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Prediction of small for gestational age neonates by combining maternal risk factors with biophysical markers

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Table 1- All types of DM versus no DM

Variables	DM n=11318	No DM n=239535	P value
Gestation age	38.70±1.85	39.12±2.22	<0.001
Maternal age	32.30±5.77	28.08±5.68	<0.001
Birth weight	3307.76±530.79	3175.16±532.5	<0.001
Tear	2374 (21.0)	44916 (18.8)	<0.001
1st	2045 (18.1)	36773 (15.4)	<0.001
2nd	265 (2.3)	6745 (2.8)	0.01
3rd	20 (0.2)	316 (0.1)	0.20
Episiotomy	1887 (16.7)	40174 (16.8)	0.78
Vacuum	452 (4.0)	8646 (3.6)	0.03
Nullipara	2166 (19.1)	56794 (23.7)	<0.001
Grandmuliparity	3373 (29.8)	50011 (20.9)	<0.001
SP CS	1049 (9.3)	17121 (7.1)	<0.001
IVF	450 (4.0)	3764 (1.6)	<0.001
Preterm delivery	848 (7.5)	15146 (6.3)	<0.001)
PET	1200 (10.6)	9905 (4.1)	<0.001
Apgar 1 ≤7	456 (4.1)	7578 (3.3)	<0.001
Apgar 5 ≤7	59 (0.5)	1380 (0.6)	0.40
Multivariate analysis for the prediction of tears			
Variables	OR	95% CI	P value
Diabetes	**1.13**	**1.07-1.18**	**<0.001**
Birth weight	1.00	1.000-1.001	<0.001
Maternal age	0.99	0.99-0.995	<0.001
Nuliparity	1.41	1.38-1.45	<0.001

Table 2- Pre-gestational DM versus gestational DM

Variables	Pregestational n=1012	Gestational n=10322	P value
Gestation age	37.56±2.11	38.81±1.78	<0.001
Maternal age	33.84±5.71	32.15±5.76	<0.001
Birth weight	3258.05±662.61	3312.74±520.48	0.01
Tear	225 (21.8)	2149 (20.9)	0.47
1st	162 (15.7)	1883 (18.3)	0.04
2nd	51 (5.0)	214 (2.1)	<0.001
3rd	5 (0.5)	15 (0.1)	0.03
Episiotomy	69 (6.7)	1818 (17.7)	<0.001
Vacuum	41 (4.1)	412 (4.0)	0.93
Nullipara	126 (12.5)	2041 (19.8)	<0.001
Grandmuliparity	391 (38.6)	2990 (29.0)	<0.001
SP CS	136 (13.4)	914 (8.9)	<0.001
IVF	42 (4.2)	409 (4.0)	0.77
Preterm delivery	154 (15.2)	695 (6.7)	<0.001
APD	15 (1.5)	52 (0.5)	<0.001
Ethnicity jew	488 (48.6)	6467 (63.2)	<0.001
Bedouin	517 (51.4)	3771 (36.8)	
Pet	156 (15.4)	1047 (10.1)	<0.001
Apgar 1≤7	52 (4.0)	404 (4.0)	0.07
Apgar 5 ≤7	7 (0.7)	52 (0.5)	0.45

173 Prediction of small for gestational age neonates by combining maternal risk factors with biophysical markers

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OBJECTIVE: Studies have suggested a role for biophysical markers (BPM) including uterine artery Doppler (UAD) and maternal mean arterial pressure (MAP) in prediction of neonatal SGA. We sought to determine if the addition of flow velocities in spiral artery (SA), UAD, MAP and maternal risk factors could improve prediction of neonatal SGA, compared with using maternal risk factors alone.

STUDY DESIGN: This is a prospective longitudinal study over a 5-year period. We measured SA UAD and MAP at: 11 to 13 + 6, 18 to 22 + 6/7 and 28 to 34+ 6/7 weeks of gestation. Prediction models for SGA were constructed using backward and forward logistic regression including minor and major maternal risk factors for SGA (RCOG Green top guideline #31: RCOG 2014) alone; and when combined with BPM. SA, UAD Doppler indices and MAP, converted to z-scores adjusted for gestational age (GA). Crown rump length and estimated fetal weight were included in the model as appropriate for the GA. SGA was defined as birth weight < 10th percentile for GA. Goodness of fit of the models were assessed using Hosmer-Lemeshow test. Area under ROC curves (AUC) were used to compare the detection rates between the models.

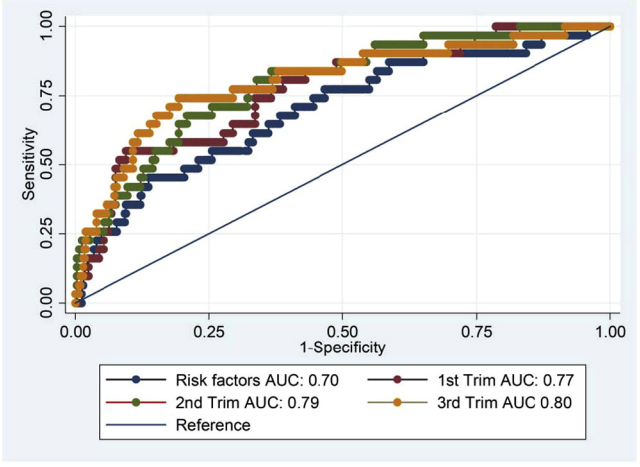
RESULTS: Among 581 pregnancies included, 43 (7.4%) had SGA neonates. The model using maternal risk factors only detected 53.5% of neonates with SGA. Including BPM resulted in an improvement

in sensitivity of the second and third-trimester models: 65.8% and 72.5%, respectively and the specificity: 79.4% and 81.8% for second and third trimesters, respectively. The resulting increase in the AUC between using maternal risk factors, 0.70; and the third-trimester prediction model 0.80, was statistically significant, p< 0.004. (Table).

CONCLUSION: When compared with using maternal risk factors alone, models incorporating BPM such as the spiral artery, uterine artery Doppler and mean arterial pressures result in improved prediction of SGA, particularly in early third trimester.

Model (n)**	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC	p-value*
Maternal risk factors (43/581)	53.5	76.9	15.6	95.4	0.70	Baseline
Maternal risk factors + First trimester BPM (36/530)	50.0	84.0	18.6	95.8	0.77	0.22
Maternal risk factors + Second trimester BPM (38/514)	65.8	79.4	20.3	96.7	0.79	0.07
Maternal risk factors + Third trimester BPM (40/507)	72.5	81.8	25.4	97.2	0.80	0.004

*AUC compared with using maternal risk factors only; **numbers vary with trimester due to missing data on biophysical markers.



174 Allostatic Load and Adverse Perinatal Outcomes

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OBJECTIVE: Mortality and adverse perinatal outcomes (APO) affect approximately 13-20% of pregnant women. Allostatic load (AL) uses biomarkers to estimate chronic stress and may be associated with APOs. Thus, we assessed the relationship between AL and APOs in a large, diverse longitudinal cohort.

STUDY DESIGN: This was a secondary analysis of NuMom2b, a large prospective observational cohort study. Participants were recruited in their first trimester of pregnancy and followed through delivery. This analysis included women who had biomarkers assessed in serum from 6w0d to 13w6d weeks' gestation. Our primary exposure was dichotomous high AL defined as 4 or more out of 12 biomarkers in the worst quartile: systolic blood pressure (SBP), diastolic blood pressure (DBP), insulin, cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides, body mass index (BMI), high sensitivity C-reactive protein (hsCRP), creatinine, albumin and glucose. 'Worst' quartile was lowest for HDL, creatinine and albumin, and highest for the rest. The primary outcome was a composite APO (cAPO): hypertensive disorders of pregnancy (HDP), preterm birth (PTB), small for gestational age (SGA), and stillbirth (SB); each component was analyzed as a secondary outcome. Multivariable logistic regression was used to test the association between high AL and cAPO adjusted for potential confounders.

RESULTS: Among 4,266 women, cAPO was identified in 1,371 (32%): 14% HDP, 16% PTB (50.7% spontaneous and 49.3% induced, respectively), 11% SGA, and 0.3% SB. In this cohort high AL was present in 36%; after adjustment for maternal age, gravidity, smoking, alcohol use, bleeding in first trimester, poverty level, and health insurance, high AL was significantly associated with cAPO (aOR 1.5, 95% CI: 1.3, 1.8), HDP (2.5, 2.0-3.0), preterm birth (1.3, 1.1-1.6), but not SGA (Figure 1). SB (n=12) was too infrequent for adjusted modeling.

CONCLUSION: High AL is associated with composite adverse perinatal outcomes, particularly hypertensive disorders of pregnancy, and preterm birth.

Table 1. Demographic and clinical characteristics of women allostatic load exposure and women with and without composite adverse perinatal outcomes.

Variables	Study N (%) N = 4,266	High AL N (%) N = 1,530	Low AL N (%) N = 2,736	P-value	Composite APO N (%) N = 1,371	No Composite APO N (%) N = 2,895	P-value
Maternal Age > = 35	409 (9.6)	179 (11.7)	230 (8.4)	0.0005	149 (10.9)	260 (9.0)	0.05
Race (Non-Hispanic Black)	566 (13.3)	200 (13.1)	366 (13.4)	0.778	320 (17.9)	320 (11.1)	< 0.0001
Education (Some college or less)	1625 (38.1)	596 (39.0)	1029 (37.6)	0.386	606 (44.2)	1019 (35.2)	< 0.0001
Gravidity > = 3	268 (6.3)	113 (7.4)	155 (5.7)	0.026	91 (6.6)	177 (6.1)	0.51
Smoking	682 (16.0)	269 (17.6)	413 (15.1)	0.033	245 (17.9)	437 (15.1)	0.02
Alcohol Use	2662 (74.9)	954 (73.8)	1708 (75.4)	0.289	840 (72.5)	1822 (76.0)	0.027
Prior Miscarriage	640 (15.0)	262 (17.1)	378 (13.8)	0.004	206 (15.0)	434 (15.0)	0.977
Prior Abdominal Surgery	423 (9.9)	156 (10.2)	267 (9.8)	0.647	133 (9.7)	290 (10.0)	0.747
Prior Bleeding at First Trimester	294 (6.9)	125 (8.2)	169 (6.2)	0.014	100 (7.3)	194 (6.7)	0.472
≤ 200% of fed poverty level	1086 (30.8)	371 (28.8)	715 (31.9)	0.060	370 (34.1)	716 (29.3)	0.004
Government Health Insurance	1163 (27.4)	370 (24.3)	793 (29.1)	0.0008	422 (31.0)	741 (25.7)	0.0003

Abbreviations: APO, adverse perinatal outcomes. Data are expressed as binary variables and as either n(%) or mean ± standard deviation unless stated as otherwise.