# Diabetes Mellitus and Glucose Metabolism

## METABOLIC DISEASE IN CHILDREN

### *HOMA-IR Levels in US Youth Ages 12–18 Years From 1999–2018*

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**Introduction:** The Homeostasis Model Assessment of insulin resistance (HOMA-IR) is a validated surrogate measure of insulin sensitivity and beta-cell function for epidemiological studies. Insulin resistance is closely associated with obesity and shares dysmetabolic state with other cardiometabolic risk factors. The aim of this study was to analyze the change in HOMA-IR levels in US youth from 1999 to 2018.

**Methods:** Serial cross-sectional data of fasting insulin and glucose levels measured in youth aged 12 to 18 years enrolled in National Health and Nutrition Examination Surveys representative of US population from 1999 to 2018 were used. Two-year survey cycles were combined to derive 4-year survey periods, and NHANES recommended adjustments were made for glucose and insulin levels for forward conversion to 2017–18 instrument levels. Median HOMA-IR was compared across the survey periods in subgroups by age, gender, race/ethnicity and levels of obesity. Association of HOMA-IR with selected cardiometabolic risk factors was assessed. Change of HOMA-IR levels were analyzed using design adjusted multivariable regression models, association of HOMA-IR with cardiometabolic risk factors was assessed and percentiles were derived.

**Results:** In an analysis of 5,541 youth, the unadjusted median HOMA-IR increased from 1.83 (95% CI 1.77–1.89) in 1999-02 to 2.41 (95% CI 2.29–2.54) in 2007–10 and has remained in this range till 2015–18. Youth with obesity (Body mass index > 95$^{th}$ percentile or waist circumference > 90$^{th}$ percentile), female gender, those of Hispanic and Black origin, and those aged 12–16 years had higher levels of HOMA-IR (p <.001). While adjusting for age category, sex, race/ethnicity, obesity represented by waist circumference z-score with its quadratic term and interaction with gender, HOMA-IR increased by 26% (95% CI 15–37) in 2015–18 as compared to 1999-02. For waist-circumference z-score (WCZ) > 1, the HOMA-IR levels were higher in boys compared to girls. The addition of total body fat from DXA scans in the model, when available, explained the variance related to gender, but not the interaction between gender and WCZ. No change was observed in the higher levels of HOMA-IR by ethnicity when high sensitivity CRP level as a measure of inflammation was added to the model. There was a positive association of HOMA-IR with triglycerides (29 %/unit, 95% CI 25–33), non-HDL cholesterol (8 %/unit, 95% CI 6–10), systolic blood pressure (2% /unit, 95% CI 1–2) and alanine transferase (11 %/unit, 95% CI 8–14) while controlling for age, sex, race/ethnicity, obesity and survey period. In youth with BMI between 5-85$^{th}$ percentile, HOMA-IR decreased with increase in age from 12 to 18 years.

**Conclusions:** HOMA-IR levels in US youth have increased since 1999-02 and may herald future cardiometabolic risks.

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### *Hyperglycemia Requiring Insulin Among Pediatric Patients Diagnosed With Hemophagocytic Lymphohistiocytosis*

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**Introduction:** Hemophagocytic lymphohistiocytosis (HLH) is a rare, life-threatening disorder marked by massive cytokine release due to macrophage and T-cell activation. Hallmarks of the diagnosis include fever, splenomegaly, cytopenias, hypertriglyceridemia, hypofibrinogemia, and elevations in ferritin and soluble IL-2 receptor. Given HLH is associated with critical illness, elevation in inflammatory markers, and treated with glucocorticoids, the development of hyperglycemia during its course is not unexpected. However, detailed descriptions of the severity of hyperglycemia and strategies in insulin management among HLH patients are lacking. We describe 10 years' experience at a single tertiary pediatric health center with HLH patients who developed insulin dependent hyperglycemia.

**Objectives:** To describe the demographics, clinical and laboratory findings, treatment regimens, and outcomes for children with HLH treated with insulin due to hyperglycemia.

**Study Design:** Retrospective chart review from 2010 through 2019 of youth 0 to 21 years of age who required insulin therapy during or shortly after a hospitalization where they were diagnosed with HLH using established criteria. Descriptive statistics were used to characterize the population of interest.

**Results:** Of 30 patients diagnosed with HLH, 33% (n=10) required insulin therapy. Half (n=5) were female and half (n=5) male. The mean age was 8.4 years (7.8 months - 17 years). The majority (80%) were non-Hispanic white. Mean BMI at admission was 53$^{rd}$ percentile (5$^{th}$ - 87$^{th}$ percentile). Max serum glucose ranged from 267 to 725 mg/dL (mean 421 mg/dL). Marked inflammation was present (max CRP 2.6 - 44.9 mg/dL, max ferritin 1,091 - 90,219 ng/mL). All were treated with dexamethasone, doses ranging from 5 to 11 mg/m$^2$/day and duration from 2 to 70 days. Most (90%) received parenteral nutrition (PN) with a mean max GIR of 8 mg/kg/min (SD=2.7). Intravenous infusions of regular insulin were used in 80% of patients, though 2 patients were later transitioned to long and short acting subcutaneous insulin. Mean duration of IV insulin therapy was 9.5 days (2–24 days); however, 2 patients died while on IV insulin therapy. The majority (70%) needed insulin within 5 days of starting steroids. Two patients (20%) were treated with subcutaneous insulin only (no IV). Only 1 patient was discharged home on insulin therapy. Mean hospital stay was 60 days (10–202 days). Mortality was 50% (n=5).