Vaccine 32 (2014) 7065–7069

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Surveillance of congenital rubella syndrome (CRS) in tertiary care hospitals in Hanoi, Vietnam during a rubella epidemic

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ARTICLE INFO

Article history:
Received 5 August 2014
Received in revised form 28 October 2014
Accepted 30 October 2014
Available online 11 November 2014

Keywords:
Rubella
Congenital rubella
Congenital rubella syndrome
Vietnam

ABSTRACT

Objective: To describe the epidemiology and clinical features of congenital rubella syndrome (CRS) in Hanoi, Vietnam.
Methods: Prospective surveillance of CRS between May 2011 and March 2012 in Hanoi, Vietnam. CRS burden was assessed by clinical examination and collection of serum samples from infants in neonatology, cardiology and pediatric departments of two tertiary care hospitals in Hanoi. All infants born during the study period with clinical manifestations of CRS and seropositivity (IgM) for rubella were included in this study.
Results: During the surveillance period 113 infants were identified with confirmed CRS (clinical features and positive rubella IgM). Their mean age at diagnosis was 38.4 days (range 1–152 days) and 61% were female. Clinical manifestations of CRS included low birth weight <2500 g (86.0%), congenital heart disease (63.7%), hearing impairment (63.7%) and ophthalmological abnormalities (46.9%). Other clinical features at birth included: thrombocytopenia (85.0%), neonatal purpura (74.3%), splenomegaly (63.7%), hepatomegaly (62.8%) and blueberry muffin rash (61.1%). Among the mothers of infants with confirmed CRS none had received a rubella vaccine in the past and 88.4% gave a history of rubella contact during the pregnancy under study. In most cases (84.1%) maternal infection occurred in the first trimester. During the surveillance period the estimated annual incidence of CRS was 1.13/1000 live births (95% CI 0.92–1.34).
Conclusions: These preliminary baseline data show a high burden of CRS in Hanoi, Vietnam and the urgent need for universal vaccination. Surveillance to determine and monitor the national burden of CRS is essential.

1. Introduction

Rubella is generally considered as a mild, self-limiting illness in children and adults. However, infection in pregnancy, particularly during the first trimester, may result in miscarriage or a spectrum of congenital anomalies in the newborn knows as congenital rubella syndrome (CRS) [1,2]. The typical triad of CRS is sensorineural deafness, eye abnormalities (retinopathy, cataract and microphthalmia) and congenital heart disease (e.g. pulmonary artery stenosis (PAS) and patent ductus arteriosus (PDA)) [1].

The frequency of CRS varies in different parts of the world, depending on levels of naturally acquired immunity, overcrowding and immunization policies and practices [3]. During epidemics of rubella, the incidence of CRS has been reported at between 0.6 and 2.2 per 1000 live births [4,5]. According to World Health

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http://dx.doi.org/10.1016/j.vaccine.2014.10.087
0264-410X/

Organization (WHO) estimates, about 238,000 children are born with CRS every year, the majority in developing countries [6]. This estimate confirms CRS as the leading cause of vaccine preventable congenital anomalies.

Currently 130 WHO member countries have rubella vaccine included in their national immunization program. However, 59 remaining WHO member states, representing 60% of the world's child population, do not have rubella in their routine immunization schedule, Vietnam being one of those countries [7]. By 2013 goals to eliminate rubella had been established in two World Health Organization (WHO) regions: the Region of the Americas by 2010 and the European Region by 2015 [3,6,8]. Targets for accelerated rubella control and CRS prevention have been established for the Western Pacific Region (WPR) [9].

The WHO has developed guidelines for surveillance of CRS and rubella [10] which recommend both case-based CRS surveillance and rubella sero-surveillance among women of childbearing age and pregnant women. In 2004–2005, at least 2 rubella epidemics were suspected in Vietnam [11,12] and between November 2010 and May 2011 epidemics of rubella were confirmed [13,14]. However, apart from few sero-epidemiological studies there is a paucity of data on the burden of CRS in Vietnam [15]. During 2012, the WHO passive surveillance system reported 7259 cases of rubella and 189 cases of CRS in Vietnam; however, this is likely a gross underestimate of the actual burden [14].

In Vietnam, the rubella virus of genotype 2B circulates [16], however the rubella vaccine, well-known for its effectiveness [17,18], has not been incorporated into the national immunization schedule. In view of efforts to incorporate rubella vaccine into the national immunization program in Vietnam, it is important to establish baseline data of disease burden due to CRS. In this prospective surveillance study we aimed to assess the clinical epidemiology and burden of CRS in infants born during a rubella epidemic in Hanoi, Vietnam.

2. Population and methods

2.1. Study design, period and location

This project was undertaken in collaboration with the University of Sydney's Australia Vietnam Medical Foundation (Hoc Mai). The study was conducted in the province of Hanoi, Vietnam between May 2011 and March 2012 in neonatology, cardiology and pediatric departments of Bach Mai tertiary teaching hospital and the National Hospital of Paediatrics (NHP) in Hanoi. Bach Mai is a multidisciplinary university hospital with 1800 beds (60 Pediatric and 50 Gynecology). NHP is a 1200 bed tertiary hospital with 165 neonatal, 40 cardiology, and 90 infectious disease beds. NHP and Bach Mai hospitals are the sole providers of tertiary care paediatric services in Hanoi, Vietnam.

During and after the 2010–11 rubella epidemic which occurred throughout Vietnam between November 2010 and May 2011, the Ministry of Health organized several seminars to educate health care professionals at primary and tertiary care services about the diagnosis and need for referral of CRS cases. Several TV and radio messages were developed to raise awareness in the general population in every provincial town and city including Hanoi. Hanoi is the second largest province in Vietnam and according to the national census in 2009 the population estimated was 6,451,909 with an average birth rate of 16.5 births/1000 population [19].

Clinicians from all levels of health facility were encouraged to refer any clinically suspected CRS cases (newborns to 6 months of age) to one of two tertiary level surveillance hospitals in Hanoi for our study. While reviewing infants with possible CRS at the surveillance hospitals, clinicians followed the WHO health-care facility recommendations for standard precautions for infection control within hospitals (e.g. hand hygiene, personal protective equipment) [20].

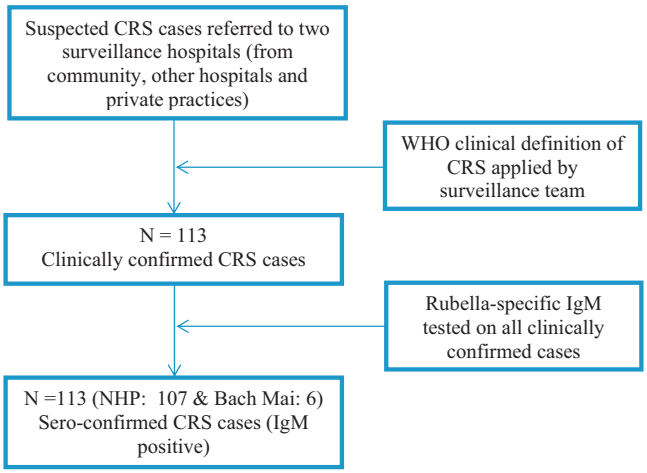

Fig. 1. Outline of CRS surveillance in Hanoi, Vietnam.

At the tertiary referral centers study investigators collected detailed demographic and clinical information and performed laboratory investigations to confirm the diagnosis of CRS (Fig. 1). Specialized tests, including otoacoustic emission (OAE) testing or automated auditory brainstem response (AABR) testing, echocardiogram (ECHO), head ultrasound and ophthalmological examination were performed on infants with suspected CRS. The WHO diagnostic criteria for CRS were applied [21]. The WHO definition for a clinically confirmed case of congenital rubella syndrome (CRS) requires fulfillment of ≥two major criteria or one major and ≥one minor criteria, in the absence of any other obvious cause. Major criteria are sensorineural hearing impairment, congenital heart disease, pigmentary retinopathy, cataract and congenital glaucoma. Minor criteria are purpura, splenomegaly, microcephaly, developmental delay, meningoencephalitis, radiolucent bone disease and jaundice with onset within 24 h of birth) [21].

2.2. Laboratory methods

Whole blood samples were taken using plain bottles, preserved in vaccine thermos, and then transported within 1 h to the laboratory of the Virology section of the Microbiology department of Bach Mai hospital (WHO's microbiology reference laboratory for the Asia Pacific region). Serum was separated and stored at −70 °C. Sera from infants with suspected or clinically confirmed CRS were tested for rubella-specific IgM by electro-chemiluminescence immunoassay (ECLIA) (Roche). The threshold value for IgM was ≥0.3.

2.3. Statistical methods

The incidence of CRS in Hanoi province was calculated with 95% confidence interval (95% CI) per 1000 births, using reported cases and the number of live births for that year [19]. We performed one-sample binomial tests (including *t*-tests) to compare proportions in demographic variables in CRS cases and other births using Vietnam birth record data from the study period [19]. A p value of <0.05 was considered as significant. The software used for data handling and analysis was Stata 10 for Mac and the Statistical Package for Social Sciences (IBM SPSS® 19, Chicago, IL, USA).