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The differential impact of adverse childhood experiences in the development of pre-diabetes in a longitudinal cohort of US adults

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ABSTRACT

Background: ACEs have a dose-response relationship with diabetes. The relationship between ACEs and pre-diabetes is not well known and may represent an effective area for prevention efforts.
Methods: Data from 1054 participants from two waves of the longitudinal MIDUS study were used. Multivariate general linear regression models assessed the relationship between ACEs and biomarker outcomes. Correlation tests and mediation models investigated the relationship between ACE and pre-diabetes.
Results: Individuals reporting ACEs were statistically significantly more likely to have higher BMI (1.13 (0.34–1.92)), higher waist circumference (2.74 (0.72–4.76)), elevated blood fasting insulin levels (2.36 (0.71–4.02)) and higher insulin resistance (HOMA-IR (0.57 (0.08–1.06)). BMI/waist circumference and insulin resistance did not maintain independent relationships with ACEs once HOMA-IR was included in the dichotomized ACE model ($p = 0.05$ and $p = 0.06$, respectively), suggesting the relationship between BMI and ACEs may be mediated by insulin resistance.
Conclusions: These results represent one of the first studies to examine the differential impact of ACEs on a diverse set of clinical pre-diabetes measures. Findings suggest sexual and physical abuse, and financial strain during childhood are important factors associated with higher risk for pre-diabetes, and should be considered during intervention development.

1. Introduction

Adverse childhood experiences (ACEs) represent a broad cascade of events occurring before the age of 18, such as abuse, neglect, and family instability, that produce a state of chronic stress throughout childhood and confer risk for poor health in adulthood.[1–3] Well documented as being predictors of adult morbidity and mortality,[4–8] a single endorsement of an ACE significantly increases risk for diabetes in adulthood, with risk increasing as number of reported ACEs increases.[1,9,10] A growing body of evidence supports the relationship between overall ACEs and diabetes,[9,11,12] the cumulative impact of ACEs and diabetes,[13] and the differential impact of specific ACEs and diabetes.[12,14,15] However, less is known about the mechanisms of influence, and how best to intervene to disrupt the impact of ACEs on developing diabetes.[9] The ACE literature suggests that lifestyle, such as physical activity and nutrition, play an important role in leading to adult morbidity.[16] Specifically, obesity has been suggested as a pathway between ACEs and diabetes.[15] However, this has not been examined in a pre-diabetic population. Additionally, little has been done to provide clinicians with a model for treating patients who have ACEs and are at risk for developing diabetes.[9]

Pre-diabetes is a widely unexplored area in the literature for understanding the impact of ACEs on diabetes and may be an important area of emphasis for intervention in individuals exposed to ACEs.[17] Pre-diabetes is characterized by elevated glucose levels and is consistent with a Hemoglobin A1c (HbA1c) ranging from 5.7–6.4%, fasting plasma glucose (FPG) of 100 mg/dL to 125 mg/dL, or oral glucose tolerance test (OGTT) of 140 mg/dL to 199 mg/dL.[18] Additional risk factors for pre-diabetes include being overweight, being over the age of 45, and family history of diabetes.[19] While designation of pre-diabetes does not necessarily determine a future diagnosis of diabetes, risk increases significantly, and little is known as to whether ACEs serve to compound risk for pre-diabetes, ultimately leading to diabetes. Li and colleagues recently examined whether exposure to ACEs significantly predicts insulin sensitivity and glucose intolerance in a sample of adults and found that among adults endorsing ACEs, greater insulin sensitivity was

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demonstrated among those with ACEs compared to those without as measured by an OGTT, however individual ACE categories were not explored.[17]

As diabetes remains the 7th leading cause of death in the US, representing significant economic burden and hospitalization,[19] two important gaps in the literature warrant greater attention: 1) the biological pathways and the latency period between exposure to ACEs and diabetes development, and 2) the differential impact that individual ACEs have on insulin sensitivity and diabetes related outcomes, i.e. are certain ACEs more detrimental to the development of diabetes compared to others. Addressing these gaps will provide clinicians and researchers with evidence to guide screening and response to ACEs in the healthcare setting. Given the growing focus on trauma informed care,[20] new information is needed to structure screening and treatment for individuals who experiences ACEs. Using a longitudinal cohort of US adults, this study aimed to examine the impact of six ACE categories on the development of pre-diabetes as measured by glycemic control, glucose measures, insulin measures, and obesity markers.

2. Material and methods

2.1. Sample

Data was obtained from the first two waves of the longitudinal study "Midlife in the United States: A National Longitudinal Study of Health and Well-Being" (MIDUS). MIDUS is funded by the National Institute on Aging and is a publicly available dataset. The first phase of dataset was initiated in 1995–1996. The first wave included 7108 participants between the ages of 25 and 74 who completed telephone interviews and self-administered questionnaires (SAQ). Participants were non-institutionalized adults from the contiguous US. Surveys included questions that explored a wide range of demographic characteristics, personality traits and behaviors. Participants from the first wave then participated in a second phase of MIDUS from 2002 to 2004 during which biological and neurological data was collected from 1054 participants. Individuals who accepted the invitation for collection of biologic specimens during the second wave spent 24 h in one of three General Clinical Research Centers, received a physical exam, collection of fasting blood samples, and a urinalysis in the morning after an overnight stay. Biological measures collected as part of the MIDUS wave 2 study included height, weight, waist circumference, waist to hip ratio, blood pressure, hemoglobin A1c, blood fasting glucose levels, and blood fasting insulin levels. Details of recruitment strategy, data collection methods, and detailed sample description have been described elsewhere.[23] MIDUS replaced missing values with respondents mean value. When valid responses were not available responses were recorded as missing and, in some cases, responses were imputed for missing data.[24] The Institutional Review Board provides a waiver to conduct this secondary data analysis using publicly available data.

2.2. Measures

2.2.1. Adverse childhood experiences

The ACE Study Questionnaire[1] was used to identify measures of adverse events experienced during childhood. The MIDUS study collected information on a number of possible ACEs included in the Felitti et al definition of ACE, as well as questions categorized by the MIDUS investigators as additional ACEs surrounding family instability and financial strain. Therefore, a combined set of ACE categories was created to include: emotional abuse, physical abuse, sexual abuse, substance abuse by parents during childhood, family instability, and financial strain.

ACE categories included:

1) Emotional abuse. This item was derived from childhood family background questions in wave 1 and Childhood Trauma Questionnaire (CTQ) completed by participants at the biomarker collection.
2) Physical abuse. This item was derived from childhood family background questions and CTQ, as well questions regarding "ever physically assaulted" before age 18 from wave 2 SAQ.
3) Sexual abuse. This item was also derived CTQ, and question regarding "ever sexually assaulted" before age 18 from wave 2 SAQ.
4) Parental substance abuse. This item referred to substance abuse from a parent during childhood and was derived from childhood background question "what was the main reason father/mother was not working for pay during most of your childhood years? – Alcohol or drug abuse"; additional items assessing this category were derived from the CTQ questions "My parents were too drunk or high to take care of me"; Wave 2 phone interview question "lived with alcoholic during childhood" and "Ever parent drank caused problems" and "Ever parent drugs caused problems".
5) Family instability. This item was measured using the following questions: "Did you live with both of your biological parents up till you were 16?"; "Who was the male head of your household for most of your childhood"; "ever parents divorced" before age 18 at wave 2 SAQ.
6) Financial strain. This item was derived from childhood background questions regarding receipt of welfare; a mother or father having less than a high school education for father; and; report of being 'worse off' than other families.

Each type of ACE was dichotomized. A count of reported ACEs was additionally created for each individual to indicate the number of ACE categories the individual responded positive, as commonly seen in the ACE literature.[1] Finally, a dichotomized ACE variable was created to indicate yes if an individual responded positive to any of the six categories, and no if they responded negative to all six categories.

2.2.2. Biological measures

Biological markers were taken from the second wave of the MIDUS study. The following markers were selected for analysis and categorized based on national recommendations:

1) Body mass index (BMI). BMI was categorized as underweight (<18.5), normal (18.5 to <25), overweight (25.0 to <30), obesity (30.0 or higher), and morbid obesity (40 or higher).[25]
2) Waist circumference in centimeters. Waist circumference was categorized by sex. For men: low (<94), high (94–<102), and very high (102 and greater. For women: low (<80), high (80–<88), and very high 88 and greater).
3) Waist-to-hip ratio. Waist-to-hip ratio was categorized by sex. For men: ideal-very low risk (<0.90), low risk (0.90–0.95), moderate risk (0.95–1.0), and high risk (1.0 and greater). For women: ideal-very low risk (<0.70), low risk (0.70–0.80), moderate risk (0.80–0.85), and high risk (0.85 and greater).
4) Systolic and diastolic blood pressure. Blood pressure was categorized as normal (<120/<80 mm Hg), prehypertension (120–<140/<80 mm Hg), stage 1 hypertension (140–<160 or 90–100 mm Hg), and stage 2 hypertension (≥160 or ≥100 mm Hg).[26]
5) Blood fasting glucose. Blood fasting glucose was categorized as normal (<100), pre-diabetes (100–<126), and diabetes (126+).[27]
6) Blood fasting Insulin. Blood fasting insulin was categorized as normal (<8), low risk (8–<12), moderate risk (12–<25), and high risk (25+).[27]
7) Insulin resistance. Insulin resistance (IR) was categorized as normal (<2), low IR (2–<3), moderate IR (3–<5), and severe IR (5+).[27] Insulin resistance (IR) was determined using the homeostatic model assessment of insulin resistance = HOMA IR calculated as a product of glucose (G0, mg/dL) and insulin (I0, μU/L) divided by the constant 405: HOMAIR = (G0 × I0) / 405. HOMA-IR was a precalculated variable provided in the publicly available dataset. Details of variable calculations can be found through MIDUS ICPSR Codebook.[21,22]

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