The Relationships Among Acculturation, Body Mass Index, Depression, and Interleukin 1-Receptor Antagonist in Hispanic Pregnant Women

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Objective: The purpose of this study was to determine relationships between acculturation, body mass index (BMI), and depressive symptoms with the Interleukin 1-mediated inflammatory response marker IL-1RA in pregnant Hispanic women at 22–24 weeks gestation.

Design: An observational, prospective design with data collected at 22–24 weeks gestation.

Setting: Public prenatal health clinics and private physician practices in central and south Texas serving low-income women.

Main Outcome Measures: Body mass index (BMI), depression scores on the Center for Epidemiological Studies of Depression (CES-D), years in the United States, the Language Proficiency Scale (LPS), and Interleukin 1 receptor antagonist levels (IL-1RA)

Results: The longer the Hispanic women were in the United States, the higher the IL-1RA levels in plasma (F=4.55; P=.002). IL-1RA plasma levels were significantly different between low and normal BMI vs overweight and obese categories of BMI (F=8.54; P<.001). IL-1RA levels were significantly higher between those women who had high scores for depressive symptoms on the CES-D (using a cut off of 20) and those who had scores less than 20 (t-value=−2.41; P=.018). In structural equation modeling, years in the United States significantly positively predicted increased depressive symptoms, increased BMI, and increased IL-1RA levels with a good model fit.

Conclusions: We found that increasing years of residency in the United States is associated with the elevated inflammatory marker IL-1RA, and increased BMI. Increased depressive symptoms also predict IL-1RA levels among Hispanic women at 22–24 weeks of pregnancy. The significance of these findings is discussed in relationship to the development and course of disease. (*Ethn Dis*. 2007;17:338–343)

Key Words: Acculturation, Body Mass Index, Depression, IL-1RA

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Introduction

The major pro-inflammatory cytokine, interleukin-1(IL-1), and its naturally occurring anti-inflammatory counterpart interleukin-1 receptor antagonist (IL-1RA), have been extensively studied in many diseases, as well as in normal physiological conditions including in pregnancy.[1] Interleukin-1RA may be readily produced in numerous chronic inflammatory and infectious diseases, and increases with increasing levels of its counterpart IL-1.[1] Interleukin-1 (IL-1) has been implicated in the destruction of the islets of Langerhans in the pancreas related to the development of diabetes, the development of atherosclerotic plaques, and inflammation associated with arthritis and colitis.[2] A recent study has identified IL-RA's role in countering the development of atherosclerosis and metabolism of cholesterol.[3] Therefore, IL-1RA is important as a counter regulator, or balancer, of IL-1 in the development of diabetes, cardiovascular disease, and other chronic diseases.[4] IL-1RA must be produced abundantly in local tissues to block the effects of IL-1.[5]

Determining what factors predict IL-1 and IL-1RA levels is of particular interest. Depression and stress have both been linked to IL-1RA levels in the general population.[6,7] In obesity there is an increase in the amount of adipose tissue and this has been associated with IL-1RA levels.[8] However, what has not

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> *IL-1RA is important as a counter regulator, or balancer, of IL-1 in the development of diabetes, cardiovascular disease, and other chronic diseases.[4]*

been studied is the effect of acculturation on the inflammatory response in Hispanic women, particularly in relationship to depression and obesity. We hypothesized that acculturation would have an effect on obesity and depression that would influence the effect on IL-1RA, potentially deregulating the immune system that influences the health and well being of pregnant Hispanic women.

There are limited reports about IL-1RA serum and plasma levels in normal, healthy pregnancy. In one report, no significant increase of IL-1RA level was found in healthy pregnant women during the first, second, and third trimester compared to pre-pregnancy levels. However, a significant decrease of IL-1RA occurred from 6 to 12 weeks postpartum, suggesting that the endocrine system is also involved in IL-1RA regulation[9]

Psychological and physical stressors increase the levels of pro-inflammatory cytokines such as IL-1.[6] IL1-RA levels have been shown to be higher in persons with major depression than in persons in non-depressed control groups.[7] Other studies demonstrated that even with successful antidepressant treatment, serum levels of IL-1RA remained un-

affected.[10] Since the risk of major depression seems to be greater for US-born Mexican Americans than for immigrants,[11–13] it is of special interest to investigate the relationship of IL-1RA and depression in Hispanics, particularly in relationship to acculturation.

Acculturation is defined as the development of new cultural traits when two previously culturally distinct groups interact with one another.[14] In one study, Mexican immigrants who had lived in the United States more than five years had higher parity, more pregnancy complications, fewer planned pregnancies, and smoked more than recent Mexican immigrants.[15] Higher prenatal stress or anxiety was associated with greater acculturation, and was related to preterm birth.[15]

In Hispanics, acculturation may influence the development of obesity and consequently IL1-RA. This increases Hispanics risk for numerous chronic illnesses and their factors: high serum insulin, non-insulin dependent diabetes, and hypertension. In a large study,[16] acculturation status was significantly associated with waist circumference and abdominal obesity. US-born Spanish-speaking women had the largest waist circumference and obesity. Furthermore, when examining adolescents, a recent study demonstrated that a striking increase in overweight existed between the first and subsequent generations of US residence.[17] Other research[18] has verified that acculturation among Mexican Americans was also associated with increasing body mass index (BMI) for both men and women in the second and third generation.

In the National Health and Nutrition Examination Survey (NHANES) III study, more healthful nutrition profiles were found among the persons born in Mexico; however, the second generation became further removed from dietary heart healthy traditions of their native country.[19] Physiologically, IL-1RA in obesity comes from white adipose tissue, is markedly increased,

and is related to insulin resistance.[8] It may be concentrated in the liver, spleen, kidney and muscle.[8] IL-1RA plays an important role in lipid metabolism to regulate insulin levels.

The purpose of this research study was to determine if depressive symptoms, acculturation (measured by years in the United States) and BMI predicted IL-1RA levels in Hispanic pregnant women in the second trimester of pregnancy.

MATERIAL AND METHODS

Participants

This report is part of a larger study focused on identifying mechanisms leading to preterm delivery and low birth weight in Hispanic women living in Texas. For this analysis, we included 206 healthy Hispanic women who met the following criteria: ability to read and speak either English or Spanish, self-identified as Hispanic, between 14 to 40 years old, less than 22 weeks pregnant with a singleton pregnancy confirmed by ultrasound, and signed an English or Spanish version of the informed consent to participate in this study. We excluded women with a diagnosis of preeclampsia, had a history of autoimmune disorders including systemic lupus erythematous and rheumatoid arthritis, insulin dependent diabetes or diabetes requiring medication, thyroid disorders, or a diagnostic and treatment history of current mental illness, such as schizophrenia or manic depression. We did not include women with asthma requiring use of steroids, as well as all women who were having active cervical bleeding or placenta previa.

Sociodemographic Variables

Detailed information was collected about age, ethnicity, current marital status, and education.

Acculturation was measured by the Bidimensional Acculturation Scale for

Hispanics (BAS).[20] The scale measures bidirectional changes in behavior that are important to a person in two cultural domains, Hispanic and non Hispanic. We used the Language Proficiency subscale, as it is a shorter version that provides a quick but efficient measure of acculturation. The alpha coefficient for the Linguistic Proficiency subscale is 0.97.[21] Psychometric analysis has shown that language items, as compared to other constructs, explain most of the variance of acculturation scales.[20] A score of 2.5 was used as a cutoff score to indicate a low or high level of adherence to each cultural domain. For purposes of analysis we grouped the bicultural with the English acculturated. In addition, we used years in the United States as a linear measure of acculturation.

Body mass index was calculated as weight in kilograms divided by the square of the height in meters. According to the National Heart, Lung, and Blood Institute (NHLBI) definitions,[22] the lean or underweight subject is defined as BMI $<18.5 kg/m^2$, normal weight as BMI between 25.0 and 29.9, and obese as BMI $\geq 30 kg/m^2$. Pre-pregnancy body weight was self-reported or obtained from existing medical records. Height was measured and recorded by a bilingual research nurse during data collection.

The Center of Epidemiological Studies Depression Index (CES-D)[23] was used to evaluate depressive symptoms in subjects participating in the study. All subjects completed the CES-D during the same prenatal visit as when the blood samples were collected. The CES-D uses a 20-item, 4-point Likert scale ranging from 0 (never) to 3 (most of the time). It is used to assess the overall level of depressive symptoms experienced in the past week. Possible scores range from 0-60, with higher scores indicating greater depressive symptoms. It is suitable for use in general populations, as well as pregnant populations, and has strong psychomet-

ric properties (alpha=.85).[24] We defined depressive symptoms as a CES-D score of > 20. Although a cutoff of 16 has been used by many investigators,[20] we chose to use a higher CES-D cutoff point to account for the possibility that symptoms of normal pregnancy may overlap with symptoms of depression. This is consistent with several other studies.[25,26]

Interleukin 1-RA levels were measured in plasma. Peripheral venous blood was drawn into vacutainer tubes containing EDTA (Becton Dickinson and Co., San Jose, CA). The tubes were centrifuged at 2000×g for 15 minutes and collected plasma was stored in multiple aliquots at −80°C until thawed for assay. IL-1RA was measured by an enzyme-linked immunosorbent assay (ELISA) kit (R&D Systems, Minneapolis, MN). The range for IL-1RA detection by this ELISA kit was 31.2 pg/mL–2000 pg/mL and sensitivity measured by a minimum detectable dose of 22 pg/mL. In some cases, because of initial high concentrations, we used diluted plasma samples to measure IL-1RA concentrations.

Data Analysis

Descriptive statistics for all variables were computed using the Statistical Program for the Social Sciences (SPSS 14.0). The frequencies of the variables were evaluated for non-normal distributions. A log linear transformation was used to normalize the distribution for IL-1RA.

Pearson's correlations were run to establish relationships between research variables. We ran *t* tests between participants with higher CES-D scores (>20), and those with lower scores (< 20). A series of analysis of variance (ANOVA) computations using SPSS were conducted comparing the key variables related to the IL-1RA levels. With ANOVA, when the between subjects test was significant, post-hoc tests were done to compare differences between groups on IL-1RA levels by

Table 1. Demographic characteristics of the study sample

Characteristic	Mean	Standard Deviation	N	%	N Missing
Age	23.2	4.69			2
Marital status					
Single			104	50.5	4
Married			78	37.9	4
Separated or divorced			20	9.9	4
Ethnicity					
Mexican American			102	49.5	2
Mexican			77	37.4	2
Puerto Rican			4	1.9	2
South or Central American			7	3.4	2
Other Hispanics not specifically identified			14	6.8	2
Education					
K-12			117	56.8	5
High school graduate			79	38.3	5
College degree			5	2.4	5

every five years in the United States and by categories of BMI.

A path analysis was performed using the structural equation modeling software package AMOS 4.0[27] Goodness of fit was examined using chi-square, the comparative fit index (CFI), normed fit index (NFI), and non-normed index. Rules of thumb for the indices suggest that an NFI, CFI, and NNFI over .95 indicate good model fit.[28]

RESULTS

Demographics of the participants are shown in Table 1. The sample was predominantly single, Mexican-American, and women whose highest level of education was less than the 12th grade.

Thirty three (33%) of the sample had high depressive symptoms (> 20 score). The IL-1RA was significantly different in a *t* test between those who had high CES-D scores and those who had scores below 20; *t* value=−2.41, *P*=.018. Figure 1 displays the differences in mean levels of IL-1RA by levels of depressive symptoms.

We divided the years in the United States into five-year increments in relation to acculturation. Table 2 gives results related to years in the United States and the Language Proficiency Scale. Low acculturation correlates with

Spanish language proficiency, and high acculturation correlates with English language proficiency. This table demonstrates that the majority of the lower acculturated women (51%) were in the United States <5 years, with decreasing numbers at 5–9 and then 10–14 years, and no lower acculturated women here >15 years. The more acculturated (high scores) begin at 15–20 years, and the majority of the women with the high acculturation scores were here more than 20 years (59%). Table 2 also illustrates years in the United States by generation, with the majority of women who were foreign born being here either <5 years, or 5–9 years. The majority of women in the second generation (born
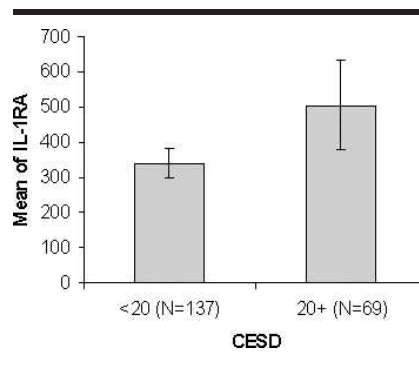

Fig 1. Differences in IL-1RA levels by CES-D scores for depression using a cut-off of 20 total score

Table 2. Correlation among years in US, generation and acculturation

	N (%) of years in US				
	<5	5–9	10–14	15–20	20+
Acculturation*,**					
Low	36 (51.43)	25 (35.71)	9 (12.86)	0 (0.00)	0 (0.00)
High	3 (2.21)	5 (3.68)	7 (5.15)	41 (30.15)	80 (58.82)
Generation*†					
First	38 (44.19)	28 (32.56)	14 (16.28)	4 (4.65)	2 (2.33)
Second	1 (0.83)	2 (1.67)	2 (1.67)	37 (30.83)	78 (65.00)
Total	39 (18.93)	30 (14.56)	16 (7.77)	41 (19.90)	80 (38.83)

* $P<.0001$ by Pearson chi-square test.

** Acculturation is measured by a language-based acculturation scale.

† Generation is measured by country of birth. Women who were born outside US are regarded as first generation.

in the United States) were here 20 years or longer (coinciding with age).

We then compared the IL-1RA levels for participants over the 5-year increments that they were in the United States. The levels of IL-1RA remained stable for the first 15 years and then significantly increased at 15–19 years and again at >20 years; F=4.5, (*df* 4), ($P<.002$). Using a Bonferroni post-hoc test, the data showed significant differences between women who had been in the United States <5 years and those who had been here >20 years. Figure 2 illustrates the changes for participants in levels of IL-1RA over these 5-year increments. Because of potential relationships of age and years in the United States with IL-1RA, we correlated age to IL-1RA. There was no significant cor-
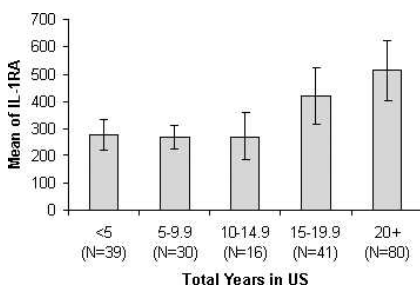
relation of IL-1RA levels with maternal age, $r = -.09$, $P = 0.13$. We also evaluated correlations between maternal age and years in the United States and found no significant relationship, $r = .01$, $P = 0.76$.

In order to determine the influence of pre-pregnancy BMI levels on IL-1RA levels, we divided the BMI into four groups: less than 18.5 (underweight); 18.5–24.9 (normal); 25–29.9 (overweight); and >30 (obese). The differences between the IL-1RA levels by BMI were highly significant; F = 8.54, (*df* 3), $P <.001$. However, a Bonferroni post-hoc test revealed that the major differences were not between the overweight and obese groups, but rather between the normal weight women and the obese group ($P <.000$), and the underweight women and the overweight
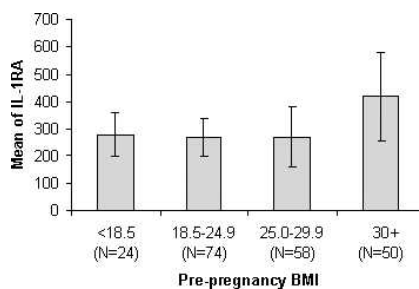
($P < .04$) and obese groups ($P < .001$). Figure 3 illustrates the IL-RA levels by BMI. We did examine if there was an interactive effect of depression with BMI. The chi square was not significant between the higher depression scores and the higher BMI categories (chi square=3.55, (*df* 2), $P=0.16$.

Finally, a structural equation model was tested to establish if the total years in the United States predicted both depressive symptoms measured by the CES-D and increased BMI, and if all three predicted IL-1RA. Figure 4 shows the model with standardized regression weights of each of the variables regressed onto IL-1RA. All of the coefficients are significant. The values for the standardized regression weights are noted next to
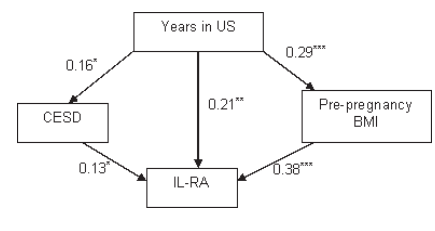

Fig 2. Differences in IL-1RA levels by years in the United States
1. Bars show means of IL1-RA; 2. Error bars show 95% CI of mean; 3. ANOVA: *F* value=4.55, *P*=.002; 4. Multiple comparisons with Bonferroni adjustment: <5 vs 20+: *P*=.01, 5–9.9 vs 20+: *P*=.02, other comparisons: *P*>.05

Fig 3. IL-1RA levels by BMI categories
1. Bars show means of IL1-RA; 2. Error bars show 95% CI of mean; 3. ANOVA: *F* value=8.54, *P*=.001; 4. Multiple comparisons with Bonferroni adjustment: <18.5 vs 25.0–29.9: *P*=.047, <18.5 vs 30+: *P*=.001, 18.5–24.9 vs 30+: *P*<.001

Fig 4. Structural equation model with standardized regression coefficients
Significance level: *P*<.05; *P*<.01; *P*<.001. Note: The following statistics indicate an excellent fit of the model: Pr > Chi-Square 0.637; Bentler's Comparative Fit Index 1.000; Bentler & Bonett's (1980) Non-normed Index 1.056; Bentler & Bonett's (1980) NFI 0.998; All standardized residuals are less than 0.5. No significant modification index by Lagrange Multiplier test.

The variable years in the United States significantly predicted increased depressive symptoms.

the arrows and the *P* values are noted with the asterisks. In examining goodness of fit, all fit indices indicate an excellent model fit.

DISCUSSION

The finding that depressive symptoms predicted IL-1RA levels is consistent with previous evidence.[6,7] The variable years in the United States significantly predicted increased depressive symptoms. The length of time in the United States may increase stress related to acculturation that is also related to increasing depression. Future study is expected to include a more multi-dimensional measure of acculturation related to depression.

The percent of high depressive symptoms is noteworthy (as it was about 33% of the sample), and is consistent with recent acculturation literature.[11] Both the amount of depressive symptoms and the subjects with higher depression scores having a higher inflammatory response have potentially disturbing health consequences. A screen for depression in pregnant Hispanics, particularly those who have been here 15 years or more, may identify those in need of interventions for depression. Further investigation is also warranted as to how depression may influence eating habits related to BMI, or if the effect of depression is on IL-1RA through the brain only (via neurotransmitters).

Years in the United States had strong predictive ability for both pre-pregnancy BMI and IL-1RA levels. This is consistent with previous evidence that, with acculturation, there is a deterioration in nutrition and an increase in obesity, particularly among Mexican Americans.[15–17] It is alarming to note that in this medically low-risk sample, IL-1RA was so high in women the longer they were in the United States. The levels of inflammation related to obesity, which IL-1RA counter-regulates, are particularly related to the development of diabetes and cardiovascular disease.[3,4] This study provides evidence that in Hispanics, particularly low-income Mexican Americans, acculturation affects BMI and inflammation. This may be one explanatory mechanism related to the potential development of diabetes and cardiovascular disease in Hispanics, particularly Mexican Americans. Future longitudinal study is needed to determine when the impact of acculturation on the inflammatory response actually becomes disease.

A limitation of this study is that it used a linear measure of acculturation (years in the United States) and a language-based measure of acculturation. We acknowledge that acculturation is a complex process both conceptually with measurement issues,[14] and we recommend further investigation using multi-dimensional measures to further refine the results presented here to allow for development of interventions. However, years in the United States is a starting point as it: a) does provide information as to when the changes occur over time and b) is consistent with country of birth and language proficiency measures of acculturation. The evidence presented here has potential important implications for Hispanic women's health the longer they are in the United States.

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