Congenital Rubella Syndrome Surveillance in Honduras

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Introduction. Congenital rubella syndrome (CRS) surveillance was established in Honduras to determine the scope of the problem and assess the impact of vaccination.

Methods. Implementation of the surveillance system required the drafting of national CRS epidemiological surveillance guidelines, the development of a laboratory diagnostic method, and training of physicians, nurses, and microbiologists in the Honduran hospital network and social security system on CRS surveillance guidelines.

Results. Honduras' experience with the surveillance of other vaccine-preventable diseases facilitated the implementation of hospital-based CRS surveillance. The surveillance system operates in 23 of the 25 public hospitals that offer services to children and at 2 social security hospitals; the private sector has not been integrated into this system. Clinical and technical staff, including representatives from various disciplines such as pediatrics, neonatology, general medicine, epidemiology, nursing, and microbiology, participate in the hospital network, as well as follow up on cases in accordance with the standardized guidelines, depending on their areas of expertise.

Conclusions. Implementation of the CRS surveillance system requires technical guidelines, laboratory diagnostic capacity, and trained multidisciplinary human resources for its systematization and operation.

Rubella was endemic in Honduras, constituting a public health problem; however, the true magnitude of congenital rubella syndrome (CRS) was unknown. From 1990 to 1997, a total of 15 cases was reported. A high degree of underreporting is suspected during this period given that there was no surveillance system in place [1–9].

Beginning in 1979 with the creation of the Expanded Program on Immunization, the country initiated the vaccination of the infant population against measles. In 1992 a “catch-up” campaign was implemented to vaccinate the group aged 1–14 years. Beginning in 1996 a “follow-up” campaign was conducted to protect the population aged 1–4 years against measles; these campaigns were carried out, on average, every 4 years.

In 1997, the decision was made to include the measles, mumps, and rubella (MMR) vaccine in the national vaccination program to be administered at 12 months of age. That same year, the national rubella and CRS surveillance system was established in the health services network to evaluate the impact of vaccination on long-term rubella and CRS control [10, 11].

During the period 2002–2003, the country implemented a mass national vaccination campaign against measles and rubella, vaccinating females aged 5–49 years and males aged 5–39 years. This campaign impacted the incidence of the disease from 2003 onward.

In light of the approval of Resolution CD44.R1 (2003) to eliminate rubella and CRS by 2010 by the Directing Council of the Pan American Health Organization/World Health Organization (PAHO/WHO) [12–15] and given the vast country experience with vaccine-preventable diseases surveillance systems (ie, for polio and measles), it is important to share the experience of Honduras with CRS surveillance with other developing countries embarking on these efforts.
METHODS

The CRS surveillance system was implemented under the Ministry of Health’s Expanded Program on Immunization (EPI), pursuant to the national guidelines in place, which included case definitions, a surveillance algorithm, standard laboratory methods, and system operations. The training of health personnel in the technical guidelines of CRS surveillance has been essential for the implementation of the system. The roles of various health personnel were defined as follows:

Epidemiologists and EPI nurse coordinators: Responsible for the ongoing training of physicians through the dissemination of guidelines developed at the central level, the reporting of cases and laboratory test results, and supervision of the process at all levels within the health services network.

Pediatricians and neonatologists: Responsible for detecting suspected CRS cases in neonatal wards and outpatient visits at hospitals and for immediately notifying the hospital’s epidemiology department. These individuals complete epidemiology-related forms, request the collection of serological samples, and provide case management.

Cardiologists, neurologists, and ophthalmologists: Responsible for identifying children with congenital cardiac, neurologic, and ophthalmologic anomalies during pediatric outpatient visits to national hospitals, following the procedure above.

Microbiologists: Responsible for the collection of blood samples from CRS suspected cases at hospitals and sending samples to the department-level laboratory, which in turn ships them to the national reference laboratory for processing and analysis.

The recommendations and case definitions proposed by the PAHO Technical Advisory Group (TAG) on Vaccine-preventable Diseases were taken into account in developing the case definitions and were modified over time to ensure for a sensitive surveillance system.

A surveillance algorithm based on the case definitions was developed and includes case detection and reporting, sample taking, laboratory follow-up, research using standardized case reporting instruments (the epidemiological reporting form, which must be filled out completely), outbreak response, data management, information analysis, final classification, and feedback [16, 17].

The main goal of the definitions adopted for surveillance was to identify children <12 months of age with suspected CRS. Under the definitions established, a health worker suspects CRS in a newborn whose mother had tested positive for rubella infection during pregnancy and who presented 1 or more of the following signs: congenital cataracts, hepatosplenomegaly, persistence of the arterial duct, hypoacusis, and purpura. [18–20].

Laboratory diagnosis has been centralized at the national level in the central virology laboratory where skilled human resources are available. This is the only laboratory with sufficient capacity to carry out the necessary procedures. PAHO has supported the laboratory by providing a continuous supply of reagents; national funds have also provided the necessary laboratory supplies.

As per the case definition, a serological test for rubella immunoglobulin M (IgM) should be conducted in any suspected CRS case. To aid in laboratory diagnosis, a flowchart was designed for processing samples in these cases. Serological diagnostics were implemented in which 2 mL samples of blood were taken and then centrifuged to separate out the serum, which was kept under refrigeration at temperatures from 2° to 8°C. They were then transported in thermoses with cold packs to the national Virology Laboratory. Reagents from different companies (Rubenostika, Organon Técnika, and Diamedix) were used in the processing. The enzyme-linked immunosorbent assay (ELISA) test was employed for titration of rubella IgM as per the flowchart. IgM-negative samples were ruled out as CRS cases, and positive results were confirmed with clinical findings following the case definition. Nasopharyngeal swabs and urine samples were used for isolation of the virus. External quality control was conducted at the Gorgas Reference Laboratory in Panama [21].

Final case classification was based on the standardized flowchart as a laboratory- or clinically confirmed case, a clinical infection, or a discarded case. A confirmed CRS case is defined as a child in whom CRS was initially suspected, who exhibits congenital anomalies compatible with CRS, and shows evidence of a rubella virus infection during the first year of life. A clinically confirmed case is one in which a health worker suspects CRS, but it was not laboratory-confirmed. This is considered a failure of the surveillance system. A case confirmed as congenital rubella infection is not classified as CRS because the child does not exhibit clinical signs or symptoms compatible with CRS together with a positive rubella laboratory test [22].
In 2005, a national committee was formed to classify suspected measles, rubella, and CRS cases in order to review special cases prior to final classification.

RESULTS

Prior to implementation of the CRS surveillance system, passive CRS case-finding was conducted using statistical information from the Ministry of Health. It was found that during the period 1990–1997, 15 CRS cases were reported at the national level. They were classified in the hospital using clinical and laboratory criteria without considering case definitions.

From 2000 to 2008, a total of 268 suspected CRS cases were detected through the national epidemiological surveillance system. The main reporting sources of suspected cases were the public sector (n = 260 suspected cases), followed by the social security system (n = 6) and the private sector (n = 2).

During that period, a total of 8 CRS cases were confirmed by applying the established case definitions: 5 cases in 2000, 2 cases in 2001, and 1 case in 2002. Cases were reported from the departments of Francisco Morazán (4 cases), El Paraiso (1 case), Choluteca (1 case), and Cortés (1 case). The characterization of these cases demonstrated that 37.5% were identified between 0 and 28 days of age, 37.5% between 1 and 5 months of age, and 25% between 6 and 11 months of age. In regards to sex, 62.5% were female and 37.5% were male. Cases were identified at the hospital level at birth, during well-baby check ups, during consultations with pediatricians, during visits to specialists, and, beginning in 2007, through sentinel surveillance of congenital malformations in infants <1 month of age in 6 hospitals in the country. All cases were reported by the public sector and were children of women who had not received the rubella vaccine.

The most important clinical manifestations identified were the following: hepatosplenomegaly in 62.5% of cases, purpura in 37.5%, cataracts in 37.5%, and cardiac manifestations in 12.5% (Table 1). Serological specimens were collected from 98% (n = 263) of the suspected cases, with IgM-positive results for rubella in 8 (3%), negative IgM results for rubella from 254 cases (97%), and for 2% (5 cases) no specimen was collected. No virus was isolated from those cases where viral specimens were collected. The primary reasons for discarding cases were the laboratory diagnosis of toxoplasmosis and syphilis [9].

The last confirmed CRS case was reported in 2002. A higher rate of case detection was observed following the implementation of the surveillance system; however, these results are not comparable since there was no systematized surveillance prior to the implementation of the system (Figure 2).

The established surveillance system facilitated the detection of an average of 30 suspected CRS cases per year from 2000 to 2008, the majority of which were reported through the public sector. CRS surveillance has been systematized in 22 of the 25 public-sector hospitals and 2 national social security hospitals that provide neonatology and outpatient pediatric services for children. There were problems with 3 hospitals located in the departments of Islas de la Bahía, Yoro, and Lempira, which did not report any suspected cases during this period. The greatest number of suspected CRS cases was reported in national reference hospitals; these cases come from different health regions, with low notification by social security and private facilities.

Training of health workers on the use of technical guidelines for CRS surveillance has raised awareness and fostered active participation. This was evident in the detection of cases that met the established case definitions, immediate reporting to the appropriate levels, proper completion of the epidemiological form, the timely collection of serological samples, and their

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>2000–2002</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>n = 8</td>
</tr>
<tr>
<td>0–28 days</td>
<td>3 (37.5)</td>
</tr>
<tr>
<td>1–5 months</td>
<td>3 (37.5)</td>
</tr>
<tr>
<td>6–11 months</td>
<td>2 (25.0)</td>
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<tr>
<td>Sex</td>
<td></td>
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<tr>
<td>Male</td>
<td>3 (37.5)</td>
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<tr>
<td>Female</td>
<td>5 (62.5)</td>
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<tr>
<td>Clinical manifestations</td>
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</tr>
<tr>
<td>Purpura</td>
<td>3 (37.5)</td>
</tr>
<tr>
<td>Hepatosplenomegaly</td>
<td>5 (62.5)</td>
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<tr>
<td>Congenital malformations</td>
<td></td>
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<tr>
<td>Cataracts</td>
<td>3 (37.5)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>1 (12.5)</td>
</tr>
</tbody>
</table>

Source: Secretary of Health, EPI, CRS database.

Figure 2. Congenital rubella syndrome surveillance, Honduras, 2000–2008.
storage and proper transport to the national reference laboratory based on the established flowcharts.

Over 90% of the cases studied during the period have been fully investigated and documented. There were problems with completing the epidemiological form at the Mario Cantarino Rivas national hospital.

Following the established laboratory algorithms, external quality control was performed on 100% of the indeterminate samples and 10% of the negative samples at the Centro Conmemorativo Gorgas reference laboratory in Panama. There was a 90% concordance rate during this period. One of the primary facilitators was the budget for hiring a company to transport samples from hospitals to the national virology laboratory.

The national laboratory has continued to meet the indicators for the timely receipt of samples and the reporting of results to the EPI. The results are sent by fax to the EPI Coordinators, who are responsible for providing feedback to hospital epidemiologists, who then provide follow-up.

To support surveillance efforts, a poster was designed showcasing the flowchart for case definition and case management and was placed in strategic areas in neonatal wards, pediatrician’s offices, and laboratories in the public and social security hospital networks. The poster supported case detection and continues to be used.

Supervision and evaluation of CRS surveillance system operations are carried out in conjunction with that of other vaccine-preventable diseases, allowing for the identification and strengthening of the deficiencies in the system.

Surveillance problems were encountered in <9% of cases in terms of documentation and the collection of serological samples and cultures. These issues were attributed to the high turnover of health personnel, lack of follow-up on reported cases, and work stoppages.

DISCUSSION

PAHO’s goal of accelerating the control of rubella and the prevention of CRS and later the elimination of these diseases created an enabling environment to develop a standardized surveillance system throughout the Americas.

In Honduras, the surveillance system was implemented in tandem with the introduction of the MMR vaccine, which facilitated the compilation of national information on the associated burden of disease following introduction of the vaccine. However, it is impossible to measure the impact of the intervention because there is limited information from the period prior to vaccine introduction.

Beginning in 2002, active CRS case search was implemented in national and area hospitals where established information systems were reviewed, including ATA and clinical records, and were analyzed to identify those cases compatible with CRS. These systems were reviewed for clinical manifestations, laboratory exams, and differential diagnosis, which had implications for the quality of the surveillance based on whether case identified during the given time period of the study had been previously captured through the established surveillance system.

Factors that were fundamental to the successful implementation of the national CRS surveillance system included (1) country experience in surveillance of other preventable disease accumulated over a decade, (2) the development of technical guidelines for CRS surveillance, (3) the availability of human resources in the hospital network, (4) national and external financial resources that supported training activities for key health personnel at hospitals and for services identified in the CRS surveillance guidelines (such as hospital neonatology, pediatric, and outpatient services), (5) the existing capacity of the central virology laboratory for implementing a centralized diagnostic method, and (6) the monitoring, supervision, and evaluation of system performance.

Supervision to ensure that activities are carried out is fundamental to the operation of the system implemented, requiring competence of epidemiologists at the different levels—hospital, regional, and national—and of EPI nurse coordinators in the departments who monitor the operations of the system and must review and consolidate the information of the forms developed for the information system.

In addition, monitoring and evaluation of surveillance system operations is performed through surveillance performance indicators, the revision of weekly and monthly reports based on the flow of information at the departmental and national level, as well as through the analysis of information.

Monitoring, supervision, and systematic evaluation are crucial to identifying strengths, weaknesses, and challenges to surveillance operations.

Important among the many lessons learned is the need to keep the staff and new hires at hospitals current on the CRS surveillance guidelines. Staff that have received training also need refresher courses to ensure compliance with the surveillance standards established for all personnel. For the system to function, professionals from different disciplines must be involved, because their diverse knowledge helps to strengthen the system. Case definitions are essential for case detection. The use of flowcharts helps with case management in different health-care settings. Case follow-up at all levels contributes to the adequate investigation and final classification of cases, thereby preventing underreporting of information.

Feedback is needed on surveillance results to keep relevant personnel informed and motivated to take steps to correct the shortcomings identified in the process, as well as to strengthen strategies to improve the surveillance system.

The main challenges identified include the need to integrate CRS surveillance into TORCHES (toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and syphilis) and congenital malformations surveillance, because systematic programs for the
detection of congenital malformations in newborns would facilitate the early detection of CRS cases, increasing the sensitivity of these programs through interprogrammatic technical efforts at the national level. This would prevent the duplication of human, physical, and financial resources, improve surveillance in the social security hospital network, and bring the private hospital network into the system.

The process of establishing CRS surveillance in Honduras helped identify the strengths and weaknesses in the surveillance of this syndrome and to implement strategies to improve it, thus capitalizing on existing opportunities, given the national priority of accelerating the reduction of infant mortality through prevention with vaccination. Evaluation of the process at all levels, from the service delivery level to the regional level, has ensured the sustainability of the surveillance system and maintained the topic on the agenda of health managers and technical personnel at all levels.

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**References**