

DOI: <https://doi.org/10.36489/nursing.2021v24i280p6235-6246>

Congenital rubella syndrome: analysis of cases notified in Brazil from 1990 to 2016

ABSTRACT | Objective: to analyze the cases of Congenital Rubella Syndrome notified in Brazil from 1990 to 2016. Method: cross-sectional study conducted in Brazil, whose sample consisted of 122 cases notified with Congenital Rubella Syndrome. Data were made available by the Departamento de Informática do Sistema Único de Saúde. Data collection was conducted during February and March 2021. The data were processed using univariate statistical analysis. Results: prevalence was observed in the state of São Paulo, whose capital city had the highest number of these notifications. The year in which there was prevalence of the diagnosis was 2008, and the month of greatest notification was December. All patients were less than one year old, female, with final confirmation of the disease through laboratory criteria, and progression to cure. Conclusion: Age was significant in this study. Therapy proved to be efficient for a better prognosis of cure, as well as vaccination as a preventive measure.

Keywords: Rubella syndrome, congenital; Rubella; Rubella virus; Disease notification; Health information systems.

RESUMEN | Objetivo: analizar los casos de Síndrome de Rubéola Congénita notificados en Brasil entre 1990 a 2016. Método: estudio transversal realizado en Brasil, cuya muestra fue 122 casos notificados con Síndrome de Rubéola Congénita. Los datos fueron facilitados por el Departamento de Informática del Sistema Único de Salud. La recogida de datos se realizó durante los meses de febrero y marzo de 2021. El tratamiento de los datos se realiza mediante un análisis estadístico univariante. Resultados: se observa una prevalencia en el Estado de São Paulo, cuya capital presenta el mayor número de notificaciones. El año y mes en que se produjo la prevalencia del diagnóstico fue 2008 y diciembre. Todos los pacientes presentaban una edad inferior a un año, sexo femenino, con confirmación final de la enfermedad mediante criterios de laboratorio y evolución para la cura. Conclusión: la edad presentó un significado en el estudio. El tratamiento es eficiente para un mejor pronóstico de curación, así como la vacunación como medida preventiva.

Palabras claves: Síndrome de rubéola congénita; Rubéola (sarampión alemán); Virus de la rubéola; Notificación de enfermedades; Sistemas de información sanitaria.

RESUMO | Objetivo: analisar os casos de Síndrome da Rubéola Congênita notificados no Brasil durante o período de 1990 a 2016. Método: estudo transversal realizado no Brasil, cuja amostra foi de 122 casos notificados com Síndrome da Rubéola Congênita. Os dados foram disponibilizados pelo Departamento de Informática do Sistema Único de Saúde. A coleta de dados foi realizada durante os meses de fevereiro e março de 2021. O tratamento dos dados se deu por análise estatística uni-variada. Resultados: observa-se prevalência no Estado de São Paulo cuja capital apresentou o maior número destas notificações. O ano em que houve prevalência do diagnóstico foi em 2008 e o mês de maior notificação foi dezembro. Todos os pacientes apresentavam idade menor que um ano, sexo feminino, com confirmação final para a doença por meio de critérios laboratoriais, e evolução para a cura. Conclusão: a idade apresentou significância no estudo. A terapêutica mostrou-se eficiente para um melhor prognóstico de cura, bem como a vacinação como medida preventiva.

Palavras-chaves: Síndrome da rubéola congênita; Rubéola (sarampo alemão); Vírus da rubéola; Notificação de doenças; Sistemas de informação em saúde.

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Received on: 06/27/2021

Approved on: 07/05/2021

INTRODUCTION

Rubella is a serious public health problem, which has been subject to compulsory notification since 1996, carried out via the Diseases and Notifications Information System (SINAN), characterized as an infectious contagious viral disease, of high transmissibility and contagiousness, also known as German measles, which can be clini-

cally described by the presence of mild symptoms, the most common being: acute exanthema, febrile, lymphadenopathy and, in some cases, arthropathy. However, approximately 25% to 50% of cases can be asymptomatic. The etiologic agent of the disease is a virus of the Rubivirus genus, of the Togaviridae family.^(1,2)

The factor that generates the greatest epidemiological impact related to this virus is when it affects pregnant women, as there is the possibility of vertical transmission (from the mother to the fetus), especially the earlier the infection in relation to the gestational age (GA), since by crossing the placental barrier, the rubella virus can infect the fetus, causing Congenital Rubella Syndrome (CRS), which may be responsible for congenital defects in the newborn child, such as malformation, otological problems (deafness), eye problems (blindness), heart problems, neurological problems (mental retardation), bone problems during fetal development or even death itself.

⁽¹⁾ The virus only affects humans, being transmitted when healthy individuals come into direct contact with respiratory secretions expelled by talking, coughing, breathing and sneezing, from infected people, however this contagion can be established even in the subclinical stage of the disease.^(1,3)

Thus, the period of transmissibility occurs about five to seven days before and after the onset of the rash, with an index of greater transmissibility two days before and two days after the onset of symptoms. The viral incubation period comprises the range of 14 to 21 days after infection.⁽⁴⁾ In 1997, approximately 30.000 cases of rubella were reported, and from 1999 to 2001 there were outbreaks in several states of the country. In order to eradicate CRS from the country, the MMR vaccine (measles, mumps and rubella) was gradually implemented between 1992 and 2000, and in 2008 there was the Vaccination Campaign against Rubella in which they were vaccinated about 67,9

million men and women, aged between 20 and 39 years, including people from 12 to 19 years old from the states of Rio de Janeiro, Minas Gerais, Rio Grande do Norte, Mato Grosso and Maranhão, representing approximately 96,7% of the target audience for vaccination.⁽⁵⁾

Treatment varies according to the symptoms presented and requires special care for pregnant women, especially in the first trimester. Serological diagnosis is basically performed using the Enzyme-Linked Immunosorbent Assay (ELISA) method, due to its specificity, sensitivity and low cost. (1,6) On April 23rd, 2015, Brazil received from the Strategic Advisory Group of Experts on Immunization (SAGE) the document verifying the eradication of Rubella and CRS. (5) Therefore, it is essential to carry out a bibliographic survey on the aforementioned problem, with the aim of providing current information on epidemiological data and its variant factors in CRS.

The so-called CRS causes numerous complications for the fetus, such as deafness, vision problems and even miscarriage. Rubella and SRC have been officially eliminated in Brazil and other countries in the Americas since 2015.⁽¹⁻⁵⁾ As a result, the year 2015 is justified as the deadline for capturing the data collected with a view to eradicating the disease through the vaccine given from this year on.

Therefore, this study aimed to analyze the cases of Congenital Rubella Syndrome reported in Brazil during the period from 1990 to 2016.

METHODS

This is a descriptive, exploratory, retrospective, cross-sectional study with a quantitative approach, carried out in all states of Brazil, a country located in South America. The sample of this study consisted of 122 cases of patients notified with Congenital Rubella Syndrome, via the Diseases Information System and Notification (SINAN - Sis-

tema de Informação de Agravos e Notificação), in the national territory from January 1990 to December 2016. The epidemiological variables were made available through the Database of the Informatics Department of the Unified Health System (DATASUS), Ministry of Health (MH), Health Surveillance Secretariat (SVS - Secretaria de Vigilância à Saúde). Data collection was carried out in the 1st semester of 2021, during the months of February and March, by the responsible researcher.

Brazil, a vast South American country, stretches from the Amazon Basin in the north to vineyards and the gigantic Iguazu Falls in the south. It is the largest country in South America and in the region of Latin America, being the fifth largest in the world in territorial area (equivalent to 47,3% of the South American territory) and sixth in population. It has 27 states, with the city of Brasília, located in the Federal District (DF), as its national capital. It also has a gross domestic product (GDP) of US\$1,869 trillion and a population of 209,5 million inhabitants in the year 2018.⁽⁷⁾

The following inclusion criteria were adopted for participation in the research: (1) being Brazilian and residing in the country, (2) having the data notified during the stipulated period, (3) having the notification forms duly completed. A structured form prepared in-house was used based on the SINAN notification form as a data collection instrument. The form presented the following independent variables: place of notification (State and municipality); period (year of diagnosis and month of notification); and socioeconomic and clinical profile (age group in years, sex, final classification, confirmation criteria, case evolution).

Data collection was carried out at DATASUS whose most recent data are reported until the year 2015 and after that there is no more information on patients notified with CRS with a view to its eradication in Brazil and in the world.

Furthermore, the data are publicly available, via online, at the following website: <http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sinanet/cnv/srubeolacbr.def>. Data were stored in a statistical program, which is the Statistical Package for Social Sciences (SPSS®), version 15.0, and presented in tables with absolute frequencies and percentages, as well as Central Trend Measures (CTM), which are the weighted arithmetic mean (WAM) and Standard Deviation (SD), prepared using Microsoft Excel®, version 2010. Data treatment was performed using bivariate statistical analysis. This includes all Descriptive Statistics methods that allow the analysis of each variable separately with a 95% confidence interval (CI95, p≤0,05). Epi Info, a publicly accessible statistical program, was applied.

The study followed the ethical precepts established by Resolution No. 466, of December 12th, 2012, of the National Health Council (CNS), which regulates research with human beings. (8) Considering that the study is a research with secondary databases in the public domain, the submission of the research project for consideration and approval by the Research Ethics Committee (CEP - Comitê de Ética em Pesquisa) was not necessary/mandatory.

RESULTS

According to data made available by DATASUS, there is a prevalence of confirmed cases in the State of São Paulo (46,0%), whose capital (São Paulo) had the highest number of these notifications by CRS (32,4%). Still, the Federal District, represented by its capital (Brasília), holds the second position with the highest number of cases (7,5%) (Table 1).

In the period stipulated for the study, from 1990 to 2016, the year in which the highest prevalence of diagnosis for the disease occurred was in 2008 (39,3%), followed by the year 2007 (24,5%). Regarding the month

with the highest notification of rubella cases, there was a higher prevalence in December (9,8%), followed by April

and May, both with the same absolute frequency and percentage (9,0%). It is noteworthy that in 20,4% of the sample

Table 1 – Prevalence by state and municipality of confirmed cases of CRS in Brazil. (n=122)

State/Municipality	n	%	State/Municipality	n	%
São Paulo	56	46,0	Ceará	04	3,4
São Paulo	39	32,4	Fortaleza	04	3,4
Santo André	04	3,2	Maranhão	03	2,4
Campinas	03	2,4	São Luís	02	1,6
Ribeirão Preto	03	2,4	São Raimundo das Mangabeiras	01	0,8
Itapeverica da Serra	02	1,6	Mato Grosso	03	2,4
Araçariquama	01	0,8	Cuiabá	01	0,8
Biritiba Mirim	01	0,8	Luciara	01	0,8
Carapicuíba	01	0,8	Várzea Grande	01	0,8
Mogi das Cruzes	01	0,8	Pará	03	2,4
Sumaré	01	0,8	Belém	01	0,8
Distrito Federal	09	7,5	Santarém	01	0,8
Brasília	09	7,5	Tucuruí	01	0,8
Rio Grande do Sul	08	6,5	Paraíba	03	2,4
Porto Alegre	05	4,1	João Pessoa	01	0,8
Bagé	02	1,6	Mamanguape	01	0,8
Pelotas	01	0,8	Sapé	01	0,8
Minas Gerais	07	5,6	Amapá	02	1,6
Belo Horizonte	04	3,2	Macapá	01	0,8
Alfenas	01	0,8	Santana	01	0,8
Cambuí	01	0,8	Espírito Santo	02	1,6
Caratinga	01	0,8	São Mateus	01	0,8
Goiás	06	5,0	Serra	01	0,8
Goiânia	04	3,4	Alagoas	01	0,8
Itaberai	01	0,8	Maceió	01	0,8
Itumbiara	01	0,8	Paraná	01	0,8
Rio de Janeiro	06	5,0	Pinhão	01	0,8
Rio de Janeiro	04	3,4	Pernambuco	01	0,8
Niterói	01	0,8	Escada	01	0,8
Petrópolis	01	0,8	Rio Grande do Norte	01	0,8
Bahia	04	3,4	Natal	01	0,8
Salvador	02	1,8	Rondônia	01	0,8
Feira de Santana	01	0,8	Porto Velho	01	0,8
Itabuna	01	0,8	Tocantins	01	0,8
			Palmas	01	0,8

Source: Author, 2021.

Table 2 – Prevalence of confirmed cases of CRS in Brazil according to year and month. (n=122)

Variables	n	%	WAM±SD	CI 95%
Year of diagnosis				
1990	01	0,8	10,16±13,673	7,736
1997	01	0,8		
2004	01	0,8		
2007	30	24,5		
2008	48	39,3		
2009	09	8,0		
2010	05	4,0		
2011	05	4,0		
2012	08	6,5		
2013	03	2,4		
2014	03	2,4		
2015	08	6,5		
Notification Month				
January	05	4,0	9,38±4,875	2,650
February	10	8,1		
March	07	5,7		
April	11	9,0		
May	11	9,0		
June	08	6,5		
July	10	8,1		
August	07	5,7		
September	08	6,5		
October	05	4,0		
November	04	3,2		
December	12	9,8		
Ignored/Blank	24	20,4		

Source: Author, 2021. WAM = Weighted arithmetic mean. SD = Standard deviation. CI 95 = 95% Confidence Interval (p<0,05).

Table 3 – Socioeconomic and clinical profile of confirmed CRS cases in Brazil. (n=122)

Variables	n	%	WAM±SD	CI 95%
Faixa etária (anos)				
< 1	122	100,0	122±0	< 0,01
Sex				
Male	56	45,9	40,66±27,535 31,159	
Female	64	52,4		
Ignored/Blank	02	1,7		
Final classification				
Confirmed	78	63,9	61,0±17,0	
Congenital Infection	44	36,1	23,560	

there was no such record. The year of diagnosis and the month of notification were not statistically associated with the disease in the analysis (Table 2).

The socioeconomic and clinical profile of the prevalence of cases in Brazil for CRS reveals that all notified patients were children under one year, with a female prevalence (52,4%), the final diagnostic classification was confirmed (63,9%) through laboratory criteria (77,8%) whose case evolution was cure (58,1%). It should be noted that age group was the only variable that was associated with the disease in the bivariate analysis (p ≤ 0,05) (Table 3).

With the advent of the vaccine against measles, mumps and rubella, the epidemiological findings had a good prognosis regarding the evolution of the disease until its eradication worldwide during the year 2015. After this period, there were no other notifications of this disease, and vaccination was intensified during the routine and in campaigns for children from one year old and young people and adults up to 49 years old.

DISCUSSION

Until the 1980s, Brazil was unaware of the magnitude of CRS cases because it did not have surveillance systems for the disease. It was only in 1996 that CRS was included in the list of compulsory notification diseases along with rubella. However, it was not until 1999, with the integrated surveillance of measles and rubella as a strategy to achieve the measles eradication goal, that the circulation of the rubella virus in Brazil began to be documented in a more evident and representative way and, consequently, of the CRS cases. ⁽⁹⁾

Among the Brazilian states, São Paulo stands out for having the largest population, the highest demographic density, the highest degree of urbanization and one of the best socioeconomic indicators. ^(9,10) In this study, the State of São Paulo, compared to other States,

Confirmation Criteria

Laboratory	95	77,8	40,66±38,681 43,770
Clinical	19	15,5	
Ignored/Blank	08	6,7	

Case Evolution

Cure	71	58,1	30,5±25,144 24,641
Death from the notified offense	11	9,0	
Death for another cause	08	6,5	
Ignored/Blank	32	26,4	

Source: Author, 2021. WAM = Weighted arithmetic mean. SD = Standard deviation. CI 95 = 95% Confidence Interval (p<0,05).

was the one with the highest number of notifications by CRS, therefore, it is clear that CRS was prevalent in municipalities with a higher rate of migration resulting from large works, stores, existence of airports and industries, especially exporters, among others.

The results of the present study converge with the findings of another study carried out in São Paulo where all the participants, being pregnant women, presented positive serological results for IgG/IgM for the rubella virus. Among newborns (NB), 14 were positive for IgG antibodies and 11 samples of newborns were positive for antibodies to IgM. Of the 25 samples analyzed, 24 were reactive to RT-PCR. Ultrasonographic changes were observed in 60% of the 25 fetuses infected with the rubella virus. Occurrence of fetal death and spontaneous abortion were reported in 40% of the analyzed cases. Rubella virus was amplified by PCR in all fetuses that showed changes on ultrasonography, compatible with rubella. ⁽¹¹⁾

In 1999, most outbreaks occurred in states that had not yet implemented rubella vaccination, with the most affected population being those under 15 years of age. In 2000, the outbreaks reached states that were already applying the rubella vaccine. Between 2000 and 2001, there was an increase in the number of CRS cases, as an effect of the outbreak, but also reflecting the structure of CRS surveillance in the country. ^(3,9)

In Brazil, vaccination against ru-



In 1999, most outbreaks occurred in states that had not yet implemented rubella vaccination, with the most affected population being those under 15 years of age.



bella was gradually implemented by the States between 1992 and 2000. Rubella and CRS have been notifiable diseases in Brazil since 1996. The Triple Viral (TV) vaccine consists of fragments of live attenuated virus (measles, mumps and rubella), and was gradually implemented between 1992 and 2000. ^(2,5) In this study, the epidemiology of rubella and CRS is documented, showing a higher prevalence in the months of December (9,8%), May and April (9,0%), both with similar percentage frequencies.

The Epidemiological Surveillance (ES) of rubella and CRS was intensified after the elimination of measles, with a reduction in confirmed cases of 80% between 2003 and 2006. ⁽¹²⁾ Note that in the present study there was an increase in the incidence of cases in 2008 (39,3%). According to the MS, in 2008 vaccination campaigns were carried out to eliminate rubella in both men and women whose age range is between 20 and 39 years old. After 2009, according to MS data, there was greater control of the disease, with no more cases of rubella being verified in Brazil, indicating the interruption of autochthonous transmission of the rubella virus. ^(1,2,5) Thus, ES becomes imperative to know the magnitude of rubella and CRS and to assess the impact of vaccination strategies, as well as the detection, notification and investigation of suspected cases, seeking to provide guidance on appropriate control measures and what refers to the disclosure of information. ⁽¹⁾

In an ecological study, in which surveillance data on rubella cases reported to the Pan American Health Organization (PAHO) and the World Health Organization (WHO) between 2007 and 2018 were evaluated. A prevalence of 139.486 reported rubella cases was observed, of which 11% were vaccine-eligible. The annual incidence ranged from 13,9 cases per million in 2007 to 1,7 cases per million in 2018. It is noto-

rious that there was a significant reduction in this time interval.⁽¹³⁾

In the present study, the prevalence of diagnosis in Brazil was in 2008 (39,3%), in order to present the same evolution as in the previous study, with a decrease in rates over the following years.

In this study, all confirmed CRS cases were younger than one year of age. In newborns, the immune system is under development regarding the production of antibodies, thus being more susceptible to the acquisition of the disease, as well as complications and, consequently, death. Studies prove that rubella vaccination is highly effective and has resulted in the elimination of rubella and CRS from the Western Hemisphere and several European countries. Furthermore, they document the duration of protection over 10-21 years after a dose of the vaccine.^(3,6,9,10,14,15) Still, the female

sex proved to be prevalent in order to go against previously published studies.^(15,16) The performance of early serology for diagnostic confirmation was present in 77,8% of the patients in this study after the onset of symptoms. Through this, the pharmacological treatment was established so that 71% of the sample evolved to a cure. These same diagnostic criteria were established in other studies.⁽¹¹⁻¹³⁾

CONCLUSION

The study design is one of the limitations given the difficulty in investigating conditions of low prevalence. Still, the scientific literature was limited to recent publications considering the eradication of the disease in the country. In this study, female children under one year were more susceptible to the disease. Diagnostic confirmation via laboratory criteria proved to be ef-

fective and efficient, leading to cure with the immediate start of treatment and follow-up.

With the advent of the rubella vaccine, the disease has been eradicated since 2015, with the Rubella Elimination Certification by PAHO/WHO, with no more confirmed and notified cases of the disease in Brazil so far. Thus, in the country, the last epidemic event with the highest prevalence of confirmed cases of rubella was registered in 2007 and 2008, with an imported case of the disease in 2014.

Currently, Brazil is making efforts to maintain the sustainability of the elimination of the circulation of the rubella virus in the country. Age was significant in the study. The therapy proved to be efficient for a better cure prognosis, as well as vaccination as a preventive measure in order to increase survival and quality of life, as well as reduce early mortality from rubella. 🐣

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