Utilizing Infant Cry Acoustics to Determine Gestational Age

*Mustafa Sahin, †Suzan Sahin, ‡Fatma N. Sari, §Emel C. Tatar, ‡Nurdan Uras, ‡Suna S. Oguz, and §Mehmet H. Korkmaz, *†*Aydın and* ‡§*Ankara, Turkey*

Summary: Objectives/Hypothesis. The date of last menstruation period and ultrasonography are the most commonly used methods to determine gestational age (GA). However, if these data are not clear, some scoring systems performed after birth can be used. New Ballard Score (NBS) is a commonly used method in estimation of GA. Cry sound may reflect the developmental integrity of the infant. The aim of this study was to evaluate the connection between the infants' GA and some acoustic parameters of the infant cry.

Study Design. A prospective single-blind study was carried out.

Methods. In this prospective study, medically stable infants without any congenital craniofacial anomalies were evaluated. During routine blood sampling, cry sounds were recorded and acoustic analysis was performed. Step-by-step multiple linear regression analysis was performed.

Results. The data of 116 infants (57 female, 59 male) with the known GA (34.6 ± 3.8 weeks) were evaluated and with Apgar score of higher than 5. The real GA was significantly and well correlated with the estimated GA according to the NBS, F0, Int, Jitt, and latency parameters. The obtained stepwise linear regression analysis model was formulized as $GA = (31.169) - (0.020 \times F0) + (0.286 \times GA\ according\ to\ NBS) - (0.003 \times Latency) + (0.108 \times Int) - (0.367 \times Jitt)$. The real GA could be determined with a ratio of 91.7% using this model.

Conclusions. We have determined that after addition of F0, Int, Jitt, and latency to NBS, the power of GA estimation would be increased. This simple formula can be used to determine GA in clinical practice but validity of such prediction formulas needs to be further tested.

Key Words: Infant cry–Acoustic analysis–Cry analysis–Gestational age–New Ballard Score.

INTRODUCTION

Crying is the primary method of communication for infants to express their physical status. Infant cry is not just a simple reflex sound. It contains complex acoustic signals produced by combined proper interactions between central and peripheral nervous systems, respiratory system, larynx, acoustic tract, and motor activities of many muscles.[1] Studies of cry analysis in infants have had a fast and growing evolution. In particular, there has been a greater appreciation for the complexities of crying. Studies investigating the association of acoustic features of infant cry with the biological condition of infant have been performed since 1940s.[2,3] Easily recorded cry sound can be analyzed by widespreading voice analysis programs which will be achieved without difficulty in the future. In the studies of LaGasse et al (pain-induced cry) and Wermke et al (spontaneous cry) performed with this aim, it was reported that the acoustic cry characteristics of preterm infants or infants with neurological problems may be different from that of healthy term infants; so it has been stated that cry may reflect neuromuscular integrity and maturation of the infants.[4,5] Michelsson et al (pain-induced cry) determined that shorter gestational age (GA) was significantly associated with higher fundamental frequency and shorter total cry duration.[1]

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From the *Department of Otolaryngology, Medical School, Adnan Menderes University, Aydın, Turkey; †Department of Neonatology, Medical School, Adnan Menderes University, Aydın, Turkey; ‡Department of Neonatology, Zekai Tahir Burak Research and Training Hospital, Ankara, Turkey; and the §Department of Otolaryngology, Diskapi Yildirim Beyazit Research and Training Hospital, Ankara, Turkey.

Address correspondence and reprint requests to Mustafa Sahin, Department of Otorhinolaryngology, Faculty of Medicine, Adnan Menderes University, Aydın 09100, Turkey. E-mail: iskebaha@gmail.com

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The determination of GA at birth is of vital importance in terms of appropriate clinical and therapeutic approach, assessment of morbidity and mortality risks, and the accuracy of institutional and social infancy statistics.[6] In determination of GA, the most commonly benefited data are the date of last menstrual period (LMP) and the first trimester ultrasonography (USG) (obstetric estimation of gestation) findings. Many women can state the first day of their LMP but the reliability of this approach depends on a number of factors including the woman's accurate recall of the LMP, regularity of menstrual cycles, use of contraceptives or breastfeeding that could influence the timing of ovulation, and her sociocultural status. Because of such potential errors, estimation of GA based on LMP is considered to be not reliable enough.[7] Although, estimating GA by prenatal USG is considered to be more reliable than LMP, USG dating may not always take into consideration biological variations of fetal growth and length of pregnancy. Some factors such as maternal malnutrition and intrauterine growth restriction reduce the reliability of USG. It was stated that USG examination provides a younger estimate of GA than that of estimated by the LMP.[8] Especially, low socioeconomic status may result in: not to know the date of LMP, inadequate prenatal follow-up, and late enrollment for antenatal care.[9] Absence of prenatal follow-up and uncertainty of LMP are two negative common grim realities in developing countries (like us) where prenatal care is usually inadequate which makes infant management more difficult. If appropriate prenatal USG is absent or LMP is not known, after delivery in estimation of GA, some subjective scoring systems such as Dubowitz, Farr, New Ballard Score (NBS), and Eregie depending on the data obtained by the physical and neurological examinations of infants may be beneficial.[6,7,9] NBS is a commonly used technique of GA assessment. NBS uses seven physical and six neurological criteria obtained by the physical examination of infants; sum of all criteria (total score) is then extrapolated to the GA by use of a maturity rating sheet. NBS relies on the intrauterine changes and maturation that the fetus undergoes during the pregnancy period. The neurological criteria depend mainly upon muscle tone and the physical criteria mainly rely on anatomical changes.[9,10] The NBS was reported as a valid and accurate gestational assessment tool for all infants. The strong correlation between NBS and USG/LMP was also reported.[10] Despite all, there is still no general consensus on USG examination criteria or a clinical formula employed to determine GA. Thus, possible systematic errors within studies will cause variations and mistakes.[7]

The current gold standards (USG and LMP) used to measure GA are not available always and they are sometimes inadequate; it's that acoustic parameters may be another "tool" in the "toolbox" as a means to provide a more accurate estimate of GA. The reports of LaGasse et al and Wermke et al provided us an insight as acoustic features of infant cry could supply additional measures while determining GA of infants as a noninvasive tool.[1,4,5]

Another rationale for the study is that when GA cannot be readily calculated via anthropometric measurements and physical examination, some other current methods (such as biochemical parameters in amniotic fluid, lens capsule vascularity) were studied to obtain "real" GA. However, these methods are invasive, compared to acoustic parameters.[11]

The aim of this study was to investigate the usability of acoustic cry analysis parameters together with NBS, that is one of the most commonly performed methods in this topic, in the estimation of GA of infants and to develop a method for clinical practice.

METHODS

Study design

This is a multidisciplinary, prospective study performed by the collaboration of ear-nose-throat diseases and newborn diseases clinics. The study was approved by the Clinical Investigations Ethics Committee (Decision No.: 13/2014; Decision date: 18 February 2014).

Patients

Mother and/or father of all patients included in the study were informed about the study in detail by the specialists of the subject, and the parents signed the informed consent forms comprehending the data about the procedures that will be performed during the study. After delivery in newborn unit, in the first 72 hours while they were with their mothers, a complete routine newborn physical examination and flexible fiberoptic laryngeal examination were performed to the patients having the required inclusion criteria. Prenatal and maternal histories of infants, known GA (KGA), gender, and birth weight were recorded. The inclusion criteria were as follows: regular follow-up during pregnancy and to know the exact GA, absence of congenital craniofacial anomalies, absence of any abnormal physical or neurological findings regarding infant's GA in first examination after delivery, to have an Apgar score of higher than 5 in the fifth minute after delivery, not to be intubated, and absence of any form of respiratory failure and laryngeal anomaly. Patients who were not stable medically, and who had severe hypoglycemia or hyperbilirubinemia requiring phototherapy in follow-up were not included in the study.

Estimation of GA by NBS

Three different experienced neonatologists in NBS assessment, who were blind for the clinical features of cases, independently examined the infants according to the NBS system and estimated GA was recorded. A universally declared ready score sheet was used to estimate GA using total NBS. This was stated as estimated GA in this study. The comment of criteria in the NBS system may vary depending on the evaluator. The compatibility between NBS evaluators was analyzed using Fleiss' kappa and intraclass correlation tests prior to the study and was determined as statistically significant (87%, $P = 0.01$).

Cry analysis

The cry sounds were recorded during routine blood sampling procedures to avoid causing additional discomfort. To diminish the environmental noise as much as possible, recordings were obtained during evening hours in separate, quiet examination rooms free of any background noise that could potentially confound acoustic variables.

Cry sounds were recorded by high-quality and 24-byte sound cards (Creative Audigy; Creative Labs Inc., Milpitas, California) and circular all-direction microphone (Shure SM48; Shure Inc.). The sounds were recorded by the same otolaryngologist who was experienced on this topic and blind to the patients. During sound recording, babies were lying on an open cradle on flat, supine position. During the records, the distance between the microphone and the mouth was approximately 15 cm. The sampling frequency of records was selected as 44,100 Hz and the resolution was set as 16 bytes. The recorded cry sounds were analyzed via Computerized Speech Lab (CSL; KayPENTAX CSL model 4500, Montvale, New Jersey) operating system. The cry sounds containing at least three crying signals and lasting for at least 10 seconds were included. After the latency time was measured, the analyses were performed after elimination of first seconds of parts at the beginning and at the end of the records to prevent the disorders on sounds. The five acoustic parameters analyzed in this study were as follows: mean fundamental frequency (Fo), jitter % (Jitt), shimmer % (Shim), noise-to-harmonic ratio (NHR), and Intensity (Int). As the temporal patterns of crying, latency in milliseconds (time period passed between the painful stimuli and the first signal of crying), total cry time (TCT) in seconds, and mean utterance duration time (MUDT) in milliseconds (the mean of standstill periods between crying signals) were determined manually.

Statistical analysis

The statistical analyses were performed with *Statistical Package for the Social Sciences (SPSS)*, Version 22.0 (IBM Corp, New York). To determine the power of sound analysis parameters together with NBS in estimation of GA, stepwise linear regression analysis was performed. To define the variables that will be used in estimation of KGA, the correlation analysis was performed between all variables included in the study and KGA. Before the correlation analysis, the variables were analysed if they corresponded to the parametric assumptions or not. It was determined that in Kolmogorov-Smirnov test, the variables were not normally distributing, and for that reason, nonparametric Spearman's rank order correlation analysis was performed. The statistical differences between the KGA of girls and boys were determined by Mann-Whitney *U* test and because there was not a statistically significant difference ($P = 0.190$), different models were not developed for different genders. The variables determined to be associated with the KGA in these analyses were included in the regression analysis. Later, variables were included in the step-by-step multiple linear regression analysis one by one to define their effects on estimation of KGA as a whole.

RESULTS

The data of a total of 116 newborns (57 girls and 59 boys) were evaluated. Acoustic analysis could not be obtained in 11 infants (either because of issues with acoustic signal recordings, or because the infants did not cry during the blood drawl). The mean KGA of 116 infants was 34.6 ± 3.8 weeks (min 22, max 41); the mean birth weight was 2317 ± 820 g (min 775, max 4340); and the mean fifth minute Apgar score was 8.6 ± 0.8 (min 6, max 10). The mean values of these three parameters according to the gender are summarized in Table 1.

The mean time passed between the delivery and performing NBS was 1.9 ± 0.7 days. In NBS, the mean score of neuromuscular maturity part was 13.5 ± 5.3 while it was 13.3 ± 5.4 for physical maturity part, and the mean total NBS score was 26.4 ± 10.5. The mean values of GA estimated with NBS and acoustic cry analysis parameters are summarized in Table 2.

The KGA, estimated GA according to NBS, and the means of acoustic analysis parameters performed with cry sounds according to genders are summarized in Table 3. There was not any statistically significant difference between genders regarding these parameters.

The results of correlation analyses of KGA with estimated GA according to NBS and acoustic cry analysis parameters are shown in Table 4. There was a statistically significant positive correlation with very good level between KGA and estimated GA according to NBS ($P < 0.001$, $r = 0.892$). The correlation between KGA and F0, Int, and Latency was determined as statistically significant at a very good level (for F0, $r = -0.873$; for Int,

TABLE 1.
The Mean Birth Weight, Known Gestational Age, and Apgar Scores According to Gender

	Number	Birth Weight (g) ± SD	Known GA ± SD	Apgar Score
Girls	57	2313 ± 736	34.0 ± 3.7	83 ± 0.6
Boys	59	2329 ± 828	35.2 ± 3.6	8.8 ± 0.7
Total	116	2317 ± 820	34.6 ± 3.8	8.6 ± 0.8

Abbreviations: GA, gestational age; SD, standard deviation.

TABLE 2.
Estimated Gestational Age According to New Ballard Score and the Mean Values of Acoustic Cry Analysis Parameters

	Mean ± SD	Min–Max
GA according to NBS	35.7 ± 4.1	23–44
F0	434 ± 61.9	312–601
Int	58.1 ± 5.3	46.1–71.3
Jitt	2.6 ± 0.9	0.6–5.1
Shim	8.4 ± 2.5	4.2–20.6
NHR	0.42 ± 0.14	0.23–0.98
Latency (ms)	1227 ± 281	650–1990
TCT (s)	11.8 ± 1.5	8–16
MUDT (ms)	2262 ± 381	1330–3120

Abbreviations: F0, fundamental frequency; GA, gestational age; Int, intensity; MUDT, mean utterance duration time; NBS, New Ballard Score; NHR, noise-to-harmonic ratio; SD, standard deviation; TCT, total cry time.

TABLE 3.
The Gestational Age, Estimated Gestational Age According to New Ballard Score, and the Means of Acoustic Cry Analysis Parameters According to Gender

	Girls (n = 57)	Boys (n = 59)	*P*
Known GA	34.0 ± 3.7	35.2 ± 3.6	0.123
GA according to NBS	35.6 ± 4.2	36.4 ± 3.9	0.072
F0	430.3 ± 63.9	438.6 ± 56.2	0.186
Int	57.8 ± 5.1	58.1 ± 5.4	0.155
Jitt	2.7 ± 0.9	2.6 ± 0.9	0.144
Shim	8.2 ± 2.8	8.6 ± 2.1	0.131
NHR	0.41 ± 0.11	0.44 ± 0.16	0.087
Latency (ms)	1234.4 ± 293.4	1220.7 ± 271.8	0.798
TCT (s)	11.8 ± 1.3	11.9 ± 1.7	0.689
MUDT (ms)	2195.3 ± 324.3	2326.0 ± 422.4	0.069

Abbreviations: F0, fundamental frequency; GA, gestational age; Int, intensity; MUDT, mean utterance duration time; NBS, New Ballard Score; NHR, noise-t-harmonic ratio; SD, standard deviation; TCT, total cry time.

TABLE 4.
The Correlation Analysis Performed Between Known Gestational Age and Estimated Gestational Age According to New Ballard Score and Acoustic Analysis Parameters

	Pearson Correlation Coefficient	*P*
GA according to NBS	0.892	<0.001
F0	–0.873	<0.001
Int	0.860	<0.001
Jitt	–0.731	<0.001
Shim	–0.696	<0.001
NHR	0.074	0.439
Latency (ms)	–0.805	<0.001
TCT (s)	0.512	<0.001
MUDT (ms)	0.794	<0.001

Abbreviations: F0, fundamental frequency; GA, gestational age; Int, intensity; MUDT, mean utterance duration time; NBS, New Ballard Score; NHR, noise-to-harmonic ratio; TCT, total cry time.

TABLE 5.
The Variables Defining Real Gestational Age (Stepwise Linear Regression Model)

	Regression Coefficient (95% CI)	Standardized Regression Coefficient	*P*
Constant value	31.169 (24.364–37.973)		
GA according to NBS	0.286 (0.196–0.375)	0.327	<0.001
F0	−0.020 (−0.026—0.013)	−0.316	<0.001
Latency	−0.003 (−0.004—0.001)	−0.188	<0.001
Int	0.108 (0.028–0.187)	0.153	0.009
Jitt	−0.367 (−0.698—0.036)	−0.089	0.030

Abbreviations: F0, fundamental frequency; GA, gestational age; Int, intensity; MUDT, mean utterance duration time; NBS, New Ballard Score; TCT, total cry time.

r = 0.860; for latency, r = −0.805). Moreover, KGA statistically significantly correlated with Jitt, Shim, and MUDT at a good level (for Jitt, r = −0.731; for Shim, r = −0.696; for MUDT, r = 0.794). There was a statistically significant positive correlation between KGA and TCT at a moderate level (r = 0.512). The relationship between KGA and NHR was not statistically significant ($P = 0.439$).

When the data of cases were analyzed with stepwise linear regression analysis, the variables obtained in the model were mean GA according to NBS, F0, Latency, Int, and Jitt. The regression coefficients of these parameters are summarized in Table 5. According to this model, by using only GA according to NBS, 80.2% of real GA could be explained. When other four parameters included in the model were added (mean F0, Latency, Int, Jitt), this ratio increased to 91.7%. The significance level of this model was $P < 0.001$.

As a result, the obtained stepwise linear regression analysis model was formulized as

$$\begin{aligned}\text{The real GA} = {} & (31.169) - (0.020 \times \text{mean F0}) \\ & + (0.286 \times \text{GA according to NBS}) \\ & - (0.003 \times \text{Latency}) + (0.108 \times \text{Int}) \\ & - (0.367 \times \text{Jitt}).\end{aligned}$$

DISCUSSION

The area of acoustic cry analysis has advanced significantly over the past 10–15 years. Infant cry is a complex, multimodal, and dynamic behavior and is related to basic neurophysiological parameters.[12] Cry sound includes rhythmic cycles which are composed of utterances (expiratory phase with sound) and short inspiratory phases (unvoiced). The time passed between the painful stimuli and the beginning of crying (cry latency) is determined to be associated with the activation of sympathetic system while TCT and MUDT are assessed as the parameters associated with neural-respiratory control of cry sound. Intensity is closely associated with respiratory control and subglottal pressure.[13,14] Infants with different GAs also have different neurophysiological maturities. With an increase in GA, subglottal vocal tract maturates, while expiration capacity increases and the control of central nervous system and vagal tonus on vocal tract becomes more regular.[15,16] Increasing GA reverberates as shorter latency, longer cry activity, and higher intensity in acoustic analyses. The results of our study were also compatible with these data. We have determined that, with an increase in GA, latency decreases while intensity, TCT, and MUDT significantly increase. It was defined that especially the latency and intensity values may be used in estimation of GA.

F0 of the vocal folds' vibration corresponds to the number of glottic cycles per second. It is a base frequency heard as the voice pitch. It has been described as the essential acoustic feature that affects the auditory perception of a cry. F0 is the most commonly studied acoustic parameter of the infant cry sound. The F0 of cry sounds of normal healthy and small infants was reported to be between 350 and 600 Hz.[1] The fundamental frequency of cry sound triggered by pain in preterm infants was defined to be higher than that of full-term infants, and higher F0 was specified to be able to show the development of an infant.[1,17] Zeskind and Lester reported that among the parameters of neonatal cry sound, latency, total amount of time of cry, and fundamental cry frequency were associated with the fetal growth level of an infant.[18] With an increase in GA, vagal activity inhibiting the laryngeal muscle contraction also increases. In this way, the tension of vocal folds and F0 of cry sound decreases.[4,15] Similarly in our study, the significant increase in mean F0 with a decrease in GA was determined to be a valuable acoustic parameter in estimation of GA.

The perturbation parameters of sound such as frequency (jitter) and amplitude (shimmer) are the noninvasive values that give information about the laryngeal vibratory function by measuring the vocal fold vibration stability. Measuring perturbations (mostly jitter and shimmer) are routinely made for sustained vowel productions and introduction of noise into the acoustic signal renders these measures restricted.[19] The increases in jitter and shimmer in acoustic analyses of children and adults are evaluated as the sign of irregularities on vibratory pattern and are thought to be indicative of voice pathology. However, this finding has been shown to occur in nonpathological voices also.[19,20] There are many unknowns about the perturbation parameters of infant cry sound. Aperiodicity is a probable feature of infant cry. Although aperiodic voice signals of cry have been researched as a sign of a pathology like central nervous system disturbance, these signals occur in the cries of most infants regardless of health status. Many bifurcations (sudden qualitative change in laryngeal behavior) and aperiodic segments are normally determined in phonatory features for infant cry.[20] Besides, biphonation feature was found more frequently in cries of infants with central nervous system disturbances.[21] Therefore, the jitter and shimmer values of infant cry sound may be expected to be higher when compared with advanced ages, but this has not been clarified yet in literature. One of the disadvantages of using jitter and shimmer is this uncertainty. On the other hand, irregularity of infant cry and its possible relationship with the maturity of infant makes analyzing of perturbation parameters reasonable and even advantageous. To comment on the mean Jitt (2.6) and Shim (8.4) values of cry sound determined in our study properly, further studies are warranted about this topic. In infants, it is thought that with an increase in neuromuscular coordination between vocal tract and nervous system, vocal vibration will be more stable. In cry acoustics of preterm infants, sudden alterations in basic frequency (glide), harmonic duplications, and noise segments (associated with higher NHR) were determined more commonly.[20,22] More variability in frequency and intensity preoccupies the instability and/or immaturity in control of motor coordination of neural system because these rapid alterations reflect the balance of inhibitor and activator autonomy mechanisms.[3,15] In our study, the decreases in Jitt and Shim with an increase in GA may also be commented as the indicator of an improvement in that stability and/or maturity. As the F0 showed highly significant results associated with GA in our study, we thought that Jitt showing the frequency variability between periods is another acoustic parameter that may be used for this purpose.

Although it is reasonable that with the acoustic analysis of cry sound, the data associated with the development of infants may be obtained, the validity of this hypothesis has not been studied yet on large, prospective clinical studies.

The main potential advantages of our model were as follows: ease of use, cost-effectiveness, objective measurements, and noninvasiveness. It is not possible to make a clear clinical statement about this formula yet. Validated prediction models evaluating different acoustic parameters, more patients with different diagnoses, and different analysis programs are needed. Evaluating some perturbation (jitter and simmer) and spectral (NHR) parameters was a favored feature of this study because far less is known about these parameters' normative values. Another positive side of this study was evaluating infants with a wide gestational week spectrum together with NBS. One of the main limitations of this study was the exclusion of infants with craniofacial or systemic different pathologies. Data of our study can be used as normative values. Another limitation is the lack of comparisons performed with portable, simpler recording methods (such as microphones with internal sound card).

Acoustic features of pain cries are different from spontaneous (hunger, fussy) cries, and cry frequency could be altered by pain stimuli. One of the limitations of this study was lack of spontaneous cry analysis because there was much noise in the rooms where the infants were with their mothers.

Most cry researchers would either discard cries that contained aperiodicity (harmonic doubling, Fo shifts, noise) and focus exclusively on cries with periodicity. In the present study, we selected (a minimum of) three cry signals that were at least 10 seconds in duration. Analyzing aperiodic cry signals can be considered as both an advantage and a disadvantage. In addition, when it comes to infants, periodic acoustic signals may not always be feasible.

Future directions

The results of this study can be applied to future studies involving premature/underdeveloped infants. Accuracy of GA estimates becomes much more critical when determining course of management in premature infants or in high-risk pregnancies. Future studies are needed to determine whether the regression model will fit acoustical parameters in atypical populations also.

Periodic acoustic signals of infant cry, especially with disordered or preterms, may not always be feasible. Preterm infants can exhibit vocal fold paralysis at birth, or can have underdeveloped lungs (affecting vocal tract aerodynamics), which all can play a role in acoustic parameters. In recent years, there has been a shift way from the use of spectral analyses in favor of cepstral analysis, which can more accurately analyze aperiodic acoustic signals, as analysis does not depend on time domains. It is recommended that cepstral measures, such as CPP (cepstral peak prominence), be included in future studies in this line of work, in conjunction with the jitter and shimmer parameters, for improved ecological validity and applicability.

CONCLUSION

In our study, the additive effects of the data obtained by the acoustic analysis of cry sound to the physical and neurological findings were evaluated in estimation of GA, and highly promising results were obtained.

Results of this study support the potential use of the acoustic cry analysis as a noninvasive tool to detect GA with combination of scoring systems like NBS. A mathematical model developed via data obtained through examination and cry acoustics to determine GA may ease management of infants with unknown GA.

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