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Stressful life events are associated with insulin resistance among Chinese immigrant women in the United States

Carolyn Y. Fang [a,*], Guenther Boden [b], Philip T. Siu [c], Marilyn Tseng [d]

[a] Cancer Prevention and Control Program, Fox Chase Cancer Center, Philadelphia, PA 19111, USA
[b] Department of Medicine, Section of Endocrinology, Diabetes and Metabolism, Temple University School of Medicine, Philadelphia, PA 19140, USA
[c] Chinatown Medical Services, Greater Philadelphia Health Action, Inc., Philadelphia, PA 19147, USA
[d] Department of Kinesiology, California Polytechnic State University, San Luis Obispo, CA 93407, USA

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ABSTRACT

Background. Chinese immigrants experience increased chronic disease risk following migration to the US. Although the impact of lifestyle changes (e.g., diet) on disease risk has been extensively studied, associations of psychosocial stress and disease risk have attracted less attention. Thus, the objective of the present study was to examine associations between stress and insulin resistance in foreign-born Chinese American women.

Methods. From October, 2005 to April, 2008, 423 women recruited from southeastern Pennsylvania completed questionnaires reporting stressful life events. Blood samples were analyzed for fasting insulin and fasting glucose levels, which were used to estimate insulin resistance according to the homeostasis model assessment ($HOMA_{IR}$).

Results. In logistic regression analyses, a greater number of negative life events were associated with insulin resistance (OR = 1.17, 95% CI = 1.02–1.34), controlling for age, level of acculturation, marital status, body mass index, and waist circumference. Similarly, greater negative life event impact ratings were also associated with insulin resistance (OR = 1.08, 95% CI = 1.01–1.16) controlling for relevant covariates.

Conclusions. This is one of the first studies to examine the associations between psychosocial stress and insulin resistance in Chinese immigrant women. These findings contribute to a growing body of literature on stress and diabetes risk in an immigrant population.

Introduction

Type 2 diabetes mellitus represents a significant threat to global human health. In the United States (US) alone, the annual health spending attributed to treating type 2 diabetes and preventing complications was estimated at $245 billion in 2012 (American Diabetes Association, 2013), and these costs are projected to continue to rise dramatically over the next decade.

One group at increased risk is Asian Americans, which is the fastest growing US racial group (Pew Research Center, 2012). Chinese Americans comprise the largest subgroup, and over 76% of Chinese Americans are foreign-born (Pew Research Center, 2012). Interestingly, prevalence rates of diabetes are higher among Chinese Americans (~12–13%) compared with non-Hispanic white Americans (4–7%) (Boykin et al., 2011) despite being thinner (Lee et al., 2011). Although the increased disease risk has been attributed primarily to dietary changes and weight gain following immigration (Pan et al., 1999), data from large-scale studies suggest that Asian Americans actually have a healthier dietary profile (e.g., overall higher fruit and vegetable consumption and lower soda consumption) than non-Hispanic whites (Kruger et al., 2007). Thus, the disease risk transition may not be explained by behavioral risk factors (e.g., diet, obesity) alone.

A biopsychosocial model of immigrant health

There is growing awareness that immigration to the US and other Western countries increases risk for chronic disease independent of traditional risk factors, such as the acquisition of Western lifestyle behaviors (Lear et al., 2009). Yet, while the behavioral changes that occur following immigration (e.g., diet) have been extensively studied (Oster and Yung, 2010), the impact of psychosocial stress on immigrant health and disease risk is less well-understood. Thus, a biopsychosocial model of immigrant health was put forward in an effort to understand the various factors that may influence disease risk in immigrant populations (Acevedo-Garcia et al., 2012; Zhang and Ta, 2009). Within this

Abbreviations: BMI, body mass index; GEQ-A, General Ethnicity Questionnaire—American; $HOMA_{IR}$, homeostasis model assessment-estimated insulin resistance; OR, odds ratio; CI, confidence interval.

* Corresponding author at: Fox Chase Cancer Center, 333 Cottman Avenue, Philadelphia, PA 19111, USA. Fax: +1 215 728 2707.
E-mail address: carolyn.fang@fccc.edu (C.Y. Fang).

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framework, it is proposed that immigrants experience considerable stress, which may arise from a variety of sources including language difficulties (Zhang et al., 2012), separation from family and social networks (Pickett and Wilkinson, 2008), and greater exposure to racism and discrimination not previously experienced in one's country of birth (Gee et al., 2009). Over time, continued stress exposure may contribute to the excess disease risk observed (Acevedo-Garcia et al., 2012; Zhang and Ta, 2009).

Indeed, these experiences may have implications for the health of Chinese Americans, as it has been noted that stronger social connections (e.g., family cohesion, friend support) are associated with better self-reported physical and mental health, whereas limited English language proficiency in recent immigrants was associated with poorer health (Zhang and Ta, 2009). And national data suggest that negative attitudes toward Chinese Americans are pervasive, with a majority of Chinese Americans reporting common and frequent exposure to discrimination (Brown et al., 2006; Chae et al., 2008). In other populations, chronic exposure to unfair treatment has been associated with diabetes risk (Williams and Mohammed, 2009).

Further, Chinese American women may be more vulnerable to the effects of these experiences, particularly stressors related to the loss of social networks and implicit support (Anderson, 1991; Taylor et al., 2007). Generally, the stress-diabetes association has been more consistently observed in women than in men (Heraclides et al., 2012; Zhao et al., 2006), as women tend to show a stronger physiologic response to stress than men (Lundberg, 2005).

In light of prior studies noting that psychosocial stress is associated with insulin resistance and the development of diabetes in non-immigrant populations (Bjorntorp et al., 1999; Heraclides et al., 2012; Pyykkonen et al., 2010; Rosmond, 2005), the objective of the present analysis was to examine associations between psychosocial stress and insulin resistance, a predictor of the future development of type 2 diabetes, in a sample of foreign-born Chinese American women. It was hypothesized that greater exposure to stress would be associated with insulin resistance in this immigrant population.

Methods

Study participants

This study is a secondary analysis of data obtained between October, 2005 and April, 2008, from a study of breast density in 436 healthy, premenopausal women. Eligibility criteria included Chinese heritage, migration from Asia ≤20 years ago, and being of mammography screening age. Exclusion criteria were: postmenopausal status (no menstruation in the past year); history of breast augmentation/reduction, prophylactic mastectomy, or any cancer except non-melanoma skin cancer; current pregnancy; current breastfeeding or breastfeeding within the last 9 months; or symptoms of new breast problem, such as palpable lump, skin changes, or nipple discharge. The study was approved by the Fox Chase Cancer Center Institutional Review Board, and all women provided written informed consent prior to participating in the research study.

Procedures

Participants were recruited through Chinese community organizations, local medical practices, and newspaper advertisements. Trained research staff administered interviews in the participant's preferred dialect (Mandarin, Cantonese, or Fujianese) to assess demographic characteristics, level of acculturation, and psychosocial stress. Participants were asked to fast overnight for 8–12 h prior to providing a morning blood sample. Trained personnel collected 1–2 tubes of blood in 10 mL red top tubes, and blood samples were transported to the Biosample Repository Core Facility (BRCF) at Fox Chase Cancer Center for processing and storage. Blood samples were centrifuged, and aliquots of serum were stored at −80 °C until analysis. At the time of blood draw, research staff also conducted an anthropometric examination for weight, standing height, and waist circumference using standard protocols as previously reported (Tseng and Byrne, 2011). All measurements were taken and recorded in duplicate, with the mean value used in analyses.

Measures

Demographic background and acculturation

Participant age, education, occupation and spouse's occupation, length of US residence, marital status, smoking status, and current medications were assessed. Weight and height were used to compute body mass index (BMI). Acculturation was measured using an abridged version of the General Ethnicity Questionnaire—American (GEQ-A) (Tsai et al., 2000). GEQ-A items are scored on a five-point Likert type scale, with higher scores representing greater endorsement of American culture. The GEQ-A demonstrated good validity and reliability in Chinese immigrants in previous studies (Tsai et al., 2000) and demonstrated high internal reliability ($\alpha = 0.91$) in the present sample.

Responses regarding the highest level of education completed were collapsed into three categories: (1) 0–8 years, (2) 9–12 years, with or without completion of high school or vocational/technical school, and (3) at least some college, university, or graduate school. Participant's occupational category was based on her spouse's occupation, similar to a previous analysis (Tseng and Fang, 2012). Occupational categories included: (1) not employed, farmer/farm worker, machine or vehicle operator, craftsworker, or service worker; (2) clerical or sales worker; and (3) manager/administrator or professional/technical. The participant's own occupation was used ($n = 44$) if she was unmarried or her spouse was not employed. For 3% ($n = 13$) of the sample, no occupation was specified for either the participant or her spouse because both the participant and her spouse were unemployed, or because the participant was unemployed and unmarried.

Psychosocial stress

Life event stress was assessed using the Life Experiences Survey (LES) (Sarason et al., 1978), which is a widely utilized instrument that assesses the presence and impact of both positive and negative life experiences over the past year. The scale has been demonstrated to have good reliability and validity (Sarason et al., 1978). In brief, participants are instructed to mark any life events that occurred, and then the impact of each life event is rated on a 7-point scale ranging from −3 (extremely negative) to +3 (extremely positive). If an event did not occur, the item was coded as 0.

Standard procedures were used to calculate scores based on events reported (Sarason et al., 1978). Every event that occurred was coded as one "life change unit." Positive and negative life events were differentiated based on whether respondents reported a positive (1 to 3) or negative (−1 to −3) impact for the event. Positive and negative impact rating scores then were calculated by summing the impact ratings of positive and negative events, respectively, with the absolute value of impact ratings used for negative events.

Risk markers

Blood samples were transported to Quest Diagnostic Laboratories and tested using standard clinical laboratory methods for fasting glucose (with spectrophotometry) and insulin (by immunoassay). Insulin resistance was estimated according to the homeostasis model assessment (HOMA) as $\text{HOMA}_{IR} = \text{fasting insulin } (\mu U/mL) \times \text{fasting glucose } (mmol/L) / 22.5$ (Matthews et al., 1985). HOMA_{IR} is widely used to estimate insulin resistance in research, and previous studies have generally used distribution-based cutpoints between the 75th and the 90th percentile, with most cutpoints ranging from 1.6 to 3.8. We used a cutpoint of 2.69, representing the 75th percentile of HOMA-IR in a large ($n > 10{,}000$) epidemiological study of adults in China (Chen et al., 2013; Xing et al., 2004).

Statistical analyses

Of the 436 women enrolled in the study, thirteen were excluded for not having completed the questionnaire (n = 4) or providing a blood sample (n = 9), leaving a sample of 423. Descriptive analyses were used to characterize the study variables. Preliminary analyses were performed using correlational analyses, analysis of variance (ANOVA), or chi-square analyses depending on the nature of the variables, to examine potential sociodemographic correlates of insulin resistance and confounders of an association between stress and insulin resistance. These variables included age, menopausal status, country of birth, marital status, level of education, occupational category, and level of acculturation. BMI and waist circumference were also considered as possible confounders due to their strong association with insulin resistance. Variables associated with insulin resistance at the $p < 0.20$ level were included as covariates in subsequent analyses.

Next, logistic regression analyses were performed to estimate odds ratios (ORs) as measures of the stress-insulin resistance association, along with corresponding 95% confidence intervals (CI) with adjustment for potential sociodemographic confounders. In these analyses, the number of positive and negative life events and positive and negative life event impact rating scores were modeled as continuous variables. Results were similar when we used modified Poisson regression models to estimate prevalence ratios as an alternative measure of association. Goodness-of-fit of the model was assessed using the Hosmer–Lemeshow statistic (Hosmer and Lemeshow, 2000), and the pseudo R-square value was estimated using the Nagelkerke R^2 (Nagelkerke, 1991), which is similar to the coefficient of determination (R^2) in linear regression, ranges from 0 to 1, and provides an indication of how useful the explanatory variables are in "predicting" the outcome variable. All statistical analyses were conducted using SAS (version 9.2, 2008, SAS Institute, Cary, NC).

Results

Participant characteristics

Participant characteristics are presented in Table 1. Over 97% of participants were born in China, with the remaining 3% originating from another (non-US) country. Participants were relatively low acculturated; notably, mean GEQ-A score was 2.1 (SD = 0.7) and 68% reported speaking no English at home. Mean BMI was 23.5 kg/m^2 (SD = 2.8) and mean waist circumference was 79.5 cm (SD = 7.7). Mean $HOMA_{IR}$ was 1.1 (SD = 2.0), with 7% of participants having $HOMA_{IR}$ values indicative of insulin resistance. Participants reported a mean of 1.1 negative life events (SD = 2.0) and 0.5 positive life events (SD = 1.1) in the 12-month period prior to the study. The mean impact rating score was 2.1 (SD = 4.0, range 0–36) for negative life events and 0.9 (SD = 2.2, range 0–16) for positive life events.

Sociodemographic correlates of stress and insulin resistance

Greater acculturation, as measured by the GEQ-A, was significantly associated with a greater number of negative life events ($r = 0.24$, $p < 0.001$) and positive life events ($r = 0.25$, $p < 0.001$), as well as greater impact ratings of negative events ($r = 0.24$, $p < 0.001$) and positive events ($r = 0.24$, $p < 0.001$). Unmarried women reported a greater number of negative life events (M = 2.13, SD = 2.83) and positive life events (M = 0.97, SD = 1.96) compared to married women (negative life events: M = 1.02, SD = 1.94; positive life events: M = 0.45, SD = 1.04), both p-values < 0.01. Similarly, unmarried women reported greater impact ratings of negative events (M = 4.47, SD = 6.14) and positive events (M = 1.84, SD = 3.78) compared to married women (negative event impact ratings: M = 1.85, SD = 3.77; positive event impact ratings: M = 0.81, SD = 2.04), both p-values < 0.01.

Table 1
Participant characteristics (N = 423).

	%
Born in China	97
Married	92
Education	
<8 years	48
9–12 years/technical school	35
at least some college	17
Occupational category[a]	
Machine operator, farm, craft, or service worker, or not employed	80
Clerical or sales worker	8
Manager, administrator, or professional	12
Speak English at home[b]	
Not at all	68
A little	23
Somewhat or higher	9
$HOMA_{IR} \geq 2.69$	7
	Mean (SD)
Age (years)	43.9 (4.5)
Length of US residence (years)	7.5 (4.8)
GEQ-A	2.1 (0.7)
Number of positive life events	0.5 (1.1)
Impact rating score for positive life events	0.9 (2.2)
Number of negative life events	1.1 (2.0)
Impact rating score for negative life events	2.1 (4.0)
Body mass index (kg/m^2)	23.5 (2.8)
Waist circumference (cm)	79.5 (7.7)
$HOMA_{IR}$	1.1 (2.0)

Participants were recruited from the Philadelphia region between 2005 and 2008.
[a] Due to missing values, n = 411 for occupational category.
[b] Due to missing values, n = 412 for English language use at home.

Correlational analyses indicated that both BMI ($r = 0.21$, $p < 0.001$) and waist circumference ($r = 0.25$, $p < 0.001$) were positively correlated with $HOMA_{IR}$. In addition, age ($r = 0.08$, $p = 0.09$) and acculturation ($r = 0.09$, $p = 0.08$) were positively associated with $HOMA_{IR}$ at the $p < 0.20$ level. No other demographic variables were associated with $HOMA_{IR}$ at the $p < 0.20$ level. Therefore, age, acculturation, marital status, waist circumference, and BMI were included as covariates in subsequent analyses.

Associations between stressful life events and insulin resistance

In logistic regression analyses (Table 2), a greater number of negative life events were associated with insulin resistance in multivariate models. In fully adjusted models, each additional negative life event

Table 2
Associations of negative life events and negative event impact rating scores with insulin resistance (N = 423).

	OR (95% CI)	p
Model 1 — number of positive and negative life events		
Age	1.12 (1.02 to 1.23)	0.01
Acculturation	2.24 (1.21 to 4.15)	0.01
Marital status	0.16 (0.02 to 1.51)	0.11
BMI	1.06 (0.86 to 1.31)	0.59
Waist circumference	1.10 (1.01 to 1.19)	0.03
Positive life events	0.98 (0.69 to 1.39)	0.91
Negative life events	1.17 (1.02 to 1.34)	0.02
Hosmer–Lemeshow goodness of fit $\chi^2 = 8.36$, df = 8, $p = 0.40$; Nagelkerke $R^2 = 0.23$		
Model 2 — impact ratings of positive and negative events		
Age	1.12 (1.02 to 1.23)	0.02
Acculturation	2.29 (1.24 to 4.25)	0.01
Marital status	0.16 (0.02 to 1.49)	0.11
BMI	1.06 (0.86 to 1.31)	0.58
Waist circumference	1.10 (1.01 to 1.19)	0.03
Impact rating scores for positive life events	0.97 (0.81 to 1.16)	0.75
Impact rating scores for negative life events	1.08 (1.01 to 1.16)	0.03
Hosmer–Lemeshow goodness of fit $\chi^2 = 8.59$, df = 8, $p = 0.38$; Nagelkerke $R^2 = 0.22$		

Participants were recruited from the Philadelphia region between 2005 and 2008.

reported was associated with an OR for insulin resistance of 1.17 (95% CI 1.02–1.34). Importantly, the inclusion of BMI and waist circumference (both significantly associated with insulin resistance) had little impact on effect estimates. Similarly, greater negative life event impact ratings were significantly associated with insulin resistance (OR = 1.08, 95% CI 1.01–1.16). In contrast, number of positive life events and positive life event impact ratings were not associated with insulin resistance in these analyses. For both models, the Hosmer–Lemeshow test suggested good model fit ($p \geq 0.38$).

Discussion

This study is the first to our knowledge to report a significant association between negative life stress and insulin resistance among Chinese immigrant women. These findings are consistent with prior studies in which greater stress was associated with increased risk of insulin resistance and diabetes (Mooy et al., 2000; Pyykkonen et al., 2010). To date, no studies of which we are aware have focused on Chinese immigrants, a population that experiences considerable stress following migration, as well as a dramatic upsurge in the incidence of type 2 diabetes (Lee et al., 2011).

As previously noted, stress may increase diabetes risk through behavioral (e.g., diet) and biological (e.g., inflammation) pathways (Bjorntorp et al., 1999; Rosmond, 2005). With respect to diet, stress can lead to poorer dietary patterns that contribute to weight gain and disease risk (Torres and Nowson, 2007). Data suggest that under conditions of stress, humans prefer highly palatable foods that are energy dense (Ng and Jeffery, 2003; Oliver et al., 2000) and show a reduction in vegetable consumption (Mikolajczyk et al., 2009). This stress-associated shift to unhealthy dietary patterns may contribute, in part, to chronic disease risk.

With respect to biological pathways, higher levels of stress are associated with pro-inflammatory cytokines such as IL-6 and C-reactive protein (Steptoe et al., 2007), which in turn can interfere with insulin signaling and lead to insulin resistance (Xi et al., 2011). It is well-established that inflammatory processes play a central role in contributing to diabetes in both obese and non-obese individuals (Mohan et al., 1997). Prospective epidemiologic studies have demonstrated that elevated levels of inflammatory markers, such as IL-6 and CRP, predicted the subsequent development of diabetes in women 4 years later (Pradhan et al., 2001).

The current study has several limitations. First, the present analyses were carried out within a cohort of foreign-born Chinese women who were participating in a study of breast density. While this unique cohort offers an important opportunity to explore questions related to immigrant health, potential limitations exist with the use of secondary data for addressing such questions. Notably, the sample size is relatively modest compared to other studies of stress and insulin resistance. However, it should be noted that this study represents one of the largest samples of foreign-born Chinese women. Few cohorts are comprised entirely of first-generation Americans; as a result, this limits our ability to address important questions regarding factors that may be associated with disease risk in populations undergoing rapid changes in health status. Another limitation of secondary data analysis involves the possibility that the confounders assessed in the parent study are incomplete or imperfect for the present analysis. We acknowledge that the potential omission of important confounders may lead to an overestimate of the observed association and thus constrain the conclusions that can be drawn (Weng et al., 2009). Nonetheless, the present study represents a significant first step toward identifying how factors other than lifestyle behaviors may be associated with disease risk in an immigrant population.

Second, our cohort was limited to women, and therefore, it is unknown whether these associations would be observed among Chinese immigrant men. Previous studies have reported stronger associations between stress and diabetes risk in women than in men (Heraclides et al., 2012), and it has been proposed that women are more vulnerable to stress-related alterations in physical and mental health (Kajantie and Phillips, 2006). Thus, further exploration of gender-specific pathways in stress and insulin resistance is warranted. Third, the cross-sectional nature of the data precludes any causal inferences regarding the direction of the observed associations and limits our ability to determine cause and effect. Longitudinal studies are needed to delineate the temporal nature of such associations. Fourth, we acknowledge that insulin resistance represents an intermediate risk marker of disease. However, a significant body of work suggests that insulin resistance is a major predictor of type 2 diabetes (Kahn, 2003), and thus represents a clinically relevant endpoint. Finally, our focus on an immigrant population may limit generalizability to other populations. On the other hand, immigrant populations are uniquely informative for identifying pathways contributing to chronic disease given that these subgroups undergo the most rapid transitions in disease risk.

Conclusions

The present study suggests that negative life stress is associated with insulin resistance in an immigrant population that is undergoing significant health transition. Future studies that characterize immigrant psychosocial experiences in conjunction with the behavioral and lifestyle changes that occur following migration to the US are critically needed. These findings will not only increase our understanding of the various social, behavioral, and biological pathways that underlie disease risk, but will also inform the development of future chronic disease prevention efforts in this growing population.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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