

## Abstract

**Background:** Assessment of glucose and insulin resistance by oral glucose tolerance test is commonly used for screening asymptomatic adults who are interested in longevity and risk assessment for metabolic disorders. In general, absolute values at various time intervals are used as the cutoff for normal vs. abnormal. Little is reported about the glucose or insulin rise and fall profile (shape). We assessed the glucose and insulin peak profile in normal and in prediabetics.

**Method:** We performed a cross-sectional analysis of 46 consecutive asymptomatic subjects (M: F 18:28, age 52±11 yrs.) without chronic illness, who underwent clinical assessment including serial glucose and insulin measurement (baseline (fasting), 30-, 60-, and 90-minute post-oral 75-gram glucose loading).

**Results:** 34 subjects had normal fasting glucose (<100 mg/dL), 12 were prediabetic (≥100, <126 mg/dL) and no one was diabetic (>126 mg/dL). The maximum rise in glucose and insulin levels was at either 30 minutes or 60 minutes. The average Insulin rise was higher (98±105 vs. 46±49 uIU/ml, p=0.04) and reached a peak later (at 60-min compared to 30-min) in prediabetics than in normal (figure). Individually, more prediabetics had discordant timing of insulin rise (i.e., max insulin time differed from max glucose time) than normal (54% vs. 32%, p = 0.03). All subjects had monophasic rise and fall patterns, no one had a biphasic pattern (initial rise then fall, and then rise again).

**Conclusions:** Insulin profile (shape) in prediabetics differs significantly from normal subjects. A larger study is needed to validate and understand the basis as well as the clinical utility of this relationship.

## Background

Simultaneous measurements of glucose and insulin have shown a cyclical oscillation at the basal state with an average glucose cycle preceding the insulin cycle by at least 2 minutes.[1] Similarly, a pulsatile pattern of both glucose and insulin in the post-prandial state has been shown by Polonsky et al. [2] In that study, the peak pattern of glucose and insulin showed concomitancy (i.e. insulin peaks occurred at the same times or a bit delayed than glucose peaks), especially in the post-prandial state in normal subjects. Subsequently, Mitrakou et al. [3] have shown that there is an increased amount as well as a delayed rise in insulin levels in subjects with impaired glucose tolerance compared to normals. However, the absolute peak attained by insulin was not different. They suggested that the late hyperinsulinemia (measured as mean concentration over 5 hours) may be the consequence of inadequate early beta-cell response rather than insulin resistance.

Little is reported about the glucose or insulin rise and fall profile (shape), especially in patients with impaired fasting glucose (defined as prediabetic in this study) in contrast to impaired glucose tolerance. We assessed the glucose and insulin peak profiles in normals and in prediabetics.

## Purpose

The purpose of this study is to understand and compare the glucose and insulin profiles (shape) in normal and prediabetic subjects. Questions related to the profile are 1- is there a significant difference in the profile? 2- if yes, what component of the profile is different? 3- what is the clinical significance of the findings? Components of the profile that can be studied are 1- Baseline value, 2- the rate of rise, 3- peak, 4- the rate of fall, and 5- the overall shape.

## Methods

We performed a cross-sectional analysis of 46 consecutive asymptomatic subjects (M: F 18:28, age 52±11 yrs.) without chronic illness, who underwent clinical assessment including serial glucose and insulin measurement (baseline (fasting), 30-, 60-, and 90-minute post-oral 75-gram glucose loading).

34 subjects had normal fasting glucose (<100 mg/dL), 12 were prediabetic (≥100, <126 mg/dL) and no one was diabetic (>126 mg/dL).

## Table

Variables	Mean	SD
Gender (N=42)	M=18 (39%), F=28 (61%)	
Age (years)	51	11
SBP (mm Hg)	123	16
DBP (mm Hg)	80	11
Weight (lbs)	198	49
Baseline (fasting) glucose (mg/dL)	93	12
30 min glucose (mg/dL)	152	29
60 min glucose (mg/dL)	138	44
90 min glucose (mg/dL)	116	41
Baseline fasting insulin (uIU/ml)	9	9
30 min insulin (uIU/mL)	69	73
60 min insulin (uIU/mL)	64	69
90 min insulin (uIU/mL)	43	45

SBP=systolic blood pressure, DBP=diastolic blood pressure

## Summary of Results

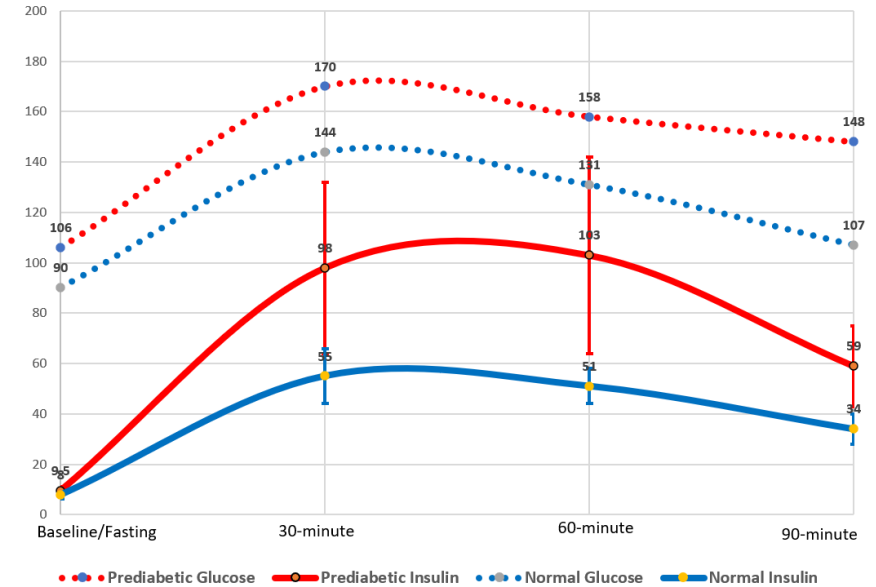
- The maximum rise in mean glucose was at 30 minutes and mean insulin levels were between 30 to 60 minutes.
- The average Insulin rise was higher (98±105 vs. 46±49 uIU/ml, p=0.04) and reached a peak later (at 60-min compared to 30-min) in prediabetics than in normal (graph).
- Individually, more prediabetics had discordant timing of insulin rise (i.e., max insulin time differed from max glucose time) than normal (54% vs. 32%, p = 0.03).
- All subjects had monophasic rise and fall patterns, no one had a biphasic pattern (initial rise then fall, and then rise again).

## Conclusions

- Insulin profile (shape) in prediabetics differs significantly from normal subjects.
- The higher insulin profile may not only be due to impaired early release but also heightened delayed release of insulin so the curve could tend higher than normal.
- A larger study is needed to validate and understand the basis as well as the clinical utility of this relationship.

## Graph

Higher and Delayed Onset of Insulin Peak in Prediabetics Compared to Normals



The above graph shows that insulin levels (solid red line) were higher in prediabetics than normal (solid blue line). The peak was higher and delayed in prediabetics than normal. The prediabetics have higher glucose levels (dotted red line) than normal (dotted blue line).

## References

- Lang DA, Matthews DR, Peto J et al. Cyclic oscillations of basal plasma glucose and insulin concentrations in human beings. N Engl J Med. 1979;301(19):1023-7
- Polonsky KS, Given BD, Van Cauter E. Twenty-four-hour profiles and pulsatile pattern of insulin secretion in normal and obese subjects. J. Clin. Invest. 1988;81:442-448
- Mittrakou A, Kelley D, Mookan M et al. Role of reduced suppression of glucose production and diminished early insulin release in impaired glucose tolerance. N Engl J Med. 1992;326:22-9