Congenital Rubella Syndrome profile of audiology outpatient clinic in Surabaya, Indonesia

Elsa Rosalina,[1] Nyilo Purnami[2]

[1]Faculty of Medicine, Universitas Airlangga, Surabaya; [2]Department of Otorhinolaryngology – Head and Neck Surgery, Faculty of Medicine, Universitas Airlangga – Dr. Soetomo Hospital, Surabaya, Indonesia

Abstract

Congenital Rubella Syndrome (CRS) consists of hearing impairment, ophthalmology abnormalities, and congenital heart disease in children, resulting from rubella infection during pregnancy. Rubella vaccine has been implemented as national immunization program in Indonesia since 2017, and needed to be evaluated. This study aimed to report the CRS patients' profile of Audiology Outpatient Clinic in Surabaya. A descriptive study from patient's medical record was conducted in Dr. Soetomo Hospital Surabaya from January 2016 to December 2017. CRS was categorized using World Health Organization classification. Suspected infants with CRS burden were assessed by Otoacoustic Emission and rubella antibody test. Ninety five infants suspected with CRS classified as laboratory-confirmed CRS (58.95%), clinically confirmed CRS (15.79%), and discarded CRS (25.26%). Clinical manifestations included combination of congenital heart disease and hearing impairment (17.89%), congenital heart disease, ophthalmology abnormalities, and hearing impairment (16.84%), and hearing impairment and ophthalmology abnormalities (13.68%). The data show a high burden of CRS in Surabaya. These implies the urgent need for national rubella immunization program.

Introduction

Congenital Rubella Syndrome (CRS) consists of hearing impairment, ophthalmology abnormalities, and heart disease resulting from rubella virus infection during pregnancy. Hearing impairment is the most common clinical manifestation, account for about 96% of all CRS cases. Early detection of CRS cases is needed to determine congenital abnormalities in infants. The CRS profile is needed to collect for determining the strategy of CRS prevention.[1,2]

A total of 110,000 babies in 78 develop-ing and recurrent outbreak of rubella countries are born with CRS, and 103,000 babies are born with CRS and 46% are from Southeast Asia, especially in countries that do not have rubella immunization programs. Ninety percent baby that are born to mothers infected with rubella virus a 11 weeks of pregnancy will have CRS. The decrease of CRS incidence rate can be seen in countries with immunization programs as preventive strategy.[3–5]

World Health Organization (WHO) strategic plan for 2012-2020 were to eliminate measles, rubella, and CRS. Routine surveilans system is needed to identify children under 1 year old for immediately diagnosing CRS and get the appropriate treatment.[3,5,6] Strategy to prevent rubella infection and CRS is achieved through vaccination programs. The rubella vaccine was introduced as the Indonesian national routine immunization program in 2017.[7] The aim of this study is to report the CRS profile in Audiology outpatient clinic of Dr. Soetomo Hospital Surabaya during the period January 1st 2016 to December 31st 2017.

Materials and Methods

This descriptive study was conducted retrospectively using secondary data derived from the CRS case surveillance form in Audiology Outpatient Clinic of Dr. Soetomo Hospital, Surabaya, Indonesia, from January 1st 2016 to December 31st 2017. CRS was categorized according to WHO classification. Suspected children under 1 year old with CRS burden was assessed by clinical examination using Otoacoustic Emission (OAE) twice and rubella antibody test, based on rubella IgM test at infants under 6 months old, and rubella IgG test twice at infants beyond 6 months old.[4,8] The data included in the CRS case surveillance form are patient identity, clinical symptoms, anti-rubella immunoglobulin test, and CRS classification. All data collected are organized into tables based on age, sex, place of residence, clinical symptoms, and CRS classification based on WHO classification.[4]

Congenital rubella syndrome classification surveillance is based on clinical, epidemiological features, and laboratory data. The CRS classification is divided into 4, namely suspected CRS, clinically confirmed CRS, laboratory confirmed CRS, and discarded CRS. Suspected CRS is a <1 year old infants with ≥1 clinical symptoms from group A and no other obvious cause or the mother has a history of suspected rubella or definitely rubella during pregnancy whether the baby has symptoms or not.

Clinically confirmed CRS is a <1 year old infants with two clinical symptoms from group A or one symptom from group A and one symptom from group B and no laboratory confirmation yet. Laboratory confirmed CRS is an infant with a clinically confirmed CRS that meets CRS laboratory criteria. Discarded CRS is a CRS Suspect that does not meet clinical and certain criteria of CRS.[4]

Results

During the period, 95 patients were obtained in this study, which were 45 patients in 2016 and 50 patients in 2017. The age of patients in this study ranging 14 days old to 11 months old. Age distribution is divided into 4 categories based on Newborn Hearing Screening to ensure

infants are screened for hearing loss by 1 month of age, diagnosed by 3 months of age, and enrolled in early intervention programs no later than 6 months of age.[9] The 1-<3 months age group is the group with the most patients, while the 6- <12 months age group has the least patients. Patients aged ≤ 1 month in this study were 21. The ratio of male to female in this study was 1.06:1 (Table 1).

Newborn hearing screening patients came from various regions especially in East Java, province in Indonesia where this study was conducted. Patients also came from other provinces like West Java, Central Kalimantan, West Kalimantan, East Kalimantan, North Sulawesi, and Papua (Table 1). This diversity is caused by Dr. Soetomo Hospital being a national tertier hospital in eastern Indonesia.

Clinical symptoms of newborn hearing screening patients were varied. The clinical symptoms are divided into two, namely clinical symptoms of group A and group B. The most common clinical symptom in Group A was hearing impairment, which were 18 patients (18.94%). Combination of congenital heart disease and hearing impairment as the second most which were 17 patients (17.89%). Combination of congenital heart disease, ophthalmology abnormality and hearing impairment as the third most which were in 16 patients (16.84%). The most common clinical symptoms of group B were 24-hours postpartum jaundice in 43 patients (45.26%) (Table 2).

The WHO classification of CRS is divided into 4 categories.

Fifty-six patients (58.95%) were included in the laboratory confirmed CRS, while 15 patients (15.79%) were in clinically confirmed CRS, 20 patients (21.05%) were in suspect CRS, and 4 patients (4.21%) were in discarded CRS. Bilateral hearing impairment was found highest in 40 patients (71.43%) with laboratory confirmed CRS while the unilateral one was found in 11 patients (19.64%) with laboratory confirmed CRS (Table 3).

In the anti-rubella IgM test results, there were 26 samples with positive results, consist of 15 samples less than 6 months old, and 11 samples more than 6 months old. In the anti-rubella IgG test, there were 79 samples with positive results, 62 samples at less than 6 months of age, and 17 samples at more than 6 months of age (Table 4).

Table 1. Characteristic of Congenital Rubella Syndrome in Dr. Soetomo Hospital, Surabaya.

Characteristic	Total (%)
Age (month)	
0-<1	21 (22.11)
1-<3	35 (36.84)
3-<6	22 (23.16)
6-<12	17 (17.89)
Gender	
Female	46 (48.42)
Male	49 (51.58)
Place of Residence	
East Java	89 (93.68)
West Java	1 (1.05)
Kalimantan (Central, West, East)	3 (3.16)
North Sulawesi	1 (1.05)
Papua	1 (1.05)

Table 2. Clinical Symptoms of Congenital Rubella Syndrome.

Clinical Symptoms	Total (%)
Group A	
Congenital Heart Disease	9 (9.47)
Ophtalmology abnormalities	0 (0.00)
Hearing impairment	18 (18.94)
Combination of Congenital Heart Disease and Ophtalmology abnormalities	0 (0.00)
Combination of Congenital Heart Disease and Hearing Impairment	17 (17.89%
Combination of Ophtalmology abnormality and Hearing Impairment	13 (13.68)
Combination of Congenital Heart Disease, Ophtalmology abnormality, and Hearing Impairment	16 (16.84)
Group B	
Microcephaly	9 (9.47)
Developmental Delay	17 (17.90)
24 hours postpartum jaundice	43 (45.26)

Table 3. Classification and Hearing Impairment in Congenital Rubella Syndrome.

Congenital Rubella Syndrom Classification	Total (%)	Hearing Impairment (%) Bilateral	Unilateral	Without Hearing Impairment (%)
Suspect	20 (21.05)	2 (10.00)	1 (5.00)	17 (85.00)
Clinically confirmed	15 (15.79)	6 (40.00)	4 (26.67)	5 (33.33)
Laboratory confirmed	56 (58.95)	40 (71.4)	11 (19.64)	5 (8.93)
Discarded	4 (4.21)	0 (0.00)	0 (0.00)	4 (100.00)

Table 4. Anti-rubella immunoglobulin test results.

Age	Result	Immunoglobulin M (%)	Immunoglobulin G (%)
<6 months	Positive	15 (15.79)	62 (65.27)
	Negative	56 (58.95)	9 (9.47)
6-12 months	Positive	11 (11.58)	17 (17.89)
	Negative	13 (13.68)	7 (7.37)

Discussion

A total of 103,000 babies are born with CRS and 46% are from Southeast Asia including Indonesia.[3–5] Indonesia strategy to prevent rubella infection and CRS is achieved through national routine immunization programs in 2017.[7] The profile of CRS is necessary to know the prevention strategy and handling infants with CRS. A surveillance system involving both private and public hospitals, and other health services needs to be established to find out the CRS profile. The resources that are needed to build a CRS surveillance system are huge that it is only implemented in a few hospitals present.

Most patients were in the age group 1-<3 months (22.11%). The most of the research in Indonesia focused on patients of <6 months of age.[10] Research in Tokyo included patients of <1 month of age (81.3%).[11] The results in this study were different from those of Indonesia and Tokyo: this is due to the large number of patients still receiving treatment in the pediatric department that were only referred for hearing screening at the age above 1 month.

The ratio of male to female patients in this study was 1.06:1. Research in Tokyo found that the ratio of male to female was 1:1.[11] Research in Fiji and Yogyakarta found that the ratio males compared to females were 1.1:1 and 1.16:1.[12,13] The highest number of patients was from East Java (93.68), the province where the study was conducted. The research by the Indonesian Ministry of Health found 30,463 cases of rubella in 2010-2015, Banten and East Java were provinces with a significant increase in rubella cases.[14]

Clinical symptoms of CRS consist of group A and group B (Table 2). Criteria for laboratory confirmed CRS cases are detection of anti-rubella IgM ≥1 IU/mL or the presence of anti-rubella IgG with a level of ≥10 IU/mL in at least two examinations in the 6-12 month age range without rubella vaccine.[3,15] Hearing impairment was the most common clinical symptoms of Group A in 18 patients (18.94%). Research in the United States reported that hearing impairment is the most common clinical symptoms in about 73% of infants with suspect CRS, while reseach in Australia reported this symptom in 38.62% of the patients.[16,17] Different results were obtained in studies in Indonesia, Yogyakarta, Tokyo, and Hanoi, with congenital heart disease as the most common clinical symptoms, which is reported in 56.56%, 90%, 75%, and 63.7% respectively.[10,11,13,18]

Twenty-four hours post partum jaundice was the most clinical symptoms of group B in 43 patients (45.26%). The results were different with research in Indonesia which was found that most clinical symptoms of group B are microcephaly.[10]

Bilateral hearing impairment was the most common type of hearing impairment found in this study, and were obtained the most in the laboratory confirmed CRS classification with 40 patients (71.43%). A London study revealed hearing impairment in infants with CRS were 61% bilaterally.[19] Research in Yogyakarta and Vietnam reported that bilateral hearing impairment was the most common hearing impairment type in laboratory confirmed CRS.[20,21]

Positive anti-rubella IgG test results were the most test results obtained in this study as 79 samples. The IgM result were obtained in 26 samples. Research in Vietnam found positive IgM results of 70%.[22]

Twenty-six patients with positive IgM test results and 30 patients with positive anti-rubella IgG results on two examinations were classified as laboratory confirmed CRS. Research in Vietnam found that 68.9% CRS cases were laboratory confirmed CRS.[18]

The retrospective nature of this study made high levels of missing data, such as pregnancy history and vaccination history, which may have biased the results. Most of the patients comes from East Java, while many data of patient from other province may not recorded due to limitation in referral process.

Conclusions

The study found that most patients were in the age group 1-<3 months old, and ratio of male was higher than that of female. Hearing impairment was the most clinical symptom of Group A and 24 hours postpartum jaundice was the most clinical symptom of Group B. Anti-rubella immunoglobulin test results were obtained positive IgG in most patients. Laboratory confirmed CRS was obtained in 58.95% patients. Bilateral hearing impairment was the most type found in laboratory confirmed CRS.

References

1. McLean H, Fiebelkorn A, Temte J, Wallace G. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013. MMWR 2013;62:1–38.
2. Reef SE, Redd SB, Abernathy E, et al. The epidemiological profile of rubella and congenital rubella syndrome in the United States, 1998-2004: The evidence for absence of endemic transmission. Clin Infec Dis 2006;43:S126-32.
3. World Health Organization. Regional office for South East Asia. Strategic Plan for Measles Elimination and Rubella and Congenital Rubella Syndrome Control in the South-East Asia Region; 2014.
4. The Regional Office for Europe of the World Health Organization. Surveillance guidelines for Measles, Rubella and Congenital Rubella Syndrome in the WHO European Region-updated December 2012. WHO Reg Off Eur. 2009:24-33.
5. Martínez-quintana E, Castillo-solórzano C, Torner N, Rodríguez-González F. Congenital rubella syndrome: a matter of concern. Rev Panam Salud Publica 2015;37:179–86.
6. Kementerian Kesehatan Indonesia. Pengendalian rubela melalui surveilans rubela dilaksanakan secara terintegrasi dengan surveilans campak. 2016:15-16.
7. Kementerian Kesehatan Indonesia. Pedoman Surveilans Congenital Rubella Syndrome 2018. Jakarta: Kementerian Kesehatan Indonesia; 2018. pp.1-13.
8. World Health Organization (WHO). Manual for the Laboratory-based Surveillance of Measles, Rubella, and Congenital Rubella Syndrome. 2019:3-5.
9. Winston-Gerson R, Ditty K. New Born Screening. Chapter 2, EHDI E-b. 2016:1-14. doi:10.1159/000144207
10. Kemenkes sub direktori surveilans. Surveillance Congenital Rubella Syndrome Indonesia 2015-2017. Jakarta: Indonesia Ministry of Health; 2018. pp.3-21.
11. Sugishita Y, Shimatani N, Katow S, et al. Epidemiological characteristics of rubella and congenital rubella syndrome in the 2012–2013 epidemics in Tokyo, Japan. Jpn J Infect Dis. 2015;68:159-165.
12. Singh S, Bingwor F, Tayler-Smith K, et al. Congenital rubella syndrome in Fiji, 1995-2010. J Trop Med 2013;86:1-5.
13. Herini ES, Gunadi, Triono A, et al. Clinical profile of congenital rubella syndrome in Yogyakarta, Indonesia. Pediatr Int. 2018;60:168-172.
14. Pusat Data dan Informasi Kementrian Kesehatan RI. Situasi Campak dan Rubella di Indonesia. 2018:6.
15. WHO. Global Measles & Rubella Strategic Plan. 2012:1-44. http://www.who.int/about/licensing/cop

yright_form/en/index.html.

16. Ugnat AM, Grenier D, Thibodeau ML, Davis MA. The Canadian Paediatric Surveillance Program: Celebrating 15 years of successful paediatric surveillance. Paediatr Child Health (Oxford). 2011;16:203-205.

17. Khandaker G, Zurynski Y, Jones C. Surveillance for congenital rubella in Australia since 1993: Cases reported between 2004 and 2013. VACCINE. 2014;32:6746-6751.

18. Van Bang N, Van Anh NT h., Van VT h. T, et al. Surveillance of congenital rubella syndrome (CRS) in tertiary care hospitals in Hanoi, Vietnam during a rubella epidemic. VACCINE. 2014;32:7065-7069.

19. Wild NJ, Sheppard S, Smithells RW, et al. Onset and severity of hearing loss due to congenital rubella infection. Arch Dis Child. 1989;64(9):1280-1283.

20. Herini ES, Gunadi, Triono A, et al. Hospital-based surveillance of congenital rubella syndrome in Indonesia. Eur J Pediatr. 2017;176(3): 387-393.

21. Toizumi M, Nguyen GTH, Motomura H, et al. Sensory defects and developmental delay among children with congenital rubella syndrome. Sci Rep. 2017;7:1-11.

22. Toda K, Reef S, Tsuruoka M, et al. Congenital rubella syndrome (CRS) in Vietnam 2011-2012-CRS epidemic after rubella epidemic in 2010-2011. VACCINE. 2015;33:3673-3677.