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Fetal Nasal Flow Doppler and Breathing Patterns for Prediction of Preterm Labor: A Prospective Cohort Study

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ABSTRACT

Background: *Expectation of preterm birth is very hard for obstetricians although there are various ways such as fetal fibronectin, different cytokines, cervical length measurement and elastography was implemented for this reason. Doppler might be used to evaluate fetal nasal fluid flow but this test was not made in expecting preterm labour til now.*

Aim: *To study the value of fetal breathing movement patterns and nasal flow Doppler in women with symptomatic preterm labor.*

Patients and Methods: *This prospective study was conducted at tertiary care hospital at Helwan University Hospital from April 2022 till October 2022 and performed on a total of 81 pregnant women at 28 to 37 weeks gestation with symptomatic preterm labor.*

Results: *During this study, 100 patients were assessed for eligibility and 81 patients were included in the study. Of all eligible patients, 12 patients were excluded from the study based on the inclusion criteria and 7 patients refused to participate in of the study. Ultimately, the analysis was based on the data of 81 pregnant women at 24 to 37 weeks gestation with symptomatic preterm labor. The current study revealed that the age, Body mass index, Gestational age, Cervical dilation and Cervical length was 27.4 ± 4.8 years, 29.4 ± 2.5 kg/m^2 , 31.2 ± 2.3 weeks, 3.3 ± 0.6 cm and 15.6 ± 2.2 mm respectively and 25.9% of cases were nulli parous. Our study results revealed that breath movement was not detected in (14.8%) of cases, was irregular in (17.3%), while it was regular in more than two thirds (67.9%) of cases and 44.4% of the studied cases had delivery within day 1 (24 hours).*

Conclusion: *Adding Doppler study to the upper respiratory tract tests could help in assessment of fetal nasal fluid flow. Inspiration/ expiration number ratio ≤1.12 had highest sensitivity and PPV in predicting delivery in day-1. As a result, only inspiration/expiration number ratio was related to higher possibility for preterm delivery.*

Keywords

Fetal breath movment, Fetal nasal flow Doppler.

Introduction

Preterm labor (PTL) is characterized by frequent uterine rhythmic contractions leading to cervical dilatation which begins before

37 weeks of gestation [1], About 6 to 10% of all pregnant womenworldwide experience preterm delivery [2], despite advances in health screening, there was no decrease in the rate of spontaneous preterm delivery. Therefore, it is highly important to be able to foresee the probability of spontaneous preterm birth at an earlier stage [3]. It is extremely important to predict and anticipate pregnant women having preterm labor) PTL) to save time for health staff and expectant mothers to take the appropriate steps. The mainstay is to transfer women who were predicted to have amenable preterm delivery to the nearest tertiary center with a well-equipped Neonatal Intensive Care Unit (NICU) [4].

It was found that the absence of FBM is considered a good predictor of premature birth in symptomatic patients. It was also found that the absence of breathing movement is more effective in predicting the occurrence of premature birth than cervical length and other biochemical markers within 48 hours or seven days [5]. As we know that the analysis of the fetal breathing patterns and its related Doppler measurements to predict premature birth are limited, and as regards to previous studies, the fetal breathing movement will decrease before birth, we will hypothesize that there will be distinctive patterns for these movements indicating the imminent occurrence of birth and we will investigate the use of fetal nasal flow Doppler as a predictive measure to anticipate preterm delivery [6].

Material & Methods

This prospective study was conducted at tertiary care hospital at Helwan University Hospital from April 2022 till October 2022 and performed on a total of 81 pregnant women at 28 to 37 weeks gestation with symptomatic preterm labor.

Study Population

Singleton pregnant patients aged 18–45 years old about 28 and 37 weeks of gestation diagnosed with preterm labor after informed consent is included in the analysis according to inclusion and exclusion criteria.

Inclusion Criteria

1. Women with ages: 18-45 years old 2. Body mass index (BMI): 20-35 kg/m2 3. Pregnant between 28-37 gestational weeks with symptomatic preterm labor: Uterine contractions ≥4 in number in 20 minutes or ≥ 8 in number in 60 minutes. 4. Cervical dilation: 2-5 cm 5. Transvaginal cervical length.

Study Procedure

1. An ultrasound unit (LOGIQ P5, GE ultrasound CO, Ltd, Korea) with a 3.5 MHz convex probe or 7.5 MHz endo- vaginal probe was used for the ultrasonographic routine assessment and measurements which done once at time of diagnosis.
2. The width of each fetal nostril was determined and the mean value was registered.
3. The presence of FBM was checked by both visual inspections of fetal diaphragmatic movements and by color Doppler of fluid movements through fetal nostrils. If both are present, a Doppler gate (2 mm) is placed on eithemostril while keeping the insonation/vessel angle less than 45° on the sagittal plane (if the sagittal plane is not possible due to fetal position a transverse nasal plane was used) and then spectral Doppler flow pattern was recorded for later offline analysis.
4. If there are five consecutive inspiration and expiration patterns and flow waveforms were identical, the breathing pattern would be classified as **'regular'.**
5. Flow waveform for regular inspiration and expiration patterns analysis was done and the following measurements will be performed: Mean inspiration duration, mean mean expiration duration, mean expiration peak velocity, mean expiration volume (Mean values were calculated from spectral analysis of five consecutive Primary outcomeinspiration peak velocity, mean inspiration volume regular breathing cycles), total breathing duration (inspiration + expiration), inspiration/ expiration peak velocity ratio and inspiration/ expiration.

If FBM was present but no regular FBM was recorded for Doppler analysis during a maximum period of 30 min of study, FBM would be graded as 'irregular' It would be classified as 'no FBM' if there was no FBM forthe entire duration of the Examination. Prediction of preterm labor by analysis of fetal nasal flow Doppler and breathing Patterns at time of presentation with symptoms of preterm labor.

Secondary outcome

1. Study and analyze fetal nasal flow Doppler measurementsin symptomatic PTL.
2. Relationship between FBM patterns and PTL within 24 hours and within 7 days.
3. Relation between fetal nostril width and PTL.

Statistical Analysis

The collected data was coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package forSocial Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013 and Microsoft Office Excel 2007.

Ethical approval

The study was approved by the Ethical Committees of Faculty of Medicine, Helwan University Hospital.

Results

This prospective study was conducted at tertiary care hospital at Badr Hospital from April 2022 till October 2022 and performed on a total of 81 pregnant women at 24 to 37 weeks gestation with symptomatic preterm labor. During this study, 100 patients were assessed for eligibility and 81 patients were included in the study. Of all eligible patients, 12 patients were excluded from the study based on the inclusion criteria and 7 patients refused to participate in of the study. Ultimately, the analysis was based on the data of 81 pregnant women at 24 to 37 weeks gestation with symptomatic preterm labor. The current study revealed that the age, Body mass index, Gestational age, Cervical dilation and Cervical length This prospective study was conducted at tertiary care hospital at Badr Hospital from April 2022 till October 2022 and performed on

a total of 81 pregnant women at 24 to 37 weeks gestation with symptomatic preterm labor. During this study, 100 patients were assessed for eligibility and 81 patients were included in the study. Of all eligible patients, 12 patients were excluded from the study based on the inclusion criteria and 7 patients refused to participate in of the study. Ultimately, the analysis was based on the data of 81 pregnant women at 24 to 37 weeks gestation with symptomatic preterm labor. The current study revealed that the age, Body mass index, Gestational age, Cervical dilation and Cervical length.

Table 1: Comparison according to time of delivery regarding fetal nostril width and breath movement among the studied cases.

Pattern	**No movement**	11 (30.6%)	1 (2.2%)	**#<0.001***
	Irregular	9 (25.0%)	5 (11.1%)	
	Regular	16 (44.4%)	39 (86.7%)	
Mean nostril width (mm)		4.1 ± 1.0	3.8 ± 0.6	^0.111
Mean inspiration duration (minutes)		471.1 ± 125.1	504.3 ± 116.0	^0.271
Mean expiration duration (minutes)		413.8 ± 125.1	449.5 ± 115.8	^0.237
Inspiration/ expiration duration ratio		1.16 ± 0.09	1.13 ± 0.05	^0.102
Total breathing duration (minutes)		885.0 ± 250.0	953.8 ± 231.5	^0.253
Mean inspiration peak velocity (mL/sec)		17.0 ± 4.7	19.3 ± 6.2	^0.108
Mean expiration peak velocity (mL/sec)		12.9 ± 4.8	15.0 ± 6.2	^0.136
Inspiration/expiration peak velocity ratio		1.40 ± 0.27	1.39 ± 0.34	^0.887
Mean inspiration volume (mL)		11.2 ± 4.2	12.5 ± 4.1	^0.220
Mean expiration volume (mL)		9.8 ± 4.2	11.1 ± 4.1	^0.214
Inspiration/ expiration number rate		1.06 ± 0.30	1.23 ± 0.20	**^0.014***

Table show that: No statistical significant differences according to time of delivery regarding fetal nostril width and breath movement except no/irregular movement; were significantly more frequent in cases with delivery in day-1 as well as Inspiration/ expiration number rate; was significantly lower in cases with delivery in day-1.

Expectation of preterm birth is very hard for obstetricians although there are various ways such as fetal fibronectin, elastography, different cytokines, cervical length dimension was implemented for this reason [7]. Although there was a previous systematic review that compared data about various tests could have a role in the short-term prediction of preterm birth in women with signs and symptoms of preterm labor, but this systematic review did not evaluate the diagnostic accuracy of these investigations in depth. Doppler might be used to evaluate fetal nasal fluid flow but this test was not made in expecting preterm labour til now [8].

Table 2: Fetal nostril width and breath movement among the studied cases.

Variables		**N**	**%**
Pattern	**No movement**	12	14.8%
	Irregular	14	17.3%
	Regular	55	67.9%
		Mean ± SD	**Range**
Mean nostril width (mm)		4.0 ± 0.8	3.0–6.0
Mean inspiration duration (minutes)		492.3 ± 119.5	227.0–729.0
Mean expiration duration (minutes)		436.6 ± 119.6	153.0–674.0
Inspiration/ expiration duration ratio		1.14 ± 0.07	1.06–1.48
Total breathing duration (minutes)		928.8 ± 238.9	380.0–1403.0
Mean inspiration peak velocity (mL/ sec)		18.5 ± 5.7	6.9–34.1
Mean expiration peak velocity (mL/sec)		14.3 ± 5.8	2.4–29.3
Inspiration/expiration peak velocity ratio		1.39 ± 0.31	1.15–2.88
Mean inspiration volume (mL)		12.0 ± 4.2	2.5–21.8
Mean expiration volume (mL)		10.6 ± 4.2	1.0–20.5
Inspiration/ expiration number rate		1.17 ± 0.25	0.45–1.68

Table 2 show that: Fetal nostril width and breath movement among the studied cases. Breath movement was not detected in (14.8%) of cases, was irregularin (17.3%), while it was regular in more than two thirds (67.9%) of cases.

Table 3: Fetal nostril width and breath movement among thestudied cases.

Variables	**AUC**	**SE**	**p- value**	**95% CI**
Mean nostril width (mm)	0.566	0.065	0.311	0.438–0.694
Mean inspiration duration (minutes)	0.567	0.072	0.356	0.426–0.709
Mean expiration duration (minutes)	0.575	0.072	0.303	0.434–0.716
Inspiration/ expiration duration ratio	0.604	0.069	0.153	0.469–0.740
Total breathing duration (minutes)	0.572	0.072	0.321	0.431–0.713
Mean inspiration peak velocity (mL/sec)	0.613	0.068	0.122	0.479–0.746
Mean expiration peak velocity (mL/sec)	0.598	0.069	0.180	0.463–0.733
Inspiration/expiration peak velocity ratio	0.560	0.071	0.414	0.420–0.699
Mean inspiration volume (mL)	0.543	0.073	0.553	0.400–0.686
Mean expiration volume (mL)	0.545	0.073	0.537	0.402–0.688
Inspiration/ expiration number rate	0.665	0.070	**0.023***	0.528–0.802

Table 3 show that: Fetal nostril width and breath movement statistically had no significant diagnostic performance in predicting delivery in day-1 except Inspiratin/ expiratioon number rate, significantly had low diagnostic performance.

In the current study, as regards the time of delivery, results revealed that no/irregular breathing movement was significantly more frequent in cases with delivery in day-1 (p=0.014). In concordance with our results, Esin et al. [2], reported that the time interval between admission to delivery was statistically different between FBM present patients (Group 2 and Group 3) when compared to FBM absent patients (Group 1). Also, in the present study, there was a statistically significant difference in nasal width measurement between FBM present patients (Group 2 and Group 3) when compared to FBM absent patients (Group 1). The comparisons of sensitivity and specificity amongst the 3 tests showed no statistically significant differences in predicting delivery within 48 hours and within 7 days. However, FBM at 48 hours showed statistically significant better specificity than fFN and TVS (P = 0.024 and P = 0.046 for fFN and TVS, respectively). Similarly, the specificity of FBM at 7 days was statistically greater than the other 2 modalities (P = 0.0000 and P = 0.0005 for fFN and TVS, respectively Also, Honest et al. [9] conducted a systematic reviewand diagnostic meta-analysis to determine the accuracy with which the absence of fetal breathing movements on ultrasound examination predicts spontaneous preterm birth and revealed that absence of fetal breathing movements was accurate in predicting birth within 48 h or within 7 days of testing inwomen who present with threatened preterm labor. The points of strength in the current study is that is a prospective research with no lost follow up ladies and it is considered the first research to reach a cut off for inspiration/expiration rate in a regular formFBM to expect delivery in this group of women. To be able to distinguish if there are FBM or not and to compare between irregular and regular FBM, you have to do a thorough scan to the fetus [10]. As regards the diagnostic accuracy, our study results revealed that No breath movement had highest specificity and PPV, while Inspiration/ expiration number ratio ≤1.12 had highest sensitivity and PPV in predicting delivery in day-1. Over all Diagnostic accuracy and Youden's index were highest in No/irregular breath movement and Inspiration/ expirationnumber ratio ≤1.12.

These results are in agreement with results of previous studies done by Esin et al. [2] who reported that the sensitivity rate, specificity rate, positive and negative predictive values were 88.2%, 42.9%, 42.9% and 88.2%, respectively. The diagnostic accuracy rate was 57.6% at this point of 1.25. By using fetal nasal Doppler, combination of absence of FBM or irregular FBM or regular FBM with I/E<1.25 detects 94.6% of patients who will eventually deliver in the first 24 h after admission. Boots et al. [11] conducted a systematic review and meta-analysis to test the precision of fetal fibronectin (fFN), (FBM), and cervical length (CL) for the short-term guess of preterm birth in symptomatic women and showed that the pooled sensitivity and specificity of fetal breathing movements for prediction of preterm labor within 48 hours of testing were 0.75 (95% CI, 0.57-0.87) and 0.93 (95% CI, 0.75-0.98) respectively and within 7 days of testing were 0.67 (95% CI, 0.43-0.84) and 0.98 (95% CI, 0.83-1.00) respectively.

Conclusion

Adding Doppler study to the upper respiratory tract tests could help in assessment of fetal nasal fluid flow. Inspiration/ expiration number ratio ≤1.12 had highest sensitivity and PPV in predicting delivery in day-1. As a result, only inspiration/expiration number ratio was related to higher possibility for preterm delivery.

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