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Objective and quantitative evaluation of fetal hiccups by computerized cardiotocography: a prospective observational study

M. La Verde[1], M. Torella[1], G. Lanza[2], A. M. C Rapisarda[2], M. Morlando[1], S. Cianci[1], N. Colacurci[1], C. Capristo[3], C. Torre[1], P. De Franciscis[1], G. Riemma[1]

[1]Department of Woman, Child and General and Specialized Surgery, Obstetrics and Gynecology Unit, University of Campania Luigi Vanvitelli, Naples, Italy
[2]Department of General Surgery and Medical Surgical Specialties, University of Catania, Catania, Italy
[3]Department of Neonatal Intensive Care, University of Campania Luigi Vanvitelli, Naples, Italy

ABSTRACT

The physiological function of fetal hiccup and its correlation with fetal well-being is a debated topic.
We conducted a prospective observational study in a Tertiary care University Hospital to correlate the fetal hiccups with the antepartum computerized cardiotocography parameters.
Fifty-one nonlaboring women with a term pregnancy were enrolled. We collected data regarding maternal perception of fetal hiccups and the computerized cardiotocographic examination. The pregnant were divided into three groups depending on fetal hiccups perception. There was a statistical difference for the number of fetal movements in an hour between the group of daily perception and the group of no perception.
Changes in fetal movements frequency are essential to recognize pregnancies at increased risk for adverse fetal outcomes. No one studies in the medical literature utilized the computerized cardiotocographic machine to explore fetal hiccups. Then our study showed that a mother with daily fetal hiccups could be considered a low risk considering the significant numbers of fetal movements revealed by computerized cardiotocography. Nevertheless, randomized controlled trials are required to evaluate the fetal hiccups evaluation and its influence on fetal outcomes.

SOMMARIO

La funzione fisiologica del singhiozzo fetale e la sua correlazione con il benessere fetale è un argomento dibattuto.
Abbiamo condotto uno studio prospettico osservazionale in un ospedale universitario di terzo livello per valutare correlazioni tra il singhiozzo fetale ed i parametri della cardiotocografia computerizzata antepartum. Sono state arruolate 51 pazienti gravide a termine non in travaglio attivo. Abbiamo raccolto dati riguardanti la percezione materna del singhiozzo fetale e l'esame cardiotocografico computerizzato. Le gravide sono state divise in tre gruppi a seconda della percezione del singhiozzo fetale. È stata riscontrata una differenza statisticamente significativa per il numero di movimenti fetali attivi in un'ora tra il gruppo con percezione quotidiana del singhiozzo e il gruppo con nessuna percezione.
I cambiamenti nella frequenza dei movimenti fetali sono essenziali per riconoscere le gravidanze ad aumentato rischio di esiti fetali avversi. Nessuno studio nella letteratura medica ha utilizzato la cardiotocografia computerizzata per indagare il singhiozzo fetale. Quindi il nostro studio ha dimostrato che una madre con singhiozzo fetale quotidiano potrebbe essere considerata a basso rischio considerando il numero significativo di movimenti fetali rilevati dalla cardiotocografia computerizzata. Tuttavia, sono necessari studi randomizzati controllati per confermare l'impatto del singhiozzo fetale sugli outcome neonatali.

Corresponding Author: Gaetano Riemma
E-mail: Gaetano.riemma@unicampania.it

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Key words
Fetal hiccups; fetal movement; computerised cardiotocography; cardiotocography; fetal heart rate; computerized analysis.

INTRODUCTION

Fetal hiccups are considered quick fetal movements that all mothers can perceive during pregnancy (1). However, current evidence does not fully explain this physiological mechanism, although fetal hiccups are considered healthy and normal fetal functions (2). The prevalence and duration of such phenoms are still unclear. Fetal hiccups can be seen with faltering on the mother's abdomen, and, since it is not a widespread phenomenon, we need much time is usually needed to appreciate it. Additionally, several reports showed no substantial difference in fetal hiccups bouts across different gestational weeks, although the frequency decreases with advanced gestational age, particularly after 28 weeks. Hiccups have been reported during the first trimester of pregnancy (3-5), with increased frequency during the third trimester (6). Other studies have shown a reduced umbilical arterial and venous flow during fetal hiccups (7, 8). However, this finding has not been correlated with adverse fetal outcomes and might be considered a physiological phenomenon (8). During the second trimester, fetal hiccups have not influenced the fetal heart rate (7). In term, hiccups have been related to a modest improvement in fetal heart rate (9), and, as such, it is considered a sign of fetal wellbeing. The best noninvasive indicator of fetal wellbeing in clinical practice remains fetal heart rate (FHR) monitoring through Cardiotocography (CTG) monitoring, which has been recently advanced by the computerized CTG (cCTG) analysis, thus improving fetal surveillance. Normal FHR baseline is indicated as normal in the ranges of 110 to 160 beats per minute (bpm) (10). Computerized CTG is an automatic analysis tool that provides further diagnostic criteria and objective parameters: the baseline fetal heart rate (Basal FHR), the accelerations and decelerations, the long-term FHR variation (LTV), the short-term FHR variation (STV), the episodes of high/low FHR variation, and the number of fetal movements for an hour (FM) (11). We hypothesize the possible analytical correlation between the presence of the fetal hiccups and the maternal perception of the fetal movements can be identified and so applied for future fetal well-being monitoring.

MATERIALS AND METHODS

Subjects and assessment

This prospective observational study was conducted between April 01, 2019, and March 01, 2020, in a single University tertiary care Center. Fifty-one pregnancies were enrolled (**table I**), we included nonlaboring term singleton pregnancies (37 0/7 - 41 6/7 weeks of gestation), who were referred for the fetal antepartum surveillance to the outpatient clinic of the "Obstetrics and Gynecology Unit, AOU Luigi Vanvitelli, University of Campania Luigi Vanvitelli of Naples (Italy)". Gestations complicated by fetal malformations, stillbirths, preterm deliveries, maternal comorbidity (12) or patients with missing data were excluded. For each patient, data on demographics and pregnancy information, including maternal age, maternal height and weight, body-mass index (BMI), gestational age (GA) at delivery, gravity, parity, and smoking, were collected. GA was determined according to the first-trimester ultrasound exam. A cCTG was carried out for each patient using a Sonicaid Team 3 (Huntleigh Healthcare Ltd, Cardiff, United Kingdom) computerized cardiotocography machine. External cCTG was performed at least 20 minutes (maximum 60 minutes), with two transducers fixed on the maternal abdomen: one above the fetal heart level and the other one at the uterine fundus. When evaluating cCTG data, the following measures were assessed: basal FHR (beats per

minute), number of accelerations and decelerations, LTV (minutes), STV (milliseconds), episodes of high/low FHR variation in minutes, and number of FM for an hour (13). Only one tracing per fetus was included. We chose the last tracing before the onset of labor, which occurred within 24 hours. To evaluate the maternal fetal hiccups perception, a trained clinician (M.L.V.) administered an *ad hoc* questionnaire focusing on fetal hiccups perception in the last two weeks to all patients, who took approximately 15-30 minutes to complete it. The questionnaire included if the mother felt the fetal hiccup's presence and, if present, its intensity and frequency, *i.e.*, if the hiccups were perceived daily, occasionally (from two episodes to almost daily perception), or if it was perceived one time only. If one of these questions was not clear for the mother and unable to answer it satisfactorily, it was reported as "does not know". Based on the answers from this questionnaire, we divided our population into three groups: no fetal hiccups perception (G1); occasionally (not daily) fetal hiccups perception (G2); and daily maternal perception (G3). The different parameter of computerized analysis of fetal heart rate (FHR, LTV, STV, episodes of high/low FHR variation in minutes, acceleration and deceleration and FM) were evaluated in each group.

Ethical approval

The confidentiality of all participants was maintained during the whole experimental procedure. Ethical approval was not required since the study was classified as a hospital audit of current clinical practice. The study was registered on www.clinicaltrials.gov database (ID no. NCT04366076) and performed according to the "Strengthening the Reporting of the Observational studies in Epidemiology" (STROBE) guidelines (14).

Sample size

According to available literature, assuming an *a priori* calculation of the minimum sample size to report a significant difference between groups, given 80% power and an alpha level of 0.05, including a 9% opt-out rate, a minimum of 42 women was necessary.

Table I. *Clinical and demographic characteristics of the three groups of women enrolled.*

	No perception (n = 25) (G1)	**Occasionally (n = 14) (G2)**	**Daily (n = 10) (G3)**		
					p-value
Maternal age (years)					
Median, DS	31.1 ± 7.1	34.6 ± 5.6	33.3 ± 7.2	G1 *vs* G2	0.28
Range	18-42	21-43	19-46	G2 *vs* G3	0.87
				G3 *vs* G1	0.67
Body mass index, kg/m^2				G1 *vs* G2	0.22
Median, DS	30.6 ± 6.5	27.5 ± 4.2	26.6 ± 2.9	G2 *vs* G3	0.90
Range	21-50	22-34	23-30	G3 *vs* G1	0.12
Smokers,	4	2	0	G1 *vs* G2	0.97
				G2 *vs* G3	0.56
				G3 *vs* G1	0.39
GA at cCTG,					
weeks, DS	39.1 ± 1.1	39.2 ± 0.6	39.1 ± 1.2	G1 *vs* G2	0.93
range	37.1-40.6	37.1-39.2	37.1-40.4	G2 *vs* G3	0.95
				G3 *vs* G1	0.99
Birth weight, gr					
Median, DS	3,152 ± 859	3,146 ± 567	3,204 ± 455	G1 *vs* G2	0.99
Range	1,900-5,280	2,350-4,070	2,510-3,730	G2 *vs* G3	0.98
				G3 *vs* G1	0.98
Fetuses					
Male	9	4	7	NS	
Female	16	10	5		
Maternal comorbidities					
Gestational Diabetes	4	1	2	NS	
Intrauterine growth restriction	3	3	2		
Pre-eclampsia	2	0	0		
Macrosomia	0	0	0		
Total	9	4	4		

GA: gestational age; cCTG: computerized Cardiotocography.

Statistical analysis

Parametric or non-parametric statistics were used, as appropriate. Namely, the multivariate analysis combined the cCTG parameters to correct for potential confounders during data analysis. The independent variables observed were the following: baseline FHR, number of accelerations and decelerations, episodes of high/low FHR variation in minutes, LTV (min), STV (ms), signal loss (%), and FM. The binary outcome was represented by fetal hiccups (present *vs* absent). The multivariate analysis joined together the cCTG results to correct for potential confounders during data analysis.
All variables are displayed as the means ± standard deviation. Data were compared using a one-way analysis of variance test (ANOVA) followed by the Tukey's honestly significant difference (HSD) test. A P-value (p) < 0.05 was used to indicate a statistically significant difference. Stata 14.1 (Stata corp., College Station, TX, 2013) was used for all data analysis.

RESULTS

Fifty-one pregnancies were initially enrolled (**table I**). Based on the maternal fetal hiccups perception during the last two weeks, the G1 group consisted of 25 women, the G2 of 14 women, and the G3 of 10 women. From the original sample of 51 patients, two were excluded because they were unable to provide any information about the hiccups perception. As shown in **table I**, there could not significative difference between maternal age, BMI, GA, fetal sex, and maternal comorbidity between the three groups. The maximum interval between cCTG and delivery was 24 hours. In order to evaluate whether the fetal weight might have produced a bias, we recorded the fetal weight at the delivery, and no significant difference between the groups was observed. The analysis of cCTG parameters between the three groups showed no significant difference in the percentage of signal loss, baseline FHR, number of accelerations and decelerations, episodes of high/low FHR variation, LTV, and STV at both univariate and multivariate analysis (**table II**). Conversely, we found a statistically significant difference for the number of FM in an hour between the group of daily perception (G3) compared to the group of no perception (G1) (72 *vs* 37 FM, p < 0.05). This statistically significant difference was also confirmed by the multivariate analysis (**table III**).

DISCUSSION

Counting fetal movements is a popular approach used to prevent stillbirths. In addition to fetal movements count, the maternal fetal hiccups perception is usually applied. Nevertheless, limited knowledge about its role in healthy pregnancies is available. Fetal hiccups seem to be shared in primates, but their origin and meaning remain unknown (15). Several theories have been proposed to explain hiccups in fetal life, including respiratory muscles' development, providing the infant for suckling and controlling amniotic fluid in early gestation (15, 16). Some studies reported the qualitative and quantitative aspects of fetal function through continuous real-time ultrasound observations and demonstrated that the fetal hiccups happened episodically with a fluctuating incidence (17-19). A study revealed its increase in maternal perception of fetal hiccups, probably due to a better maternal perception in late gestation (20). Additional researches have focused on the natural aspect of fetal hiccups and its relationship with reduced risk of late stillbirth (21, 22). In this scenario, the present study suggests that the daily perception of the fetal hiccups might be related to an increased number of fetal movements, measured by the cCTG, which seem to be almost twice compared to mothers with no fetal hiccups perception. Given the lack of previous evidence on this topic, this study's finding might significantly support clinicians in screening pregnant women with a real decrease in fetal activity. As such, fetal daily hiccups perception might be considered a marker of normal fetal activity and fetal well-being (23, 24). This study's strength is the prospective design, which allows detailed reporting information on the maternal perception of fetal hiccups concerning the cCTG. Moreover, the assessment of fetal hiccups was performed by an expert physician in order to minimize the maternal questionnaire bias. Another strength was the attempt to reduce the heterogeneity of demographic characteristics of the sample by considering several factors (GA at the cCTG, smoking, age (25), BMI (26), fetus sex, and all maternal comorbidity (27-31). Further, in order to exclude bias related to the fetal size (32), we recorded all the fetal weights at the birth. Finally, this study's peculiarity is the use of cCTG to objectively estimate the real number of fetal movements and all the other cCTG parameters. Several previous publications,

Table II. *Report of maternal fetal hiccups perception during the last two weeks.*

	No perception (n = 25) (G1)	Occasionally (n = 14) (G2)	Daily (n = 10) (G3)		
					p-value
cCTG Duration time, min					
Median, DS	42 ± 17	40 ± 16	40 ± 15	G1 *vs* G2	0.91
Range	20-60	20-60	20-60	G2 *vs* G3	1.00
				G3 *vs* G1	0.92
Signal loss, %					
Median, DS	3.4 ± 4.8	1.6 ± 2.6	5.1 ± 6.7	G1 *vs* G2	0.55
Range	0-20.6	0-8.7	0-18.8	G2 *vs* G3	0.22
				G3 *vs* G1	0.62
FHR, bpm					
Mean, DS	131 ± 7	136 ± 9	129 ± 8	G1 *vs* G2	0.15
Range	121-149	120-150	119-143	G2 *vs* G3	0.09
				G3 *vs* G1	0.77
FM, 1 h					
Mean, DS	37.3 ± 26.2*	42.7 ± 50	72.7 ± 44.6*	G1 *vs* G2	0.90
Range	7-107	4.1-178	21-161	G2 *vs* G3	0.15
				G3 *vs* G1	0.042*
Accelerations, n.					
Mean, DS	9.2 ± 5.9	8.8 ± 6.4	10.5 ± 6	G1 *vs* G2	0.98
Range	0-25	3-24	2-19	G2 *vs* G3	0.79
				G3 *vs* G1	0.84
Decelerations, n.					
Mean, DS	0.1 ± 0.3	0.2 ± 0.5	0 ± 0	G1 *vs* G2	0.68
Range	0-1	0-2	0-0	G2 *vs* G3	0.35
				G3 *vs* G1	0.69
Episode of high variation, n.					
Mean, DS	22.5 ± 13	22.0 ± 14.0	23 ± 14.1	G1 *vs* G2	0.99
Range	0-47	7-57	5-47	G2 *vs* G3	0.98
				G3 *vs* G1	0.99
Episode of low variation, n.					
Mean, DS	8 ± 13.3	9 ± 15.0	5.8 ± 6.8	G1 *vs* G2	0.96
Range	0-52	0-52	0-50	G2 *vs* G3	0.81
				G3 *vs* G1	0.88
LTV, ms					
Mean, DS	50.3 ± 15.9	50.6 ± 17.8	57.9 ± 13.2	G1 *vs* G2	0.99
Range	20-89	19-82	35-76	G2 *vs* G3	0.51
				G3 *vs* G1	0.41
STV, ms					
Mean, DS	9.6 ± 3.5	9.7 ± 3.3	11.8 ± 3.4	G1 *vs* G2	0.99
Range	3.9-21.9	4.9-14.1	7.1-18.6	G2 *vs* G3	0.32
				G3 *vs* G1	0.22

cCTG: computerized Cardiotocography; FHR: Fetal Heart Rate; FM: Fetal Movement; LTV: Long Term Variability; STV: Short Term Variability.

Table III. *Multivariate analysis on fetal movements for an hour.*

			95% CI		
Clinical feature	**B Coefficient**	**SE**	**Lower limit**	**Upper limit**	**p-value**
Age	- 0.137	0.974	- 2.098	1.824	0.889
Body-mass Index	- 2.040	1.217	- 4.492	0.410	0.101
Birth Weight	- 0.009	0.009	- 0.029	0.001	0.305
Gestational age	2.514	8.277	- 14.146	19.176	0.763

indeed, evaluated the importance of fetal movements in women with reduced frequency to prevent stillbirth (33-35), but none of them have been focused on fetal hiccups evaluated with cCTG parameters. This study's main limitations are the relatively small sample size and the lack of fetal outcomes and their correlation with the maternal perception of fetal hiccups.

CONCLUSIONS

Daily maternal perception of fetal hiccups correlated with a double number of fetal movements for an hour than women without perception. Adding support to the evidence that when fetal hiccups are present daily, the number of fetal movements can be adequate. Therefore, these women might not need to contact the maternity care provider. Further randomized and prospective studies are needed to replicate our findings in order to fully include the maternal perception of fetal hiccups in the management of fetal wellbeing.

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CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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