Diagnostic Performance of a Modified Biophysical Profile for Fetal Acidemia in High-Risk Pregnancies

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Objective : *To determine the diagnostic performance of NST, AFI and modified-BPP for screening fetal acidemia in high-risk pregnancies.*
Design : *Diagnostic tests.*
Setting : *Srinagarind (tertiary) Hospital, Faculty of Medicine, Khon Kaen University.*
Material and Method : *Between April 2000 and August 2001, we included 185 high risk singleton pregnancies, GA> 37 weeks, with NST and AFI once a week until delivery. Immediately after delivery, the umbilical artery blood gases were evaluated. Fetal acidemia was defined as an umbilical artery pH < 7.15. An abnormal modified-BPP was identified when either the NST was non-reactive or the AFI was ≤ 5 cm.*
Results : *Thirteen high risk pregnancies were excluded because the last test was more than 7 days before delivery. Of the remaining 172 pregnancies, total fetal acidemia was identified in 19 cases. The incidence of fetal acidemia was 11.05% (95% CI 6.63-15.73). Among the 19 cases, eight had non-reactive NST, and 11 had AFI ≤ 5 cm but 14 with abnormal modified-BPP. The sensitivity of NST, AFI and modified-BPP was 42.11% (95% CI 34.73-49.48), 57.89% (95% CI 50.52-65.27), and 73.68%. (95% CI 67.10-80.27), respectively. The specificity, PPV, NPV, accuracy of NST, AFI and modified-BPP were high but not statistically different.*
Conclusion : *The modified-BPP had a significantly higher sensitivity than NST or AFI alone in screening for fetal acidemia, so a modified-BPP should be used to screen for fetal acidemia in high-risk pregnancies.*

Keywords : *Modified biophysical profile, Non-stress test, Amniotic fluid index, Fetal academia.*

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Two mechanisms indicate a fetal response to hypoxia and acidosis:[1] 1) "Acute fetal adaptive response," which can be detected by changes in heart rate, breathing, movement and power of movement; and, 2) "Chronic fetal adaptive response, "which increases blood flow to vital organs, results in decrease amniotic fluid and retardation of fetal growth. Hypoxia and acidosis also cause neonatal respiratory distress and postpartum infective enteritis.

Early diagnosis of fetal acidosis improves the success of treatment. According to the ACOG guidelines, fetal monitoring includes counting movement and measuring the heart rate[2]. Each method has both advantages and disadvantages. Counting fetal movement is inexpensive, simple, convenient and the mother can perform the test herself. The downside is a lack of sensitivity because mother is not always conscious of all the fetal movement.

The most common type of test for fetal heart rate is the nonstress test (NST), which measures the change in fetal heart rate in response to fetal movement. Since heart rate is a good indicator of the fetal autonomous nervous system, if there is no heart rate response, it could mean that the fetus is asleep or the central nervous system (CNS) is suppressed. One possible cause of CNS suppression is acidemia. There is no contraindication for NST and it is a reliable predictor of good fetal health for the coming week; however, it is costly and requires an experienced interpreter.

The biophysical profile (BPP) is a test which includes both acute and chronic fetal adaptive responses to acidemia. The acute adaptive responses

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measured include the change in fetal heart rate, respiration, fetal movement and muscle tension. The chronic adaptive response includes the reduction of amniotic fluid, measured by the amniotic fluid index.

Vinzileo *et al* (1991)[3] found that a change in heart rate was the first response to fetal acidosis. Later when the acidemia increased, fetal movement was also affected. Consequently, the use of a modified-BPP, which includes the nonstress test (NST) and amniotic fluid index (AFI), is proposed. AFI is a measure of amniotic fluid volume using ultrasound, which can be performed with a less training.

Seelbach-Gobel *et al* (1999)[4] found that pregnant women at between 37 and 42 weeks gestation with prolonged low fetal oxygen saturation is significantly related to an umbilical artery pH < 7.15; therefore, this study used an umbilical artery pH < 7.15 as the indication of fetal acidemia.

This study sought the sensitivity, specificity, positive and negative predictive values, and accuracy of the NST, AFI and modified biophysical profile as clinically useful tests for evaluating fetal acidemia.

Material and Method

Using the Helsinki Declaration, the Human Ethics Committee of Khon Kaen University approved the protocols used in this study. Data were gathered from 185 pregnant women who had high-risk singleton pregnancies at ≥ 37 weeks with no premature rupture of the amniotic sac. These women had their prenatal care and delivery at Srinagarind Hospital, Khon Kaen Thailand, between April 1, 2000 and August 31, 2001.

The inclusion risk factors comprised poor maternal weight gain (less than 1,000 g. per month or less than 11.5 kg. throughout pregnancy), decreased fetal movement by maternal perception (less than 10 movements per day), postterm pregnancy (pregnancy reach 42 completed weeks), maternal anemia ,diabetes mellitus (DM), hypertension, teenage pregnancy, elderly gravida (maternal age over 35) and small for the gestational age. All of these pregnancies received weekly NST and AFI tests on their prenatal care visits until deliveries.

Patients were excluded if the presence of fetal anomalies was detected or their last visit was more than seven days. All pregnancies were examined by the same physician using the same equipment.

The NST fetal monitor used in this study was the Corometrics R fetal monitor model 150. The semi-Fowler position (at 30-45) was used with the mother lying slightly on her left side. Maternal blood pressure was checked before the examination. The fetal heart rate was monitored with a Doppler ultrasound transducer. Uterine contractions were measured with a tocodynamometer and the mother pressed the switch every time she felt fetal movement, which was recorded for 20 minutes[5].

If the fetal heart rate increased at least 15 beats/minute for two or more accelerations each lasting 15 seconds or more ,the test was terminated as 'reactive'. If there was non-reactive pattern, the fetus was stimulated with acoustic vibrator over the region of the fetal head. The test was continued for the next 20 minutes; if there was still non-reactive pattern, the test was interpreted as 'non-reactive'.

The AFI was measured with an ALOKA high frequency ultrasound model SSD-2000 using a 3.5-MHz probe[6]. The mother was examined while lying on her back. Using an imaginary transverse across the umbilicus and the *linea nigra*, the uterus was partitioned into quadrants. In each quadrant, the probe was placed parallel to the *linea nigra* and perpendicular to the floor. The deepest vertical position, excluding the umbilical cord or any other parts of the fetus, in each quadrant was summed to obtain the AFI. The measurement was interpreted at the time of examination. If the AFI was ≤ 5 cm, it was interpreted as abnormal.

If the result from either one or both of the tests was abnormal, the mother had an 'abnormal' modified BPP and was admitted for observation in the delivery room and treatment, by judgement of obstetricians, which include repositioning of patient, oxygen administration and intravenous dextrose-saline infusion. When the result of treatment was not improved, termination of pregnancy was considered. The route of delivery was judged by obstetricians. If both tests were normal, the next regular appointment was made and mothers were sent home. The same tests were done weekly until delivery.

After delivery and before cutting the cord, a sample of fetal blood was obtained from the fetal side of the umbilical artery using the double-clamp technique. Blood gases were measured within 10 minutes. If the pH of the blood from the fetal umbilical cord was < 7.15[4], fetal acidemia was interpreted.

Statistics were done using SPSS version 10.0 and STATA 6.

Results

Of the 185 patients, 13 were excluded because their NST and AFI were performed more than 7 days

before their last visit. We found that among the 172 high risk pregnancies the mean maternal age was 27.6 years, range15-43 years. Most were the first and second pregnancies, 75 and 68 patients respectively. 21 were on their third pregnancy, and 8 were on more than their third pregnancy. The most common risk factors were poor maternal weight gain, maternal age over 35, and decreased fetal movement (Table 1). Some women had many risk factors.

The rank of delivery modes was spontaneous, cesarean, forceps and vacuum extraction and of these 8.1, 13, 20 and 16.7 percent, respectively, had fetal acidemia. (Table 2) Of the 46 cesarean deliveries, fetal distress was indicated in 11 and 4 (36%) of these had fetal acidemia; and all of these had an abnormal modified-BPP. Among the cesareans done for other indications, 2 of the 35 had fetal acidemia (6%) and both had an abnormal modified-BPP. All 6 cesareans with fetal acidemia had been performed under general anesthesia.

The common complication was fetal distress before delivery and the Apgar score at 1 minute was < 7, and the birth weight was < 2500 g. There was one fetal death and the umbilical artery pH was 6.83 (Table 3). The maternal risks in this case were high maternal age, DM and decreased fetal movement at the 37th week. The causes of fetal death were fetal chronic hypoxia and acidosis. In cases of fetal distress before delivery, 36% had fetal acidemia. In cases with an Apgar score at 1 minute < 7, 41.3% had fetal acidemia. None of the infants with a birth weight < 2500 g had fetal acidemia. Some of the infants had more than one complication. The birth weight averaged 3128.5 g (maximum 4330 g; minimum 1590 g). In total, 19 cases had fetal acidemia (incidence = 11.05). From the 14 cases of non-reactive NST, 8 had fetal acidemia. Among the 18 cases with an AFI < 5 cm, 11 had fetal acidemia. Among the 25 cases with an abnormal modified-BPP, 14 had fetal acidemia.

The sensitivity of each test for assessing fetal acidemia were: NST 57.9%, AFI 42.1%, and for modified-BPP 73.7% (*i.e.* modified-BPP had a significantly higher sensitivity with a 95% CI 67.1-80.3). All three methods gave a high specific negative predictive value and accuracy up to 90%. The positive predictive values were low for all three methods due to the low incidence of fetal acidemia (*i.e.* 11.1%).

Table 1. Risk factors during prenatal care

	Risk Factors	Number (%)
Poor maternal weight gain	101	36.9
Maternal age more than 35	33	12.0
Decreased fetal movement	26	9.5
Maternal anemia from thalassemia	19	6.9
Postterm pregnancy	17	6.2
Teenage pregnancy	13	4.7
Pregnancy with diabetic complications	12	4.4
Pregnancy with hypertensive complications	8	2.9
Fetal growth lower than normal gestational growth	4	1.5
Others	41	15.0
Total	274	100

Table 2. Relationship between the mode of delivery and fetal acidemia

	Mode of delivery	Number	Fetal acidemia (%)
Spontaneous	99	8	8.1
Cesarean section	46	6	13.0
Forceps	15	3	20.0
Vacuum	12	2	16.7
Total	172	19	11.0

Table 3. Relationship between infant complication and fetal acidosis

Result of delivery	Number	Fetal acidemia	(%)
Normal	129	7	5.4
Fetal death	1	1	100.0
Fetal distress	25	9	36.0
Apgar scores 1 min < 7	12	5	41.7
Low birth weight (< 2,500 g)	12	0	0.0
Admit NICU	6	2	33.3

Discussion

We found that an abnormal modified biophysical profile had a high specificity, accuracy, and negative predictive value, but a low positive predictive value because the incidence of fetal acidemia was low (11.1%). When comparing with NST or AFI alone, the modified-BPP had a significantly higher sensitivity (95% CI 67.1-80.3).

The results of the study should be reliable because: 1) the same population was used to test both the NST and AFI; 2) the same examiner and equipment were used, thus reducing inter-observer variation[7];

Table 4. Relationship between NST, AFI and modified BPP and umbilical artery pH

	pH < 7.15	pH ≥ 7.15	Total
NST			
Non-reactive	8	6	14
Reactive	11	147	158
AFI			
≤ 5 cm.	11	7	18
> 5 cm.	8	146	154
Modified BPP			
Abnormal	14	11	25
Normal	5	142	147

Table 5. Diagnostic performance of NST, AFI and modified BPP

	NST	AFI	Modified BPP
Sensitivity (%)	42.1	57.9	73.7
(95% CI)	(34.7-49.5)	(50.5-65.3)	(67.1-80.3)
Specificity (%)	96.1	95.4	92.8
(95% CI)	(93.2-99.0)	(92.3-98.6)	(89.0-96.7)
PPV (%)	57.2	61.1	56.0
(95% CI)	(49.8-64.5)	(53.8-68.4)	(48.6-63.4)
NPV (%)	93.0	94.8.	96.6
(95% CI)	(89.2-96.8)	(91.5-98.1)	(93.9-99.3)
Accuracy (%)	90.1	91.3	90.7
LR+	10.7	12.7	10.3
LR-	0.6	0.4	0.3
Incidence (%)	11.1 (6.4-15.7)		

LR+ : Likelihood ratio of a positive test result
LR- : Likelihood ratio of a negative test result

3) the sample size was adequate; and, 4) a specific cut-off point (umbilical artery pH < 7.15) was used to define fetal acidemia. Moreover, Piazze *et al* (2000)[8] also used a modified-BPP in predictive of fetal acidemia and even though they used different criteria for fetal acidemia (*i.e.* an umbilical artery pH < 7.2), they observed a similar sensitivity of 80%.

We included postterm pregnancy as one of our inclusion criteria. In postterm pregnancy, the amniotic fluid might decreased to < 5 cm;[9] however, the fetal acidemia in these cases might not occur depending on the functionality of the placenta. Among 17 postterm pregnancies, 3 had an AFI < 5 cm and all had fetal acidemia. Among the 14 with a normal AFI, only one had fetal acidemia - perhaps because of intrapartum placental insufficiency.

This study did not exclude any particular delivery mode. Of the 99 spontaneous deliveries, 8 had fetal acidemia, 6 of which had an abnormal modified-BPP, resulting in a rate of 8%. Among the cesareans with fetal distress, all of the fetuses with fetal acidemia had an abnormal modified-BPP and the 2 cesareans with fetal acidemia done for other indications also had an abnormal modified-BPP. In forceps deliveries, 3 cases had fetal acidemia: 2 had an abnormal modified-BPP, and one with a normal modified-BPP was a breech birth.

In breech deliveries, the head of the fetus is stuck in the birth canal longer, so the possibility of cord compression is a concern. It is possible that a vaginally delivered breech birth has fetal acidemia. Since this could cause a false positive result, breech delivery should be excluded in future studies.

Among 12 cases of vacuum deliveries, 2 had fetal acidemia and non of them had abnormal modified-BPP, vacuum deliveries probably cause stress to the fetuses and subsequent fetal acidemia.

Epidural anesthesia could reduce uteroplacental blood flow and cause changes in the fetal acid-base balance. Sendag *et al.* (1999)[10] compared epidural anesthesia and general anesthesia and found that epidural anesthesia was correlated to a lower umbilical artery pH than general anesthesia, especially at pH < 7.19. The study also found that the number of infants with fetal acidemia was significantly higher in the epidural block than in the spinal block group. When each of these groups was compared to general anesthesia, the group with spinal anesthesia had an OR of 4.7(95% CI 2.7-8.0) and the group with epidural anesthesia had an OR of 2.4 (95% CI 1.4-4.4).

In our study, of the 46 cases delivered by cesarean all 6 with fetal acidemia were done under general anesthesia and all 6 had an abnormal modified-BPP. Therefore, acidemia in these cases was unlikely the result of general anesthesia but rather it was a pre-existing fetal acidemia.

Andes *et al* (1999)[11] defined pathological fetal acidemia as a condition in which the fetal umbilical artery pH is < 7 and has metabolic complications (*i.e.* a base deficit or low bicarbonate) regarding the PO_2 value. We had one fetal death. The maternal risks in this case were high maternal age, DM and decreased fetal movement at the 37th week. The modified-BPP was abnormal and the umbilical artery pH was 6.83, which was considered to be pathological fetal acidemia.

Casey *et al* (2000)[12] found that decreased amniotic fluid was correlated to fetal death *in utero*, aspiration of amniotic content during delivery, NICU,

admission and infant death. They found that an AFI < 5 cm had a specificity and negative predictive value > 90% in assessing fetal acidemia (pH < 7.15), but a sensitivity of only 58%. Therefore, other tests are needed to improve sensitivity in determining fetal acidemia.

Casey *et al* (2001)[13] found that pH values at birth, and 2 hours after birth, < 7.2 predicted neonatal health. The use of the Apgar score alone is insufficient in evaluating birth asphyxia. They suggested that correcting postpartum acidosis helped improve neonatal health. Modified-BPP can help in assessing neonatal health so that timely intervention and immediate postpartum treatment can be administered.

The modified-BPP has high sensitivity, specificity and accuracy and is easy to perform: we recommend it be used as frontline screening of high-risk pregnancies.

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การใช้ค่าดัชนีน้ำคร่ำและการตอบสนองของอัตราการเต้นของหัวใจทารก เพื่อประเมินภาวะเลือดเป็นกรดของทารกในครรภ์ที่มีความเสี่ยงสูง

โกวิท คำพิทักษ์, อรพิน เฟื่องทวีโชค

วัตถุประสงค์ *: เพื่อศึกษาความไวของการใช้ค่าดัชนีน้ำคร่ำ (AFI) การตอบสนองของอัตราการเต้นของหัวใจทารก (NST) และการตรวจทั้งสองอย่าง (Modified biophysical profile) ในการประเมินภาวะเลือดเป็นกรดของทารกในครรภ์ที่มีความเสี่ยงสูง*

รูปแบบการวิจัย *: เป็นการวิจัยชนิด "Diagnostic Test"*

สถานที่ทำการวิจัย *: ห้องฝากครรภ์และห้องคลอด โรงพยาบาลศรีนครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น*

กลุ่มตัวอย่าง *: สตรีตั้งครรภ์ที่มีความเสี่ยงสูง เป็นครรภ์เดี่ยวและอายุครรภ์มากกว่าหรือเท่ากับ 37 สัปดาห์ ที่มาฝากครรภ์และคลอดที่โรงพยาบาลศรีนครินทร์ ตั้งแต่ 1 เมษายน 2543 ถึง 31 สิงหาคม 2544 จำนวน 185 ราย และไม่มีภาวะถุงน้ำคร่ำแตกก่อนการตรวจ ทารกไม่มีความพิการหรือเสียชีวิตตั้งแต่อยู่ในครรภ์ก่อนการตรวจ*

วิธีการวิจัย *: สตรีดังกล่าวได้รับการฝากครรภ์ตามปกติ ร่วมกับได้รับการตรวจวัดดัชนีน้ำคร่ำ (AFI) และตรวจการตอบสนองของอัตราเต้นของหัวใจทารก (NST) ทุกสัปดาห์จนกระทั่งคลอด และใช้ค่าการตรวจครั้งสุดท้ายมาประเมินผล เมื่อผลตรวจผิดปกติ (Abnormal modified biophysical profile) หมายถึงการมี non-reactive NST และ/หรือ AFI ≤ 5 ผู้ป่วยจะได้รับการดูแลในห้องคลอด และทำการเก็บเลือดแดงจากสายสะดือทารกทันทีหลังคลอด และส่งตรวจหาค่ากรด-ด่างของเลือด*

ตัวชี้วัดหลัก *: ค่าความไว ดัชนีน้ำคร่ำน้อยกว่าหรือเท่ากับ 5.0 เซนติเมตร และ/หรือการตอบสนองของอัตราเต้นของหัวใจทารกที่ผิดปกติ และค่ากรด-ด่างของเลือดจากสายสะดือ น้อยกว่า 7.15*

ผลการวิจัย *: สตรีตั้งครรภ์ที่มีความเสี่ยงสูงถูกคัดออกจากการวิจัย 13 ราย เนื่องจากผลการตรวจครั้งสุดท้ายจนกระทั่งคลอดนานเกิน 7 วัน เหลือ 172 รายที่นำมาวิเคราะห์ พบว่าทารกมีภาวะเลือดเป็นกรดทั้งหมด 19 ราย คิดเป็นอุบัติการณ์ร้อยละ 11.05 (95% CI 6.63-15.73) ในจำนวนนี้ตรวจ NST ผิดปกติ (non-reactive) 8 ราย คิดเป็นความไวเท่ากับร้อยละ 42.11 (95% CI 34.73-49.48) ค่าดัชนีน้ำคร่ำน้อยกว่าหรือเท่ากับ 5.0 ซม. 11 ราย คิดเป็นความไวเท่ากับร้อยละ 57.89 (95% CI 50.52-65.27) ส่วน Modified biophysical profile ผิดปกติ 14 ราย มีความไวเท่ากับร้อยละ 73.68 (95% CI 67.10-80.27) ความจำเพาะ ค่าพยากรณ์บวก ค่าพยากรณ์ลบ และความถูกต้องของ NST AFI และ Modified biophysical profile สูงไม่แตกต่างกัน*

สรุป *: การตรวจทั้งค่าดัชนีน้ำคร่ำและการตอบสนองของอัตราเต้นของหัวใจทารกร่วมกัน มีความไวสูง เหมาะในการประเมินภาวะเลือดเป็นกรดของทารกในครรภ์ จึงควรนำมาใช้ดูแลสตรีตั้งครรภ์ที่มีความเสี่ยงสูง*