The correlation between levels of Immunoglobulin M (IgM) specific rubella with examination result of brainstem evoked response audiometry on congenital rubella syndrome patients.

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Abstract

Background: Congenital Rubella Syndrome is a disease caused by infection with rubella or German measles virus. The clinical symptoms are not typical rubella infection and diagnosis with clinical symptoms is inaccurate. Investigations to determine levels of antibody (IgG and IgM) against rubella play an important role in the diagnosis of rubella. One of the clinical manifestations of CRS is hearing loss. Investigations are good enough to detect hearing loss is Brainstem Auditory Evoked Response (BERA). The aim of this study is analyze the correlation levels of immunoglobulin M (IgM) with threshold hearing on Congenital Rubella Syndrome patients in the Dr. Sardjito Hospital.

Method: Study is a cross sectional study on the correlation of the levels of immunoglobulin M in patients with Congenital Rubella Syndrome BERA examination results in patients with Congenital Rubella Syndrome. Inclusion criteria are children diagnosed with congenital rubella syndrome. Subject is less than 24 month of age. Hearing impairment by BERA analysis. Serology tested for rubella specific immunoglobulin. Exclusion criteria are subjects with incomplete medical records.

Results: The samples were 47 patients with IgM Positive, Imunoglobulin M and BERA were examined and the result of correlation between immunoglobulin M and BERA result with p value 0.001 with correlation coefficient 0.606.

Conclusion: There is a positive correlation between specific rubella immunoglobulin M (IgM) level and BERA test results, the higher the specific rubella immunoglobulin M (IgM) level, the greater the hearing loss.

Keywords: Congenital rubella syndrome, Immunoglobulin M, Brainstem evoked response auditory, BERA.

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Background

Congenital Rubella Syndrome is a disease caused by a rubella virus infection or German measles. In children, the infection usually causes little or no symptoms. If rubella virus infection occurs in pregnancy, especially the first trimester often causes Congenital Rubella Syndrome (CRS). CRS results in abortion, stillborn, premature and disabling infants when the baby is alive. Between 1962 and 1965 rubella became an endemic disease and an estimated 12.5 million cases of rubella occurred in the United States area with the results of 2000 cases of encephalitis, 11,250 abortus, 2,100 cases of neonatal death and 20,000 cases of infant birth with CRS. The administration of rubella vaccine started in 1969 and gave a very significant effect [1,2].

Rubella infection during first trimester of pregnancy will cause congenital rubella syndrome. Clinical manifestations of CRS include blindness, hearing loss, congenital heart disease, and mental retardation. Infection that occurs in the first 12 weeks of pregnancy will cause a congenital rubella infection of 90% with a risk of congenital defects of almost 100%. Infection at 13 to 17 weeks has an infection risk of about 60% and the risk of defects is about 50%. Infection at the 18^{th} to 24^{th} week is at risk of infection of about 25% and almost no risk of congenital defects [3].

Fetal organ damage is caused by various factors, for example by cell damage due to cell division of the rubella virus which causes focally dispersed necrosis regions in the villi korealis epithelium and capillary endothelial cells. Cells infected with the rubella virus have a short lifespan, the infected fetus's organs have lower cell numbers than healthy fetuses. This is because during a young pregnancy the fetal defense mechanism is immature [4,5].

Congenital Rubella Syndrome has one of the major defects of neurosensory hearing loss, caused by histopathologic hearing loss in maternal rubella infections in the fetus, indicating that temporal bone changes in the cochleosaccular whereas utricles, semicircular canals, and ganglion are usually unaffected. The tektoria membrane was found rolled up and floated inside the sulcus [4,5].

Clinical symptoms of rubella infection are not typical and the diagnosis with clinical symptoms is not accurate. Investigations to determine the levels of antibodies (IgG and IgM) to rubella play an important role in the diagnosis of rubella. Laboratory inspection materials for IgG and IgM antibody levels can be either oral fluid (OF) or with dried blood spot (DBS) with sensitivity and specificity of 96% to 100%. If antibody screening is performed before the patient's age of 3 months and

positive IgG and IgM levels are obtained then the CRS diagnosis can be confirmed as a confirmed CRS [3].

Investigations are suspected of hearing loss, there are several tests that can be done and the results of the examination is good enough and widely used is Auditory Brainstem Response Testing/Brainstem Evoked Response Auditory (ABR/BERA), Auditory Steady-State Response (ASSR), Otoacoustic Emission Testing (OAE). The main purpose of an autotoustic emission check is to assess the state of the cochlea, in particular the function of hair cells. The results of the examination can be useful for: a) Hearing screening (especially in neonates, infant or individuals with developmental disorders), b) Estimating sensitivity of hearing within a certain range, c) Distinguishing sensory and neural disturbances in sensorineural hearing loss, d) Examination of functional hearing loss (pretend). BERA is an important electrophysiological procedure for hearing evaluation. The development of BERA has clinical significance in two main areas: a) Evaluation and diagnosis of peripheral auditory systems and associated abnormalities. b) Assess the integrity of the acoustic nerve and the acoustic nerve pathway at the caudal level of the brainstem [6-8].

Objectives

Knowing whether there is a correlation of specific rubella-specific IgM Immunoglobulin (IgM) levels with hearing threshold values in patients with Congenital Rubella Syndrome at Dr. Sardjito Hospital Yogyakarta.

Methods

This observational analytical study determines the correlation between the levels of specific rubella-specific IgM with the results of the BERA examination. The research design is cross sectional. The subjects of the study were all pediatric patients with a diagnosis of Surveillance Congenital Rubella Syndrome (P.35.0) of Dr. Sardjito Hospital Yogyakarta, from 2011 to December 2016 meeting the inclusion and exclusion criteria. The study was conducted in April 2017. Pediatric patients with diagnosed Congenital Rubella Syndrome must have done IgM and BERA examination. Research variable is the content of rubella specific IgM and BERA examination results then tested the data normality with Kolmogorov-Smirnov with the results of abnormal data distribution, and tested the correlation with spearman correlation test and the result is plotted pair of data on cartesian diagram called scatterplot or scatter diagrams.

Results and Discussion

The subjects of this study were 47 patients of Congenital Rubella Syndrome who have been examined levels of specific rubella IgM and examination of BERA.

Table 1: Subjects Characteristics.

Characteristics		n	%
Age of diagnosis (month)	Mean (min-max)	7.02	0-23
Sex	Male	27	57.40
	Female	20	42.60
CHD	Yes	38	80.90
	No	9	19.10
Cataract	Yes	30	63.80
	No	17	36.20
Deafness	Yes	45	95.70
	No	2	4.30
BERA	Normal	2	4.30
	Mild	3	6.40
	Moderate	1	2.10
	Severe	9	19.10
	Profound	32	68.10
IgM	Positive	46	89.70
	Negative	1	10.30

In this study the age of the sample when diagnosed with Congenital Rubella Syndrome was the youngest of 0 months and the oldest was 23 months, the mean age of the sample was 7.02 months at the time of diagnosis of Congenital Rubella Syndrome. In contrast to research conducted by Herini et al. at Dr. Sardjito Hospital Yogyakarta is between 0-11 months.

Sexes of the sample in this study were 27 patients (57.4%) and female were 20 patients (42.6%). The sample of male sex is more than the sample of female sex. This is in accordance with the research of Council et al. which mentions no difference in the incidence of Congenital Rubella Syndrome must be based on sex.

The condition of hearing loss in this study sample was found as many as 45 patients (95.7%) while there was no hearing loss as much as 2 patients (4.3%). Hearing loss in research conducted by Board et al. as much 48.5% of all samples were positive for serum-specific serologic examinations. In contrast to Herini et al. research suggests that there is a 100% hearing loss in CRS patients who have a specific serologic examination. Clinical symptoms of congenital heart disease found in this study sample of 38 patients (80.9%) and who did not suffer from congenital heart disease as much as 9 patients (19.1%), Research conducted by Board et al. get 46% of cases with congenital heart defects examined with a specific serologic examination were found to be positive. The results of Herini et al. found the same that congenital heart abnormalities were 5 (45.5%) of CRS patients confirmed with a specific serology of rubella. Congenital cataracts were found in this study sample of 30 patients (63.8%) while samples that did not have congenital clinical symptom of 17 patients (36.2%), Council study of prevalence of congenital cataract incidence in patients with Congenital syndrome is 10-15% of the population suffering from congenital rubella syndrome. In the Herini et al. study, the congenital census was ranked second after hearing loss of 72.7% of all CRS patients who had serologic-specific serologic examinations[9].

Results of BERA with results <25 db were found in 2 patients (4.3%), 26-40 db in 3 patients (6.4%), 41-60 db in 1 patient (2.1%), 61-80 db was found in 9 patients (19.1%) and >81 db in 32 patients (68.1%), Board et al. conducted a study of 140 infants tested BERA, 70 normal babies, and 70 infants with various risk factors including congenital rubella syndrome, obtained 44 infants (31.3%) with various risk factors showed abnormal BERA results. In the study of Herini et al. of all samples of the study of 47 patients obtained all samples 100% there is abnormal BERA results. Herini et al. study assessed the BERA results in both patients' ears, but only 1 sample ear looked normal [10].

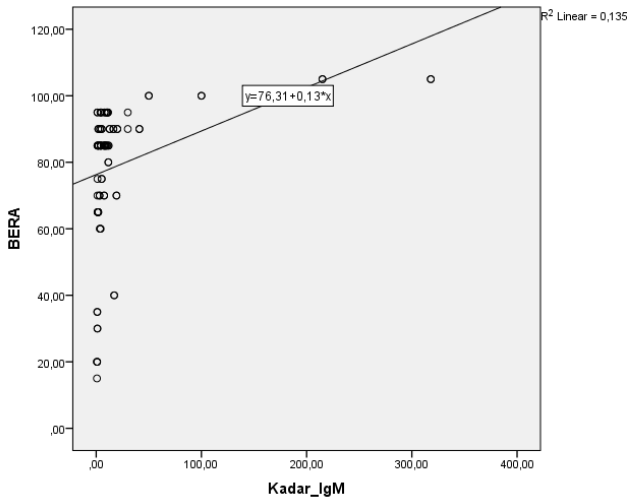

Figure 1: Scatterplot Correlation Between Levels of Immunoglobulin M (IgM) Specific Rubella with BERA.

Linearity test is also done in this research; it is intended to know the relationship between the two research variables in this case IgM levels and BERA examination results. The correlation coefficient value of 0.606 is a strong correlation strength category and has a higher mean IgM-based rubella, the greater the occurrence of deafness seen from the result of BERA in the form of profound.

Table 2: Correlation test between IgM and BERA.

IgM level	BERA
correlation coefficient	0.606*
p value	<0.001

*Spearman correlation test, p<0.05

Correlation test results, according to Dahlan can be seen significance level, meaning if p <0.05 or not significant if p>0.05, correlation strength (very weak: 0.000-0.199, weak: 0.200-0.399, medium: 0.400-0.599, strong: 0.600-0.799 and very strong: 0.800-1.00), as well as direction of relationship between two variables tested (positive direction or negative direction). Positive direction can be interpreted that the greater the value/score of immunoglobulin M variable, followed by the greater the value/score of the BERA variable [11].

Conclusion

There was a positive correlation between the specific immunoglobulin M (IgM) content of the rubella with wave V (five) on the examination of BERA, it can be concluded that the higher the specific IgM level of rubella, the higher the hearing loss.

Declaration

Ethics approval and consent to participate

Ethics Committee Approval

Medical and Health Research Ethics Committee (MHREC) Faculty of Medicine Gadjah Mada University-Dr. Sardjito Hospital

Ref: KE/FK/0453/EC/2017

The Medical and Health Research Ethics Committe (MHREC) states that the protocol meets the ethical principle outlined in

the Declaration of Helsinki 2008 and therefore can be carried out.

Competing Interest

The authors declare that they have no competing interests.

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