Duration of Fasting, Serum Lipids, and Metabolic Profile in Early Childhood

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Objectives To evaluate the association between fasting duration and lipid and metabolic test results.

Study design A cross-sectional study was conducted in healthy children aged 0-6 years from The Applied Research Group for Kids! (TARGet Kids!) primary care practice network, Toronto, Canada, 2008-2013. The associations between duration of fasting at blood collection and serum lipid tests and metabolic tests were evaluated using linear regression.

Results Among 2713 young children with blood tests the fasting time ranged from 0 to 5 hours (1st and 99th percentiles). Fasting duration was not significantly associated with total cholesterol ($\beta = 0.006$; $P = .629$), high-density lipoprotein (HDL) ($\beta = 0.002$; $P = .708$), low-density lipoprotein ($\beta = 0.0013$; $P = .240$), non-HDL ($\beta = 0.004$; $P = .744$), or triglycerides ($\beta = -0.016$; $P = .084$) adjusted for age, sex, body mass index, maternal ethnicity, and time of blood draw. Glucose, insulin, and homeostasis model assessment of insulin resistance were significantly associated with fasting duration, and the average percent change between 0 and 5 hours was –7.2%, –67.1%, and –69.9%, respectively. The effect of fasting on lipid or metabolic test results did not differ by age or sex; HDL and triglycerides may differ by weight status.

Conclusions In this cohort of healthy young children, we found little evidence to support the need for fasting prior to measurement of lipids. The effect of fasting on glucose was small and may not be clinically important. When measuring serum lipid tests in early childhood, fasting makes a very small difference. *(J Pediatr 2016;■■:■■-■■).*

Trial registration ClinicalTrials.gov: NCT0186953.

Measuring serum lipid and metabolic tests in early childhood may be important for population health surveillance, cardiometabolic disease prevention, and clinical disease management.[1] Adverse lipid and metabolic profiles in early childhood may lead to increased risk of adult-onset cardiometabolic disease.[2-4] Fasting is recommended prior to blood collection for testing lipids (except non-high-density lipoprotein [HDL]), glucose, and insulin in childhood,[1] but there are no harmonized guidelines on the duration of fasting time required. In adults, overnight fasting, or fasting for >8 hours is recommended prior to lipid testing.[5,6] However, recent studies among adults have suggested that fasting has minimal impact on total cholesterol, HDL, and possibly low-density lipoprotein (LDL), but somewhat larger changes, up to 15%-20%, for triglycerides.[7-9] In infants and young children, it is challenging to collect fasting blood samples because of frequent meals throughout the day, and fasting for some young children may not be safe.[10,11] Few studies have explored whether fasting is necessary for blood testing in children.[12,13]

The primary objective of our study was to evaluate if fasting duration was associated with serum lipid (total cholesterol, HDL, LDL, non-HDL, triglycerides) and metabolic testing results (insulin, glucose, and homeostasis model assessment of insulin resistance [HOMA-IR]) in healthy children 0-6 years of age. The secondary objective was to evaluate if the association between fasting and lipid and metabolic profile variables differs by sex, adiposity, and age.

BMI	Body mass index
HDL	High-density lipoprotein
HOMA-IR	Homeostasis model assessment of insulin resistance
LDL	Low-density lipoprotein
NHANES	National Health and Nutrition Examination Surveys
TARGet Kids!	The Applied Research Group for Kids!
zBMI	BMI z-score

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Methods

A cross-sectional analysis was conducted in children 0 to 6 years of age. Children were recruited between July 2008 and December 2013 from scheduled health supervision visits through The Applied Research Group for Kids! (TARGet Kids!) primary care practice-based research network (ClinicalTrials.gov: NCT0186953).[14] Children were recruited from 9 pediatric or family practice primary care clinics in Toronto, Canada and followed at annual health supervision visits.

Children were eligible for inclusion if they were considered healthy by parent report and were younger than 6 years of age at the first visit. Children were excluded if they had severe developmental delay, health conditions affecting growth, any acute or chronic illness (other than asthma), or if their families were unable to complete English questionnaires. Consent was obtained from parents, and this study was approved by the Research Ethics Boards at The Hospital for Sick Children and St. Michael's Hospital.

Time of blood sample collection was recorded by the research assistants. Children were not advised on duration of fasting prior to blood draw. The time of last meal or snack and time of last drink (except water) were measured from parent report. Fasting duration was calculated by subtracting the time of last meal or drink (whichever was closest to blood sample time), from the blood sample time.

The outcomes were total cholesterol, HDL, LDL, non-HDL, triglycerides, insulin, glucose, and HOMA-IR. Blood samples were collected in the primary care office by trained pediatric phlebotomists and transported to Mount Sinai Services Laboratory, Toronto, Ontario. Laboratory analyses were performed daily using standard procedures as follows. Glucose was measured using enzymatic reference method with hexokinase; lipids (total cholesterol, triglycerides, HDL, and non-HDL) were measured using enzymatic colormetric on the Roche Modular platform (Roche Diagnostics, Risch-Rotkreuz, Switzerland); and insulin was measured using electrochemiluminescence immunoassay. LDL was calculated using the Friedewald equation. LDL was not calculated for children with triglycerides >4.5 nmol/L (n = 20). The HOMA-IR index was calculated by first converting insulin from pmol/L to uIU/mL by dividing by 6.945 and then dividing the product term of glucose (mmol/L) and insulin (uIU/mL) by 22.5.[15]

Covariates identified through a review of the literature included age, sex, maternal ethnicity, time of blood draw, and body mass index (BMI) z-score (zBMI). Height and weight were measured by trained research staff using a precision digital scale (SECA, Hamburg, Germany), and stadiometer (SECA) for standing height or length board for children under 2 years old.[16] zBMI were defined using the World Health Organization growth standards,[17] which are the recommended standards for our population.[18]

Statistical Analyses

For our primary analysis, we performed linear regression modeling using cross-sectional data from the first TARGet Kids! visit. We fit separate multiple linear regression models for each of the 8 outcomes using both unadjusted and fully adjusted models. Adjustment for potential confounders included all a priori specified covariates (see above). Triglycerides, insulin, and HOMA-IR were log-transformed in all models to achieve a normal distribution, and regression coefficients were back-transformed to the original units and are reported as the change in median concentration. For the secondary analysis, all linear regression models were stratified by age group, sex, and weight status. Statistical analysis was conducted using SAS statistical software v 9.3 (SAS Institute Inc, Cary, North Carolina). All statistical tests were 2-sided, and statistical significance was defined as $P < .05$.

Results

A total of 5161 children participated in TARGet Kids! between 2008 and 2013. Blood samples were obtained at 1 or more visits from 3191 children, and there were 2747 children with a visit between 0 to 6 years of age with time of blood draw and time of last meal or drink recorded. Children with time of last meal or drink recorded as after the time of blood draw (n = 33) or fasting time greater than 12 hours (n = 1) were excluded from the analysis. Among the 2713 children included in the primary analysis, the mean age was 35 months, 46% were female, 68%

Table I. Descriptive characteristics among children 0-6 years of age in TARGet Kids! (n = 2713)

Variables	First visit with blood testing
Age (mo), mean (SD)	34.6 ± 19.9
zBMI, mean (SD)	0.14 ± 1.09
Fasting duration (h), mean (SD)	1.87 ± 1.26
<1 h, no. (%)	478 (18%)
1 h, no. (%)	561 (21%)
2 h, no. (%)	805 (30%)
3 h, no. (%)	551 (20%)
4 h, no. (%)	250 (9%)
≥5 h, no. (%)	68 (2%)
Sex	
Female, no. (%)	1258 (46%)
Male, no. (%)	1455 (54%)
Maternal ethnicity	
European, no. (%)	1775 (68%)
East Asian, no. (%)	178 (7%)
Southeast/South Asian, no. (%)	237 (9%)
Other, no. (%)	411 (16%)
Weight	
Obese (zBMI >2.0), no. (%)	121 (5%)
Overweight (zBMI >1.0 and ≤2.0), no. (%)	379 (14%)
Normal (zBMI ≥ −2.0 and ≤1.0), no. (%)	2081 (79%)
Wasting (zBMI <−2.0), no. (%)	64 (2%)
Cholesterol (mmol/L), mean (SD)	4.02 ± 0.69
HDL (mmol/L), mean (SD)	1.26 ± 0.32
LDL (mmol/L), mean (SD)	2.16 ± 0.65
Non-HDL (mmol/L), mean (SD)	2.75 ± 0.68
Triglycerides (mmol/L), mean (SD)	1.31 ± 0.74
Insulin (pmol/L), mean (SD)	63.27 ± 56.58
Glucose (mmol/L), mean (SD)	4.63 ± 0.64
HOMA-IR, mean (SD)	1.97 ± 2.02

Conversion factors: To convert to mg/dL for cholesterol, HDL, LDL, and non-HDL divide by 0.0259; for triglycerides divide by 0.0113; and for glucose divide by 0.0555. To convert insulin to μIU/mL divide by 6.945.

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