and Gynaecology. 1987;94(5):387-402.

SALUD COLECTIVA. 2019;15:e1863. doi: 10.18294/sc.2019.1863

29. Morris JK, Mutton DE, Alberman E. Revised estimates of the maternal age specific live birth prevalence of Down's syndrome. Journal of Medical Screening. 2002;9(1):2-6.

30. Langer A. Unwanted pregnancy: impact on health and society in Latin America and the Caribbean. Revista Panamericana de Salud Pública. 2002;11(3):192-204.

31. Goisis A, Schneider D, Myrskylä M. Secular changes in the association between advanced maternal age and the risk of low birth weight: a cross-cohort comparison in the UK. Population Studies. 2018;27:1-17. doi: 10.1080/00324728.2018.1442584.

32. Campaña H, Ermini M, Aiello HA, Krupitzki H, Castilla EE, López-Camelo JS, Latin American Collaborative Study of Congenital Malformations Study Group. Prenatal sonographic detection of birth defects in 18 hospitals from South America. Journal of Ultrasound in Medicine. 2010;29(2):203-212.

33. Gorlin RJ, Cohen MM, Hennekam RCM. Syndromes of the head and neck. 4a ed. New York: Oxford University Press; 2001.

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