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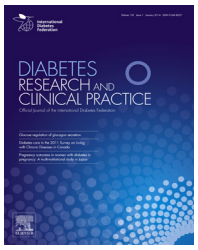

Effect of a mixed meal on plasma lipids, insulin resistance and systemic inflammation in non-obese Indian adults with normal glucose tolerance and treatment naïve type-2 diabetes

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ABSTRACT

Aim: Asian Indians are believed to have a lower capacity to clear a glucose load even during normoglycemia. High post meal glucose levels have been linked to postprandial dyslipidemia and generation of proinflammatory cytokines. Since humans spend most of their time in the postprandial state, the present study aims to evaluate the relationship of insulin resistance (IR) in the basal state with dyslipidemia and systemic inflammation (hs-CRP, IL-6 and TNF-a), in the fasting state, 2 h and 4 h after a mixed meal, in Indian adults with normal glucose tolerance, and new onset type-2 diabetes.

Methods: Forty-eight people with type 2 diabetes and 32 individuals with normoglycemia, 30–70 years age, not on medications, underwent blood sampling after overnight (12 h) fast and 2 and 4 h after a mixed meal (carbohydrates, proteins and fat content 79.1%, 7.7% and 13.2%, respectively).

Results: Triglyceride (TG), TG/HDL-C (high density lipoprotein), HDL-C/LDL-C (low density lipoprotein) ratios, IR parameters, and inflammatory markers were significantly higher among patients with diabetes. There was a fall in total cholesterol (TC), HDL-C and LDL-C at 2 and 4 h after the meal in both groups. Compared with fasting, 4-h postprandial TC, TG and HDL-C were significantly better positively correlated with IR in normal individuals. Postprandial hs-CRP was not significantly different to fasting in both groups. Postprandial IL-6 and TNF-α were significantly lower in both groups.

Conclusion: Consumption of a carbohydrate rich meal is associated with a rise in TG and fall in TC, HDL-C, LDL-C, IL-6 and TNF-α among normal individuals and people with type 2 diabetes.

1. Introduction

Dyslipidemia in individuals with metabolic syndrome is characterized by elevated serum triglyceride, decreased high density lipoprotein cholesterol (HDL-C) and increased small dense low density lipoprotein (sd-LDL) particles [1]. Individuals with insulin resistance, especially after a fatty meal have higher postprandial triglyceride rich lipoprotein particles [chylomicrons and very-low-density lipoproteins (VLDL-C)], a result of both higher peak concentration and delayed clearance from the circulation [2]. These particles are

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subsequently metabolized to atherogenic remnants which penetrate the endothelium and contribute to the formation of foam cells [3], increased cytokines and C-reactive protein (CRP) in people with type 2 diabetes (T2DM) [4,5]. Elevated cytokines [interleukin-1β (IL-1β), IL-6] and CRP are believed to be predictive of development of diabetes in individuals with metabolic syndrome [6].

Estimation of lipid parameters has traditionally being done in the fasting state, without definitive evidence to suggest that fasting concentrations are superior to postprandial in terms of predicting metabolic outcomes and cardiovascular risk. Humans spend most of their time in a postprandial state. Hence it may be expected that postprandial lipid values would be a better predictor of insulin resistance (IR) and the associated systemic inflammation. However there are very few studies addressing this issue of postprandial dyslipidemia in relation to IR among people with diabetes and normal individuals [7,8]. The relationship between postprandial dyslipidemia and inflammatory markers (IL-6 and TNF-α) has not been studied extensively, with conflicting reports [9–11].

Hence the aim of this study was to study the relationship of IR in the basal state with dyslipidemia and systemic inflammation (hs-CRP, IL-6 and TNF-α) fasting, and 2 and 4 h after a mixed meal, in normal individuals and individuals with new onset T2DM.

2. Patients and methods

Family members of patients of T2DM, 30–70 years of age, attending the diabetic clinic of department, who did not have any history of diabetes and gave consent, were screened with 75 g anhydrous glucose oral glucose tolerance test with estimation of blood glucose at fasting (FBG) and 2 h post glucose (2hPGBG). Individuals with FBG < 100 mg/dl (5.5 mmol/l) and 2hPGBG < 140 mg/dl (7.8 mmol/l) were considered for the study. In addition, individuals with recent diagnosis of T2DM (<3months), treatment naïve, 30–70 years age, clinically and biochemically stable, without any acute metabolic complications of diabetes were also considered for the study. Individuals with history of recent alcohol use (<6 months), use of anti-lipid medications, drugs, or severe co-morbid state were excluded. The study period was from January 2010 to August 2012. The study was approved by the institutional ethics committee. The study was explained to all the initially considered individuals and only those who gave informed written consent were finally included.

The included individuals attended the OPD services after a 12 h fast. The individuals underwent detailed clinical evaluation along with measurement of anthropometric parameters (weight, height, waist and hip circumference). Blood sample was drawn fasting for estimation of FBG, fasting insulin, lipid profile, hs-CRP, IL-6 and TNF-α. The individuals were then given a mixed breakfast of 576 kcal in the form of biscuits (Good-day Butter®, Britannia, Bangalore, India; 81 g, 398 kcal) and sweetened milk beverage (Amul Kool Elaichi®, Anand, Gujarat, India; 200 ml, 178 kcal). Carbohydrates, proteins and fat constituted 79.1%, 7.7% and 13.2%, respectively, of the test meal Table 1. Blood samples were also collected at 2 h and 4 h after the meal for the same parameters except insulin.

Table 1 – Composition of mixed meal breakfast.

Composition	Biscuits (Good-day Butter)®	Sweetened milk (Amul Kool Elaichi)®
Weight/volume	81 g	200 ml
Total energy (kcal)	398	178
Carbohydates (g)	57.7	24
Sugar (g)	24	16
Protein (g)	4.8	3.2
Fat (g)	18.5	8
Saturated fatty acid (g)	9.8	3.8
MUFA (g)	7	–
PUFA (g)	1.7	–
Trans-fatty acid (g)	0	–
Cholesterol (mg)	12.3	16.6

Blood glucose and lipid profile were estimated using autoanalyzer (Dade Diamension RXL Max, Siemens, UK). Serum insulin, hs-CRP, IL-6 and TNF-α were estimated using solid phase, enzyme labelled chemiluminescent immunometric assay (Immulite 1000, Siemens, Gwynedd, UK).

Insulin resistance in the basal state was calculated using HOMA2-IR and basal beta cell activity was estimated using HOMA2-β. The HOMA2 calculator was used for calculation Downloaded from http://www.dtu.ox.ac.uk [12]. Quantitative insulin sensitivity check index (QUICKI) is also a validated method for estimation of insulin resistance in obese, non-obese diabetic and non diabetic individuals (downloaded from https://sasl.unibas.ch/11calculators-QUICKI.php) [QUICKI Score = 1/{log(fasting insulin) + log(fasting sugar)}]. QUICKI index correlates well with glucose clamp studies ($r = 0.78$) and values typically range between 0.45 for healthy individuals and 0.30 in diabetics [13].

3. Statistical analysis

Results were expressed as mean ± standard deviation. Independent sample t tests, paired sample t tests, correlation and regression were used in the analysis of the data. P value < 0.05 was considered statistically significant.

4. Results

Thirty-two individuals with normal glucose tolerance (Group-I) from 51 initially screened individuals were included. Six and two individuals were found to have prediabetes and T2DM respectively on OGTT and hence excluded. Four individuals were on medications for dyslipidemia and were excluded. Four individuals were lost to follow up. Forty-eight patients with newly diagnosed treatment naive T2DM (Group-II) from 81 initially screened patients were included in the study. Of the 32 excluded patients, 16 patients were on medications for dyslipidemia, 4 patients had uncontrolled hypothyroidism, 3 patients had CKD, 2 were on OCPs, and 1 patient each had chronic alcoholism and chronic liver disease. Four patients refused to consent for the study. Patients with diabetes