

## The effect of very low birth weight on otoacoustic emissions

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**Key-words.** Very low birth weight; universal newborn hearing screening; screening; hearing; otoacoustic emissions; neonatal intensive care unit

**Abstract.** *The effect of very low birth weight on otoacoustic emissions. Objectives:* The aim of this study was to examine the effect of very low birth weight (VLBW) on the measurement of transiently evoked otoacoustic emissions (TEOAEs) in newborns.

*Methods:* TEOAEs were recorded in all VLBW newborns (birth weight <1500 g) who were admitted in the Neonatal Intensive Care Unit of the Iaso Maternity Hospital, during a period of 1 year. Twenty-four VLBW newborns were included in the study. Their mean birth weight was 1283 g and they had mean gestational age 31.3 weeks. Forty full-term newborns with absence of any risk factor for hearing impairment were used as controls.

*Results:* TEOAEs were present in 97.5% of controls, but only in 79.2% of the VLBW group. Statistically significant differences were found between VLBW newborns and controls in most TEOAE measures.

*Conclusions:* Increased rate of initial 'fail' in hearing screening, in conjunction with statistically confirmed lower TEOAE measures in VLBW newborns, justifies special care and long term follow-up for this group of newborns.

### Introduction

Early identification of congenital hearing loss is an important issue in clinical audiology, because late remediation has a negative impact on hearing, cognitive, emotional and social development.<sup>1,2</sup> The incidence of moderate to profound congenital hearing loss is estimated to range from 1 to 4 per 1000 live births,<sup>3</sup> but is much higher for babies from neonatal intensive care units (NICU): 1 to 5 per 100 births.<sup>4</sup>

The development and application in clinical practice of otoacoustic emissions, marked the beginning of a new era in the field of screening for congenital hearing loss.<sup>5</sup> Measuring otoacoustic emissions yields an objective evaluation of cochlear function and is possible as soon as the babies are born. In particular, transiently evoked otoacoustic

emissions (TEOAEs) have been widely adopted by many universal hearing screening (UNHS) programs, because they are simple, easy to perform, relatively cheap and fast.<sup>6,7</sup> An alternative technique for newborn hearing testing uses auditory brainstem responses, and is used by many UNHS programs as well.<sup>8</sup>

In contrast to the 1994-recommendations of the Joint Committee on Infant Hearing, however, neonatal hearing screening is not available to all neonates.<sup>9</sup> A compromise between no screening and universal screening has been the implementation of screening in NICU newborns with risk factors for hearing loss, such as prematurity, low Apgar score, etc.<sup>10</sup>

Very low birth weight (VLBW) has been identified as one of the major risk factors for hearing loss since 1973 in the United States.<sup>11</sup>

In 1982 the Joint Committee on Infant Hearing<sup>12</sup> formally established a high-risk registry, which listed seven risk factors for hearing loss in newborns, including a birth weight less than 1500 g. In 1994 the high-risk criteria were extended to ten indicators,<sup>9</sup> again including VLBW. It has been reported that in newborns with VLBW, the prevalence of bilateral moderate to severe hearing loss is approximately 2-4 per cent. The overall prevalence of unilateral and bilateral mild to severe hearing impairment in this high risk infant population is 10-100 times higher than in newborns without risk factors.<sup>13</sup>

Universal hearing screening in both well-baby and NICU newborns, yields a large amount of data on the presence and features of otoacoustic emissions measured in these groups. The aim of the present study was to evaluate

the effect of VLBW on otoacoustic emissions.

## Methods

The study was performed as part of the newborn hearing screening program with TEOAEs in the "Iaso" maternity hospital. Our study group included all VLBW newborns (birth weight <1500 g) who were admitted in the NICU of the hospital, during a period of 1 year.

Twenty-four newborns were included in this study. Their mean birth weight was 1284 g (range 930-1500) and their mean gestational age was 31.3 weeks (range 26.3-36.6). Their mean post-conceptual age on the day of hearing screening was 38.2 weeks (range 35-42) weeks and the mean *post partum* age was 6.9 weeks (range 0-12.5 weeks). A control group of 40 full-term newborns without any risk factor was randomly recruited from a pool of neonates born and screened at Iaso maternity hospital.<sup>14</sup> These neonates were tested in exactly the same way as the NICU-babies. Their birth weights were between 2010 and 5300 g (mean 3230 g) and the mean gestational age of the newborns varied between 36.0 and 43.2 weeks (mean 39.1 weeks). All the newborns of the control group were examined during the third or fourth day after birth.

Hearing screening was performed just before hospital discharge, by an otolaryngologist experienced in neonatal screening. The equipment used for TEOAE measuring and analysis was an ILO-88 Otodynamics analyzer (Otodynamics, London, software version 3.94 H) connected to a portable personal computer. The

Quickscreen program was used for all testing. The exact parameters used for screening and details of the screening procedure are described elsewhere.<sup>15,16</sup> Newborns were tested in their cribs and the right ear was screened first. In case of doubtful results or failures, immediate retesting with TEOAEs was performed in order to reduce false positive results. When otoacoustic emissions could be measured during the second trial, only these data were used for further analysis and the data from the first trial were discarded. In case of a new failure, the newborns were scheduled for rescreening after 1 month, according to our protocol.<sup>16</sup>

For each test, different metrics were extracted from the recorded signal: (1) overall response level (dB SPL); (2) signal to noise ratios (SNR) at the frequency zones centered at 1.0 (SNR1), 1.5 (SNR1.5), 2.0 (SNR2), 3.0 (SNR3) and 4.0 kHz (SNR4); (3) overall reproducibility (%); (4) reproducibility scores of the signal within frequency bands centered at 1.0, 1.5, 2.0, 3.0 and 4.0 kHz; (5) noise rejection level; (6) intensity and stability of the stimulus. The "pass-fail" criteria were a SNR  $\geq 6$  dB SPL, in four out of five  $\frac{1}{2}$  octave frequency bands centered at 1.0, 1.5, 2.0, 3.0 and 4.0 kHz.

The noise rejection level was initially set at 46 dB SPL. When the noise level was so high that hardly any data could be collected, the noise rejection level was increased, up to the maximum of 52 dB SPL. If the noise level was very low and hardly any data were being rejected then the noise rejection level was decreased, down to a minimum of 40 dB SPL.

**Statistical methods:** Data were imported in a statistical computer program (SPSS 12.0) for further evaluation and analysis. The Kolmogorov-Smirnov and the Shapiro-Wilk tests of normality were used to test data for normal distribution. When normal distribution was found, a two-tailed *t*-test for independent groups was used to compare mean otoacoustic emission measures in the two groups. The Mann-Whitney U-test was used for data that did not show a normal distribution. An analysis of covariance was used to test the difference between the mean otoacoustic measures of the two groups, while controlling for gestational age. The Fisher's exact test was employed for comparison of categorical data. The adopted level of statistical significance was 0.05.

## Results

In 19 VLBW newborns TEOAEs were present in both ears, in 4 of them TEOAEs were absent, and in 1 newborn TEOAEs were present in only 1 ear (Table 1). From the 4 newborns with bilateral involvement, 3 were lost for follow-up and the remaining newborn was normal on re-examination one month later. The newborn with unilateral involvement was also found normal on re-examination. In the control group, only 1 newborn had no TEOAEs, but at follow-up retesting, normal otoacoustic emissions were found as well. The "pass-fail" rate of these two study groups differed at a statistically significant level (Fisher's exact test).

The stimulus level measured in the ear canal of the VLBW newborns ranged from 75 to 88 dB SPL, with a mean of 82.1 dB SPL.

Table 1  
'Pass-fail' of VLBW newborns and controls

|      | VLBW newborns                                   | Controls                  |
|------|---|---------------------------|
| Pass | 19 (79.2%)                                      | 39 (97.5%)                |
| Fail | 5 (20.8%)<br>(4 bilaterally and 1 unilaterally) | 1 (2.5%)<br>(bilaterally) |

Fisher's exact test:  $p < 0.001$ .

Table 2

Means (M) of response levels and reproducibility, standard deviations (SD) and range (R) comparing the ears with present TEOAEs of the group of VLBW newborns (N = 39) and controls (N = 78)

| Response (dB SPL)              |    | SNR1  | SNR1.5  | SNR2  | SNR3  | SNR4  | Overall   |
|--------------------------------|----|-------|---------|-------|-------|-------|-----------|
| Very low birth weight newborns | M  | 0.9   | 3.2     | 11.2  | 13.9  | 14.1  | 20.3      |
|                                | SD | 2.2   | 3.0     | 4.9   | 4.5   | 5.7   | 4.1       |
|                                | R  | 0-8   | 0-9     | 0-21  | 0-24  | 0-29  | 11.6-30.4 |
| Controls                       | M  | 4.9   | 15.3    | 20.6  | 23.0  | 22.3  | 20.6      |
|                                | SD | 6.2   | 6.7     | 5.6   | 5.9   | 6.6   | 4.2       |
|                                | R  | 0-27  | 0-32    | 6-36  | 7-35  | 5-35  | 11.5-29.8 |
| Reproducibility (%)            |    | 1 kHz | 1.5 kHz | 2 kHz | 3 kHz | 4 kHz | Total     |
| Very low birth weight newborns | M  | 23    | 60      | 89    | 94    | 93    | 72        |
|                                | SD | 31    | 27      | 12    | 5     | 8     | 10        |
|                                | R  | 0-87  | 0-89    | 40-99 | 80-99 | 54-99 | 53-90     |
| Controls                       | M  | 55    | 92      | 98    | 98    | 98    | 91        |
|                                | SD | 37    | 16      | 2     | 2     | 3     | 9         |
|                                | R  | 0-99  | 0-99    | 80-99 | 85-99 | 78-99 | 53-99     |

The corresponding values for controls were 75 to 87 dB SPL for the range, and 81.7 dB SPL for the mean. The stability of the stimulus ranged from 62 to 100%, with a mean of 86.7%. In 90% of the cases, the stability was over 80%. The corresponding values for controls were: range, 69-100%, and mean, 89.4%. The noise rejection level was adjusted between 41 and 52 dB SPL, with a mean of 46.1 dB SPL for the VLBW newborns and 45.3 dB SPL for the controls. Mean test time was 111 seconds (range, 74-282) for the ears of the VLBW group and 97 seconds (range, 69-215) for the control ears.

Descriptive statistics (average, standard deviation, and range) of the overall response level and reproducibility of all measured TEOAEs (39 ears of the VLBW group and 78 ears of the control group) are listed in Table 2 for the two groups. The overall response level ranged from 11.6 to 30.4 dB SPL (mean 20.3 dB SPL) and overall reproducibility ranged from 53 to 90% (mean 72%) in the VLBW group. Corresponding values in the control group were: overall response level range from 11.5 to 29.8 dB SPL (mean 20.6 dB SPL) and overall reproducibility range from 53 to 99% (mean 90.7%).

Tests for normal distribution of the extracted metrics showed that overall response and band SNR followed a normal distribution, but the distributions of overall and partial reproducibilities were significantly skewed. Accordingly, a *t*-test for two-independent samples was used for response level measures and a Mann-Whitney U-test was used for reproducibility measures. In Table 3 the statistical analysis of the results of all ears with measurable otoacoustic emissions for the two groups is shown. These results reveal statistically significant differences in both response and reproducibility measures, with the exception of the overall response. Since gestational age could be a confounding factor in statistical analysis of the results, the mean overall response and band SNR of the ears with present otoacoustic emissions of the two groups were tested by analysis of covariance, with gestational age as the covariate. After controlling for gestational age, group differences in all band SNR measures were highly significant, but overall response mean difference between the ears of the two groups remained non significant (Table 4). These findings show that the observed differences in response measures between VLBW newborns and controls are not explained by the lower post-conceptual age of the first group, but are due to very low birth weight *per se*.

## Discussion

VLBW has been consistently identified as one of the high risk criteria for congenital hearing loss.<sup>9,11</sup> Our study corroborates this fact, because we found increased rate of 'fail' newborns in VLBW

Table 3

Mean differences, statistical values (*t* and *z*), and levels of statistical significance (*p*) in otoacoustic emissions, comparing the ears with present TEOAEs of the VLBW group (N = 39) and the control group (N = 78). The *t*-test for two independent samples was used for response measures and the Mann-Whitney U-test was used for reproducibility measures

| Response              | Mean difference (dB SPL) | <i>t</i> | <i>p</i> |
|-----------------------|--------------------------|----------|----------|
| SNR1                  | 3.9                      | 5.0      | <0.001   |
| SNR1.5                | 12.1                     | 13.4     | <0.001   |
| SNR2                  | 9.4                      | 8.8      | <0.001   |
| SNR3                  | 9.0                      | 8.3      | <0.001   |
| SNR4                  | 8.2                      | 6.6      | <0.001   |
| Overall response      | 3.2                      | 0.4      | ns*      |
| Reproducibility       | Mean difference (%)      | <i>z</i> | <i>p</i> |
| 1 kHz                 | 32.1                     | 4.3      | <0.001   |
| 1.5 kHz               | 32.0                     | 7.9      | <0.001   |
| 2 kHz                 | 8.3                      | 7.0      | <0.001   |
| 3 kHz                 | 4.0                      | 6.6      | <0.001   |
| 4 kHz                 | 4.3                      | 5.9      | <0.001   |
| Whole reproducibility | 18.7                     | 7.2      | <0.001   |

\* ns: non significant.

newborns, in comparison with full-term newborns. Unfortunately, three of the four cases with absent otoacoustic emissions were lost at follow-up, and we could not confirm hearing loss in any case of the VLBW group studied. In the 3 newborns available to rescreen (2 from the VLBW group and 1 control), normal otoacoustic emissions were finally found. These findings underscore the necessity of rescreening at a later moment, and suggest the presence of a postnatal maturation period for middle ear and cochlea.

The lack of an effective follow-up protocol in our UNHS program is a major problem.<sup>17</sup> Several reasons may account for this, such as lacking information or referral to other public pediatric hospitals, because a maternity hospital is not considered suitable to provide adequate facilities for follow-up, diagnosis and intervention. Additionally, a complete diagnos-

tic work-up in a private unit is quite expensive, and many parents are reluctant to pay for this. However, we have taken various measures described elsewhere,<sup>6</sup> resulting in decrease of the missed-to-follow-up rate.

However, useful conclusions may be obtained from this study of otoacoustic emissions in the VLBW group of newborns. In our study, statistical comparison between this group and controls showed significant differences in all TEOAE measures, indicating a degree of cochlear malfunctioning in VLBW babies. This may be attributed to several factors, including hypoxemia, acidosis, and immature metabolic function. Ototoxic drugs, which quite often are administered to these newborns because of co-existing disease, may be another cause.<sup>4,13</sup>

Several studies have measured otoacoustic emissions of VLBW newborns. The aims were various:

Table 4

Statistically adjusted for gestational age mean differences in response measures, *F* statistical values, and levels of statistical significance (*p*) comparing the ears with present TEOAEs of the VLBW group (N = 38) and controls (N = 78)

| Response | Mean difference (dB SPL) | <i>F</i> | <i>p</i> |
|----------|--------------------------|----------|----------|
| SNR1     | 6.2                      | 7.6      | <0.001   |
| SNR1.5   | 13.5                     | 56.9     | <0.001   |
| SNR2     | 6.5                      | 39.8     | <0.001   |
| SNR3     | 11.2                     | 35.0     | <0.001   |
| SNR4     | 8.7                      | 21.8     | <0.001   |
| Overall  | 3.5                      | 1.3      | ns*      |

\* ns: non significant.

gather screening outcomes in VLBW newborns<sup>18</sup>; report the characteristics of otoacoustic emissions in this high risk group in comparison to full-term babies<sup>13,19</sup>; follow-up the long term progress of these children's health, registering defects in their overall physical and neuropsychologic development,<sup>20</sup> including hearing. Long term follow-up long of development and status of the child's health has a particular interest in extremely low birth weight babies (<1000 g),<sup>21</sup> because prematurity is more severe and the risk for permanent health problems is higher. In the present study 3 newborns had birth weight less than 1000 g, but all of them had measurable TEOAEs.

From the above mentioned studies, van Zanten *et al.*<sup>19</sup> reported lower TEOAE response level in VLBW pre-term born infants, which agrees with our findings. However, most reports focus on the 'pass-fail' results of hearing screening testing, in conjunction with the prevalence of hearing impairment in the VLBW population. Roth *et al.*<sup>22</sup> reported a pass rate of 87.2% in VLBW newborns, compared with 92.2% in the full-term control group.

Additionally, they reported low incidence of sensory-neural hearing loss in VLBW newborns (0.3%), but they found a relatively high incidence of conductive hearing loss (2.7%), which was attributed to bronchopulmonary dysplasia and low Apgar score. Valkama *et al.*<sup>23</sup> found that 6 out of 51 (11.7%) VLBW pre-term infants had bilateral hearing loss. According to these authors, TEOAEs is not a sensitive test, due to the high prevalence of retrocochlear hearing loss in this group of patients and they recommended auditory brainstem response screening. Gill *et al.*<sup>18</sup> reported a pass rate of 84% (considering only one ear mandatory to pass the test). Among the cases who failed TEOAEs, 3 infants (2%) had conductive hearing loss and another 8 (5.5%) had confirmed sensorineural deafness. Finally, Uchoa *et al.*<sup>4</sup> using distortion product otoacoustic emissions found 6.3% prevalence of hearing loss in VLBW newborns, but not yet definitively confirmed.

In our study, the pass rate in VLBW newborns was 79.2%, but data for confirmed permanent hearing loss are not yet available. Discrepancies among the various reports may be attributed to the different populations studied (e.g. presence of numerous risk factors, besides VLBW), and different protocols and equipment used. However, lower pass rates in TEOAE testing and increased incidence of hearing loss in VLBW newborns were found in most reports. It should be mentioned at this point that the effectiveness of our protocol can also be testified by the efficiency of our UNHS program in full-term newborns as reported elsewhere,

which ensures a screening procedure of high standard.<sup>6,7</sup>

VLBW is related to prematurity that might affect otoacoustic emissions as well. Several studies have reported growth of otoacoustic emissions as age proceeds from immaturity to full-term age.<sup>2,19,24</sup> However, comparison of pre-term and fullterm babies yielded contradictory results. Bonfils *et al.*<sup>25</sup> did not find statistically significant differences between the level of otoacoustic emissions of neonates with postconceptional age (PCA) ranging from 32 to 21 weeks. Eshraghi *et al.*<sup>24</sup> longitudinally studied the otoacoustic emissions of neonates at different postconceptional weeks and found that neither the spectrum nor the level of the otoacoustic emissions changed. However, the presence of the otoacoustic emissions was not always stable and these could disappear temporarily and reappear later. Van Zanten *et al.*<sup>19</sup> reported similar instability before the PCA of 40 weeks and attributed it to unfavourable conditions in the middle ear. They also reported an increase by 10 dB SPL in the emission amplitude between 31 and 42 weeks PCA. Morlet<sup>26</sup> and Briennesse *et al.*<sup>27</sup> supported this finding. Smurzynski *et al.*<sup>28</sup> found that otoacoustic emissions of pre-term neonates were comparable to the highest values of those of full-term newborns screened during the first two or three days of life. They argued that when pre-term neonates were tested several weeks *post partum*, the influence of environmental conditions outside the womb on the middle ear, lead to very strong otoacoustic emissions. To resolve these conflicting results, we performed an analysis of covariance to disentangle gestational age and

birth weight and we found that VLBW is an independent factor of low performance in TEOAE testing.

It would be very interesting to know if any of the 3 newborns of the present study, who failed screening but were lost at follow-up, have actually hearing loss. Efficient follow-up is a common problem for most UNHS programs.<sup>18</sup> However, the finding of increased rate of initial 'fail', in conjunction with statistically confirmed lower TEOAE measures in VLBW newborns, warrants special care and long term follow-up for this group of newborns.

## Conclusions

In the present study we found an increased rate of initial 'fail' in hearing screening based on TEOAEs in VLBW newborns compared to normal newborns. Moreover, TEOAEs of VLBW newborns have lower intensity and reproducibility compared to normal newborns.

To resolve the confounding effect of prematurity, we performed an analysis of covariance controlling for gestational age on the otoacoustic emission measures, and we found that VLBW is an independent factor that reduces level and reproducibility of otoacoustic emissions. Our results support the special care and long term follow-up of hearing of VLBW-newborns.

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