Hyperinsulinemia Trends in U.S. Adults without Diabetes: A Joinpoint Analysis

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ABSTRACT

Hyperinsulinemia is associated with various chronic diseases and cardiovascular disease risk factors. Investigating changes in hyperinsulinemia over time is important due to its association with pervasive clinical outcomes. PURPOSE: Estimate the prevalence and examine trends in hyperinsulinemia among U.S. adults without diabetes between 1999 and 2018. METHODS: Weighted data from adults ≥20 years of age from the 1999-2018 cycles of the National Health and Nutrition Examination Survey (NHANES) were analyzed. Exclusion criteria included pregnancy, history of diabetes or blood glucose ≥126 mg/dL, and taking diabetes medications (n=23,447). The 20-year trend for hyperinsulinemia (defined as the 75th percentile of log-transformed insulin) was nonlinear. The 2009-2010 cycle was identified as a joinpoint, creating two segments – 1999/2000 to 2009/2010 and 2009/2010 to 2017/2018. Each segment was examined for significant trends. RESULTS: Overall, an initial rise in hyperinsulinemia was followed by a drop and plateau. The age-adjusted prevalence of hyperinsulinemia increased by ~18% in the study population between 1999/2000 and 2017/2018 (21.5% to 25.3%, P for trend 0.0034). The age-adjusted prevalence of hyperinsulinemia increased by ~65% in the first joinpoint segment (21.5% to 35.4%, P for trend <0.0001). The prevalence of hyperinsulinemia decreased ~29% in the second joinpoint segment, but not significantly (35.4% to 25.3%, P for trend=0.10). CONCLUSION: Hyperinsulinemia rates in U.S. adults without diabetes significantly increased at the turn of the century, however, the more recent decline and steadying of rates may be due to improved medication regimens and lifestyle modifications. Both warrant further investigation in this population.

INTRODUCTION

Diabetes continues to be an epidemic in the United States (U.S.) and around the world. There has been an increase in both type 1 (1) and type 2 diabetes (T2D) (2), however, most cases continue to be T2D (90-95%). The estimated age-adjusted prevalence of diabetes in U.S. adults has increased approximately 46% over the past two decades, going from 9.8% in 1999-2000 to 14.3% in 2017-2018 (3). The antecedent to T2D is insulin resistance (IR) and compensatory hyperinsulinemia (4), which have both been shown to be associated with various cardiometabolic risk factors (5), the aggregation of risk factors (6), and mortality (7, 8). Recent evidence suggests that hyperinsulinemia and IR may result from an adaptive process to a physiological environment including augmented fat mass and circulating free fatty acids (9).

Nearly three out of four U.S. adults ≥20 years of age are classified as either overweight (31.1% [BMI = 25.0-29.9]) or obese (42.5% [BMI ≥30.0]) (10). With overweight and obesity maintaining epidemic proportions in U.S. adults, IR and hyperinsulinemia will remain ubiquitous. Utilizing data from the National Health and Nutrition Examination Survey (NHANES), Li et al. (11) examined trends in hyperinsulinemia in U.S adults between 1988-1994 and 1999-2002 and 1999-2002 and reported a 35.1% increase in the age-adjusted prevalence. The primary aim in this study was to provide updated estimates of trends in hyperinsulinemia in U.S. adults, utilizing 1999-2018 NHANES data. A secondary aim was to examine the potential associations with various measures of adiposity. Similar to Li et al. (11), we utilized fasting serum insulin concentrations as a proxy for IR, due to more precise measures of glucose disposal not being available in NHANES.

PURPOSE

Estimate the prevalence and assess the trends in hyperinsulinemia is U.S. adults without diabetes between 1999 and 2018.

METHODS

This study utilized 20 years of data from the 1999-2018 NHANES, a continuous survey conducted by the National Center for Health Statistics (12). The NHANES provides national estimates of the health and nutritional status of non-institutionalized U.S. civilians over the age of two months.

Sample

A fasting sub-sample of male and nonpregnant females (n=23,447) (≥20 years of age) without diabetes, who completed the in-home interview questionnaire and visited a mobile examination center to provide anthropometric measurements (WC and BMI), and serum blood samples necessary for the measurement of fasting insulin and other clinical biomarkers that were used in the analyses.

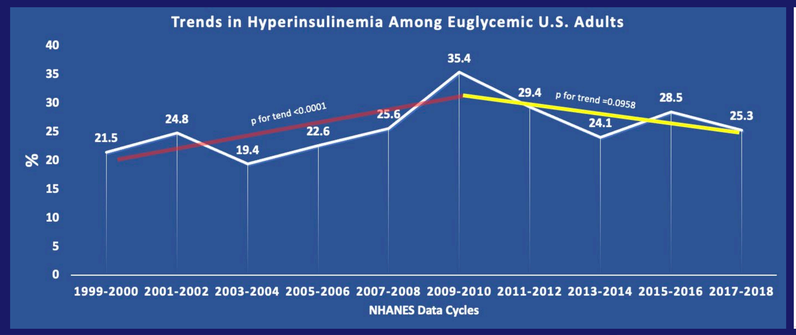
Hyperinsulinemia

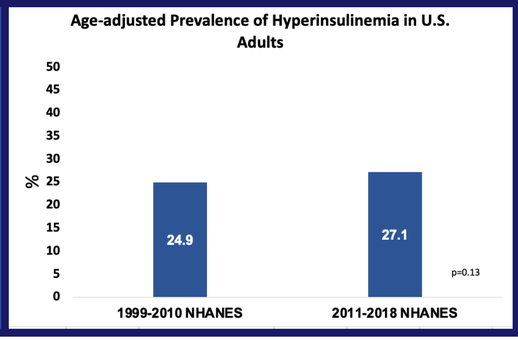
Hyperinsulinemia was calculated using the weighted 75th percentile of log-fasted insulin among adults who had fasting blood glucose values <126 mg/dL, answered no to a diabetes question, and reported taking no diabetes medications.

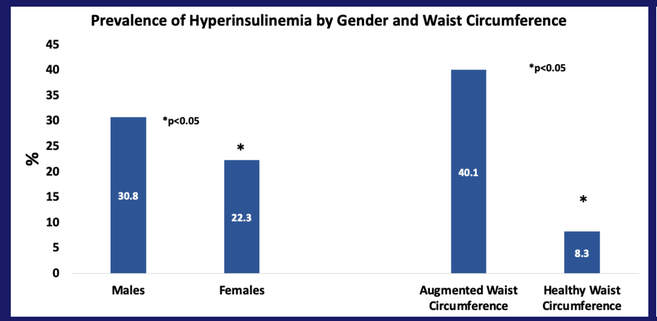
Statistical Analyses

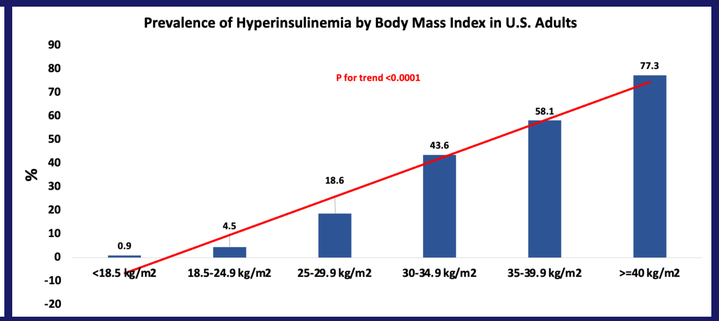
The data in this study were managed using SAS 9.4 (13). SAS was used to conduct complex variable recodes, data coding validation and to establish the p for trend for each segment. SAS-SURVEY procedures were subsequently used to conduct the analyses, incorporating sampling weights within the context of the correlated multi-stage complex sampling design inherent to NHANES. Joinpoint 4.1 software was used to determine the best joinpoint (14).

RESULTS









DISCUSSION

This observational study utilized data from 10 consecutive two-year cycles of NHANES since the turn of the century. Our findings illustrate a significant upward trend in the prevalence of hyperinsulinemia between 1999 and 2010, which is similar to what was reported by Li et al. (11) when analyzing earlier NHANES data. However, this upward trend is followed by a slight downward trend (p=0.10) between 2010 to 2018. We also illustrate a consistent and significant positive dose-response relationship between BMI and hyperinsulinemia, and an estimated five-fold difference between the prevalence of hyperinsulinemia in U.S. adults with and without an augmented waist circumference. These observations are congruent with the hyperinsulinemia obesity relationship reported by Ormazabal et al. (5) and the adaptive mechanistic response reported by Fryk et al. (9). Furthermore, males continue to possess a greater prevalence of hyperinsulinemia.

CONCLUSIONS

Overall, hyperinsulinemia rates have significantly increased among U.S. adults during the past 20 years. Central adiposity and BMI are both strongly associated with hyperinsulinemia.

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