
Catalina Correa a,⁎, Christina Mallarino b, Rafael Peña a, Luis Carlos Rincón a, Gloria Gracia c, Ignacio Zarante b,c

a Hospital Militar Central, Bogotá, Colombia
b Instituto de Genética Humana, Pontificia Universidad Javeriana, Bogotá Colombia
c Secretaría de Salud de Bogotá

ABSTRACT

Article history:
Received 19 June 2013
Received in revised form 1 March 2014
Accepted 4 March 2014

Key words:
Congenital anomalies
Pediatric surgery
Prevalence
Surveillance
Birth defects
ECLAMC

Background: Congenital anomalies (CAs) cause nearly one third of infant deaths worldwide. Various surveillance systems have been established, such as the Bogota Congenital Malformations Surveillance Program (BCMSP). Some CAs are of special interest to pediatric surgeons: omphalocele, gastroschisis, intestinal and esophageal atresia, anorectal malformations, vascular anomalies, diaphragmatic hernias, hypospadias and cryptorchidism. The aim of this study is to determine the prevalence of such CAs, and identify possible risk factors.

Methods: Data from the BCMSP were collected between January 2005 and April 2012. CAs were classified in accordance with the ICD-10 and grouped for analysis purposes. Data on CA frequencies were obtained from the BCMSP. Association analyses were performed using the case–control methodology.

Results: 282,523 births were registered. 4682 (1.66%) had one or more CAs at birth. The prevalence of CAs requiring pediatric surgery was 1 in 1000. The most frequent CAs were vascular anomalies, hypospadias, and anorectal malformations. Exposure to external factors was significantly associated with selected CAs. 51% of selected birth defects were not diagnosed in prenatal ultrasound.

Conclusions: This study highlights the importance of evaluating the local prevalence of congenital malformations. We propose the creation of specialized centers in Bogotá to manage patients with CAs.

© 2014 Elsevier Inc. All rights reserved.

In 2007, for the first time in the history of Colombia, congenital anomalies (CAs) became the most frequent cause of infant mortality [1]. This study highlights the importance of evaluating the local prevalence of CAs to identify potential areas of intervention in their prevention and treatment. CAs should be diagnosed and treated in a timely fashion in order to reduce the burden of disease and disability associated with most of them.

CAs are structural abnormalities that are present at birth and now constitute the main cause of infant mortality in many countries around the globe [2–4]. Accounting for nearly one third of infant deaths worldwide [5], their contribution to morbidity and mortality presents geographic variations [6] due to the burden of other competing causes of death, such as malnutrition and infections, access to quality health care, and the availability of specialized institutions to treat CAs [7].

Some CAs, such as abdominal wall defects, intestinal and esophageal atresia, anorectal malformations, vascular anomalies, diaphragmatic hernias, hypospadias and cryptorchidism, are of special interest to pediatric surgeons. Newborns with such CAs require immediate attention and opportune surgical management in order to ensure the best possible prognosis regarding both mortality and potential disability [8]. The objective of this study is to determine the prevalence of selected CAs that require surgical management, documented in the Bogota Congenital Malformations Surveillance Program (BCMSP) between January 2005 and April 2012 and identify possible factors associated with these CAs. Frequency of other CAs in Colombia has been previously reported [9,10].

1. Methods

Data from the BCMSP were collected in order to determine the prevalence of selected CAs between January 2005 and April 2012. This surveillance program is managed by the local health authorities (Secretaría de Salud de Bogotá) as well as the Human Genetics Institute (HGI) of the Pontificia Universidad Javeriana; its data collection...
formats correspond to the Latin American Collaborative Study for Congenital Malformations (ECLAMC) [11].

The BCMSP is a hospital-based surveillance program that covers over 90% of all hospital births in the city. In Bogota, 98% of births occur in hospitals [12]. The BCMSP is a member of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR) [13]. Data on CA frequencies were obtained from the BCMSP and prevalence was calculated using as a denominator the number of births registered in the surveyed hospitals during the study period. Association analyses were performed using the case-control methodology.

General practitioners previously trained to carry out a systematic physical examination searching for CAs evaluated all newborns born in the hospitals that belong to the BCMSP program. If a CA was diagnosed, the physician filled out a standardized questionnaire, previously designed by the ECLAMC, [11] collecting information about the pregnancy, the newborn, the mother’s medical history, ethnicity and educational attainment, amongst others. All participants signed an informed consent before the form was completed. Cases were defined as all live newborns and those stillborn weighing more than 500 g, who were born in one of the 46 hospitals under surveillance, and who presented with one or more of the selected CAs. Multiple Congenital Anomalies were defined as the presence of a major CA in two or more organ systems. Controls were defined as any live newborn that had been born in the same hospital during the same month as the case, and had no CA at time of birth. The controls were not sex-matched. The case-control ratio was 1:4.

CAs were classified in accordance with the 10th Revision of International Classification of Diseases (ICD-10) and grouped into ten different subgroups for analysis purposes. All data were recorded in Microsoft Excel® 2010. All analyses were performed with SPSS version 17.0 (SPSS Corp. Chicago, IL) and Epi Info 7.1.0.6 (Epi Info™ Centers for Disease Control and Prevention, Atlanta GA). Student’s t test was performed to compare variables relating to the mother, the newborn, and pregnancy. P < 0.05 was considered statistically significant.

The information on prenatal diagnosis was obtained from the interview with the newborn’s mother, describing the results of all prenatal exams and ultrasounds (US). The US results were considered positive if the clinical diagnosis of the newborn was consistent with the CAs reported in the US. The diagnosis of CAs was considered to be ‘missed’ if none of the US described the CAs identified at birth.

Maternal age (~16 years, 16–34 years, >34 years), parity, socio-economic class, newborn’s gestational age, birth weight, size, gender and size for gestational age, exposure to diseases during pregnancy (acute or chronic), concurrence of external factors (trauma, environmental hazards, x-ray exams), and use of “recreational” drugs (cocaïne, marijuana) were studied. Maternal smoking and drinking habits were also studied, considering the amount of cigarettes smoked, and the period of smoking or drinking (first, second, third trimester). All quantitative data are expressed as mean ± standard deviation (SD).

2. Results

In the period between January 2005 and April 2012, 282,523 births were registered in the BCMSP. Of these, 4682 (1.66%) presented with one or more CAs at the time of birth, 243,193 (86%) were live newborns, 1153 (0.4%) were stillbirths, and 38,177 (13%) had no information on viability of the newborn. There were 125,637 (48.8%) female and 131,357 (51.1%) male newborns. A total of 132 (0.1%) newborns had disorders of sex development and 25,397 had no information registered for the sex variable. The sex ratio was 1.05 (Male:Female ratio), meaning that there was a greater prevalence of CAs in male newborns. Of the 4682 (1.6%) newborns with CAs, 284 (6.07%) had one or more of the selected CAs. Thus, the prevalence of selected CAs in this dataset was 1 per 1000 newborns.

The most frequently seen CAs were vascular anomalies, with a prevalence of 3 per 10,000 births, followed by hypospadias (2.8 per 10,000), and anorectal malformations (2.2 per 10,000). The prevalence of cryptorchidism was 5.4 per 10,000 male births. Regarding abdominal wall defects, the prevalence of gastroschisis was 2.1 per 10,000 births, and 1.2 per 10,000 for omphalocele. Esophageal and Intestinal atresias had a prevalence of 2 and 0.8 per 10,000, and congenital diaphragmatic hernia 1.7 per 10,000. Multiple CAs had a total prevalence of 4.4 per 10,000 births.

Regarding vascular anomalies, 84% were hemangiomas, 8% lymphangiomias, and 7% cystic hygromas. In order of frequency, craniofacial hemangiomas were the most frequently diagnosed vascular anomalies after birth, followed by hemangiomas of the extremities, thorax and abdomen. Vascular anomalies were rarely detected in prenatal US. Only 12 of 84 cases (14%) had prenatal diagnosis, mainly corresponding with lymphatic malformations such as cystic hygroma.

2.1. Analysis of selected malformations

Average maternal age for cases was 25 ± 6.3 years, and average maternal age for controls was 26 ± 7 years. Mothers were separated into age groups, and in both groups, the most frequent range of maternal age was 16–34 years. There was no statistically significant difference for the maternal age of the cases and the controls (p = 0.007).

Gestational age lower than 37 weeks was significantly associated with the presence of all selected CAs, with a relative risk (RR) of 2.13 (CI: 1.72–2.64) and a p-value <0.01. Average weight was 2950 g (SD ± 520 g) for the total population, 2670 g (SD ± 680 g) for the cases, and 2970 g (SD ± 490 g) for the control group. There was also a significant association between low birth weight (<2500 g) and all of the selected CAs (RR 2.39, CI: 1.94–2.96, p < 0.01).

Concurrence of external factors showed a positive association with selected CAs (RR 1.746, CI: 1.13–2.70). There was no relation between the selected CAs and exposure to alcohol (RR 1.425, CI: 0.94–2.15), recreational drugs (RR 1.14, CI: 0.36–4.97), tobacco (RR: 0.86, IC: 0.517–1.446), and acute or chronic diseases during pregnancy.

2.2. Prenatal diagnosis

In the ECLAMC dataset, selected CAs were diagnosed by ultrasound (US) in 49% of the cases. The most commonly diagnosed CAs using this test were abdominal wall defects, followed by diaphragmatic hernias. Eighty-eight per cent of anorectal malformations were not detected by US. The mean number of US per pregnancy was 4.95 (SD 5.79) (Tables 1–4).

3. Discussion

In the present study, we document the prevalence of CAs that are of particular interest to pediatric surgeons, using data registered in the BCMSP between January 2005 and April 2012. A total of 282,523 births were registered. This accounts for 31% of the births documented by the National Administrative Department of Statistics (DANE) during the same period [14]. The total prevalence of CAs found in this population was 1.6%, which is similar to the reports of other surveillance systems (usually around 2% or 3%) [2,15], and to previous reports by our group [9]. However, the prevalence of CAs reported in other programs, such as ECLAMC (2009), EUROCAT (2006–2010), MACPD (2009), and CREC (2009), was higher than that found on BCMSP. This might be due to the different surveillance strategies, the case definition established by each program, and the total coverage, as well as the type of hospitals under surveillance.
A review study by Ozgediz and Poenaru concluded that significant congenital anomalies and CAs both represent an important burden of disease and essential to improve the health of children, since pediatric surgical conditions require evaluation and treatment by pediatric surgeons every birth in Bogota yearly, an estimated 115 babies are born with CAs

Table 1

<table>
<thead>
<tr>
<th>CONGENITAL ANOMALY</th>
<th>ICD - 10 SUBGROUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemangioma, any site</td>
<td>D18.0 Vascular</td>
</tr>
<tr>
<td>Angioma NOS (Angioma Cavernosum)</td>
<td>D18.0 Anomaly</td>
</tr>
<tr>
<td>Hemangioma and lymphangiomia, any site</td>
<td>D18</td>
</tr>
<tr>
<td>Cystic Higroma</td>
<td>D18.1</td>
</tr>
<tr>
<td>Lymphangiomia, any site</td>
<td>D18.1</td>
</tr>
<tr>
<td>Atresia of esophagus with tracheo-esophageal fistula</td>
<td>Q39.1 Esophageal</td>
</tr>
<tr>
<td>Atresia of esophagus without fistula</td>
<td>Q39.0</td>
</tr>
<tr>
<td>Congenital malformations of esophagus</td>
<td>Q39</td>
</tr>
<tr>
<td>Congenital absence, atresia and stenosis of duodenum</td>
<td>Q41.0 Intestinal</td>
</tr>
<tr>
<td>Congenital absence, atresia and stenosis of jejunum</td>
<td>Q41</td>
</tr>
<tr>
<td>Apple peel syndrome. Imperforate jejunum</td>
<td>Q41.1</td>
</tr>
<tr>
<td>Undescended testicle, unspecified. Cryptorchidism NOS</td>
<td>Q53.9</td>
</tr>
<tr>
<td>Gastrochisis</td>
<td>Q79.3</td>
</tr>
<tr>
<td>Congenital diaphragmatic hernia</td>
<td>Q79.0</td>
</tr>
<tr>
<td>Hypospadias, balanic. Hypospadias: coronal, glandular</td>
<td>Q54.0</td>
</tr>
<tr>
<td>Hypospadias, penile</td>
<td>Q54.1</td>
</tr>
<tr>
<td>Hypospadias, penoscrotal</td>
<td>Q54.2</td>
</tr>
<tr>
<td>Hypospadias, perineal</td>
<td>Q54.3</td>
</tr>
<tr>
<td>Ectopic anus</td>
<td>Q43.5</td>
</tr>
<tr>
<td>Congenital absence, atresia and stenosis of anus with fistula</td>
<td>Q42.2 Malformation</td>
</tr>
<tr>
<td>Congenital absence, atresia and stenosis of ileum</td>
<td>Q42.3</td>
</tr>
<tr>
<td>Exomphalos. Omphalocele. Excludes: umbilical hernia</td>
<td>Q79.2</td>
</tr>
<tr>
<td>Multiple congenital malformations, not elsewhere classified</td>
<td>Q89.7 Multiple Congenital Anomalies</td>
</tr>
</tbody>
</table>

The prevalence of selected CAs found in the current study was 10 per 10,000 births. This means that if there is an average of 115,000 births in Bogota yearly, an estimated 115 babies are born with CAs that require evaluation and treatment by pediatric surgeons every year. This highlights the importance of creating specialized centers dedicated to the management of these pathologies, where physicians can acquire good experience in the treatment of CAs, which ultimately improves the prognosis of these patients. Such interventions are essential to improve the health of children, since pediatric surgical conditions and CAs both represent an important burden of disease and significantly contribute to infant morbidity and mortality worldwide [16]. A review study by Ozgediz and Poenaru concluded that opportune surgical management of children with CAs is cost-effective and comparable with other essential health interventions, since it results in an important reduction of disease burden and disability-adjusted life years (DALYS) [16]. Also, specialized centers would also facilitate an interdisciplinary approach, which is indispensable in the management of these patients, who usually have other conditions derived from the CAs, such as a failure to thrive and delayed neural development, amongst others [8].

Programs such as ECLAMC and EUROCAT receive data from sentinel hospitals that are usually reference centers, where one would expect to see a higher amount of high-risk pregnancies and, consequently, a higher prevalence of CAs. BCMSP receives data from 46 medical institutions, [17] which represent 90% coverage of hospital births in Bogota. Even though it continues to be a hospital-based surveillance program, BCMSP almost behaves as a population-based system because deliveries occurring outside health institutions are very rare in Bogota. Therefore, we would expect to see a lower amount of CAs in a program that includes a higher proportion of low-risk pregnancies in the total population being evaluated. It has also come to our attention that the MACDP, which is a population-based program, also reported a higher prevalence of CAs than that found in the current study. This is probably due to the fact that MACDP utilizes multiple sources of information and includes cases of CAs detected up to the first year of life, while the BCMSP only uses a single source of information and includes cases identified prenatally or at the time of birth. This is an important limitation of the current study, since some CAs that need surgical management may be difficult to diagnose before birth or at the initial evaluation of the newborn.

Another important limitation, as will be discussed below, is the fact that a significant number of malformations are not detected by ultrasonography during the prenatal period. This may delay the time of diagnosis of certain CAs that are not clinically evident at the time of birth, affecting the true prevalence of these malformations.

The prevalence of esophageal atresia was found to be lower than that usually reported in the literature [18,19] and other surveillance systems such as MACDP and ECLAMC. It is possible that this malformation is under-registered in the BCMSP since it should be diagnosed during the first physical evaluation of the newborn. Anorectal malformations and intestinal atresia, on the other hand, may be more difficult to diagnose during the initial examination of the newborn and their prevalence has been reported to be 2 and 1.3–2.9 per 10,000 live newborns, respectively [20,21]. The prevalence of vascular anomalies was 3 per 10,000 births. Interestingly, none of the surveillance programs that were reviewed reported these CAs, probably because they usually manifest later in life, and are not easy to define or to classify; these elements have historically made these malformations difficult to evaluate and treat [22].

Possible factors associated with the development of selected CAs were evaluated. Various studies have found associations between CAs and advanced maternal age, low birth weight and male sex [6,10,23,24]. The results presented in this study are consistent with these findings and other local studies [9]. A gestational age lower than 37 weeks was found to be significantly associated with the appearance of the evaluated CAs (RR 2.13 CI: 1.72–2.64). This association was also reported for urological CAs in Colombia [25,26]. Even though this analysis does not allow us to establish a causal relationship between gestational age and CAs, it does suggest that preterm newborns should be evaluated for CAs in cases where the cause of prematurity is not clear. Exposure to external factors was significantly associated with selected CAs. However, it is important to bear in mind that there may be a memory bias, since mothers of newborns with CAs probably make a greater effort to remember details of the pregnancy. Also, there may be other confounding variables, which may have contributed to this association. Further studies are needed to understand the true relationship between these variables.

Table 2

<table>
<thead>
<tr>
<th>Demographic variables</th>
<th>BCMSP Data</th>
<th>Cases</th>
<th>Controls</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight g (SD)</td>
<td>2954 (±516.4)</td>
<td>2672 (±67.3)</td>
<td>2972 (±486.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>&lt;2500 (%)</td>
<td>35245 (11.7)</td>
<td>85 (30.8)</td>
<td>135 (11.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>≥2500 (%)</td>
<td>220967 (86.2)</td>
<td>191 (88.0)</td>
<td>992 (69.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Length cm (DS)</td>
<td>49 (±3)</td>
<td>47.5 (±4.4)</td>
<td>48 (4.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Materinal age, years</td>
<td>26 (±6.5)</td>
<td>25 (±6.3)</td>
<td>26 (±7)</td>
<td>0.007</td>
</tr>
<tr>
<td>&lt;16 (%)</td>
<td>4222 (1.7)</td>
<td>5 (1.8)</td>
<td>21 (1.9)</td>
<td>0.049</td>
</tr>
<tr>
<td>≥16–34 (%)</td>
<td>216871 (89.4)</td>
<td>251 (88.4)</td>
<td>924 (82.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>&gt;34 (%)</td>
<td>25729 (10.6)</td>
<td>28 (9.9)</td>
<td>174 (15.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Gestational age, weeks (SD)</td>
<td>38 (±2.2)</td>
<td>36 (±3.4)</td>
<td>37 (±2.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>&lt;37 (%)</td>
<td>28568 (11.4)</td>
<td>82 (29)</td>
<td>143 (13)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>≥37 (%)</td>
<td>221827 (88.6)</td>
<td>198 (71)</td>
<td>960 (87)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Female (%)</td>
<td>125637 (48.8)</td>
<td>107 (38)</td>
<td>495 (44)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male (%)</td>
<td>131357 (51.1)</td>
<td>174 (61)</td>
<td>641 (56)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Disorders of sex development (%)</td>
<td>132 (0.1)</td>
<td>3 (1)</td>
<td>0 (0)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
There were no significant associations between CAs and variables that have been previously identified as risk factors for CAs, such as the consumption of alcohol, tobacco or drugs during pregnancy [27–29]. There are various reasons that might explain these findings, including memory bias and unwillingness of the mother to disclose such information. It is also possible that our data set lacks power to detect a relationship between these variables. Nevertheless, it is important to mention that, even though the relationship between alcohol and CAs was not statistically significant, there is a positive tendency between these variables. Finally, another association reported in the literature that was not seen in this analysis was the positive correlation between gastrochisis and young maternal age [30,31].

A high percentage of selected CAs were not diagnosed by US (51%), even though the test was performed around four times in each pregnancy. This means that only 49% of selected CAs were diagnosed, which is a much lower overall sensitivity than that which has been reported previously, mainly in the EUROFETUS study, where the sensitivity of prenatal US for identifying CAs was 61.4% [32]. Anorectal malformations and esophageal atresia are the most commonly missed CAs, but the sensitivity for correct diagnosis was much lower than previously reported [32]. Another study of prenatal US carried out with data from the Paris Registry of Congenital Malformations showed results similar to ours, except for the diagnosis of diaphragmatic hernias and abdominal wall defects, which was reported at a much higher frequency in the French study [33]. Nevertheless, we still consider that the lack of diagnosis is high, especially since the mean number of US carried out per pregnancy is higher than that which is currently recommended for low-risk pregnancies (which was the classification of these pregnancies since no prenatal diagnosis of CAs had been made). Even though US has a marked difference in its sensitivity for different CAs [32], these results suggest that there is a need to enhance the quality – rather than quantity – of US, probably by improving the type of equipment used, as well as the training of physicians that are in charge of doing these tests [26]. Achieving a good level of prenatal diagnosis is crucial in order to refer patients to specialized centers at an opportune moment, as well as making decisions such as the preferred route of delivery. Being able to assure that babies with CAs are born in institutions that are equipped with neonatal ICUs and pediatric surgeons has an important impact on their prognosis [34,35].

### 4. Conclusion

The current study highlights the importance of evaluating the local prevalence of CAs and possible risk factors, in order to compare our data with other programs, detect problems that are of public health interest, and identify potential areas of intervention. The most significant problem found in this population was the lack of prenatal diagnosis using ultrasonography. We consider that it is imperative to improve the level of training of physicians that carry out prenatal ultrasounds as well as the equipment that is being used.

The BCMSP has proven to be a good surveillance strategy enforced by local health authorities. Pediatric surgeons, as well as other health personnel, are summoned to participate as active agents in the surveillance and management of this particular public health issue, in order to detect and treat CAs in a timely fashion. We propose the creation of specialized centers in Bogota that can offer the interdisciplinary management of patients with CAs, in order to improve their diagnosis and probably decrease costs of their medical and surgical treatment in the long-term. The obvious benefits of such specialized centers justify further cost-effectiveness studies.

### References