RENAC: National Registry of Congenital Anomalies in Argentina

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ABSTRACT

Introduction. The National Registry of Congenital Anomalies (Registro Nacional de Anomalías Congénitas, RENAC) is a hospital-based surveillance system for newborn infants with major morphological congenital anomalies (CAs). The objective of this study was to describe the characteristics and operation of the RENAC registry and the prevalence at birth of 56 specific selected CAs, compared to other registries.

Population and Methods. The organization of the RENAC registry was initiated in public hospitals with 1000 or more births per year or which are the referral hospitals in a determined health region. Neonatologists are in charge of data collection, and a central coordination department is in charge of encoding, statistical analyses and regular reports. The RENAC registry uses an online forum for data submission and for guidance and interaction regarding the initial management of cases.

Results. Between November 1st, 2009 and June 30th, 2012, 98 hospitals were included in the registry, the annual coverage of these hospitals is 65% in the public sector and 35% of births in Argentina. In this period, 294 005 newborn infants were examined, and 5165 cases with major CAs were detected (1.76%; 95% CI: 1.71-1.80). The most frequent CAs were septal heart defects (prevalence per 10 000: 28.6), Down’s syndrome (prevalence per 10 000: 19.2), cleft lip +/- palate (prevalence per 10 000: 12), and a set of neural tube defects (prevalence per 10 000: 11.9).

Conclusions. The RENAC has reached a high coverage in the public sector and the differences in prevalence with other registries can be related to operational aspects or actual differences, depending on the case. The RENAC deals with the collection, analysis and dissemination of information about CAs in Argentina, and also contributes with local interventions.

Key words: Argentina, congenital anomalies, information systems, registries, health surveillance.

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INTRODUCTION

Congenital anomalies (CAs) are morphological or functional alterations of prenatal etiology which are present since birth, even if detected later in life.¹ The prevalence of CAs in newborn infants ranges between 3% and 5%, and they can be classified as major or minor.² Major CAs have a significant effect on health and generally require medical or surgical treatment (e.g., cleft lip and palate, gastroschisis, Down’s syndrome); minor CAs are clinical signs with no implications on health (e.g., prominent ears, epicanthal fold, preauricular sinus). With the management of infectious and nutritional diseases, the relative significance of CAs in child mortality has increased.³ CAs accounted for 11% in 1980, for 25% in 2010, and are now the second cause of child mortality in Argentina.⁴

CAs have a varied etiology, and 50% of them are still of unknown origin.⁵ The known causes include mutations in a major gene or chromosomal anomalies, prenatal exposure to teratogenic factors, and the effect of predisposing genes expressed when triggered by environmental factors. Traditionally, CAs were regarded as “non-reducible;” however, there are multiple preventive actions that can be applied throughout the different stages of life.⁶⁻⁹

CAs are individually uncommon events, and therefore epidemiological studies require a large number of individuals.

For this reason, CA surveillance systems with large databases, an adequate level of diagnostic quality and continuous operation over time are useful for studying causative agents, such as environmental pollutants, nutritional factors or maternal diseases.

Such systems first appeared in the 1960s, after the so-called “thalidomide tragedy,”¹⁰ and their initial objective was to closely monitor any change in...
prevalence, for the early detection and prevention of any similar epidemics. Since that time, the objectives of surveillance have widened their scope. Now objectives include the comparison of regions, the analysis of trends or the discovery of new determining factors, and also the evaluation of prevention strategies, the interconnection of patients with healthcare services, and the collaboration in resource allocation.11-13

In Argentina, deaths caused by CAs are reported in the Death and Fetal Death Statistical Reports. However, Live Birth Statistical Reports do not include information on CAs, and although the Perinatal Information System does include CAs, it establishes that only one anomaly can be coded per child, selected from a predefined, non comprehensive list of options.14 In addition, several Argentine hospitals are part of the Latin-American Collaborative Study of Congenital Malformations EstudioColaborativoLatinoamericano de Malformaciones Congénitas, ECLAMC), a voluntary network of South American maternity centers with a case and control design.15 Although, for decades, data provided by the ECLAMC was the only epidemiological information available, its coverage is not wide and its design is operatively complex. The relative increase of CAs in child mortality, that we mentioned above, and the lack of statistical tools for establishing their prevalence were determining factors for the creation of a national registry, in addition to the need of information to evaluate recent warning signs indicative of a relationship between CAs and environmental pollutants. In this context, and prior to conducting a feasibility pilot study,16 the National Registry of Congenital Anomalies (RegistroNacional de Anomalías Congénitas de Argentina, RENAC) was organized in 2009 within the framework of the “National Genetic Medicine Network” Program of the National Ministry of Health, which is coordinated by the National Genetic Medical Center (Centro Nacional de GenéticaMédica, CNGM and the National Administration of Health Institutes and Lab (ANLIS).

The objective of this study was to describe the characteristics and operation of the RENAC registry and the prevalence at birth of 56 specific selected CAs, compared to other registries.

**POPULATION AND METHODS**

**Material**

The target population of the RENAC is made up of all newborn infants born in Argentina. This study was restricted to the data reported by the first 98 hospitals included in the study between November 1st, 2009 and June 30th, 2012.

The case definition was that of newborn infants with major morphological CAs, whether external or internal, identified from birth until hospital discharge and detected during physical examination or using supplementary tests, interventions or an autopsy. The definition includes all live newborn infants and stillbirths with a weight of 500 g or more, and excludes those who have only minor or functional CAs (e.g., hearing loss).

**Methods**

Data collection (Figure 1) is done using a form attached to the medical record of women hospitalized to give birth, on which the presence of a congenital anomaly in the newborn infant is recorded. If the infant has a CA, this is described and additional outcome measures are filled in as per the standard procedures indicated in an operational manual. The RENAC’s team in every hospital is made up of two neonatologists or a neonatologist and a member of the health team. At the end of each month, they retrieve all cases of congenital anomalies and enter the data in an electronic file, including the total number of live births and stillbirths for that month. Using a web site hosted at Amazon Web Services and the vBulletin 4 software, with a password-restricted access to participants, the electronic file is sent to the coordination department, made up of four professionals from the CNGM (authors BG, MPB, PB and RL), with the help of a professional who provides statistical support (author JAG). The coordination department reviews the quality of descriptions and compliance with the inclusion of additional outcome measures, and corrections are made if the information provided is incomplete or not clear.

CA coding is the responsibility of geneticists, and it is performed as per the International Classification of Diseases 10th Revision, adapted by the British Pediatric Association.17 Following the analysis, data are disseminated to participating hospitals and health authorities (Figure 1).

The RENAC’s web site is organized as a communication system with forums. Each responsible team uses a hospital exclusive forum to submit data and the coordination
department makes the necessary corrections; the forums common to all hospitals are used to solve operational problems, discuss selected cases and publish academic resources. Each neonatologist has a profile with their name and picture, and they can access the web site at any time to submit questions or comments. At the same time, forum exchanges are made in a clinical context and to provide guidance on the initial management of affected newborn infants. Depending on the case, pictures and additional tests are submitted to the forum and analyzed, once the parents’ informed consent is obtained. Additionally, the coordination department helps to refer cases to genetic departments and submit samples for lab tests.

Analysis
Newborn infants with congenital anomalies were classified as follows: isolated or multiple CAs or CA syndromes, sequences or associations; sex; status at birth; twin pregnancy; status at the time of data submission; gestational age; weight; and maternal age. The percentage of total newborn infants and the prevalence per 10 000 individuals were calculated for 56 specific CAs selected based on their clinical significance, their impact on morbidity and mortality, or the presence of at least 5 reports. Prevalences were calculated as per Poisson’s distribution, with a 95% confidence interval, and were compared to those obtained by the Consortium of the European Surveillance of Congenital Anomalies (EUROCAT) (2005-2009 period) and those obtained by the ECLAMC (2005-2007 period). For each specific CA, a “Z” value was obtained using the RENAC as a reference (expected value) and the ECLAMC (Z1) and EUROCAT (Z2) as comparator values (observed value) \[Z = \frac{(observed\ value - expected\ value)}{\sqrt{expected\ value}}\]. The statistical significance was established using Bonferroni’s correction for multiple comparisons, in \[Z = \pm 3.5\], corresponding to a p value of 0.00025. The Stata statistical software was used.
RESULTS

Figure 2 summarizes the activities performed in relation to the RENAC organization. A total of 98 hospitals were included and the coordination department was expanded to four CNGM members. The National Ministry of Health committed to printing products (reports) and supplies (forms, operational manual) and to providing funds for annual meetings. These meetings were attended by neonatologists, members of other health programs, clinical geneticists and health authorities; annual reports were presented and electronic databases and individual reports were delivered to the responsible teams from each hospital. Also, personal interaction was encouraged, new members were trained, clinical cases were discussed, and awards were given for the timely input of data, the quality of descriptions, the use of local data and the submission of cases for discussion in the web forum. Figure 3 summarizes the main characteristics of the RENAC as per the attributes used to evaluate surveillance systems.19

The 98 hospitals were progressively included (Table 1 and Figure 2), until a 65% annual coverage of the public subsector and 35% of all births in Argentina were reached. Between November 1st, 2009 and June 30th, 2012, 294,005 newborn infants were examined and 5743 cases of congenital anomalies were reported.

Of these, 5165 had major CAs (positive predictive value= 89.94%); the remaining 578 cases (10.06% false positive cases) were newborn infants who did not meet the inclusion criteria.

Table 1. Coverage evolution of the RENAC according to jurisdiction

<table>
<thead>
<tr>
<th>Jurisdictions</th>
<th>RENAC Total estimated annual birthsa</th>
<th>Annual coverage of RENAC for the total number of birthsb</th>
<th>Annual coverage of RENAC of births in the public sectorb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buenos Aires</td>
<td>23 409</td>
<td>51 737</td>
<td>100 670</td>
</tr>
<tr>
<td>CABA</td>
<td>26 938</td>
<td>30 561</td>
<td>30 849</td>
</tr>
<tr>
<td>Catamarca</td>
<td>22 242</td>
<td>23 782</td>
<td>23 990</td>
</tr>
<tr>
<td>Chaco</td>
<td>46 98</td>
<td>55 382</td>
<td>56 550</td>
</tr>
<tr>
<td>Chubut</td>
<td>24 20</td>
<td>22 112</td>
<td>0%</td>
</tr>
<tr>
<td>Córdoba</td>
<td>14 85</td>
<td>15 426</td>
<td>0%</td>
</tr>
<tr>
<td>Corrientes</td>
<td>28 56</td>
<td>31 167</td>
<td>31 111</td>
</tr>
<tr>
<td>Entre Rios</td>
<td>6 544</td>
<td>7 364</td>
<td>0%</td>
</tr>
<tr>
<td>Formosa</td>
<td>3 240</td>
<td>3 282</td>
<td>3 295</td>
</tr>
<tr>
<td>Jujuy</td>
<td>3 908</td>
<td>3 736</td>
<td>3 728</td>
</tr>
<tr>
<td>La Pampa</td>
<td>1 864</td>
<td>2 172</td>
<td>0%</td>
</tr>
<tr>
<td>La Rioja</td>
<td>1 844</td>
<td>2 062</td>
<td>0%</td>
</tr>
<tr>
<td>Mendoza</td>
<td>8 724</td>
<td>9 168</td>
<td>0%</td>
</tr>
<tr>
<td>Misiones</td>
<td>4 500</td>
<td>4 963</td>
<td>5 139</td>
</tr>
<tr>
<td>Neuquén</td>
<td>2 544</td>
<td>2 618</td>
<td>0%</td>
</tr>
<tr>
<td>Río Negro</td>
<td>2 104</td>
<td>1 980</td>
<td>0%</td>
</tr>
<tr>
<td>Salta</td>
<td>8 324</td>
<td>8 585</td>
<td>11 602</td>
</tr>
<tr>
<td>San Juan</td>
<td>6 680</td>
<td>7 312</td>
<td>0%</td>
</tr>
<tr>
<td>San Luis</td>
<td>2 100</td>
<td>2 102</td>
<td>0%</td>
</tr>
<tr>
<td>Santa Cruz</td>
<td>1 084</td>
<td>1 128</td>
<td>0%</td>
</tr>
<tr>
<td>Santa Fe</td>
<td>4 824</td>
<td>17 414</td>
<td>20 594</td>
</tr>
<tr>
<td>Santiago del Estero</td>
<td>5 844</td>
<td>6 373</td>
<td>6 763</td>
</tr>
<tr>
<td>Tierra del Fuego</td>
<td>1 421</td>
<td>1 328</td>
<td>0%</td>
</tr>
<tr>
<td>Tucumán</td>
<td>9 148</td>
<td>16 233</td>
<td>17 606</td>
</tr>
<tr>
<td>Total RENAC</td>
<td>15 294</td>
<td>103 569</td>
<td>206 578</td>
</tr>
</tbody>
</table>

a. The RENAC total number of annual births in each jurisdiction was calculated based on an estimation of annual births occurred in each jurisdiction hospitals.

b. For each year, coverage is estimated based on the total number of births reported by the DEIS for the previous year.
Incorporación de hospitales

Inician 4 hospitales de la región NEA

27 nuevos hospitales:
- 22 región Centro
- 5 región NOA

Total: 31 hospitales

47 nuevos hospitales:
- 29 región Centro
- 11 región Patagonia
- 4 región Cuyo
- 2 región NOA

Total: 78 hospitales

21 nuevos hospitales en la región Centro
Total: 98 hospitales

**Estructura y actividades del RENAC**

- Dos integrantes en la coordinación.
- Diseño e impresión del Formulario.
- 1º Encuentro Anual de capacitación.
- Incorporación del Manual Operativo.
- Implementación de la comunicación mediante Foro-online.
- 2º Encuentro Anual de capacitación.

- La coordinación pasa de 2 a 3 integrantes; se incorpora 1 profesional externo y 1 administrativo.
- Actualización del Manual Operativo.
- Presentación del primer Reporte Anual.
- Capacitaciones regionales.
- 3º Encuentro Anual de capacitación.

- La coordinación pasa de 3 a 4 integrantes.
- Nueva actualización del Manual Operativo.
- Segundo Reporte Anual.
- Afiche con flujograma que se distribuye en los hospitales.
- Inicio de proyectos de investigación especiales.
- Incorporación del RENAC como miembro de la International Clearinghouse of Birth Defects Surveillance and Research - ICBDSR.
- 4º Encuentro Anual de capacitación.

**Figura 2.** RENAC’s activities and coverage evolution of births monitored in the first 98 hospitals (from November 1st, 2009 to June 30th, 2012)
### Health surveillance systems’ attributes and RENAC’s characteristics

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Definition</th>
<th>Characteristics of the RENAC Registry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simplicity</td>
<td>It refers to the structure and ease of operation of the registry. A surveillance system has to be as simple as possible without leaving its objectives behind.</td>
<td>It includes a single source of data and does not require case follow-up; exposure factors are not assessed. Case confirmation is based on the neonatologists’ clinical judgment and is supported by routine supplementary tests. Additional outcome measures are obtained from medical records and do not require interviewing mothers. The appointment of responsible teams was agreed upon by neonatologists who were willing to participate and local authorities. The reporting and communication system is useful in the clinical context.</td>
</tr>
<tr>
<td>Acceptability</td>
<td>It reflects individuals’ will and the agreement of organizations to take part in the surveillance system.</td>
<td>No changes were made in the definition of case, additional sources of data or technological resources, but the original form has been recently amended to include new outcome measures in a seamless fashion.</td>
</tr>
<tr>
<td>Flexibility</td>
<td>It refers to the system’s capability to adapt to any change in relation to information needs or operation conditions without taking up additional time, resources or funding.</td>
<td>An open description field is used to characterize congenital anomalies, thus allowing an interpretation process before coding the event. This would not be possible if a predefined list of options was used because it usually does not include less frequent CAs and it is an obstacle for the inclusion of multiple CAs. A centralized coding by geneticists warrants technical suitability and criteria homogeneity.</td>
</tr>
<tr>
<td>Quality of data</td>
<td>It reflects the completeness and validity of data recorded in the surveillance system.</td>
<td>The data collection process at the RENAC registry starts by attaching the form to the mother’s medical record, thus ensuring case detection right at the labor room. Including multiple sources of data (children hospitals, genetic medicine departments, etc.) so as to increase sensitivity may make the system more complex (longer time, higher cost) and threaten its stability. It cannot be estimated because there is no Gold Standard for sensitivity. However, it has been observed that the prevalence of specific CAs observed by the RENAC is similar to that of other registries.</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>It refers to the proportion of cases with a disease detected by the surveillance system. In addition, it may refer to the power of the system to detect epidemics by monitoring any change in the number of cases over time.</td>
<td>The time elapsed from the occurrence of a health event until it is reported is usually one month, followed by a request for corrections, coding and analysis. In the case of potentially life-threatening events, ambiguous genitalia or multiple CAs, neonatologists report and contact the coordination department through the web forum immediately after birth takes place.</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>It is the proportion of reported cases that actually have the health event under surveillance.</td>
<td>Since the creation, the RENAC registry has been continuously operating. People in charge of reporting events are part of the hospitals’ full-time staff. The coordination department increased from two to four members, and operates as an institution of the CNGM. The RENAC registry has progressively included hospitals and has received funds from the National Ministry of Health, these funds are allocated to annual training meetings, printing forms, operational manuals and reports.</td>
</tr>
<tr>
<td>Representativity</td>
<td>It is the capacity to accurately describe the event over time and its distribution in the population by place and by subject.</td>
<td>In the November 2009-June 2012 period, the observed positive predictive value was 89.94%</td>
</tr>
<tr>
<td>Opportunity</td>
<td>It reflects the speed at which each step in a public health surveillance system takes place.</td>
<td>In Argentina, 99.4% of births take place in a health facility; therefore, the number of lost cases is negligible. It is possible that the prevalence is overestimated due to the referral of cases detected at smaller health facilities or hospitals by antenatal ultrasonography. However, it is expected that such effect will be reduced as maternity centers are regionalized and as smaller maternity centers are included. At present, the RENAC registry is restricted to hospitals in the public subsector; as a consequence, there is a selection bias resulting from the systematic exclusion of a population sector.</td>
</tr>
<tr>
<td>Stability</td>
<td>It refers to the capacity of adequately collecting, managing and providing data, and also to a sustained operation.</td>
<td>The time elapsed from the occurrence of a health event until it is reported is usually one month, followed by a request for corrections, coding and analysis. In the case of potentially life-threatening events, ambiguous genitalia or multiple CAs, neonatologists report and contact the coordination department through the web forum immediately after birth takes place.</td>
</tr>
</tbody>
</table>

**RENAC**: National Registry of Congenital Anomalies in Argentina
The classification of cases is presented according to the different outcome measures (Table 2). The overall prevalence of major CAs at birth was 1.76% (95% CI: 1.71-1.80).

The prevalence observed for each one of the 56 specific selected CAs is presented together with a comparison with the data from the ECLAMC and the EUROCAT (Table 3).

Compared to the ECLAMC, it has been observed that the RENAC has a significantly higher prevalence of cleft palate, kidney cysts, and septal and valvular heart defects, and a significantly lower prevalence of hydrocephalus, anorectal atresia, diaphragmatic hernia, total hypospadias, preaxial polydactyly, postaxial polydactyly, talipes equinovarus and talipes calcaneovalgus.

Compared to the EUROCAT, it has been observed that the RENAC has a significantly higher prevalence of hydrocephalus, cleft lip +/− palate, ambiguous genitalia, and gastroschisis, and a lower prevalence of heart diseases, cleft palate, hypospadias, unspecified polydactyly, syndactyly, hip subluxation/dislocation, and talipes equinovarus.

Table 2. Characteristics of cases with major congenital anomalies as per different outcome measures. RENAC, November 2009 - June 2012

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Categories</th>
<th>Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification*</td>
<td>Isolated</td>
<td>3418</td>
<td>66.18</td>
</tr>
<tr>
<td></td>
<td>Multiple congenital anomalies</td>
<td>866</td>
<td>16.77</td>
</tr>
<tr>
<td></td>
<td>Syndromes, sequences or associations</td>
<td>858</td>
<td>16.61</td>
</tr>
<tr>
<td></td>
<td>UN</td>
<td>23</td>
<td>0.45</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>2701</td>
<td>52.29</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2341</td>
<td>45.49</td>
</tr>
<tr>
<td></td>
<td>Undetermined</td>
<td>103</td>
<td>1.99</td>
</tr>
<tr>
<td></td>
<td>UN</td>
<td>20</td>
<td>0.39</td>
</tr>
<tr>
<td>Status at birth</td>
<td>Alive</td>
<td>4927</td>
<td>95.39</td>
</tr>
<tr>
<td></td>
<td>Deceased</td>
<td>234</td>
<td>4.53</td>
</tr>
<tr>
<td></td>
<td>UN</td>
<td>4</td>
<td>0.08</td>
</tr>
<tr>
<td>Twin pregnancy</td>
<td>Twin</td>
<td>182</td>
<td>3.52</td>
</tr>
<tr>
<td></td>
<td>Nottwin</td>
<td>4753</td>
<td>92.02</td>
</tr>
<tr>
<td></td>
<td>UN</td>
<td>230</td>
<td>4.45</td>
</tr>
<tr>
<td>Status at the time of data submission</td>
<td>Discharged alive</td>
<td>3438</td>
<td>66.56</td>
</tr>
<tr>
<td></td>
<td>Discharged deceased</td>
<td>963</td>
<td>18.64</td>
</tr>
<tr>
<td></td>
<td>Still hospitalized</td>
<td>726</td>
<td>14.06</td>
</tr>
<tr>
<td></td>
<td>UN</td>
<td>38</td>
<td>0.74</td>
</tr>
<tr>
<td>Gestational age</td>
<td>&lt;37 weeks</td>
<td>1456</td>
<td>28.19</td>
</tr>
<tr>
<td></td>
<td>≥37 weeks</td>
<td>3452</td>
<td>66.83</td>
</tr>
<tr>
<td></td>
<td>UN</td>
<td>257</td>
<td>4.98</td>
</tr>
<tr>
<td>Weight</td>
<td>&lt;2500 g</td>
<td>1608</td>
<td>31.14</td>
</tr>
<tr>
<td></td>
<td>≥2500 g</td>
<td>3540</td>
<td>68.54</td>
</tr>
<tr>
<td></td>
<td>UN</td>
<td>17</td>
<td>0.33</td>
</tr>
<tr>
<td>Maternal age</td>
<td>&lt;20</td>
<td>1100</td>
<td>21.30</td>
</tr>
<tr>
<td></td>
<td>20-24</td>
<td>1468</td>
<td>28.42</td>
</tr>
<tr>
<td></td>
<td>25-29</td>
<td>1013</td>
<td>19.61</td>
</tr>
<tr>
<td></td>
<td>30-34</td>
<td>740</td>
<td>14.33</td>
</tr>
<tr>
<td></td>
<td>35-39</td>
<td>517</td>
<td>10.01</td>
</tr>
<tr>
<td></td>
<td>40-44</td>
<td>253</td>
<td>4.90</td>
</tr>
<tr>
<td></td>
<td>45+</td>
<td>35</td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>UN</td>
<td>39</td>
<td>0.76</td>
</tr>
</tbody>
</table>

*Isolated, when the case presents a single congenital anomaly, or two or more congenital anomalies in the same system organ class which do not account for a known syndrome, association or sequence.

Multiple, when the case presents major congenital anomalies affecting different, unrelated system organ classes, which do not correspond to a known syndrome, association or sequence; known syndromes, associations or sequences (e.g., Down’s syndrome, Patau’s syndrome, Edwards’ syndrome, prune belly sequence, etc.) if they correspond to specific entities.

UN: unspecified.
<table>
<thead>
<tr>
<th>Specific selected CAs</th>
<th>RENAC</th>
<th>ECLAMC</th>
<th>EUROCAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>N Prevalence x10'000 CI 95%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anencephaly (Q00)</td>
<td>105</td>
<td>3.6</td>
<td>2.9-4.3</td>
</tr>
<tr>
<td>Encephalocoele (Q01)</td>
<td>57</td>
<td>1.9</td>
<td>1.5-2.5</td>
</tr>
<tr>
<td>Microcephaly (Q02)</td>
<td>89</td>
<td>3.0</td>
<td>2.4-3.7</td>
</tr>
<tr>
<td>Spinabifida (Q05)</td>
<td>189</td>
<td>6.4</td>
<td>5.5-7.4</td>
</tr>
<tr>
<td>Hidrocefealy (Q13)</td>
<td>267</td>
<td>9.1</td>
<td>8.0-10.2</td>
</tr>
<tr>
<td>Holoprosencephaly (Q41.0-41.42)</td>
<td>76</td>
<td>2.6</td>
<td>2.0-3.2</td>
</tr>
<tr>
<td>Anophthalmia (Q11.1)</td>
<td>16</td>
<td>0.5</td>
<td>0.3-0.9</td>
</tr>
<tr>
<td>Microphthalmia (Q11.2)</td>
<td>36</td>
<td>1.2</td>
<td>0.9-1.7</td>
</tr>
<tr>
<td>Anota (Q16.0)</td>
<td>8</td>
<td>0.3</td>
<td>0.1-0.5</td>
</tr>
<tr>
<td>Microtia (Q17.2)</td>
<td>123</td>
<td>4.2</td>
<td>3.5-5.0</td>
</tr>
<tr>
<td>Anota + microtia (Q16.0, Q17.2)</td>
<td>131</td>
<td>4.5</td>
<td>3.8-5.3</td>
</tr>
<tr>
<td>Transposition of the great vessels (Q20.3)</td>
<td>44</td>
<td>1.5</td>
<td>1.1-2.0</td>
</tr>
<tr>
<td>Tetralogy of Fallot (Q21.3, Q21.82)</td>
<td>66</td>
<td>2.2</td>
<td>1.7-2.9</td>
</tr>
<tr>
<td>Attrial septal defect (Q21.1-Q21.18)</td>
<td>374</td>
<td>12.7</td>
<td>11.5-14.1</td>
</tr>
<tr>
<td>Ventricular septal defect (Q21.0)</td>
<td>538</td>
<td>18.3</td>
<td>16.8-19.9</td>
</tr>
<tr>
<td>Total seaptal heart defects (Q21.0-Q21.9)</td>
<td>833</td>
<td>28.6</td>
<td>26.7-30.6</td>
</tr>
<tr>
<td>Total valvular heart defects (Q22-Q23.9)</td>
<td>213</td>
<td>7.3</td>
<td>6.4-8.4</td>
</tr>
<tr>
<td>Hypoplastic left heart (Q23.4)</td>
<td>45</td>
<td>1.5</td>
<td>1.1-2.1</td>
</tr>
<tr>
<td>Aorta coartation (Q25.1-Q25.19)</td>
<td>46</td>
<td>1.6</td>
<td>1.2-2.1</td>
</tr>
<tr>
<td>Choanal atresia (Q30.0)</td>
<td>9</td>
<td>0.3</td>
<td>0.1-0.6</td>
</tr>
<tr>
<td>Cleft palate (Q35)</td>
<td>95</td>
<td>3.2</td>
<td>2.6-4.0</td>
</tr>
<tr>
<td>Cleft lip +/ - palate (Q36-Q37)</td>
<td>352</td>
<td>12.0</td>
<td>10.8-13.3</td>
</tr>
<tr>
<td>Esophageal atresia (Q39.0-Q39.11)</td>
<td>98</td>
<td>3.3</td>
<td>2.8-4.1</td>
</tr>
<tr>
<td>Intestinal atresia (Q41.1-Q41.9)</td>
<td>47</td>
<td>1.6</td>
<td>1.2-2.1</td>
</tr>
<tr>
<td>Duodenal atresia (Q41.0)</td>
<td>49</td>
<td>1.7</td>
<td>1.2-2.2</td>
</tr>
<tr>
<td>Anorectal atresia (Q42.0-Q42.3)</td>
<td>104</td>
<td>3.5</td>
<td>2.9-4.3</td>
</tr>
<tr>
<td>Diaphragmatic hernia (Q79.0-Q79.01)</td>
<td>98</td>
<td>3.3</td>
<td>2.7-4.1</td>
</tr>
<tr>
<td>Cryptorchidism (Q53.2)</td>
<td>23</td>
<td>0.8</td>
<td>0.5-1.2</td>
</tr>
<tr>
<td>UN cryptorchidism (Q53.3, Q53.4)</td>
<td>9</td>
<td>0.3</td>
<td>0.1-0.6</td>
</tr>
<tr>
<td>Ambiguous genitalia (Q56.4)</td>
<td>40</td>
<td>2.1</td>
<td>1.8-3.0</td>
</tr>
<tr>
<td>Hypospadias (Q54.1-Q54.3)</td>
<td>7</td>
<td>0.2</td>
<td>0.1-0.5</td>
</tr>
<tr>
<td>UN hypospadias (Q54.9)</td>
<td>37</td>
<td>1.3</td>
<td>0.9-1.7</td>
</tr>
<tr>
<td>Total hypospadias (Q54)</td>
<td>44</td>
<td>1.5</td>
<td>1.1-2.0</td>
</tr>
<tr>
<td>Bilateral renal agenesis (Q60.1)</td>
<td>33</td>
<td>1.1</td>
<td>0.8-1.6</td>
</tr>
<tr>
<td>Renal cysts (Q61.1-Q61.90)</td>
<td>144</td>
<td>4.9</td>
<td>4.1-5.8</td>
</tr>
<tr>
<td>Epispadias (Q64.0)</td>
<td>8</td>
<td>0.3</td>
<td>0.1-0.5</td>
</tr>
<tr>
<td>Bladder extrophy (Q64.1)</td>
<td>7</td>
<td>0.2</td>
<td>0.1-0.5</td>
</tr>
<tr>
<td>Hip subluxation or dislocation (Q65)</td>
<td>66</td>
<td>2.1</td>
<td>1.7-2.9</td>
</tr>
<tr>
<td>Talipes calcaneovalgus (Q66.4)</td>
<td>51</td>
<td>1.7</td>
<td>1.3-2.9</td>
</tr>
<tr>
<td>Talipes equinovarus (Q66.0)</td>
<td>205</td>
<td>7.0</td>
<td>6.1-8.0</td>
</tr>
<tr>
<td>UN talipes (Q66.8)</td>
<td>117</td>
<td>4.0</td>
<td>3.3-4.8</td>
</tr>
<tr>
<td>Preaxial polydactyly (Q69.00, Q69.1, Q69.20)</td>
<td>48</td>
<td>1.6</td>
<td>1.2-2.2</td>
</tr>
<tr>
<td>Postaxial polydactyly (Q69.02, Q69.22)</td>
<td>155</td>
<td>5.3</td>
<td>4.5-6.2</td>
</tr>
<tr>
<td>UN polydactyly (Q69.9)</td>
<td>14</td>
<td>0.5</td>
<td>0.3-0.8</td>
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<tr>
<td>Syndactyly (Q70.0-Q70.30, Q70.4-Q70.90)</td>
<td>122</td>
<td>4.2</td>
<td>3.5-5.0</td>
</tr>
<tr>
<td>Transverse limb defect (Q71.2-Q71.30)</td>
<td>93</td>
<td>3.2</td>
<td>2.6-3.9</td>
</tr>
<tr>
<td>Preaxial limb defect (Q71.31, Q72.5)</td>
<td>52</td>
<td>1.8</td>
<td>1.3-2.3</td>
</tr>
<tr>
<td>Postaxial limb defect (Q71.5, Q72.6)</td>
<td>13</td>
<td>0.4</td>
<td>0.2-0.8</td>
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<td>Intercalary limb defect (Q71.7, Q73.1)</td>
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<td>0.1</td>
<td>0.0-0.2</td>
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<tr>
<td>UN limb defect (Q71.8-Q71.9, Q72.8-Q72.90)</td>
<td>75</td>
<td>2.6</td>
<td>2.0-3.2</td>
</tr>
<tr>
<td>Omphalocele (Q73.2)</td>
<td>86</td>
<td>2.9</td>
<td>2.3-3.6</td>
</tr>
<tr>
<td>Gastrochisis (Q79.3)</td>
<td>262</td>
<td>8.6</td>
<td>7.9-10.1</td>
</tr>
<tr>
<td>Prune belly sequence (Q79.4)</td>
<td>17</td>
<td>0.6</td>
<td>0.3-0.9</td>
</tr>
<tr>
<td>Down’s syndrome (Q90)</td>
<td>563</td>
<td>19.2</td>
<td>17.6-20.8</td>
</tr>
<tr>
<td>Trisomy 13 (Q91.4-Q91.7)</td>
<td>15</td>
<td>0.5</td>
<td>0.3-0.8</td>
</tr>
<tr>
<td>Trisomy 18 (Q91.0-Q91.3)</td>
<td>38</td>
<td>1.3</td>
<td>0.9-1.8</td>
</tr>
</tbody>
</table>


Z1: Z value obtained by comparing the frequencies observed by ECLAMC vs. RENAC. Positive values indicate a higher rate as per the ECLAMC system, negative values indicate a higher rate as per the RENAC.

Z2: Z value obtained by comparing the frequencies observed by EUROCAT vs. RENAC. Positive values indicate a higher rate as per the EUROCAT system, negative values indicate a higher rate as per the RENAC.

UN: unspecified.
DISCUSSION

The observed prevalence (1.76% cases) is within expected rates if only major morphological CAs are considered. The most common CAs were heart diseases, Down’s syndrome, oral clefts and the set of neural tube defects (anencephaly, spina bifida, encephalocoele), consistent with ECLAMC and EUROCAT reports, and with the literature.23

Of the specific CAs with significantly different prevalences between the RENAC and the ECLAMC, talipes equinovarus, preaxial polydactyly and postaxial polydactyly had a lower prevalence in the RENAC; however, such differences disappeared when analyzing the total number of cases with talipes equinovarus, which included unspecified forms of these anomalies. It is considered that these cases were detected by the RENAC, but they were not specifically described (for example, the term “polydactyly” was described instead of “postaxial polydactyly”, or “club foot” instead of “talipes equinovarus”). In addition, the RENAC recorded a higher rate of septal and valvular heart defects, which could be attributed to the fact that ECLAMC data correspond to a previous period (2005-2007) than that of the RENAC (2009-2012), probably with a lower availability of heart studies and prior to the National Heart Disease Program, which started in 2008.

In relation to the specific CAs which had significantly different prevalences between the RENAC and the EUROCAT, some differences could be explained by the fact that the registries of the consortium include a follow-up period of newborn infants until they turn one year old. For example, heart diseases and hip subluxation/dislocation might not be evident at birth and, therefore, it is assumed that the EUROCAT has a better detection capacity. The higher prevalence of hypospadias in the EUROCAT can be attributed to a previously reported increasing trend.20

In relation to gastroschisis, it is known that its rate is higher in the descendants of young women;21 therefore, the lower prevalence found by the EUROCAT can be attributed to differences in the structure of maternal age.22 The higher frequency of a cleft lip +/- palate observed by the RENAC can be explained by the American Indian component present in our population, previously associated with this anomaly.23 The differences observed in the prevalence of the remaining CAs could be due to operational aspects or actual differences.

There are no ideal systems or a single possible organization for the surveillance of CAs. In some countries, surveillance is conducted passively, through health statistics; in others, surveillance is active and involves the staff in charge of searching cases.24 The sensitivity of birth certificates, using active surveillance registries as reference, showed an under-recording that ranges between 30% and 60% in the United Kingdom,25,26 and between 50% and nearly 90% in the United States.27,28 In Brazil, under-recording was variable, depending on the CAs considered and the methods used.29,30

The RENAC conducts a mixed surveillance, with data collected by neonatologists, who are part of the hospital’s personnel, but they are also part of this special registry, which is centrally coordinated. Given that 99.4% of births in Argentina take place in health facilities, and within framework of birth regionalization process currently taking place in the country,31 the organization of a hospital-based registry was the selected strategy. Priority was given to the public subsector hospitals which are considered a referral center in their health region or which have more than 1000 births per year, thus ensuring a high number of births, adequate diagnostic resources (trained doctors, X-rays, ultrasounds, etc.) and a sufficient number of cases to implement systematic registration. Although the RENAC has a high coverage in the public sector, births taking place in social security and private facilities are still not recorded; therefore, there would be a bias resulting from their systematic exclusion. It is expected that non public and smaller maternity centers will start being included.

This study offers a first baseline regarding the prevalence of certain specific CAs. This is the initial step of the first objective of the RENAC, i.e., to monitor the prevalence of specific CAs, detect geographic variations or temporary trend changes, generate the hypothesis regarding determining factors, and evaluate the impact of population interventions. Additionally, in a country like Argentina, where genetic services have not been sufficiently developed,32 the RENAC also proposes to contribute to the early management of newborn infants with CAs. As a consequence, the system does not only involve the flow of data from hospitals to the coordination department, it is also based on a continuous exchange and the remote support of health teams. Health surveillance is taken as the production of the data-information-knowledge triad, and also as the communication-action processes for its use towards the reduction of inequalities.33

The system collects, processes and shares
information, and at the same time, acts as a management support by training and motivating health teams. This strategy seems fundamental, both to favor medical care of affected newborn infants and to reach a purely epidemiological goal. But having a continuous surveillance system with a high coverage and quality in place does not seem possible without the strong commitment of participants based on their conviction regarding the system’s usefulness for local management.

Some of the RENAC’s strengths include its high coverage in the public sector; its operational simplicity, which could be expanded at a national level; the guidelines established in an operational manual with standard procedures; the use of an open source field for describing CAs instead of having a multiple choice list; a centralized coding in the hands of geneticists, thus ensuring its suitability and homogeneous criteria; and the use in the clinical context for the initial management of affected newborn infants.

In relation to the system’s weaknesses, we could mention the fact that non-public facilities have not yet been included; that CAs detected upon the hospital discharge are not recorded; that there is a possible prevalence over-estimation of the CAs detected prenatally and referred to hospitals with a higher level of care, i.e., those which are part of the RENAC; and that risk factors are not systematically recorded but only through special research projects.

CONCLUSIONS

Since it started operating, the RENAC has expanded and reached a high coverage of the public sector thanks to the support provided by the authorities and the commitment of the participating health teams. Differences observed in the prevalence of CAs between the RENAC and other registries could be attributed to operational aspects or actual differences, depending on the case.

In addition to the objective of producing information relevant to the surveillance and epidemiological research of congenital anomalies, the RENAC works through the continuous exchange among its participants, which allows to comply with another objective of the registry: to provide support to health teams in relation to the initial management of affected newborn infants. The RENAC deals with the collection, analysis and dissemination of information regarding CAs in Argentina, and also collaborates with local interventions in the different prevention levels of these anomalies.

REFERENCES


ANEX

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