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Ethnic Differences in Maternal Cytokines and Adipokines and Their Association With Spontaneous Preterm Delivery

Yelizavet D. Lomakova
Rowan University

Xinhua Chen
Rowan University

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Yelizavet D. Lomakova OMS-III, Dr. Xinhua Chen MD

Department of OB/GYN Research, Rowan University School of Osteopathic Medicine, Stratford, NJ

Introduction

Spontaneous preterm delivery (SPTD, birth at <37 weeks' gestation) is a leading cause of infant mortality in the United States [1]. Infants born prematurely are more likely to suffer from both short and long-term complications including neurodevelopmental delay, visual and hearing impairment, and chronic diseases such as heart disease, hypertension and diabetes in later life [2-4]. African American women have a 2-fold increased risk of preterm delivery compared to Caucasian women [5]. The reasons for this disparity are poorly understood. This limits the ability to predict and prevent preterm delivery in the most high-risk populations.

Objectives

To investigate racial/ethnic differences in maternal serum inflammatory biomarkers and their associations with spontaneous preterm delivery.

Methods

Pregnant women (n = 2029) were from a large prospective cohort study in Camden, NJ (African-American 37.0%; Hispanic 47.8%; Caucasian 15.2%). Serum IL6, IL8, IL10, TNFα, Granulocyte-macrophage colony-stimulating factor (GMCSF), adiponectin and resistin were measured at entry (week 16.8) and at 3rd trimester (week 30.7) using the Luminex xMapTechnology. Potential confounding variables were controlled for including BMI. IRB approval was obtained for this study.

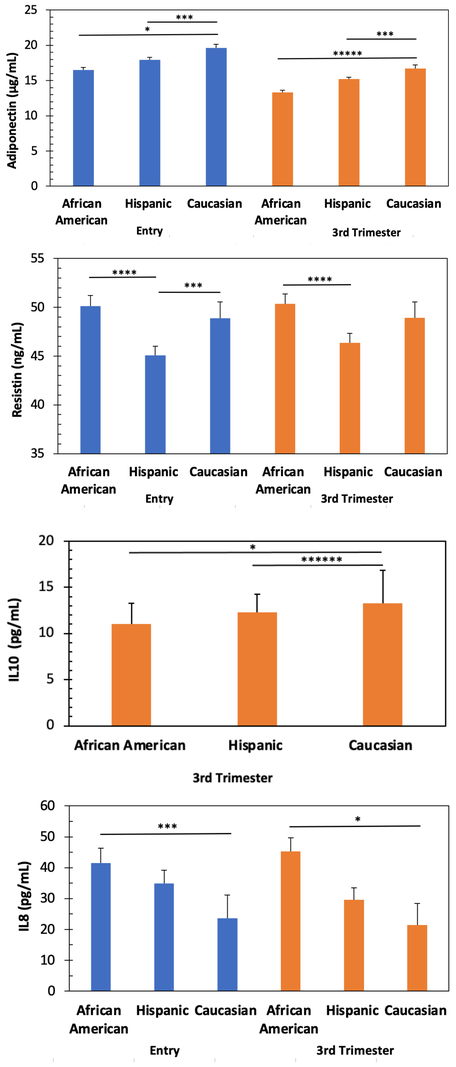
Results

Table 1. Characteristics of study participants at entry by ethnicity.

Characteristics	All Participants	African American	Hispanic	Caucasian	p-value
n	2029	750	970	309	
Age (years)	22.00 ± 5.23	21.33 ± 4.94[a,b]	22.11 ± 5.18[c]	23.31 ± 5.74	<0.0001
Pre-pregnant BMI (kg/m^2)	25.72 ± 6.28	26.08 ± 7.06[c]	25.77 ± 6.79[b]	24.68 ± 5.62	<0.01
Obese (BMI ≥ 30)	411 (20.31)	165 (22.00)	192 (19.79)	55 (17.80)	<0.01
Gestational age at blood sampling (week)					
Entry	16.83 ± 5.47	16.92 ± 5.55[d]	16.99 ± 5.54[d]	16.12 ± 5.47	NS
3rd trimester	30.68 ± 3.60	30.72 ± 3.63	30.66 ± 3.61	30.63 ± 3.51	NS
Cigarette smoking	375 (18.48)	146 (19.47)	117 (12.06)	112 (36.25)	<0.0001
Nulliparity	783 (38.54)	276 (36.80)	384 (39.59)	122 (39.48)	NS
Insurance					
Medicaid	1955 (97.41)	745 (99.33)	970 (100)	278 (89.97)	
Other	74 (3.60)	5 (0.67)	0	31 (10)	<0.0001
Pregnancy outcome					
Gestational age at delivery (week)	38.65 ± 2.25	38.55 ± 2.40	38.69 ± 2.19	38.75 ± 2.07	NS
Infant birth weight (g)	3209 ± 582	3128 ± 592[a,b]	3241 ± 568	3301 ± 577	<0.0001
Preterm delivery	222 (10.94)	93 (9.59)	97 (12.93)	32 (10.36)	NS
Preeclampsia	176 (7.93)	87(11.60)	63 (6.49)	26 (8.41)	<0.001
Gestational diabetes	88 (4.34)	16 (2.13)	52 (5.36)	20 (6.47)	<0.001

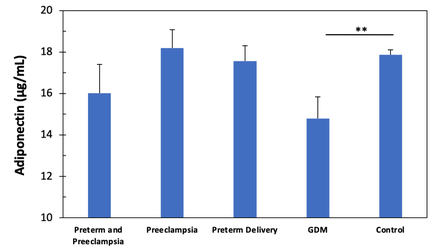
Data are mean ± SD or n (%). P-value reflects p for trend by ANOVA or p-value by chi-square test. [a] p<0.0001 vs. Caucasian; [b] p<0.01 vs. Hispanic; [c] p<0.001 vs. Caucasian; [d] p<0.05 vs. Caucasian.

Figure 1. Differences in cytokine/adipokine concentrations by ethnicity.



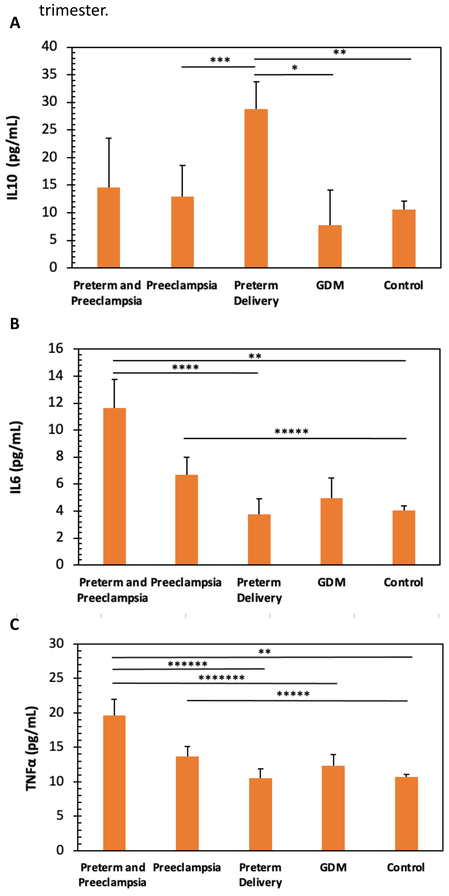
Data are mean ± SE. Means were adjusted for age, BMI, smoking, and parity. *P* values reflect log transformed data. $^{*}p$<0.01 vs. Caucasian; $^{**}p$<0.0001 vs. African American; $^{***}p$<0.05 vs. Caucasian; $^{****}p$<0.01 vs. African American; $^{*****}p$<0.0001 vs. Caucasian; $^{******}p$<0.001 vs. Caucasian.

Figure 2. Differences in adiponectin levels by outcome at entry.



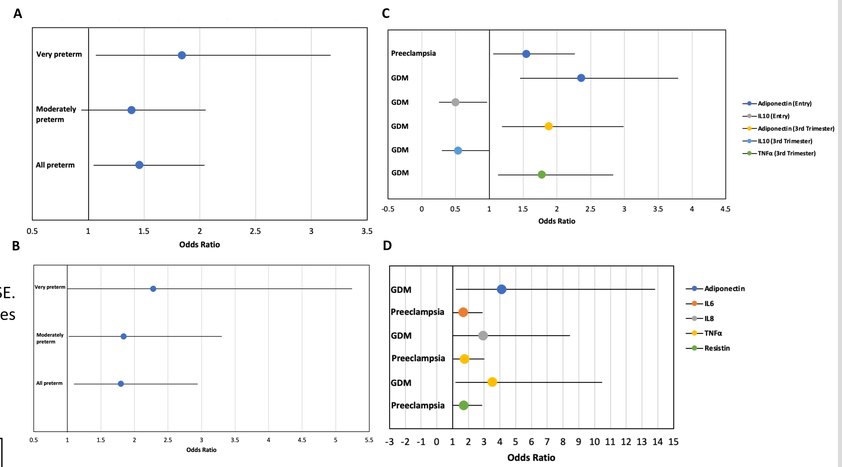
GDM, gestational diabetes mellitus. Data are mean ± SE. Means were adjusted for ethnicity and BMI. *P* values reflect log transformed data. $^{**}p$<0.001 vs. control.

Figure 3. Differences in cytokine levels by outcome at 3rd trimester.



Differences in IL10 (A), IL6 (B), and TNFα (C) levels by outcome at 3rd trimester. GDM, gestational diabetes mellitus. Data are mean ± SE. Means were adjusted for ethnicity and BMI. *P* values reflect log transformed data. $^{*}p$<0.015 vs. GDM; $^{**}p$ <0.001 vs. control; $^{***}p$ <0.05 *vs.* preeclampsia; $^{****}p$<0.05 vs. preterm delivery; $^{*****}p$<0.05 vs. control; $^{******}p$ <0.001 vs. preterm delivery; $^{*******}p$ <0.05 vs. GDM.

Figure 4. Multiple logistic regression analysis.



Multiple logistic regression analysis of low adiponectin with preterm birth for cohort at entry (A), low adiponectin with preterm birth in African Americans at entry (B), low adiponectin/high cytokine with adverse outcomes for cohort at entry and at 3rd trimester (C), low adiponectin/high cytokine with adverse outcomes for African Americans at 3rd trimester (D). AOR, adjusted odds ratio; 95% CI, 95% confidence interval; Low adiponectin was defined as the lowest quartile (<11.35 ug/mL) as compared to quartiles two, three, and four pooled; High IL6 was defined as the highest quartile (>2.64 pg/mL) as compared to quartiles one, two, and three pooled; High IL8 was defined as the highest quartile (>13.87 pg/mL) as compared to quartiles one, two, and three pooled; High IL10 was defined as the highest quartile (>11.51 pg/mL) as compared to quartiles one, two, and three pooled; High TNFα was defined as the highest quartile (>9.97 pg/mL) as compared to quartiles one, two, and three pooled. High resistin was defined as the highest quartile (>60.52 ng/mL) as compared to quartiles one, two, and three pooled. Model adjusted for age, ethnicity, cigarette smoking, and parity.

Summary

Ethnic differences in mean levels of adiponectin, IL8, IL10 and resistin were observed. Adiponectin levels were significantly decreased in African American and Hispanic women (*P*<.05 - *P*<.0001) compared to Caucasians at early and late gestation. Higher levels of IL8 (p<.05) and resistin were also found in African Americans as compared to Caucasian and/or Hispanic women (*P*<.05 - *P*<.01). Results of multiple logistic regression analysis showed that low (lowest quartile) adiponectin was associated with an increased risk for very preterm delivery (<34 weeks, adjusted odds ratio (AOR) 1.79, 95% confidence interval (CI) 1.07-3.17) and for all preterm delivery (<37 weeks, AOR 1.46, 95% CI 1.05-2.04) for the cohort at entry. When analysis was separated by ethnic group, significant association was only obtained in African Americans (AOR 2.20, 1.84 and 1.80 for very preterm, moderately preterm and all preterm delivery respectively, P<.05 for each). Multiple logistic regression analysis also showed low adiponectin was associated with preeclampsia (AOR 1.55, *P*<0.05), and gestational diabetes mellitus (GDM, AOR 2.36, *P*<0.05) at early gestation. High IL10 (highest quartile) was protective against GDM development at both early and late gestation (AOR 0.49, *P*<0.05). When separated by ethnic group, significantly low adiponectin (AOR of 4.12, 95% CI 1.23-13.80), and high IL8 (AOR 2.94, 95% CI 1.00-8.69) and TNF-α (AOR 3.54, 95% CI 1.20-10.44) levels were associated with GDM in African Americans at late gestation. High IL6 (AOR 1.69, 95% CI 1.00-2.88) and resistin (AOR 1.71, 95% CI 1.02-2.85) levels were associated with preeclampsia in African Americans at late gestation.

Conclusions

Our data suggest a significant association between decreased maternal adiponectin concentration at early pregnancy and risk of preterm delivery, particularly in African American women. High IL10 concentration early in gestation may protect against GDM development. This association is independent of maternal adiposity.