

# Profiling of audiological characteristics in infants with congenital rubella syndrome

## Abstract

Rubella (German measles) is a contagious viral infection caused by Rubella virus (RuV) and most frequently it occurs in the fetus during pregnancy. Congenital rubella infection is one of the most common causes of hearing loss in newborns. The aim of the present study is to evaluate the audiological profile in two infants with Congenital Rubella Syndrome. The infants underwent detailed audiological evaluation including otoscopic examination, behaviour observation audiometry, immittance audiometry, otoacoustic emission and auditory brainstem response test. Based on the audiological evaluation the infants were diagnosed as having bilateral symmetrical sensorineural hearing loss. However, the degree of hearing loss varied among the infants as one exhibited mild and the other exhibited severe to profound hearing loss. To conclude, it is crucial to evaluate the hearing mechanism in infants with rubella syndrome as most often they exhibit sensorineural hearing loss. Early intervention can diminish the consequences of hearing loss on child development.

**Keywords:** rubella, viral infection, rubella virus, congenital rubella syndrome, hearing loss

Volume 7 Issue 6 - 2017

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**Received:** May 29, 2017 | **Published:** June 23, 2017

**Abbreviations:** RuV, rubella virus; CRS, congenital rubella syndrome; BOA, behaviour observation audiometry; DPOAE, distortion product otoacoustic emission; OHC, outer hair cell

## Introduction

Congenital hearing loss is a sensory impairment affecting the speech and language development of a child. There are various causes leading to the congenital loss of hearing. One of the most common causes is the infection due to Rubella virus.<sup>1</sup> Rubella (German measles) is contagious viral infection caused by Rubella virus (RuV) to the fetus during pregnancy<sup>2</sup> WHO (World health organisation) estimate that worldwide more than 100,000 children are born with CRS.<sup>1</sup> It is Togaviridae family of the genus Rubivirus which affects multiple organs.<sup>2</sup>

Rubella infection in pregnant women may cause fetal death or congenital defects known as congenital rubella syndrome (CRS) in newborns.<sup>2</sup> The effect of rubella infection varies depending on time of gestational rubella infection. Cooper,<sup>3</sup> Miller et al.,<sup>4</sup> reported that the frequency of occurrence of congenital infection is greatest (80%) during first trimester & progressive smaller risk at the end of the second trimester.

Congenital rubella infection lead to varies congenital abnormalities with wide spectrum of clinical manifestation in fetus i.e. auditory deficits, vestibular deficits, cataracts, cardiac defects, nerve deafness and cerebral lesion with late onset complications including thyroid disease, diabetes, growth hormone deficiency and panencephalitis in newborns.<sup>2,5</sup> Studies reported that hearing loss results in delayed development of speech & language milestone.<sup>6</sup> Mental retardation and cerebral palsy are the consequences of the cerebral damage due to CRS.<sup>7</sup> It was also reported that sensorineural hearing loss is second most commonly noted among wide variety of congenital abnormalities in CRS.<sup>5,8</sup>

Histopathological studies reported that inner ear is most susceptible to damage during sixth to twelve weeks of pregnancy.<sup>8</sup> Thus sensorineural hearing loss in newborns with CRS is attributed to hemorrhagic damage of sensory end organ of hearing i.e. organ

of corti.<sup>9,10</sup> In addition to these, CRS can also lead to interruption in further development of different parts of inner ear and auditory nerve.<sup>10</sup> Previous studies done by Wild et al.,<sup>11</sup> in children with CRS for identifying late onset hearing loss. It was reported that profound hearing loss was more evident than mild to moderate hearing loss. Most of the studies reviewed were carried out only in children with CRS but not in infant and studies focusing on profiling audiological characteristics during early infancy (before 6months of age) with CRS were sparse. Thus, the current study aimed at profiling the audiological characteristics of infants with CRS. The evaluation is performed by using state of art technological instruments for a comprehensive view of hearing mechanism, which aids in channelizing to accurate diagnosis and to plan the early intervention.

## Case report

The present study evaluated two infants who were first child to the parents (Participant A: 2months old male and participant B: 6-month-old male). Both the infants were admitted to the hospital due to congenital eye abnormalities & heart disease. As a part of detail health check up, infants underwent various routine medical investigations including, ophthalmological, cardiac examination, laboratory tests, audiological and speech & language evaluation. The reports of ophthalmological evaluation revealed cataract in both eyes. Cardiac examination indicated congenital heart deficits. A laboratory test for Complete TORCH evaluation (by ELISA) revealed high IgM and IgG antibody for only rubella infection. This is an indication of gestational rubella infection transmitted from pregnant women to fetus. Speech and language evaluation indicated significant delay in the development of speech and language abilities. Evaluation by the physiotherapist reported delayed motor milestone development for both the infants. Followed by the evaluations both infants were diagnosed as CRS. Prenatal history of both participants showed positive history of rubella infection to mothers and had no history of elderly pregnancy, ototoxicity, smoking, alcoholic mother. Natal & postnatal history revealed positive history of premature delivery and fetal distress only in participant and APGAR score was lower in both participants.

## Method and materials

A structured detailed history was taken for both the participants A and B. Prior to the evaluation of hearing mechanism, visual inspection of the ear was performed by otolaryngologist using otoscope. Followed by otoscopic examination, a detail audiological evaluation including behaviour observation audiometry (BOA) using Paediatric audiometer (PA-5), immittance evaluation using MAICO Easy Tymp, Otoacoustic emissions (Mimosa diagnostic OAE) and Auditory brainstem response (Biologic Natus Pro (ver 7.2.1) were performed.

## Procedure

### Otoscopic examination

Otoscopic examination was performed using otoscope (Mini 3000 HEINE). To examine, the pinna of the child's ear is grasped and pulled backwards to straighten the ear canal. On visual examination, the structure of the ear canal, presence of wax, foreign tissues or discharge, colour and structure of the tympanic membrane were evaluated.

### Behaviour observation audiometry (BOA)

A free field handheld paediatric audiometer (PA-5) was used for BOA testing. In this test, pure tone of 75 to 90dBHL was presented for a brief period (2-3seconds) at 500Hz & 4000Hz parallel to the ear canal at a distance of 50cm from the ear. The behavioural responses of the child such as start crying or stop crying, eye blinking, eye widening, gaze shifting, body movement, limb movement, startle response, arousal from sleep were observed for 10-15sec and documented.

### Immittance evaluation

Calibrated Maico Easytymp was used for Immittance Evaluation. Immittance evaluation includes tympanometry and reflexometry. Tympanometry was performed bilaterally using 1000Hz probe tone to evaluate the status of middle ear. Reflexometry was performed to estimate acoustic reflex thresholds at octave frequencies from 500, 1000, 2000 and 4000Hz in both ipsilateral and contralateral conditions for both ears. The immittance measures were repeated once again immediately to cross check the reliability of the measures.

### Otoacoustic emission

Distortion product otoacoustic emission (DPOAE) was performed in both ears to evaluate the function of outer hair cells. DPOAE testing was performed by setting the frequency band from 1000Hz to 6000Hz at stimulus intensity  $L1=65\text{dB SPL}$  &  $L2=55\text{dB SPL}$ , frequency ratio  $F2: F1=1.2:1$  and signal to noise ratio of at least 6dB with a reproducibility score of at least 70%.

### Auditory brainstem response

Biologic Natus Pro (ver 7.2.1) instrument was used. Click-evoked ABR was performed in both ears monaurally. The testing was performed after sedation in sleeping status of patient. Single channel recording was used in which non-inverting electrode was placed on upper forehead (Fz); the inverting electrode was placed on mastoid of test ear and ground electrode was placed on mastoid of non-test ear. Electrode impedances were less than  $5\text{k}\Omega$ , and inter-electrode impedances were less than  $2\text{k}\Omega$ . Eartone-3A insert earphone was used to present the stimuli. The click stimuli of 2000 sweeps in rarefaction polarity were presented at 11.1 click/sec repetition rate. Potentials were recorded in band-pass filter setting 30Hz-3000Hz with an amplification factor of 1, 00,000. Recordings were started from

90dBnHL and lowered by 10dB steps until the threshold is reached<sup>12</sup> i.e., the minimum intensity at which the Vth peak is present. The replicability of the waveform at each intensity is verified by providing the click stimuli again and by overlapping the obtained waveform with the earlier response for at the same intensity. ABR waveforms were analysed at 20msec time window setting. All the testing was performed in a sound-treated room in which ambient noise levels were well within the permissible limits as per ANSI S3.1, 1991 standards.

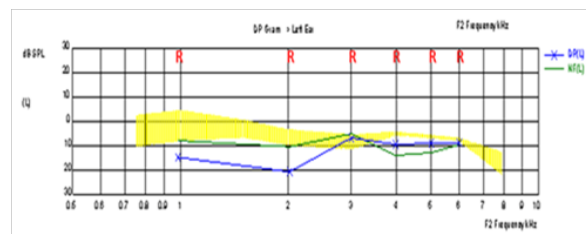


Figure 1 DPOAE test result for left ear (L) in participant A.

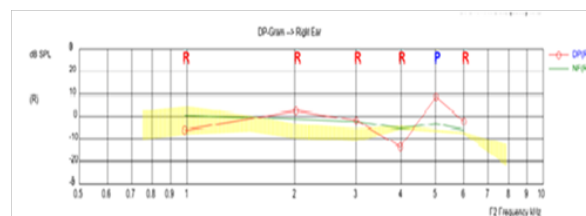


Figure 2 DPOAE test result for right ear (R) in participant A.

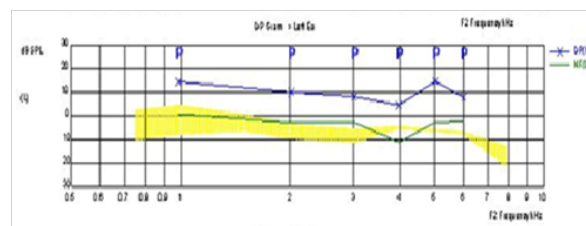


Figure 3 DPOAE test result for right ear (R) in participant A.

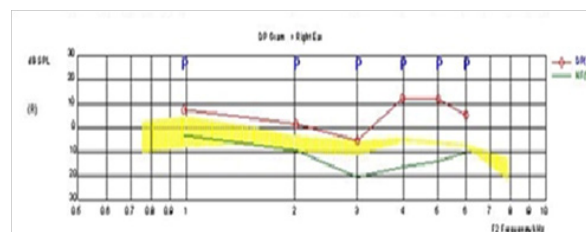


Figure 4 DPOAE test result for right ear (R) in participant A.

## Results

### Otoscopic examination

Otoscopic examination of the both ears of the participants indicated that there are no structural abnormalities of ear canal or tympanic membrane and also the ear can be clean without any presence of foreign bodies and occluded wax.

### Behaviour observation audiometry

There were no responses for both the participants at lower levels of the paediatric free field audiometer. Participant A did not respond even at higher levels, whereas participant B had occasional responses at higher level i.e., 70dBHL in free field BOA testing of infants.

## Immittance audiometry

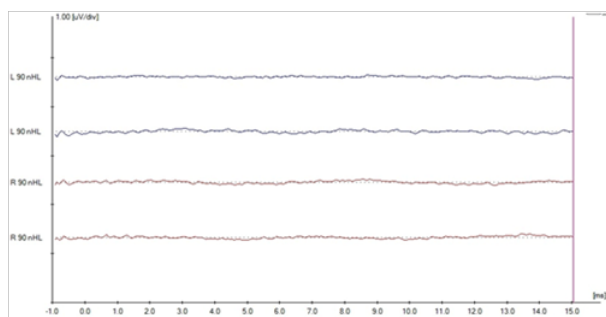
In both infants, Immittance findings revealed bilateral “A” type tympanogram with absent ipsilateral & contralateral reflex in both ears. The findings are suggestive of bilateral indication of no middle ear pathology.

## Distortion product otoacoustic emission

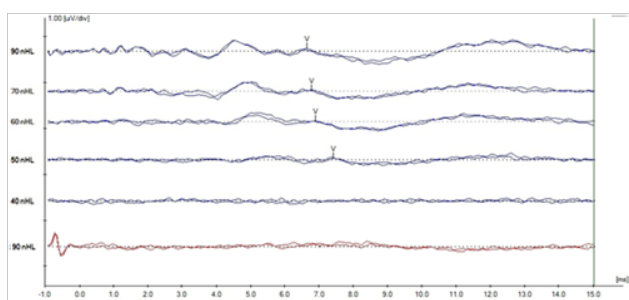
DPOAE results of participants were measured at distortion product frequency from 1 KHz to 6KHz. Across all the frequencies the DPOAE’s were absent for participant A in both the ears except at 3328 Hz in right ear. The Figure 1 & 2 indicates the results of DPOAE for left ear and right ear with a letter “R” across the frequencies. “R” indicates “refer” i.e. there is no response from the outer hair cells in both the ears. The Figure 3 & 4 depicts participant B’s DPOAE response from the outer hair cells, indicating pass with the letter “P” across frequencies.

## Brainstem evoked response audiometry

The results of ABR in participant A indicated no Vth peak even repeated trail at 90 dBnHL in both ears suggestive of bilateral severe to profound hearing loss as depicted in Figure 5. Whereas, the ABR results in participant B indicated a clear Vth peak at 70dBnHL & 60dBnHL but not at 50dBnHL in both ears. This finding is suggestive of bilateral mild hearing loss as shown in Figure 6.



**Figure 5** ABR finding of participant A for left ear (blue color) and right ear (red color).



**Figure 6** ABR finding of participant B for left ear (blue color) and right ear (red color).

## Discussion

The present study outlines audiological outcomes in infants with congenital rubella syndrome. The results of the visual examination through otoscope indicated no structural abnormalities of ear canal and tympanic membrane in both infants with CRS. Followed by otoscopic examination the patient was subjected to BOA to evaluate the behavior responses of presented sound.<sup>13</sup>

In the present study, eye shifting, arousal from sleep, eye blinking behaviour was not observed in participant A and occasional eye shifting was observed in participant B at the higher levels of paediatric free field audiometer i.e., 70dBHL. However, studies reported that BOA has poor sensitivity (66.7% ) and specificity (86.9%) and this behavioural technique is unreliable for unilateral hearing loss, delayed cognitive, speech & language development motor development infants.<sup>14</sup> and immature neurodevelopment process in high-risk newborns.<sup>15</sup> To overcome the limitations of the evaluations based on BOA responses, objective assessment of hearing procedures were adapted.<sup>12</sup> In current study, immittance audiometry, otoacoustic emission, and auditory brainstem response were used to evaluate the hearing based on objective measures.

Immittance Audiometry was used to detect the admittance of ear. Immittance evaluation includes tympanometry and Reflexometry.<sup>16</sup> Tympanometry used to detect movement of tympanic membrane and middle ear functioning and reflexometry measures the contraction of stapedius muscle at higher intensity level.<sup>16</sup> The results indicated compliance and ear canal volume were within normal range for both ears reflecting the adequate mobility of tympanic membrane and no perforation of tympanic membrane or presence of impacted wax. Thus, the overall findings suggestive of no bilateral abnormalities in the middle ear in both participant A & B. Reflexometry test result indicated absent of ipsilateral and contralateral acoustic reflexes at all frequencies in both ears. This finding suggestive of both participant A & B may have bilateral sensorineural hearing loss. In support of this finding, Gelfand<sup>17</sup> reported that acoustic reflex threshold may be absent sensorineural hearing loss.

DPOAE test was administered to detect outer hair cell (OHC) function as emission generated from cochlea.<sup>18</sup> In the current study; for participant “A” had absent DPOAE’s in both ears indicative of abnormal OHC functioning. This implies cochlear pathology in both ears. In Participant B, DPOAE’s were present in both ears indicative of normal OHC functioning. In the previous study, it was found that DPOAE was absent in 41% children who have positive history of gestational rubella infection and degree of hearing loss confirmed by ABR.<sup>19</sup> The sensorineural hearing loss in CRS due to histopathological changes in inner ear which interrupt developmental process of embryonic cochlea.<sup>9</sup> Thus, this affects the effectiveness of cochlear electromechanical transduction functioning.

ABR testing was performed for threshold estimation.<sup>20</sup> It is also used to check the reliability of hearing thresholds by comparing with pure tone behaviour threshold.<sup>18</sup> In participant A, no Vth peak was found even repeated trail at 90dBnHL in both ears (Figure 5). This finding is suggestive of client having bilateral severe to profound hearing loss. In Participant B, clear Vth peak with replicable waveform was found even repeated trail at 70dBnHL & 60dBnHL but not at 50dBnHL in both ears (Figure 6). This finding is suggestive of client having mild sensorineural hearing loss. In the previous study, it was found that abnormal ABR obtained in children with the previous history of gestational rubella infection in which profound hearing loss are more evident than lesser degree of hearing loss.<sup>17,19</sup> Thus, in the current study, participant “A” had bilateral severe to profound sensorineural hearing loss & participant “B” had mild sensorineural hearing loss.<sup>21,22</sup>

## Conclusion

The present study focused on profiling the audiological outcome in infants with CRS as hearing loss is often not noticed by the health

care professionals as hearing loss is invisible. This study included two participants who exhibited symmetrical sensorineural hearing loss even though there were differences in the degree of loss. No drug therapy exists for sensorineural hearing loss but early identification and intervention can facilitate development of communication. Finally, it is important to get sensitized to the effect of congenital rubella infection on hearing system and refer every newborn with congenital rubella syndrome for detail audiological evaluation.

## Acknowledgments

We would like to thank the coordinator of BASLP course, HOD of ENT and Pediatric Department, Netaji Subhash Chandrabose Medical College cum Hospital for allowing us to carry out the research study. Our sincere thanks to the participants included in the study.

## Funding

No financial support from any organization/ Institute was used for the current study.

## Disclosure of potential conflicts of interest

No potential conflict of interest was reported by the authors.

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