Original Article

Risk of hearing loss in small for gestational age neonates

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Abstract

Background Small for gestational age (SGA) neonates often have intrauterine growth restriction due to placental insufficiency and chronic hypoxia. These conditions may cause developmental impairment, psychosocial disabilities, or metabolic dysfunction in later life. Previous studies have shown greater incidence of speech and language disabilities, learning impairment, and neuromotor dysfunction in term SGA infants compared to term appropriate for gestational age (AGA) infants.

Objective To compare hearing loss in SGA and AGA neonates using otoacoustic emission (OAE) tests and to study correlations between maternal risk factors and hearing loss in SGA neonates.

Methods A cross-sectional study was performed in St. Borromeus Hospital, Limijati Hospital, and Melinda Hospital in Bandung from February to May 2010. Study subjects consisted of full-term neonates born in these three hospitals. A retrospective medical record review was performed for this study. Statistical analysis was done by multivariable logistic-regression.

Results There was a total of 4279 subjects in our study, including 100 SGA neonates and 4179 AGA neonates. We observed a greater percentage of OAE 'refer' (indicating abnormal OAE) results in the SGA group compared to the AGA group (P<0.001, Z=13.247). For subjects with OAE 'refer' results, we also analyzed the correlation to the following maternal risk factors: smoking, hypertension, diabetes mellitus and asthma. We also found significant differences between those with and without each of the four maternal risk factors studied (P<0.001). By using multivariant analysis to compare SGA and AGA neonates, we found the odds ratio (OR) to be 4.34 (95% CI 2.52 to 7.49, P = 0.001), meaning the SGA group had a 4.34 times higher risk of hearing loss than the AGA group.

Conclusion SGA neonates had a higher risk of hearing loss than AGA neonates. In addition, maternal smoking, hypertension, diabetes mellitus and asthma significantly correlated to hearing loss in all newborns. [Paediatr Indones. 2011;51:52-7].

Hearing loss in children is one of the most common congenital defects. It is usually a sensory-neural type defect, bilateral, and severe to very severe in degree.[1] According to the WHO, the incidence of severe, bilateral, sensory-neural hearing loss in neonates is 1 to 3/1000 in a normal infant population, and 2 to 4/100 neonates requiring neonatal intensive care.[1,2]

Small for gestational age (SGA) is defined as infants with birth weight and/or length less than the 10th percentile, according to the Lubchenco gestational age curve.[3-5] SGA babies have intrauterine growth restriction due to placental insufficiency and chronic hypoxia, possibly causing glucose tolerance impairment, insulin resistance, and developmental

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impairment that may affect the growth hormone-insulin like growth factor (GH-IGF) axis.[3-6] SGA children may have impaired catch-up growth related to short stature, psychosocial disabilities, and metabolic dysfunction later in life.[7-9] Speech and language disabilities, hyperactivity, learning impairment, and neuromotor dysfunction are more commonly seen in term SGA babies than in AGA babies.[10,11] In addition, several mothers' risk factors including maternal smoking habits, diabetes mellitus (DM), severe hypertension, and moderate-to-severe asthma during pregnancy may cause placental insufficiency, chronic hypoxia, and hearing impairment for neonates.[12-17]

Previous studies have evaluated hearing disabilities in SGA babies.[10,11,18,19] The purpose of this study was to compare hearing loss in SGA and AGA neonates by otoacoustic emission (OAE) tests. OAE testing is considered useful for early detection. Identifying maternal risk factors can lead to better hearing screening in infants born to such mothers.

Methods

We conducted a cross-sectional study with subjects from three private hospitals in Bandung. These hospitals routinely use OAE screening for early detection of hearing loss in all newborns. Subjects were compiled from St. Borromeus Hospital (3287 term births, January 2008-December 2009), Melinda Hospital (668 term births, January-December 2009), and Limijati Hospital (324 term births, October 2009-March 2010). OAE examinations were conducted by the ENT specialist from the Department of Otolaryngology of each hospital.

This study was approved by the Ethics Commitee of Medical Faculty of Padjajaran University/Hasan Sadikin General Hospital, Bandung. Subjects were excluded if their medical records did not contain information on birth weight, length, head circumference, or the mother's first day of last menstrual period (LMP). Also excluded were those suspected of having neonatal sepsis, severe neonatal hyperbilirubinemia, severe asphyxia at birth, or needed mechanical ventilation.

We followed three steps for gathering data from medical records. First, all medical records were divided by month of birth and the mother's medical record was then paired with that of her child to be submitted into the study form. Second, we recorded neonatal information on weight, length, head circumference, sex, date of birth, APGAR score, form of delivery and OAE examination. Anthropometrical data was plotted into a Lubchenco curve to divide the subjects into two groups, SGA and AGA. The form of delivery data was divided into four groups: spontaneous, caesarean section, vacuum extraction, and forceps extraction. APGAR scores were not grouped, but were recorded. OAE results were divided into two groups, 'refer' indicating abnormal OAE and 'pass' indicating normal OAE. Third, we recorded mothers' information including age, first day of last menstrual period, and risk factors during pregnancy. Four types of maternal risk factors were noted: smoking, hypertension, diabetes mellitus and asthma. The first day of the last menstrual period (LMP) was used to calculate due dates and gestational ages. Mothers' ages were divided into three age groups.

SGA and mothers' risk factors were analyzed by multivariable logistic-regression analysis. Odds ratio (OR) with 95% confidence intervals (CI) were calculated for each factor. P values less than 0.05 were considered statistically significant. We used SPSS software version 16.0 for Windows 2008, SPSS Inc., Chicago-Illinois, USA, for all statistical analyses.

Results

We had 4279 subjects in our study, 100 (2.3%) in the SGA group and 4179 (97.7%) in the AGA group. In agreement with our data, previous studies have estimated that 2-10% of babies are born SGA.[9,10] Characteristics of the infants and their mothers are shown in **Table 1**. Most mothers were 30-39 years old and delivered spontaneously.

A comparison of OAE examination results from both groups is shown in **Table 2.** We observed a higher percentage of OAE 'refer' results in the SGA group than in the AGA group, 48% versus 9%, respectively. (P<0.001, Z=13.247).

A univariant analysis of risk factors and OAE 'refer' results are shown in **Table 3**. Four mothers' risk factors (smoking, hypertension, DM, and asthma) as

Table 1. Characteristics of mothers and infants in SGA and AGA groups

Subject Characteristics	Group	
	SGA (n=100)	AGA (n=4179)
Sex		
Male	52	2,111
Fe male	48	2,068
Birth weight (g)		
Mean (SD)	2,065.38 (99.70)	3,229.69 (264.25)
Range	1,800-2,250	2,100 – 4,000
Birth length (cm)		
Mean (SD)	48.00 (2.34)	50.14 (1.09)
Range	42 – 50	45 – 53
Head circumference (cm)		
Mean (SD)	32.73 (1.51)	34.21 (0.94)
Range	30 – 35	31 – 37
Gestational age (weeks)		
Mean (SD)	38.26 (0.82)	38.82 (0.86)
Range	37 – 41	37 – 39
Delivery method		.
Spontaneous	46	2,246
Caesarean section	53	1,830
Forceps extraction	1	100
Vacuum extraction	0	3
Mother's age (years)		
20 -29	26	832
30-39	73	3,237
≥40	1	110

Table 2. Comparison of OAE examination results between the SGA and AGA groups

Variable	SGA		AGA		P
	n = 100	%	n = 4179	%	
OAE					<0.001
Pass	52	52	3,805	91	
Refer	48	48	374	9	

Note: Z-test was used to analyze differences in the 2 groups; Z=13.247, P<0.001

Table 3. Risk factors associated with OAE 'refer'

Risk factor	OAE 'refer' n (%)	P *
SGA vs AGA neonates	48 (48%) vs 374 (9%)	<0.001
Smoking vs non-smoking mothers	50 (67.6%) vs 400 (9.2%)	<0.001
Hypertensive vs non-hypertensive mothers	120 (50.2%) vs 330 (7.9%)	<0.001
Mothers with DM vs non-DM	34 (36.6%) vs 416 (9.6%)	<0.001
Mothers with asthma vs non-asthma	54 (41.9%) vs 396 (9.3%)	<0.001

Note: * Chi-square test

Table 4. Multivariant analysis between risk factors and OAE 'refer' results

Risk factor	OR	OR (95% CI)	P
SGA	4.34	2.52 to 7.49	<0.001
Maternal smoking	31.48	18.56 to 53.40	<0.001
Maternal hypertension	18.95	14.00 to 25.64	<0.001
Maternal diabetes mellitus	24.98	13.35 to 46.72	<0.001
Maternal asthma	13.48	9.16 to 19.85	<0.001

well as SGA/AGA status in newborns were analyzed for correlation to newborns' OAE 'refer' results. Two groups for each risk factor (those with the risk factor and those without) were compared by chi-squre test. There were significant differences between each of the two groups (those with the risk factor and those without it) for all four mothers' risk factors (P<0.001).

We also compared the risk factors influencing OAE examination results by multivariant analysis with logistic regression. Results are shown in **Table 4.** The odds ratio (OR) of every risk factor (SGA, smoking, hypertension, DM, and asthma) was calculated. The OR for SGA was 4.34 (95% CI 2.52 to 7.49), which means that the SGA group had an OAE 'refer' result 4.34 times more often than the AGA group. Mothers' smoking had the highest OR, 31.48 (95% CI 18.56 to 53.40), meaning that neonates born from a smoking mother had OAE 'refer' results 31.48 times more often than non-smoking mothers.

Discussion

We found SGA newborns had 4.34 times greater OAE 'refer' results than AGA newborns. SGA neonates may have intrauterine growth restriction due to placental insufficiency and chronic hypoxia. Auditory organs needs an adequate oxygen supply, especially the organs of Corti. Hypoxia causes auditory cell death and can affect aerobic respiration in the cochlea. Placental insufficiency and chronic hypoxia in SGA can damage the cochlear outer hair cells and cause sensorineural hearing loss.[3,20,21]

The SGA group consisted of 100 term babies, with 48% (48/100) having OAE 'refer' results. There were only 9% (374/4179 babies) OAE 'refer' results in the AGA group. Similarly, Martikainen[18] showed that asymmetrical SGA babies have lower visual and auditory perception than other babies. Another study by Todorovich *et al*[19] showed that SGA babies' responses toward auditory stimulation were lower than those of AGA babies. Hearing loss in AGA newborns is generally suspected to be related to such factors as stiff neonatal auricle or the presence of cerumen that may interfere with the OAE results. Furthermore, congenital TORCH infection, family history of deafness, and a history of ototoxic or teratogenic drug

consumption (e.g. salicylic acid, quinine, neomycin, gentamycin, thalidomide, and barbiturate) may affect organogenesis and destroy cochlear hair cells.[22,23]

A statistical analysis was also conducted between other risk factors and the OAE 'refer' results. We found maternal smoking, hypertension, diabetes mellitus and asthma to significantly correlate to OAE 'refer' results. Similarly, Fried and Watkinson[12] showed that maternal smoking was a risk factor in SGA babies for hearing response impairment in babies. In addition, mothers with diabetes mellitus (DM) may suffer various complications causing impairment in hearing organ development and craniofacial anomalies, which exacerbate congenital hearing disabilities.[13-15] A study by Wells[16] showed the presence of massive bleeding in the inner and middle ear based on histopathological examination of a 29-week fetal temporal bone of a child born to a mother with severe hypertension. Furthermore, moderate-to-severe asthma during pregnancy may cause placental insufficiency and chronic hypoxia. This was believed to trigger pre-eclampsia and cause low birth weight.[17]

There are a number of limitations of this study. First, OAE was used only as an early detection method to check the possibility of hearing loss. To determine the hearing threshold and the type of hearing loss, further examination is needed, such as with brainstem evoked response audiometry (BERA). This tool has 98% sensitivity and 96% specificity.[24,25] Also, since this study was cross-sectional, further studies with cohort and prospective design using BERA to evaluate the incidence of hearing disabilities between SGA and AGA babies are needed. In addition, some medical records were incomplete and not objective. The researcher also had difficulties due to hospital regulations in accessing patients' private medical data.

We conclude that SGA neobates have a higher risk of hearing loss than AGA neonates. Therefore, OAE should be performed for early detection of hearing loss, especially for SGA newborns. In babies with suspected hearing loss, diagnosis should be verified with BERA at 4-6 months of age. The community should be warned about maternal risk factors for infant hearing loss, and the importance of early detection and early intervention for congenital hearing loss before the age of 2 years. Screening programs must be well-

prepared and coordinated between ENT specialists, pediatricians, and obstetricians.

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